

# Establishing stroke systems of care from the bottom to the top: A global perspective

SHEILA CRISTINA OURIQUES MARTINS,<sup>1</sup> YOHANNA KUSUMA,<sup>2</sup> UDAYA RANAWAKA,<sup>3</sup>  
MOHAMMAD WASAY,<sup>4</sup> MARIA EPIFANIA COLLANTES<sup>5</sup>

<sup>1</sup> Professor of Neurology, Universidade Federal do Rio Grande do Sul; Chief of Neurology and Neurosurgery Hospital Moinhos de Vento; President-Elect World Stroke Organisation, Porto Alegre, Brazil.

<sup>2</sup> Consultant Neurologist; Head of Hyperacute Stroke Team & Neurosonology Services, PhD Candidate, National Brain Centre, Airlangga University, Jakarta, Indonesia; Deakin University, Waurn Ponds, Victoria, Australia.

<sup>3</sup> Professor of Neurology, Faculty of Medicine, University of Kelaniya; Honorary Consultant Neurologist, North Colombo Teaching Hospital, Ragama, Sri Lanka

<sup>4</sup> Consultant Neurologist, Aga Khan Hospital; Professor of Neurology, Aga Khan University, Karachi, Pakistan

<sup>5</sup> Consulting Neurologist, Philippine General Hospital, University of the Philippines, Manila, Philippines

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## Abstract

Five international stroke experts shared their experiences establishing stroke services in low- and medium-income countries (LMIC) in a symposium sponsored by Boehringer Ingelheim at the Virtual 13th World Stroke Congress on Thursday, October 28th of 2021. Stroke is a major cause of death and disability worldwide and its incidence and mortality are increasing. Both age-standardised stroke mortality and rates of disability-adjusted life years have decreased. However, in people under 70 years of age, stroke incidence increased, and the highest stroke-related mortality and DALY rates are in low-income groups. These factors disproportionately affect LMICs around the world. As the experts from Brazil, Indonesia, Sri Lanka, Pakistan, and Philippines explain, LMICs face many challenges in stroke care due to deficiencies in healthcare systems and socioeconomic factors. Despite these challenges, measures can be implemented to effectively improve stroke care and prevention.

**KEYWORDS:** ACUTE STROKE CARE, ANGELS, LOW- AND MEDIUM-INCOME COUNTRIES, THROMBOLYSIS, THROMBECTOMY

**Corresponding author:** Sheila Cristina Ouriques Martins - sheila@redebrasilavc.org.br

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## Introduction

### Sheila Cristina Ouriques Martins

According to the most recent global burden of disease study, in 2019 there were 12.2 million strokes, 143 million disability-adjusted life years (DALYs), and 6.55 million deaths due to stroke. Between 1990 and 2019, stroke incidence and mortality increased by 70% and 43%, respectively. Stroke is the second cause of death (11.6%) and the third cause of death and disability (5.7%) worldwide. While both age-standardised stroke mortality and rate of DALYs decreased by 36%, in people <70 years of age stroke incidence increased (15%) and the highest stroke-related mortality and DALY rates are in low-income groups.<sup>1</sup> Low- and medium-income countries (LMICs) face many challenges in stroke care. Stroke awareness in the general population is low and access to stroke centres is poor. Few hospitals are organised to assist acute stroke care (ASC) patients and emergency medical service (EMS) staff are untrained. Stroke services only partially implement the recommended protocols and structure, including basic low-cost strategies such as swallowing assessments, blood glucose, temperature, and early mobilisation. They also suffer from a general lack of rehabilitation inside and outside the hospital, aetiological investigation, screening, and treatment of risk factors in primary care, evidence-based secondary prevention, and national plans for stroke in public health.

## Brazil

### Sheila Cristina Ouriques Martins

Brazil is a country of >213 million people<sup>2</sup> where a public health system paid by the federal government covers 100% of the population, and only 20% of people have additional private health insurance. Stroke is the second cause of death and incidence increased by 14% between 2009 and 2019.<sup>2</sup> Most strokes (80%) are attended in public institutions, and there are huge disparities within the country and its cities. The EMS, Serviço de Atendimento Móvel de Urgência (SAMU), is well organised.

Since tissue plasminogen activator (tPA) was approved in 1996 by the FDA,<sup>3</sup> the Brazilian Stroke Society (BSS) has discussed the implementation of ASC with the Ministry of Health (MOH). However, the MOH experienced many obstacles and competing priorities to ASC implementation before 2007. For example, tPA being potentially unsafe in Brazilian emergency rooms (ERs) due to lack of intensive care

units or dedicated stroke beds, delays performing computer tomography (CT) scans in public hospitals, inability to treat patients in the short time window required for tPA, tPA's high cost for Brazil's healthcare budget, and lack of clinical trial data on thrombolysis in Brazilian public hospitals.

To face these challenges and answer each of their concerns, the BSS demonstrated to the MOH what was being done in Brazil. Then, there were 400,000 strokes/year and stroke had been the leading cause of death for the previous 20 years with >100,000 deaths/year.<sup>4</sup> Vascular units were created to respond to the problem of overcrowded ERs which underlies many of the obstacles to thrombolysis. In these units, intravenous (IV) thrombolysis can be performed to treat acute stroke and myocardial infarction. They include emergency physicians, nurses, and on-call neurologists. In 2007, the conglomerated Brazilian Hospitals registries showed that 1000 patients underwent thrombolysis in 35 hospitals. This demonstrated that thrombolysis was feasible in Brazil including in public hospitals, implemented with local resources. In Brazil, the organisation of ASC had similar results as in international studies: it reduced the need for intensive care unit beds, disability, mortality, and the length of hospital stay.<sup>5-7</sup> A cost-effectiveness study based on public health data from 2005 to 2007 showed that tPA administered within 3 hours of stroke onset resulted in an incremental cost-effectiveness ratio in one year of USD 28,956/QALY for men and USD 26,171/QALY for women, with an incremental cost of USD 1063 and 858 respectively, and saves money after the second year of treatment.<sup>8</sup>

Based on these data, the MOH decided to implement thrombolysis in Brazil and in 2008 it launched the Stroke Pilot Project, which showed that IV thrombolysis increased functional independence outcomes (modified ranking scale 0-2) 2.54-fold without increasing death rates and the rate of haemorrhagic transformation was similar to that of other clinical trials (5.8%).<sup>4</sup> The Brazilian Stroke Project and Network were also founded to improve assistance, education, and research in stroke.<sup>4</sup> Dr Martins then visited each Brazilian state and met with health authorities, hospital directors, SAMU coordinators, and neurologists to learn about their local situation, to explain the importance of organising ASC, and to decide jointly which hospitals could implement stroke centres. As a result, they drafted a plan tailored to accommodate the high inter-regional variability in terms of

local resources and hospital structure. Local and national health managers were engaged to ensure continuity.<sup>1</sup> Once these steps were taken, the MOH enacted the Brazilian National Stroke Policy in April of 2012 approving the use of tPA in the public health system, the creation of stroke centres with stroke units, and local lines of stroke care including prevention, treatment, and rehabilitation.<sup>4</sup>

Additionally, awareness campaigns have been conducted since 2009 together with the World Stroke Organisation (WSO). These include children through the Angels “Fast Heroes” initiative, designed to teach them how to recognise stroke signs and to call SAMU. During the COVID-19 pandemic the campaign was virtual and engaged all of Latin America.

When the pilot project started in 2008, there were 35 stroke centres (5 with stroke units) and 8 comprehensive stroke centres. By 2020, they increased to 193 stroke centres (90 with stroke units) and 68 comprehensive stroke centres. For the areas that are still without dedicated centres, a smartphone app (JOIN App, Allm, Tokyo, Japan) to share clinical and imaging data was evaluated in a study. It was found that it reduced door to needle (DTN) times by 26 minutes ( $P=0.03$ ), and the decisions seem to be as accurate as the physical presence of stroke experts.<sup>9</sup> With this validation, a telestroke programme was created.

Regarding thrombectomy for large vessel occlusion, the MOH supported a clinical trial (RESILIENT) to evaluate feasibility, efficacy, and cost-effectiveness in stroke patients treated within the Brazilian public healthcare system.<sup>10</sup> It found that thrombectomy within 8 hours after stroke onset in conjunction with standard thrombolysis resulted in better functional outcomes at 90 days despite the many limitations encountered in the public healthcare system of a developing country.<sup>10</sup> This study's results supported the MOH approval of thrombectomy for public hospitals.

Regarding regional initiatives, in 2018 the Latin American Stroke Ministerial meeting was created. In these meetings 13 countries discuss the gaps, best models, and possible solutions for the region to improve stroke care. One of its achievements is the declaration of Gramado with the

commitment to implement all the best evidence-based strategies for the treatment, prevention, and rehabilitation of stroke patients.<sup>11</sup> In 2020, the certification of Latin American stroke centres was implemented through a collaboration between the WSO and the SIECV/IASO (Ibero-American Stroke Organization). To date, 27 hospitals are pre-certified; 11 are in Brazil of which 4 received full certification in September 2021.

Brazil has achieved significant progress in ASC beginning with the collection of data and obtaining the support of the MOH to implement and conduct further evaluation of initiatives to improve stroke care.

## Indonesia

### Dr Yohanna Kusuma

Indonesia is a country of 273 million people<sup>12</sup> where stroke is a major burden. Dr Kusuma described how in 2018, 10.9/1000 residents were diagnosed with stroke vs 7/1000 in 2013. Stroke is the main cause of mortality and disability in Indonesia and incidence increased by 26% between 2009 and 2019.<sup>13</sup> Most ischaemic and haemorrhagic strokes are of mild (91%) or moderate (77%) severity; severe or very severe strokes are less frequent (9% and 23%, respectively).

There are many challenges to ASC in Indonesia. Time to referral is >30 minutes, stroke onset upon arrival is >60 minutes, and DTN time is also >60 minutes. A limited number of neurologists are available for 24-hour standby, and nurses are often not trained to provide stroke care. Administrative processes also cause delays in treatment. There are limited stroke-ready hospitals or with stroke dedicated beds, CT, and magnetic resonance imaging (MRI) equipment. The EMS is not stroke-ready. Families need to find referral hospitals on their own and insurance coverage for acute stroke treatment is still inadequate. A Stroke National Guideline was approved in 2019 but has not been fully disseminated to neurologists and training is lacking.

The key actions that have helped improve these reperfusion therapy rates have included forming multidisciplinary stroke teams that are regularly trained, and implementing stroke awareness campaigns for patients and families to recognise stroke symptoms and seek care at the NBC in a timely fashion

<sup>1</sup> Coordinators of the Ministry of Health, State and City Secretaries of Health, EMS Coordinators, Hospital Directors

(<4.5 hrs from stroke onset). Moreover, DTN at the NBC decreased between 2017 and 2020 from 105 to 58 minutes. Dr Kusuma confirmed that based on the Stroke Registry of the National Brain Centre and Registry for Stroke Care Quality (RES-Q) Annual Reports, the actions that underlie this improvement are the provision of on-site neurologists 24/7 in the ER, simplifying the admission process, not waiting for complete blood test results unless coagulation indicators are concerning, and administering bolus IV thrombolysis at the CT room in the absence of contraindications.

Dr Kusuma notes that other indicators are also improving. While both ischaemic and haemorrhagic stroke cases at the NBC have increased from 987 to 4068 and 466 to 1075, respectively, the case fatality rate decreased between 2016 and 2020.<sup>14</sup> As of 2020, 28% vs 72% of ischaemic stroke patients are treated within vs outside of the 4.5-hour time limit from stroke onset. According to data from the RES-Q annual reports, there was a slight increase in the NBC, and in Indonesia overall, in the percentage of stroke patients that received a CT or MRI between 2019 and 2020. Nevertheless, CTs and MRIs <1 hr after admission decreased due to COVID-19-related protocol changes between those years.

Dr Kusuma states that progress has been achieved in Indonesia. In 2018, the NBC was a pilot hospital for the implementation of RES-Q, and in subsequent years, many hospitals received awards from the Angels initiative for their ASC services.

## Sri Lanka

### Udaya Ranawaka

Sri Lanka is a country of 21.9 million people with high population density (350 people/km<sup>2</sup>) and a per capita gross national income of USD 3582.<sup>15</sup> Health expenditure is extremely low, and human resources, infrastructure, and training are limited. Meanwhile, the country is undergoing demographic and epidemiological change as the population is rapidly ageing: 12.4% of people are ≥60 years of age and the ageing index increased from 18.8% in 1981 to 49.1% in 2015.<sup>16</sup> As a consequence, chronic non-communicable diseases (NCDs) are the main cause of death (71%)<sup>16</sup> and stroke is naturally a large burden (10.4 strokes/1000 people)<sup>17</sup> as the second leading cause of death and the third cause of combined mortality and disability.<sup>18</sup>

### Stroke systems of care in Sri Lanka

According to the American Stroke Association task force on stroke systems, the key links in the chain of stroke survival and the domains required to improve stroke care are community education, primordial prevention, primary prevention, EMS response, acute stroke treatment, secondary prevention, stroke rehabilitation, and continuous quality improvement.<sup>21</sup>

In Sri Lanka, community education was targeted after data from three studies revealed gaps in stroke awareness among adults, children, stroke patients, and general practitioners (GPs).<sup>22</sup> The Sri Lankan Stroke Association has led improvement in stroke awareness through the declaration of a National Stroke Day (stroke walks and ambassadors such as famous cricket professionals), and the development of educational materials in local languages. These initiatives target healthcare professionals, workers, school children, and emergency departments.

Primordial and primary prevention are fostered through health promotion on healthy eating habits, physical activity, and school curricula on healthy lifestyles. In addition, there is taxation of tobacco and legislation mandating health-related labelling on cigarette and food packaging, and the establishment of 922 Healthy Lifestyle Centres through which 62% of the target population (individuals aged 40–65 years) were screened for vascular risk factors between 2012 and 2018.<sup>23</sup>

For emergency response, the establishment of a free EMS response system, Suwa Sariya, increased hospital arrivals by ambulance from 2011 to 2020 and the number of people admitted within 3 hours. Patients are also encouraged to go to a hospital where thrombolysis is available through the website of the Association of Sri Lankan Neurologists. EMS operators and ambulance crews will soon be trained in ASC; they will be provided with validated tools and instructed to transport patients suspected of stroke to the nearest hospital with thrombolysis services.

ASC is provided by hospitals and 43 neurologists (1/500,000 people), however, there are no trained stroke neurologists or physicians. Of the state-sector hospitals, 30 have neurology units, only 9 have stroke units or dedicated stroke beds, and none are stroke-certified. In comparison, in Africa only

three countries have stroke units (South Africa, Ghana, and the Central African Republic)<sup>24</sup> and in Latin America there are many countries with no stroke units.<sup>25</sup> Thrombolysis is available in 31 hospitals, yet the rate of thrombolysis is low (3%) among stroke patients eligible for the procedure.<sup>26</sup> Mechanical thrombectomy is only available in two hospitals. To improve this situation, a National Stroke Centre and 10 new stroke units are being planned or built. A collaboration with the MT 2020+ (Mission Thrombectomy) initiative of the Society of Vascular and Interventional Neurology of the United States seeks to improve access to thrombectomy.

Data from a survey among neurologists in 21 public hospitals in 2018 revealed that while the availability of medicines for secondary prevention (antihypertensives, antiplatelets, statins, anticoagulants, and antidiabetic drugs) was rated as good in 95–100% of hospitals, rehabilitation facilities and services remain limited.<sup>19</sup>

With regards to continuous quality improvement, quality of stroke care has been evaluated through several stroke audits. In 1998, stroke care was rated 'Very poor' or 'Poor' for 58.3% of the items tested in an audit using the Royal College of Physicians package.<sup>27</sup> In 2001, after the establishment of a stroke unit, there were significant improvements for 83.3% of the audit items.<sup>28</sup> A more recent audit (2015/2016) from another stroke unit using the Acute Stroke Data Tool from the Stroke Foundation of Australia showed the quality of stroke care was satisfactory for most of the domains tested.<sup>29</sup>

To conclude, the limitations in ASC in Sri Lanka are largely related to the socio-economic problems typical of a LMIC. Despite this, social and health indicators are improving thanks to universal healthcare coverage, and an excellent primary healthcare network. Although the country lags behind on newer advances such as mechanical thrombectomy and mobile stroke units, much has been achieved in other areas of the stroke systems of care.

## Pakistan

### Mohammad Wasay

Pakistan is the fifth most populated country in the world (224 million people) and it has a very young population with a life expectancy of 67 years.<sup>30</sup> The health budget is <1% of the GDP (<11 USD/capita/year), and 70% of the healthcare costs are paid by individuals.<sup>31</sup>

Stroke is the third cause of mortality in Pakistan and incidence increased by 19% between 2009 and 2019.<sup>30</sup> It affects a relatively young population (mean age 55 years). Notably, 20% of people <40 years have strokes including 60% of women during pregnancy or post-partum. Stroke mortality is 16% within 30 days, and 40% after one year. The burden of stroke risk factors is high considering that 34% of people >45 years of age are hypertensive, >10 million are diabetic, 23% of adults use tobacco, and the air quality index is 130–250 in large cities. Moreover, stroke risk factors in Pakistan are unique; 7% of people have rheumatic heart disease, 10% have hepatitis B or C, and 30% have intracranial disease.<sup>32–36</sup>

According to the WSO stroke road map, 85% of the population have access to minimal healthcare services (rural areas and small cities), 15% to essential stroke services (large cities, private hospitals), and <1% to advanced stroke services (few private hospitals in large cities, none in the public sector).

In terms of resources, there are 240 neurologists (1/million people) and only 20% have training in stroke. There are 10 stroke units – 8 in private hospitals and 2 in public hospitals; there are >250 CT/MRI facilities (80% private) within 3 hrs driving range for 70% of the population. Thrombolysis is available in 6 private centres; tPA was recently approved by the Drug Regulatory Authority of Pakistan but it is not yet marketed; thrombectomy is available in 3 centres, 2 private and 1 public; and rehabilitation centres (>200) only offer outpatient services.

Pakistan's Stroke Society (PSS) is working with the government to establish 20 stroke units able to administer tPA by 2022. ASC training is being provided to GPs (>12 stroke continuing medical education (CME) credits for GPs per year), nurses, and EMS staff. GPs are also being trained on post stroke care. The PSS organises an annual stroke meeting that is usually attended by up to 300 people, and is updating the 2010 stroke guidelines for GPs. A total of four thrombectomy workshops were organised in 2021 with plans to continue training GPs, nurses, and EMS staff in 2022.

Stroke research is in development. There is a National Stroke Registry that enrolls approximately 1000 patients/year, a cerebral venous thrombosis registry with >1500 patients, and a database of COVID-19-related stroke. In addition, a stroke research trial network provides training for centres on

research procedures, and international trials are ongoing.

Public stroke awareness is low and <50% of GPs are knowledgeable about primary ASC. World Stroke Day, media, social media activities, and educational campaigns on stroke symptoms are being implemented in local languages to improve awareness.

One of the main obstacles to adequate ASC in Pakistan is that the government does not consider stroke and NCDs to be a priority, and most healthcare funds are currently focused on COVID-19. Another challenge is that many people go to local healers. GPs are not well trained on stroke care, so individuals often do not receive appropriate care. There is a high and increasing burden of stroke risk factors with remarkably poor awareness of the relationship between stroke, diabetes, and obesity. Community reintegration is extremely low resulting in stroke patients frequently becoming disabled long-term and very few return to work. Finally, there are no patient support groups or social support services.

Fortunately, there are opportunities thanks to a great proportion of the population using mobile phones (10 million). Many people are involved in entrepreneurship and philanthropy, contributing 20% of healthcare funds.<sup>31</sup> Health awareness gained importance with COVID-19 and Dr Wasay hopes this will help obtain more assistance to treat stroke. Healthcare finance is increasing and the PSS is collaborating with other organisations to improve stroke care.

Despite many challenges, momentum is growing to move the WSO stroke agenda forward. The PSS has been working on awareness, training, research, and advocacy with the government for 8 years. There is now a long-term strategic plan in place for the next 10 years to improve stroke care.

## Philippines

### **Maria Epifania Collantes**

The Philippines is a country of 7640 islands with a population of 112 million people. In 2019, stroke was the second cause of death and incidence increased by 20% between 2009 and 2019.<sup>37</sup>

Stroke care faces many challenges in the Philippines. Urban hospitals are better equipped resulting in inequality of

healthcare service delivery. Different hospitals have different stroke protocols. People with higher economic status can afford better stroke care while poorer people die from stroke without medical care. Healthcare workers are inadequately trained in stroke and there is poor community stroke awareness. All of these factors result in high stroke mortality and morbidity.<sup>38</sup>

The Stroke Society of the Philippines (SSP), the Department of Health, medical societies, hospital administrations, local government, and Angels initiatives are working together to improve stroke prevention and management.

In 2017, after evaluating the stroke needs and gaps, a national stroke training day was implemented in all regions of the country. More than 5000 stroke leaders (neurologists, internists, general practitioners, and nurses) were trained on the WSO cardinal principles of stroke treatment, and attended thrombolysis workshops and simulations. After the training, stroke-ready hospitals and acute stroke units were established in different regions of the country. In 2014, there were only 17 acute stroke-ready hospitals and 5 years later thanks to stroke training provided by the WSO, this number increased to 42. During the COVID-19 pandemic, the Bringing Evidence-Based Stroke Treatment to Philippine Hospitals (BEST-PH) initiative was launched, resulting in a total of 56 stroke-ready hospitals.

In December 2020, after 2 years of meetings and close coordination with health policy makers, the Philippine government approved the National Stroke Policy creating a framework for prevention, control, and management of ASC in the country.<sup>38</sup> This policy ensures availability and access to holistic, standardised, and quality stroke care (prevention, early detection and diagnosis, treatment, and rehabilitation until recovery) to reduce stroke-related deaths, minimise lifetime disability, and improve outcomes. The government will facilitate capacity building, establish more acute stroke-ready hospitals, a National Stroke Registry, health promotion campaigns, and referral pathways. Access to essential medicines will also be provided through the Stroke Medicine Access Programme and a comprehensive stroke benefit package.<sup>38</sup> An executive order in February 2020 improved access further through price regulation reducing the price of stroke medicines (tPA by 50%), antihypertensive, antithrombotic, and antidiabetic drugs.

Other aspects of the National Stroke Policy include drafting and implementing national stroke clinical practice guidelines and certification of acute stroke-ready hospitals and stroke units through collaboration between SSP and the Department of Health. A stroke hospital tracker is available to patients and their families through the SSP website (<https://www.strokesocietyphilippines.org/>) to direct them to the nearest stroke-ready hospital. Stroke training will become mandatory in public hospitals with regular CME for GPs and nurses. A National Stroke Registry, using a format similar to the RES-Q database will be set up. Public stroke awareness campaigns will be intensified using social media, TV, radio, Run for Stroke and World Stroke Day events. Healthy lifestyle modification and control of modifiable risk factor programmes will also be implemented. Our greatest challenges are the following: establishing a stroke referral network, including telemedicine in remote areas, and the improvement of government insurance coverage for stroke, especially for thrombectomy. Additional government programmes are in place to improve stroke facilities and stroke prevention by establishing acute stroke units and brain centres together with NCD prevention and nutrition programmes.

As a result of these efforts, the Philippines have progressed from only one hospital receiving the WSO Angels award in 2019, to 5 hospitals in 2020, and 6 hospitals in 2021. Key actions have been the evaluation of the situation of stroke care in the country – the organisation, collaboration, and planning of initiatives, the provision of nationwide stroke training, conducting stroke awareness campaigns, and setting up acute stroke units and acute stroke-ready hospitals in different regions of the Philippines. The overarching milestone that facilitated these achievements was the approval of the National Stroke Policy.

Dr Collantes concludes that improving ASC in resource-poor areas is possible through close coordination and support from the government, medical societies, and the community. Strong government support can help improve facilities, financing, and access to medicines. Stroke training, stroke prevention, and health promotion have a significant impact on stroke incidence in low resource areas.

## CONCLUSION

The steps to improve ASC in LMICs include:

- Evaluating the country's situation
- Organising stroke centres (or units) and the EMS
- Organising courses, awareness campaigns, and telemedicine for areas without trained doctors
- Implementing thrombectomy in one centre to each 1–1.5 million people
- Monitoring data quality
- Conducting stroke research to support the implementation of new strategies
- Organising collaboration with regional countries

A good example of these steps in action is a pilot project that the African task force conducted together with the WSO to implement ASC in countries with no access to thrombolysis. They established minimal stroke units in five hospitals: three to implement thrombolysis and two rural hospitals without CT scans in South Africa to evaluate the benefits of organized stroke care. First, the hospital structure was evaluated using the WSO roadmap,<sup>2</sup> then virtual visits were made to evaluate the structure of the hospitals, and to meet the directors and doctors. As a result, the programme 'Telemedicine without Borders'<sup>3</sup> was implemented in three hospitals through the JOIN App and tPA is now being used in Ethiopia. Early rehabilitation and ASC training are being provided as well.

Dr Martins concludes that the scientific evidence supports these strategies. If evidence is lacking, then local studies should be designed and implemented to obtain it. GPs in LMICs should not feel improvement in ASC is impossible or unfeasible. The best initiative to take is to join like-minded people that believe they can make a difference in all levels.

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<sup>2</sup> An online road map to improve access to quality stroke care. This tool helps users to identify their hospitals' situation and informs them about the elements they need to fulfil to reach the next level

<sup>3</sup> International stroke specialists that provide advice in real time to LMIC GPs

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