Neurocrit Care
https://doi.org/10.1007/s12028-022-01568-2

NEUROCRITICAL CARE SOCIETY

REVIEW ARTICLE

Providing Neurocritical Care in Resource-Limited Settings: Challenges and Opportunities

Morgan L. Prust[1*†], Amir Mbonde[2,3†], Clio Rubinos[4], Gentle S. Shrestha[5], Morenikeji Komolafe[6], Deanna Saylor[7,8] and Halinder S. Mangat[9]

Abstract

Acute neurologic illnesses (ANI) contribute significantly to the global burden of disease and cause disproportionate death and disability in low-income and middle-income countries (LMICs) where neurocritical care resources and expertise are limited. Shifting epidemiologic trends in recent decades have increased the worldwide burden of noncommunicable diseases, including cerebrovascular disease and traumatic brain injury, which coexist in many LMICs with a persistently high burden of central nervous system infections such as tuberculosis, neurocysticercosis, and HIV-related opportunistic infections and complications. In the face of this heavy disease burden, many resource-limited countries lack the infrastructure to provide adequate care for patients with ANI. Major gaps exist between wealthy and poor countries in access to essential resources such as intensive care unit beds, neuroimaging, clinical laboratories, neurosurgical capacity, and medications for managing complex neurologic emergencies. Moreover, many resource-limited countries face critical shortages in health care workers trained to manage neurologic emergencies, with subspecialized neurocritical care expertise largely absent outside of high-income countries. Numerous opportunities exist to overcome these challenges through capacity-building efforts that improve outcomes for patients with ANI in resource-limited countries. These include research on needs and best practices for ANI management in LMICs, developing systems for effective triage, education and training to expand the neurology workforce, and supporting increased collaboration and data sharing among LMIC health care workers and systems. The success of these efforts in curbing the disproportionate and rising impact of ANI in LMICs will depend on the coordinated engagement of the global neurocritical care community.

Keywords: Global health, Global neurology, Capacity-building, Resource-limited health care delivery

Introduction

Acute neurologic illnesses (ANI) are key drivers of global disability and death and disproportionately affect populations in low-income and middle-income countries (LMICs) where access to critical care and neurologic expertise is highly constrained [1]. A number of disease conditions are associated with this high burden of ANI in LMICs, including stroke, traumatic brain injury (TBI), epilepsy, and neurological infections. Stroke is the second leading cause of death worldwide and carries a higher mortality in LMICs compared with high-income

*Correspondence: morgan.prust@yale.edu
†Morgan L. Prust and Amir Mbonde contributed as co-lead authors.
[1] Department of Neurology, Division of Neurocritical Care and Emergency Neurology, Yale School of Medicine, PO Box 208018, New Haven, CT CT 06520-8018, USA

Full list of author information is available at the end of the article

Springer

countries (HICs) [2]. More than 80% of the global burden of TBI occurs in LMICs [3]. Control of epilepsy is limited by access to antiseizure medications [4, 5], whereas HIV-related and non-HIV-related central nervous system (CNS) infections such as tuberculosis, malaria, and neurocysticercosis remain highly prevalent [6–8].

Resource limitations in many LMIC health care settings create significant challenges in providing adequate critical care to patients with ANI. Critical care is a resource-intensive enterprise requiring significant investment in material and human resources. Critically ill patients are often underserved in resource-limited countries, which may lack the infrastructure to meet the needs of patients requiring critical care [9]. More than 70 countries have fewer than five intensive care unit (ICU) beds per 100,000 population [10], with shortages occurring disproportionately in LMICs [11] (Fig. 1). Major gaps also exist between wealthy and poor countries in effective triage systems, specialized training, material resources, and protocolized care required to provide life-saving care to the sickest patients [12]. Diagnostic studies are essential for the appropriate management of people with ANI; however, even if electroencephalography (EEG) and computerized axial tomography (CT) are available, they are usually inequitably concentrated in the private sector and only in major cities, and therefore may be unaffordable and/or inaccessible to the majority of the population [13, 14]. There is a critical shortage of health care workers trained to manage neurologic emergencies in LMICs, where there is a median of 0.13 neurologists per 100,000 population compared with 4.75 in HICs [15]. Subspecialized neurocritical care expertise is largely absent outside of HICs [16–18], and differences in patient populations and constrained health care delivery systems in LMICs may limit the applicability of best practices established for the care of ANI in high-resource settings to resource-challenged environments.

Despite these challenges, promising opportunities exist for improving outcomes of neurologic emergencies in resource-limited countries. Broadly, these include expanding research on needs and best practices for ANI management in LMICs, developing systems for effective triage, and broadening the neurology workforce through training pathways that foster and retain local expertise in LMICs. Indeed, the most promising capacity-building interventions are likely to be driven by leading health care workers from LMICs with sustained longitudinal commitments to the communities they serve. To consolidate gains made on these fronts, networks that foster collaboration and dissemination of promising care innovations will be essential for maximizing the benefits of this work.

Although much of the critical care delivered in HICs serves older patients with complications of chronic disease, the majority of individuals with ANI in resource-limited settings are young adults, many with excellent potential for recovery [12]. Neurologic disorders are the leading cause of disability-adjusted life-years among all disease categories worldwide [1], and incur tremendous

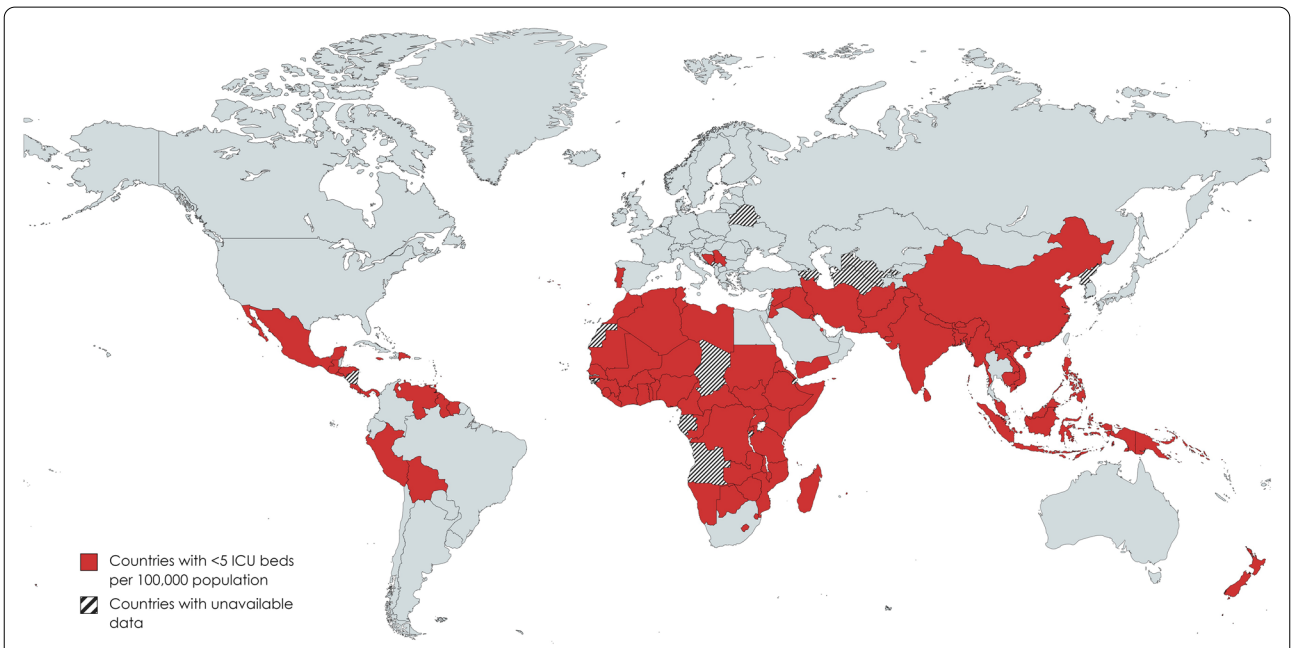

Fig. 1 Global availability of ICU beds. Countries with fewer than five ICU beds per 100,000 population are shaded in red. Figure created using Mapchart.net with data published in Ma & Vervoort, *Journal of Critical Care*, 2020 [10]. ICU, intensive care unit

social and economic costs within communities served by vulnerable health systems. Expanding worldwide capacity to provide effective and context-appropriate care for patients with ANI in resource-limited settings is likely to deliver benefits to individual patients and their communities in terms of total life-years saved, reintegration to society, and return to productive work. The burden of ANI and its disproportionate morbidity and mortality in LMICs highlight the unmet global need for neurocritical care capacity building in resource-limited settings.

The Unmet Burden of Acute Neurologic Illness in LMICs

The worldwide epidemiology of ANI has evolved in recent decades, reflecting a global rise in noncommunicable diseases attributable to aging populations, rising living standards promoting greater exposure to cardiovascular risk factors, and advances in the treatment of infectious diseases [19]. These shifts have given rise to a "double burden" of disease in many LMICs [20] where a rising burden of noncommunicable diseases coexist with a persistently high burden of communicable diseases. The precise global incidence of ANI is difficult to quantify due to underdeveloped systems for epidemiologic surveillance in LMICs for in-hospital and out-of-hospital deaths, which leads to widespread underreporting of disease prevalence in resource-limited settings. Underdiagnosis and misdiagnosis of ANI are also prevalent in regions with limited access to diagnostic testing and few specialist physicians, where care for ANI may be provided primarily by nonphysician health care workers.

The Global Burden of Disease study has provided the most comprehensive review of available data to date on worldwide neurologic disease epidemiology. Neurologic diseases are the greatest driver of worldwide disability-adjusted life-years, with stroke accounting for nearly half of this disease burden [1]. Stroke is the leading cause of disability and the second leading cause of death worldwide [2]. More than half (58%) of strokes, and 67% of stroke-related deaths occur in LMICs annually, with the risk of death per incident stroke being 50% higher in LMICs compared with HICs [2]. These differences in outcomes likely reflect gaps in prehospital care, acute stroke interventions such as thrombolysis and endovascular thrombectomy, and neurosurgical interventions such as decompressive hemicraniectomy [21]. Survivors of stroke experience a significantly greater burden of long-term disability in LMICs, where access to longitudinal stroke rehabilitation may be absent or significantly constrained [22].

In recent decades, there has also been a steep rise in the burden of TBI in LMICs. Increasing access to motor vehicles in many LMICs has outpaced the development of driving and vehicle regulations, with numerous countries worldwide lacking laws for speeding, seatbelts, child restraints, drunk driving, and vehicle safety standards [23]. Road traffic collisions are the leading cause of death worldwide among individuals 15–29 years of age and account for 1.3 million deaths per year [23]. Fall-related trauma remains a key driver of TBI worldwide, with the overwhelming majority of incident cases occurring in patients above age 70 [3]. As the global population ages, the incidence of fall-related TBI will continue to increase, especially in LMICs where gains in life expectancy have been substantial in recent decades. Beyond road traffic–related and fall-related trauma, a complex array of sociocultural factors contribute to the epidemiology and natural history of TBI in LMICs, including concentration of limited health care resources in urban centers, underdeveloped infrastructure for prehospital care including emergency response, transport, and communications, and racial and wealth inequities in access to care [24, 25]. In addition to considerable heterogeneity in outcomes by location, genetic factors may also explain some of the worldwide variance in TBI outcomes, but this remains a subject of active investigation [26].

Large population-based studies have estimated an annual global incidence of TBI ranging from 27 to 69 million [3, 27], with disproportionately greater incidence and related mortality in LMICs [24, 28, 29]. Importantly, however, existing data likely provide an underestimate of the true global burden of TBI due to underdeveloped epidemiologic monitoring systems throughout much of the world, resulting in the under-allocation of health care resources. A notable study that recruited all health workers from an urban center in New Zealand to report all incident TBI cases found a significantly greater disease burden than previous reports from other HICs [30]. The methodological rigor of the New Zealand study suggests that prevailing population estimates of TBI incidence suffer from underreporting, even in high-resource settings.

The global burden of epilepsy is concentrated disproportionately in LMICs, where exposure to underlying risk factors such as endemic pediatric and adult CNS infections, TBI, and birth injury is high and where access to antiseizure medications and longitudinal epilepsy care is limited [31]. The vast majority of prevalent epilepsy cases and related deaths and disability occur in LMICs compared with HICs [32]. Limited access to neuroimaging and EEG in most LMICs precludes early diagnosis of the cause of seizure disorders, and the range of available medications to treat these disorders is highly limited, often to phenytoin, phenobarbital, and sodium valproate. Continuous EEG monitoring is largely unavailable in resource-limited settings, limiting the capacity to detect and manage nonconvulsive status epilepticus. A recent

study of inpatients with altered mental status undergoing routine EEG in a tertiary hospital in Zambia found that nearly 9% of patients who underwent EEG monitoring met electrographic criteria for nonconvulsive status epilepticus, with nearly 20% of patients demonstrating interictal epileptiform discharges [33]. Reductions in case fatality rates associated with epilepsy in recent decades have predominantly benefited wealthy nations, whereas significant gaps in access to preventive care and treatment persist in LMICs worldwide [32].

CNS infectious diseases have long been a global driver of ANI and neurologic mortality. Although advances in antimicrobial and vaccine availability have helped to curb the burden of meningitis and encephalitis in recent decades, these conditions continue to cause significant death and disability in sub-Saharan Africa [34]. Diagnostic resource limitations commonly result in failure to diagnose life-threatening CNS pathogens, leading to delays in initiation of appropriate antimicrobial therapy. Gaps in access to antiviral medications result in high rates of untreated encephalitis. Limited capacity for comprehensive supportive care, such as advanced airway management, control of intracranial hypertension, and detection and treatment of nonconvulsive status epilepticus, further contributes to the excess morbidity and mortality due to neurologic infections in LMICs. And although tremendous progress has been made in the global fight against HIV/AIDS, many nations continue to struggle with high rates of HIV infection, which, when poorly controlled, predisposes to an array of CNS opportunistic infections, immune reconstitution inflammatory syndromes, cerebrovascular disease, and neuromuscular syndromes, all of which can be acutely life threatening.

Beyond primary neurologic causes of ANI, life-threatening systemic complications including sepsis, shock, respiratory failure, and systemic thromboembolism commonly arise in the management of inpatient neurologic illness due to impaired airway protection and prolonged immobility. Patients with severe neurologic injury frequently require prolonged intubation for airway protection, which may be particularly challenging in many LMIC settings where resources for tracheostomy placement and prolonged ventilatory support outside of an ICU setting are limited. Moreover, prolonged intubation for airway protection may present resource utilization challenges in settings with limited ICU beds, leading to low rates of intubation for comatose patients with severe brain injury [35].

Key drivers of mortality for patients with acute brain injury likely differ between well-resourced and resource-limited settings. Limitations in prehospital care in LMICs result in delayed presentation to care and more severe neurologic injury at the time of presentation [24, 27]. In the inpatient setting, limited access to basic critical care resources and neurologic expertise mean that most neurologic emergencies are managed on low-acuity wards by staff who have received limited focused training in care for ANI [17, 36, 37]. A recent survey of physicians from sub-Saharan Africa revealed that, although nearly all reported caring for patients with ANI, only 58% had cared for those patients in an ICU [38]. Only 20% of countries worldwide have specialized inpatient neurology wards [15]. CT scanners are severely limited in LMICs, with only 1.3 scanners per 1 million population compared with 21.2 in HICs [14, 39]. For patients who survive to hospital discharge, access to inpatient and outpatient rehabilitation services is severely limited in LMICs compared with HICs [22], and optimal strategies for providing effective rehabilitative services in resource-limited settings remain uncertain [40, 41]. A summary of key challenges for global neurocritical care delivery and opportunities for health system strengthening in resource-limited settings is provided in Table 1.

Expanding Research for ANI in LMICs

Limited Applicability of Literature from HICs in LMICs

Recognizing that material resource limitations in most LMICs preclude the wholesale adoption of standard neurocritical care practices as currently implemented in HICs, data gathering is essential for generating "the right solutions for the right setting" [42]. The particular challenges in caring for patients with ANI may vary considerably among countries and health care settings as a result of local epidemiology, affordability of care, health system financing, and resource availability. Furthermore, because practice in resource-limited settings is rarely informed by local clinical trials, it is often necessary to extrapolate from HIC-derived literature whose applicability may be severely limited in LMICs. Comprehensive acute stroke guidelines from North America and Europe, for example, have limited use in settings without ready access to a CT scanner [21]. Even when feasible to implement, interventions with proven benefits in HIC settings may be unhelpful or even harmful in resource-limited settings, in which context-specific drivers of mortality, including routine clinical monitoring, underlying pathology, genetics, and stage of illness at the time of presentation to care, may differ from those encountered in high-income settings. For example, fluid resuscitation for septic shock, an established cornerstone of sepsis care in HICs, has been shown to increase mortality in a randomized sample of adults with sepsis in Zambia [43].

For patients with acute brain injury, invasive intracranial pressure (ICP) monitoring has become a core tool in neurocritical care management. ICP monitoring is recommended as the standard of care by the Brain Trauma

Table 1 Summary of the challenges to providing neurocritical care in resource-limited settings and opportunities for advancing global neurocritical care capacity

Challenges	Opportunities
•"Double burden" of noncommunicable and infectious diseases in many LMICs •Limited availability of health care workers with neurocritical care expertise •Limited availability of essential material resources (ICU beds, ventilators, CT scanners, MRI scanners, EEG, laboratory medicine, neurosurgical capacity, essential medicines) •Scarcity of data on epidemiology of ANI and clinical outcomes •Limited applicability of treatment protocols from HICs to resource-limited settings •Lack of triaging protocols for patients with ANI in resource-limited settings •Limited opportunities for education and training in neurocritical care in LMICs	•Increasing data collection on ANI epidemiology and clinical outcomes in LMICs to guide context-appropriate innovations in care •Developing systems for triage that optimize use of available resources and align with local ethical and legal priorities •Expanding educational partnerships between HICs and LMICs that foster self-sustaining training pathways for growing local neurocritical care expertise •Strengthening national, regional, and international networks for data sharing and care innovation in resource-limited settings

ANI Acute neurologic illnesses, *CT* Computerized tomography, *EEG* Electroencephalography, *HIC*, High-income country, *ICU* Intensive care unit, *LMICs* Low-income and middle-income countries, MRI Magnetic resonance imaging

Foundation for all patients with TBI presenting with abnormal head CT and a Glasgow Coma Scale score of 3–8 [44]. However, results from resource-limited settings have failed to reveal a benefit for ICP monitoring. The Benchmark Evidence from South America: Treatment of Intracranial Pressure study, a notable multicenter randomized trial of 324 patients with severe TBI in Bolivia and Ecuador, revealed no benefit of invasive ICP monitoring over a protocol of serial clinical examinations and CT scans on survival or functional outcomes [45]. A recent prospective cohort study of 2395 patients with acute brain injury in 42 countries revealed an association between ICP monitoring and survival only in HICs, with no benefit in LMICs [46].

The reasons for this discrepancy are likely multifactorial. First, much of the benefit derived from neurocritical care is conferred through the prevention of secondary brain injury after an acute neurologic insult. Substantial improvements in patient outcomes can be achieved with basic quality assurance measures, such as regular vital sign monitoring, prompt treatment of fevers and hypoxemia, and prevention of complications such as aspiration pneumonia and acute symptomatic seizures. It is likely that, for advanced modalities such as invasive neuromonitoring to be beneficial in LMIC settings, an array of more fundamental resource needs must first be met, such as ready access to acute neuroimaging, mechanical ventilation, EEG monitoring, nursing staff with specific neurocritical care training, and anticonvulsants, to name a few. Recently published protocols informed by evidence from LMICs and expert opinion provide promising guidance for the management of TBI in resource-limited settings without invasive monitoring [24, 29]. The CREVICE protocol, derived from the methods of the Benchmark Evidence from South America: Treatment of Intracranial Pressure study, provides an evidence-based system for low-cost noninvasive neuromonitoring for LMIC settings with ready access to a CT scanner and capacity for close bedside monitoring of the neurologic examination [47].

In resource-limited settings, attempts to replicate best practices for prehospital, inpatient, and postdischarge care as developed in HICs are likely to encounter prohibitive challenges in the near term and may not result in improved outcomes even if successfully implemented. For example, after the implementation of a standardized protocol for critical care management of tetanus in Tanzania, reduced mortality from airway obstruction and respiratory failure was negated by an increase in deaths from sepsis, at the cost of significantly higher clinical resource utilization [48]. Thus, capacity-building efforts must recognize the challenges introduced by so-called best practices in resource-limited settings, where the complexity of local epidemiology and resource availability may often render standard practice patterns from HICs inapplicable and counterproductive. The greatest progress, therefore, is likely to arise from longitudinal efforts led by health care workers from LMICs to develop systems of care informed by local knowledge and expertise.

The Need for Context-Specific Research and Global Data Sharing

Abundant opportunities exist to expand the study of ANI in LMICs. These include needs assessments that define the local epidemiology of ANI and gaps in care and outcomes research that assesses the feasibility and impact of clinical interventions. There are currently 137 countries designated by the World Bank as a LMIC [49], and considerable heterogeneity in ANI burden and resource availability exists among these nations. Access to acute

neurological care varies widely by region of the world [50], and within individual LMICs, health care resources are typically concentrated major urban centers, further complicating care delivery for patients with acutely life-threatening neurologic emergencies in rural areas [51, 52]. To facilitate progress in a particular LMIC setting, a critical initial step is the establishment of hospital-based, national, and regional registries that capture key clinical data from patients with acute brain injury. Registry data serve to define the burden of ANI within a particular health system and can highlight drivers of mortality and common hospital-acquired complications in order to guide effective interventions [53]. It can further aid in prospectively monitoring the implementation of care protocols for patients with ANI and assessing their clinical impact. Such data-driven assessments can strengthen efforts to reorganize care around locally established best practices and may be applicable across an array of analogous LMIC contexts beyond the local institution. At the administrative level, inpatient registries can support clinicians in leadership positions as they engage stakeholders in hospital administration and national health ministries to advocate for resources that serve proven interventions for management of ANI in resource-limited settings. Hospital-based registries of inpatient neurologic disease have previously been shown to be feasible in resource-limited settings [54]. A critical component in these efforts is a local champion with interest in neurologic care who can initiate and oversee a hospital registry that compiles bedside clinical data for patients with ANI.

Beyond the local level, strengthening global networks for research and data sharing is likely to broaden the reach of individual investigators and accelerate the innovation of care worldwide [55]. The recently published Point Prevalence in Neurocritical Care study revealed significant international heterogeneity in resources, epidemiology, practice patterns, and clinical outcomes for patients in need of neurocritical care and serves as a promising model for international collaborations in neurocritical care research [56, 57]. The Point Prevalence in Neurocritical Care study, however, had limited participation from resource-limited regions, most notably sub-Saharan Africa, highlighting the need to establish networks that bring together practitioners from a broader array of LMICs. Indeed, the overwhelming majority of clinical research pertinent to the management of ANI is generated in HICs [58], with significantly lower representation in the literature from those regions with the greatest burden of ANI [59]. Supporting the development of systems for data collection and publication in LMICs, championed by LMIC investigators, is likely to have the greatest and most sustainable impact in advancing applicable and context-specific clinical practice guidelines for patients with ANI in LMICs. Moreover, networks that investigate and give voice to the needs of patients with ANI in resource-limited settings may play an important role in securing funding for high-value resources that expand neurocritical care capacity over the longer term and provide data to guide resource allocation and implementation of care innovations to settings where they may have the greatest impact and where those resources have been identified as a priority need by local health care providers. Furthermore, additional resources and capacity building are needed to ensure rigorous postimplementation program evaluation systems are in place that can evaluate the impact of new resources and programs and assess the net benefits of these programs. Robust evaluation and monitoring programs are essential, as prior work has repeatedly shown that programs that work in one setting do not always have the same beneficial impact in other diverse settings.

For example, in 2018, the Ibero-American Stroke Organization, the World Stroke Organization, and the American Heart Association/American Stroke Association organized the first Latin American Stroke Ministerial meeting in Gramado, Brazil. Stroke and public health experts from 13 Latin American countries convened to establish priorities for improving the prevention and management of stroke in Latin America [60]. A 2-year follow-up survey of attendees from the Gramado conference indicated significant increases in public stroke awareness, uptake of strategies for primary stroke prevention, and the number of stroke centers in Latin America [61]. These findings underscore the tangible benefits that can be derived from organizing local expertise and maximizing its potential through collaborative networks and data sharing to improve the care of patients with ANI. A list of national and international organizations working toward improving care for patients with ANI is provided in Table 2 (this list is not intended to be comprehensive).

Developing Systems for Effective and Ethical Triage

In most LMICs, the volume of patients with ANI requiring critical care vastly exceeds the supply of available ICU resources. In addition, considerable global heterogeneity exists in the clinical and legal approach to death by neurologic criteria and withdrawal of life-sustaining care. Fewer than half of countries worldwide have established protocols for death by neurologic criteria [62, 63] (Fig. 2), and many have laws prohibiting the withdrawal of mechanical ventilation before cardiac death. In these settings, patients with irreversible neurologic injury may require the prolonged use of limited critical care resources with very limited prospects for a favorable outcome.

Table 2 Regional organizations supporting collaboration and research in neurology and critical care around the world

Organization	Region	Web site
African Stroke Organization (ASO)	Sub-Saharan Africa	http://twitter.com/africanstroke
African Network for Perioperative and Critical Care (N4PCC)	Sub-Saharan Africa	http://n4pcc.com/
African Academy of Neurology	Sub-Saharan Africa	http://www.afaneurology.org/
Stroke Investigative Research and Education Network (SIREN)	Sub-Saharan Africa	http://h3africa.org/index.php/consortium/stroke-investigative-research-educational-network-siren/
Latin American Brain Injury Consortium (LABIC)	Latin America	http://labic.org/
Latin American Intensive Care Network (LIVEN)	Latin America	http://www.redliven.org/web/
Middle East and North African Stroke Organization (MENA Stroke)	Middle East and North Africa	http://menastroke.org
Asian and Oceanian Association of Neurology (AOAN)	Asia and Oceania	http://www.aoaneurology.org/
Association of Southeast Asian Nations Neurological Association (ASNA)	Southeast Asia	http://www.neurology-asia.org/asna.php

This list is not comprehensive

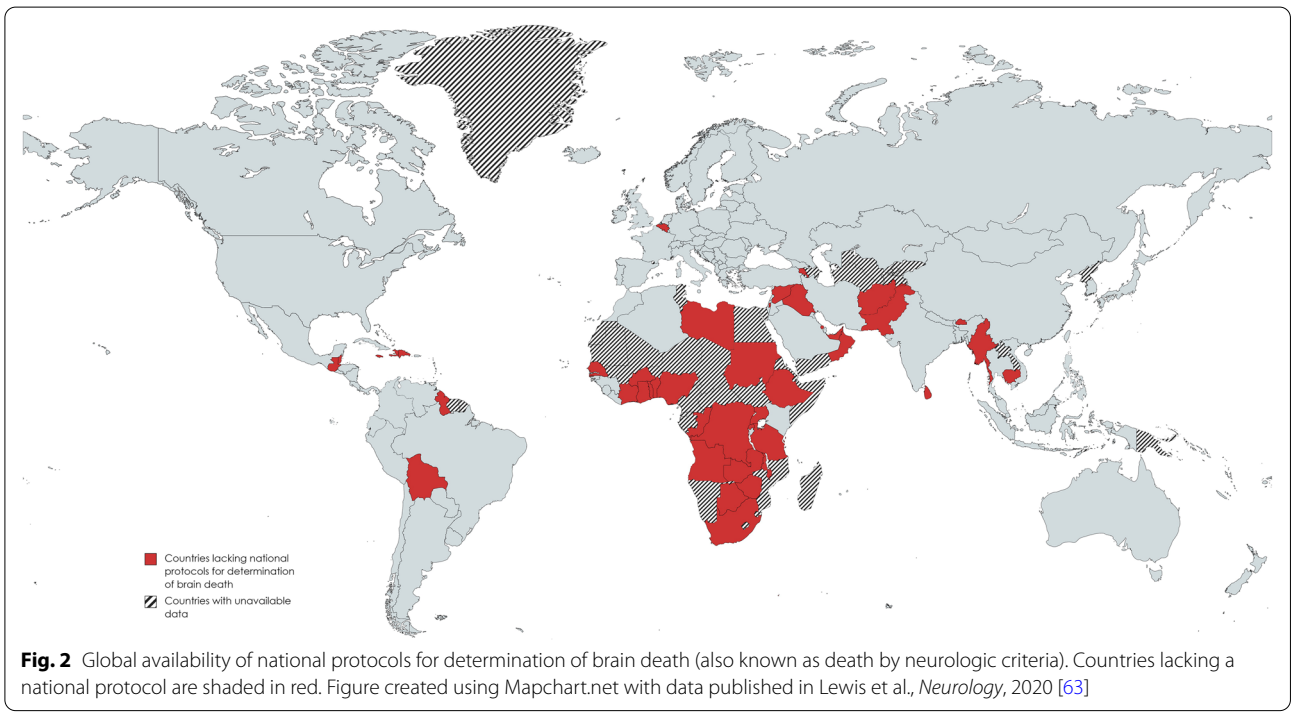

Fig. 2 Global availability of national protocols for determination of brain death (also known as death by neurologic criteria). Countries lacking a national protocol are shaded in red. Figure created using Mapchart.net with data published in Lewis et al., *Neurology*, 2020 [63]

Many hospitals lack formal triage systems responsive to the acuity and potential reversibility of patients' illnesses [9]. Triaging systems developed in LMICs have shown promise in improving outcomes in emergency departments [64], obstetrical emergencies [65], and pediatric emergencies [66], but no validated tools for triaging neurologic emergencies in resource-limited settings have been developed. Developing triage protocols for patients with ANI in LMIC health care settings may serve to maximize the clinical benefit of available resources and to support ethical and transparent resource allocation that is governed by established protocols and context-specific cultural values.

Evidence-based systems for identifying patients with ANI with (1) A high risk of deterioration and (2) Good potential for clinical reversibility with available resources would help clinicians allocate limited resources more efficiently to those with greatest likelihood of benefit. Development of effective triaging systems for patients with ANI will require context-specific assessments that characterize the local epidemiology of ANI and available critical care and neurosurgical modalities and their

associated outcomes within individual health care settings. Identifying patient populations likely to benefit—or not to benefit—from locally available ICU resources can increase the efficiency of triage and optimize the survival benefit of the limited critical care capacity available to patients with ANI in these settings.

The weighting of ethical priorities for ANI triage protocols is likely to vary worldwide as a function of culture, resource availability, and clinical demand. In settings where clinical demand far exceeds available critical care resources, the principle of maximizing clinical benefit for the patient population must be weighed against prevailing attitudes toward individual autonomy and allocating care on a first-come, first-served basis [67]. Institutional protocols should be developed with input from physicians and local community leaders. They should be implemented with transparency to best align with locally relevant clinical, legal, and cultural factors while minimizing moral distress for patients, families, and triaging physicians.

Expanding the Neurocritical Care Workforce

Perhaps the most valuable intervention for transforming management of ANI in LMICs is the establishment of training pathways that expand and maintain the workforce with expertise in caring for this patient population. Many physicians in LMICs emigrate to HICs for subspecialty training and do not return to their home countries, causing a gap in local expertise that severely limits the human resource capacities of underserved health systems.

Numerous critical care short courses have been deployed to resource-limited settings and have the advantage of reaching a large number of health care workers with targeted training in specific content areas [42, 68], although resource limitations may limit their applicability in LMIC contexts. The Emergency Neurological Life Support (ENLS) course, developed in 2012 by the Neurocritical Care Society, provides an educational framework for the acute management of neurologic emergencies, and is typically delivered as a 1-day course centered around disease-specific modules [69]. The feasibility and impact of providing ENLS training in resource-limited settings has been studied across multiple studies among physicians from numerous LMICs [38, 70, 71]. The use of a virtual format in sub-Saharan Africa may serve as a useful model for expanding the accessibility of ENLS to a wider audience and allow for training in areas with limited local expertise [38]. The consistent theme emerging from these studies, however, is that ENLS training significantly increases physicians' knowledge of neurocritical care content areas and self-reported confidence in managing neurologic emergencies, but that there is a need to adapt the course content to increase relevance for LMIC settings where resource limitations continue to limit the adoption of guidelines derived from data from HICs. Whether ENLS training improves clinical outcomes in resource-limited settings has not been evaluated.

Although short-focused training courses like ENLS have the advantage of rapidly transmitting knowledge to a large number of clinicians, long-term capacity-building partnerships between institutions in HICs and LMICs are likely to have the most transformative impact on expanding the global neurocritical care workforce. Training programs that foster neurocritical care expertise within LMICs promise increased retention of skilled practitioners within resource-limited health systems and create a self-reinforcing and self-sustaining cycle of training and education, in which locally trained physicians contribute not only to the neurocritical care workforce but also to the training of subsequent generations of trainees. The establishment of a neurology training program at the University Teaching Hospital in Lusaka, Zambia in partnership with the Johns Hopkins University School of Medicine has led to a quadrupling of the number of trained neurologists in that country in the past 4 years and has significantly expanded capacity in Zambia's national referral hospital, which sees a high volume of stroke and other ANIs (Saylor and colleagues, personal communication).

The partnership between the Muhimbili Orthopaedic Institute in Dar es Salaam, Tanzania, and the Weill-Cornell Global Neurotrauma Group has supported numerous neurosurgical trainees from the North America and Europe in a 1-year global neurotrauma fellowship aimed at building capacity for clinical care, training, and research in neurocritical care in Tanzania. This effort has resulted in sequential increase in rates of mechanical ventilation, CT scans, surgical intervention, and 20% mortality reduction over 7 years of capacity building (Mangat and colleagues, personal communication). Bidirectional longitudinal partnerships of this kind have the potential to broaden the health care workforce through education and training, to increase awareness of global health challenges and opportunities for engagement among HIC health workers, and to allow innovations derived from resource-limited settings to inform high-quality and cost-effective care in HICs.

Conclusions

The global burden of ANI represents a major unmet need for international health care. This burden falls disproportionately on vulnerable health systems in LMICs, where the availability of expertise and resources for the management of complex neurologic emergencies is often severely limited. Implementing systems of care,

clinical training, and research that improve outcomes for in resource-limited environments is a vital, if challenging, public health goal. Progress in this area will depend on sustained longitudinal efforts in LMICs to build systems that account for local complexities in epidemiology and resource availability, to improve care and foster clinical research output. Acknowledging the heterogeneity of ANI disease burden across LMIC contexts globally, we propose to avoid a "one-size fits all" approach to the management of neurologic emergencies in resource-limited settings, and instead call upon the global neurocritical care community to scale up its support of capacity-building efforts aimed at the large and expanding worldwide burden of ANI.

Author details
[1] Department of Neurology, Division of Neurocritical Care and Emergency Neurology, Yale School of Medicine, PO Box 208018, New Haven, CT CT 06520-8018, USA. [2] Mayo Clinic, Scottsdale, AZ, USA. [3] Mbarara University of Science and Technology, Mbarara, Uganda. [4] University of North Carolina at Chapel Hill, Chapel Hill, NC, USA. [5] Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu, Nepal. [6] Obafemi Awolowo University, Ife-Ife, Nigeria. [7] Johns Hopkins University School of Medicine, Baltimore, MD, USA. [8] University Teaching Hospital, Lusaka, Zambia. [9] University of Kansas Medical Center, Kansas City, KS, USA.

Acknowledgements
Dr. Rubinos wishes to acknowledge the Medical Scientist Training Program at the University of North Carolina School of Medicine.

Author contributions
Dr. Prust contributed to conceptual design, literature review, preparation of article, tables and figures, and editing, drafting the article, and revising it critically for important intellectual content. Dr. Mbonde contributed to conceptual design, literature review, preparation of article, tables and figures, and editing, drafting the article, and revising it critically for important intellectual content. Dr. Rubinos contributed to literature review, drafting the article, and revising it critically for important intellectual content. Dr. Shrestha contributed to literature review, drafting the article, and revising it critically for important intellectual content. Dr. Komolafe contributed to literature review, drafting the article, and revising it critically for important intellectual content. Dr. Saylor contributed to conceptual design, literature review, drafting the article, and revising it critically for important intellectual content. Dr. Mangat contributed to conceptual design, literature review, drafting the article, and revising it critically for important intellectual content. The final manuscript was approved by all authors.

Source of support
This work received no funding.

Declarations

Conflicts of interest
The authors have no conflicts to disclose.

Ethical approval/informed consent
Because this is a review article that did not involve any clinical investigation or human subjects, no ethical/institutional review board approval or informed consent was obtained for the preparation of this article.

Publisher's Note

Received: 26 April 2022 Accepted: 23 June 2022
Published online: 16 July 2022

References

1. Feigin VL, Nichols E, Alam T, et al. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(5):459–80.
2. Johnson CO, Nguyen M, Roth GA, et al. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(5):439–58.
3. James SL, Bannick MS, Montjoy-Venning WC, et al. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(1):56–87.
4. Beghi E, Giussani G, Abd-Allah F, et al. Global, regional, and national burden of epilepsy, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(4):357–75.
5. Newton CR. Status Epilepticus in the Resource Poor Countries. Epilepsia. 2009;50(Suppl 12):54.
6. Donovan J, Figaji A, Imran D, Phu NH, Rohlwink U, Thwaites GE. The neurocritical care of tuberculous meningitis. Lancet Neurol. 2019;18(8):771–83.
7. Thakur K, Zunt J. Tropical Neuroinfectious Diseases [Internet]. Contin Lifelong Learn Neurol. 2015;21(6):1639–61.
8. White AC. Calcifications and the Global Burden of Neurocysticercosis: not just rocks in your head. Clin Infect Dis. 2021;73(9):e2604-6.
9. Baker T. Critical care in low-income countries. Trop Med Int Health. 2009;4(2):143–8.
10. Ma X, Vervoort D. Critical care capacity during the COVID-19 pandemic: Global availability of intensive care beds. J Crit Care. 2020;58:69–97.
11. Phua J, Faruq M, Kulkarni A, et al. Critical care bed capacity in Asian Countries and Regions. Crit Care. 2020;48(5):654–62.
12. Kerry VB, Sayeed S. Leveraging opportunities for critical care in resource-limited settings. Glob Heart. 2014;9(3):275–9. https://doi.org/10.1016/j.gheart.2014.09.002/.
13. World Health Organization. Atlas : epilepsy care in the world. 2005.
14. World Health Organization. Global atlas of medical devices [Internet]. 2017. Available from: https://apps.who.int/iris/handle/10665/255181.
15. WHO. WHO | ATLAS Country Resources for Neurological Disorders. WHO [Internet] 2017 [cited 2020 Nov 27];Available from: http://www.who.int/mental_health/neurology/atlas_second_edition/en/.
16. Mateen F. Neurocritical care in developing countries. Neurocrit Care. 2011;15(3):593–8.
17. Shrestha G, Goffi A, Aryal D. Delivering neurocritical care in resource-challenged environments. Curr Opin Crit. 2016;22(2):100–5.
18. Prust M. (2020) Neurocritical care and global health | Neurodiem [Internet]. Neurodiem. 2020 [cited 2022 Mar 4];Available from: https://www.neurodiem.com/news/neurocritical-care-and-global-health-7kCL4jDQ9dOQWPUI14sM9n.
19. WHO. WHO | Noncommunicable diseases country profiles 2018. WHO [Internet] 2018 [cited 2020 Nov 28];Available from: http://www.who.int/nmh/publications/ncd-profiles-2018/en/.
20. Stafford RE, Morrison CA, Godfrey G, Mahalu W. Challenges to the provision of emergency services and critical care in resource-constrained settings. Glob Heart. 2014;9(3):319–23.
21. Prust ML, Saylor D, Zimba S, et al. Inpatient management of Acute Stroke of unknown type in resource-limited settings. Stroke. 2022. https://doi.org/10.1161/STROKEAHA.121.037297.
22. Langhorne P, O'Donnell MJ, Chin SL, et al. Practice patterns and outcomes after stroke across countries at different economic levels (INTERSTROKE): an international observational study. Lancet. 2018;391(10134):2019–27.
23. World Health Organization (2018) Global status report on road safety 2018: summary. Geneva.
24. Godoy DA, Rabistein AA. How to manage traumatic brain injury without invasive monitoring? Curr Opin Crit Care. 2022;228(2):111–22.
25. Bonow RH, Barber J, Temkin NR, et al. The outcome of severe traumatic brain injury in Latin America. World Neurosurg. 2018;111:e82.
26. Kals M, Kunzmann K, Parodi L, et al. A genome-wide association study of outcome from traumatic brain injury. eBioMedicine. 2022;77:103933.

27. Dewan MC, Rattani A, Gupta S, et al. Estimating the global incidence of traumatic brain injury. J Neurosurg. 2018;130(4):1080–97.
28. Mangat HS, Wu X, Gerber LM, et al. Severe traumatic brain injury management in Tanzania: analysis of a prospective cohort. J Neurosurg. 2021;135(4):1190–202.
29. Rubiano AM, Griswold DP, Jibaja M, Rabinstein AA, Godoy DA. Management of severe traumatic brain injury in regions with limited resources. Brain Inj. 2021;35(11):1317–25.
30. Feigin VL, Theadom A, Barker-Collo S, et al. Incidence of traumatic brain injury in New Zealand: a population-based study. Lancet Neurol. 2013;12(1):53–64.
31. Ngugi AK, Bottomley C, Kleinschmidt I, Sander JW, Newton CR. Estimation of the burden of active and life-time epilepsy: a meta-analytic approach. Epilepsia. 2010;51(5):883.
32. Beghi E, Giussani G, Abd-Allah F, et al. Global, regional, and national burden of epilepsy, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019;18(4):357–75.
33. Buback C, Siddiqi O, Titima I, Selioutski O, Birbeck G. Estimating the period prevalence of non-convulsive status epilepticus among comatose adults at the University Teaching Hospital in Lusaka Zambia. Epilepsia Open. 2019;4(4):555–62.
34. Zunt JR, Kassebaum NJ, Blake N, et al. Global, regional, and national burden of meningitis, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2018;17(12):1061.
35. Eaton J, Hanif AB, Grudziak J, Charles A. Epidemiology, management, and functional outcomes of Traumatic Brain Injury in Sub-Saharan Africa. World Neurosurg. 2017;108:650–5.
36. Banerdt JK, Mateyo K, Wang L, et al. Delirium as a predictor of mortality and disability among hospitalized patients in Zambia. PLoS One. 2021;16(2):e0246330. https://doi.org/10.1371/journal.pone.0246330.
37. Dart PJ, Kinnear J, Bould MD, Mwansa SL, Rakhda Z, Snell D. An evaluation of inpatient morbidity and critical care provision in Zambia. Anaesthesia. 2017;72(2):172–80. https://doi.org/10.1111/anae.13709.
38. Tiamiyu K, Suarez JI, Komolafe MA, Kwasa JK, Saylor D. Effectiveness, relevance, and feasibility of an online neurocritical care course for African healthcare workers. J Neurol Sci. 2021;431:120045.
39. Hc M, Al B, Bn P, et al. Availability, accessibility, and affordability of neurodiagnostic tests in 37 countries. Neurology. 2015;85(18):1614–22.
40. Zhou B, Zhang J, Zhao Y, et al. Caregiver-delivered Stroke Rehabilitation in Rural China. Stroke. 2019;50(7):1825–30.
41. ATTEND Collaborative Group (2017) Family-led rehabilitation after stroke in India (ATTEND): a randomised controlled trial. Lancet 390(10094):588–99
42. Diaz JV, Riviello ED, Papali A, Adhikari NKJ, Ferreira JC. Global critical care: moving forward in resource-limited settings. Ann Glob Heal. 2019;85(1):5465. https://doi.org/10.5334/aogh.
43. Andrews B, Semler MW, Muchemwa L, et al. Effect of an early resuscitation protocol on in-hospital mortality among adults with sepsis and hypotension: a randomized clinical trial. JAMA. 2017;318(13):1233–40.
44. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe Traumatic Brain Injury Fourth Edition. Neurosurgery. 2017;80(1):6–15.
45. Chesnut RM, Temkin N, Carney N, et al. A trial of intracranial-pressure monitoring in traumatic brain injury. N Engl J Med. 2012;367(26):2471–81. https://doi.org/10.1056/nejmoa1207363.
46. Robba C, Graziano F, Rebora P, et al. Intracranial pressure monitoring in patients with acute brain injury in the intensive care unit (SYNAPSE-ICU): an international, prospective observational cohort study. Lancet Neurol. 2021;20(7):548–58.
47. Chesnut RM, Temkin N, Videtta W, et al. Consensus-Based Management Protocol (CREVICE Protocol) for the treatment of severe traumatic brain injury based on imaging and clinical examination for use when intracranial pressure monitoring is not employed. J Neurotrauma. 2020;37(11):1291–9.
48. Aziz R, Colombe S, Mwakisambwe G, et al. Pre-post effects of a tetanus care protocol implementation in a sub-Saharan African intensive care unit. PLoS Negl Trop Dis. 2018;12(8):e0006667. https://doi.org/10.1371/journal.pntd.0006667.
49. Low & middle income | Data [Internet]. [cited 2022 Jun 7];Available from: https://data.worldbank.org/country/XO
50. Punchak M, Mukhopadhyay S, Sachdev S, et al. Neurosurgical care: availability and access in low-income and middle-income Countries. World Neurosurg. 2018;112:e240-54.
51. Aluisio AR, Waheed S, Cameron P, et al. Clinical emergency care research in low-income and middle-income countries: opportunities and challenges. BMJ Glob Heal. 2019;4(Suppl 6):1289.
52. Estenssoro E, Alegría L, Murias G, et al. Organizational Issues, Structure, and Processes of Care in 257 ICUs in Latin America: A Study From the Latin America Intensive Care Network. Crit Care Med. 2017;45(8):1325–36.
53. Prust ML, Nutakki A, Habanyama G, et al. Aspiration Pneumonia in Adults Hospitalized with Stroke at a Large Academic Hospital in Zambia. Neurol Clin Pract. 2021;11(6):e840-7.
54. Nutakki A, Chomba M, Chishimba L, et al. Risk factors and outcomes of hospitalized stroke patients in Lusaka. Zambia J Neurol Sci. 2021;424:117404.
55. Schwalbe N, Wahl B, Song J, Lehtimaki S. Data sharing and global public health: defining what we mean by data. Front Digit Heal. 2020. https://doi.org/10.3389/fdgth.2020.612339.
56. Venkatasubba Rao CP, Suarez JI, Martin RH, et al. Global Survey of Outcomes of Neurocritical Care Patients: analysis of the PRINCE Study Part 2. Neurocrit Care. 2020;32(1):88–103.
57. Suarez JI, Martin RH, Bauza C, et al. Worldwide Organization of Neurocritical Care: Results from the PRINCE Study Part 1. Neurocrit. 2020;32(1):172–9.
58. Griswold DP, Khan AA, Chao TE, et al. Neurosurgical Randomized Trials in Low- and Middle-Income Countries. Neurosurgery. 2020;87(3):476–83.
59. Tropeano MP, Spaggiari R, Ileyassoff H, et al. A comparison of publication to TBI burden ratio of low- and middle-income countries versus high-income countries: how can we improve worldwide care of TBI? Neurosurg Focus. 2019;47(5):E5.
60. Ouriques Martins SC, Sacks C, Hacke W, et al. Priorities to reduce the burden of stroke in Latin American countries. Lancet Neurol. 2019;18(7):674–83.
61. Martins SCO, Lavados P, Secchi TL, et al. Fighting against Stroke in Latin America: a joint effort of medical professional societies and governments. Front Neurol. 2021. https://doi.org/10.3389/fneur.2021.743732.
62. Greer DM, Shemie SD, Lewis A, et al. Determination of Brain Death/Death by Neurologic Criteria: the world brain death project. JAMA. 2020;324(11):1078–97.
63. Lewis A, Bakkar A, Kreiger-Benson E, et al. Determination of death by neurologic criteria around the world. Neurology. 2020;95(3):E299-309.
64. Bruijns S, Wallis L, Burch V. A prospective evaluation of the Cape triage score in the emergency department of an urban public hospital in South Africa. Emerg Med J. 2008;25(7):398–402.
65. Umar A, Manu A, Mathai M, Ameh C. Development and validation of an obstetric early warning system model for use in low resource settings. BMC Pregnancy Childbirth. 2020;20(1):1–9. https://doi.org/10.1186/s12884-020-03215-0.
66. Robison J, Ahmed Z, Durand C, et al. Implementation of ETAT (Emergency Triage Assessment And Treatment) in a central hospital in malawi. Arch Dis Child. 2011;96(Supplement 1):A74–5.
67. Nyman DJ, Sprung CL. International perspectives on ethics in critical care. Crit Care Clin. 1997;13(2):409–16.
68. Joynt GM, Zimmerman J, Li TST, Gomersall CD. A systematic review of short courses for nonspecialist education in intensive care. J Crit Care. 2011;26(5):533.e1-533.e10.
69. Smith WS, Weingart S. Emergency Neurological Life Support (ENLS): what to do in the first hour of a neurological emergency. Neurocrit Care. 2012;17(Suppl 1):1–3.
70. McCredie VA, Shrestha GS, Acharya S, et al. Evaluating the effectiveness of the Emergency Neurological Life Support educational framework in low-income countries. Int Health. 2018;10(2):116–24.
71. Barkley AS, Medina-Beckwith J, Sothea S, Pak S, Durfy SJ, Lele AV. Teaching the Emergency Neurologic Life Support Course at Two Major Hospitals in Phnom Penh, Cambodia. World Neurosurg. 2020;141:e686-90.