THE WORLD STROKE ORGANIZATION - *LANCET NEUROLOGY* COMMISSION: PRAGMATIC SOLUTIONS TO REDUCE THE GLOBAL BURDEN OF STROKE

The World Stroke Organization – Lancet Neurology Commission Stroke Collaboration Group*

†Corresponding authors:

†Prof. Valery L. Feigin, MD, PhD, FRSNZ, FRAS, FAAN
National Institute for Stroke and Applied Neurosciences, Faculty of Health and Environmental Sciences, Auckland University of Technology, 90 Akoranga Dr, Northcote, Auckland 0627, New Zealand. Telephone: +64 9 921 9166; Email: valery.feigin@aut.ac.nz

†Prof. Mayowa O. Owolabi, DrM, MD, FAAN, FANA, FRCP, FAMedS, FAAS, FAS
Centre for Genomics and Precision Medicine, College of Medicine, University of Ibadan; University College Hospital, and Blossom Specialist Medical Centre, Ibadan, Nigeria.
Tel: +234 802 077 5595 Email: mayowaowolabi@yahoo.com

Words count: 20,053 (excluding panels, tables, figures and references)

Tables: 13

Figures: 8

References: 284

Supplementary materials: 136 pages

* Full list of the core writing group authors, authors contributing to separate sections of the manuscript as well as other authors of the WSO – *The Lancet Neurology* Commission Stroke Collaboration Group and authors' contributions can be found at the end of the manuscript. Suggested citations of the manuscript (including conference presentations and media) "WSO – *The Lancet Neurology* Commission Stroke Collaboration Group".
†There are two leading corresponding authors who equally contributed to the manuscript.

EXECUTIVE SUMMARY 617 words

Stroke is the second leading cause of death worldwide and its burden is increasing at a faster pace in low- and middle-income countries (LMICs) than in high-income countries (HICs), largely because of increasing and aging populations worldwide. The number of people who develop stroke, die from or remained disabled from stroke has continuously increased over the last 30 years and is projected to further increase from 2020 to 2050 by 50%, disproportionally affecting LMICs. Should the current trends continue, the Sustainable Development Goals (SDGs) for reducing the burden of stroke (as part of the general target to reduce burden from non-communicable disorders [NCDs] by a third by 2030) will not be met.

The growing burden of stroke across the globe prompted us to conduct a situational analysis of current stroke services and a critical appraisal of four sections of the stroke quadrangle: stroke surveillance, prevention, acute care, and rehabilitation (Figure 1). A qualitative study with thematic analyses identified barriers and facilitators of surveillance systems (capacity, information technology, and governance), prevention (system capacity, universal health coverage, and governance), acute care (barriers were awareness, investment, and strategy; facilitators were training, innovation, and networks), and rehabilitation, (barriers included complexity, scope, and awareness; facilitators were evidence-based care, universal healthcare and capacity building).

Based on these findings we identified and prioritized the highest grade of recommendations supported by the highest level of evidence (including that from the best stroke guidelines) globally (Supplementary materials "Overview of Methods" pp 3-5) and proposed pragmatic solutions for implementation of evidence-based interventions to reduce the global stroke burden (described in seven interconnected sections of the Commission work: stroke burden projections from 2020 to 2050, thematic analysis of implementation barriers and facilitators to evidence-based interventions in stroke, stroke surveillance, prevention, acute care, rehabilitation, and costs). The estimated losses due to direct (treatment and rehabilitation) and indirect (including productivity loss) costs for stroke globally were in excess of US$891 billion annually. It is expected that solutions we recommend for urgent implementation (a summary of our key findings and suggested solutions are presented in the Panel) will mitigate these losses, reduce the global burden of stroke, and contribute towards achieving the SDG 3·4, the World Health Organization (WHO) Intersectoral Global Action Plan against epilepsy and other neurological disorders and WHO Action Plan for Prevention and Control of NCDs.

Urgent measures to reduce stroke burden across the globe, particularly in LMICs, by implementation of more effective primary and secondary stroke prevention strategies, and evidence-based acute care and rehabilitation services are urgently needed (Panel 1). These measures include, but are not limited to, the following: (i) establishing a framework for regular monitoring and evaluation of the burden of stroke and its risk factors, stroke services at a national level via a range of validated and practicable community-based surveys and electronic health records; (ii) implementation of integrated population-wide and individual-level prevention strategies for people at any level of increased stroke/CVD risk to reduce the burden of modifiable risk factors, with a range of novel approaches such as task-shifting and motivational mobile technology, with the emphasis on early detection and control of elevated blood pressure; (iii) effective planning and delivery of acute stroke care services including reperfusion therapies (chemical and mechanical), workforce training and capacity building, with monitoring of quality indicators nationally, regionally and globally; (iv) promoting access to interdisciplinary care and infrastructure, training for care-givers, and capacity building of community health workers and other

healthcare providers for stroke rehabilitation; and (v) active and joint stroke advocacy and implementation ecosystem including all relevant organizations and stakeholders aimed at involving the general population, healthcare policy makers and governments (Figure 2). This will facilitate the implementation, impact and monitoring of the effects of these pragmatic solutions using suggested key performance indicators.

Panel 1. KEY MESSAGES

Fast growing stroke burden, with widening gap between HIC and LMICs:

- Worldwide, stroke remains the second leading cause of death, the third leading cause of combined death and disability and a leading cause of dementia. Stroke prevalence has been increasing significantly since 2005, largely due to increasing and aging populations worldwide. The absolute number of people affected by stroke who die or remain disabled from stroke has almost doubled over the last three decades, with most of the stroke burden (86% of global deaths and 89% of global disability-adjusted life years (DALYs) lost due to stroke in 2020) residing in LMICs.
- Our forecast shows that the global burden of stroke (deaths and disability-adjusted life years [DALYs]) will continue to grow, with widening gaps between HICs and LMICs. Multiple factors contribute to the burden in LMICs including undetected and uncontrolled hypertension, lack of easily accessible high quality health services, insufficient attention to and investment in prevention, in-house air pollution, population growth and changing demographics, an earlier age of stroke onset, greater proportion of intracerebral haemorrhagic strokes and the coexistent burden of infectious diseases competing for limited healthcare resources.

Barriers, facilitators and economic case for reducing the global burden of stroke:

- Few countries worldwide, particularly lower income countries, have comprehensive, contemporary stroke surveillance systems that can provide accurate data on stroke events, outcome, and risk factors.
- Qualitative analysis of in-depth interviews of stroke experts from 6 HICs and 6 LMICs across all six WHO world regions unravelled key barriers and facilitators to high-quality stroke surveillance, prevention, acute care and rehabilitation across the globe. Major barriers were: (1) low awareness of stroke including evidence-based management by the community, health professionals and policy makers; (2) limited data on stroke risk factors, events, management, and outcomes to drive quality improvement and priority setting. Major facilitators included: (1) well developed stroke organizations and networks that could advocate and build capacity for stroke care and research; (2) universal health coverage which provided population-wide access to evidence-based stroke care for pre-hospital, acute care, rehabilitation, and prevention.
- Stroke is highly preventable and treatable. The aim of SDG 3.4 is to reduce premature mortality from non-communicable diseases (NCDs) by one-third through better prevention and treatment by 2030. Global investment in the suggested stroke prevention, treatment and rehabilitation strategies will have a central role in determining the success in achieving the SDGs.
- Based on our economic analysis, the estimated treatment, rehabilitation, and indirect costs for stroke will rise from US$891 billion per year in 2017 to up to US$2.31 trillion in 2050. We make an economic case to governments, health ministries and other policy makers for interventions to mitigate this massive expense and reduce the burden of stroke globally. It is vital to promote brain health, brain capital and overall health and wellbeing across the globe.

Key solutions for stroke surveillance:

- To adequately guide prevention and treatment, we propose various relatively low-cost surveillance systems and electronic means that could provide the required accurate epidemiological data on stroke.
- We recommend incorporation of stroke surveillance into national stroke action plans or existing monitoring systems for NCDs, processes to identify and ascertain stroke cases in the community, and inclusion of surveillance of dominant stroke risk factors in the national census.

Key solutions for stroke prevention:

- Wider implementation of population-wide primary prevention strategies because many strokes (particularly in young people) occur among individuals with a predicted risk of stroke and cardiovascular disease (CVD) that is below recommended thresholds for intervention.
- Raise public awareness and action to improve health and prevent stroke by population-wide deployment of validated mobile and digital technologies (so-called motivational mass individual strategy for stroke prevention) with simple, inexpensive screening for a history of CVD and presence of modifiable risk factors (particularly smoking, vaping, obesity, elevated blood pressure, alcohol, illicit drugs, sedentary behaviour, diet low in vegetables, excessive dietary sodium intake, lack of physical exercise) and potentially modifiable risk factors (diabetes mellitus, atrial fibrillation/flutter) for lay people reinforced by healthcare professionals through validated motivational digital technologies for person-centred primary and secondary stroke/CVD prevention, linked to local, regional and/or national healthcare electronic databases.
- For implementation of primary stroke prevention on the individual level in people with any level of increased stroke/CVD risk, especially in LMICs, we recommend shifting/sharing of tasks from the limited number of health professionals to more widely accessible healthcare workers to facilitate stroke prevention interventions and use of polypill whenever appropriate with (for secondary stroke prevention after ischaemic stroke or transient ischaemic attack [TIA]) or without aspirin (for primary prevention).
- Health systems should have processes to identify, screen, and manage risk factors in individuals at any level of increased risk of stroke. Effectiveness of the primordial and primary stroke prevention measures should be assessed by monitoring of stroke incidence, mortality, prevalence, and risk factors at the individual and population levels.

Key strategies for improving acute stroke care:

- Prioritizing effective planning of acute stroke care services, capacity building and training of sustainable workforce, provision of evidence-based and appropriate equipment, treatment and medicines, and adequate resource allocation at national and regional levels.
- Establishment of acute stroke centres in hospitals through regional stroke systems of care and accelerating access to acute stroke treatments including intravascular thrombolysis and mechanical thrombectomy for ischaemic stroke that can reduce mortality and long-term disability. In centres with no access to emergency thrombolysis, early administration of antiplatelet drugs after ischaemic stroke is essential.
- Regional networks including primary stroke centres, thrombectomy-capable centres and comprehensive stroke units should be created to properly and timely triage, transfer and treat acute ischaemic stroke, especially those with large vessel occlusion (LVO).
- Planning and establishment of regionally coordinated pre-hospital services that are educated in stroke and LVO recognition scales and follow optimized triage protocols are critical for rapid access to reperfusion therapy including intravenous thrombolysis and/or mechanical thrombectomy.
- Tele-stroke-based networks should be implemented to improve equity to adequate service access in the rural and underserved areas where stroke specialists are lacking. It is still very important for the government to invest in stroke education for lay people (e.g., regular F.A.S.T. campaigns) and medical

professionals, including workforce development for health professionals (not just clinicians with an interest and expertise in stroke, but also nurses and allied health professionals [physiotherapists, occupational therapists, speech therapists, social workers, psychologists etc]), especially for LMICs.

- Simple nurse-driven strategies like fever management, swallow assessment, blood sugar control, prevention or early detection and adequate management of medical and neurological complications and secondary prevention measures should be implemented. It is also important to measure key indicators of quality of care and risk factors management on national, regional and international levels.

Key strategies for improving stroke rehabilitation:

- Delivery of stroke rehabilitation services in a multidisciplinary setting is highly recommended, emphasizing the need for education, training programs and capacity building for stroke rehabilitation healthcare workers, community health workers and caregivers, as well as increasing resource allocation for acute stroke rehabilitation and reducing out-of-pocket expenses.
- The huge variability of capacities and rehabilitation professionals available across geographic regions necessitates an adaptation of evidence-based rehabilitation to the regional organizational settings, including training and support of family members and caregivers to assist in stroke care, and long-term follow-up as appropriate.
- Digital portals can potentially be used to enhance stroke rehabilitation care by targeting all stakeholders using multiple suitable interactive channels to communicate and deploy solutions and training.

INTRODUCTION 508 words

The global burden of stroke remains a huge public health issue. In 2019, stroke was the second leading cause of death (6.6 million) and the third leading cause of combined death and disability (143 million DALYs) worldwide, only after neonatal disorders (in children) and ischaemic heart disease (in adults).[1] Stroke is also a leading cause of depression and dementia.[2, 3] Most countries have made little progress towards achieving Sustainable Development Goal (SDG) 3.4, which calls for a reduction in premature mortality from non-communicable diseases (NCDs) by a third from 2015 to 2030.[4] Achieving this worldwide would require US$140 billion in new spending over 2023–30, but 39 million deaths could be averted and $2·7 trillion in net economic benefits could be generated, with benefit outweighing costs by a factor of nineteen-to-one.[4] Globally, stroke costs over US$891 billion annually as at 2017.[5] Thus, pragmatic solutions to reduce the burden of stroke and related NCDs are urgently needed to save lives and improve brain health and human capital globally.[5, 6] Any genuine effort to reduce the global burden of stroke must utilize solutions that are appropriate and implementable globally.

The World Stroke Organization - *Lancet Neurology* Commission on Stroke is a collaboration instigated by the World Stroke Organization (WSO)[5, 7-9] and *The Lancet Neurology,* supported by the World Health Organization (WHO) to tackle the global burden of stroke. This Commission aims to provide evidence-based pragmatic solutions for reducing the global burden of stroke and related NCDs across the four sections of the stroke quadrangle (surveillance, prevention, acute care, and rehabilitation).[10] The strategic pathways for implementation were created for the identified evidence-based solutions based on thematic analysis of barriers and facilitators. These goals align with SDG 3.4 (reducing premature mortality from non-communicable diseases (NCDs) by a third) and the WHO Global Action

Plan for the prevention and control of NCDs.[11, 12] SDG 3.4 is closely related to the accomplishment of nine other SDGs.[13]

A conceptual framework was designed to characterize and forecast the burden of stroke, identify and prioritize evidence-based interventions against stroke, characterize the barriers and facilitators to their implementation, and proffer pragmatic solutions for maximal accelerated impact globally (Figure 1). We also identified gaps in evidence and practice and provided future directions for research, policy, and practice to control stroke across the globe. Experts with skills in the various sections led the seven interconnected sections of the Commission work: stroke burden projections from 2020 to 2050, multiple case studies mixed methods analysis of implementation barriers and facilitators to evidence-based interventions in stroke, stroke surveillance, prevention, acute care, rehabilitation, and costs (Figure 2) using multiple case study mixed methods of stroke services analysis (Supplementary Figure 1). Commissioners carried out a situational and gap analysis by reviewing existing stroke-related literature, guidelines and recent surveys.[5, 8, 9] Pragmatic interventions to reduce stroke burden utilized implementation science theories[14] and sustainable multisectoral implementation ecosystem with iterative implementation cycle[15] (Figure 3). In three to five years, we plan to analyse and report achieved impact, progress, and remaining challenges in reducing stroke burden in the world.

SECTION 1: PROJECTION OF STROKE BURDEN FROM 2020 TO 2050 2453 words

Introduction and methods

Previous estimates of the burden of stroke by the Global Burden of Disease (GBD) Study were limited to the 1990-2019 period[1] and forecast life expectancy, years of life lost (YLL), and all-cause and cause specific mortality for 2016-2040.[16] However, long-term stroke healthcare planning, priority setting and resource allocation require projections of the stroke burden for at least 10-30 years after the last actual estimates. In this section we provide estimates of stroke burden as determined by stroke deaths and disability-adjusted life-years lost (DALYs) by age groups (total, under 60 years, 60 years and older), stroke pathological type (ischaemic stroke [IS], intracerebral haemorrhage [ICH], subarachnoid haemorrhage [SAH]), region (global, GBD super regions), and World Bank country economic levels (High income countries [HICs], low- and middle-income countries [LMICs]) for the period 2020 to 2050. The methodology for determining stroke types has been reported elsewhere.[1] Forecasts of stroke burden were produced from cause specific GBD 2019 estimates of mortality, incidence, and prevalence for IS, ICH and SAH.[1, 17] (details on the methodology are presented in Supplementary Materials section "Methods used to forecast stroke burden," pp 5-6). In this section, we do not include projections of stroke on a national level or projections of incidence, prevalence, YLL and years of healthy life lost due to disability (YLD), as that report will be presented in a separate paper.

Results

Projections of stroke deaths

The absolute number of people who die from stroke in the world is estimated to increase by 50% - from 6.6 million [95% UI 6.0-7.1] in 2020 to 9.7 million [95% UI 8.0-11.6] in 2050 (Table 1, Figure 4).

Age

There is an estimated increase in stroke deaths in people aged 60 and older (5.6 [5.1-6.1] million in 2020; 8.7 [7.3-10.4] million in 2050), while in younger people there will be almost no change in the

number of deaths in 2050 (1.0 [0.7-1.3]) compared to 2020 (1.0 [0.9-1.1]). We also forecasted a decrease in the age-standardized rates in both younger (under 60 years; from 13.3/100,000 [12.1-14.5] in 2020 to 9.9/100,000 [7.2-13.6] in 2050) and older (60 and over; from 565.6/100,000 [508.6-613.4] in 2020 to 361.7/100,000 [299.1-431.9] in 2050) people (Table 2 and 3; Supplementary Figures 2 and 3), which indicate progress in prevention and treatment.

World Bank country economic levels

Projections of stroke deaths from 2020 to 2050 by World Bank country income level (Table 3, Figure 4) show that while age-standardized stroke mortality rates will continue declining in both HIC and LMICs (33.7/100,000 [95% UI 29.1-36.9] and 105.8 [95% UI 95.2-115.0] in 2020, 18.9 [95% UI 15.7-22.2] and 64.0/100,000 [95% UI 52.5-77.9] in 2050 respectively), the absolute number of people who are projected to die from stroke will only slightly decrease in HIC (from 0.9 million [95% UI 0.79-1.02] in 2020 to 0.91 million [95% UI 0.74-1.06] in 2050) and sharply increase in LMICs (from 5.7 million [95% UI 5.1-6.2] in 2020 to 8.8 million [95% UI 7.3-10.6] in 2050). The proportion of global stroke deaths in LMICs was projected to increase from 86% in 2020 to 91% in 2050.

Region

Among seven GBD super-regions, the highest proportion of stroke deaths (51%; 4.9 million [4.1-5.9]) is projected to occur in 2050 in Southeast Asia, East Asia, and Oceania, followed by South Asia (16%; 1.6 million [1.2-2.0]), Sub-Saharan Africa, and high-income regions (8%; about 0.8 million in each). Although the age-standardized death rates will be reduced from 2020 to 2050 across all GBD regions (Figure 4) with the most significant reductions in the high-income region (45% reduction) and Central Europe, Eastern Europe, and Central Asia (52% reduction), the absolute number of deaths was projected to increase in Southeast Asia, East Asia, Oceania, Latin America, and Caribbean, North Africa and Middle East, South Asia, and Sub-Saharan Africa, with the most significant increase in Southeast Asia, East Asia, and Oceania (3.1 [2.6-3.5] million in 2020, 4.9 [4.1-5.9] million in 2050).

Stroke pathological type

Our forecast of age-standardized stroke mortality rates from 2020 to 2050 by pathological types of strokes in the world and by HICs, LMICs and GBD regions (Table 2, 3; Figure 4) showed that there will be a trend towards an increasing proportion of deaths due to ICH among all strokes from 44.3% in 2020 globally to 52.4% in 2050. This is largely attributable to the proportional increase of ICH related deaths in LMICs (2.7 [2.4-2.9] million in 2020 and 4.8 [4.1-5.4] million in 2050), especially among people aged 60+ years old (2.0 [1.8-2.2] million in 2020 and 4.1 [3.5-4.6] million in 2050). The proportion of ICH in LMICs in 2050 is projected to be 1.5 times greater than that in HIC - 54% and 37%, respectively. The ICH death rate among the younger population (below 60 years) is projected to decrease in HIC, from 3.3/100,000 (3.0-3.5) deaths in 2020 to 2.5/100,000 (2.0-3.1) deaths in 2050. Among GBD regions the highest number of ICH deaths in 2050 is projected to be in Southeast Asia, East Asia, and Oceania – 1.5 (1.3-1.7) million in 2020 and 2.9 (2.4-3.3) million in 2050, but the fastest growth of ICH deaths in 2050 is projected to be in Sub-Saharan Africa (98% growth). We forecast that globally age-standardized mortality rates over 2020-2050 will be reduced for each pathological type of stroke in both age groups (<60 and 60+ years), with most reductions (over 2-fold) projected for IS mortality rates (from 42.6/100,000 [38.2-46.2] in 2020 to 20.5/100,000 [16.8-24.7] in 2050, especially in HIC (from 20.1/100,000 [17.1-22.2] in 2020 to 8.0/100,000 [6.4-9.3] in 2050) (Table 3;

Supplementary Figures 2 and 3). The least reduced age-standardized mortality rates were projected for SAH (4.6/100,000 [4.1-5.2] in 2020 and 4.1/100,000 [2.9-5.7] in 2050).

Projections of stroke DALYs

Similar global changes in the stroke burden over the next three decades are expected for DALYs (Table 1, 2-5, Figure 5; Supplementary Figures 3 and 4). The total number of DALYs from stroke will increase over the 2020-2050 period by 31% - from 144.8 million [95% UI 133.9-156.9] to 189.3 million [95% UI 161.8-224.9].

Age

Age-standardized DALYs rates in HIC are expected to significantly decrease from 699.0/100,000 [95% UI 629.9-761.1] in 2020 to 488.3/100,000 [95% UI 415.0-571.1] in 2050 (Table 3, Figure 4) in both age groups (under 60 and 60+ years old), but the absolute number of DALYs overall will only be slightly (non-significantly) decreased from 15.9 million [95% UI 14.3-17.4] to 15.6 million [95% UI 13.3-17.8]. The decrease in the absolute number of DALYs will only be observed in people under 60 years old (from 20.1 [17.6-23.0] million in 2020 to 13.9 [11.1-17.1] million in 2050), while in older people we expect a significant increase of DALYs from 47.0 (40.7-53.1) million in 2020 to 74.1 (62.8-86.8) million in 2050.

World Bank country economic levels

Although the age-standardized DALYs rates in LMICs are also expected to decrease from 2,131.9/100,000 [95% UI 1,964.6-2,315.5] in 2020 to 1,391.9/100,000 in 2050 [95% UI 1,161.3-1,678.4], the absolute number of DALYs will increase over the same period from 128.8 million [95% UI 118.5-139.8] to 173.7 million [95% UI 146.8-207.7] (Table 3).

Region

Similar decreases in age-standardized DALYs rates were projected to happen across all GBD regions, with the largest decrease (40%) in Central Europe, Eastern Europe, and Central Asia. However, for North Africa and Middle East, and South Asia (Table 4, Supplementary Figure 4) we projected an increase, though not statistically significant, in the age-standardized rates of DALYs in people younger than 60 years.

Pathological type of stroke

Globally, among DALYs due to various pathological types of stroke, the largest contributor to DALYs in 2020 was ICH (69.4 [63.5-75.3) million or 48% of total stroke DALYs), and in 2050 it is projected to increase to 97.0 (82.7-113.9) million or 51%, especially in people younger than 60 year (64%).

Age-standardized rates of DALYs are projected to decrease from 2020 to 2050 across all types of stroke and age groups, except for SAH where these rates are expected to increase non-significantly in people younger than 60 years – from 97.5/100,000 (84.0-115.5) in 2020 to 103.7/100,00 (65.7-152.0) in 2050 (Table 5; Supplementary Figure 4).

We forecast the highest rate of age-standardized DALYs to be observed in 2050 from ICH in Southeast Asia, East Asia, and Oceania (992.4/100,000 [832.7-1153.4]), followed by ICH related DALYs in Sub-Saharan Africa (848.5/100,000 [708.8-1,018.3]), IS related DALYs in North Africa and Middle East (656.0/100,000 [515.1-845.5]) and Central Europe, Eastern Europe, and Central Asia (649.9/100,000

[547.8-762.4]) (Figure 4). The latter will also experience the highest age-standardized rates of DALYs due to SAH (167.6/100,000 [119.1-225.71]).

Why is the global stroke burden rising disproportionately?

For stroke as for all chronic diseases, the population growth and aging in most countries is contributing most to the increasing total numbers of death and DALY events. However, the role of prevention and treatment to contain the increasing number of events is crucial. There is suboptimal and inequitable detection and control of risk factors, limited infrastructure for acute stroke care and rehabilitation, particularly in LMICs. In our situational analysis, approximately half of the countries had implemented less than half of the recommended elements for acute care with low-income countries (LICs) meeting only 30% of the acute care recommendations. Europe and Central Asia had services that best aligned with evidence-based guidelines while services in sub-Saharan Africa had implemented the fewest. Among LMICs, availability of physicians with expertise in stroke management was better in North Africa, Middle East, Eastern Europe, and Central Asia and least in Sub-Saharan Africa. Many of these countries also had low general doctor-to-population ratios and inadequate workforce of multi-disciplinary healthcare workers with training on how to provide acute and chronic care for patients with transient ischaemic attack and stroke.

Implications

This is the first study that reports projections of stroke burden estimates, as determined by deaths and DALYs from stroke by age groups (total, under 60 years, 60 years and older), stroke pathological type (IS, ICH, SAH), region (global, GBD super regions), World Bank country economic development level (HIC, LMICs) for the period from 2020 to 2050. Globally, we found that the absolute number of people who die from stroke in the world will continue to increase – from 6.6 million [95% UI 6.0-7.1] in 2020 to 9.7 million [95% UI 8.0-11.6] in 2050, with DALYs increasing over the same period from 144.8 million [95% UI 133.9-156.9] to 189.3 million [95% UI 161.8-224.9], although age-standardized mortality and DALYs rates will continue to decrease – from 83/100,000 (75-90) and 1747/100,000 (1612-1892) in 2020 to 54/100,000 (44-66) and 1229/100,000 (1030-1477) in 2050, respectively. The rate of increase of stroke deaths and DALYs for the 2020-2050 period compared to 1990-2019 period[1] decelerated (deaths from 43% to 50%; and DALYs from 31% to 32%), but it was not statistically significant.

While the proportions of stroke deaths in LMICs and HICs in the total global stroke deaths in 2020 were 86% and 14%, respectively, in 2050 it was projected to increase to 91% in LMICs and decrease to 9% in HICs. Similarly, the proportions of stroke DALYs in LMICs and HICs in total global stroke DALYs in 2020 were 90% and 10%, respectively, while in 2050 it was projected to amount to 92% in LMICs and 8% in HICs. These findings suggest widening gaps in stroke burden between HIC and LMICs. Among the GBD regions the largest proportion of stroke DALYs compared to global DALYs in 2050 will continue residing in the Southeast Asia, East Asia, and Oceania region (46%).

Our findings also indicate a relative (compared to the 1990-2019 period) increase in the contribution of ICH to the overall increase in stroke burden in the world, especially in Southeast Asia, East Asia, and Oceania. However, the fastest growth of ICH deaths in 2050 is projected to be in Sub-Saharan Africa (98% growth). As the main risk factor for stroke and particularly for ICH is elevated blood pressure (hypertension),[1, 18] our forecasts support a call for improving prevention and treatment of hypertension in the world.[19]

A recent pooled analysis of 104 million study participants from 1201 population-representative studies[19] showed that the number of people aged 30-79 years with hypertension doubled from 1990 (331 [95% CI 306-359] million women and 317 [292-344] million men) to 2019 (626 [584-668] million women and 652 [604-698] million men), despite stable global age-standardized prevalence and among those with hypertension only 23% (95% CI 20-27) of women and 18% (16-21) of men had their blood pressure under control. This may be related to the wide use of high CVD risk threshold for initiation of pharmacological treatment of elevated blood pressure.[20-24] Targeting individuals with high CVD risk and applying treatment thresholds for primary CVD prevention might be adequate for an identifiable minority, but this approach precludes access to prevention and effective treatment for a large proportion of the population.[25-27] There is reliable evidence from recent meta-analyses of large randomized controlled trials that a pharmacological reduction of blood pressure reduces the risk of stroke and CVD irrespective of the baseline level of blood pressure across all age groups.[28] Based on the totality of evidence, the World Stroke Organization and the World Federation of Neurology recently called for revision of currently used primary prevention guidelines for stroke and CVD,[29] and switching attention from high CVD risk strategy to primary prevention strategies in people with any level of increased stroke/CVD risk, with focus on early detection and adequate management of hypertension.

Although a key driver in forecasting estimates of stroke deaths and DALY counts is population growth and aging, our survey analysis also suggests an insufficient level of, and inequity in, access to high quality prevention, acute and rehabilitation services across the globe will drive stroke-related deaths and DALYs, particularly in LMICs.

Gaps and future directions for stroke burden projections

While this is the first report on stroke burden projections for the 2020-2050 period, we do not include projections of stroke on a national level or projections of incidence, prevalence, YLL and years of healthy life lost due to disability (YLD), as that report will be presented in a separate paper. Planned forecasts of the future burden of stroke include modelling of the effects of various preventative (primary and secondary), treatment and rehabilitation interventions on stroke burden and its economic cost at global, regional, and national levels.

Conclusions

Our forecast shows the burden of stroke in the world will continue growing, with widening gaps between HIC and LMICs, although the pace of the increase in 2020-2050 period is slower than that in the 1990-2019 period. Projected failure to meet the Sustainable Development Goals 3.4.1 and further increase in stroke burden in the world, particularly in LMICs and especially in Southeast Asia, East Asia, Oceania and Sub-Saharan Africa regions, calls for urgent actions to improve stroke prevention and treatment across the globe (Panel 2).

Panel 2. KEY MESSAGES FOR STROKE BURDEN PROJECTIONS

Findings: Consistent with the increasing population size and aging in most countries, we found that the absolute number of people who die from stroke in the world will increase by 50% - from 6.6 million [95% UI 6.0-7.1] in 2020 to 9.7 million [95% UI 8.0-11.6] in 2050, with DALYs increasing over the same period by 31% - from 144.8 million [95% UI 133.9-156.9] in 2020 to 189.3 million [95% UI 161.8-224.9] in 2050. However, age-standardized mortality rates will continue decreasing – from

83/100,000 (75-90) and 1747/100,000 (1612-1892) in 2020 to 54/100,000 (44-66) and 1229/100,000 (1030-1477) in 2050, respectively. While 86% of the total global stroke deaths in 2020 occurred in LMICs, this was projected to increase to 91% by 2050. Similarly, 88% of the global stroke DALYs in 2020 occurred in LMICs while it was projected to amount to 92% by 2050.

Implications:

- Our findings provide evidence that the stroke burden in the world, as measured by the number of people who die or remain disabled, will continue increasing, disproportionally affecting LMICs, with the disparities in stroke burden between HICs and LMICs increasing even further.
- Should the current strategies in stroke prevention, risk factors prevalence and demographic trends continue, the Sustainable Development Goals for stroke burden reduction will not be met.
- Urgent measures to reduce stroke burden across the globe are needed, with the emphasis on LMICs and implementation of more effective primary stroke prevention strategies targeting first of all early detection and adequate management of hypertension.

Key research gaps and future directions for stroke burden projections:

- Ongoing forecasting of various stroke burden metrics (including costs) at global, regional, national and sub-national levels.
- Development of interactive tools (including maps and figures) showing the expected impact (short-term and long-term) of various preventative (including control of various risk factors), treatment, healthcare and rehabilitation interventions on global, regional and national stroke burden metrics (incidence, prevalence, deaths, YLLs, YDLs, DALYs, and economic benefits).
- Determination of impact of stroke burden on brain health burden at global, regional and national levels.

SECTION 2: ECONOMIC IMPLICATIONS OF STROKE FROM 2017 TO 2050 1022 words

Global medical care expenses associated with stroke have been estimated to be as high as US$ 315 billion in 2017, with a further US$ 576 billion foregone in income losses.[5] Given that stroke incidence rises with age, a combination of growing populations and aging demographic changes is likely to result in large increases in global deaths and disability from stroke in the future unless major improvements are seen in population prevention programs that reduce the risk of stroke. The GBD team forecasts that the annual number of deaths from stroke would rise from 6.6 million in 2020, to almost 9.9 million by 2050, and DALYs lost from stroke would increase from 145 million in 2020 to 185 million by 2050. The forecasts also indicate the number of stroke deaths would become more concentrated in Asia, rising from 4.1 million in 2020 (61.3% of the global total) to 6.6 million in 2050, or about 68.9% of global deaths from stroke. The share of Sub-Saharan African countries in annual global stroke deaths, although smaller relative to Asia, will also rise, from 6.2% in 2020 to 8.0% in 2050. Therefore, by 2050, not only will the economic implications of stroke be significantly higher than their current levels but will also more likely to be felt in Asia and Africa, and more generally, in LMICs.

Although income/indirect losses can be expected to rise over time, the rise is less sharp than for direct expenses and is primarily the result of two factors (for methodology of the global stroke economic burden estimates for 2050, see Supplementary materials pp.29-31). The first is that the working age

population (aged 15-64 years), the primary driver of income losses from stroke in our projection model, is expected to increase only slightly from 2020 to 2050 but is expected to fall sharply in China and in countries that are currently classified as high-income according to UN projections.[30] The second is our assumption that people will retire at age 65, the same as used to estimate income losses from stroke in 2017, as in Owolabi et. al.[5] If work participation rates at older ages were to increase over time, particularly after age 65, the projections will underestimate income losses from stroke in 2050 (Supplementary Tables 1 and 2).

The estimated aggregate economic costs of stroke, including direct costs and income losses, range from US$0.74 trillion to US$1.07 trillion in 2017 prices. But by 2050, these costs are projected to rise to between US$0.88 trillion to US$2.31 trillion in 2017 prices (Table 6).

Figure 7 highlights trends in direct costs and income/indirect losses from stroke between 2017 and 2050. Both project large increases in the direct costs and income losses from stroke in middle income countries and increases in direct costs in high-income countries (HICs). Projections also provide evidence of increased economic impacts of stroke in low-income countries but overall, their share in global costs is likely to remain small.

These projections of the economic consequences of stroke should best be thought of as indicative owing to the considerable uncertainties involved in predicting future direct costs and income losses. The accuracy of our projected economic implications of stroke in 2050 is crucially dependent first on the economic forecasting model used. We used a particularly simple model that relied solely on demographics, regional characteristics and starting GDP per capita for each country. While our model captures key elements of standard empirical growth models, richer models of economic growth would also account for projected changes in educational attainment, capital investments, changes in the policy environment and climate implications. However, predicting these variables may further add to the imprecision of the projected effects on income losses. Further, our estimates of the direct costs of stroke are dependent on assumptions about the relative rate of price increase of non-medical goods and stroke treatment. The prices of these goods and treatment will in turn depend on treatment practices, emergence of new treatment technology and diffusion of stroke treatment practices from HICs to the rest of the world, some of which will raise costs of treatment. Conversely, economies of scale and scope might lower treatment costs. Our strategy was to assume two different rates of expenditure growth in stroke treatment to try to account for this – 1% above non-medical expenditure inflation, and 3% above non-medical expenditure inflation.

Economic case for interventions to reduce the burden of stroke 2017 to 2050

The projected large increases in the economic cost of stroke between 2017 and 2050 imply major declines in the wellbeing of people who have had a stroke and their households, far into the future. These financial implications underline the importance of identifying interventions to prevent and manage stroke cases in a cost-effective manner. Large economic gains from effective interventions are potentially available from reduced treatment and rehabilitation expenses in both HICs and LMICs. There is a sufficient body of evidence to show that achieving the UN Sustainable Development Goals and WHO health targets with low-cost interventions (e.g., <US$1 per person a day in LICs and <$3 a day in MICs) could reduce the mortality rate for stroke and ischaemic heart disease by 10%. Another promising strategy to reduce stroke incidence and mortality is to reprioritize health investment streams towards population-wide primary prevention across the lifespan. It has been estimated that, for every US$1 spent on the prevention of stroke and cardiovascular disease, there is a more than $10

return on investment and that the most cost-effective preventive interventions are those that are focused on risk factors. Recent estimates of scaling up prevention of neurological disorders, including stroke, in just 11 countries (USA, Brazil, Colombia, China, Japan, Germany, Italy, Romania, UK, Kenya and Lebanon) to adequate levels by 2030 could save US$2.4 trillion, while scaling up treatment rehabilitation to the required level would save US$911 billion and US$727 billion, respectively.[31] Additionally, primary prevention efforts directed at stroke are likely to yield large gains due to the secondary effects of reducing the risk of heart disease, type 2 diabetes, dementia, and some types of cancer that share common risk factors, thus supporting achievements of a range of SDGs.

SECTION 3: STROKE SURVEILLANCE 2813 words

Introduction

Epidemiological surveillance systems are fundamental for evidence-based planning, resource allocation and priority determination for the reducing the burden of stroke.[32] When well designed and implemented, these systems provide comprehensive and contemporary information on risk factors, incidence, prevalence, and outcomes of stroke. Data from these systems can be used to develop, implement and evaluate programs for stroke prevention, acute care and rehabilitation.[33] The WHO Intersectoral Global Action Plan on Epilepsy and other Neurological Disorders[34] acknowledged the role of surveillance data in reducing the burden of neurological diseases. The Global Action Plan sets a target of 50% of countries to regularly collect and report on core indicators for neurological diseases, by 2031. In this section, we provide evidence on the progress of stroke surveillance towards this goal. We also highlight gaps in current surveillance systems and explore pragmatic strategies for improving stroke surveillance systems globally.

Situational and gap analysis

An ideal stroke surveillance system should include nationally representative data on the incidence, prevalence, quality of care, and outcomes (e.g., death, disability) of stroke, and prevalence of risk factors. These indicators are essential for informing strategies to reduce the burden of stroke. Here, we report the current level and gaps in stroke surveillance across the world. Countries are summarized by: (a) the level of economic development, i.e., low-income country (LIC), lower middle-income country (MIC), upper MIC, or developed/high-income country (HIC); and (b) the GBD region. GBD super regions include HICs; Latin America and Caribbean; Sub-Saharan Africa; North Africa and Middle East; Southeast Asia, East Asia, and Oceania; South Asia; Central Europe, Eastern Europe, and Central Asia.

Review of the current state of surveillance of stroke events and outcomes

Surveillance of stroke events can come from stroke incidence studies, registries or population-level data on hospitalizations and stroke outcomes.[35, 36] Stroke incidence and case fatality are traditionally monitored using 'ideal' incidence studies.[37] However, these studies are resource-intensive and often impractical to undertake. For example, in the recent review of the Global Stroke Statistics,[36] the authors identified only seven ideal incidence studies undertaken globally in the last decade. In contrast, stroke registries continued to be abundant globally.[36]

National stroke registries can be a relatively inexpensive supplement or substitute for monitoring fatal and non-fatal strokes, with relatively limited resources. Despite the value of these registries, there are

limitations affecting their use for optimal surveillance of stroke, including error in data entry (selection bias) or coding (classification bias),[38] and lack of precision of hospital diagnostic coding regarding the cause of stroke.[39] Examples include the use of the ICD I64 code (stroke, not specified as ischaemic or haemorrhagic), or incorrectly coding TIA or haemorrhagic stroke as ischaemic stroke. Another major challenge is the nationwide coverage of national stroke registries. In a review of data collected in the Global Stroke Statistics,[36] we found that only 31 of 216 WHO member countries/territories (14%) had some capacity for optimal stroke surveillance through their national stroke registries. All but seven of these countries were HICs. National registries were scant in the super regions of Central Europe, Eastern Europe, and Central Asia (1 registry); South Asia (1 registry); and Southeast Asia, East Asia, and Oceania (3 registries in total). No national registry was identified in North Africa and Middle East, and Sub-Saharan Africa, indicating that fewer resources are available for surveillance in these regions, a situation that is likely to continue unless there is significant investment from government. Only a few countries (e.g., Bahrain, Finland, Israel, Russian Federation, Singapore) had stroke registries with the nationwide coverage required for evidence-based healthcare planning and resource allocation for stroke care.

Nationally representative data on mortality due to stroke are those collected in national civil registration and vital statistics systems and submitted to WHO. Although these data are not without limitations, e.g., submission of incomplete data or lack of up-to-date data,[36] they remain the most robust source of statistics on stroke mortality. However, only 138 of the 216 WHO member countries/territories (64%) submitted stroke-specific mortality data to WHO in the last three decades.[36] The majority of the 78 countries without data were from sub-Saharan Africa (42 countries; 54%), and South East Asia, East Asia & Oceania (18 countries; 23%), potentially reflecting the lack of capacity for surveillance of stroke mortality in these regions. In the absence of data from the national registration systems of countries, mortality estimates are often extrapolated from non-representative studies or international demographic and epidemiological statistical models,[40] which may not be reliable. Given the rising population in these regions (estimated to be home to 45% of the global population in 2030), and their ongoing demographic and epidemiological transitions, reliable data on stroke events and outcomes are needed to inform public health policy and actions.

Review of the current state of surveillance of risk factors for stroke

To reduce the burden of stroke, there is a need for population-wide monitoring of risk factors for stroke. In limited-resource settings, efforts are focused on collecting high-quality data on risk factors that (1) strongly predict stroke,[18] (2) are highly prevalent,[41] (3) are amenable to individual- or population-level interventions,[5, 42] and (4) are relatively easy and cheap to monitor. An ideal comprehensive surveillance of risk factors for stroke would include monitoring of blood pressure (BP), anthropometrics (e.g., weight, waist circumference), biochemical measures (e.g., lipids, blood glucose), and lifestyle factors (e.g., smoking, diet, physical activity, alcohol intake, illicit drugs, stress, overweight/obesity, dyslipidaemia, diabetes, atrial fibrillation, and air pollution). Therefore, in September 2022, we undertook a search of published and grey literature for the latest national health surveys for surveillance of these risk factors in 216 WHO member countries/territories. For this review, a survey is considered as comprehensive for stroke surveillance if it comprises measurements from at least one of each of the above-listed risk factors.

We found information on national health surveys in 196 countries/territories (91%; Supplementary Table 3), with different capacities for the surveillance of risk factors for stroke (Figure 6). Information was unavailable for 4 HICs/territories, 8 countries in Latin America, 6 countries in Sub-Saharan Africa and in RyuKyu Islands (Southeast Asia). The most measured risk factors included lifestyle factors (181 countries; 92%), anthropometrics (164 countries; 84%), and diagnosis of metabolic conditions (159 countries; 81%). Most surveys lacked comprehensiveness and recency. Five countries (Cameroon, Congo Democratic Republic, Sao Tome and Principe, Senegal, and Tunisia) did not measure any risk factor for stroke in their latest national survey. Although, LMICs assessed more risk factors in their last surveys than HICs (Figure 11-a), their surveys were often not recent (i.e., undertaken before 2018). Compared to LMICs, HICs more often had recent and/or comprehensive survey of risk factors. Overall, 112 countries lacked recent surveys (undertaken from 2018 onwards), 109 (97%) of which were non-HICs. Of 84 countries with a recent survey, only 32 (38%) included BP measurement, and only 27 countries (32%) had comprehensive surveillance of risk factors for stroke. It is evident from these findings that capacity is required for collecting comprehensive and contemporary information on important risk factors for stroke across the globe, but particularly in low- and middle-income countries.

Thematic analysis of surveillance services

As shown in Supplementary Table 4, several main themes were identified from the semi-structured interviews with experts from 12 countries (Supplementary materials, pp. 8-28) acting as both facilitators and barriers to the delivery of high-quality stroke surveillance services. These themes include surveillance capacity, information technology, and governance of surveillance activities.

Surveillance capacity covered activities and availability of a trained workforce to capture stroke events or risk factors. Countries with good stroke surveillance had a well-funded and trained workforce. They had established nationwide registries to monitor treatment and outcome as well as regular risk factors surveys from population-based approaches including being integrated into the census. In contrast, countries with limited surveillance capacity lacked nationally representative or standardized data on stroke treatment or outcomes. This was due to lack of government-coordinated efforts with stroke surveillance activities undertaken by individual institutions or academic research networks.

Information technology influenced the ability to deliver high-quality stroke surveillance services. Countries with a strong health information system performed well in stroke surveillance. Web-based systems allow data collection in real-time, improving data quality. Digitalization of medical records, mortality, and other health databases enhanced the analysis and use of data to inform policies. Electronic databases increased accessibility and enabled data linkage to conduct complex studies on stroke. High-performing countries used data from stroke surveillance systems to raise awareness of stroke and its risk factors in the community and government, enhancing strategic investment. Poorer performing countries had fragmented health databases limiting the comprehensiveness and use of data for decision making.

Strong governance facilitated high-quality national stroke surveillance systems. This included political commitment, funding, and advisory bodies for stroke surveillance. Countries with strong governance often had strong health information systems to facilitate data-driven decision making. Stroke surveillance activities were often government-led, with technical support from experts. A lack of

government commitment to stroke surveillance hindered the ability to establish a strong stroke surveillance system. The lack of data on stroke hampers setting priorities and funding for stroke services. Countries with strong commitment to stroke surveillance still reported limited funding.

Pragmatic solutions for improving stroke surveillance

It is recommended by WHO that each country have a program that achieves near universal monitoring of the important indicators of the burden of stroke.[43] A good example of that is the Stroke Service Tracker in Europe as part of the European Action Plan for Stroke 2018-2030.[44] For regions with limited resources, WHO developed a three-step standardized surveillance system for stroke in 2002 - STEPS.[43] In a review of seven studies from nine LMICs incorporating the WHO STEPS protocol,[45] adherence to the surveillance methods was variable.[46] Particularly, there were challenges with collecting data on neuroimaging and non-fatal events in the community.[46] This and other challenges could be overcome through training to improve capacity to undertake surveys, having feasible surveillance protocols that are co-designed with local experts, electronic data collection, and including stroke in existing monitoring systems for NCDs to facilitate easy identification of cases in the community.[46]

One of the most popular and commonly used epidemiological methods for surveillance of stroke in LMICs is a door-to-door survey. If a stroke prevalence survey is undertaken in a sufficiently large sample size (25-30,000 people), and combined with data from death certificates (e.g., using verbal autopsy procedures) collected over at least 3 years in the same community, it may be possible to derive relatively accurate incidence and mortality estimates in the study population. The central tenet of this approach is that nonfatal first-ever stroke events within the preceding 3 years in the defined population are identified through a prevalence survey, and then combined in the analysis with fatal first-ever stroke events, in the same population for the same study period, to calculate cumulative stroke incidence rates.[47] This approach was first used in Italy[48] and China,[49] shown to be valid,[49] and successfully used to study stroke incidence and mortality in a large nation-wide cross-sectional study in China.[50] Another epidemiological approach for stroke surveillance in LMICs is repeated community-based studies in the same population at different time periods,[51] as previously undertaken in Brazil.[52] However, the latter approach is resource-intensive and often challenging to undertake .

Key recommendations and solutions for improving stroke surveillance are summarized in Table 7 and Panel 3. National stroke registries can be used to monitor hospitalizations for stroke.[53] Where these registries have nationwide coverage, they can be coupled with national death registries to give a near complete picture of the burden of stroke.[54] However, in countries with less access to hospital services, registries should be supplemented by case ascertainment of at least fatal and, if possible, non-fatal cases occurring in the community. This could be undertaken through WHO standard verbal autopsy instrument[55] that has been validated for use electronically in developing countries.[56]

There is also an increasing interest in using other large, routinely collected, administrative data for monitoring hospitalizations, quality of care, and outcomes following stroke.[35] However, there is a need to develop standardized methods and systems for using these data to provide timely and reliable estimated stroke burden. Countries should establish national electronic health records or information systems, that could facilitate greater coverage of electronic medical records and interoperability between systems to prevent duplication of data capture. Likely barriers include resources required to establish and maintain this infrastructure, particularly in limited resource settings, where access to

electricity is limited, and technological literacy of health workers is inadequate. Also, concerns have been raised about the validity of administrative health data for diagnosis of stroke and comorbidities,[57] and privacy of electronic health records.[58, 59] These concerns can be overcome through appropriate training of staff on data coding, entry and handling, undertaking regular review of variables and validation of data entry and coding methods, and appropriate encryption of data.[32, 60-62]

Regardless of the monitoring system used, consulting community groups, clinicians, providers, policy makers, funders, and implementation partners at each stage of development and implementation is paramount. This will ensure that ethical, legal, and social considerations are met,[5, 15] and that the system meets the needs of the community and other stakeholders.

Establishing national monitoring systems for risk factors

There is a need for countries to establish a national framework and capacity, including funding and reporting mechanisms, for regular monitoring of important risk factors for stroke,[45] with geographical and ethnic/racial representativeness. Countries without existing frameworks can implement one of the three main types of surveys widely used to assess risk factors for stroke: the World Health Organization (WHO) STEPS, Demographic and Health Survey (DHS), and European Health Interview Survey (EHIS).

The WHO STEPS system is a valid and reliable system for the surveillance of risk factors,[45] with emphasis placed on high-quality collection on fewer variables, rather than large numbers of poor-quality data. The DHS is largely funded by the United States Agency for International Development (USAID), with support from host countries and other agencies (e.g., The DHS Program). A major benefit of the DHS is the concurrent capacity building of workers through training and support tools, to maximize the collection of high-quality data. The EHIS is a collaborative effort between all member states of the European Union (EU) to collect standardized, high-quality, self-reported health data. EHIS is complemented by the European Health Examination Survey (EHES) which collects information on blood pressure and biochemical measures.

Comprehensive surveillance of risk factors for stroke requires additional resources for staff, training, data management and collection and processing of samples. There is potential for using digital tools for remote, large-scale collection of data on NCD risk factors. However, methods for sampling to ensure representativeness, sharing of data, and validation of these tools, require development before implementation in national risk factor surveillance systems. An example of a comprehensive fully digitalized national level survey of risk factors was recently undertaken in India.[63] It was adapted from the STEPS system and is part of the Indian national NCD monitoring framework.

Future strategies for research, dissemination, and implementation

Stroke surveillance systems are important for developing, implementing, and evaluating national programs to reduce the burden of stroke. These systems are relevant across prevention, acute care, and rehabilitation sections of stroke. Stroke surveillance is a key element of the WSO Global Stroke Care Guidelines (e.g., 'key stroke quality indicators' sections), along with several other international plans, such as the WHO Intersectoral Global Action Plan on Neurological Disorders.[34]

Future research should be focused on methods, implementation and evaluation of stroke surveillance systems including quality improvement. For research, there is a need to develop and validate methods

for measuring incidence, prevalence, and outcomes of stroke, using administrative data. Research focused on the implementation and evaluation of models to improve the surveillance of stroke, drawing on mixed methods approaches is necessary, including how these data can be used for quality improvement activities.

The stakeholders of the WSO-*Lancet Neurology* Stroke Commission implementation ecosystem (Figure 3) will ensure the implementation, monitoring and evaluation of pragmatic solutions recommended by this Commission. Commissioners and national stroke societies will champion co-implementation activities at the national level. The ecosystem will leverage global partners to undertake several activities to improve stroke surveillance (Table 7, Panel 3), including: implementing national strategies for surveillance of stroke (e.g., via digital technologies, where possible), particularly for countries with limited data, and building capacity and resources (governance, training, and infrastructure) in LMICs for electronic medical records system that could facilitate surveillance and data linkage.

To implement the recommendations of this Commission, countries should establish sustainable programs for regular country-wide monitoring and evaluation of stroke burden, its modifiable risk factors, and stroke-related health services, integrated within existing national stroke plans. Regardless of the surveillance method used, collaboration and co-design is necessary among stakeholders to provide inputs and use outputs in developing and implementing stroke surveillance systems.[35] This will help ensure that stroke surveillance systems meet the needs of all stakeholders, enhance uptake and ensure sustainability.

Panel 3. KEY MESSAGES FOR STROKE SURVEILLANCE

Strategies and Solutions to Improve Stroke Surveillance

- Governments need to establish nationwide and representative systems for monitoring stroke, through registries, electronic health records, and vital statistics systems that achieve near universal surveillance of important indicators of stroke burden and risk factors, to reliably inform the development of programs for stroke prevention, acute care, and rehabilitation. These include incorporating surveillance in national stroke plans or existing monitoring systems for NCDs, processes to identify stroke cases in the community; and including stroke risk factors or in national census. Countries with limited capacity or resources could benefit from assistance, collaboration, and funding from international development agencies, e.g., WHO, USAID. For countries with capacity and resources, there is a need for sustainable funding to ensure routine data collection.
- All countries should have a program of surveys with identified priorities, and clearly defined cycles and scope of data collection, and invest in surveillance and analysis in a manner that ensures efficient use of resources. This should include assessing the incidence, prevalence, management and control of cardiovascular risk factors at the population level, based on reliable and valid measurements. e.g., measurement of blood pressure rather than self-report of hypertension. These surveys should be undertaken at regular intervals to determine changes over time. Countries should also develop capacity to regularly analyse the data collected and generate quality evidence to support decision-making.

- Governments should establish and fund national stroke registries of hospitalized, non-hospitalized, fatal and non-fatal stroke and TIA, to complement existing surveillance systems. Such registries should be facilitated by linkage of population data on risk factors to hospitalization and national death registries, to determine the relationship between the population burden of risk factors and stroke burden. For countries with capacity for stroke surveillance through registries, there is a need to expand coverage nationwide. When combined with data being collected in national death registries, data from nationally representative stroke registries could provide a near complete picture of the burden of stroke.
- There is a need to maximise the potential of digital tools and national registries for large-scale collection of data on stroke. Countries should establish national electronic health information systems, with interoperability between systems, to prevent duplication of data. In countries with established electronic or web-based platforms for data collection, there is a need to encourage or incentivise collection of data on stroke and its risk factors to increase coverage. This could, in turn, facilitate linkage of large population-based data for surveillance purposes. For such platforms to be valuable and sustainable, there is a need for training to ensure appropriate documentation and coding, and secure handling of electronic health data,
- Regardless of the surveillance system used, consulting community groups, clinicians, providers, policymakers, payers, and implementation partners at each stage of development and implementation is paramount. This will ensure that political, legal, ethical, anthropological, and socioeconomic considerations are applied, and that the system meets the needs of the community and other stakeholders.

Future Directions and Key Research Gaps for Stroke Surveillance and Epidemiology

- Need for mixed methods research focused on the development, implementation, and evaluation of models to improve the surveillance of stroke, particularly in countries with limited resources and capacity. Such research could be focused on developing feasible surveillance protocols that address local priorities and needs, while ensuring collection of standardised and representative data that can be used for quality improvement. This could involve adapting well established standard surveillance protocols, e.g. WHO STEPs, DHS, EHIS, and exploring less costly but successful surveillance methods, such as repeated cross-sectional and community-based studies undertaken in strategic locations.
- Introduction of nationwide representative community-based stroke surveillance in health and demographic surveillance sites, and high-quality national stroke registries, to monitor hospitalisations, resources, treatments, and outcomes.
- Linkage of population data on risk factors to national hospitalisation and death registries to determine the relationship between the population burden of risk factors and stroke burden.
- Need for validation studies to determine the quality and coverage of data on risk factors available in administrative datasets (e.g., admitted patient record and primary care).
- Surveillance systems should incorporate data collection for discovery science to unravel the genomic architecture and pathobiology of stroke, its risk factors and outcomes, across populations of diverse ancestries. Combined with translational trans-omics research and precision medicine, this will facilitate the development of novel predictive, diagnostic, and prognostic biomarkers, and better prophylactic, diagnostic, therapeutic, and restorative interventions for preventing stroke and its risk factors. Including underserved populations from LMICs in such genomic and multi-omic studies is crucial to enhance the discovery potential by increased diversity, and to ensure that derived biomarkers and interventions are applicable to high-risk populations.[64]

- Development and validation of novel personalized digital and mobile health tools for population wide surveillance of stroke and its risk factors

SECTION 4: STROKE PREVENTION 3186 Words

Introduction - Focus on secondary stroke prevention

Recurrent strokes and transient ischaemic attacks (TIA) contribute significantly to the overall burden of acute cerebrovascular diseases[65] as about 20-30% of strokes occur in people with a previous stroke or TIA.[65-67] Patients with stroke and TIA are at increased risk of recurrent stroke, which is particularly high within the first days after the index event.[66, 68] These recurrent strokes are more disabling and have poorer outcomes than first strokes.[69] There is evidence that 45-80% of recurrent strokes and TIAs could be prevented.[70-72] Although post-stroke survival probabilities have improved over the last two decades, no major trends in stroke recurrence rates have been observed over the last two decades in many,[67, 73, 74] but not all,[75, 76] countries.

In this section we focus on stroke prevention strategies in people with previous stroke or TIA, paying particular attention to the level, barriers, and facilitators for the implementation of current recommendations, identifying deficiencies in existing guidelines and offering pragmatic solutions for implementation. As strategies on secondary stroke prevention also include strategies for primary stroke prevention, we reiterate some primary stroke prevention strategies described previously.[5]

Situational and gap analysis

Definition: Secondary stroke prevention is commonly defined as the prevention of stroke in individuals who have already had a stroke or transient ischaemic attack (TIA). *Principles*: The principles of secondary stroke prevention are to urgently evaluate, identify and treat the underlying causal pathologies and minimize long-term exposure to causal risk factors, and to reduce the immediate and distant risk of recurrent stroke. *Components*: The evidence-based components of effective secondary stroke prevention comprise lifestyle, pharmacological and surgical interventions (in eligible patients) that are targeted to the cause and are aligned to the risk of recurrent stroke and complications of any intervention.[65, 72] Examples include antithrombotic therapy, carotid endarterectomy or stenting, and patent foramen ovale closure in those with ischemic stroke, aneurysm coiling/clipping in those with subarachnoid haemorrhage, and control of vascular modifiable risk factors known to reduce the risk of stroke (similar to what was previously described by us for primary prevention of stroke), of which blood pressure control is the most prominent.[5]

Current strategies

Whereas primary prevention is targeted at the population as a whole and at individuals without clinically established stroke and TIA, similar measures are applied to individuals in secondary prevention. Tangible global strategies and pragmatic solutions for improving management of vascular risk factors on an individual level as part of the primary stroke prevention strategies have been published elsewhere.[5] In summary, these strategies overlap and include both population-wide and individual-based strategies that cover all or most of the population, with priority directed towards population-wide strategies and early detection and control of hypertension (Figure 8). At the population level it has been estimated that a 2 mm Hg decrease in systolic blood pressure would result in a 24% decrease in stroke incidence.[77]

Individual-based primordial and primary stroke prevention strategies can be best accomplished on the population level by population-wide stroke/CVD prevention strategies and on the individual level by using mobile technology (so-called motivational mass individual strategy for stroke prevention)[25] and by shifting/sharing of tasks from highly trained health professionals to healthcare workers, particularly community-based health workers.[78, 79] Primary and secondary stroke prevention strategies can be further augmented by using polypills.[80, 81]

Secondary stroke prevention has conventionally been individual-based around the doctor-patient relationship. The diagnosis of stroke and its cause(s) have been made by a doctor, and the secondary prevention program has been generated and managed by the doctor in conjunction with the patient. Other complementary inputs include access to family support, community services for education and monitoring (e.g., nursing, allied health), public education and population-based primary stroke prevention strategies.

Despite these efforts, stroke recurrence rates in many countries remain at unacceptably high levels (20-30%), although a recent international cohort study showed that with proper management, there is only a 10% risk of subsequent disabling or fatal stroke at 5 years after TIA and minor ischaemic stroke.[82] The failure of current secondary prevention strategies to contain stroke recurrence rates may be attributed to several known barriers for effective secondary prevention. These barriers include a lack of specialized training by the doctor, lack of education of patients on the cause of the index stroke, the long-term risk of recurrence, or the importance of long-term monitoring of risk and health and maintenance of lifestyle behaviour and medical therapy, as well as medical workforce deficiency and low affordability of preventative medications (especially in LMICs), lack of doctor's time and efficient digital tools for developing person-specific and motivational secondary stroke prevention recommendations. Failure by doctors and patients to appreciate that these factors compromise motivation and effective self-management strategies, may be compounded by post-stroke sedentary behaviour, mood, speech and cognitive disorders, and likely achieve inadequate adherence to secondary stroke prevention recommendations.[83]

Our recent WSO-*Lancet Neurology* commissioned international survey of stroke services[8] from 84 countries showed that overall, secondary stroke prevention activities were at an acceptable level (score 50+) in only 40-46% of participating hospitals (Supplementary Tables 5 and 6). While this survey did not cover all countries, the findings contributed to developing better prevention strategies. The lowest ('poor') secondary prevention activity scores were observed for routinely available education about stroke and lifestyle management for stroke patients and their families. The strategies most often adopted were for the use of antiplatelet, anticoagulant, blood pressure-lowering and lipid-lowering medications. The most widely available medicines were aspirin (available in 90% countries), metformin (87% countries), and thiazide diuretics (87% of countries). There were also disparities between regions, e.g., while 92% of countries in the European Region reported availability of angiotensin II receptor blockers (ARBs), only 36% of countries in the African Region reported such availability. It is important to note that availability of outpatient stroke/TIA clinics or stroke prevention clinics is better in upper-middle- and HICs than other income groups. There was also a lack of digital tools to support clinicians for implementing and monitoring evidence-based and patient-centred secondary stroke prevention strategies,[84] and low stroke awareness among the populations.[85-87]

Our analysis of the utilization of guidelines addressing evaluation/measurements and management of various risk factors in people with stroke and TIA for secondary stroke prevention by country income level also showed an extremely low level of such assessment and management in LICs, and significantly lower levels in MICs as compared to HICs. However, even in HICs the level of evaluation of risk factors for secondary stroke prevention was suboptimal.[88] Routinely available secondary stroke prevention activities across all country economic levels were particularly low in areas such as recurrent stroke risk assessment score (even in patients with atrial fibrillation), risk factor assessment, lifestyle assessment, and education about stroke and lifestyle management.

Previous surveys[89] and the results of our survey on the low utilization of secondary stroke prevention strategies are in line with those from a recent survey of national scientific societies and stroke experts in Europe,[90] China[91] and a recent systematic review of ischaemic stroke prevention guidelines.[92] We also found a lack of organization of follow-up systems after TIA and stroke. However, there is currently much emphasis on the fact that follow-up should be multimodal and structured and include not only preventive issues but also other key components after a stroke as identified in the post-stroke checklist endorsed by the WSO. Scientific evidence supporting such an integrated approach is emerging.[93]

In 2019, we estimated global stroke DALYs of 143 million,[1] with economic burden of stroke of US$891 billion per year.[5] In 2050 we project to have 190.8 million stroke DALYs in the world. A simple extrapolation of the cost suggests that by 2050, the global economic burden of stroke is expected to be over US$1.19 trillion per year.

Thematic analysis of prevention services

The three themes identified as facilitators and barriers to high-quality stroke prevention services in interviews (details of the interviews can be found in Supplementary materials pp.10-11) with nine interviewees worldwide were: system capacity, universal health coverage, and governance of stroke prevention (Supplementary Table 6).

System capacity covered the distribution of services across urban and rural areas, continuum of services, and availability of trained health workforce. Lack of trained health staff was a major barrier to providing primary and secondary stroke prevention services. The unequal distribution of health staff and socioeconomic differences between urban and rural areas created inequality in access to services that negatively impacted health literacy. On the contrary, countries with a wide network of service delivery with a mixture of staff (doctors, community health workers) with stroke-specific training provided a wide range of stroke prevention services.

Universal healthcare influenced the accessibility of stroke prevention services. Countries with universal health coverage (e.g., affordable access for all people to the quality health services they need) had a wide range of stroke prevention services (e.g., regular health checks, lifestyle programs, medications) provided free of charge or at low cost. A lack of universal healthcare exacerbates inequality in accessing stroke prevention services with out-of-pocket costs seeing patients prioritizing treatment rather than prevention, e.g., less, or no regular health check to control stroke risk factors. The lack of government-led primary stroke prevention activities was linked to lower population health literacy on stroke prevention.

Strong governance in stroke prevention facilitated high-quality stroke prevention services. A political commitment to stroke prevention and national strategy to control risk factors of stroke (e.g., tobacco control or blood pressure) enhanced primary and secondary stroke prevention. Active participation of stroke organizations enhanced governance. Countries with strong governance in stroke prevention used health information for decision making, whereas low government priority to prevent cardiovascular diseases/stroke and no clear national prevention guidelines hinders stroke prevention.

Pragmatic solutions for improving stroke prevention

Problems to overcome, and suggested strategies for policy makers to achieve sustainable and appropriate primary and secondary stroke prevention are presented in Tables 8 and 9, Panel 4 (Supplementary Figures 6 and 7). A summary of identified barriers and facilitators for improving stroke prevention services is shown in Supplementary Table 6. It has been suggested that effective collaboration between various healthcare sectors, government policies and campaigns, together with evidence-based individual management approaches would allow successful implementation of primordial, primary and secondary prevention strategies across the globe.[5, 94, 95] A tripartite approach to primary stroke prevention, comprising behavioural, pharmacological, and structural interventions which is superimposed on the socioecological model could minimize the current fragmentation and inefficiency of primary stroke prevention.[42]

The development and implementation of action plans for primordial, primary, and secondary stroke prevention should align with internationally recommended goals and targets for reducing NCDs.[96] These country-specific and financially sustainable action plans and consensus statements should be developed by recognized experts from the region on the basis of the best available evidence, endorsed by government agencies, and contain adequate and well-developed indicators, goals, concrete steps, timelines and accountable people. These action plans must be facilitated by national, culturally appropriate, and up-to-date guidelines for primordial, primary, and secondary stroke prevention. Unfortunately, there is a shortage of operational national plans aligned with the Global Action Plan on NCDs.[96] In addition, while there are national guidelines for primary and secondary stroke prevention in a number of HICs,[65, 96-99] there is a paucity of evidence-based, context-appropriate pragmatic stroke prevention guidelines in LMICs,[95] including those related to secondary stroke prevention. The only currently available digital tool to support clinicians in evidence-based primary and secondary stroke prevention interventions in both hospital and outpatient settings is the PreventS-MD webapp.[84, 100]Although mainstream preventative strategies should be similar in HICs and LMICs, differences in the population-attributable risks, lifetime risk of stroke and availability and affordability of resources should be considered when setting realistic and country/culturally-appropriate goals and priorities.

Based on our survey results and literature review we propose key recommendations for healthcare providers and policy makers to improve primary and secondary stroke prevention, with the emphasis on LMICs. Solutions and supporting evidence for primordial, primary and secondary stroke prevention on the population and individual levels are presented in Tables 8 and 9.

Guidelines and risk estimation

The most recent guidelines for primary prevention of stroke and CVD[101-103] and secondary stroke prevention in patients with stroke and TIA[65, 104, 105] are recommended for use and adaptation for local conditions. There is enough evidence to suggest that the traditional high CVD risk approach to risk

factor control is complex, expensive, and only modestly successful,[25, 27, 106] and the absolute-risk treatment thresholds should not be the main and sole criteria for selecting individuals for pharmacological management of elevated blood pressure, diabetes and lipid lowering therapies.[26, 29, 107] The WSO and World Heart Federation also proposed that the categorization of people into low, moderate (mild), and high absolute cardiovascular risk (including use of risk-stratified heat maps) should be abandoned.[78, 108] More effective and widely applicable motivational preventative strategies, with emphasis on lifestyle modification, should be implemented for people at any level of risk of stroke and cardiovascular disease.

Building capacity for stroke prevention

We suggest that all countries should have government endorsed policies, guidelines, and ongoing stroke awareness campaigns (via media, schools, churches etc.). Meaningful engagement of such campaigns can include global user-friendly educational programs that target children's families and grandparents to successfully identify stroke symptoms and respond appropriately to this health emergency (e.g., the FAST Heroes initiative).[109, 110] Realistic, country/culturally appropriate, and financially sustainable action plans for secondary stroke prevention can be integrated with both the corresponding primary prevention strategies and development/improvement of stroke services. Specific plans should also be established for upskilling of staff, including community health workers. Countries should develop a plan for prioritization of these multisectoral and cost-effective accessible and affordable interventions, including those utilizing proven effective telemedicine, mobile and other digital technologies.

Monitoring and evaluation

The key performance indicators for primordial and primary stroke prevention should include accurate measurement of stroke incidence and prevalence of risk factors (particularly blood pressure, overweight and smoking status) over time. As stated in our surveillance section, all countries should also have a nationwide and representative system for measuring and monitoring effects of primary and secondary stroke prevention activities. This should undergo a stepped approach that highlights the elements required for minimum (hospitalized events), essential and advanced monitoring, i.e., incorporating the WHO stepwise approach[111] or similar.[37, 47, 112] Key performance indicators for secondary stroke prevention should include proportion of patients with: (1) ischaemic stroke and TIA whose co-morbidities (such as hypertension, DM) are under control during follow-up; (2) ischaemic stroke and TIA who are prescribed an antiplatelet agent; (3) ischaemic stroke and TIA who are prescribed a statin agent (system indicator: availability of statin medications in region); (4) ischaemic stroke and TIA with atrial fibrillation/flutter who are prescribed an anticoagulant agent; (5) carotid territory ischaemic stroke and TIA and symptomatically relevant extracranial carotid artery disease who undergo carotid revascularisation; (6) ischaemic or haemorrhagic stroke on blood pressure-lowering medication(s); (7) who have their blood pressure controlled; and (8) time from stroke onset to carotid revascularization. It was also suggested that the identified gaps in secondary stroke prevention can be addressed through national and international policy initiatives, clinical guidelines, registries and direct reimbursement for specific interventions.[90] Successful implementation of appropriate secondary prevention strategies in individuals with stroke and TIA has the potential to reduce the burden of stroke by up to a quarter.[66]

Future strategies for research, dissemination, and implementation

The importance of developing adequate prevention services for stroke is being emphasized in several recent international initiatives/programs, such as the WHO Global Action Plan (GAP) on Neurological disorders, Brain Health Initiative, OneNeurology, Heart and Brain Initiative, Non-communicable Disease (NCD) Alliance, Circulatory Health, and WHO Strategic Technical Advisory Group (TAG) NCD-related Research and Innovation. As risk factors for stroke are common for other major NCDs such as ischaemic heart disease, peripheral vascular disease, diabetes mellitus, vascular dementia, chronic obstructive pulmonary disease, and some cancers (Supplementary Figure), reducing exposure to these risk factors on individual and population levels would prevent not only stroke but also other major NCDs.

The most recent WSO Global Stroke Guidelines and Action Plan concerning secondary stroke prevention[113] emphasizes the importance of involvement of healthcare providers who have expertise in stroke care with designated prevention clinics, vascular risk reduction programs, educational and preventative tools (e.g. the Stroke Riskometer app), chronic disease management programs, acute care hospitals, emergency departments, primary care and other community settings and in the home, based on resource and facility availability. Digital technologies have also been proposed as a new strategy for improving both primary and secondary stroke prevention.[84, 100] Educational campaigns implemented both digitally and face-to-face have been found to advocate acute stroke care by successfully increasing learning about stroke symptomatology and the necessary steps that need to be followed.[114]

Further research is needed to: (a) identify the best balance of population-wide and risk targeted stroke/CVD prevention strategies, including various digital technologies, to maximize cost effectiveness and minimize inequalities; (b) develop and validate innovative, pragmatic, scalable and cost-effective interventions (educational, prognostic, diagnostic, and therapeutic), including motivational digital tools, to be used for stroke prevention by healthcare practitioners and lay people; (c) increase wide-scale implementation research of various evidence-based primordial, primary and secondary stroke prevention strategies in different populations, including testing of low-risk preventative interventions in routine clinical care.

Discovery science and translational research leveraging genomics, trans-omics and precision medicine to develop and test novel prophylactic, diagnostic, therapeutic, prognostic and restorative biomarkers and interventions for stroke and its risk factors are crucial to enhance the discovery.[115] These approaches should include underserved populations from the LMICs. This will ensure that derived biomarkers and interventions are applicable to populations with the greatest burden of stroke.

To implement, monitor and evaluate the pragmatic solutions recommended by this Commission, the WSO Task Force on Stroke (Figure 3) and implementation ecosystem are being established (Figure 1). This ecosystem will harness and leverage global resources, including WHO and United Nations non-communicable disease control plan and the WHO Intersectoral Global Action Plan Against Neurological Diseases to: (i) address key environmental factors via policy change – social determinants of health, making default choices healthy (e.g., healthy cities, healthy food value chain); (ii) enhance stroke literacy through key community influencers who can deliver culturally tailored messages, using strategies such as social media (social media influencers with impact), the arts (music, comedy, film, TV); (iii) address motivation, self-efficacy, self-management skills; (iv) facilitate inclusion of the

primary and secondary prevention recommendations outlined in this section into national stroke/CVD management guidelines; and (v) empower the stroke commissioners (country ambassadors for stroke prevention) to be the champions and advocates ensuring rigorous implementation and evaluation via national policy makers across the globe. The WSO Task Force on Stroke commissioners and ecosystem are planned to operate at country, regional and global levels in collaboration with relevant policy makers and implementation partners, including World Hypertension League, World Federation for Neurorehabilitation, NCD Alliance, WHO, Resolve To Save Lives, Ministries of Health, national and regional stroke organizations (African Stroke Organization, European Stroke Organization, Middle East and North Africa Stroke Organization, Asian Pacific Stroke Organization, American Heart Association, Registry of Stroke Care Quality , etc.), neurology, CVD and NCD organizations and relevant alliances. Key performance indicators will be monitored using the United Nations Theory of Change approach.[116]

Panel 4. Key messages for cost-effective individual primordial, primary and secondary stroke prevention

Suggested solutions for improving stroke prevention on individual level:

- Mobile and digital technologies (so-called motivational mass individual strategy for stroke prevention)[25] which enable lay people to engage in simple, inexpensive screening for a history of CVD and presence of modifiable risk factors (particularly smoking/vaping, obesity, atrial fibrillation, elevated blood pressure) in collaboration with their healthcare professionals; afford linkage to local, regional and/or national healthcare electronic databases, and utilize validated motivational digital technologies to assess stroke/CVD risk; and implement and monitor person-centred, lifestyle behavioural primary and secondary stroke/CVD prevention strategies.
- Motivational strategies for improving compliance to prescribed medications and lifestyle modifications, improving access to affordable medications and procedures for primary and secondary stroke prevention strategies, with the focus on essential medications/procedures (including polypills with blood pressure and lipid lowering medications in the WHO list of essential medications). Essential drugs for primary and secondary prevention should be subsidized by the government and made available at all hospitals and outpatient clinics.
- Shifting/sharing of tasks from highly trained health professionals to paramedical healthcare workers, particularly community-based health workers, with less training, qualifications, and education to facilitate stroke prevention interventions on the individual level.[78, 79] Establish a continuum of care for stroke prevention and improve population health literacy on stroke prevention.
- Primary and secondary stroke prevention services should be covered by national health insurance/universal health coverage. Governments need to set a fixed proportion of annual health funding for stroke prevention activities. This funding could come from taxation on tobacco, salt, sugar, and alcohol.[25]

Key research gaps and future directions for improving stroke prevention:

- There is an urgent need to develop/update national guidelines for stroke prevention[29] and enhance the involvement of key stakeholders, including stroke organizations, in advocacy and policy development in stroke prevention.[5]

- Identification of the best balance of population-wide and risk-targeted stroke/CVD primary prevention strategies to maximize cost effectiveness and minimize inequalities.[25]
- Validation studies to determine the effectiveness of various types and combinations of the four primary stroke and vascular dementia prevention strategies recommended by the WSO (population-wide prevention; motivational mobile technologies; low dose combination of generic blood pressure and lipid-lowering therapies in one polypill for middle age and older adults having at least two behavioural or clinical stroke risk factors; and facilitation of the implementation of primary prevention strategies on the individual level by community health workers) in different populations.
- Identification of causes (including socio-economic factors) of ethnic/racial disparities in the risk of stroke occurrence (including various stroke pathological types and etiological sub-types) occurrence and recurrence and developing and testing culturally appropriate primary and secondary prevention strategies to mitigate these disparities. Improving the incentives for health staff in rural areas to encourage relocation and retention.
- High quality population-based epidemiological studies to determine and monitor the global, regional, national and sub-national changes in the burden, distribution (frequency, prevalence, population-attributable risk) and significance of stroke (including the various stroke pathological types and etiological sub-types) and dementia risk factors across different populations.
- Validation studies to determine the effectiveness of strategies to promote good health and wellbeing in children for an early start to healthy living and primary stroke prevention in adulthood.
- Evaluation of disparities in access to stroke prevention within and among countries and regions.
- Systematic evaluation and optimization of transportability of evidence-based risk prediction tools across various populations (race/ethnicity, etc) to reduce health inequalities.[117]

Practical examples of implementation of the suggested solutions:

- The validated (including cross-cultural validation) and free Stroke Riskometer app[94, 118-120] which is available in 19 languages in 78 countries, potentially covering 5.3 billion people, and the PreventS-MD webapp for clinicians for primary and secondary stroke prevention.[84, 100]
- Government funded evidence-based stroke secondary stroke prevention program in Austria.[93]
- Transferring/sharing tasks from highly trained health professionals to paramedical health-care workers was implemented in several areas of India for improving BP control and secondary stroke prevention.[79, 121, 122]
- A scalable public health hypertension control in India yielded substantial BP control improvements, especially in the primary care setting.[123]
- WSO stroke survey,[8] WHO health survey,[124] GBD Study.[125]

SECTION 5: ACUTE STROKE CARE 3883 words

Introduction

The organization of acute stroke care is a (cost-)effective way to decrease disability and mortality in stroke.[126] It includes the implementation of the following three major level 1A evidence-based strategies:[12] (1) Admission to a stroke unit, neuroimaging with CT scan within 24 hours, starting aspirin

in ischaemic stroke within 48 hours, swallowing assessment, early mobilization when medically stable, appropriate blood pressure and glucose management, prevention of deep venous thrombosis and aspiration pneumonia, early initiation of secondary prevention measures. Compared with the alternative service (e.g., general wards), organised inpatient (stroke unit) care was associated with improved outcomes at the end of scheduled follow-up (median one year): poor outcome (odds ratio (OR) 0.77, 95% confidence interval (CI) 0.69 to 0.87; moderate-quality evidence), death (OR 0.76, 95% CI 0.66 to 0.88; moderate-quality evidence), death or institutional care (OR 0.76, 95% CI 0.67 to 0.85; moderate-quality evidence), and death or dependency (OR 0.75, 95% CI 0.66 to 0.85; moderate-quality evidence).[126] (2) Implementation of reperfusion treatments for ischaemic stroke with either intravascular thrombolysis or mechanical thrombectomy (MT). The benefits of reperfusion therapy are highly time-dependent, and systems need to be well-coordinated to minimize time from symptom onset to treatment. Thrombolysis reduces disability in a third of patients increasing the absolute proportion of patients with minimal or no disability by 10% if treated within 4.5 hours of onset[127] and some benefit can be derived in selected patients up to 9 hours.[128] Thrombectomy increases functional independence by 19.5% and decreases mortality by 15% in strokes attributable to large vessel occlusion if treated within 6 hours of onset and some well-selected patients can benefit if treated as late as 24 hours, increasing independence by 36% with an additional 20% absolute reduction in death or severe disability.[129-132] (3) Organization of a regional acute stroke care network. The stroke unit, which is a specialized, geographically defined area dedicated to the management of stroke patients with an interdisciplinary stroke team,[113, 126, 133] is a highly effective tool in acute care assistance and rehabilitation to save lives and to improve outcomes. Despite over 30 years of evidence showing its benefit, several countries do not have any stroke units or the number of beds available in them are not enough to cover all stroke patients.[8, 126, 133, 134]

Implementation of intravascular thrombolysis requires trained doctors and nurses. Brain imaging by CT or MRI scan, availability of thrombolytic drugs and a monitored bed for the treatment are essential. intravascular thrombolysis was the first approved specific and efficacious treatment for ischaemic stroke. But it is still underutilized in many parts of the world.[8] It has been suggested that at least 12% of patients with ischaemic strokes should be treated with thrombolysis.[135, 136] Many pre-hospital and hospital related barriers that decrease utilization have been identified.[137] Additionally, thrombectomy implementation requires angiographic imaging by CT and DSA, neuro-interventionalists, anaesthetist, neurosurgeon and, in most cases, an intensive care unit bed. Despite its enormous treatment effect, thrombectomy is not implemented in several countries in the world.[8]

Stroke centre teams are best placed to take responsibility for organizing an effective regional stroke network, educating the population including young children and health professionals about stroke symptoms, training pre-hospital staff, and implementing pre-hospital pathways that are fundamental to faster access to the right hospital, as well as creating a coordinated pathway utilizing excellent communications to transfer the patient from a lower to a higher complexity hospital. The stroke centre specialists can also provide support to health managers to create a regional strategic plan for stroke. In this report we discuss the current situation of acute stroke care across the world, the gaps, recommended protocols, and the main strategies for effective implementation, including partnerships, creative solutions, and successful models.

Situational and gap analysis of stroke unit services

Definition: Acute stroke care is the care of patients within the first 24-72 hours following symptom onset. The implementation of coordinated acute stroke management through a multidisciplinary team plays an important role in influencing and improving patients' long-term outcomes. Fast evaluation and treatment in a stroke-ready hospital is the key for the success of the reperfusion therapy. *Components*: The main components of acute stroke care are acute reperfusion therapies (thrombolysis and thrombectomy) for appropriate patients with ischaemic stroke and, for all stroke – concurrent and immediate organized care by an interdisciplinary team in a stroke unit; secondary prevention of recurrent stroke; prevention and treatment of complications and, for those who can participate, rehabilitation. In our WSO - *The Lancet Neurology* commissioned study, the structure of stroke services was evaluated through the recommendations of the WSO Roadmap. The WSO provided a framework for implementation, monitoring and evaluation of stroke services.[113] Stroke services were divided into minimal, essential, and advanced based on a set of minimal resources required for hospitals to attain each category. If the hospital had some characteristics but did not meet all the minimum requirements, the hospital was classified in the lower category. Minimal services could be hospitals without doctors in poor areas, but the WSO suggested minimal low-cost protocols that could be implemented to improve the patient's outcomes. Essential stroke services should have an emergency service for stroke, CT scan, IV thrombolysis and doctors trained to assist acute stroke patients on site or through telemedicine. In the United States (US) these hospitals are called primary stroke centres. Most stroke centres across the globe are essential and they do not need a high level of technology. The Advanced centre should also include a physician/neurologist specialist in stroke, neurosurgical facilities, acute endovascular treatment, inpatient rehabilitation and ideally should be able to investigate and to treat any complex stroke cases. They are called comprehensive stroke centres in the US. Our WSO-Lancet Neurology Commission Survey[8] evaluated the structure of hospitals for stroke care according to the availability of resources, professionals and protocols implemented compared to all elements recommended in each category of the WSO Roadmap.

The effectiveness of the organized stroke care in low-resource settings was demonstrated in Conakry, Guinea, where a minimal stroke unit was set up, consisting of a dedicated area with three acute beds, heart rate, blood pressure and blood oxygen saturation monitoring equipment. Implementation of this simple stroke unit, without reperfusion therapy, was associated with lower mortality (7.2 versus 22.3%; $P < 0.0001$), fewer clinical complications (4.1 versus 27.7%; $P < 0.001$) and less pneumonia (3.3 versus 14.5%; $P < 0.001$).[138] On the other hand, an epidemiological population-based Brazilian study sponsored by the Ministry of Health showed that cities without any stroke centre had 90 day mortality rate of 49% compared with 18% in a city with full implementation of a stroke network.[139]

Current situation with acute stroke treatment

Despite the well-established benefit of acute interventions on post-stroke outcomes, their implementation has been very slow and mostly partial, especially in the most socio-economically disadvantaged countries[8] and also in Europe.[140] Reperfusion therapies will achieve better outcomes if bundled with care in an inter-disciplinary acute stroke unit or at least under the care of a mobile stroke team to ensure adequate swallowing assessment, early physiotherapy and mobilization, blood pressure and glucose management, and prevention of deep venous thrombosis in order to avoid post-acute stroke complications. In addition, all stroke patients benefit from acute stroke unit (ASU) while only a subset benefit from reperfusion therapy. Both acute interventions are important to reduce the stroke burden and go hand in hand.

Substantial efforts have been made to increase the number of acute stroke centres around the world and to certify them, implementing reperfusion treatment and stroke units.[132–135] This is particularly significant as the time window for effective reperfusion treatment is increasing. Our WSO-Lancet Neurology commissioned international survey of stroke services[8] provided data on 314 hospitals in 84 countries and showed that only 35% of hospitals had the minimum structure to be considered a stroke centre, with the organization of acute stroke care and intravenous (IV) thrombolysis implemented. Supplementary Table 7 shows the unmet needs in each country based on the survey and, when the survey had only 1 or 2 hospitals representing the country, the comments are based on the survey and the recent literature.[134, 141-143]

The availability of stroke units was 91% in hospitals evaluated in high-income countries (HICs) and 18% in low-income countries (LIC), with acute stroke treatments available in 60% of hospitals in HICs and upper-MIC and only 26% in LIC (P=0.009). Protocolized swallowing assessment and strategies to minimize aspiration pneumonia (e.g., appropriate diet and fluids or tube feeding) - a very simple no cost intervention that can reduce the morbidity of stroke - was available in only 34% of hospitals. Substantial inequalities were demonstrated, with the availability of recommended service features increasing with income, as measured by the World Bank's 2019 country income classification (p=0.029). Guidelines and protocols were more commonly implemented in upper-MICs (46%) and HICs (42%) compared to lower-MICs (27%) and LICs (11%), P=0.04. The lowest availability of stroke centres and the worst structure of centres (only 28.7% of the recommended structure by the WSO Roadmap) occurred in the African region.

A WHO report on the state of stroke services across the globe (194 Countries)[8] showed that globally, 72% of countries reported that services for acute stroke care were available (defined as reaching 50% or more of patients in need) and care for acute stroke was available in at least half of the countries in all regions. The European region performed best with acute stroke care available in all but three countries (94%). Acute stroke care was available in approximately two thirds or more countries in all other regions, except for the African Region. Disparities across income groups were marked, with around a third of LIC having acute service available, compared to around half of lower-MICs, and two thirds or more of upper-MICs, and HICs.

Europe was the region with the best structured hospitals for acute care (57%) in our survey (Supplementary Table 7).[8] However, the evaluation of the burden of stroke in Europe[134] showed that only about 30% of patients receive stroke unit care and the proportion of people treated in a stroke unit varies from 10% to 80% between countries.[134, 140] In addition, most hospitals do not have data to monitor stroke care, which makes it difficult to improve quality. It is essential to implement a minimum number of quality indicators to monitor stroke care, at least at the individual hospital, but ideally at a national level (see pragmatic solution section).[113] Stroke unit certification may be a helpful framework to encourage and monitor improvements to drive the quality of acute stroke care.

Another gap in acute stroke care is the implementation of effective reperfusion treatment even though alteplase/streptokinase is included in the WHO Model List of Essential Medicines (2021 Edition)[144] and devices for thrombectomy in the List of Priority devices (2021 Edition). In well-resourced and organized healthcare systems around 20% acute ischaemic stroke patients can be treated with thrombolysis. In LMICs less than 1% of patients with ischaemic stroke are treated with thrombolysis,[141, 145-147] and some countries do not have any hospital able to deliver thrombolysis.[148-150] The rates of hospital use of intravascular thrombolysis increase according to the country-level income

status. In our survey, 47% of hospitals have IV thrombolysis available to treat stroke patients, with more access in the HICs. If we compare with the Registry of Stroke Care Quality (RES-Q) data, an international stroke centres quality indicators registry in which participating hospitals are mostly stroke centres, all hospitals have a CT scan, many hospitals had thrombolysis available, but the rates of reperfusion treatment increased according to income level, demonstrating gaps in access to the best treatments and disparities among countries and inside the same country.[8]

Although mechanical thrombectomy is very cost effective, there is a big demand-supply mismatch in LMICs. A recent survey in India showed that the number of MTs done in India are only 1000 to 1500 per year but there is more than 270,000 mechanical thrombectomy needed per year.[151] This is mostly due to the cost of the treatment, very few trained interventionalists and angiography equipped centres and potentially a lack of awareness among the physicians.

A recent review of stroke care in Africa[148] showed a 3-year fatality rate greater than 80%. In 2015 a geospatial analytic study demonstrated that 71% of Africans took more than 2 hours to arrive at the hospital. Only ten countries have stroke units:[152] Morocco, Tunisia, Algeria, Egypt, Mauritania, Ghana, Nigeria, Guinea, Central African Republic, and South Africa. The availability of neuroimaging services (CT or MRI) is very limited in many African settings and the access to acute reperfusion therapies are limited but growing. These treatments are now available in Morocco, Tunisia, Algeria, Egypt, Central African Republic, and South Africa. Several countries do not have thrombolytic agents. A recent global survey on disparities in the cost of alteplase (tPA) and its impact on each country's health expenditure resources was conducted. Despite a significantly higher per capita GDP and health expenditure in HICs, alteplase costs account for 217% of purchasing-power-parity adjusted per capita health expenditure in LMICs compared to 18% in HICs ($p<0.0001$).[150]

In Latin American Countries significant improvement has occurred in acute stroke care organization over recent years.[141, 153] The number of stroke centres increased from 322 (2018) to 448 (2020), all of them providing thrombolysis, with an increase in the number of countries with dedicated stroke units. All countries deliver thrombectomy in some centres, but mostly restricted to a few private hospitals. Pre-hospital organization remains limited in several countries. The utilization of telemedicine has increased but is restricted to a few hospitals and is not widely available throughout each country. Regardless of the increasing number of stroke centres, in some countries the patient must pay for reperfusion therapies, at least in part. For example, in public hospitals, thrombolysis needs full payment by the patient in 8% of countries whereas in 23% of the countries half of the costs are paid by the patient. The situation is worse for mechanical thrombectomy. It is less available, and the payment is covered by the government in only 32% of public hospitals and 42% by healthcare insurance in the private hospitals. Non-reimbursement of reperfusion treatment limits access for many patients. Despite this situation, there is evidence that supports the feasibility of mechanical thrombectomy in Latin America with the same efficacy as in HICs, especially in the private practice setting.[154]

The reasons for governments not implementing evidence-based strategies for acute care in LMICs are several, including concerns about the efficacy of the treatment and complications in these settings, lack of knowledge about cost-effectiveness and insufficiently trained staff.[145] Good quality national research and service evaluation demonstrating improved outcomes from implementation of reperfusion therapies can help drive change.[155]

The findings of our survey reinforced the importance of a global ecosystem to improve stroke care in the world and ensure that recommendations are implemented. This global WSO Task Force on Stroke commissioners has a diverse membership with adequate representation from LMICs.

Thematic analysis of acute stroke care in high performing stroke services

Interviews with experts about acute stroke care from nine countries (Supplementary materials pp. 8-9, Supplementary Table 8) identified barriers and facilitators for acute stroke services. Major barriers identified fell into the following themes: awareness, investment, and strategy. Awareness describes the lack of understanding of stroke care that affected access and availability. There was agreement that low community awareness of stroke decreased access to evidence-based care. The lack of awareness among bureaucrats about stroke care resulted in low prioritization and funding of stroke services. The limited training and knowledge of health professionals, particularly 'generalists' that provided most care to most people, decreased access to the best care. Investment encompasses that all respondents agreed that funding for stroke care was inadequate. A lack of investment resulted in inequalities in access to care by geography or socioeconomic factors. It was almost universal that the best care was only available in major cities. The result was limited access to stroke units, thrombolysis and thrombectomy to people outside major cities or without means to pay out of pocket. Strategy refers to the fact that many regions lacked a national strategy or guidelines for stroke care. There were often no professional organizations for health professionals interested in stroke. This limited a national approach to training, data collection, accreditation, and advocacy on stroke.

The major facilitators for the delivery of high-quality acute stroke services fell into the following themes: training, innovation, and networks (Panel 5). Training describes that the provision of regular, structured training was vital for building a stroke care workforce. The best training services were interdisciplinary, captured general practitioners that provided the most care with a variety of funding sources. The increasing demand for thrombectomy was creating an urgent need for more interventionalists. Some countries addressed this by allowing multiple specialities to perform thrombectomy. In other countries, tight restrictions on who could perform this service meant that access was limited. Innovation means that a highly motivated and invested workforce was driving investment to improve stroke care. The best examples were formal, e.g., government-funded, and informal, e.g., What'sApp groups, telehealth networks providing connected, regionalized stroke care. Governments in some regions were investing in mobile stroke units to increase coverage of care. Innovations in data collection on stroke care were driving quality improvement activities with public recognition of high performing centres seen as important. Networks refers to the fact that well organized national bodies for stroke care with strong leadership increased access to high quality care for stroke. The most effect networks were connected to government, resulting in endorsed guidelines and funding. 'Living' guidelines provide the potential for harmonised, internationally recognized stroke care guidelines that could be locally adapted. We present models of acute stroke care in LMICs such as China, India, Brazil, Chile, Colombia, Uruguay, Egypt, and Ethiopia (Supplementary materials, pp. 15-18). Various successful global initiatives for acute stroke care (The Angel's Initiative, Mission Thrombectomy 2020+, Latin American Stroke Ministerial Meeting, Global Stroke Alliance, WSO Certification of Stroke Centres Program, free international Registry of Stroke Care Quality – RES-Q, Safe Implementations in Treatments in Stroke – SITS-QR, WSO Implementation Task Force, and various American Stroke Association programmes) are presented in Supplementary materials pp. 18-21.

Pragmatic Solutions

Key evidence-based recommendations for improving acute stroke care worldwide by pathological type of stroke are presented in Tables 10 and 11. The suggested quality indicators for acute stroke care are: (1) door-to-needle time (median and proportion of patients with door-to-needle time < 60 min with a target > 50%); (2) door-to-puncture time (median and proportion of patients with door-to-puncture < 120 min with a target > 50%, for Advanced Centres only); (3) proportion of patients eligible for reperfusion among total ischaemic stroke patients; (4) Proportion of thrombolysed patients among total number of ischaemic stroke patients arriving ≤ 4.5h of symptom onset (for Advanced Stroke Centres - a proportion patients final TICI 2b-3; time of puncture-to-recanalization); (5) proportion of symptomatic intracranial haemorrhage; (6) proportion of patients with swallowing assessment before feeding (all stroke patients); (7) Proportion of patients with suspected stroke who performed Neuroimaging (CT/MRI); (8) Proportion of patients discharged with prescription of antiplatelet agents in non-cardioembolic ischaemic stroke patients (target 100%); (9) proportion of patients discharged with prescription of oral anticoagulants in patients with AF (target 90%); (10) proportion of all stroke patients (ischaemic, haemorrhagic or TIA) attended in a stroke unit (target 90%); (11) proportion of patients with modified Rankin score (mRs) 0-2 at 3 months (or at least at discharge); (12) proportion of patients with ischaemic stroke/TIA with mRS 6 (death) at 3 months; and (13) proportion of patients with haemorrhagic stroke with mRS 6 (death) at 3 months.

Starting system-level planning and implementing minimum basic acute stroke care

Effective stroke care planning, on a national or regional level, and adequate resource allocation are key to improving stroke outcomes, thus facilitating a decrease of the burden of stroke. For the organization of acute stroke care and implementation of guidelines, it is fundamental to meet the minimum structural requirement and make CT imaging available to all stroke patients, to, as a minimum, distinguish between haemorrhagic and ischaemic stroke. In our survey only 57% of hospitals have CT imaging available. Even where no CT scanners can be made available, care improvement is still feasible. In 2014, the World Stroke Organization launched the global stroke services guidelines and action plan[103] creating the WSO Roadmap with recommendations to regions with low resources, without physicians and without CT imaging, suggesting general basic stroke care that can be implemented anywhere (including swallowing assessment, fever management, early mobilization, etc.). These strategies depend only on health professionals' training. Several international initiatives provide free virtual training for basic organization of stroke services and stroke unit protocols such as World Stroke Academy in English and Spanish,[156] Angels Initiative in several languages and Global Stroke Alliance in Portuguese and Spanish.

Accelerating Improvement of Acute Care Services

The action plan suggests centres gradually work to improve their status to achieve a superior category. Measurement is key to achieve improvement over time. To facilitate the evaluation of services, since 2021 the WSO Roadmap for quality of services is available online at no cost in English, Spanish and Portuguese, as a self-assessment tool. A centre can easily evaluate its status, and the proportion of elements implemented compared with the full list of recommendations. The tool clearly shows what needs to be implemented to improve the quality in the same stroke centre level and what they need to upgrade to a higher level. The tool can be used by the hospital, the stroke or neurological society and by the health managers to evaluate the regional or national situation.

Implementation of ASUs and reperfusion treatments

It is strategically important to encourage dialogue between stroke physicians, policy makers and government officers to create awareness and understanding of the importance and impact of implementing evidence-based strategies. A key step in stepping up a stroke unit is convincing the director and other health managers that it is (cost-) effective, citing the evidence and showcasing examples from other hospitals and/ or countries. It depends on the organization and team of professionals usually already available in the hospital, with some additional training and coordination of bed utilization for geographical co-location.

To implement IV thrombolysis and mechanical thrombectomy the drug and devices should be available at affordable cost. Despite these treatments being cost-effective, access to them in low resource settings are limited. Governments could discuss with companies to negotiate lower costs in LMICs. Over the years, the WSO has helped in the discussions with Ministries of Health worldwide. The use of intervention conceptual frameworks like the behaviour change wheel which is based on the COM-B behaviour system can aid countries and regions in the identification, design, and implementation of evidence-based complex interventions like this one.[15]

It is imperative that the regional stroke centres be fully equipped, including with the ability to deliver and teach mechanical thrombectomy. The training of providers in these techniques can follow the model of regional surgical training centres established in response to the 2015 *Lancet* Report on the provision of essential surgical care in LMICs.[157] In telemedicine, the lack of trained doctors for acute stroke care is an important gap in several countries in the world. Telemedicine can be used to increase the access to acute treatments in these areas.[158-163] Mobile telemedicine can be a lower cost alternative.[160]

PANEL 5: KEY SOLUTIONS FOR IMPROVING ACUTE STROKE CARE

Recognition of gaps: The organization of acute stroke care starts by recognizing the gaps in structure and care locally. As many countries have huge intra-country disparities, mainly in LIC and lower-MIC, the interventions should be tailored to each country region. Our situational analysis combined with the literature review, helped to identify these barriers that may hinder implementation of evidence-based recommendations. The online WSO Roadmap also can help to evaluate the structure of stroke services.

Discussion with local health authorities:

- The next step is to discuss these gaps and the recommendations with the directors of hospitals and local or national health authorities, supported by the local WSO-Lancet Neurology on Stroke commissioners and societies, to elaborate action plans. It is crucial to surmount the barriers of cost, availability, and affordability of reperfusion therapies, including access to mechanical thrombectomy.
- There is a significant variability in the cost (higher in LMICs) and availability of alteplase across countries. Efforts should be made to provide sufficient supply of alteplase across the globe and to reduce the cost of alteplase in resource limited settings.[141] Stroke care should be included in the Universal Health Coverage package in the WHO member countries. Expensive treatments like IV thrombolysis and mechanical thrombectomy should be made affordable; governments can negotiate with companies concerned to reduce these costs as occurred in Brazil.

- Initiatives such as the Latin American Stroke Ministerial Meeting and Global Stroke Alliance can be organized in all regions of the world to bring together health managers, including the Ministers of Health, to facilitate the discussions and action plans. Identification of recognized regional and national 'stroke champions' among the WSO Task Force on Stroke commissioners may help the discussion with the local health authorities and the implementation of the evidence-based recommendations.

Structuring of the services:

- The organization of acute stroke care includes well-trained emergency medical service workers for early recognition of stroke signs and rapid rescue and transfer of the patient to a stroke centre, rapid evaluation in the emergency department and the initiation of acute stroke treatments in a timely manner, admission to a stroke unit, management by a multidisciplinary team, and early initiation of the rehabilitation interventions.[113, 133, 164]
- More important than physical and technological infrastructure, it is essential to organize the pathways for stroke care with the role of each component of the stroke team very well defined, and train personnel to establish acute stroke protocols. The multidisciplinary team ideally should include at least a physician, nurse, nurse assistant, physiotherapist and speech therapist.[113]
- It is fundamental to increase the number of stroke units (at least 50 beds per 1 million inhabitants) with a multidisciplinary approach, and implementation of evidence-based acute treatments (thrombolysis as a first step and thrombectomy as the next step in comprehensive centres).[141] Furthermore, we recommend the creation of comprehensive centres providing all necessary treatment options, with at least one centre per 2 million inhabitants).[141]
- Initiatives such as the Angels Program and WSO Task Force can help in the first steps of the stroke centre organization. Health authorities need to create national plans for stroke with regional networks to increase access to care, include evidence-based stroke care in government-funded services, implement interoperable electronic medical records systems, and establish a national strategy for stroke care.

Telemedicine: There are global disparities in the availability of neurologists to assist acute stroke care. In several countries, other medical specialities (e.g., emergency, intensive care, and internal medicine physicians) have been trained to assist and treat stroke patients in acute care. In areas without trained professionals, telemedicine can safely and effectively increase the access to acute stroke care. Good examples of the success of telemedicine in LMICs exists in Ethiopia, India, Chile, and Brazil.

Education:

- The training of health professionals in stroke care is a fundamental tool for an effective implementation of the guidelines. There are large disparities in the availability of neurology training between HICs and LMICs.[165]
- Digital solutions-based training can be utilized to build capacity among physicians and nurses to deliver evidence-based stroke care especially in remote areas without access to trained professionals.
- Success models are the Chilean MOH program with free educational virtual stroke courses for health professionals, the World Stroke Academy, Angels Initiative and Global Stroke Alliance virtual platforms, providing quality training without cost for several countries.
- The mechanical thrombectomy trained neuro-interventionalists with workshops and hands-on training to improve the quality of the procedures and the patients' outcomes. The lack of speech

therapists is quite common in LMICs, and nurses or physiotherapists can be trained to perform the swallowing evaluation in the acute phase and during rehabilitation. A good example of a peer network to advocate and facilitate the global implementation of mechanical thrombectomy is the Mission Thrombectomy 2020+ (MT2020+) initiative in the USA.

Quality monitoring: To monitor the quality of acute stroke care, a nationwide registry and essential quality control instrument of all patients with stroke admitted to hospitals should be implemented with a minimum dataset such as the RES-Q, SITS-QR or other platforms. We recommend that hospitals publicly report stroke outcomes. There is some evidence of better outcomes among institutions which publicly report mortality for stroke and myocardial infarction.[166]

Certification: The certification of Stroke Centres with an external audit by a recognised in this area national or international agency can help to improve the quality of the care delivered and to ensure the implementation of the main recommended structure and personal in the stroke centres as occurred in Latin America and China.

Research: We recommend that leaders, researchers, professional societies, and health authorities organize and fund research in stroke, especially in LMICs. All these strategies should be discussed with health managers, including governments, creating national stroke policies, as occurred in Chile and Brazil.

Key research gaps and future directions for improving acute stroke care:

- Development and evaluation of optimal strategies to increase early recognition, early hospital admission, and access to appropriate care of acute stroke in LMICs (including reperfusion therapies).
- Evaluation of the strategies of triage of stroke patients in the pre-hospital setting and determine the best strategies to distribute these patients to appropriate stroke centres in different healthcare systems (high probability of large vessel occlusion to primary stroke centre versus direct to comprehensive stroke centre).
- Evaluation of the best approach to management of hypertension in hyperacute (prehospital) and acute stroke patients in low resource settings.
- Determination of the subtypes of acute haemorrhagic stroke which do better with surgery than conservative care and evaluation of the best surgical approach in these subtypes.
- Development and evaluation of putative neuroprotective drugs for improving stroke outcomes.
- Deeper understanding of stroke and its molecular risk factors to unravel new molecular targets for novel diagnostic and prognostic tools as well as new treatments and preventive drugs especially for intracerebral haemorrhage.
- Development and evaluation of novel definitive therapies for haemorrhagic stroke.
- Development and evaluation of treatments for dysphagia.
- Evaluation of telemedicine for potentially increasing access to specialized stroke treatment in LMICs.
- Determine the capacity required of health services and workforce to manage stroke.
- Evaluation of disparities in access to stroke care and prevention within and among countries and regions.
- Discovery of neuroprotective drugs for acute stroke treatment.

SECTION 6: STROKE REHABILITATION 2829 words

Introduction

The burden of stroke constitutes a huge public health issue as it remains the third leading cause of disability.[1, 125, 167] Any genuine effort to reduce the global burden of stroke must utilize solutions which are implementable globally to address stroke-related limitations in functioning . In this part of the Commission report, we proffer pragmatic solutions to maximize implementation of, and the global impact of, evidence-based recommendations for rehabilitation of stroke survivors based on a situational analysis.

Situational and gap analysis

Purpose and principles of stroke rehabilitation

Over two-thirds of stroke survivors experience impairments leading to limitations in activities of daily living and participation restriction.[1] These include motor, sensory, visual, swallowing, language, cognitive and psychological impairments.[168] Rehabilitation adds years to life, life to years and meaning to life. Rehabilitation maintains and improves function, participation in domestic, social and work life, and health-related quality of life and mental health, and enables the achievement of a meaningful, fulfilled and prolonged life.[169, 170] However, the extent of functional recovery after stroke is variable and depends on a number of factors, including condition prior to stroke, age, the location and size of the stroke lesion, comorbidities, and the quality and quantity of rehabilitation care received after stroke.[171]

Neural repair and regeneration with the regrowth of neurons and associated circuitry, is the ideal target for recovery but the most challenging, though recent research with stem cells and growth factors provides a pathway.[169] Thus, neuroplasticity – the structural and functional changes in neural networks adjacent to the stroke lesion in response to external stimuli – is another promising target.[169] This is mainly driven by function- or task-specific and goal-directed training that is repetitive and challenging enough to maintain attention and to promote body functions and capacities beyond the perceived limits.[171] With neuroplasticity, deficits in motor and other functioning domains are reduced, and people may recover partially or fully. Moreover, rehabilitation also involves adaptative and compensatory interventions utilizing alternate behavioral strategies (coping mechanisms) and assistive products to enable specific tasks, functions and roles for stroke survivors with the aim of maximizing improvement and quality of life.[172]

Review of the current state of stroke rehabilitation

Significant gaps exist in the quality and quantity of rehabilitation services for stroke across countries of all income strata including deficiencies in the education of rehabilitation workers, patients and caregivers; inadequate use of evidence-based protocols for stroke rehabilitation, and the non-availability and quality of stroke rehabilitation services across multiple settings– in outpatient, in-patient, and community settings (Supplementary materials pp. 22-23, Supplementary Table 9).[173-175] Reports from a recent survey,[8] the World Health Organization NCD Survey,[176] and the RES-Q data[177, 178] showed that most countries had less than half of the American Heart Association recommended stroke rehabilitation services. Compared to other stroke pillars (surveillance, prevention and acute care), rehabilitation was the least available in every region in LMICs.[8] Recent studies showed LMICs had significantly lower rehabilitation services compared to HICs – in-patient rehabilitation, home

assessment, community rehabilitation, education, early hospital discharge program, rehabilitation protocol –compared to HICs.[8] The 2017 WHO Atlas for neurological disorders demonstrated that of the 105 countries responding to the survey, only 16% had specialized neurorehabilitation services and only 17% report general rehabilitation services offering neurological rehabilitation. This reduces productivity in LMICs, especially in Africa and India where stroke occurs at a younger age, thus affecting the workforce.[179] However there seems to be an increasing availability of rehabilitation services with increasing income strata.[8, 180]

An effective rehabilitation service must include the required interdisciplinary/transdisciplinary components, a lack of which markedly affects community reintegration of stroke survivors. Physiotherapy services appear to be the only available component especially in LMICs where occupational therapy, psychotherapy, speech and language therapy, nutritional therapy and social work are less available.[175, 181, 182] This alongside low-dose and intensity of services may explain differential recovery patterns for stroke survivors in LMICs compared to HICs.[183] The provision of simple interventions including education of patients on their management plan and self-management occurred in less than 25% of countries in all income categories.[8]

There is also a lack of multidisciplinary rehabilitation for stroke survivors which is associated with high rates of depression, poor quality of life and low rates of return to work.[180] Older adults, females, patients with impaired consciousness at admission and/or prior history of stroke, and patients not referred and counselled on the need for rehabilitation are less likely to undergo rehabilitation.[184, 185] A solution remains tapping into telemedicine. Despite the positive reception to telerehabilitation, there are challenges with equipment setup, limited scope of exercises,[163, 186] difficulties with patient assessment, interface problems, and time limitation in daily care.[187] Further investigations on cost, benefits, feasibility, and efficacy in different regions are needed.

Meanwhile, the lack of an efficient service structure and related protocols in LMICs and some HICs has led to prolonged wait times for rehabilitation needs assessment and intervention, hospital discharge without an on-going rehabilitation plan in place – a major requirement in early supported discharge schemes, inadequate long-term support, inadequate screening and care for depression, and lack of psychological and social support.[182, 188]

Thematic analysis of stroke rehabilitation

Interviews with experts from nine countries identified major barriers and facilitators to the delivery of high-quality stroke rehabilitation (Supplementary Table 10). The major barriers identified for the delivery of high-quality stroke rehabilitation services fell into the following themes: complexity, scope, and awareness.

Complexity encompasses that the inter-disciplinary (rehabilitation physicians, physiotherapists, speech and language therapists, psychologists, prosthetists and orthotists, occupational therapists, nutritionists and nurses) and inter-setting (acute care, outpatient care, community, home, public and private providers) nature of rehabilitation created issues for prioritizing and delivering funding, governance of workforce and services, data capture and reporting, and quality improvement and care coordination. Scope describes that most stroke rehabilitation is focused on a limited range of services, for a limited amount of time, in a limited number of settings. It was common that only physiotherapy

was available, with very limited access to other specialities, e.g., speech pathology, occupational therapy, or neuropsychology. Government-funded services were mostly restricted to those provided with acute care, not through community, home, or tele-based services. The broadest scope of services was only available to those in large cities that had the means to pay. Awareness describes that there is low awareness of the role of rehabilitation after stroke in enhancing recovery across a broad range of stakeholders (e.g., community, health professionals, policy makers). This resulted in low political will to fund services and limited advocacy stakeholders to increase access or scope of services. There was evidence of recent shifts in awareness, particularly among health professionals, linked to the growing evidence-base and professionalization of the allied health workforce.

The major facilitators for the delivery of high-quality stroke rehabilitation services fell into the following themes: evidence-based care, universal healthcare and capacity building.

The evidence-based care theme describes the role of guidelines, frameworks, or protocols for stroke rehabilitation. The development and implementation of these documents assisted with service planning and ensured quality of care. There were numerous examples of how data collection aligned with frameworks assisted in planning and evaluation. Many expressed regret that data were not used nationally to plan services or that data were restricted to counting cases of stroke in hospital settings only. Universal healthcare was a major theme providing a safety net of at least some care to most people after stroke. While most agreed that government-funded services were not perfect, there was strong agreement that allied health professionals were doing the best they could with their current resources. The importance of the private sector for providing stroke rehabilitation cannot be understated. These user pays services provided access to a wider range of services (e.g., speech pathology, occupation therapy and psychology) for a longer time in the community. Capacity building facilitated stroke rehabilitation through training (undergraduate and post-graduate) and registration of allied health professionals. There was limited capacity for allied health training outside nursing and physiotherapy in many LMICs. In several regions stroke rehabilitation leadership fell to a small number of individuals. In this context, mentoring and communities of practice contributed to capacity building. There were several examples of online, internationally led mentoring programs for people in LMICs that were seen as important to prevent the 'brain drain' that occurs when leaders leave for training.

Special Interest Group Clinical Pathways of the international survey

The World Federation for Neurorehabilitation (WFNR) issued over 150 specific evidence-based stroke rehabilitation practice recommendations in 2021, developed by 14 multi-professional international author groups.[186] From June to August 2022 the Special Interest Group Clinical Pathways of the WFNR organized an international survey asking healthcare professionals (clinicians) involved in neurorehabilitation to indicate to what degree these practice recommendations can be implemented in their region (not necessarily in their institution or by themselves), and, if they could not be implemented as indicated to provide information about the reasons why (Supplementary Tables 11 and 12). The lack of fundamental aspects of the team approach for stroke rehabilitation in 20 to 40% of healthcare settings globally raises concerns and points to a need to address such service deficiencies with a worldwide perspective. In addition, the disparities between HICs and LMICs help to focus on deficiencies at a regional level. This applies both to the establishment of interdisciplinary teams with specific training and experience in the field and the continuation of stroke rehabilitation after discharge in LMICs. Accordingly, there is a substantial need for capacity building in LMICs. And there

is the question of clinicians' knowledge and skills for a multidisciplinary team approach in the community in HICs that needs to be addressed. See Supplementary materials for further details

Gaps in stroke rehabilitation evidence-base

There is a relative paucity of deployment of evidence guidelines, especially in LMICs (Supplementary Table 12). Some LMICs guidelines recommend treatments that do not appear in the HIC guidelines and for which there is little evidence of effect (e.g., cryotherapy, range of motion exercise for paresis, and magnetotherapy for spasticity). Also, some LMIC guidelines include recommendations that might be taken for granted in HICs (e.g., to train nursing staff in early stroke rehabilitation).[189]

Equally apparent are gaps of evidence when practice recommendations that are considered important by expert opinions and international evaluation panels are not supported by evidence of at least low quality (according to GRADE).[189] Such examples are: complex interdisciplinary rehabilitation to be provided for patients with prolonged disorders of consciousness (DOCs) post-stroke, and the optimal approach to speech and language therapy for aphasia.[190] Evidence on how best to treat post-stroke neuro-visual disorders including unilateral spatial neglect is of low quality, except for prism adaptation[191] and is hardly sufficient to guide clinical decision making even though these stroke sequelae are frequent and affect activities and recovery substantially. Similarly, there are gaps in the evidence-base to support specific interventions for post-stroke cognitive, emotional, and behavioural disorders, and fatigue. These areas have a very high impact on daily life and participation and yet there is little evidence to support clinical practice.

Such evidence gaps highlight an urgent need to engage in comprehensive collaborative stroke-rehabilitation related research from bench to bedside, ideally in a global effort. Brain recovery research (basic science) needs to take a lead and help generate therapeutic concepts that can be tested with translational research. When supportive, these further lead to high-quality pivotal clinical trials and consequently systematic reviews and meta-analyses to guide clinical decision making.[192]

Evidence-based, innovative and pragmatic solutions

Pragmatic solutions to accelerate stroke rehabilitation worldwide are derived and are to be implemented through the following process and principles (Panel 6). *Theory-driven synergistic actions* based on the implementation wheel adapted to harness all resources for concerted application of the pragmatic solutions from this Commission. The proposed solutions are aligned with WHO and UN NCD SDG, Brain Health, WHO IGAP initiatives and Rehabilitation 2030 Targets and are based on: (a) evidence-based practice recommendations derived from a synthesis of evidence-based guidelines and/or best evidence based on systematic evidence-to-decision methodology including GRADE levels of evidence and strengths of recommendations. Only high quality, high impact, consistent, implementable, low-cost recommendations are selected for the continuum of care. (b) Randomized Control Trials with newer evidence covering gaps in existing guidelines. (c) Prioritization of recommendations to ensure focus on key recommendations with the potential to benefit the largest population of stroke survivors and translatability. (d) Contextualization of intervention using the political, legal, ethical, anthropological, and socioeconomic framework. *Development of a sustainable multisectoral interdisciplinary implementation ecosystem* at international, regional, national, and subnational levels (macro, meso and micro levels) which informs, inspires, collaborates with, and empowers (ICE) all stakeholders to act towards achieving the targets. Use of an integrated stroke services approach (Figure 2) addressing the continuum of surveillance, prevention, acute care, and

rehabilitation across the life-course. *Use of the principle of the iterative implementation cycle* to navigate barriers and enhance facilitators to deliver impact through effective communication with and participation of all stakeholders. (Figure 3).

Recommendations on specific interventions are derived from the leading evidence-based stroke rehabilitation guidelines globally, which require adaptation to the local setting. Political, legal, ethical, anthropological, and socioeconomic implications of the recommendations, and anticipated and observed barriers and facilitators for implementation are highlighted (Table 12 and Supplementary Tables 13).[191] In addition, the forthcoming WHO Package of Interventions for Rehabilitation for Stroke provides an overview on interventions for rehabilitation relevant to people with stroke. To implement these key recommendations, there is a great need to establish interdisciplinary rehabilitation facilities and training programs in tertiary institutions, especially in LMICs, for delivery by all categories of rehabilitation professionals worldwide. This is important in the face of the broad accumulating evidence for stroke rehabilitation and hence the necessary knowledge management implied.[192]

In the interim, enhancing self-efficacy, implementation of the forthcoming WHO Basic Rehabilitation Package[193] and supervised task-sharing with available personnel and *capable supported* family members *may* bridge the gap and help to deliver the required frequency and intensity of impairment- and task-oriented practice to facilitate neuroplasticity and recovery.[6, 194-196] However, the results of the ATTEND trial raise some doubts on the limitations.[197] Future research should perhaps also investigate caregiver-mediated interventions combined with e-health and telerehabilitation services to augment training and allow adequate feedback.[198]

Indeed, (tele)rehabilitation can be offered in various settings including intensive care, in-patient care, outpatient care, community-based and family-based care.[199-202] Therefore, the gap in education on patient management and self-management could be targeted across all countries to improve management of stroke patients by developing educational tools (including videos and apps) that can be disseminated globally. The results of the recent trial prove that video conferencing systems to connect specialists in urban areas to healthcare specialists in the rural areas is feasible in LMICs.[203]

Financing solutions including local manufacturing, health insurance systems and subsidies can improve access to these materials. Meanwhile, better organization and optimization of available resources through care protocols is essential[9] globally including them in some HICs which lack standardized follow-up care.[204] Most of the existing guidelines emanate from HICs. In the absence of alternatives, there is a need to adapt and implement them in LMIC settings until local evidence emerges. A major facilitator to overcome this barrier for implementation in LMICs is the regional adaptation of practice recommendations by making use of the evidence,[205] but actively transforming recommendations regionally into clinical pathways that reflect the local healthcare priorities, settings and capacities.[206] The 'Key Recommendations to improve Stroke Rehabilitation services worldwide' presented in the Tables 12 and 13 and supplementary Table 13 provide the means to do so.

A novel approach is the concept of 'living guidelines' whereby experts from across the world participate in the process of developing internationally agreed evidence-based guidelines that could be adapted in the local context across the globe. This could save a lot of time and resources if each country was not spending time reviewing evidence and developing their guidelines from scratch. For example, a 'living' stroke online guideline model with a dynamically updating summary of stroke evidence to guide clinical practice and policy development was recently adapted in Australia. The

success of such a concept is dependent on strong leadership and coordination, and would need to be adequately financed.

The development of genuine international evidence-based stroke rehabilitation guidelines that focus on therapeutic approaches rather than on organizational issues, could also be useful to structure regional or local stroke rehabilitation pathways directly and to develop their resources in a way that will eventually achieve effective stroke rehabilitation.[206] Such international practice recommendations for stroke rehabilitation were developed by the WFNR.[206, 207]

Given the increasing number of stroke survivors and already limited health resources for ongoing community rehabilitation, availability of effective and accessible self-management programmes/tools for stroke survivors and their caregivers is important. There is evidence that self-management programmes/tools are feasible to use and can improve survivors' self-efficacy, outcome expectations, and satisfaction with performance of self-management behaviours.[208, 209] A good example of instructional and educational tools is the WSO, World Federation for Neurorehabilitation endorsed videos on stroke self-management.[209]

The proposed recommendations presented in Supplementary Table 13 and summarized in Tables 12 and 13 can be considered as a complementary reference source that help to identify key processes (interventions) to be considered and implemented for stroke rehabilitation. These evidence-based practice recommendations are – while not limited to specific healthcare contexts while being developed – equally meant to be implemented via regionally contextualized clinical pathways. The WFNR explicitly focuses on this dual process of both the (contextual-independent) identification of evidence-based practice recommendations for interventions in stroke rehabilitation as one (globally valid) step, and their embedding in contextualized regional pathways that take regional priorities, resources, and organizational backgrounds (including healthcare structures) into account.[207] They nevertheless serve as a starting point to generate beneficial and cost-effective stroke rehabilitation structures (including healthcare services). The attribution of selected interventions to healthcare professions and the organization of implementing interventions does not follow a tight link that would conceptually be set forth but is a matter of such regional contextualization.

Key research gaps and future directions for stroke rehabilitation

Future research in stroke rehabilitation should investigate the post-stroke life-course of stroke survivors, determinants of functional dependence in different countries and populations, the equivalency or non-inferiority of supervised task-sharing with available personnel and capable supporting family members in overcoming the shortage of professionals in LMICs (as compared to traditional care model), community-delivered versus facility-based rehabilitation models, regenerative strategies, including low-cost and accessible robotics neuromodulation tools and brain-computer interfaces. We also need validation studies to determine the effectiveness of rehabilitation-based educational tools including telerehabilitation, training videos, and mobile health (including role of delivering care in COVID 19 and similar pandemics). Validation and implementation studies are required to determine the feasibility, effectiveness, and coverage of home-based rehabilitation (including self-management), community-based rehabilitation, and informal rehabilitation services as well as validation studies for locally manufactured rehabilitation and assistive devices with health economic analysis on cost benefit, cost utility, and cost effectiveness. Evaluation and improvement of the capacity of health services and workforce for stroke rehabilitation in terms of education, skill

acquisition, and availability of required tools as well as implementation research of tailored rehabilitation protocols for LICs and LMICs are also needed.

PANEL 6: KEY MESSAGES FOR STROKE REHABILITATION

Key pragmatic solutions for stroke rehabilitation

- To ensure an efficient service delivery and reduction of complications (including cognitive impairment, depression, etc.), multidisciplinary setting for multidimensional assessment and intervention should be the focus, as well as enhancing self-efficacy and supervised task-sharing combining available personnel and the support of capable family members to bridge the gap and optimize the quality of life and meaningful life after stroke.
- Where inadequate, there is an urgent need to invest in the training of a broad range of therapists and other stroke rehabilitation professionals, research to generate innovative low-cost assessments and interventions, education and cross-learning from peers, advocacy to mobilize resources and financial solutions and multidisciplinary therapy especially in LMICs.
- Development of core assessment measures and minimum standardized rehabilitation requirements which should include skin assessment, swallowing assessment, deep venous thrombosis prophylaxis and infection (pneumonia or urinary tract infection) control.
- Using conceptually broad assessment tools such as the modified Rankin Scale and the NIH Stroke Scale, much information about the type and severity of both disability and impairment could be documented with international standards without having to have each aspect to be covered by a separate assessment. The latter would still be suggested for clinically -specific assessments in specialised services having the training and resources for their implementation.
- Dissemination of rehabilitation multidimensional assessments, solutions, training videos (including self-management), and advocacy targeting all stakeholders involved in stroke care should be implemented in all regions. The spread and reach of information technology options available including smartphones and online videos across the globe provides channels that could be harnessed.
- While the ultimate goal would be equity in the array of stroke rehabilitation services available worldwide, there is an urgent need to actively adapt evidence-based effective pragmatic recommendations at the regional and national level into clinical pathways that reflect the local healthcare priorities, settings and capacities.
- Contextualization and implementation of pragmatic solutions across the globe through WSO Task Force on Stroke commissioners and ecosystem will develop, implement, and monitor strategic action plans with all stakeholders to ensure availability of stroke rehabilitation services to all eligible stroke patients in their countries and regions. They will also advocate for the training of rehabilitation personnel who can offer domiciliary services.

Key Research Gaps and Future Directions for Rehabilitation

- Multidimensional characterization of the post-stroke life-course profile of stroke survivors
- The prevalence and management of risk factors for functional dependence and mortality at a population level
- Determination of the capacity and needs of the health services and workforce for stroke rehabilitation in terms of education, skill/competencies, and availability of required tools/equipment e.g., utilizing the WHO Rehabilitation Competency Framework

- Development of agreed rehabilitation service performance indicators to monitor rehabilitation quality
- Assessment and monitoring of country coverage and outcomes of stroke rehabilitation with routine data collection from facilities, e.g., utilizing the WHO Routine Health Information Systems – Rehabilitation toolkit
- Validation studies to determine the effectiveness of educational tools for stroke rehabilitation including telerehabilitation, training videos (including self-management tools/programmes), and mobile health (including the role for delivering remote care as in COVID 19 and similar situations)
- Validation and implementation studies to determine the feasibility, effectiveness, and coverage of home-based rehabilitation (including self-management), community-based rehabilitation, and informal rehabilitation services
- Determination of the equivalency or non-inferiority of supervised task-sharing with available paramedical healthcare personnel and capable supporting family members in overcoming the shortage of rehabilitation professionals in LMICs (as compared to the traditional care model)
- Studies further investigating the cost benefit, cost utility, and cost effectiveness of locally manufacturing assistive devices
- Investigation of regenerative medicine, novel medications to modify neuroplasticity, low-cost and accessible robotics, neuromodulation tools, and brain-computer interface approaches which currently have limited evidence of effectiveness
- Determination of novel biomarkers for prognostication and quantification of neural repair and recovery and recovery
- Implementation research of tailored rehabilitation protocols for LICs and LMICs
- Investigation of the effectiveness of peer support across various settings
- Research into the effectiveness of community-based services for inter-disciplinary care
- Determination of the effective therapies for post-stroke fatigue
- Investigation of the use of digital solutions for post-stroke rehabilitation and supporting transitions, medication compliance, and discharge education
- Clinical trials for rehabilitation of stroke survivors with aphasia[210]
- Determination of the optimal dosage of therapy for physiotherapy, swallow therapy, speech and language therapy, psychotherapy, etc.
- Investigation of the role of psycho-spiritual therapy for post-stroke rehabilitation.

CONCLUSIONS 2742 words

Despite available evidence-based interventions, there are huge within- and between-country gaps in the delivery of stroke surveillance, prevention, and care across the globe, especially in LMICs. Effective planning of stroke surveillance, prevention and care services, workforce training and capacity building, monitoring of stroke burden and services quality indicators nationally, and certification of acute stroke services are major steps to control stroke global disease burden. To maximize the impact of the limited resources available, it is critical to develop and deploy cost-effective evidence-based pragmatic solutions by active engagement of all stakeholders including policy makers, and local communities. Region-specific adaptations of guidelines and their incorporation into clinical practice to guide national prevention and stroke care is essential to bridge the gaps in stroke care between high-income countries and low-income and middle-income countries. Population-wide deployment of stroke risk

factor detection and control through task sharing and digital tools is essential to reduce the incidence of stroke across the life course. Establishment of stroke units, stroke centres and rehabilitation services should be prioritized worldwide particularly in resource-limited settings. Promoting universal health coverage will enable wider usage of thrombolysis and mechanical thrombectomy. Simple interventions focusing on managing fever, swallow assessment and blood sugar control are low-cost strategies which improve stroke outcome.

Implementation ecosystem

The WSO Task Force on Stroke and proposed ecosystem (Figures 2 and 3) has the potential to play a pivotal role in supporting implementation of recommended cost-effective strategies to reduce stroke burden across the globe. The WSO Task Force on Stroke will provide independent management of the project, implementation of the Commission's recommendations (via commissioners and proposed ecosystem) and disseminations of the project findings (Figure 2). This will also involve **T**raining of personnel and providers, **R**esearch to generate innovative low-cost interventions, **E**nlightenment and empowerment of both patients and healthcare providers along the life course, **A**dvocacy to mobilize resources and financial solutions and multidisciplinary **T**herapy (TREAT). This approach will bring about transfer of knowledge from peers in the same income strata with better stroke care and rehabilitation services. Global ranking of countries for stroke surveillance, prevention, acute care, and rehabilitation services, bi-annually, will stimulate healthy competition and improvement. Efforts to mobilize financial solutions through the international stakeholders and implementation partners in the ecosystem are crucial. This is because stroke, a leading cause of disability, is also a leading cause of catastrophic spending especially in LMICs. Most LMICs rely on out-of-pocket payment for healthcare which is grossly deficient and inadequate for the life-long care required for functional recovery and secondary prevention, and most often plunges patients' families into catastrophic financial straits.[170,171]

Synergy with existing international initiatives

The world is experiencing a neurologic revolution.[211] The new WHO Intersectoral Global Action Plan (IGAP) on Epilepsy and other Neurological Disorders 2022-2031 was adopted by the 75th World Health Assembly in May 2022. It will coordinate efforts to achieve an ambitious agenda for neurological conditions such as stroke. Global targets have been set by the action plan to improve access to care and treatment, recovery, well-being, and participation of people living with neurological disorders, while simultaneously reducing mortality, morbidity, and disability. The action plan focuses on increasing access to assistive technology and products for those who need them across all levels of health services with a focus on primary care and within Universal Health Coverage (UHC). The training and education of an interdisciplinary workforce, including rehabilitation specialists trained in neurological conditions, is also a strong emphasis of the action plan.

This plan represents an integrated approach to neurology and neurological conditions throughout the life-course and envisions a world in which "brain health is valued, promoted, and protected across the life course; neurological disorders are prevented, diagnosed and treated; premature mortality and morbidity are avoided, and people affected by neurological disorders and their carers attain the highest possible level of health, with equal rights, opportunities, respect and autonomy".[34, 211-215] It also articulates strategic objectives and specific targets, indicators signifying the achievement of these targets, and the means of verification of each indicator. In a wider context, brain health and overall health depend on the sustainability of interconnectedness of all life – humans, nonhumans, and the

earth through inventing and implementing equitable economic systems and solutions across various sectors of life and environment.[216, 217] This marks a turning point for neurological disorders, brain health, animal and environmental health at their cores. The advent of the neurologic revolution,[211] leveraging the WHO IGAP, WHO Rehabilitation 2030,[34, 218] WHO NCD,[219] United Nations Joint Action Plan on One Health,[220-222] and brain health initiatives[223] is propelling neurology to the forefront of the global health and development agenda by harmonizing global neurology activities and advocacy efforts into a united, powerful force. Stroke is not only the leading cause of neurological deaths and disabilities globally, but also a leading cause of death from NCDs.

Due to the chronic nature of many neurological disorders, the importance of involving caregivers in the rehabilitative process following neurological injury such as that sustained in stroke is paramount. Challenges for carers include stress and emotional strain, financial burden and social isolation. Roles and challenges may vary depending on the age of the carer and are also different when caring for children, adolescents, or older adults. Carers who are actively involved in the rehabilitative process are a vital member of the rehabilitative team.

Overall, NCDs cause 74% of all deaths globally. But if every country were to adopt the interventions that are known to work, at least 39 million NCD deaths could be averted by 2030, and countless other lives would be longer, healthier, and happier. The drivers of the NCD deaths are social, environmental, commercial, political, and genetic, and their presence is global. Every year, 17 million people under the age of 70 die of NCDs, and 86% of them live in LMICs. Many of these early deaths are preventable. Addressing major risk factors that can lead to them – hypertension, diabetes, dyslipidaemia, tobacco use, unhealthy diet, harmful use of alcohol, physical inactivity, and air pollution – could simultaneously prevent and delay significant ill health and a large number of deaths from stroke and other NCDs. Improving access to prevention, treatment, and care particularly in LMICs could prevent or delay NCDs and their consequences.

Every member State of the United Nations has committed to the Sustainable Development Goals (SDGs), which include a target to reduce premature death from NCDs by a third by 2030. This could save millions of lives, but few countries are on track to achieve the target. Relatively small additional investments in NCD prevention and treatment could make a big difference long before 2030: spending an additional US$ 18 billion per year across all LMICs could generate net economic benefits of US$ 2.7 trillion over the next seven years. This is an investment, not simply a cost, with the benefits of action going far beyond health. The right policies for NCD prevention and treatment will have significant wins for other sustainable development concerns. Poverty and inequity can be reduced through the introduction of universal health coverage that avoids the need for catastrophic expenditure on treatment for those with an existing NCD. Food systems will be healthier for people and the planet.

However, for those who still develop stroke, the WHO Rehabilitation 2030 initiative draws attention to the profound unmet need for rehabilitation worldwide and highlights the importance of strengthening health systems to provide rehabilitation. Rehabilitation 2030 is mobilizing stakeholders to accelerate and support efforts to strengthen rehabilitation services in countries, highlighting the importance of strengthening the health system to provide rehabilitation at all levels of healthcare. Acknowledging the need to support governments efforts, the WHO has developed resources that support rehabilitation policy and planning, financing, workforce strengthening and integration of rehabilitation into health information systems, with other products planned. Rehabilitation 2030, launched in 2017, marks a new strategic approach for the global rehabilitation community by

emphasizing that: 1) Rehabilitation care should be available for the whole population and through all stages of the life course; 2) Efforts to strengthen rehabilitation should be directed towards supporting the health system as a whole and integrating rehabilitation into all levels of healthcare; 3) Rehabilitation is an essential health service and crucial for achieving universal health coverage. The call for action articulates ten strategic steps for improving access to and impact of rehabilitation care for people living with stroke and other conditions across the globe.[34, 218]

Overall, partnering with global and regional professional organizations and the WHO as well as government policy makers is essential in the dissemination and implementation of evidence-based interventions for stroke. Wider implementation of stroke quality programs which are ongoing will further scale up the expansion of stroke centres. Strong WSO Task Force on Stroke advocacy in conjunction with global and WHO organizations e.g., WHO Rehabilitation 2030 and Global Rehabilitation Alliance can help improve the situation by enhancing availability and affordability of personnel and relevant interventions, equipment, and assistive devices. Local production of appropriate assistive devices in LMICs may reduce the cost, create jobs, and improve affordability. Supplementary Tables 1-14 along with 13 Tables, 8 Figures and 6 Panels in the manuscript summarize the targets and estimated unmet needs for ensuring availability of stroke surveillance, prevention, acute care and multidisciplinary neuro-rehabilitation facilities and personnel in all countries by the year 2030, thereby making services accessible to all stroke patients worldwide. These estimates can be further improved in the future if we are able to determine the number and size of facilities required per 100,000 population and per 100 stroke survivors.

Establishment of global, regional and national plans

As stated in the Prevention and Acute Care sections of this manuscript, the WSO Task Force on Stroke will work with implementation partners including non-governmental organizations, national and regional stroke societies (where such societies do not exist, the WSO Task Force on Stroke will help establishing them) to co-create, co-implement and monitor application of pragmatic solutions to reduce the global burden of stroke. Global, regional, and national key performance indicators and targets will be co-created in conjunction with all policy makers within the WSO Task Force on Stroke ecosystem to improve stroke surveillance, prevention, acute care, and rehabilitation services. Implementation partners include the WHO (leveraging the WHO Rehabilitation 2030, WHO IGAP, and WHO NCD and WHO Brain Health Initiatives). Other implementation partners include but are not limited to NCD Alliance, Global Coalition for Circulatory Health, World Federation of Neurology, World Heart Federation, OneNeurology, Angels Initiative, Resolve to Save Lives (RTSL), and MT 2020. Regional and national Stroke Societies are crucial drivers in the ecosystem for domestication across world regions, e.g., European Stroke Organization (ESO) incorporating the Stroke Action Plan Europe (SAP-E), in cooperation with the Stroke Alliance for Europe (SAFE), African Stroke Organization (ASO), Middle East and North Africa Stroke Organization (MENASO), Asia Pacific Stroke Organization (APSO), Stroke Society of Australasia (SSA), Indian Stroke Association, International Stroke Recovery and Rehabilitation Alliance, (ISRRA), American Heart Association/American Stroke Association. An example of successful implementation of the action plan can be seen in Bulgaria.[224]

Innovative population-wide communication of solutions for maximum impact

Beyond the publication of these key recommendations and evidence-based pragmatic interventions in *The Lancet Neurology*, itself an advocacy tool, strategic steps will be taken immediately by the WSO, commissioners, and implementation partners to spread the key messages of this Commission, through

innovative deployments via social media and other media platforms. Due to the wide availability of mobile phones including smartphones, even in LMICs, mobile health and tele-rehabilitation solutions including training videos and advocacy videos can be widely disseminated in various languages to enhance stroke rehabilitation care. Using multiple and interactive channels of choice to communicate and deploy solutions, all stakeholders (patients, populace, policy makers etc.) should be targeted. The implementation cycle (Figure 3)[16] and the stroke control measures based on the behaviour change wheel approach (Supplementary Figure 5)[15] should be implemented to inform, involve, collaborate with and empower all stakeholders.

The pragmatic solutions should be packaged innovatively to suit the targeted audience – using digital solutions, social media, social marketing, applied theatre, life-course multi-sectoral approach, tele-health, data science, precision public health, educational tools, success stories, and interactive websites. In the 'Stroke Self-Management and Rehabilitation Trial," carried out in India and Nigeria, the intervention group were provided with digital video discs that they took home with them on discharge from hospital showing that such self-management strategy is feasible with local and global support.[225] A direct communication portal including a website as well as stroke-related printed materials were developed as part of the global stroke educational program FAST Heroes, that also includes principal learning strategies (e.g. spacing, repetition and pegging techniques). Furthermore, a study in Brazil showed that health promotion through social media and websites yielded positive results in advertising a stroke rehabilitation protocol.[226] Health promotion interventions should be developed and tested to improve awareness and increase demand and consumption of stroke recognition, prevention, and rehabilitation services.[227] The importance of the awareness of stroke, its risk factors, warning signs, adequate acute care, and rehabilitation is illustrated by a hypothetical clinical scenario in Panel 7.

Through the WSO Task Force on Stroke commissioners and ecosystem we plan to: (a) address key environmental factors via policy change – social determinants of health, making default choices healthy; (b) enhance stroke literacy through key community influencers who can deliver culturally tailored messages, using strategies such as social media (social media influencers with impact), the arts (music, comedy, film, TV); (c) address motivation, self-efficacy, self-management skills; and (d) empower the stroke commissioners and stroke support groups to be the champions and advocates ensuring rigorous implementation and evaluation across the globe.

The WSO Task Force on Stroke commissioners, leveraging the WHO Global Action plan against NCDs,[11, 228] will operate at country, regional and global levels in collaboration with relevant implementation partners including national and regional neurology and stroke organizations such as the European Stroke Organization, Middle East & North Africa Stroke Organization, Asia Pacific Stroke Organization, American Stroke Association, African Stroke Organization,[229, 230] Ibero-American Stroke Organization (SIECV/IASO). The Angels Initiative, Mission Thrombectomy 2020, WSO Task Force and RES-Q can work together to support the global implementation and qualification of stroke control services.

Monitoring impact

We recommend the collection and monitoring of international key quality indicators for all stroke services across the globe. For instance, for acute stroke care this will enable the quality monitoring of stroke centres, to plan actions for improvement and to compare different centres and countries. These measures are used in the main international registries such as RES-Q, SITS-QR and the main quality programs such as Get with the Guidelines, Joint Commission international, AHA/ASA Certification of

Stroke Centres, WSO Certification Program. For the certification programs the goal is to ensure continuous improvement in the measures. The better quality of acute stroke care can help to achieve the goals of SDG 3.4 to decrease the early mortality from non-communicable diseases across the globe.

A key performance indicator (KPI) is a quantifiable measure of performance over time for a specific objective. These KPIs are the critical indicators of progress toward an intended result; they provide a focus for strategic and operational improvement, create an analytical basis for decision making and help focus attention on what matters most. Managing with the use of KPIs includes setting targets (the desired level of performance) and tracking progress against that target. KPIs can be categorized into several different types: inputs and processes, outputs, and outcomes. The KPIs proposed in this section have been developed to measure performance of a healthcare system to provide rehabilitation for stroke; the performance of a healthcare system is related to its capacity to respond to population needs and rehabilitation needs of stroke survivors. Adherence to service availability and quality KPIs is consistently associated with a lower risk of death or disability after stroke.[231] Quality KPIs can be used to monitor the adherence to guidelines and support the transfer of evidence into everyday clinical practice.[232, 233] Standardized core outcome measures for stroke rehabilitation, currently lacking in LMICs,[234] are also needed for comparisons of effectiveness of interventions across settings. The global targets for neurological disorders for 2022-2031 were recently described in the WHO IGAP.[34]

Overall, if all the recommendations of this Commission are implemented and monitored, the burden of stroke will be reduced drastically across the globe this decade and beyond. It will mitigate the clinical scenario presented in Panel 7. This will accelerate the attainment of SDG 3.4, and other SDGs, as well as improve brain health, and the overall wellbeing of the human race.

PANEL 7. CLINICAL SCENARIO

P, a 39-year-old Nigerian man was going about his duties on what he thought was a typical day in a biochemistry laboratory in the University College Hospital, Ibadan, when his colleague suddenly heard him repeatedly mutter to himself “It is well!” after which he staggered and tried to grab the wall trying to avoid a fall. His colleagues rushed him to the emergency section of the hospital, where he was diagnosed with a large ischaemic stroke affecting the left side of the brain. He was also noticed to have elevated blood pressure and serum lipid values. He was not aware that he had these conditions. He was managed conservatively due to the absence of acute reperfusion therapy. He was discharged home in a wheelchair with severe functional disability after 10 days of admission. He was unable to attend to basic activities of daily living without assistance and could neither communicate nor walk unassisted.

P is recently married with a new baby, and the breadwinner of the family before stroke. The social and economic effect on his family meant there was pressure on him to return to participation in domestic, social, and work life. He had no access to health insurance. As the family income dwindled, he could not pay for private physiotherapy and nursing services, leading to joints contractures and decubitus ulcers complicating his functional impairment as the days progressed. He had no access to speech therapy. He was unable to keep his outpatient clinic appointments and his family considered traditional medicine. He developed post-stroke depression and needed support in this period as he

began to refuse medications. He subsequently had a fever, difficulty in breathing, and unilateral limb swelling about three months after discharge which meant he had to be rushed to the emergency room again.

Lessons: While P clearly had an inadequate support system due to major gaps in the availability of adequate acute care and organization of post-stroke rehabilitation services in his locale, provision of educational materials to the patient or caregiver on self-management and simple rehabilitation tips would have gone a long way in avoiding some of the complications he suffered including decubitus ulcers, musculoskeletal contractures, limb clots, and finally, the hospital re-admission.

Furthermore, community-based rehabilitation would have been useful as it is expected to be less financially demanding and improves access to health services. The use of a multidisciplinary team consisting of physicians, nurses, physiotherapists, occupational therapists, etc., in community-based settings should be considered. Even a telemedicine-based model should work in P's case.

The practical goal would have been teaching P how to attend to basic activities of daily living without assistance, to reintegrate him into family life and if possible, work, as this would reduce the burden on his wife and give his child a better opportunity to survive. Above all, the stroke could have been prevented if he was aware of his risk factors through lifestyle modifications, regular annual check-ups, and proper control of risk factors.

WSO Task Force on Stroke: Prof. Bo Norrving (Co-Chair), Prof. Valery L. Feigin (Co-Chair), Prof. Michael Brainin, Prof. Sheila Martins, Prof. Jeyaraj Pandian, Prof. Graeme J. Hankey, A/Prof. Seana Gall, Prof. Mayowa Owolabi, Dr Taskeen Khan.

Steering Committee members of this Commission: Prof. Mayowa Owolabi (Co-Chair)*; Prof. Valery L. Feigin (Co-Chair).* Other members are listed in alphabetical order by last name: Prof. Foad Abd-Allah; Prof. Rufus Akinyemi; Dr. Natalia Bhattacharjee; Prof. Michael Brainin; Jackie Cao; Bronte Dalton; Dr. Alan Davis; Joseph Duprey; Prof. Gary A. Ford; A/Prof. Seana Gall; Prof. Dorcas Gandhi; Prof. Vladimir Hachinski; Prof. Graeme Hankey; Prof. Walter Johnson; Dr. Julie Kim; Prof. Pablo Lavados; Dr. Patrice Lindsay; Prof. Ajay Mahal; Prof. Sheila Martins; Prof. Christopher Murray; Prof. Thuy Phuong Nguyen; Prof. Bo Norrving; Dr. Muideen Olaiya; Prof. Jeyaraj Pandian; Hoang Phan; Thomas Platz; Prof. Anna Ranta; A/Prof. Greg Roth; Prof. Ivy Anne Sebastian; Amanda E. Smith; Prof. PN Sylaja; Prof. Amanda Thrift; Ezinne Uvere; Prof. Stein Emil Vollset; Dr. Dileep Yagaval; Dr. Joseph Yaria.

*Co-Chairs of the Steering Committee contributed equally to management of the Commission.

Core writing group of this Commission (all members of the core writing group of this Commission contributed equally to the manuscript, therefore they are listed alphabetically by last name): Prof. Foad Abd-Allah, MD, PhD[1]; Prof. Rufus Akinyemi, MSc, PhD[2]; Natalia Bhattacharjee, PhD[3]; Prof. Michael Brainin, MD, PhD[4]; Jackie Cao, MS[3]; Bronte Dalton, BA[3]; Alan Davis, MD[5]; Joseph Duprey, MS[3]; Prof. Valery L. Feigin, MD, PhD[6]; Prof. Gary Ford, PhD[7]; A/Prof. Seana Gall, PhD[8]; Prof. Dorcas Gandhi MPT[9]; Prof. Vladimir Hachinski, MSc, MD[10]; Prof. Graeme J. Hankey, MD, PhD[11]; Prof. Walt Johnson, MD, MBA, MPH[12]; Julie Kim, MPH[3]; Dr Taskeen Khan, MD, MMed, FCPHM;[27] Prof. Pablo Lavados MPH, MD[13]; Dr. Patrice Lindsay, BScN, RN, M.Ed., PhD[14]; Prof. Ajay Mahal, PhD[15]; Prof. S. Martins, MD, PhD[16]; Dr. Christopher Murray, BA, MD, DPhil[3]; Thuy Phuong Nguyen[8]; Prof. Bo Norrving, PhD[17]; Dr. Muideen Olaiya, MSc, PhD[18]; Dr. Victor O. Olalusi, MD, PhD[19, 26]; Prof. Mayowa Owolabi, MBBS, MSc, MD, Dr.M[2, 20]; Prof. Jeyaraj Pandian, MBBS, MD, DM[9]; Dr. Hoang Phan, MBBS, PhD[8]; Prof. Thomas Platz, Dr. med.

habil[21]; Prof. Anna Ranta, MD, PhD[22]; Dr. Sabah Rehman[8]; A/Prof. Greg Roth, MPH, MD[3]; Prof. Ivy Anne Sebastian, MBBS, MD[9]; Amanda E. Smith, MPA[3]; Prof. PN Sylaja, MD, DM[23]; Dr. Rajshree Thapa, MPH, PhD[18]; Prof. Amanda Thrift, PhD[18]; Ezinne Uvere, MPH[24]; Prof. Stein Emil Vollset, MPH, MD, DrPH[3]; Dr. Dileep Yagaval, MD[25]; Dr. Joseph Yaria, MSc, MBBS[26]; on behalf of the Stroke Experts Collaboration Group** (all other members of the Stroke Collaboration Group are listed below).

Members of the writing groups sections: *Section 1: Projected Burden of Stroke:* Prof. Valery L. Feigin, MD, PhD[6], Prof. Stein Emil Vollset, PhD[3], Amanda E. Smith[3], Joseph Duprey[3], Julie Kim[3], Bronte Dalton[3], Jackie Cao[3], Natalia Bhattacharjee[3], Prof. Bo Norrving[17], Prof. Michael Brainin, MD, PhD[4], Prof. Mayowa Owolabi, MBBS, MSc, Dr.M[2,20], A/Prof. Greg Roth, MD[3], PhD, Prof. Christopher Murray, MD, PhD[3]. *Section 2: Economic Implications of stroke 2017 to 2050:* Prof. Ajay Mahal, PhD[15], Marie Ishida[15], Prof. Mayowa Owolabi, MBBS, MSc, Dr.M[2, 20]. *Section 3: Thematic Analysis:* A/Prof. Seana Gall, PhD[8], Prof. Thuy Phuong Nguyen[8], Ezinne Uvere[24], Hoang Phan[8], Dr. Muideen Olaiya, PhD[18]. *Section 4: Stroke Surveillance:* Dr. Muideen Olaiya, PhD[18], A/Prof. Seana Gall, PhD[8], Dr. Rajshree Thapa[18], Dr. Sabah Rehman, PhD[8], Prof. Valery L. Feigin, MD, PhD[6], Prof. Mayowa Owolabi, MBBS, MSc, Dr.M[2, 20], Prof. Amanda Thrift, PhD[18]. *Section 5: Stroke Prevention, with a focus on secondary prevention:* Prof. Valery L. Feigin, MD, PhD[6], Prof. Mayowa Owolabi, MBBS, MSc, MD, Dr.M[2, 20], A/Prof. Seana Gall, PhD[8], Prof. Vladimir Hachinski, CM, MD, DSc.[10], Prof. Pablo Lavados, MD, PhD[13], Prof. Walt Johnson, MD, PhD[12], Prof. Michael Brainin, MD, PhD[4], Prof. Amanda Thrift, PhD[18], Prof. Ajay Mahal, PhD[15], Dr Alan Davis, MD[5], Prof. Sheila Martins, MD, PhD[16], Prof. Graeme J. Hankey, MD, PhD[11], Prof. Gary A. Ford, PhD[7]. *Section 6: Acute stroke care:* Prof. Sheila Martins, MD, PhD[16], Prof. Jeyaraj Pandian, MD, PhD[9], Prof. Valeria Caso, MD, PhD[28] Prof. Gary Ford, MD, PhD[7], Prof. Anna Ranta, MD, PhD[22], Prof. Rufus Akinyemi, MD, PhD[2], Prof. Pablo Lavados, MD, PhD[13], Dr. Dileep Yagaval[25], Prof. PN Sylaja[23], Prof. Ivy Anne Sebastian[9], Prof. Werner Hacke, MD, PhD[29], Dr Robert Dempsey, MD[30], Prof. Foad Abd-Allah, MD, PhD[1], Hoang Phan[8], Nijasri Suwanwela[31], Prof. Walter Johnson, MD, PhD[12], Prof. Valery L. Feigin, MD, PhD[6], A/Prof. Seana Gall, PhD[8], Dr Wayne Feng[32], Prof. Bo Norrving, MD, MBA, MPH[17], Prof. Mayowa Owolabi, MBBS, MSc, Dr.M[2, 20]. *Section 7: Stroke rehabilitation:* Prof. Mayowa Owolabi, MBBS, MSc, MD, Dr.M[2, 20], Prof. Jeyaraj Pandian, MD, PhD[9], Prof. Foad Abd-Allah, MD, PhD[1], Dr. Joseph Yaria, MBBS, MPH[26], Wuwei Feng[33], Prof. Thomas Platz, Dr. med. habil[21], David Good[34], Dr Patrice Lindsay, PhD[14], Prof. Stein Emil Vollset, MD, PhD[3], A/Prof. Gregory Roth, MD, PhD[3], Prof. Dorcas Gandhi[9], A/Prof. Seana Gall, PhD[8], Prof. Ajay Mahal, PhD[15], Dr. Victor O. Olalusi[19,26]. *Introduction, Methods, Conclusions and Impact sections:* Prof. Mayowa Owolabi, MBBS, MSc, MD, Dr.M[2, 20], Dr. Joseph Yaria MBBS, MPH[26], Prof. Valery L. Feigin, MD, PhD[6]

Affiliations of the core writing group and writing groups of the sections

1. Faculty of Medicine, Cairo University, Egypt
2. Centre for Genomics and Precision Medicine, College of Medicine, University of Ibadan, Nigeria
3. Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA
4. Danube University Krems, Austria
5. Te Whatu Ora/Health New Zealand
6. National Institute for Stroke and Applied Neurosciences, Auckland University of Technology, Auckland, New Zealand; Institute for Health Metrics Evaluation, University of Washington, Seattle, USA; Research Centre of Neurology, Moscow, Russia
7. Radcliffe Department of Medicine, University of Oxford, Oxford, UK
8. Menzies Institute for Medical Research, University of Tasmania, Tasmania, Australia

9. Christian Medical College & Hospital, Ludhiana, India
10. Schulich School of Medicine and Dentistry, Western University, Toronto, Ontario, Canada
11. UWA Medical School, The University of Western Australia, Perth, Australia; Perron Institute for Neurological and Translational Science, Perth, Australia
12. Loma Linda University Schools of Medicine and Public Health, Loma Linda, CA, USA
13. Clinica Alemana, Universidad del Desarrollo; Universidad de Chile, Santiago, Chile
14. Heart and Stroke Foundation of Canada
15. Melbourne School of Population and Global Health, The University of Melbourne, Victoria, Australia
16. World Stroke Organization; Medical School of Universidade Federal do Rio Grande do Sul; Hospital de Clínicas de Porto Alegre; Hospital Moinhos de Vento, Brazil
17. Department of Neurology, Lund University, Skåne University Hospital, Lund, Sweden
18. Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia
19. Faculty of Clinical Sciences, National Research Medical University, Moscow, Russia
20. Faculty of Clinical Sciences, University of Ibadan, Ibadan, Nigeria
21. BDH Klinik Greifswald; Institute for Neurorehabilitation and Evidence-based Practice, University of Greifswald and University Medical Centre, Greifswald, Germany
22. University of Otago, Wellington, New Zealand
23. Sree Chitra Tirunal Institute for Medical Sciences and Technology, Kerala, India
24. Department of Medicine, University of Ibadan, Nigeria
25. University of Miami, FL, USA
26. University College Hospital, Ibadan, Nigeria
27. World Health Organization
28. University of Perugia Stroke Unit, Perugia, Italy
29. University of Heidelberg, Heidelberg, Germany
30. University of Wisconsin School of Medicine and Public Health, WI, USA
31. Faculty of Medicine, Chulalongkorn University, Thailand
32. Medical University of South Carolina, Charleston, SC, USA
33. Dept of Neurology, Duke University School of Medicine, Durham, NC, USA
34. Penn State Health, Pennsylvania, USA

****List of other members of the WSO-The Lancet Neurology Commission Stroke Collaboration Group** (in alphabetical order by last name):

Abanto C., MD, MPH[1], Abera S.F., PhD[2], Addissie A., MD, PhD[3,] Adeleye A., MD[4], Adilbekova Y., MD[5], Adoukonou T.A., MD,[6] Aguiar de Sousa D., MD, PhD,[7] Prof. Akhmetzhanova Z., MD, MSc[5] Akpalu A., MB. ChB,[8] Ameriso S.F., PhD,[9] Andonova S., MD, PhD, DSc[10], Arsovska A., MD, PhD[11], Awoniyi F.E., MSc,[12,] Bakhiet M., MD, PhD[13], Basri H., MD[14], Bath P.M., DSc, FMedSci[15], Bereczki D., MD, PhD, DSc[16], Beretta S., MD, PhD[17], Berkowitz A.L., MD, PhD[18], Bernhardt J. MD[19], Berzina G., MD, PhD[20], Bhavsar B., MSc[21], Bisharyan MD, DSc[22], Bohara M., MD, PhD[23], Bovet P., MD, MPH,[24,] Budincevic H., MD[25], Prof. Cadilhac D A., PhD[26], Čerimagić D., MD, PhD[27], Charway-Felli A., MD, PhD[28], Chen C., MD,[29] Chin J.H., MD, PhD, PPH[30], Christensen H, MD, PhD, DMSCi[31], Chwojnicki K., MD[32], Conforto A.B., MD[33], Correia M., MD[34], Cruz V.T., MD, PhD[35], Cuervo D.L.M., MD[36], Członkowska A., MD[37], D'Amelio M., MD[38], Danielyan K.E., PhD[39], Prof. Davis, S. MD[40], Prof. Demarin V, MD, PhD[41], Demchuk A.M., MD[42], Prof. Dichgans M., MD[43], Prof. Dokova MD, PhD[10], Prof. Donnan G. MBBS, MD[44], Duran J., MD[45], Ekeng G., MSc[46], Elizondo M.A.B., MD, MSc[47], Elkind M.S., MD, MS[48], Endres M., MD[49], Etedal I., MD[50], Faris

M.E., MD[51], Fischer U., MD[52], Flomin Y., MD, PhD[53], Gankpe F., MD[54], Gavidia M., MD[55,] Gaye-Saavedra A., MD[56], Gebreyohanns M., MD[57], George M., MD[58], Gierlotka M., MD[59], Prof. Giroud M., MD[60], Prof. Gnedovskaya E.V., MD, PhD[61], Gonçalves I.P., MD[62], Gongora–Rivera F., MSc, PhD[63], Gunaratne P.S., MD[64], Hamadeh R.R., BSc, MSc, DPhil[65], Hamzat T.K., PhD[66], Heldner M.R., MD, MSc[67], Prof. Ibrahim N.M., MBBCH[68], Ihle-Hansen H., MD, PhD[69], Jee S., MD, PhD[70], Jiann-Shing J., MD[71], Johnston S. C., MD, PhD[72], Prof. Jovanovic D., MD, PhD[73], Jurjāns K., PhD[74], Kalani R., MD[75], Kalkonde Y., MD, MSc[76], Kamenova S., MD[77], Kang Z.L., MD[68], Karaszewski B., MD, PhD[78], Kelly P., MD MS[79], Kiechl S., MD[80], Kondybayeva A., MD[81], Prof. Kõrv J., MD, PhD[82], Prof. Kozera G., MD, PhD[83], Kravchenko M., MD, DMSCI[61], Krespi Y., MD[84], Prof. Krishnamurthi R., BSc, MApplSc, PhD[85], Kutluk K., MD[86], Prof. Langhorne P., MD, PhD,[87] Kruja J., MD, PhD[88], Lebedynets D., MD[89], Leung T.W., MBChB[90], Liebeskind D.S., MD[91], Liu L., MD, PhD[92], López-Jaramillo P., MD, PhD[93], Lotufo P.A., MD, DPH[94], Machline-Carrion M.J,, MD, PhD[95], Maia L.F., MD, PhD[96], Malojcic B., MD, PhD[97], Prof. Markus H.S., MD, PhD[98], Marquez-Romero J.M., MD, MS[99], Medina M.T., PhD[100], Medukhanova S., MD, MPH[101], Prof. Mehndiratta M.M., PhD[102], Miglāne E., MD, PhD[103], Mihejeva I., MD, PhD[104], Prof. Mikulik R., MD, PhD[105], Prof. Mirrakhimov E., MD[106], Mohl S., MD[107], Munakomi S., MCh[108], Murphy S., MD[109,] Musa K.I., PhD[110], Nasreldein A., MD[111], Nogueira R., MD[112], Nolte C.H., MD[113], Noubiap J.J., MD, MMed[114], Novarro-Escudero N., MD[115], Ocampo C., MD[116], Prof. O'Donnell M., PhD[117], Prof. Ogun Y., BSc, MBChB, MPH[118], Prof. Ogunniyi A, MBChB[119], Oraby M.I., PhD[120], Prof. Ovbiagele B., MD, MAS[121], Prof. Õrken D.N., MD, PhD[122], Õzdemir A.O., PhD[123], Ozturk S., MD[124], Paccot M., MD[125], Pereira T., PhD[126], Peeters A., MD[127], Prof. Piradov M., MD, PhD, D.Med.Sci[61], Potpara T., MD, PhD[128], Rathore F.A., MBBS, MSc[129], Prof. Sacco R.L., MD, MS[130], Sahathevan R., MD, PhD[131], Sandset E.S., MD, PhD[132], Santos I.R., MD, MHA[133], A/Prof. Saposnik G., MD, MSc, PhD[134], Sarfo F.S., MD, PhD[135], Sargento-Freitas J., MD, PhD[136], Sharma M., PhD[137], Shaw L., MBChB[138], Sheth K.N., MD, PhD[139], Shin Y., MD, PhD[140], Shobhana A., MD[141], Silva, S.N., MD[142], Thakur K., MD[143], Thapa L., MD, DM[144], Toni D., MD[145], Topcuoglu M.A., MD[146,] Torales J., MD, MS[147], Towfighi A., MD[148], Truelsen T., MD, PhD[149], Tsiskaridze A., MD, PhD, DSc[150], Lee T.H., MD, PhD[151], Tulloch-Reid M., MD, DSc[152], Useche J.N., MD[153], Vanacker P., MD[154], Vassilopoulou S., MD, PhD[155], Vukorepa G., MD[156], Vuletic V., MD, PhD[157], Wahab K.W., MD, MPH, MSc[158], Wang W., PhD[159], Prof. Wijeratne T., MD[160], Wojtyniak B., PhD[161], Prof. Wolfe C, MD[162], Yacouba M.N., MD[163], Yang J., MD, PhD[164], Yifru M.Y., MD, MSc[165], Yock-Corrales A., MD, MSc[166], Yonemoto N., PhD[167], Yperzeele L., MD, PhD[168], Zagożdżon P., MD[169]

Affiliations of these members of the WSO – The Lancet Neurology Commission Stroke Collaboration Group:

1. Departamento de Enfermedades Neurovasculares, Instituto Nacional de Ciencias Neurológicas, Lima, Peru
2. School of Public Health, College of Health Sciences, Mekelle University, Mekelle, Ethiopia
3. School of Public Health, Addis Ababa University, Ethiopia
4. College of Medicine, University of Ibadan/Department of Neurological Surgery, University College Hospital, Ibadan, Nigeria
5. Department of Neurology of NpJSC "Astana Medical University", Astana, Kazakhstan
6. EBU Neurology, Faculty of Medicine, Université de Parakou, Benin
7. Stroke Center, Lisbon Central University Hospital and Institute of Anatomy, Faculdade de Medicina, Universodade de Lisboa, Lisbon, Portugal
8. University of Ghana Medical School, Accra, Ghana

9. Department of Neurology, Institute for Neurological Research, FLENI, Montañeses, Buenos Aires, Argentina
10. Medical University/University Hospital "St. Marina', Varna, Bulgaria
11. University Clinic of Neurology, University SS Cyril and Methodius, Skopje, North Macedonia
12. Department of Linguistics, Osun State University of Technology, Nigeria
13. Department of Molecular Medicine, College of Medicine and Medical Sciences, Princess Al-Jawhara Center for Genetics and Inherited Diseases, Arabian Gulf University, Manama
14. Department of Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia
15. University of Nottingham, United Kingdom
16. Semmelweis University, Budapest, Hungary
17. San Gerardo Hospital ASST Monza, University of Milano Bicocca, Italy
18. University of California, San Francisco, USA
19. The Florey Institute of Neuroscience & Mental Health, University of Melbourne, Australia
20. Riga East University Hospital, Riga, Latvia
21. Shah Hospital, Nairobi, Kenya
22. Yerevan State Medical University after Mkhitar Heratsi, Yerevan, Armenia
23. Department of Neurosurgery, HAMS Hopsital, Kathmandu, Nepal
24. University Center of Primary Care and Public Health (Unisanté), Lausanne, Switzerland
25. Sveti Duh University Hospital, Zagreb, Croatia
26. Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia
27. Poliklinika Glavić, Dubrovnik, Croatia; Department of Neurology, Dubrovnik General Hospital, Croatia
28. Military Hospital medical Division, Accra, Ghana
29. Department of Pharmacology, Yong Loo Lin School of Medicine, National University of Singapore
30. New York University School of Medicine, New York, NY, USA
31. Copenhagen University Hospital, Bispebjerg og Frederiksberg Hospital, Denmark
32. Medical University of Gdansk, Poland
33. University of São Paulo, São Paulo SP, Brazil
34. Universidade do Porto Instituto de Ciências Biomédicas Abel Salazar, Porto, Portugal
35. School of Medicine, Johns Hopkins Medicine, Baltimore, MD, USA
36. Pontificia Universidade Católica do Rio Grande do Sul, Brazil
37. Department of Neurology, Institute of Psychiatry and Neurology, Warsaw, Poland
38. University of Palermo, Italy
39. Institute of Biochemistry named after H. Buniatyan, NAS RA, Yerevan, Armenia
40. Royal Melbourne Hospital, Australia
41. Department of Medical Sciences of the Croatian Academy of Sciences and Arts, Zagreb, Croatia
42. Clinical Neurosciences, Cumming School of Medicine, University of Calgary, Canada
43. Institute for Stroke and Dementia Research (ISD), Ludwig-Maximilians University (LMU) Munich, Medical Center, München, Germany; Munich Cluster for Systems Neurology (SyNergy), Munich, Germany
44. University of Melbourne, Australia
45. La Paz, Bolivia
46. Stroke Care International, London, United Kingdom
47. Escuela de Medicina, San José Universidad de Costa Rica

48. Department of Neurology, Vagelos College of Physicians and Surgeons and Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, USA
49. Department of Neurology with Experimental Neurology, Charité – Universitätsmedizin, Berlin
50. Alneelain University, Khartoum, Sudan
51. Mohamed V University, Rabat, Morocco
52. University Hospital Basel, University of Basel; University Hospital Bern, Switzerland
53. Stroke and Neurorehabilitation Unit, MC Universal Clinic 'Oberig' Kyiv, Ukraine
54. CHU Hassan II of Fez, Morocco
55. Medico Neurologo, Clinica Angloamericana, Lima, Peru
56. Unidad de ACV, Instituto de Neurología, Hospital de Clínicas, Uruguay
57. Department of Neurology, UT Southwestern Medical Centre, Dallas, TX, USA
58. Centre for Disease Control, Atlanta, GA, USA
59. Department of Cardiology, University Hospital in Opole, Poland
60. Dijon Stroke Registry, University Hospital of Dijon, University of Burgundy, France
61. Research Center of Neurology, Moscow, Russia
62. Assoc Hospitalar Moinhos De Vento, Brazil
63. Department of Neurology and Stroke Unit, University Hospital Jose Eleuterio Gonzalez, Universidad Autonoma de Nuevo Leon, Mexico
64. National Hospital of Sri Lanka, Colombo, Sri Lanka
65. Department of Family and Community Medicine, College of Medicine and Medical Sciences, Arabian Gulf University, Bahrain
66. Department of Physiotherapy, College of Medicine, University of Ibadan, Nigeria
67. Bern University Hospital/Department of Neurology, University of Bern, Bern, Switzerland
68. UKM Medical Center, Kuala Lumpur, Malaysia
69. Oslo University Hospital, Oslo, Norway
70. Department of Rehabilitation Medicine, College of Medicine, Chungnam National University Hospital, Daejeon, South Korea
71. Department of Neurology, National Taiwan University Hospital, Taipei, Taiwan
72. Medical school, University of Texas, Austin, USA
73. Dept. of Emergency Neurology, Medical Faculty, University of Belgrade, Serbia
74. Department of Neurology and Neurosurgery, Riga Stradins University, Latvia
75. University of Washington, Seattle, WA, USA
76. SEARCH for Health, Maharashtra, India
77. Al-Farabi Kazakh National University Kazakhstan
78. Department of Adult Neurology, Medical University of Gdansk, Gdansk, Poland
79. Mater Misericordiae University Hospital, Dublin, Ireland
80. Department of Neurology, Medical University of Innsbruck and VASCage, Research Centre on Vascular Ageing and Stroke, Innsbruck, Austria
81. Asfendiyarova Kazakh National Medical University, Almaty, Kazakhstan
82. Department of Neurology and Neurosurgery, University of Tartu, Tartu, Estonia
83. Medical Simulation Center, Medical University of Gdańsk, Gdańsk, Poland
84. Department of Neurology, University of Istanbul, Istanbul, Turkey
85. National Institute for Stroke and Applied Neurosciences (NISAN), School of Clinical Sciences, Auckland University of Technology, New Zealand
86. Neurology Department, Dokuz Eylül University, Izmir, Turkey
87. University of Glasgow, United Kingdom
88. Faculty of Medicine, University of Medicine, Tirana, Albania
89. Department of Neurology, University of California, Los Angeles, USA

90. The Chinese University of Hong Kong
91. V.N. Karazin Kharkiv National University, Kharkiv, Ukraine
92. Beijing Tiantan Hospital, Capital Medical University
93. Universidad de Santander (UDES), and Universidad Autonoma de Bucaramanga (UNAB), Bucaramanga, Colombia
94. Department of Medicine, University of Sao Paulo, São Paulo, Brazil
95. epHealth Primary Care Solutions, Florianópolis, Brazil
96. Department of Neurology, Centro Hospitalar Universitário de Porto, Porto, Portugal
97. University Hospital Centre Zagreb, Zagreb, Croatia
98. Department of Clinical Neurosciences, University of Cambridge, United Kingdom
99. Instituto Mexicano del Seguro Social (IMSS) HGZ 2, Aguascalientes, Mexico
100. Faculty of Medical Sciences, National Autonomous University of Honduras (WHO Collaborating Centre for Research and Community Intervention in Epilepsy), Honduras
101. National Center of Neurosurgery, Astana, Kazakhstan
102. BLK-MAX, Dr. B.L.Kapur Hospital, Max Healthcare, Department of Neurosciences, New Delhi, India
103. Department of Neurology and Neurosurgery, Riga Stradins University, Latvia
104. Riga East University Hospital, Latvia
105. St. Anne's University Hospital and Masaryk University, Czech Republic
106. Department of Internal Medicine of Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan
107. American Heart Association/American Stroke Association, Dallas, TX, USA
108. Kathmandu University
109. Mater Misericordiae University Hospital, Dublin, Ireland; UCD School of Medicine, Dublin, Ireland and RCSI Medical School, Dublin, Ireland.
110. Department of Community Medicine, School of Medical Sciences, Universiti Sains, Malaysia
111. Department of Neurology and Psychiatry, Assiut University, Egypt
112. Emory University School of Medicine, Atlanta, Georgia, USA
113. Department of Neurology, Center for Stroke Research, Berlin, and Berlin Institute of Health, Charité—Universitätsmedizin, Berlin, Germany
114. Department of Medicine, Groote Schuur Hospital and University of Cape Town, South Africa
115. Hospital Punta Pacifica, En Punta Pacífica, Ciudad de Panamá, Panama
116. University of Botswana, Gaboronc, Botswana
117. NUI Galway Health Research Board, Clinical Research Coordination, Galway, Ireland
118. Lagos State University College of Medicine/Lagos State University Teaching Hospital, Lagos State, Nigeria
119. University College Hospital, Ibadan, Nigeria
120. Beni Suef University Faculty of Medicine: Beni Suef, Egypt
121. Weill Institute for Neurosciences, University of California San Francisco, USA
122. İstanbul Arel University,Turkey
123. Eskişehir Osmangazi University, Turkey
124. Selcuk University Faculty of Medicine, Turkey
125. Non-Communicable Diseases Department, Ministry of Health, Santiago, Chile
126. Polytechnic Institute of Coimbra, Coimbra Health School, Portugal
127. UCL St Luc Unité neuro-vasculaire, Bruxells
128. School of Medicine, University of Belgrade, Serbia
129. PNS Shifa Hospital, Karachi, Pakistan
130. Miller School of Medicine, University of Miami, USA
131. Ballarat Health Services, Australia

132. Department of Neurology, Oslo University Hospital, Oslo, Norway
133. Department of Neurology and Neurosurgery, Faculty of Medicine, University of Chile, Non-Communicable Diseases Department, Ministry of Health, Santiago, Chile
134. Stroke Outcomes and Decision Neuroscience Research Unit, University of Toronto, Canada; Editor-in-Chief, World Stroke Academy for the WSO
135. Kwame Nkrumah University of Science and Technology, Kumasi, Ghana
136. Department of Neurology, Hospitais da Universidade de Coimbra, Coimbra, Portugal
137. Population Health Research Institute and Hamilton Health Sciences, Canada
138. Clinical Director South West, Integrated Stroke Delivery Network at NHS England, Bath, England, United Kingdom
139. Department of Neurology and Neurosurgery, Yale School of Medicine, New Haven, CT, USA
140. Department of Rehabilitation Medicine, Rehabilitation Hospital and Research Institute for Convergence of Biomedical Science and Technology, Pusan National University Yangsan Hospital, Yangsan, Korea
141. Institute of Neuroscience, Kolkata, India
142. Ochre Medical Centre Deniliquin, Fellow; Australasian Institute of Digital Health, Australia
143. Columbia University Irving Medical Center, New York, NY, USA
144. National Neuro Center (NNC), Maharajgupi, Kathmandu, Nepal
145. Department of Human Neurosciences, Sapienza University, Rome, Italy
146. Neurology Department, Hacettepe University Hospitals, Ankara, Turkey
147. Department of Psychiatry, School of Medical Sciences, National University of Asunción, Asunción, Paraguay
148. Los Angeles County Department of Health Services, California, USA
149. Department of neurology, Rigshospitalet, University of Copenhagen, Denmark
150. Dept. of Neurology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia
151. Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan
152. University of the West Indies, Mona, Jamaica
153. Dept of Neuroradiology and radiology, Universidad El Bosque; University Hospital Fundación Santa Fe de Bogotá, Bogotá, Colombia
154. Antwerp University Hospital, Edegem; Department of Translational Neurosciences, Antwerp University, Antwerp, Belgium
155. First Department of Neurology, National and Kapodistrian University of Athens, Greece
156. University Hospital Dubrava, Zagreb, Croatia
157. University of Rijeka, Croatia
158. Department of Medicine, University of Ilorin, Ilorin, Nigeria
159. Beijing Neurosurgical Institute, China
160. Department of Neurology, The Sunshine Hospital, Australia
161. Polish Institute of Public Health, Warsaw, Poland
162. School of Population Health & Environmental Sciences, Kings College London, United Kingdom
163. Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Douala; Department of Internal Medicine, Douala General Hospital, Douala, Cameroon
164. Department of Neurology, Sichuan Provincial People's Hospital, University of Electronic Science and Technology, Chengdu, China
165. Department of Neurology, College of Health Science, Addis Ababa University, Addis Ababa, Ethiopia
166. Department of Emergency Medicine, National Children's Hospital "Dr Carlos Saenz Herrera", CCSS, San José, Costa Rica
167. Department of Public Health, Juntendo University School of Medicine, Japan

168. Stroke Unit and NeuroVascular Reference Center (NVCA), Antwerp University Hospital (UZA), Belgium
169. Department of Hygiene and Epidemiology, Medical University of Gdańsk, Gdańsk, Poland

AUTHOR'S CONTRIBUTIONS

MOO, VLF, AGT, SM, SG, AES, SEV, GR, and WJ conceptualized the structure and design of the manuscript. MOO, WJ and VLF invited other members of the Commission with relevant expertise, convened and co-led meetings, provided the initial direction, and coordinated all communications and subsequent writing. MOO wrote the first draft of the manuscript, the rehabilitation section of the manuscript, contributed to the design and source materials for the surveillance, co-designed the thematic and acute care sections, and the template for the pragmatic solutions tables. VLF wrote the first drafts of the stroke burden projection and prevention sections of the manuscript, contributed to the writing of the surveillance section, revised all sections of the manuscript and Supplementary materials, and wrote the final version of the manuscript that was circulated to all commissioners for their final review and approval. SEV, AES, VLF, GR and MOO designed the IHME projections while JD, JC, BD, NB and JK performed the IHME analyses. SG, AGT and MOO designed the thematic study. SG and AGT wrote the first draft of the surveillance section of the manuscript. SG and MOO wrote the first draft of the thematic analysis of the manuscript. SM and JP wrote the first draft of the acute care section of the manuscript. MOO, JY, FA, JP, WF and TP wrote the first draft of the stroke rehabilitation section. JO and MOO handled integration of all content and overall flow of the document. AM, MI and MOO developed the section on economic analysis. All other co-authors provided critical intellectual contribution to the manuscript. All authors reviewed the manuscript for important intellectual content and approved the final version of the manuscript. All members of the Commission contributed fully to the overall structure and concepts, the writing and editing of the executive summary, and key messages and recommendations.

DISCLOSURES

VLF states that the free Stroke Riskometer app and PreventS-MD webapp are owned and copyrighted by AUT Ventures Ltd, Auckland University of Technology, New Zealand. Bo Norrving has received honoraria for DSMB work in THALES trial (AstraZeneca). Other authors have no disclosure to make. ME reports grants from Bayer and fees paid to the Charité from Abbot, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Daiichi Sankyo, Sanofi, Novartis, Pfizer, all outside the submitted work.

ROLE OF THE FUNDING SOURCE

The survey part of the Commission was partially funded by the World Stroke Organization (WSO). Stroke burden projections 2020-2050 were funded by the Bill and Melinda Gates Foundation. Thematic analysis was partially funded by the NHMRC Synergy STOPstroke Grant (GNT1182071) and the WSO. The funders had no influence on the interpretation and presentation of the study findings.

ACKNOWLEDGEMENT

MOO is supported by SIREN (U54HG007479), SIBS Genomics (R01NS107900), and SIBS Gen (R01NS107900-02S1), ARISES (R01NS115944-01), H3Africa CVD Supplement (3U24HG009780-03S5), CaNVAS (1R01NS114045-01), Sub-Saharan Africa Conference on Stroke, SSACS, (1R13NS115395-01A1) and Training Africans to Lead and Execute Neurological Trials & Studies, TALENTS, (D43TW012030). VLF also declares grants received from the Brain Research New Zealand

Centre of Research Excellence (16/STH/36), National Health & Medical Research Council (NHMRC, Australia APP1182071) and WSO; he reports being Executive Committee member of WSO, Honorary Medical Director of Stroke Central New Zealand, and CEO of New Zealand Stroke Education (charitable) Trust, outside of the submitted work. AGT acknowledges receipt of funding from the National Health & Medical Research Council (Australia) outside the submitted work. SLG is funded by a National Heart Foundation of Australia Future Leader Fellowship (GNT102061) and a National Health and Medical Research Council Synergy Grant (GNT1182071). The thematic analysis of stroke services was funded by the WSO and NHMRC STOPstroke Synergy Grant (GNT1182071). The WFNR SIG Clinical Pathways survey was supported by the BDH Bundesverband Rehabilitation, a charity for neuro-disabilities.

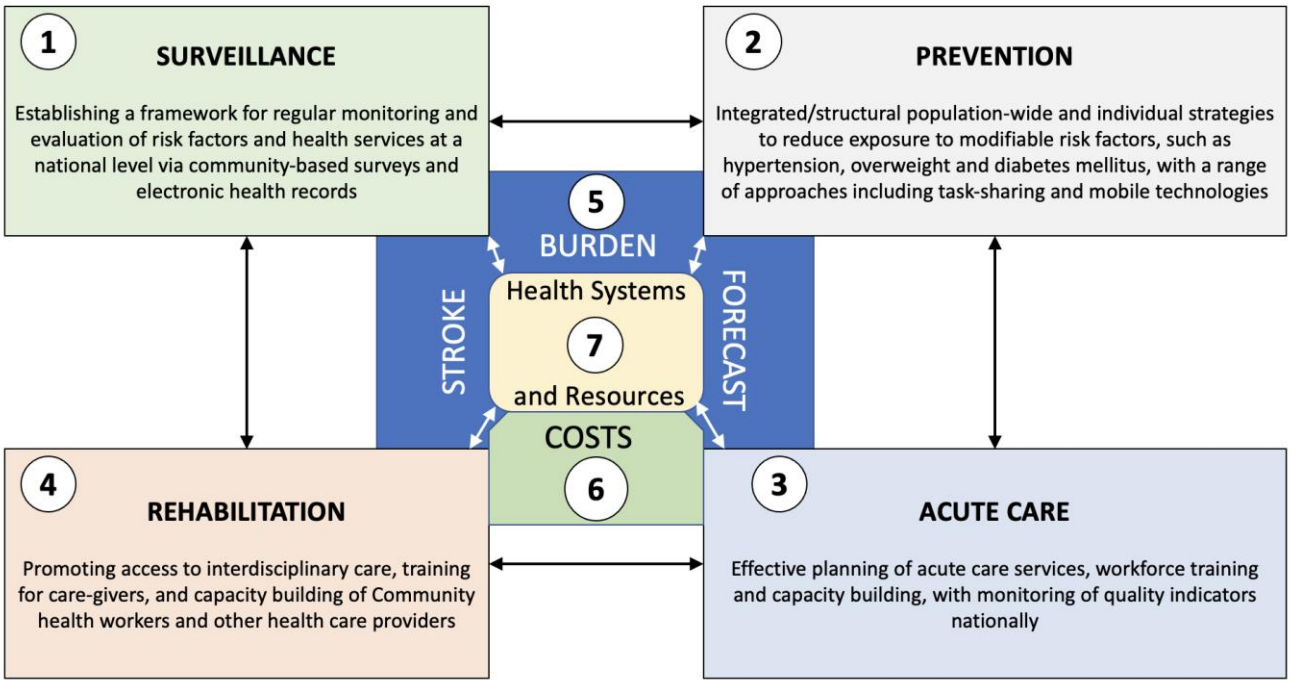
We acknowledge the contributions of Jody-Anne Mills, Alexandra Rauch, Wouter De Groote, Tarun Dua, Nicoline Schiess, Taskeen Khan, Cherian Varghese, Slim Slama, Prebo Barango, Alarcos Cieza, and Pauline Kleinitz of the World Health Organization for reviewing and editing of the manuscript.

A LIST OF FIGURES AND TABLES FOR THE MAIN TEXT OF THE MANUSCRIPT

FIGURES

TABLES

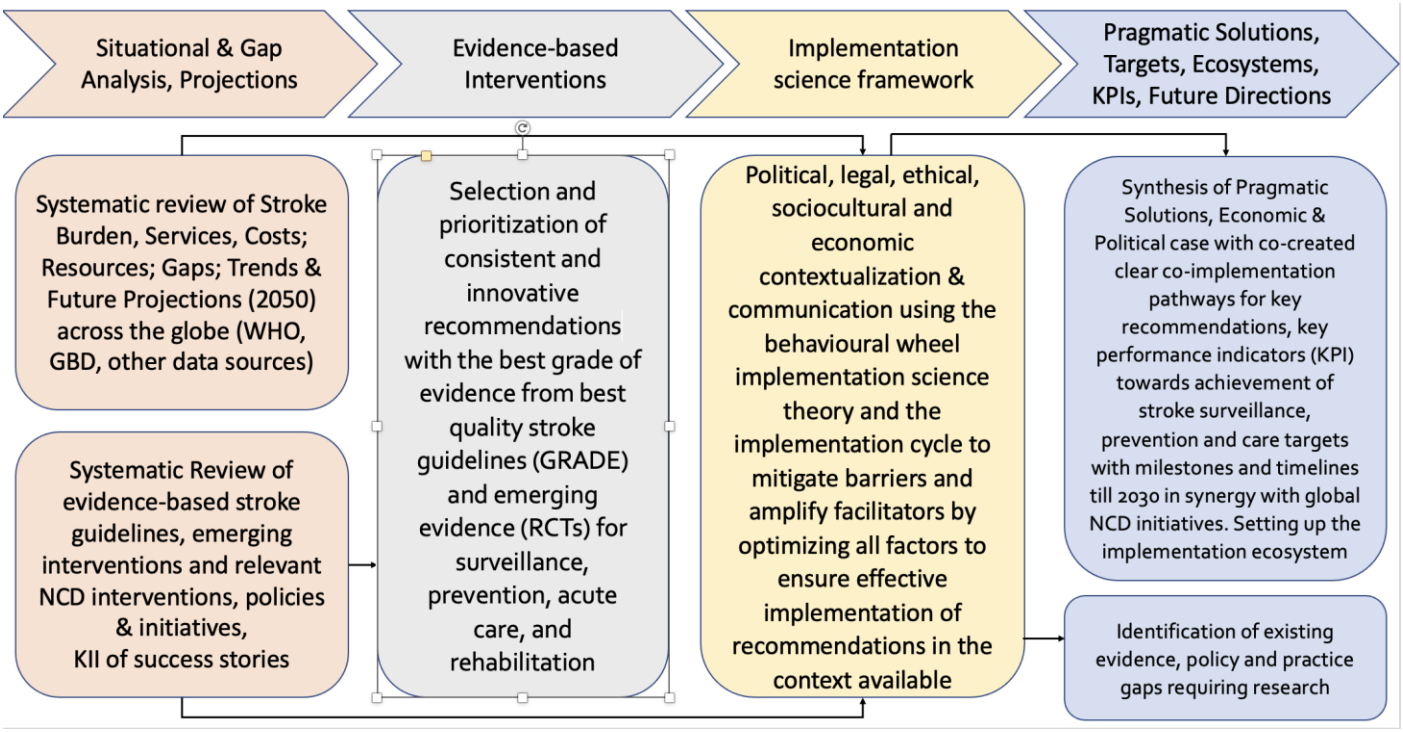
Figure 1: Manuscript stroke sections/topics interconnections



This figure shows the interconnections and harmony among the seven sections of the manuscript depicting the four sections of the stroke quadrangle (surveillance, prevention, acute care and rehabilitation) as well as organization of supporting health systems and resources.

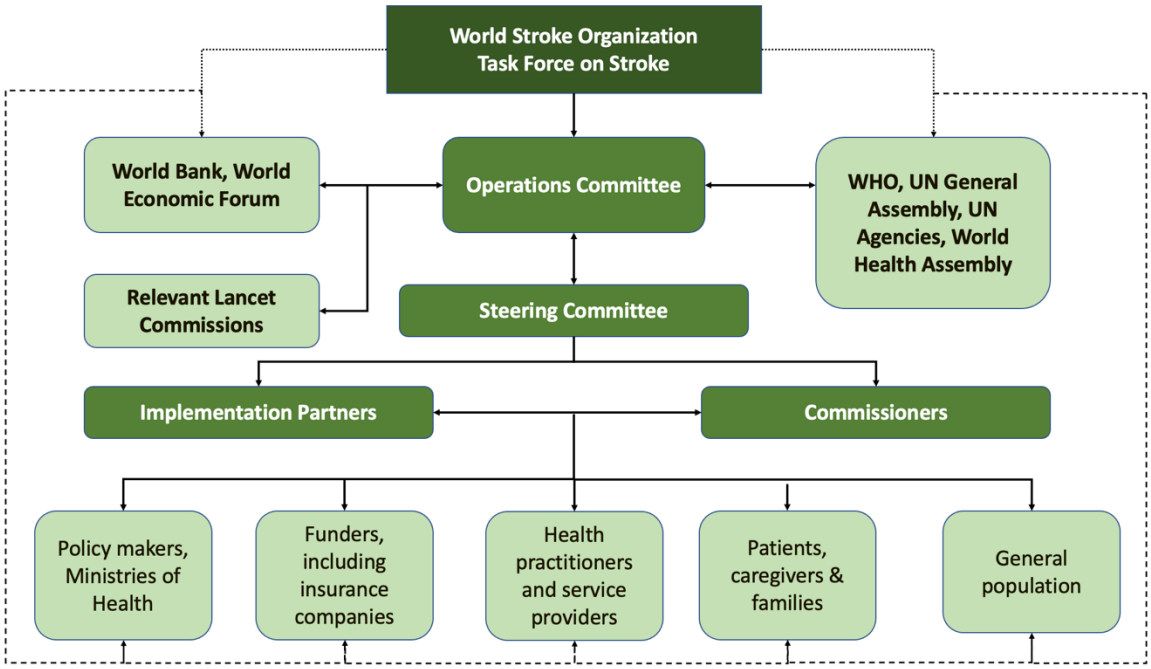
1. Establishing a framework for regular monitoring and evaluation of stroke and its risk factors and health services at a national level via community-based surveys, data linkage and electronic health records (Burden [incidence, prevalence, mortality, DALY]; Trends; Determinants of diseases and disease outcome: causes/risk factors [genomic, environmental]; (provide evidence for planning and designing interventions)
2. Implementation of integrated population-wide strategies to reduce modifiable risk factors, such as hypertension and diabetes mellitus, with a range of approaches such as task-shifting and mobile technology [Primordial, Primary, Secondary]; (reduce incidence, mortality & prevalence)
3. Effective planning of acute stroke care services, workforce training and capacity building, with monitoring of quality indicators nationally [Early and accurate diagnosis and presentation; Drug and non-drug treatment; Prognostication]; (reduce mortality)
4. Promoting access to interdisciplinary care, training for caregivers, and capacity building of community health workers and other healthcare providers for stroke rehabilitation. (Improve DALYs, improve health-related Quality of Life)
5. Global stroke burden estimates (including forecast) via Global Burden of Disease, Injury and Risk in 204 countries
6. Health economic estimates of the current and projected cost of stroke
7. Health system engineering, training, capacity building

Figure 2: Methodological workflow for deriving pragmatic solutions to reduce the global burden of stroke



WHO – World Health Organization. GBD – Global Burden of Disease, Injury and Risk Factors Study. NCD – non-communicable diseases. RCTs – randomised controlled trials. KPI – key performance indicators. WSO – World Stroke Organization.

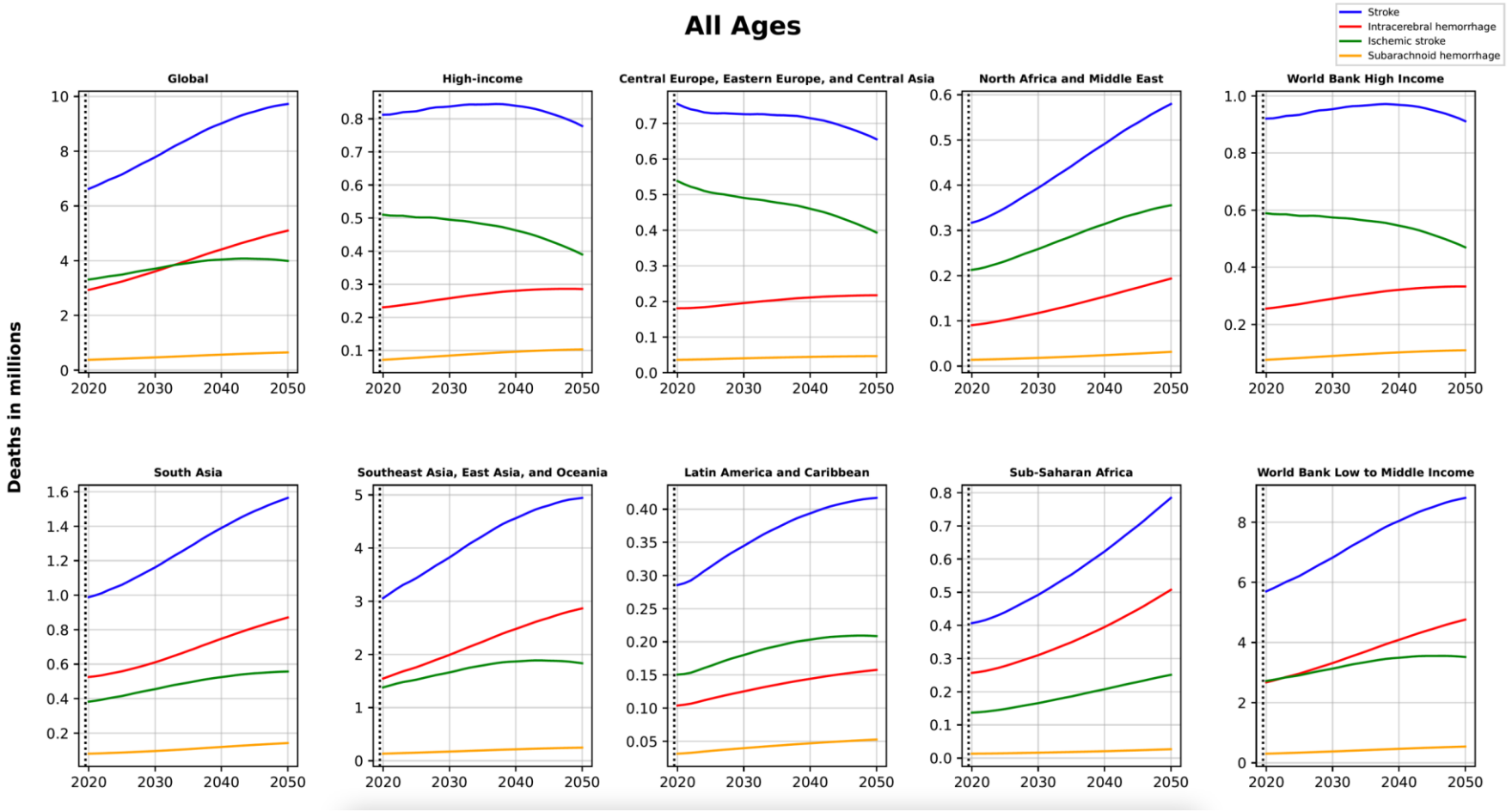
Figure 3: Ecosystem for the management, implementation and dissemination of tangible actions to reduce stroke burden in the world (interactive implementation cycle)



Led by the WSO Task Force on Stroke, partners of the Commission will include the WHO, WHF, WFN, NCD Alliance, Global Circulatory Health, Ministries of Health, and national Stroke Support Organizations. Implementation partners include Ministries of Health. The World Bank and other funders/philantropists will be approached for funding and support. Performance indicators are to be developed and monitored using Theory of Change approach. Adapted versions of the global ecosystem can be developed as regional and national ecosystems to suit the respective implementation environments. WSO-Lancet Neurology Commision on Stroke Commissioners will be country ambassadors. Criteria for selection of commissioners are:

1	Expertise	Stroke medicine or related fields/sectors including neurology, neurosurgery, neurorehabilitation, speech therapy, physiotherapy, psychotherapy, health economics, food value chain, public health, health education, communication sector, legal, information technology, and education sector, etc. Relevance to stroke had to be justified.
2	Keen Interest	Track record in stroke-related work and personal statement articulating the potential commissioner's skills, motivation, and action plan.
3	Nomination	Nomination by a member of the WSO Task Force on Stroke, WSO-Lancet Neurology Commission Steering Committee or nomination by the national stroke society, or self-nomination supported by a member of the WSO Task Force on Stroke, WSO-Lancet Neurology Commission Steering Committee in the relevant WHO world region.

Figure 4. Forecasts of stroke deaths (counts and age-standardized rates per 100,000 person-years (with 95% UI) globally by stroke pathological type (ischaemic stroke, intracerebral haemorrhage, subarachnoid haemorrhage, total strokes), GBD regions and World Bank country income level, 2020-2050



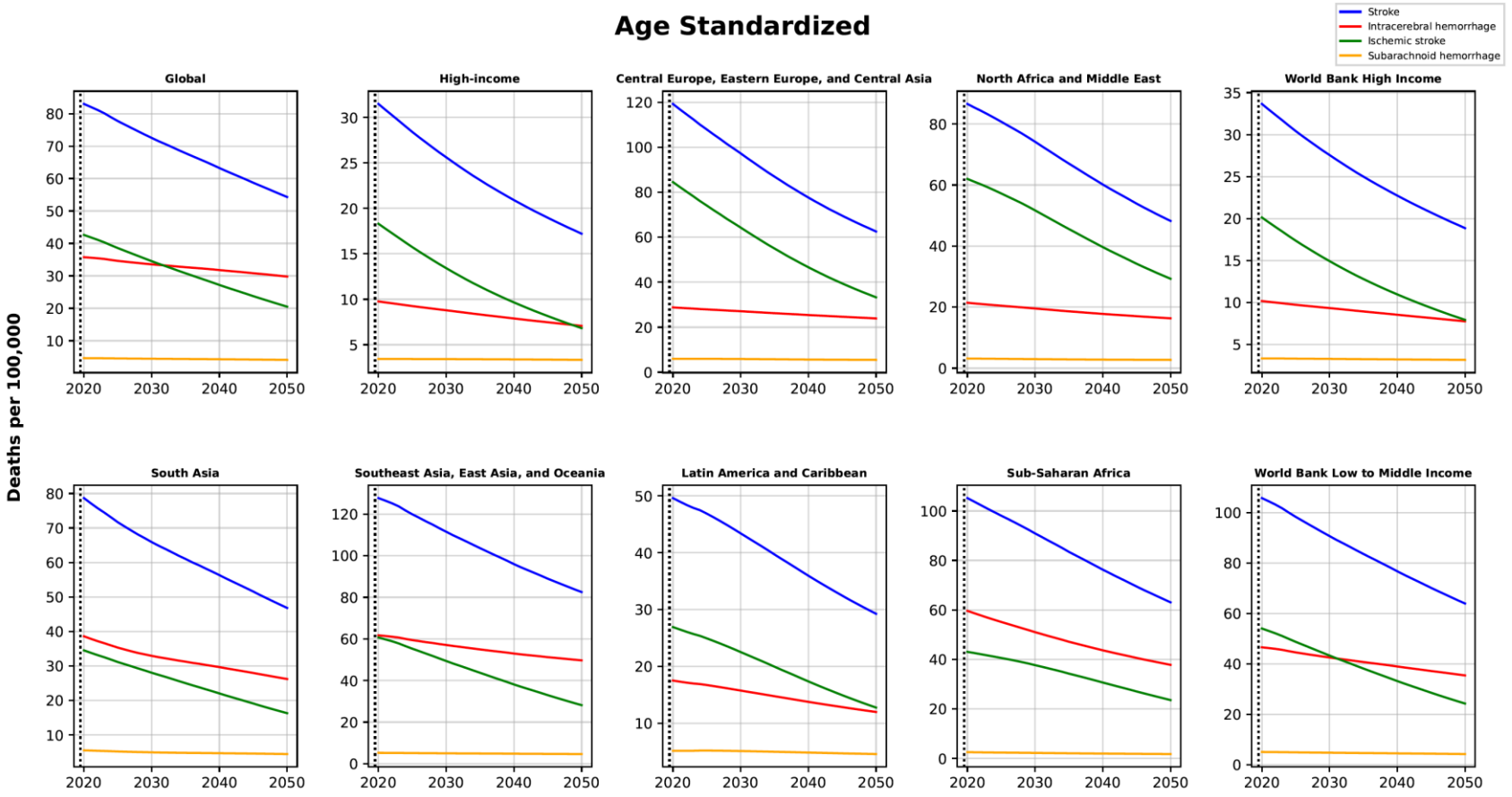
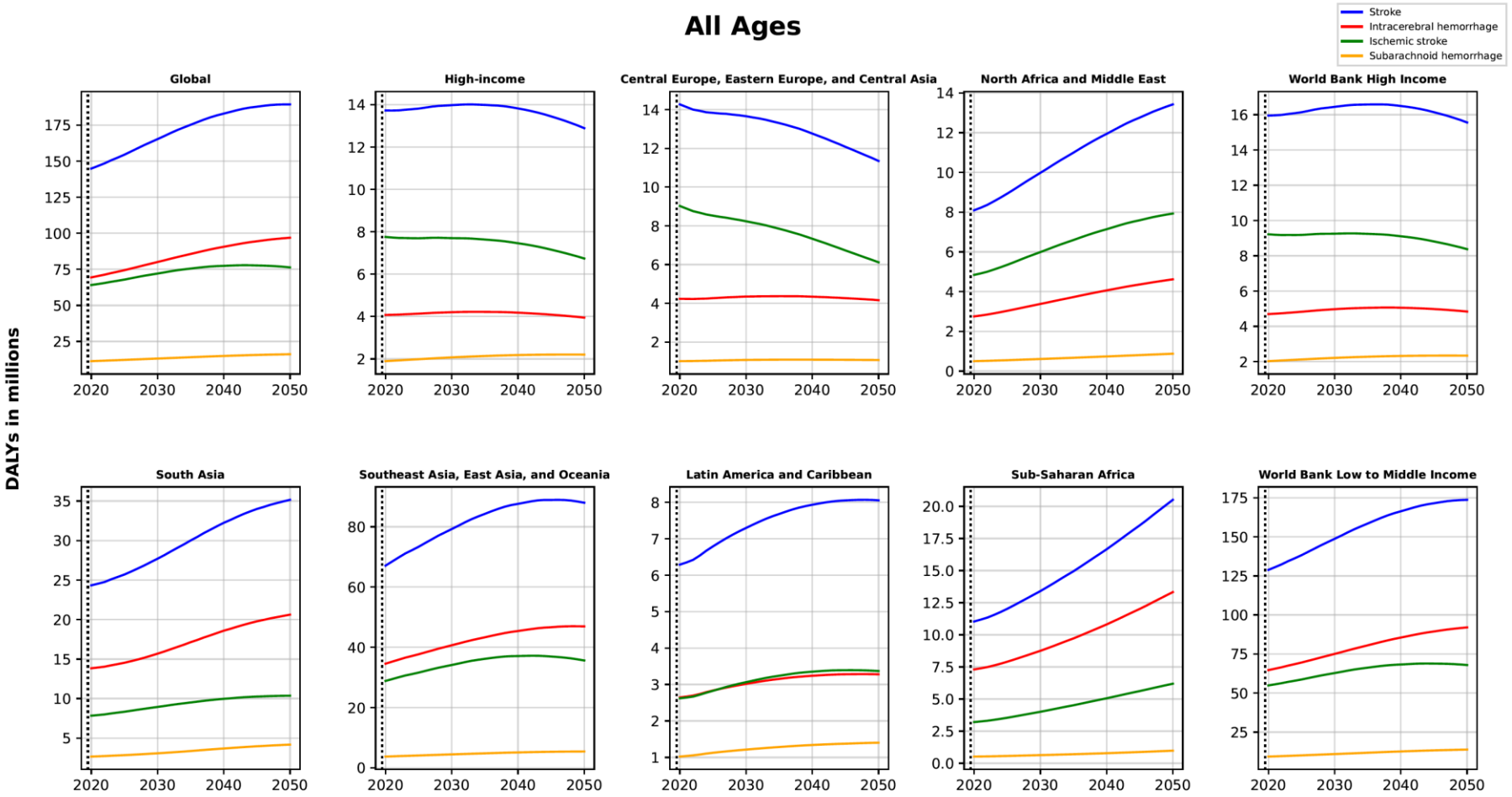

Age Standardized
Stroke
Intracerebral hemorrhage
Ischemic stroke
Subarachnoid hemorrhage
Deaths per 100,000
Global
High-income
Central Europe, Eastern Europe, and Central Asia
North Africa and Middle East
World Bank High Income
South Asia
Southeast Asia, East Asia, and Oceania
Latin America and Caribbean
Sub-Saharan Africa
World Bank Low to Middle Income

Figure 5. Forecasts of stroke DALYs (counts and age-standardized rates per 100,000 person-years (with 95% UI) globally by stroke pathological type (ischaemic stroke, intracerebral haemorrhage, subarachnoid haemorrhage, total strokes), GBD regions and World Bank country income level, 2020-2050



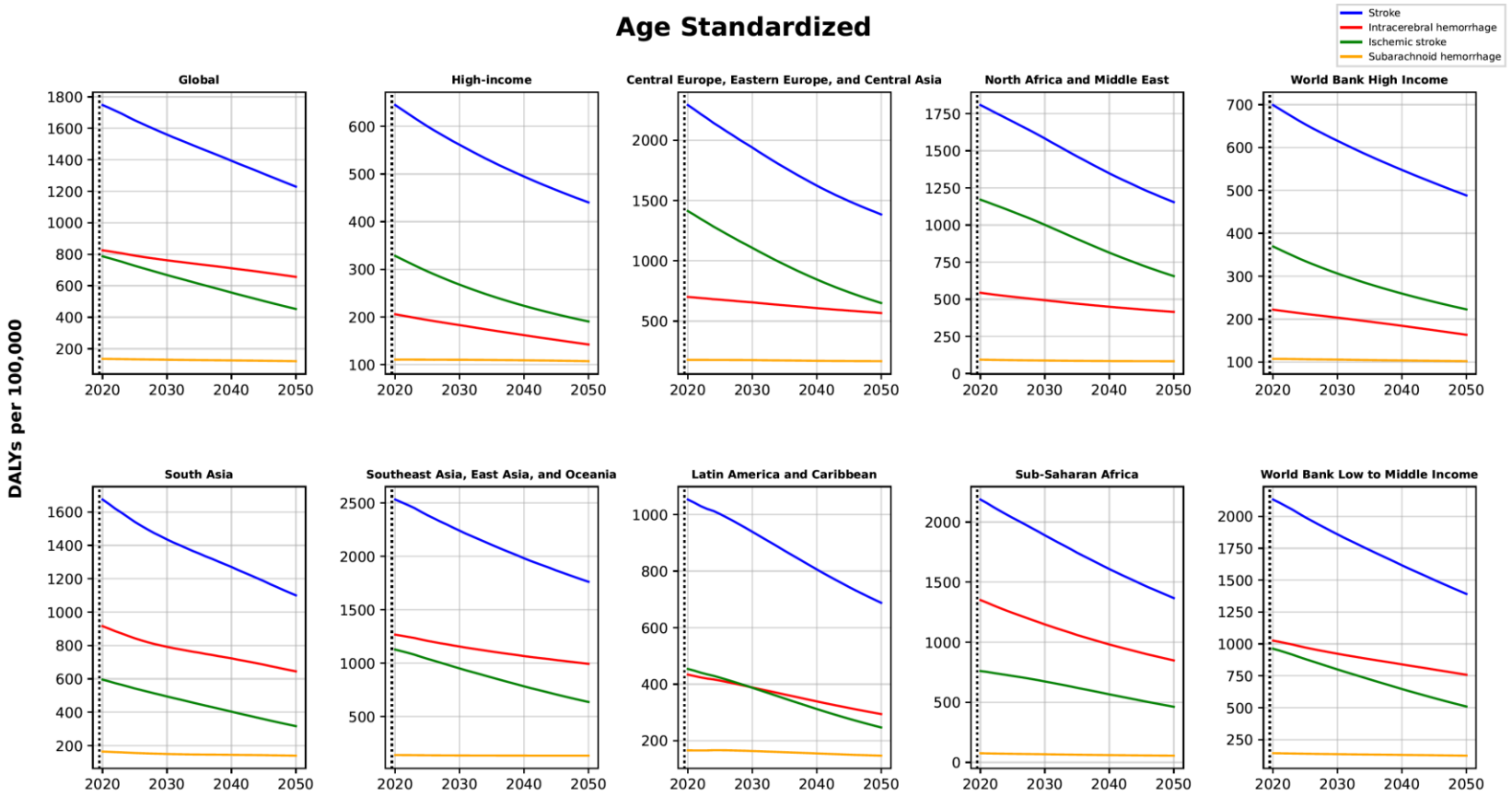

Age Standardized
Stroke
Intracerebral hemorrhage
Ischemic stroke
Subarachnoid hemorrhage
DALYs per 100,000
Global
High-income
Central Europe, Eastern Europe, and Central Asia
North Africa and Middle East
World Bank High Income
South Asia
Southeast Asia, East Asia, and Oceania
Latin America and Caribbean
Sub-Saharan Africa
World Bank Low to Middle Income

Figure 6. Heat map showing capacities for national surveillance of risk factors for stroke around the world.

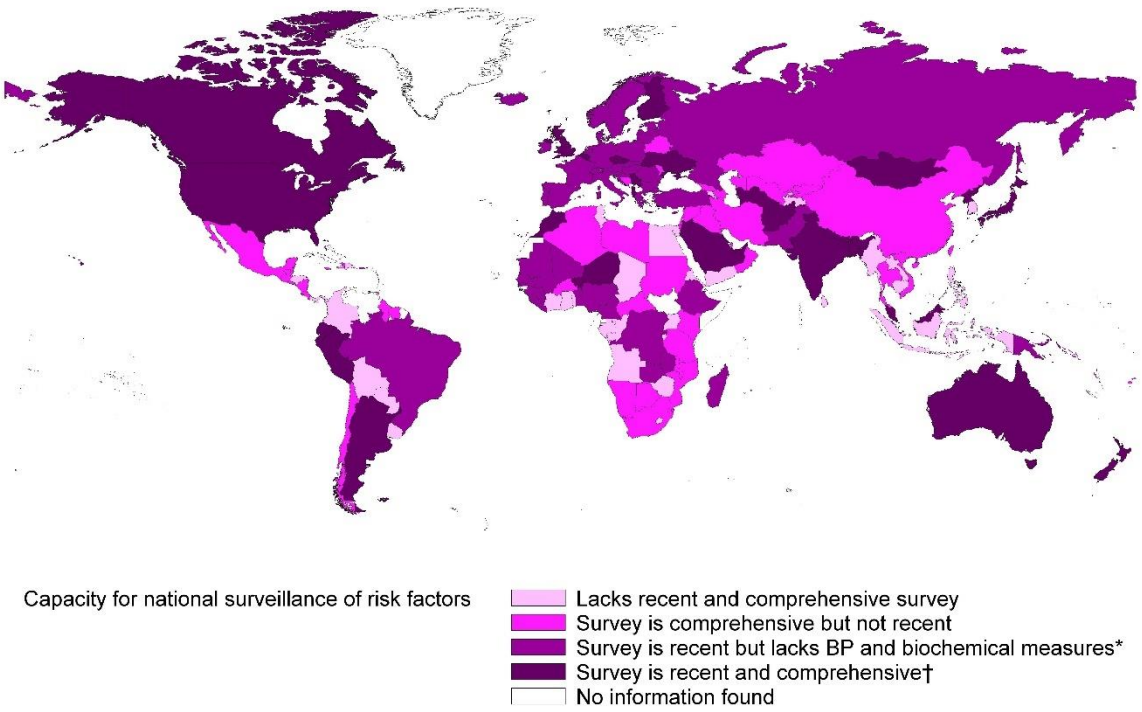
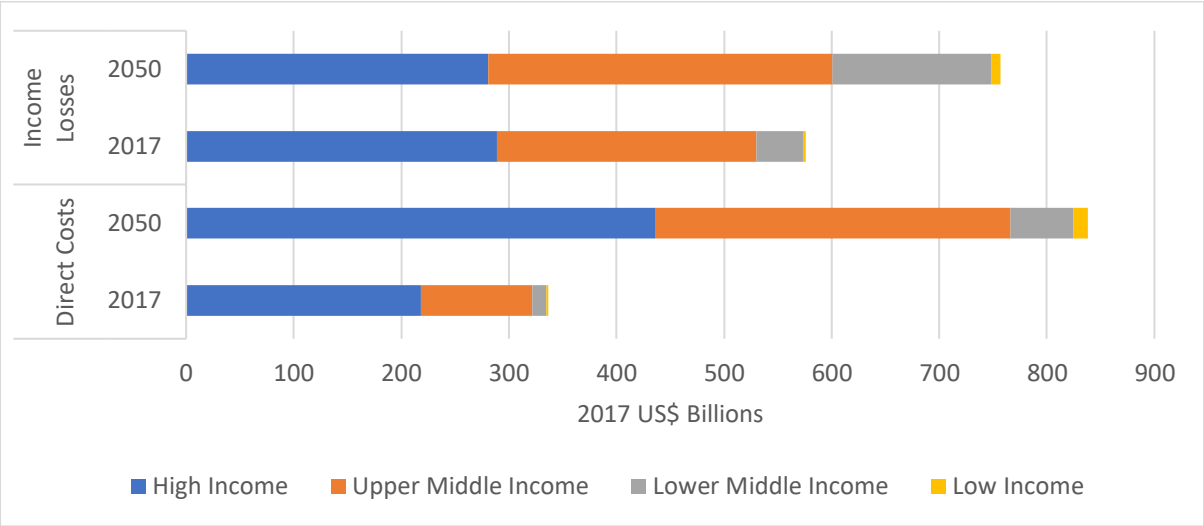


Figure 7. Economic costs of stroke, by World Bank Regions, 2017 versus 2050 (billions of 2017 US$)



Note: Estimated direct costs and income losses are based on the regional means of the ranges reported in Tables 2 and 3.

Figure 8. Diagram of major strategies for stroke risk factors control at the population and individual levels showing overlap between various primordial, primary and secondary prevention strategies

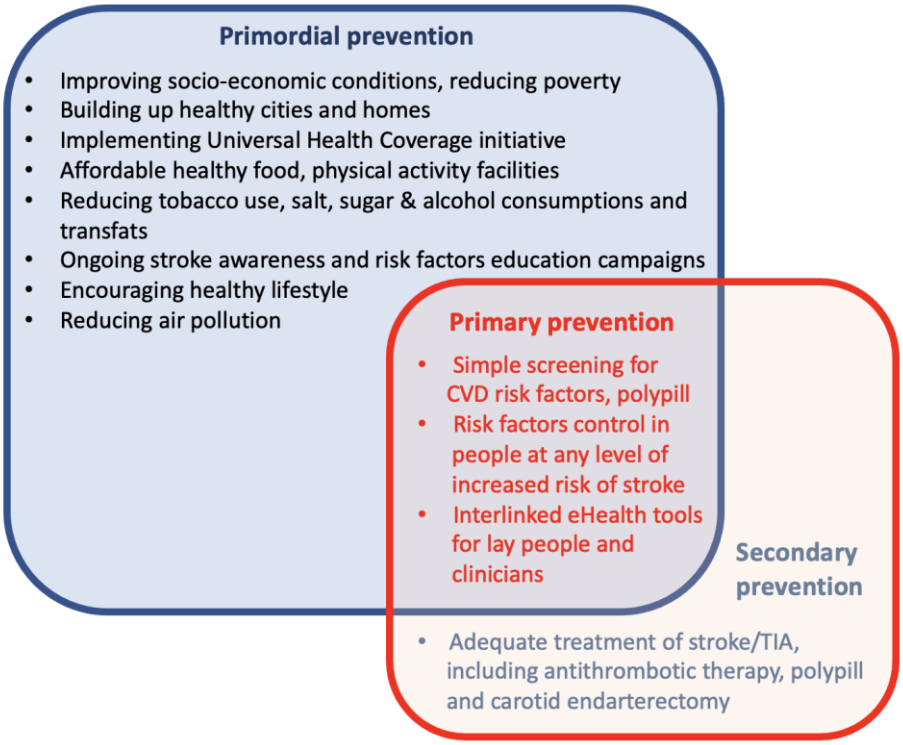


Table 1: Forecasts of global stroke deaths and DALYs (counts and rates per 100,000 person-years, with 95% UI) by age group (total, under 60 years old, 60+ years old) and year (2020 and 2050)

Outcome	Year	Age group	Metric	Counts/rates (95% UI)
Deaths	2020	All ages	Rates	84.89 (77.14-91.57)
	2050			105.18 (87.28-125.75)
	2020	Age-standardized rates		83.00 (75.32-89.61)
	2050			54.31 (44.39-66.34)
	2020	Age-standardized rates in under 60 years old		13.31 (12.10-14.47)
	2050			9.93 (7.16-13.65)
	2020	Age-standardized rates in 60+ years old		565.65 (508.59-613.37)
	2050			361.69 (299.07-431.89)
	2020	All ages	Counts	6.62 (6.02-7.14)
	2050			9.72 (8.07-11.62)
	2020	Under 60 years old		1.00 (0.91-1.09)
	2050			0.98 (0.71-1.34)
	2020	60+ years old		5.62 5.08-6.09)
	2050			8.75 (7.29-10.37)
DALYs	2020	All ages	Rates	1856.63 (1716.88-2010.86)
	2050			2048.32 (1750.41-2432.64)
	2020	Age-standardized rates		1747.70 (1612.34-1892.47)
	2050			1229.16 (1029.90-1477.44)
	2020	Age-standardized rates in under 60 years old		700.94 (638.28-767.75)
	2050			649.85 (511.34-825.96)
	2020	Age-standardized rates in 60+ years old		9184.71 (8392.76-9959.58)
	2050			6795.05 (5890.94-7887.75)
	2020	All ages	Counts	144.84 (133.94-156.88
	2050			189.36 (161.82-224.88)
	2020	Under 60 years old		47.24 (43.01-51.54)
	2050			46.40 (36.51-58.98)
	2020	60+ years old		97.61 (89.20-105.85)
	2050			142.95 (123.93-165.94)

Table 2: Forecasts of stroke deaths and DALYs (counts and rates per 100,000 person-years, with 95% UI) by age group (total, under 60 years old, 60+ years old), World Bank economic level (high-income countries, low- to middle-income countries) and year (2020 and 2050)

HIGH INCOME COUNTRIES					LOW- TO MIDDLE-INCOME COUNTRIES				
Year	**Age group**	**Outcome**	**Metric**	**Mean (95% UI)**	**Year**	**Age group**	**Outcome**	**Metric**	**Mean (95% UI)**
2020	All ages	Deaths	Rates	75.97 (64.96-83.79)	2020	All ages	Deaths	Rates	86.50 (78.04 -93.82)
2050				73.80 (60.26-85.93)	2050				109.95 (90.71-132.50)
2020	Age-standardized rates			33.65 (29.10-36.88)	2020	Age-standardized rates			105.82 (95.25-115.00)
2050				28.86 (15.71-22.24)	2050				64.00 (52.48-77.90)
2020	Age-standardized rates in under 60 years old			4.20 (3.92-4.48)	2020	Age-standardized rates in under 60 years old			15.37 (13.89-16.78)
2050				3.15 (2.46-4.13)	2050				10.95 (7.88-15.15)
2020	Age-standardized rates in 60+ years old			237.65 (203.36-262.05)	2020	Age-standardized rates in 60+ years old			732.10 (658.72-798.25)
2050				127.68 (104.70-148.94)	2050				431.31 (358.28-514.82)
2020	All ages		Counts	0.92 (0.79-1.02)	2020	All ages		Counts	5.70 (5.14-6.18)
2050				0.91 (0.74-1.06)	2050				8.81 (7.27-10.61)
2020	Under 60 years old			0.06 (0.05-0.06)	2020	Under 60 years old			0.94 (0.85-1.03)
2050				0.04 (0.03-0.05)	2050				0.93 (0.67-1.29)
2020	60+ years old			0.86 (0.73-0.95)	2020	60+ years old			4.76 (4.28-5.18)
2050				0.87 (0.71-1.01)	2050				7.87 (6.53-9.37)
2020	All ages	DALYs	Rates	1316.64 (1181.93-1435.60)	2020	All ages	DALYs	Rates	1954.66 (1798.69-2120.66)
2050				1260.12 (1075.75-1438.24)	2050				2168.44 (1832.77-2593.39)
2020	Age-standardized rates			699.00 (629.87-761.14)	2020	Age-standardized rates			2131.91 (1964.62-2315.49)
2050				488.27 (415.02-570.08)	2050				1391.95 (1161.26-1678.44)
2020	Age-standardized rates in under 60 years old			248.23 (224.59-275.23)	2020	Age-standardized rates in under 60 years old			754.92 (684.66-824.59)
2050				200.28 (166.50-245.64)	2050				533.28 (414.75-682.72)

2020	Age-standardized rates in 60+ years old			3820.45 (3413.56-4172.29)	2020	Age-standardized rates in 60+ years old			11896.98 (10830.18-12957.13)
2050				2482.53 (2125.54-2827.26)	2050				7337.88 (6301.95-8588.15)
2020	All ages		Counts	15.95 (14.32-17.39)	2020	All ages		Counts	128.81 (118.53-139.75)
2050				15.56 (13.28-17.76)	2050				173.68 (146.80-207.72)
2020	Under 60 years old			3.22 (2.93-3.55)	2020	Under 60 years old			43.98 (39.89-48.04)
2050				2.43 (2.04-2.97)	2050				43.93 (34.29-56.03)
2020	60+ years old			12.74 (11.27-13.95)	2020	60+ years old			84.83 (77.36-92.39)
2050				13.12 (11.18-14.84)	2050				129.75 (111.89-151.42)

Table 3: Forecasts of stroke related deaths (counts and rates per 100,000 person-years, with 95% UI) by age group (total, under 60 years old, 60+ years old), GBD super-regions and year (2020 and 2050)

GBD super-region	Metric	Year	All ages	Age-Standardized (AS) Mean (95% UI)	Under 60 years old	60+ years old
			Mean (95% UI)		Mean (95% UI) (Rates reported as AS)	Mean (95% UI) (Rates reported as AS)
Southeast Asia, East Asia, and Oceania	Counts	2020	3.06 (2.62-3.46)		0.44 (0.38-0.50)	2.62 (2.23-2.96)
		2050	4.94 (4.09-5.90)		0.30 (0.22-0.37)	4.65 (3.83-5.51)
	Rates	2020	141.27 (121.11-159.81)	127.68 (108.49-144.44)	16.85 (14.51-19.24)	895.16 (761.93-1014.07)
		2050	232.25 (192.44-277.01)	82.54 (68.37-98.42)	12.39 (9.35-15.59)	568.34 (467.50-677.61)
Central Europe, Eastern Europe, and Central Asia	Counts	2020	0.75 (0.68-0.83)		0.07 (0.07-0.08)	0.68 (0.61-0.75)
		2050	0.66 (0.56-0.77)		0.04 (0.03-0.07)	0.61 (0.52-0.71)
	Rates	2020	180.57 (162.50-198.46)	119.26 (107.35-131.04)	15.71 (13.89-17.55)	836.25 (751.08-917.84)
		2050	164.32 (140.17-192.41)	62.53 (51.83-75.21)	10.98 (6.89-16.45)	419.53 (357.46-492.06)
High-income regions	Counts	2020	0.81 (0.69-0.91)		0.05 (0.04-0.05)	0.77 (0.64-0.86)
		2050	0.78 (0.64-0.86)		0.03 (0.03-0.04)	0.75 (0.61-0.86)
	Rates	2020	74.69 (63.41-83.43)	31.49 (27.14-34.92)	3.66 (3.45-3.93)	224.15 (190.90-250.25)
		2050	69.50 (56.73-80.64)	17.21 (14.17-20.20)	2.80 (2.18-3.61)	116.96 (96.01-136.27)
Latin America and Caribbean	Counts	2020	0.29 (0.25-0.32)		0.05 (0.05-0.07)	0.23 (0.20-0.26)
		2050	0.42 (0.32-0.55)		0.05 (0.03-0.08)	0.37 (0.28-0.48)
	Rates	2020	48.58 (43.00-53.88)	49.61 (43.68-54.98)	9.07 (8.07-10.24)	330.39 (285.51-367.33)

		2050	61.80 (46.78-80.77)	29.26 (21.48-39.93)	6.49 (4.08-10.31)	186.95 (140.68-246.18)
North Africa and Middle East	Counts	2020	0.32 (0.28-0.36)		0.07 (0.06-0.08)	0.25 (0.22-0.28)
		2050	0.57 (0.43-0.80)		0.08 (0.05-0.12)	0.50 (0.38-0.67)
	Rates	2020	51.42 (45.70-57.70)	86.57 (77.13-96.40)	12.94 (10.83-15.52)	596.41 (531.95-660.90)
		2050	71.37 (52.93-98.35)	48.23 (36.12-65.80)	9.34 (6.05-14.37)	317.51 (243.27-418.31)
Sub-Saharan Africa	Counts	2020	0.41 (0.36-0.46)		0.11 (0.09-0.13)	0.30 (0.26-0.33)
		2050	0.78 (0.64-0.94)		0.18 (0.13-0.26)	0.60 (0.50-0.69)
	Rates	2020	36.80 (32.30-41.65)	105.19 (92.64-118.00)	17.20 (14.15-20.43)	714.50 (625.28-798.08)
		2050	38.62 (31.51-46.47)	63.06 (52.63-73.21)	11.07 (8.01-15.37)	423.04 (357.14-484.48)
South Asia	Counts	2020	0.99 (0.85-1.15)		0.21 (0.18-0.25)	0.78 (0.67-0.90)
		2050	1.56 (1.18-2.04)		0.29 (0.19-0.44)	1.27 (0.97-1.62)
	Rates	2020	54.30 (46.78-63.19)	78.65 (67.53-91.29)	14.49 (12.34-17.01)	522.96 (447.36-605.91)
		2050	75.24 (56.80-98.17)	46.82 (35.04-61.58)	11.14 (7.30-17.00)	293.92 (222.43-374.88)

Table 4: Forecasts of stroke related DALYs (counts and rates per 100,000 person-years, with 95% UI) by age group (total, under 60 years old, 60+ years old), GBD super-regions and year (2020 and 2050)

GBD super-region	Metric	Year	All ages Counts/rates (95% UI)	Age-Standardized (AS) rates (95% UI)	Under 60 years old Mean (95% UI) (Rates reported as AS)	60+ years old Mean (95% UI) (Rates reported as AS)
Southeast Asia, East Asia, and Oceania	Counts	2020	67.10 (58.43-75.85)		20.14 (17.56-22.99)	46.95 (40.65-53.10)
		2050	87.98 (74.61-103.26)		13.93 (11.08-17.13)	74.06 (62.82-86.76)
	Rates	2020	3098.72 (2698.22-3503.00)	2531.07 (2210.74-2852.43)	800.34 (695.10-911.04)	14515.87 (12576.37-16386.97)
		2050	4133.29 (3505.36-4851.04)	1760.79 (1481.49-2070.58)	616.17 (486.88-760.68)	9686.91 (8255.21-11348.06)
Central Europe, Eastern Europe, and Central Asia	Counts	2020	14.27 (12.85-15.64)		3.35 (2.98-3.76)	10.92 (9.86-11.94)
		2050	11.35 (9.72-13.10)		2.15 (1.59-2.86)	9.20 (8.09-10.40)
	Rates	2020	3415.23 (3075.35-3742.91)	2292.02 (2064.62-2511.35)	739.83 (655.81-829.48)	13040.44 (11771.67-14273.44)
		2050	2844.59 (2435.30-3283.44)	1384.40 (1148.25-1660.84)	548.22 (401.81-739.17)	7174.71 (6260.53-8178.47)
High-income regions	Counts	2020	13.72 (12.28-14.96)		2.54 (2.30-2.83)	11.17 (9.89-12.27)
		2050	12.89 (10.93-14.57)		1.99 (1.67-2.41)	10.89 (9.31-12.32)
	Rates	2020	1261.84 (1129.63-1375.59)	644.58 (578.00-706.37)	220.88 (199.20-247.14)	3578.56 (3178.25-3923.08)
		2050	1150.90 (976.25-1300.84)	440.32 (375.18-507.88)	181.82 (150.95-222.68)	2230.38 (1893.56-2519.85)
Latin America and Caribbean	Counts	2020	6.29 (5.69-6.96)		2.40 (2.13-2.69)	3.89 (3.49-4.32)
		2050	8.05 (6.47-10.20)		2.26 (1.66-3.20)	5.79 (4.71-7.09)

	Rates	2020	1069.91 (951.33-1166.16)	1053.01 (951.34-1166.16)	432.15 (383.19-484.38)	5352.31 (4787.79-5951.93)
		2050	1193.46 (958.46-1511.55)	687.61 (539.05-900.33)	319.56 (231.30-460.02)	3236.32 (2639.65-4016.78)
North Africa and Middle East	Counts	2020	8.10 (7.15-9.10)		3.60 (3.03-4.23)	4.50 (4.02-4.93)
		2050	13.42 (10.51-17.50)		4.11 (2.95-5.78)	9.31 (7.45-11.96)
	Rates	2020	1313.40 (1159.24-1476.81)	1807.75 (1596.44-2017.88)	666.19 (561.98-781.43)	9712.70 (8694.54-10725.79)
		2050	1653.14 (1294.32-2154.86)	1154.33 (895.49-1521.04)	501.50 (358.19-710.24)	5674.98 (4573.65-7234.60)
Sub-Saharan Africa	Counts	2020	11.04 (9.57-12.59)		5.39 (4.56-6.33)	5.64 (4.99-6.31)
		2050	20.51 (16.89-24.98)		9.07 (6.90-12.08)	11.43 (9.86-13.04)
	Rates	2020	998.46 (865.76-1138.49)	2187.52 (1927.11-2473.86)	788.34 (666.08-924.39)	11876.43 (10522.85-13271.60)
		2050	1009.79 (831.57-1229.82)	1367.36 (1151.33-1606.96)	533.78 (407.41-709.48)	6576.47 (5670.19-7498.59)
South Asia	Counts	2020	24.33 (21.40-28.18)		9.80 (8.50-11.43)	14.53 (12.65-16.89)
		2050	35.16 (27.82-45.23)		12.89 (9.50-17.72)	22.26 (17.97-27.69)
	Rates	2020	1336.09 (1174.54-1547.30)	1674.76 (1467.14-1945.97)	649.37 (562.23-758.80)	8775.28 (7640.72-10189.38)
		2050	1690.59 (1338.26-2175.00)	1100.40 (865.51-14.25.27)	515.61 (379.82-711.18)	5149.84 (4149.83-6403.86)

Table 5: Global forecasts of stroke related deaths and DALYs (counts and age-standardized rates per 100,000 person-years, with 95% UI) by stroke type (IS – ischaemic stroke, ICH – intracerebral haemorrhage, SAH – subarachnoid haemorrhage), age group (total, under 60 years old, 60+ years old), and year (2020 and 2050)

Type of stroke	Year	Metric	Projected estimates of deaths: Mean (95% UI)			Projected estimates of DALYs: Mean (95% UI)		
			Under 60 years	60+ years	Total	Under 60 years	60+ years	Total
IS	2020	Counts	0.18 (0.16-0.21)	3.12 (2.81-3.38)	3.31 (2.98-3.58)	11.42 (9.81-13.09)	52.70 (47.57-57.67)	64.11 (57.47-70.40)
	2050		0.11 (0.08-0.17)	3.87 (3.21-4.60)	4.00 (3.29-4.75)	9.42 (7.33-11.81)	66.91 (56.56-78.28)	76.33 (64.25-89.78)
	2020	Age-standardized rates	2.45 (2.17-2.74)	320.77 (286.71-347.95)	42.62 (38.23-46.20)	153.88 (132.32-176.66)	5170.52 (4665.88-5662.86)	786.92 (706.13-864.10)
	2050		1.16 (0.77-1.72)	154.46 (127.28-184.80)	20.50 (16.81-24.68)	101.42 (78.77-127.76)	2881.74 (2423.50-3389.98)	452.26 (376.72-535.54)
ICH	2020	Counts	0.68 (0.61-0.74)	2.25 (2.01-2.45)	2.93 (2.65-3.19)	29.25 (26.41-31.99)	40.15 (36.52-43.54)	69.40 (63.54-75.35)
	2050		0.70 (0.56-0.89)	4.39 (3.82-4.95)	5.10 (4.42-5.78)	29.57 (23.32-37.67)	67.32 (58.24-77.27)	96.90 (82.66-113.95)
	2020	Age-standardized rates	10.08 (9.06-10.97)	212.06 (189.37-230.59)	35.75 (32.20-38.85)	393.75 (355.16-430.37)	3811.23 (3462.76-4133.93)	824.99 (756.20-895.45)
	2050		9.86 (7.78-12.53)	208.80 (181.83-235.46)	29.78 (35.70-34.29)	308.55 (241.47-397.86)	3063.13 (2636.05-3545.24)	656.14 (551.13-778.87)
SAH	2020	Counts	0.13 (0.11-0.16)	0.25 (0.21-0.27)	0.38 (0.33-0.42)	6.57 (5.66-7.78)	4.76 (4.20-5.26)	11.33 (9.96-12.78)
	2050		0.16 (0.10-0.23)	0.49 (0.35-0.68)	0.65 (0.47-0.89)	7.41 (4.69-10.86)	8.71 (6.18-12.03)	16.12 (11.19-22.66)
	2020		1.81 (1.55-2.17)	24.16 (20.90-26.72)	4.63 (4.07-5.15)	90.00 (77.50-106.87)	452.89 (400.11-499.95)	135.79 (119.63-153.19)

	2050	Age-standardized rates	1.63 (1.03-2.46)	21.15 (15.03-29.17)	4.09 (2.87-5.68)	80.32 (50.56-118.35)	400.71 (280.68-555.91)	120.75 (81.48-172.88)

Table 6: Direct costs and income losses due to stroke in 2017 and 2050 (in billions 2017 US$)

World Bank country classification by income level	**2017 (Low)**	**2017 (High)**	**2050 (Low)**	**2050 (High)**
High-Income countries	417.0	597.6	436.6-655.9	578.3-997.0
Upper Middle-Income countries	279.1	410.0	273.5-743.6	334.2-1,026.4
Lower Middle-Income countries	48.3	64.8	159.5-200.4	170.4-252.5
Low Income countries	2.6	4.9	11.2-22.0	13.5-34.1
Global Total	745.9	1,077.2	880.8-1,621.9	1,096.4-2,310.0

Note: Direct costs are due to incident stroke cases and deaths in 2017 and 2050 and are calculated using the methodology described elsewhere.[5] 2017 estimates comprise the low- and high-scenario estimates[5] in Table 4 of the Supplementary Appendix. Low estimates for 2050 assume that costs of treatment and rehabilitation grow at 1% above non-medical inflation, with the range reflecting the high- and low-cost estimates for acute and post-acute care as in Table 3 of the Supplementary Appendix in Owolabi et al.[5] High estimates for 2050 assume that costs of treatment and rehabilitation grow at 3% above non-medical inflation, with the range reflecting the high- and low-cost estimates for acute and post-acute care as in Table 3 of the Supplementary Appendix in Owolabi et al.[5]

Table 7: Key recommendations for improving stroke surveillance

Key recommendations	Source	Resources required	implications /Barriers/Facilitators, for LMICs	Recommendation for contextualization and implementation through WSO Task Force on Stroke
Countries should have a nationwide and representative system for monitoring stroke.	WHO – Global Action Plan on Epilepsy and other Neurological Disorders, target 4.1	Expertise in epidemiology, data management and statistics to support ongoing monitoring of stroke.[235]	Major barriers include lack of: a) infrastructure to support a monitoring program b) expertise to develop an efficient program c) capacity to analyse the data collected and produce quality statistics d) community engagement and feedback of data to enhance demand and accountability; and e) use of data to drive decision-making. f) need for standardized and validated indicators of stroke burden from linked datasets	WSO Task Force on Stroke commissioners to develop, implement and monitor strategic action plan with all stakeholders to ensure availability of a high-quality monitoring of stroke in their countries and regions. This should include a stepped approach that highlights the elements required for minimum (hospitalized events), essential and advanced monitoring, i.e. incorporating the WHO stepwise approach, or similar.
Countries should have a nationwide monitoring program of risk factors for stroke.	WHO - Global Action Plan on Epilepsy and other Neurological Disorders, strategic objective 3, proposed action 88b; NCD-GAP; 2030 Agenda	Expertise in epidemiology, data management and statistics to support a regular cycle of national surveys and analysis.[235]	Major barriers include lack of: a) Infrastructure to support a surveillance program. b) expertise to develop an efficient program c) capacity to analyse the data collected and produce quality statistics. d) community engagement and feedback of data to enhance demand and accountability; and e) use of data to drive decision-making.	WSO Task Force on Stroke commissioners to develop, implement and monitor strategic action plan with all stakeholders to ensure availability of a high-quality surveillance system in their countries and regions. This should include a stepped approach that highlights the elements required for minimum, essential and advanced surveillance, i.e. incorporating the WHO stepwise approach, or similar.
Countries should have an electronic recording and reporting system for health care.	WHO – Global Strategy on Digital Health 2020-25; Global Action Plan on Epilepsy and other Neurological	Expertise in development and maintenance of secure online data to support rapid and simple	Major barriers include lack of: a) infrastructure to support an electronic data system b) expertise to develop and maintain a secure record-keeping system	WSO Task Force on Stroke commissioners to develop, implement and monitor strategic action plan with all stakeholders to ensure availability of a secure data record system in their countries and regions. This could include the employment of Community Health Workers to register people in the community; this

	Disorders, strategic objective 4.2 Data and information systems	input of patient-relevant data.	c) expertise to link data to other collection systems, e.g., death records, to enable assessment of outcomes; and d) need for expertise in clinical coding including use of WHO ICD system e) develop tools to increase quality and coverage of mortality data including verbal autopsy	would include a capacity-building component to train them in use of technology, transport to enable collection of information, and appropriate remuneration.
Countries should establish national stroke organizations to guide and advocate for surveillance of stroke including burden, management, and outcomes	WHO – Global Strategy on Digital Health 2020-25; Global Action Plan on Epilepsy and other Neurological Disorders, global targets 1.1 and 1.2	Expertise in governance, co-design, interdisciplinary ways of working, consumer, and government engagement	Major barriers include lack of: a) resources including cash and in-kind time to establish national networks of researchers and clinicians b) funding to prepare national policy documents including stakeholder engagement; and c) need for mentoring for leaders of new organizations	WSO Task Force on Stroke commissioners to develop national stroke organizations including mentoring and capacity building for health professionals and clinicians. This should include mechanisms to report to governments to enact meaningful and sustainable change.

Table 8: Key recommendations for healthcare providers and governments to improve primordial, primary and secondary stroke prevention

Key recommendations	Source	Level of evidence/ GRADE[236]	Resources required for implementation	Political, legal, ethical, sociocultural and economic considerations for barriers and facilitators	Recommendation for implementation through WSO Task Force on Stroke
Countries should have government endorsed policies for community-wide stroke prevention.	UN/WHO[237] Action plan for stroke in Europe,[44] AHA Guide for improving cardiovascular health at the community level[238]	Level B evidence that tobacco,[235, 239, 240] salt[241, 242] and alcohol[9–13,243-247] taxation is an effective strategy to improve health. Level A evidence for population-wide primary stroke and other NCD prevention[14–16,248-250]	Expertise in stroke and CVD epidemiology and public health	Major barriers: Industry lobbying (e.g., for reducing salt content in processed food, reducing consumption of sugary drinks, alcohol) as well as lack of: a) expertise to develop an efficient action plan b) community support for introducing taxation on salt, sugary drinks, alcohol, tobacco products c) government and health policy engagement; and d) public resources for accessible and affordable healthy food outlets, physical activity facilities, healthy ecological environment	WSO Task Force on Stroke commissioners to develop legislative changes for reducing salt content in processed food, reducing consumption of sugary drinks, alcohol, including development of policies for community-wide stroke prevention activities, monitoring effectiveness of these activities, and workforce development. Reinvestment of taxation revenue into primary (including the development of accessible and affordable healthy food outlets, physical activity facilities, reducing air pollution) and secondary prevention, health service development and health research.
Countries should have ongoing stroke awareness and prevention campaigns and interventions. The main risk factors to be targeted for primary stroke prevention are: elevated blood pressure (≥120/80), low physical activity (<2½ hours a week of moderate to vigorous exercise), poor unbalanced diet (e.g. less than 6 servings a day of fruits or vegetables), excessive sodium (>2 g/day; equivalent to 5 g/salt/day) intake, overweight (BMI ≥25 or waist-to-hip ratio	WSO,[78] WHO[256], Action plan for stroke in Europe,[44] Gramado Declaration[141]	Level B evidence.[248-250] WHO 'One Health' initiative[256] Level A evidence for risk factors control for stroke	Expertise in development and maintenance of awareness campaigns; electronic patient	Major barriers include lack of: f) engagement of stakeholders (patients, populace, providers, and policy makers) g) collaboration between multiple sectors of society (e.g.,	WSO Task Force on Stroke commissioners to develop strategies and action plans for ongoing stroke awareness and primary prevention, with a strong emphasis in LMICs on early detection and management of

≥0.8 for women and ≥0.9 for men), tobacco use, cardiac causes (coronary heart disease, atrial fibrillation (AF), valve disease, heart failure), dyslipidaemia (total cholesterol ≥5 mmol/L or 200 mg/dL; LDL-C ≥4 mmol/L or ≥150 mg/dL; HDL-C <1 mmol/L or <40 mg/dL; triglycerides >1.7 mmol/L or 150/mg/dL), persistent stress or depression, alcohol consumption (>1 standard drink a day), and diabetes mellitus. Primary stroke prevention is cost-effective: investing US$1.27 per person per year in LMICs until 2030 can save an estimated 8.2 million lives and yield a return on investment of at least US$7.[251, 252] Non-pharmacological and motivational cognitive-behavioral interventions are recommended for lifestyle risk management. For example, regular physical activity before the index event was found to be associated with reduced risk of poor functional outcome after stroke (OR 0·52, 95% CI 0·42–0·66; p<0·0001).

For primary stroke and CVD prevention, polypill containing generic BP-lowering medications and statin can be recommended in adults at intermediate (10-20% 10-year Framingham Risk Score) or greater CVD risk,[81] and no contraindications to the medications. Individuals aged 40-75 years with isolated hypercholesterolaemia of LDL-C ≥4.9 mmol/L (≥190 mg/dL) should receive high-intensity statin therapy without calculating CVD risk. Individuals of that age group with LDL-C levels ≥70 mg/dL to 189 mg/dL (≥1.8-4.9 mmol/L) should receive statin therapy if their 10-year CVD risk is 7.5-19.9% (if a decision about statin therapy is uncertain, a clinician should consider measuring coronary artery calcium)**.**[253] Aspirin should not be routinely used for primary stroke prevention, but is recommended for secondary stroke prevention after TIA or ischaemic stroke.

Pharmacological treatment of elevated blood pressure for primary stroke prevention should be initiated in (a) people with SBP ≥140 mmHg or DBP ≥90 mmHg, or (b) people with existing CVD and SBP 130-139 mmHg, or (c) people with SBP 130-139 mmHg but without CVD who are at high CVD risk (10-year Framingham Risk Score >20%), diabetes mellitus, or chronic kidney disease.[254] The use of

AHA stroke primary and secondary prevention guidelines,[65, 101, 257] WHO Guidelines,[254] INTERSTROKE Study,[18] GBD Study,[258] Framingham Study,[259, 260] White Paper for Circulatory Health,[261]

European Guidelines on CVD prevention.[262]

prevention[24,29,3065, 257, 263]

Level A evidence for use of polypill[81, 264, 265] for BP and cholesterol reduction.[23, 65, 253]

Level A evidence for use of antiplatelet therapy, oral anticoagulation, blood pressure and lipid lowering therapy, and carotid revascularization for secondary stroke prevention.[103, 253, 266-277]

Level of evidence for lifestyle modifications for secondary stroke prevention: smoking cessation and healthy balanced diet (B),[278-280] limited alcohol consumption and sodium intake, regular physical activity, normal BMI

management systems.

government, public health, research/education)

elevated BP, and on reduction of exposure to air pollution. They should develop a plan for prioritization of multisectoral and cost-effective accessible and affordable interventions, including Implementation of and digital technologies for promoting healthy lifestyle[94, 283-285] and primary /secondary stroke prevention.[28,61–655, 84, 94, 100, 118, 141, 286, 287] For example, population-wide strategies recently recommended for implementation for stroke prevention in all Latin American countries (e.g. the free Stroke Riskometer app),[141] should be one of the priorities for funders and policy makers.[141, 286] A sustained TV-led FAST education campaign led to significant improvement of stroke awareness and timely hospital admissions in the UK.[288] There is evidence that multidomain lifestyle intervention is effective for primary and secondary stroke prevention.[289] Legislative changes in South Africa led to the reduction of salt consumption.[290] Evidence-based digital tools (e.g. the PreventS-MD webapp)[84, 100] and most recent ASA/AHA guidelines for secondary stroke prevention recommend them in patients with stroke and TIA[65, 287, 291] for use and

BP-lowering medications for secondary stroke prevention in people with clinical CVD should be initiated with BP ≥130/80 mmHg.[23, 65] Most individuals with SBP ≥140 or DBP ≥90 mmHg are high risk and indicated for pharmacological treatment; they do not require CVD risk assessment prior to initiating treatment. Secondary stroke prevention interventions have been shown to be cost-effective.[255] For secondary stroke prevention, control of hypertension, blood glucose, and lipids (regardless of their level) as well as timely diagnostic evaluation are effective.[65] For those requiring pharmacological therapy, the target blood pressure should generally be <130/80 mm Hg.[23, 65, 101]		(C),[31,54,55518, 280, 281] and salt substitute (A).[282]			adaptation for local conditions, when required.
Countries should have a nationwide and representative system for measuring and monitoring effects of primary and secondary stroke prevention activities (for more details see surveillance section). This should include a stepped approach that highlights the elements required for minimum (hospitalized events), essential and advanced monitoring, i.e. incorporating the WHO stepwise approach[111] or similar.[37, 47, 112] In patients with nonvalvular AF (including paroxysmal) or atrial flutter and stroke or TIA, oral anticoagulation is recommended.[65] Ischaemic stroke patients with severe stenosis ipsilateral to a nondisabling stroke or TIA who are candidates for intervention should have the stenosis fixed, likely relatively early after their ischemic stroke.[65] The choice between carotid endarterectomy and carotid artery stenting should be driven by specific patient comorbidities and features of their vascular anatomy.[65] Large health service providers should have outpatient Stroke Clinics to facilitate GPs in better management of post-discharge stroke/TIA patients. In LMICs with high rate of rheumatic heart disease Oral Anticoagulation Clinics are also recommended.	WHO STEPs,[111] Action plan for stroke in Europe[44]	Level B evidence	Expertise in epidemiology, data management and statistics to support ongoing monitoring of stroke.	Major barriers include lack of: g) infrastructure to support a monitoring program h) expertise to develop an efficient program i) capacity to analyse the data collected and produce quality statistics j) use of data to drive decision-making.	WSO Task Force on Stroke commissioners to develop, implement and monitor reliable, simple, and fit-for-purpose strategic action plan with all stakeholders to ensure availability of a reliable monitoring of stroke and risk factors standardized surveillance systems in their countries and regions.

Table 9: Identified problems with and suggested strategies for policy makers to achieve sustainable and appropriate primary and secondary stroke prevention

Problems	Goals	Targets	Recommendations/Actions	Assessment methods
Lack of funding for primary stroke prevention across all countries, particularly in LMICs	To provide sufficient funding for primary and secondary stroke prevention	Governments and politicians	Encourage all governments and politicians to re-invest revenues from taxation on unhealthy products (e.g., tobacco, sugary drinks, alcohol, salt in processed food, reduced consumption) back to health services and preventative strategies All healthcare policy makers should be aware that for every US$1 spent on prevention of stroke and CVD there are over US$10 returns on investment	Proportion of funding allocated to primary and secondary stroke prevention
Few countries or regions have established action plans for stroke prevention. Low level of secondary prevention activities, especially in LMICs and activities related to education about stroke and lifestyle management for stroke patients and their families, stroke/TIA clinics and guidelines utilization	To establish country-specific action plans and stroke prevention guidelines for every country in the world	The whole population for population-wide prevention strategies and individuals at any level of risk for individual prevention strategies	All governments should allocate sufficient funding for the development and implementation of primary stroke prevention strategies All countries should have financially sustainable action plans for primary and secondary stroke prevention All countries should have culturally appropriate guidelines for primary and secondary stroke prevention Adults are encouraged to use the freely available and validated mobile apps for managing their risk factors (e.g., the WSO recommended free Stroke Riskometer app) Upskilling of health staff, including doctors, nurses, and other support staff, in the primary and secondary prevention of stroke, including providing advice on lifestyle changes and adherence to medications Transferring tasks of primary stroke prevention from highly trained health professionals to healthcare workers with less training, qualifications, and education should be encouraged Culturally appropriate education about healthy lifestyles should be incorporated into standard education curricula and started early in life, with reinforcement across the lifespan Service providers should ensure adequate health services for people with acute cerebrovascular diseases to reduce the risk of recurrent stroke, including multidisciplinary acute stroke units, outpatient stroke/TIA clinics and routinely available education about stroke and lifestyle management for stroke patients and their families, ongoing stroke and risk factors	Stroke incidence, mortality, and disability Prevalence of risk factors 5 or 10-year risk of CVD and/or stroke Availability of stroke/TIA and stroke prevention clinics and proportion of people at risk of stroke and people who have experienced a stroke or TIA managed in such clinics Proportion of evidence-based decisions in stroke prevention

			awareness campaigns, and availability of valid digital secondary stroke prevention tools for clinicians	
Lack of integrative approach and digital tools for primary and secondary stroke prevention interventions, particularly in LMICs	To establish collaboration between different national and international agencies and organizations involved in primary and secondary prevention of NCDs	National and international agencies and organizations	Include nationally and internationally recognized stroke experts in all relevant national and international agencies and organizations involved in primary and secondary prevention of NCDs Priority in the primary stroke prevention strategies should be given to the reduction of exposure to CVD risk factors of the whole population across the life course, with the focus on behavioural and lifestyle risk factors, thus allowing an integrative approach that also targets other major NCDs, such as dementia, diabetes, cancer, and pulmonary diseases. Absolute CVD risk treatment thresholds should not be the sole criteria for selecting individuals for pharmacological management of elevated blood pressure and lipids. Categorization of people into low, moderate (mild) and high absolute CVD risk (including use of risk-stratified heat maps) when communicating risk should be abandoned, and individual primary stroke and CVD prevention interventions should include all people at increased risk of stroke and CVD regardless of the level of the increased risk. All countries should be encouraged to adapt validated, affordable, and culturally appropriate digital tools for secondary stroke prevention.	Representation of stroke experts in all relevant national and international agencies and organizations involved in primary prevention of NCDs
Low stroke awareness across all countries	To establish national ongoing stroke awareness campaigns about stroke, its warning signs and prevention	The whole population	All national and regional stroke organizations should conduct ongoing stroke awareness campaigns about stroke, its warning signs and prevention, coordinated by the World Stroke Organization. Regular TV programmes are the preferred channel of media for such campaigns	Stroke awareness surveys
Lack of monitoring systems for evaluation of the effectiveness of preventative strategies	To establish national and subnational (for large countries) monitoring frameworks	Whole population and people at risk of stroke	All countries should have monitoring systems to evaluate the effects of primary and secondary prevention strategies In the absence of sufficient quality country-specific epidemiological data on stroke burden and risk factors, healthcare policy makers should be encouraged to use relevant Global Burden of Disease estimates Regular use of accurate data to support decision-making	Changes in the 5- or 10-year absolute risk of stroke/CVD of outpatients Registries of recurrent strokes/TIA (including their outcomes), digital tools for monitoring trends in stroke/CVD risk and risk factors
Insufficient funding of stroke prevention research	To study determinants of stroke occurrence and outcomes and the	Health research funding agencies	In consultation with recognized regional experts on stroke and public health, allocate sufficient funding for research in primary and secondary stroke prevention	Proportion of research funding allocated to primary stroke

across all countries, particularly in LMICs	best strategies to reduce stroke burden			prevention (compared to the total health research funding)
Affordability of essential drugs for primary and secondary stroke prevention across all countries	To establish a list of essential drugs for primary and secondary stroke	People at risk of stroke	All countries should have a list of essential drugs for primary and secondary stroke prevention funded by the government	Availability of government subsidized essential drugs for primary and secondary stroke prevention aligned with the WHO list of essential drugs

Table 10: Key evidence-based recommendations to improve acute stroke care worldwide

Key recommendations	Source	Level of evidence/ GRADE	Resources required for implementation	Political, legal, ethical, sociocultural and economic considerations and barriers for	Recommendation for contextualization and implementation through WSO Task Force on Stroke and implementation ecosystem
For all stroke patients					
Patients with an acute stroke should be admitted to hospital	WSO Guideline and Action Plan[113]	Level A	Hospitals available (preferably stroke centres)	Some regions without hospitals	Governments should map the country and build at least 1 hospital per region (ideally every 200-250 km, preferably a stroke centre). Online roadmap can help in the evaluation
All patients with suspected acute stroke should receive brain imaging evaluation on arrival to hospital (non-contrast CT – NCCT – or Magnetic Resonance - MRI)	AHA Guideline for Acute Stroke[164] Canadian Guidelines[133] ICH Guidelines AHA/ASA[291]	Level 1A[1] Level A Level 1A	Availability of CT scan in hospitals	Lack of resources to equip more hospitals with NCCT scan	Governments should map the country and implement at least 1 CT scan equipment every 200 km. Online roadmaps can help in the evaluation
Patients with acute stroke or TIA admitted to a hospital should be treated by an interdisciplinary stroke team (at least a physician with training in stroke care, a nurse, physiotherapist and speech therapist)	Canadian Guidelines[133] WSO Guideline and Action plan[113] Action plan for stroke in Europe[44]	Level A Level A Level A	Interdisciplinary stroke team	Lack of knowledge of health managers that interdisciplinary team is cost effective and improves the patient's outcomes Lack of training for the interdisciplinary team	WSO Task Force on Stroke commissioners to work together with the health managers to show the evidence about interdisciplinary stroke team Educational teaching courses for the stroke team (online – World Stroke Academy) and face to face with local societies
Patients with acute stroke or TIA admitted to a hospital should be treated in a stroke unit, which is a specialized, geographically defined area dedicated to the management of stroke patients with an interdisciplinary stroke team	Canadian Guidelines[133] WSO Guideline and Action plan[113]	Level A	Geographic area in the hospital Interdisciplinary stroke team	Lack of space to create stroke units Lack of resources	WSO Task Force on Stroke commissioners to work together with health managers and local societies to show the evidence about stroke units and to create plans to organize them more than built new areas

	Action plan for stroke in Europe[44] Declaration of Gramado[141]	Level A Level A		Lack of knowledge of health managers that interdisciplinary team is cost effective and improves the patient's outcomes Lack of training for the interdisciplinary team	Educational teaching courses for the stroke team members (online – World Stroke Academy) and face to face meetings with local societies
Patients should be evaluated and managed to prevent complications (early access to swallowing, nutrition and hydration status, fever, glucose, oxygen saturation, blood pressure, deep vein thrombosis, skin ulcers)	Canadian Guidelines[133] WSO Guideline and Action plan[113] Action plan for stroke in Europe[44] AHA Guidelines[164]	Level A Level A Level A Level A	Training for the stroke team	Lack of knowledge of health professionals about the importance of these general actions Lack of training for the interdisciplinary team	Educational teaching courses for the stroke team (online – World Stroke Academy) and face to face with local societies/professionals
In remote regions without doctors with stroke expertise, telemedicine in community hospitals may help to provide acute stroke treatment, including thrombolysis.	AHA,[164] Canadian,[133] Action plan in Europe,[44] Declaration of Gramado[141]	Level IIa, B-R	Tools for communication and image evaluation in real time Stroke experts to give consultation 24h/day, 7 days a week	Lack of communication and image transfer tools Low resources to pay the equipment and professionals	WSO Task Force on Stroke commissioners to work together with health managers and hospitals to develop a network to increase the access to stroke treatment in areas without doctors with stroke expertise.
Specific for Ischemic stroke/TIA					
Patients with TIA should be assessed in hospital or if not possible, in a specialized outpatient clinic to perform CT scan, evaluate stroke aetiology and immediately to start stroke prevention (within 48 hours from symptoms onset)	Canadian Guidelines[133] WSO Guideline and Action plan[113] Action plan for stroke in Europe[44]	Level A Level A	Training for health professionals Organization of TIA acute assistance	Lack of awareness of health professionals about the importance to evaluate TIA and minor stroke as a medical urgency Lack of structure for a fast evaluation of AIT aetiology and prevention treatment initiation	WSO Task Force on Stroke commissioners to develop strategies and action plans for education of health professionals to treat TIA as a medical urgency and to educate them with the best prevention strategies starting immediately after symptoms onset.
Patients with ischemic stroke should be evaluated for IV thrombolysis with tPA up to 4,5 hours of symptoms onset	AHA,[164]	Level 1A	Availability of tPA; Training for stroke professionals;	Lack of knowledge of health managers about the benefit and cost-effectiveness of the thrombolytic treatment	WSO Task Force on Stroke commissioners to work together with health managers and local societies to show the evidence about IV thrombolysis and to create plans to implement

	Canadian Guidelines,[133] WSO,[113] Action plan in Europe.[44] Declaration of Gramado[141] ESO Guideline[292]		Organization of pathways for fast treatment	lack of trained doctors and interdisciplinary team lack of thrombolytic medication in some countries cost of medication	treatment; teaching courses; telemedicine is an effective and cost-effective tool to help the implementation in areas without stroke expertise doctors.[78,79] Governments should discuss with companies to ensure affordable thrombolytic medication
Ischemic stroke patients should be given acetylsalicylic acid (ASA) as soon as possible within 48 hours from symptom onset after brain imaging has excluded intracranial haemorrhage. Thrombolysed patients should receive ASA 24 hours after treatment	AHA,[164] Canadian Guidelines,[133] WSO,[113] Action plan in Europe.[44]	Level 1A	Health professional education	Lack of medical education	Educational teaching courses for the stroke team (online – World Stroke Academy) and face to face with local societies/professionals
Patients with minor stroke (NIHSS ≤ 3) who did not receive IV alteplase or high-risk TIA (ABCD2 score >4) of non-cardioembolic origin should receive dual antiplatelet therapy (DAPT) up to 24 hours of symptoms onset with aspirin plus clopidogrel (loading dose 300 or 600 mg followed by 75 mg/day). DAPT should continue for 21 to 30 days. After, should continue antiplatelet monotherapy indefinitely	AHA,[164] Canadian Guidelines,[133]	Level 1A Level 1A	Training for the stroke team	Lack of medical education	Educational teaching courses for the stroke team (online – World Stroke Academy) and face to face with local societies/professionals
Patients with Large Vessel Occlusion (LVO) with symptoms up to 24 hours should be evaluated for mechanical thrombectomy (MT) in comprehensive stroke centres (Advanced as the WSO Roadmap classification).	AHA,[164] Canadian Guidelines,[133] WSO,[113] Action plan in Europe.[44]	Level 1A	Comprehensive stroke centres (advanced) Neurointerventionalists trained available 24h, 7 days a week, anaesthesiologist, Access to Angiography units, devices for MT	Lack of knowledge of health managers about the benefit of the treatment lack of structure in hospitals (usually LIC without any advanced hospital) lack of resources to pay the professionals and devices lack of trained neuro-interventionalists	WSO Task Force on Stroke commissioners to work together with health managers and local societies to show the evidence already available and to create plans to implement treatment, teaching courses, hands-on in high volume centres. Governments should discuss with companies to ensure affordable devices and materials

Patients eligible for IV thrombolysis should receive IV thrombolysis even if MT is being considered.	AHA,[164] Canadian Guidelines,[133] ESO Guideline.[292]	Level 1A Level 1A	Training for the stroke team	Lack of medical education	Educational teaching courses for the stroke team (online – World Stroke Academy) and face to face with local societies/professionals
Specific for intracerebral haemorrhage (ICH)					
In patients with spontaneous ICH of mild to moderate severity presenting with SBP between 150 and 220 mmHg, acute lowering of SBP to a target of 140 mmHg (maintaining in the range of 130 to 150 mm Hg) is safe and may be reasonable for improving functional outcomes	AHA ICH[291]	Level 1A	Training for the stroke team	Lack of medical education	Educational teaching courses for the stroke team
In patients with spontaneous ICH and clinical hydrocephalus, transfer to centres with neurosurgical capabilities for definitive hydrocephalus management with external ventricular derivation (EVD) placement and monitoring is recommended to reduce mortality	AHA ICH[291]	Level 1-BNR	Training for the stroke team	Lack of medical education	Educational teaching courses for the stroke team
Intermittent pneumatic compression (IPC) starting on the day of diagnosis is recommended for deep venous thrombosis and pulmonary embolism prophylaxis	AHA ICH[291]	Level 1-BR	Training for the stroke team	Lack of medical education	Educational teaching courses for the stroke team
In patients with spontaneous ICH, impaired consciousness, and confirmed electrographic seizures, antiseizure drugs should be administered to reduce morbidity	AHA ICH[291]	Level 1-CLD	Training for the stroke team	Lack of medical education	Educational teaching courses for the stroke team
In patients with clinical seizures antiseizure drugs should be administered	AHA ICH[291]	Level 1 CEO	Training for the stroke team	Lack of medical education	Educational teaching courses for the stroke team
For patients with cerebellar ICH who are deteriorating neurologically, have brainstem compression and/or hydrocephalus from ventricular	AHA ICH[291]	Level 1 BNR	Training for the stroke team	Lack of medical education	Educational teaching courses for the stroke team. If unavailability of resources, the patient

obstruction, or have cerebellar ICH volume ≥15 mL, immediate surgical removal of the haemorrhage with or without EVD is recommended in preference to medical management alone to reduce mortality			Availability of operating room and neurosurgeon 24h, 7 days	Unavailability of structure to the surgery (equipment and professional)	should be transferred to a hospital with neurosurgery Plans to transfer these patients should be coordinated with health managers as regional protocol
ICH while anticoagulated: -Acute reversal of anticoagulation using protein complex concentrate (PCC) more than fresh frozen plasma for reversal of vitamin K antagonists followed immediately by IV Vitamin K to avoid increased INR again.	AHA ICH[291]	Level 1 BR Level 1 CLD	Training for the stroke team Availability of PCC	Lack of medical education Lack of medication for anticoagulation reversal	Educational teaching courses for the stroke team. Director of hospital and Health managers should provide medication for anticoagulation reversal
- Idarucizumab for reversal of the thrombin inhibitor dabigatran -Andexanet alfa for reversal of factor Xa inhibitors such as Rivaroxaban, Apixaban, and Edoxaban.		Level 2a BNR Level 2a BNR	Training for the stroke team, availability of Idarucizumab Training for the stroke team, availability of Andexanet	Lack of medical education Lack of medication for anticoagulation reversal Lack of medical education Lack of medication for anticoagulation reversal	Educational teaching courses to the stroke team Director of hospital and Health managers should provide medication for anticoagulation reversal
Specific for subarachnoid haemorrhage (SAH)					
Acute diagnostic workup should include non-contrast head CT, which, if nondiagnostic, should be followed by lumbar puncture CTA may be considered in the workup of aSAH. If an aneurysm is detected by CTA, this study may help guide the decision for type of aneurysm repair, but if CTA is inconclusive, Diagnostic subtraction angiography still recommended (except possibly in the instance of classic perimesencephalic aSAH)	AHA SAH[293]	1B 2B, C	Availability of CT scan and lumbar puncture material in the hospital Availability of CTA	Lack of resources to equip more hospitals Lack of resources to equip more hospitals	Governments should map the country and implement at least 1 CT scan equipment every 200 km. Online Roadmap can help in the evaluation Governments should plan and implement at least 1 comprehensive (advanced) stroke centre to each 2 million inhabitants Coordinated routes to transfer these patients in the first 24 hours should be organized.

The magnitude of blood pressure control to reduce the risk of rebleeding has not been established, but a decrease in systolic blood pressure to <160 mmHg is reasonable	AHA SAH[293, 294]	Level C, 2A,	Training for health professionals	Lack of training	Educational teaching courses for the stroke team.
Patients with SAH should start oral nimodipine to improve outcomes but not to decrease vasospasm	AHA SAH[293, 294]	Level 1A	Training for health professionals	Lack of training Lack of nimodipine	Educational teaching courses for the stroke team. Health managers should ensure that essential medication is available
Surgical clipping or endovascular coiling of the ruptured aneurysm should be performed as early as feasible in the majority of patients to reduce the rate of rebleeding after aSAH	AHA SAH[293, 294]	Level 1 B	Availability of neurosurgeon or neurointerventionalists, availability of surgery room or angio-suite	Lack of equipment and professionals	Educational teaching courses for neurosurgeon, neurointerventionalists Comprehensive (advanced) stroke centre available in the region to transfer the patient
A neuroradiologist and a neurosurgeon should discuss the options for managing the culprit aneurysm (endovascular coiling or neurosurgical clipping), taking into account the patient's clinical condition, the characteristics of the aneurysm, and the amount and location of subarachnoid blood	AHA SAH[293, 294]		1B	Lack of training	Educational teaching courses to neurosurgeon, neurointerventionalist

Table 11: 2030 Targets and Recommendations for acute stroke care

Problems	Goals	Targets	Recommendations/Actions	Assessment methods for assessing adherence to recommendations
Some countries do not have acute stroke care services	To establish acute stroke services in all countries	To ensure availability of acute stroke services in all countries by the year 2030 accessible to all stroke patients worldwide	All countries without acute stroke services should have a government program to establish them and train personnel to deliver interdisciplinary care to stroke patients in pre-hospital and hospital Financing programs should be developed to facilitate access to acute stroke services in low- and middle-income countries (government or public-private partnership) Use of telemedicine to increase the access to stroke specialists	Number of countries without acute stroke services in 2022 who have established same by 2030.
Some countries do not have adequate number and quality of acute stroke services for stroke patients	To increase the number and quality of hospitals with acute stroke care, with implementation of evidence-based approach	To increase the number of acute stroke centres such that every stroke patient has access to such services by 2030. The recommended number is at least 50 beds per 1 million inhabitants with a multidisciplinary approach and implementation of evidence-based treatments: thrombolysis as a first step and thrombectomy in comprehensive centres as the next step (the suggestion is to create more high-level stroke centres providing all necessary treatment options, including thrombectomy, with at least 1 centre per 2 million inhabitants)	Countries with existing acute stroke hospitals should improve the quality of services provided according to evidence-based guidelines. Training programs should be enhanced to increase the number of personnel required to offer services. Telemedicine can be used to increase the access to stroke specialists Certification programs can help to improve and to maintain the quality of services	Number of new acute stroke services established between 2022 and 2030 in each country National or international quality indicators registries in hospitals to monitor and improve the quality Number of certified stroke services in each country

Table 12. Summary of key pragmatic solutions based on national and international stroke guidelines to improve stroke rehabilitation services worldwide

KEY RECOMMENDATIONS (Criteria: Class I and III and IIa A or B, IIbA recommendations only from best Guidelines reviewed based on COUNCIL Criteria)	**Source**	**LOE**	**Resources required for implementation**	**Barriers/Facilitators for implementation in LMICs**	**Pragmatic Solutions/Recommendation** for contextualization and implementation in LMICs through WSO Task Force on Stroke
ORGANIZATION OF REHABILITATION SERVICE					
It is recommended that early rehabilitation for hospitalized stroke patients be provided in environments with organized, interprofessional stroke care.	AHA ESAP	I A	Multidisciplinary rehabilitation facilities with rehabilitation doctor/physician/ neurologist, physiotherapist, occupational therapist, speech and language and dysphagia therapist, clinical psychologist, nurse; etc.	Major barriers to be surmounted include lack of awareness and low demand, absence of/or inadequate number of rehabilitation professionals (need to establish training institutions/program to produce adequate number of professionals); need to adapt evidence-base practice recommendations to regional capacities (need to establish regional protocols / clinical pathways); need to finance rehabilitation services to make them accessible and available to all stroke patients	WSO Task Force on Stroke commissioners to develop, implement and monitor strategic action plan with all stakeholders to ensure availability of stroke rehabilitation services to all eligible stroke patients in their countries and regions
SKIN					
In ischaemic stroke, prophylactic-dose subcutaneous heparin (UFH or LMWH) should be used for the duration of the acute and rehabilitation hospital stay or until the stroke survivor regains mobility	AHA	I A	Subcutaneous heparin	Availability of subcutaneous heparin	Provision and administration of subcutaneous Heparin for DVT prophylaxis in patients with ischaemic stroke
PAIN					

Patient and family education (i.e., range of motion, positioning) is recommended for shoulder pain and shoulder care after stroke, particularly before discharge or transitions in care	AHA	I C	Education	Education	Training of care providers to educate patients/family members
FALLS					
It is recommended that individuals with stroke be provided a formal fall prevention program during hospitalization People with stroke should be offered falls risk assessment and management as part of their stroke rehabilitation, including training for them and their family/carers in how to get up after a fall People with stroke should be offered an assessment of fear of falling as part of their falls risk assessment People at high risk of falls after stroke should be offered a standardized assessment of fragility fracture risk as part of their stroke rehabilitation People with stroke with symptoms of vitamin D deficiency, or those who are considered to be at high risk (e.g., housebound) should be offered calcium and vitamin D supplements People at high risk of falls after stroke should be advised to participate in physical activity/exercise which incorporates balance and co-ordination at least twice per week	AHA UK	I A Nil	In hospital rehabilitation programs with balance and falls risk assessment	Limited number of organized programs with assessment of balance and risk falls	Support for workshops, production of free online training materials
DEPRESSION					
In the first months post-stroke, antidepressant pharmacotherapy is only recommended if the process of rehabilitation is hindered by emotional problems. Increasing motivation for and participation in rehabilitation is the target for treatment. Selective serotonin reuptake inhibitors, SSRIs should be considered when depressive complaints or emotionalism are long lasting and become chronic while adverse effects should be monitored continuously	WFNR	LoE: 1a QoE: moderate SoR: B+			
CONSCIOUSNESS					
Amantadine for a course of amantadine treatment over a couple of weeks can be used in the beginning of the rehabilitation treatment of stroke survivors with DoC (VS-MCS) to promote recovery in the disability domain The evidence is too limited to guide clinical decision-making with respect to long-term use and discontinuation of amantadine, or the prescription of other drugs to treat DoC in stroke survivors	WFNR	LoE: 1b QoE: moderate SoR: o indirectness of evidence			
COGNITION					
Screening for cognitive deficits is recommended for all stroke patients before discharge home	AHA AHA	I B IIa C	Multidisciplinary approach should	Limited number of trained	Need to finance multidisciplinary

When screening reveals cognitive deficits, a more detailed neuropsychological evaluation to identify areas of cognitive strength and weakness may be beneficial Services for people with stroke should have a comprehensive approach to delivering psychological care that includes specialist clinical neuropsychology/clinical psychology input within the multi-disciplinary team People with stroke should be considered to have at least some cognitive impairment in the early phase. Routine screening should be undertaken to identify the person's level of functioning, using standardized measures People with communication impairment after stroke should receive a cognitive assessment using valid assessments in conjunction with a speech and language therapist. Specialist advice should be sought if there is uncertainty about the interpretation of cognitive test results Any person with stroke who is not progressing as expected in rehabilitation should receive a detailed assessment to determine whether cognitive impairments are responsible, with the results explained to the person, their family, and the multidisciplinary team People with acute cognitive problems after stroke whose care is being transferred from hospital should receive an assessment for any safety risks from persisting cognitive impairments. Risks should be communicated to their primary care team together with any mental capacity issues that might affect their decision-making People with stroke returning to cognitively demanding activities such as driving, or work should have their cognition fully assessed	UK	Nil	include trained clinical psychologist experienced in cognitive assessment (neuropsychologist)	neuropsychologists /occupational therapists	rehabilitation including neuropsychologists/ occupational therapists
DYSPHAGIA SCREENING, MANAGEMENT, AND NUTRITIONAL SUPPORT					
Early dysphagia screening is recommended for acute stroke patients to identify dysphagia or aspiration, which can lead to pneumonia, malnutrition, dehydration, and other complications	AHA Au	I B Strong	Multidisciplinary approach should include trained speech and swallowing therapist	Limited number of trained speech and swallowing therapist	Financing training program, workshops, and online materials for healthcare provider
External feedings (tube feedings) should be initiated within 7 days after stroke for patients who cannot safely swallow	AHA	I A	Implementation of a dysphagia screening program for all stroke cases	Major barriers to be surmounted include lack of awareness and low demand, absence of/or	Financing training program, workshops and online materials for healthcare provider

				inadequate number of professionals	
APHASIA					
Recommendations: Aphasia Speech and language therapy is recommended for individuals with aphasia People with communication problems after stroke should be assessed by a speech and language therapist to diagnose the problem and to explain the nature and implications to the person, their family/careers and the multidisciplinary team. Reassessment in the first four months should only be undertaken if the results will affect decision-making or are required for mental capacity assessment People with communication problems after stroke should be assessed by a speech and language therapist to diagnose the problem and to explain the nature and implications to the person, their family/careers and the multidisciplinary team. Reassessment in the first four months should only be undertaken if the results will affect decision-making or are required for mental capacity assessment	AHA Au UK WFNR	I A Strong Nil	Multidisciplinary approach should include trained speech and language therapists	Limited number of trained speech and language therapists	Financing training program, workshops and online materials for healthcare provider
SPASTICITY					
Targeted injection of botulinum toxin into localized upper limb muscles is recommended to reduce spasticity, to improve passive or active range of motion, and to improve dressing, hygiene, and limb positioning	AHA	I A	Multidisciplinary approach should include trained neurologists for Botox injection	Limited number of trained neurologists //physical and rehabilitation medicine doctors	Financing training programs, workshops, and online materials for neurologists/physical and rehabilitation medicine doctors
BALANCE					
Individuals with stroke who have poor balance, low balance confidence, and fear of falls or are at risk for falls should be provided with a balance training program For patients with balance disorders post stroke, balance training should be offered It has been demonstrated that exercising postural control with visual feedback while standing on a force platform improves the postural sway in stance of patients with a stroke Studied for early and chronic rehabilitation It has been demonstrated that exercising balance during various activities results in improved sitting and standing balance and improved performance of basic activities of daily living by stroke patients Studied for early, late, and chronic rehabilitation	AHA Ca Ne	I A Evidence Level A (Level 1)	Physiotherapists are required for balance training	Need large number of physiotherapists	Recommend training of more physiotherapists for stroke patients globally
MOBILITY					

Intensive, repetitive, mobility- task training is recommended for all individuals with gait limitations after stroke Task and goal-oriented training that is repetitive and progressively adapted should be used to improve performance of selected lower-extremity tasks such as walking distance and speed and sit to stand It has been demonstrated that training specific skills, such as exercising balance while standing and reaching to grasp objects, has a favorable effect on the specific skill being trained by stroke patients in all phases of rehabilitation People with loss of movement and/or ataxia after stroke sufficient to limit their activities should be assessed by a physiotherapist with experience in neurological rehabilitation People with loss of movement and/or ataxia after stroke should be taught task-specific, repetitive, intensive exercises or activities that will increase strength People with impaired sitting balance after stroke should receive trunk training exercises People with significant impairment of their balance and walking ability after stroke should receive progressive balance training, functional task-specific training, lower limb strengthening exercises and be considered for an ankle-foot orthosis People with moderate to severe limitation of their walking ability after stroke should be assessed for a walking aid to improve their stability People with stroke who are able to walk with or without assistance should undergo task specific walking training with a cardiorespiratory and/or muscle strength focus at sufficient intensity to improve endurance and walking speed People with limited ability to walk after stroke should be assessed by a physiotherapist with experience in neurological rehabilitation to guide management People with limited mobility after stroke should be assessed, provided with and trained in how to use appropriate mobility aids including a wheelchair to enable safe independent mobility	AHA Ca ESAP Ne UK	I A Evidence Level A Level 1 Nil	Physiotherapists are required for mobility and gait training	Need large number of physiotherapists/ physical and rehabilitation medicine doctors	Recommend training of more physiotherapists /physical and rehabilitation medicine doctors for stroke patients globally
UPPER EXTREMITY ACTIVITY, INCLUDING ADLS, IADLS, TOUCH, AND PROPRIOCEPTION					
Functional tasks should be practiced: that is, task-specific training, in which the tasks are graded to challenge individual capabilities, practiced repeatedly, and progressed in difficulty on a frequent basis	AHA Ca UK	I A (Evidence Level A),	Therapists, training	Availability of therapists	Ensure incorporation in stroke rehabilitation protocols

		Nil			
Patients should engage in training that is meaningful, engaging, repetitive, progressively adapted, task specific and goal-oriented in an effort to enhance motor cont11rol and restore sensorimotor function ii. Training should encourage the use of patients' affected limb during functional tasks and be designed to simulate partial or whole skills required in activities of daily living (e.g., folding, buttoning, pouring, and lifting) The team should promote the practice and transfer of skills gained in therapy into the patient's daily routine Therapy should include repetitive and intense use of novel tasks that challenge the patient to acquire the necessary skills needed to perform functional tasks and activities (Evidence Level A) People with stroke with potential or actual arm movement should be given every opportunity to practice functional activities. Practice should be characterized by movements that are of high intensity, repetitive and are task-specific. These activities may be bilateral or unilateral depending on the task			Same for all		
CHRONIC CARE MANAGEMENT: HOME- AND COMMUNITY-BASED PARTICIPATION					
After completion of formal stroke rehabilitation, participation in a program of exercise or physical activity at home or in the community is recommended. (Access to green areas and walking space may facilitate physical activity) Community-dwelling stroke survivors who have difficulties performing daily activities should be assessed by a trained clinician Community-dwelling stroke survivors with confirmed difficulties in personal or extended ADL should have specific therapy from a trained clinician (e.g., task-specific practice and training in the use of appropriate aids) to address these issues	AHA ESAP Au	I A Strong	Therapists and training	Training	Same
TREATMENTS/INTERVENTIONS FOR VISUAL IMPAIRMENTS					
For deficits in eye movements: Eye exercises for treatment of convergence insufficiency are recommended	AHA	I A	Therapists and training	Training	Ensure incorporating in protocols
SOCIAL AND FAMILY CAREGIVER SUPPORT					
It may be useful for the family/caregiver to be an integral component of stroke rehabilitation	AHA ESAP	IIb A	Therapists and caregivers	Training and availability of caregivers	Ensure implementation
REFERRAL TO COMMUNITY RESOURCES					
It is recommended that acute care hospitals and rehabilitation facilities maintain up-to-date inventories of community resources	AHA	I C	Therapists and caregivers	Training and availability of caregivers	Ensure implementation
RECREATIONAL AND LEISURE ACTIVITY					

It is reasonable to promote engagement in leisure and recreational pursuits, particularly through the provision of information on the importance of maintaining an active and healthy lifestyle	AHA	IIa B	Therapists and caregivers	Training and availability of caregivers	Ensure implementation

American Heart Association (e.g., Class I Level A)[82], Netherlands KNGF Stroke Guideline[83], Canada Stroke Best Practice recommendation[84], WFNR Clinical pathways in stroke rehabilitation: evidence-based clinical practice recommendations[85], European Stroke Organisation, Australian Stroke Foundation[2], United Kingdom NICE guideline for stroke[86], and World Stroke Organization. AHA: American Hypertension Association. ESAP: European Stroke Action Plan. Ca: Canada. Au: Australia. UK: United Kingdom. Ne: The Netherlands.

Table 13: 2030 Targets and Recommendations for improving stroke rehabilitation

Problems	Goals	Targets	Recommendations/Actions	Assessment methods for assessing adherence to recommendations
Some countries do not have rehabilitation services for patients with stroke	To establish and strengthen neurorehabilitation services in various settings in all countries for patients with stroke	To ensure availability of multidisciplinary neurorehabilitation facilities and personnel in all countries by the year 2030 accessible to all stroke patients worldwide	All countries without multidisciplinary neurorehabilitation services should have a program to establish these multidisciplinary neurorehabilitation services and train appropriate personnel to deliver transdisciplinary care to patients with stroke in hospital and community settings Financing solutions should be developed to facilitate access to neurorehabilitation services for patients with stroke in low- and middle-income countries	Number of countries without multidisciplinary neurorehabilitation services in 2019 for stroke patients who have established these multidisciplinary neurorehabilitation services by 2030
Many countries do not have adequate number and quality of rehabilitation services and settings for survivors of stroke	To increase the number of facilities offering quality multidisciplinary care for patients with stroke and to increase adherence to best practice guidelines along the "continuum of care" including inpatient, outpatient, community, and home-based rehabilitation with an inter-setting organisation.	To increase the number of facilities offering quality multidisciplinary care for patients with stroke with a "continuum of care" approach and inter-setting organisation such that every patient with stroke has access to these quality multidisciplinary care services by 2030. The specific numbers and types of facilities required will depend on the population burden of patients with stroke in each region and country	Multidisciplinary care and inter-setting organisation along the "continuum of care" with inpatient, outpatient, community and home-based rehabilitation should be available for patients with stroke. Countries with existing stroke rehabilitation facilities should improve the quality of services provided according to evidence-based guidelines. Training programs should be enhanced to increase the number of personnel required to offer services. Development of agreed performance indicators for rehabilitation that address major impairments and patient and carer needs. Creation of a repository for best practice rehabilitation protocols for sharing and adaptation to different countries and settings.	Number of new rehabilitation services established between 2019 and 2030 in each country Improved adherence to clinical practice guidelines

References

1. Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, et al. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurology*. 2021;20:795-820 doi.org/710.1016/S1474-4422(1021)00252-00250
2. Mijajlović MD, Pavlović A, Brainin M, Heiss W-D, Quinn TJ, Ihle-Hansen HB, Hermann DM, Assayag EB, Richard E, Thiel A et al. Post-stroke dementia - a comprehensive review. *BMC medicine*. 2017;15:11-11
3. Medeiros GC, Roy D, Kontos N, Beach SR. Post-stroke depression: A 2020 updated review. *Gen Hosp Psychiatry*. 2020;66:70-80
4. Watkins DA, Msemburi WT, Pickersgill SJ, Kawakatsu Y, Gheorghe A, Dain K, et al. NCD Countdown 2030: efficient pathways and strategic investments to accelerate progress towards the Sustainable Development Goal target 3.4 in low-income and middle-income countries. *The Lancet*. 2022;399:1266-1278
5. Owolabi MO, Thrift AG, Mahal A, Ishida M, Martins S, Johnson WD, Pandian J, Abd-Allah F, Yaria J, Phan HT et al. Primary stroke prevention worldwide: translating evidence into action. *The Lancet Public Health*. 2022;7:e74-e85
6. Owolabi MO, Suwanwela NC, Yaria J. Barriers to implementation of evidence into clinical practice in low-resource settings. *Nature Reviews Neurology*. 2022;18:451-452
7. Johnson W, Onuma O, Owolabi M, Sachdev S. Stroke: a global response is needed. *Bull World Health Organ*. 2016;94:634-634a
8. Owolabi MO, Thrift AG, Martins S, Johnson W, Pandian J, Abd-Allah F, Varghese C, Mahal A, Yaria J, Roth GA et al. The state of stroke services across the globe: report of World Stroke Organization - World Health Organization surveys. *International Journal of Stroke*. 2021;16(8):889-901
9. Yaria J, Gil A, Akintomiwa M, Oguntoye R, Miranda JJ, Lazo-Porras M, Puhong Z, Xuanchen T, Ahlgren JÁ, Bernabe-Ortiz A et al. Quality of stroke guidelines in low- and middle-income countries: a systematic review. *Bulletin of the World Health Organization*. 2021;99:640-652E
10. Owolabi MO. Taming the burgeoning stroke epidemic in Africa: stroke quadrangle to the rescue. *West Indian Med J*. 2011;60:412-421
11. World Health Organization. Global action plan for the prevention and control of noncommunicable diseases 2013-2020. WHO, Geneva *http://www.who.int/nmh/events/ncd_action_plan/en/*. 2013
12. NCD Alliance. New submission - WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases (NCDs) 2013–2030 - Appendix 3. https://ncdalliance.org/resources/new-submission-who-global-action-plan-for-the-prevention-and-control-of-noncommunicable-diseases-ncds-2013%E2%80%932030-appendix-3 Accessed 21 October 2022.
13. Nugent R, Bertram MY, Jan S, Niessen LW, Sassi F, Jamison DT, Pier EG, Beaglehole R. Investing in non-communicable disease prevention and management to advance the Sustainable Development Goals. *The Lancet*. 2018;391:2029-2035
14. Michie S, van Stralen MM, West R. The behaviour change wheel: A new method for characterising and designing behaviour change interventions. *Implementation Science*. 2011;6:42
15. Owolabi M, Miranda JJ, Yaria J, Ovbiagele B. Controlling cardiovascular diseases in low and middle income countries by placing proof in pragmatism. *BMJ Global Health*. 2016;1
16. Foreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, Pletcher MA, Smith AE, Tang K, Yuan C-W et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. *The Lancet*. 2018;392:2052-2090

17. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, Abbasi-Kangevari M, Abbastabar H, Abd-Allah F, Abdelalim A et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet*. 2020;396:1204-1222
18. O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, Rao-Melacini P, Zhang X, Pais P, Agapay S et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet*. 2016;388:761-775
19. Zhou B, Carrillo-Larco RM, Danaei G, Riley LM, Paciorek CJ, Stevens GA, Gregg EW, Bennett JE, Solomon B, Singleton RK et al. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *The Lancet*. 2021;398:957-980
20. Ministry of Health. Cardiovascular Disease Risk Assessment and Management for Primary Care. Wellington: Ministry of Health. https://www.health.govt.nz/publication/cardiovascular-disease-risk-assessment-and-management-primary-care Accessed 26 April 2019.
21. National Institute for Health and Care Excellence (NICE) Guideline: hypertension in adults: diagnosis and management. Draft for consultation, March 2019. https://www.nice.org.uk/guidance/GID-NG10054/documents/draft-guideline Accessed 10 October 2022.
22. Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, Burnier M, Clement D, Coca A, De Simone G, Dominiczak A et al. 2018 practice guidelines for the management of arterial hypertension of the European society of cardiology and the European society of hypertension ESC/ESH task force for the management of arterial hypertension. *J Hypertens*. 2018;36:2284-2309
23. Whelton PK, Carey RM, Aronow WS, Casey DE, Jr., Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2018;138:e426-e483
24. Herrett E, Gadd S, Jackson R, Bhaskaran K, Williamson E, van Staa T, Sofat R, Timmis A, Smeeth L. Eligibility and subsequent burden of cardiovascular disease of four strategies for blood pressure-lowering treatment: a retrospective cohort study. *The Lancet*. 2019;394:663-671
25. Feigin VL, Brainin M, Norrving B, Gorelick PB, Dichgans M, Wang W, Pandian JD, Martins SCO, Owolabi MO, Wood DA et al. What Is the Best Mix of Population-Wide and High-Risk Targeted Strategies of Primary Stroke and Cardiovascular Disease Prevention? *Journal of the American Heart Association*. 2020;9:e014494
26. Feigin VL. Primary stroke prevention: useful thresholds? *The Lancet Neurology*. 2022;21:116
27. Yusuf S, Pinto FJ. The polypill: from concept and evidence to implementation. *The Lancet*. 2022;400:1661-1663
28. Rahimi K, Bidel Z, Nazarzadeh M, Copland E, Canoy D, Wamil M, Majert J, McManus R, Adler A, Agodoa L et al. Age-stratified and blood-pressure-stratified effects of blood-pressure-lowering pharmacotherapy for the prevention of cardiovascular disease and death: an individual participant-level data meta-analysis. *The Lancet*. 2021;398:1053-1064
29. Brainin M, Grisold W, Hankey GJ, Norrving B, Feigin VL. Time to revise primary prevention guidelines for stroke and cardiovascular disease. *The Lancet Neurology*. 2022;21:686-687
30. Bloom DE, Canning D, Hu L, Liu Y, Mahal AS, Yip WC-m. The Contribution of Population Health and Demographic Change to Economic Growth in China and India. *J Comp Econ*. 2010;38(1):17-33
31. The value of action. Mitigating the global impact of neurological disorders. Economist Impact 2022

https://impact.economist.com/perspectives/sites/default/files/ei_roche_executive_summary.pdf Acccessed 29 November 2022.
32. Nsubuga P, White ME, Thacker SB, Anderson MA, Blount SB, Broome CV, Chiller TM, Espitia V, Imtiaz R, Sosin D et al. Public Health Surveillance: A Tool for Targeting and Monitoring Interventions. In: Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, et al., eds. *Disease Control Priorities in Developing Countries*. Washington (DC): World Bank; 2006.
33. Truelsen T, Bonita R, Jamrozik K. Surveillance of stroke: a global perspective. *International Journal of Epidemiology*. 2001;30:S11-S16
34. World Health Organization. Intersectoral Global Action Plan on epilepsy and other neurological disorders 2022 – 2031. 2021. https://www.who.int/publications/m/item/intersectoral-global-action-plan-on-eepilepsy-and-other-neurological-disorders-2022-2031 Accessed 14 November 2022.
35. Olaiya MT, Sodhi-Berry N, Dalli LL, Bam K, Thrift AG, Katzenellenbogen JM, Nedkoff L, Kim J, Kilkenny MF. The Allure of Big Data to Improve Stroke Outcomes: Review of Current Literature. *Curr Neurol Neurosci Rep*. 2022;22:151-160
36. Thayabaranathan T, Kim J, Cadilhac DA, Thrift AG, Donnan GA, Howard G, Howard VJ, Rothwell PM, Feigin V, Norrving B et al. Global stroke statistics 2022. *Int J Stroke*. 2022;17:946-956
37. Feigin V, Norrving B, Sudlow CLM, Sacco RL. Updated Criteria for Population-Based Stroke and Transient Ischemic Attack Incidence Studies for the 21st Century. *Stroke*. 2018;49:2248-2255
38. Aboa-Eboulé C, Mengue D, Benzenine E, Hommel M, Giroud M, Béjot Y, Quantin C. How accurate is the reporting of stroke in hospital discharge data? A pilot validation study using a population-based stroke registry as control. *J Neurol*. 2013;260:605-613
39. Li L, Binney LE, Luengo-Fernandez R, Silver LE, Rothwell PM. Temporal trends in the accuracy of hospital diagnostic coding for identifying acute stroke: A population-based study. *Eur Stroke J*. 2020;5:26-35
40. Global, regional, and national burden of diseases and injuries for adults 70 years and older: systematic analysis for the Global Burden of Disease 2019 Study. *BMJ*. 2022;376:e068208
41. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, Abd-Allah F, Abdelalim A, Abdollahi M, Abdollahpour I et al. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet*. 2020;396:1223-1249
42. Bam K, Olaiya MT, Cadilhac DA, Donnan GA, Murphy L, Kilkenny MF. Enhancing primary stroke prevention: a combination approach. *The Lancet Public Health*. 2022;7:e721-e724
43. Farooq MU, Chaudhry AH, Amin K, Majid A. The WHO STEPwise Approach to Stroke Surveillance. *Journal of the College of Physicians and Surgeons--Pakistan: JCPSP*. 2008;18:665
44. Norrving B, Barrick J, Davalos A, Dichgans M, Cordonnier C, Guekht A, Kutluk K, Mikulik R, Wardlaw J, Richard E et al. Action Plan for Stroke in Europe 2018–2030. *European Stroke Journal*. 2018
45. World Health O. *WHO steps surveillance manual: the WHO stepwise approach to chronic disease risk factor surveillance*. Geneva: WHO; 2005.
46. Sajjad A, Chowdhury R, Felix JF, Ikram MA, Mendis S, Tiemeier H, Mant J, Franco OH. A systematic evaluation of stroke surveillance studies in low- and middle-income countries. *Neurology*. 2013;80:677-684
47. Feigin VL. Stroke in developing countries: can the epidemic be stopped and outcomes improved? *The Lancet Neurology*. 2007;6:94-97
48. Rocca WA, Reggio A, Savettieri G, Salemi G, Patti F, Meneghini F, Grigoletto F, Morgante L, Di PR. Stroke incidence and survival in three Sicilian municipalities. Sicilian Neuro-Epidemiologic Study (SNES) Group. *Ital.J Neurol.Sci*. 1998;19:351-356
49. Li SC, Schoenberg BS, Wang CC, Cheng XM, Bolis CL, Wang KJ. Cerebrovascular disease in the people's republic of China: Epidemiologic and clinical features. *Neurology*. 1985;35:1708-1713

50. Wang W, Jiang B, Sun H, Ru X, Sun D, Wang L, Wang L, Jiang Y, Li Y, Wang Y et al. Prevalence, Incidence, and Mortality of Stroke in China: Results from a Nationwide Population-Based Survey of 480 687 Adults. *Circulation*. 2017;135:759-771
51. Rothwell PM, Coull AJ, Giles MF, Howard SC, Silver LE, Bull LM, Gutnikov SA, Edwards P, Mant D, Sackley CM et al. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). *Lancet*. 2004;363:1925-1933
52. Cabral NL, Cougo-Pinto PT, Magalhaes PSC, Longo AL, Moro CHC, Amaral CH, Costa G, Reis FI, Gonçalves ARR, Nagel V et al. Trends of Stroke Incidence from 1995 to 2013 in Joinville, Brazil. *Neuroepidemiology*. 2016;46:273-281
53. Cadilhac DA, Kim J, Lannin NA, Kapral MK, Schwamm LH, Dennis MS, Norrving B, Meretoja A. National stroke registries for monitoring and improving the quality of hospital care: A systematic review. *International Journal of Stroke: Official Journal of the International Stroke Society*. 2016;11:28-40
54. Asplund K, Hulter Åsberg K, Appelros P, Bjarne D, Eriksson M, Johansson A, Jonsson F, Norrving B, Stegmayr B, Terént A et al. The Riks-Stroke story: building a sustainable national register for quality assessment of stroke care. *Int J Stroke*. 2011;6:99-108
55. Nichols EK, Byass P, Chandramohan D, Clark SJ, Flaxman AD, Jakob R, Leitao J, Maire N, Rao C, Riley I et al. The WHO 2016 verbal autopsy instrument: An international standard suitable for automated analysis by InterVA, InSilicoVA, and Tariff 2.0. *PLoS Med*. 2018;15:e1002486
56. Tran HT, Nguyen HP, Walker SM, Hill PS, Rao C. Validation of verbal autopsy methods using hospital medical records: a case study in Vietnam. *BMC Medical Research Methodology*. 2018;18:43
57. Varkila MRJ, Cremer OL. Is research from databases reliable? Not sure. *Intensive Care Medicine*. 2019;45:122-124
58. Ozair FF, Jamshed N, Sharma A, Aggarwal P. Ethical issues in electronic health records: A general overview. *Perspectives in Clinical Research*. 2015;6:73-76
59. Porsdam Mann S, Savulescu J, Sahakian BJ. Facilitating the ethical use of health data for the benefit of society: electronic health records, consent and the duty of easy rescue. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*. 2016;374:20160130
60. Liu K. The patient empowerment in the context of electronic health records: A comparison of the legal systems of the european union and the United States. *Medicine and Law*. 2018;37:595-608
61. Mamun Q. A conceptual framework of personally controlled electronic health record (PCEHR) system to enhance security and privacy. *Advances in Intelligent Systems and Computing*. 2018;580:304-314
62. Wilson K, Khansa L. Migrating to electronic health record systems: A comparative study between the United States and the United Kingdom. *Health Policy*. 2018;122:1232-1239
63. Mathur P, Kulothungan V, Leburu S, Krishnan A, Chaturvedi HK, Salve HR, Amarchand R, Nongkynrih B, Kumar PG, K SV et al. National noncommunicable disease monitoring survey (NNMS) in India: Estimating risk factor prevalence in adult population. *PLoS ONE*. 2021;16:e0246712
64. Mishra A, Malik R, Hachiya T, Jürgenson T, Namba S, Posner DC, Kamanu FK, Koido M, Le Grand Q, Shi M et al. Stroke genetics informs drug discovery and risk prediction across ancestries. *Nature*. 2022;611:115-123
65. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC et al. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack; A guideline from the American Heart Association/American Stroke Association. *Stroke*. 2021:E364-E467
66. Hankey GJ. Secondary stroke prevention. *The Lancet Neurology*. 2014;13:178-194

67. Rücker V, Heuschmann PU, O'Flaherty M, Weingärtner M, Hess M, Sedlak C, Schwab S, Kolominsky-Rabas PL. Twenty-Year Time Trends in Long-Term Case-Fatality and Recurrence Rates After Ischemic Stroke Stratified by Etiology. *Stroke*. 2020;51:2778-2785
68. Diener H-C, Hankey GJ. Primary and Secondary Prevention of Ischemic Stroke and Cerebral Hemorrhage: JACC Focus Seminar. *Journal of the American College of Cardiology*. 2020;75:1804-1818
69. Hankey GJ, Spiesser J, Hakimi Z, Carita P, Gabriel S. Time frame and predictors of recovery from disability following recurrent ischemic stroke. *Neurology*. 2007;68:202-205
70. Hackam DG, Spence JD. Combining multiple approaches for the secondary prevention of vascular events after stroke: a quantitative modeling study. *Stroke*. 2007;38:1881-1885
71. Richards A, Jackson NJ, Cheng EM, Bryg RJ, Brown A, Towfighi A, Sanossian N, Barry F, Li N, Vickrey BG. Derivation and Application of a Tool to Estimate Benefits From Multiple Therapies That Reduce Recurrent Stroke Risk. *Stroke*. 2020;51:1563-1569
72. Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JN, Lovelock CE, Binney LE, Bull LM, Cuthbertson FC et al. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. *Lancet*. 2007;370:1432-1442
73. Kolmos M, Christoffersen L, Kruuse C. Recurrent Ischemic Stroke - A Systematic Review and Meta-Analysis. *Journal of Stroke and Cerebrovascular Diseases*. 2021;30
74. Drescher C, Buchwald F, Ullberg T, Pihlsgård M, Norrving B, Petersson J. Epidemiology of first and recurrent ischemic stroke in Sweden 2010-2019 - A Riksstroke study. *Neuroepidemiology*. 2022
75. Flach C, Muruet W, Wolfe CDA, Bhalla A, Douiri A. Risk and Secondary Prevention of Stroke Recurrence: A Population-Base Cohort Study. *Stroke*. 2020;51:2435-2444
76. Modig K, Talbäck M, Ziegler L, Ahlbom A. Temporal trends in incidence, recurrence and prevalence of stroke in an era of ageing populations, a longitudinal study of the total Swedish population. *BMC Geriatrics*. 2019;19:31
77. Hardy ST, Loehr LR, Butler KR, Chakladar S, Chang PP, Folsom AR, Heiss G, MacLehose RF, Matsushita K, Avery CL. Reducing the Blood Pressure-Related Burden of Cardiovascular Disease: Impact of Achievable Improvements in Blood Pressure Prevention and Control. *Journal of the American Heart Association*. 2015;4:e002276
78. Brainin M, Feigin VL, Norrving B, Martins SCO, Hankey GJ, Hachinski V. Global prevention of stroke and dementia: the WSO Declaration. *The Lancet Neurology*. 2020;19:487-488
79. Gamage DG, Riddell MA, Joshi R, Thankappan KR, Chow CK, Oldenburg B, Evans RG, Mahal AS, Kalyanram K, Kartik K et al. Effectiveness of a scalable group-based education and monitoring program, delivered by health workers, to improve control of hypertension in rural India: A cluster randomised controlled trial. *PLoS Med*. 2020;17:e1002997
80. Castellano JM, Pocock SJ, Bhatt DL, Quesada AJ, Owen R, Fernandez-Ortiz A, Sanchez PL, Marin Ortuño F, Vazquez Rodriguez JM, Domingo-Fernández A et al. Polypill Strategy in Secondary Cardiovascular Prevention. *New England Journal of Medicine*. 2022
81. Joseph P, Roshandel G, Gao P, Pais P, Lonn E, Xavier D, Avezum A, Zhu J, Liu L, Sliwa K et al. Fixed-dose combination therapies with and without aspirin for primary prevention of cardiovascular disease: an individual participant data meta-analysis. *The Lancet*. 2021;398:1133-1146
82. Hobeanu C, Lavallée PC, Charles H, Labreuche J, Albers GW, Caplan LR, Donnan GA, Ferro JM, Hennerici MG, Molina CA et al. Risk of subsequent disabling or fatal stroke in patients with transient ischaemic attack or minor ischaemic stroke: an international, prospective cohort study. *The Lancet Neurology*. 2022;21:889-898
83. Adcock AK, Haggerty T, Crawford A, Espinosa C. mHealth impact on secondary stroke prevention: a scoping review of randomized controlled trials among stroke survivors between 2010-2020. *mHealth*. 2022;8:19

84. Feigin VL, Owolabi M, Hankey GJ, Pandian JD, Martins SC. Digital health in primordial and primary stroke prevention: a systematic review. *Stroke*. 2022;53:1008–1019
85. Kamran S, Bener AB, Deleu D, Khoja W, Jumma M, Al Shubali A, Inshashi J, Sharouqi I, Al Khabouri J. The level of awareness of stroke risk factors and symptoms in the Gulf Cooperation Council countries: Gulf Cooperation Council stroke awareness study. *Neuroepidemiology*. 2007;29:235-242
86. Tibebu NS, Emiru TD, Tiruneh CM, Nigat AB, Abate MW, Demelash AT. Knowledge on Prevention of Stroke and Its Associated Factors Among Hypertensive Patients at Debre Tabor General Hospital: An Institution-Based Cross-Sectional Study. *Risk Manag Healthc Policy*. 2021;14:1681-1688
87. Worthmann H, Schwartz A, Heidenreich F, Sindern E, Lorenz R, Adams H-A, Flemming A, Luettje K, Walter U, Haertle B et al. Educational campaign on stroke in an urban population in Northern Germany: influence on public stroke awareness and knowledge. *International Journal of Stroke*. 2013;8:286-292
88. Kim J, Andrew NE, Thrift AG, Bernhardt J, Lindley RI, Cadilhac DA. The potential health and economic impact of improving stroke care standards for Australia. *Int J Stroke*. 2017;12:875-885
89. Brainin M, Teuschl Y, Kalra L. Acute treatment and long-term management of stroke in developing countries. *Lancet Neurol*. 2007;6:553-561
90. Webb A, Heldner MR, Aguiar de Sousa D, Sandset EC, Randall G, Bejot Y, van der Worp B, Caso V, Fischer U. Availability of secondary prevention services after stroke in Europe: An ESO/SAFE survey of national scientific societies and stroke experts. *European Stroke Journal*. 2019;4:110-118
91. Zhang X, Lu J, Yang Y, Cui J, Zhang X, Xu W, Song L, Wu C, Wang Q, Wang Y et al. Cardiovascular disease prevention and mortality across 1 million urban populations in China: data from a nationwide population-based study. *The Lancet Public Health*. 2022;7:e1041-e1050
92. Bayona H, Owolabi M, Feng W, Olowoyo P, Yaria J, Akinyemi R, Sawers JR, Ovbiagele B. A systematic comparison of key features of ischemic stroke prevention guidelines in low- and middle-income vs. high-income countries. *J Neurol Sci*. 2017;375:360-366
93. Willeit P, Toell T, Boehme C, Krebs S, Mayer L, Lang C, Seekircher L, Tschiderer L, Willeit K, Rumpold G et al. STROKE-CARD care to prevent cardiovascular events and improve quality of life after acute ischaemic stroke or TIA: A randomised clinical trial. *EClinicalMedicine*. 2020;25:100476
94. Feigin VL, Norrving B, Mensah GA. Primary prevention of cardiovascular disease through population-wide motivational strategies: insights from using smartphones in stroke prevention. *BMJ Global Health*. 2017 Apr 4;2:DOI: 10.1136/bmjgh-2017-000306
95. Pandian JD, Gall SL, Kate MP, Silva GS, Akinyemi RO, Ovbiagele BI, Lavados PM, Gandhi DBC, Thrift AG. Prevention of stroke: a global perspective. *The Lancet*. 2018;392:1269-1278
96. World Health Organization. Seventy-fifth World Health Assembly. Provisional agenda item 14.1. Follow-up to the political declaration of the third high-level meeting of the General Assembly on the prevention and control of non-communicable diseases. A75/10 Add.8. 27 April 2022. https://apps.who.int/gb/ebwha/pdf_files/WHA75/A75_10Add8-en.pdf Accessed 14 May 2022.
97. Esenwa C, Gutierrez J. Secondary stroke prevention: challenges and solutions. *Vascular health and risk management*. 2015;11:437-450
98. Graham GD. Secondary Stroke Prevention: From Guidelines to Clinical Practice. *Journal of the National Medical Association*. 2008;100:1125-1137
99. Spence JD. Secondary stroke prevention. *Nat Rev Neurol*. 2010;6:477-486
100. Feigin VL, Krishnamurthi R, Merkin A, Nair B, Kravchenko M, Jalili-Moghaddam S. Digital solutions for primary stroke and cardiovascular disease prevention: a mass individual and

public health approach. *The Lancet Regional Health - Western Pacific*. 2022;100511:https://doi.org/10.1016/j.lanwpc.2022.100511

101. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140:e563-e595
102. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, Benetos A, Biffi A, Boavida J-M, Capodanno D et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology (EAPC). *European Heart Journal*. 2021;42:3227-3337
103. Diener H-C, Hankey GJ, Easton JD, Lip GYH, Hart RG, Caso V. Non-vitamin K oral anticoagulants for secondary stroke prevention in patients with atrial fibrillation. *European heart journal supplements : journal of the European Society of Cardiology*. 2020;22:I13-I21
104. Dawson J, Béjot Y, Christensen LM, De Marchis GM, Dichgans M, Hagberg G, Heldner MR, Milionis H, Li L, Pezzella FR et al. European Stroke Organisation (ESO) guideline on pharmacological interventions for long-term secondary prevention after ischaemic stroke or transient ischaemic attack. *Eur Stroke J*. 2022;7:I-ii
105. Fonseca AC, Merwick Á, Dennis M, Ferrari J, Ferro JM, Kelly P, Lal A, Ois A, Olivot JM, Purroy F. European Stroke Organisation (ESO) guidelines on management of transient ischaemic attack. *Eur Stroke J*. 2021;6:V
106. Emberson J, Whincup P, Morris R, Walker M, Ebrahim S. Evaluating the impact of population and high-risk strategies for the primary prevention of cardiovascular disease. *Eur Heart J*. 2004;25:484-491
107. Navar AM, Fonarow GC, Pencina MJ. Time to Revisit Using 10-Year Risk to Guide Statin Therapy. *JAMA Cardiology*. 2022;7:785-786
108. Brainin M, Sliwa K. WSO and WHF joint position statement on population-wide prevention strategies. *The Lancet*. 2020;396:533-534
109. Tsakpounidou K, van der Merwe J, Klinke ME, Webb C, Ouriques Martins SC, Proios H. FAST Heroes: Results of Cross-Country Implementation of a Global School-Based Stroke Education Campaign. *Frontiers in Public Health*. 2022;10
110. Tsakpounidou K, Loutrari A, Tselekidou F, Baskini M, Proios H. FAST 112 HEROES: A kindergarten-based educational stroke intervention for the whole family. *Health Education Journal*. 2020;79:724-734
111. Cluster WHOND, Mental H. *WHO STEPS stroke manual : the WHO STEPwise approach to stroke surveillance*. World Health Organization; 2005.
112. Pandian JD, William AG, Kate MP, Norrving B, Mensah GA, Davis S, Roth GA, Thrift AG, Kengne AP, Kissela BM et al. Strategies to Improve Stroke Care Services in Low- and Middle-Income Countries: A Systematic Review. *Neuroepidemiology*. 2017;49:45-61
113. Lindsay P, Furie KL, Davis SM, Donnan GA, Norrving B. World stroke organization global stroke services guidelines and action plan. *International Journal of Stroke*. 2014;9:4-13
114. Tsakpounidou K, Tsitiroki A, Keramydas C, Proios H. Digital implementation of originally school-based stroke educational programme in Greece due to the COVID-19 pandemic. *International Journal of Health Promotion and Education*. 2022:1-11
115. Mishra A, Malik R, Hachiya T, Jürgenson T, Namba S, Posner DC, Kamanu FK, Koido M, Le Grand Q, Shi M et al. Stroke genetics informs drug discovery and risk prediction across ancestries. *Nature*. 2022;611:115-123

116. United Nations Development Group. UNDAF Campanion Guidance: Theory of Change. https://unsdg.un.org/sites/default/files/UNDG-UNDAF-Companion-Pieces-7-Theory-of-Change.pdf Accessed 13 June 2022.
117. Martin AR, Kanai M, Kamatani Y, Okada Y, Neale BM, Daly MJ. Clinical use of current polygenic risk scores may exacerbate health disparities. *Nat Genet*. 2019;51:584-591
118. Krishnamurthi R, Barker-Colllo S, Theadom A, Bhattacharjee R, George AS, Arroll B, Ranta A, Walters D, Wilson D, Sandiford P et al. Mobile technology for primary stroke prevention: a proof-of-concept pilot randomised controlled trial - a brief report. *Stroke*. 2018;50:196-198
119. Parmar P, Krishnamurthi R, Ikram MA, Hofman A, Mirza SS, Varakin Y, Kravchenko M, Piradov M, Thrift AG, Norrving B et al. The Stroke Riskometer App: validation of a data collection tool and stroke risk predictor. *International Journal of Stroke*. 2015;10:231-244
120. Medvedev O, Truong Q, Merkin A, Borotkanics R, Krishnamurthi R, Feigin V. Cross-cultural validation of the Stroke Riskometer using generalizability theory. *Scientific Reports. Nature Portfolio*. 2021;11:19064 doi.org/19010.11038/s41598-19021-98591-19068
121. Balsari S, Phadke M, Simon G, Goyal R, Mulholland I. *Task Shifting in Indian Healthcare: reframing the AYSH Debate. Harvard University South Asia Institute 2018*.
122. Sylaja PN, Singh G, Sivasambath S, Arun K, Jeemon P, Antony R, Kalani R, Gopal BK, Soman B. Secondary prevention of stroke by a primary health care approach: An open-label cluster randomised trial. *Journal of Clinical Neuroscience*. 2021;84:53-59
123. Kaur P, Kunwar A, Sharma M, Mitra J, Das C, Swasticharan L, Chakma T, Dipak Bangar S, Venkatasamy V, Dharamsoth R et al. India Hypertension Control Initiative-Hypertension treatment and blood pressure control in a cohort in 24 sentinel site clinics. *J Clin Hypertens (Greenwich)*. 2021;23:720-729
124. World Health Organization. Assessing national capacity for the prevention and control of NCDs [Internet]. WHO. 2018 http://www.who.int/ncds/surveillance/ncd-capacity/en/ Accessed 16 October 2020.
125. Institute for Health Metrics and Evaluation (IHME). GBD Compare Data Visualization. Seattle, WA: IHME, University of Washington, 2019. Available from https://vizhub.healthdata.org/gbd-compare/. Accessed 9 November 2021.
126. Langhorne P, Ramachandra S. Organised inpatient (stroke unit) care for stroke: network meta-analysis. *Cochrane Database Syst Rev*. 2020;4:Cd000197
127. Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, Brott T, Cohen G, Davis S, Donnan G et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. *Lancet*. 2014;384:1929-1935
128. Campbell BCV, Ma H, Ringleb PA, Parsons MW, Churilov L, Bendszus M, Levi CR, Hsu C, Kleinig TJ, Fatar M et al. Extending thrombolysis to 4·5-9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data. *Lancet*. 2019;394:139-147
129. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CB, van der Lugt A, de Miquel MA et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723-1731
130. Roaldsen MB, Jusufovic M, Berge E, Lindekleiv H. Endovascular thrombectomy and intra-arterial interventions for acute ischaemic stroke. *Cochrane Database of Systematic Reviews*. 2021;14;6(6):CD007574. doi: 10.1002/14651858.CD007574.pub3.
131. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, Yavagal DR, Ribo M, Cognard C, Hanel RA et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. *New England Journal of Medicine*. 2017;378:11-21

132. Albers GW, Lansberg MG, Kemp S, Tsai JP, Lavori P, Christensen S, Mlynash M, Kim S, Hamilton S, Yeatts SD et al. A multicenter randomized controlled trial of endovascular therapy following imaging evaluation for ischemic stroke (DEFUSE 3). *Int J Stroke*. 2017;12:896-905
133. Boulanger JM, Lindsay MP, Gubitz G, Smith EE, Stotts G, Foley N, Bhogal S, Boyle K, Braun L, Goddard T et al. Canadian Stroke Best Practice Recommendations for Acute Stroke Management: Prehospital, Emergency Department, and Acute Inpatient Stroke Care, 6th Edition, Update 2018. *Int J Stroke*. 2018;13:949-984
134. The Burden of Stroke in Europe. Stroke Alliance for Europe (SAFE 2017), ISBN 978-1-5272-0857-5 http://www.strokeeurope.eu/downloads/The_Burden_of_Stroke_in_Europe_Report_-_Appendix.pdf.
135. Hoffmeister L, Lavados PM, Mar J, Comas M, Arrospide A, Castells X. Minimum intravenous thrombolysis utilization rates in acute ischemic stroke to achieve population effects on disability: A discrete-event simulation model. *J Neurol Sci*. 2016;365:59-64
136. Lavados PM, Diaz V, Jadue L, Olavarria VV, Carcamo DA, Delgado I. Socioeconomic and cardiovascular variables explaining regional variations in stroke mortality in Chile: an ecological study. *Neuroepidemiology*. 2011;37:45-51
137. Hasnain MG, Attia JR, Akter S, Rahman T, Hall A, Hubbard IJ, Levi CR, Paul CL. Effectiveness of interventions to improve rates of intravenous thrombolysis using behaviour change wheel functions: a systematic review and meta-analysis. *Implement Sci*. 2020;15:98
138. Cisse FA, Damien C, Bah AK, Touré ML, Barry M, Djibo Hamani AB, Haba M, Soumah FM, Naeije G. Minimal Setting Stroke Unit in a Sub-Saharan African Public Hospital. *Front Neurol*. 2019;10:856
139. Dos Santos E, Wollmann GM, Nagel V, Ponte HMS, Furtado LETA, Martins-Filho RKV, Weiss G, Martins SCO, Ferreira LE, França PHCd et al. Incidence, lethality, and post-stroke functional status in different Brazilian macro-regions: The SAMBA study (analysis of stroke in multiple Brazilian areas). *Front Neurol*. 2022;13: 966785. doi: 10.3389/fneur.2022.966785
140. Aguiar de Sousa D, von Martial R, Abilleira S, Gattringer T, Kobayashi A, Gallofré M, Fazekas F, Szikora I, Feigin V, Caso V et al. Access to and delivery of acute ischaemic stroke treatments: A survey of national scientific societies and stroke experts in 44 European countries. *European Stroke Journal*. 2018;4:13-28
141. Martins SC, Sacks C, Hacke W, Brainin M, Figueiredo FDA, Pontes-Neto O, et al. Priorities to reduce the burden of stroke in Latin American countries. *The Lancet Neurology*. 2019;18:674-683
142. Shahjouei S, Bavarsad-Shahripour R, Assarzadegan F, Rikhtegar R, Mehrpour M, Zamani B, Tsivgoulis G, Alexandrov A, Alexandrov A, Zand R. Acute management of stroke in Iran: Obstacles and solutions. *Iranian Journal of Neurology*. 2017;16:62-71
143. Ince B, Necioglu D. Organization of stroke care in Turkey. *International Journal of Stroke*. 2017;12:105-107
144. World Health Organization. WHO model list of essential medicines - 22nd list, 2021. https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2021.02 Accessed 13 January 2023.
145. Chimatiro GL, Rhoda AJ. Scoping review of acute stroke care management and rehabilitation in low and middle-income countries. *BMC Health Services Research*. 2019;19:789
146. Li Z, Pandian J, Sylaja PN, Wang Y, Zhao X, Liu L, Wang C, Khurana D, Srivastava MVP, Kaul S et al. Quality of care for ischemic stroke in China vs India: Findings from national clinical registries. *Neurology*. 2018;91:e1348-e1354
147. Khatib R, Arevalo YA, Berendsen MA, Prabhakaran S, Huffman MD. Presentation, Evaluation, Management, and Outcomes of Acute Stroke in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis. *Neuroepidemiology*. 2018;51:104-112

148. Akinyemi R, Ovbiagele B, Adeniji O, Sarfo F, Abdallah F, Thierry A, Ogah S, Naidoo P, Damasceno A, Walker R et al. Stroke in Africa: Profile, Progress, Prospects and Priorities *Nature Reviews Neurology*. 2021;17(10):634-656
149. Baatiema L, Otim M, Mnatzaganian G, Aikins AD-G, Coombes J, Somerset S. Towards best practice in acute stroke care in Ghana: a survey of hospital services. *BMC Health Services Research*. 2017;17
150. de Souza AC, Sebastian IA, Zaidi WAW, Nasreldein A, Bazadona D, Amaya P, Elkady A, Gebrewold MA, Vorasayan P, Yeghiazaryan N et al. Regional and national differences in stroke thrombolysis use and disparities in pricing, treatment availability, and coverage. *Int J Stroke*. 2022;17:990-996
151. Sundar K, Panwar A, Yagaval DR, Huded V, Sylaja PN. Mission Thrombectomy 2020 (MT2020)—India's Biggest Healthcare Challenge Yet. *Journal of Stroke Medicine*. 2020;3:62-71
152. Al-Rukn S, Mazya M, Akhtar N, Hashim H, Mansouri B, Faouzi B, Aref H, Abdulrahman H, Kesraoui S, Hentati F et al. Stroke in the Middle-East and North Africa: A 2-year prospective observational study of intravenous thrombolysis treatment in the region. Results from the SITS-MENA Registry. *Int J Stroke*. 2020;15:980-987
153. Martins SCO, Lavados P, Secchi TL, Brainin M, Ameriso S, Gongora-Rivera F, Sacks C, Cantú-Brito C, Alvarez Guzman TF, Pérez-Romero GE et al. Fighting Against Stroke in Latin America: A Joint Effort of Medical Professional Societies and Governments. *Front Neurol*. 2021;12:743732
154. Marquez-Romero JM, Góngora-Rivera F, Hernández-Curiel BC, Aburto-Murrieta Y, García-Cazares R, Delgado-Garzón P, Murillo-Bonilla LM, Ochoa-Solórzano MA. Endovascular Treatment of Ischemic Stroke in a Developing Country. *Vasc Endovascular Surg*. 2020;54:305-312
155. Gongora-Rivera F, Gonzalez-Aquines A, Marquez-Romero JM. Identification of Barriers to Access Endovascular Treatment for Acute Ischemic Stroke in the Health Care System of Mexico: Results From a National Survey Among Endovascular Neurologists. *Front Neurol*. 2021;12:601328
156. Saposnik G, Galanos LC, Guerrero R, Casagrande F, Adhamidhis E, Gao MMY, Grupper MF, Arsovska A. The World Stroke Academy: A World Stroke Organization global pathway to improve knowledge in stroke care. *Int J Stroke*. 2022;17:17474930221085895
157. Rose J, Weiser TG, Hider P, Wilson L, Gruen RL, Bickler SW. Estimated need for surgery worldwide based on prevalence of diseases: a modelling strategy for the WHO Global Health Estimate. *The Lancet Global Health*. 2015;3:S13-S20
158. Wechsler Lawrence R, Demaerschalk Bart M, Schwamm Lee H, Adeoye Opeolu M, Audebert Heinrich J, Fanale Christopher V, Hess David C, Majersik Jennifer J, Nystrom Karin V, Reeves Mathew J et al. Telemedicine Quality and Outcomes in Stroke: A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*. 2017;48:e3-e25
159. Demaerschalk BM, Switzer JA, Xie J, Fan L, Villa KF, Wu EQ. Cost utility of hub-and-spoke telestroke networks from societal perspective. *The American Journal of Managed Care*. 2013;19:976-985
160. Martins SO, Mont'Alverne F, Rebello LC, Abud DG, Silva GS, Lima FO, Parente BSM, Nakiri GS, Faria MB, Frudit ME et al. Thrombectomy for Stroke in the Public Health Care System of Brazil. *New England Journal of Medicine*. 2020;382:2316-2326
161. Switzer JA, Demaerschalk BM, Xie J, Fan L, Villa KF, Wu EQ. Cost-effectiveness of hub-and-spoke telestroke networks for the management of acute ischemic stroke from the hospitals' perspectives. *Circulation. Cardiovascular Quality and Outcomes*. 2013;6:18-26

162. Nelson RE, Okon N, Lesko AC, Majersik JJ, Bhatt A, Baraban E. The cost-effectiveness of telestroke in the Pacific Northwest region of the USA. *Journal of Telemedicine and Telecare*. 2016;22:413-421
163. Sarfo FS, Adamu S, Awuah D, Sarfo-Kantanka O, Ovbiagele B. Potential role of tele-rehabilitation to address barriers to implementation of physical therapy among West African stroke survivors: A cross-sectional survey. *J Neurol Sci*. 2017;381:203-208
164. Powers William J, Rabinstein Alejandro A, Ackerson T, Adeoye Opeolu M, Bambakidis Nicholas C, Becker K, Biller J, Brown M, Demaerschalk Bart M, Hoh B et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*. 2019;50:e344-e418
165. Hillis JM, Berkowitz AL. Neurology Training Worldwide. *Seminars in Neurology*. 2018;38:135-144
166. Hollenbeak CS, Gorton CP, Tabak YP, Jones JL, Milstein A, Johannes RS. Reductions in Mortality Associated With Intensive Public Reporting of Hospital Outcomes. *American Journal of Medical Quality*. 2008;23:279-286
167. Feigin VL, Norrving B, Mensah GA. Global Burden of Stroke. *Circulation Research*. 2017;120:439-448
168. Divani AA, Majidi S, Barrett AM, Noorbaloochi S, Luft AR. Consequences of stroke in community-dwelling elderly: the health and retirement study, 1998 to 2008. *Stroke*. 2011;42:1821-1825
169. Bernhardt J, Borschmann K, Boyd L, Thomas Carmichael S, Corbett D, Cramer SC, Hoffmann T, Kwakkel G, Savitz SI, Saposnik G et al. Moving rehabilitation research forward: Developing consensus statements for rehabilitation and recovery research. *Int J Stroke*. 2016;11:454-458
170. Kwakkel G, Lannin NA, Borschmann K, English C, Ali M, Churilov L, Saposnik G, Winstein C, van Wegen EE, Wolf SL et al. Standardized measurement of sensorimotor recovery in stroke trials: Consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable. *Int J Stroke*. 2017;12:451-461
171. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. *The Lancet*. 2011;377:1693-1702
172. Belagaje SR. Stroke Rehabilitation. *CONTINUUM: Lifelong Learning in Neurology*. 2017;23:238-253
173. Dieleman JL, Campbell M, Chapin A, Eldrenkamp E, Fan VY, Haakenstad A, Kates J, Li Z, Matyasz T, Micah A et al. Future and potential spending on health 2015-40: development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. *The Lancet*. 2017;389:2005-2030
174. Dieleman J, Campbell M, Chapin A, Eldrenkamp E, Fan VY, Haakenstad A, Kates J, Liu Y, Matyasz T, Micah A et al. Evolution and patterns of global health financing 1995–2014: development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. *The Lancet*. 2017;389:1981-2004
175. Tawa N, Rhoda A, Brink Y, Urimubenshi G, Giljam-Enright M, Charumbira MY, Niekerk SM, Louw Q. Human Functioning, Technology and Health. Stroke rehabilitation services in Africa – Challenges and opportunities: A scoping review of the literature. In: Louw Q, ed. *Collaborative capacity development to complement stroke rehabilitation in Africa*. Cape Town (ZA): Aosis. Copyright © Quinette Louw.; 2020.
176. World Health Organization. Assessing national capacity for the prevention and control of noncommunicable diseases: report of the 2019 global survey. Geneva: World Health Organization; 2020 https://apps.who.int/iris/handle/10665/331452 Accesssed 14 November 2022.

177. Grecu A, Simsic S, Svobodová V, Mikulík R. *REGISTRY FOR STROKE CARE QUALITY (RES-Q) – A REGISTRY TOOL FOR EVALUATING STROKE CARE QUALITY INDICES IN EASTERN EUROPE AND WESTERN ASIA*. 2017.
178. Mikulik R, Bar M, Grecu A, Herzig R, Neumann J, Sanak D, Skoda O, Skoloudik D, Svobodova V, Tomek A et al. The registry of stroke care quality (RES-Q): The first nation-wide data on stroke care quality. *Journal of the Neurological Sciences*. 2017;381:91
179. Gorthi SP, Garg D. Stroke Epidemiology among Young Persons in India: Every Step Counts. *Annals of Indian Academy of Neurology*. 2022;25:1-2
180. Walters R, Collier JM, Braighi Carvalho L, Langhorne P, Katijjahbe MA, Tan D, Moodie M, Bernhardt J. Exploring post acute rehabilitation service use and outcomes for working age stroke survivors (≤65 years) in Australia, UK and South East Asia: data from the international AVERT trial. *BMJ Open*. 2020;10:e035850
181. Roushdy T, Aref H, Kesraoui S, Temgoua M, Nono KP, Gebrewold MA, Peter W, Gopaul U, Belahsen MF, Ben-Adji D et al. Stroke services in Africa: What is there and what is needed. *Int J Stroke*. 2022;17:972-982
182. Murie-Fernández M, Laxe S. Comparison of stroke neurorehabilitation in Spain and in Europe. *Neurología (English Edition)*. 2020;35:354-355
183. Rhoda A, Smith M, Putman K, Mpofu R, DeWeerdt W, DeWit L. Motor and functional recovery after stroke: a comparison between rehabilitation settings in a developed versus a developing country. *BMC Health Serv Res*. 2014;14:82
184. Labberton AS, Barra M, Rønning OM, Thommessen B, Churilov L, Cadilhac DA, Lynch EA. Patient and service factors associated with referral and admission to inpatient rehabilitation after the acute phase of stroke in Australia and Norway. *BMC Health Serv Res*. 2019;19:871
185. Unrath M, Kalic M, Berger K. Who receives rehabilitation after stroke?: Data from the quality assurance project "Stroke Register Northwest Germany". *Dtsch Arztebl Int*. 2013;110:101-107
186. Tyagi S, Lim DSY, Ho WHH, Koh YQ, Cai V, Koh GCH, Legido-Quigley H. Acceptance of Tele-Rehabilitation by Stroke Patients: Perceived Barriers and Facilitators. *Arch Phys Med Rehabil*. 2018;99:2472-2477.e2472
187. Davoody N, Hägglund M. Care Professionals' Perceived Usefulness Of A Rehabilitation Ehealth Service In Stroke Care. *Stud Health Technol Inform*. 2015;216:992
188. Wafa HA, Wolfe CDA, Emmett E, Roth GA, Johnson CO, Wang Y. Burden of Stroke in Europe. *Stroke*. 2020;51:2418-2427
189. Bernhardt J, Urimubenshi G, Gandhi DBC, Eng JJ. Stroke rehabilitation in low-income and middle-income countries: a call to action. *The Lancet*. 2020;396:1452-1462
190. Dosage, Intensity, and Frequency of Language Therapy for Aphasia: A Systematic Review-Based, Individual Participant Data Network Meta-Analysis. *Stroke*. 2022;53:956-967
191. Longley V, Hazelton C, Heal C, Pollock A, Woodward-Nutt K, Mitchell C, Pobric G, Vail A, Bowen A. Non-pharmacological interventions for spatial neglect or inattention following stroke and other non-progressive brain injury. *Cochrane Database Syst Rev*. 2021;7:Cd003586
192. Platz T, Sandrini G. Specialty Grand Challenge for NeuroRehabilitation Research. *Front Neurol*. 2020;11:349
193. WHO. Basic Rehabilitation Package Clinical Resource. https://www.who.int/activities/integrating-rehabilitation-into-health-systems/service-delivery/basic-rehabilitation-package-clinical-resource-information-sheet Accessed 11 January 2023.
194. He M, Wang Je, Dong Q, Ji N, Meng P, Liu N, Geng S, Qin S, Xu W, Zhang C et al. Community-based stroke system of care improves patient outcomes in Chinese rural areas. *Journal of Epidemiology and Community Health*. 2018;72:630
195. Niama Natta DD, Lejeune T, Detrembleur C, Yarou B, Sogbossi ES, Alagnidé E, Kpadonou T, Selves C, Stoquart G. Effectiveness of a self-rehabilitation program to improve upper-

extremity function after stroke in developing countries: A randomized controlled trial. *Ann Phys Rehabil Med*. 2021;64:101413
196. Zhou B, Zhang J, Zhao Y, Li X, Anderson CS, Xie B, Wang N, Zhang Y, Tang X, Prvu Bettger J et al. Caregiver-Delivered Stroke Rehabilitation in Rural China. *Stroke*. 2019;50:1825-1830
197. Liu H, Lindley R, Alim M, Felix C, Gandhi DB, Verma SJ, Tugnawat DK, Syrigapu A, Ramamurthy RK, Pandian JD et al. Family-led rehabilitation in India (ATTEND)-Findings from the process evaluation of a randomized controlled trial. *Int J Stroke*. 2019;14:53-60
198. Kwakkel G, van Wegen EEH. Family-delivered rehabilitation services at home: is the glass empty? *Lancet*. 2017;390:538-539
199. Olaleye OA, Hamzat TK, Owolabi MO. Development and evaluation of the Primary Healthcare-based Physiotherapy Intervention and its effects on selected indices of stroke recovery. *International Journal of Therapy and Rehabilitation*. 2013;20:443-449
200. Olaleye OA, Hamzat TK, Owolabi MO. Stroke rehabilitation: should physiotherapy intervention be provided at a primary health care centre or the patients' place of domicile? *Disabil Rehabil*. 2014;36:49-54
201. Kuo LM, Huang HL, Huang HL, Liang J, Chiu YC, Chen ST, Kwok YT, Hsu WC, Shyu YI. A home-based training program improves Taiwanese family caregivers' quality of life and decreases their risk for depression: a randomized controlled trial. *Int J Geriatr Psychiatry*. 2013;28:504-513
202. Vloothuis JD, Mulder M, Veerbeek JM, Konijnenbelt M, Visser-Meily JM, Ket JC, Kwakkel G, van Wegen EE. Caregiver-mediated exercises for improving outcomes after stroke. *Cochrane Database Syst Rev*. 2016;12:Cd011058
203. Cramer SC, Dodakian L, Le V, See J, Augsburger R, McKenzie A, Zhou RJ, Chiu NL, Heckhausen J, Cassidy JM et al. Efficacy of Home-Based Telerehabilitation vs In-Clinic Therapy for Adults After Stroke: A Randomized Clinical Trial. *JAMA Neurol*. 2019;76:1079-1087
204. Hempler I, Woitha K, Thielhorn U, Farin E. Post-stroke care after medical rehabilitation in Germany: a systematic literature review of the current provision of stroke patients. *BMC Health Serv Res*. 2018;18:468
205. Ekechukwu END, Olowoyo P, Nwankwo KO, Olaleye OA, Ogbodo VE, Hamzat TK, Owolabi MO. Pragmatic Solutions for Stroke Recovery and Improved Quality of Life in Low- and Middle-Income Countries-A Systematic Review. *Front Neurol*. 2020;11:337
206. Platz T. Evidence-Based Guidelines and Clinical Pathways in Stroke Rehabilitation-An International Perspective. *Front Neurol*. 2019;10:200
207. Platz T. Clinical Pathways in Stroke Rehabilitation Evidence-based Clinical Practice Recommendations: Evidence-based Clinical Practice Recommendations. 2021.
208. Lo SHS, Chang AM, Chau JPC. Stroke Self-Management Support Improves Survivors' Self-Efficacy and Outcome Expectation of Self-Management Behaviors. *Stroke*. 2018;49:758-760
209. Jones KM, Bhattacharjee R, Krishnamurthi R, Blanton S, Barker-Collo S, Theadom A, Thrift AG, Wolf SL, Venketasubramanian N, Parmar P et al. Determining the feasibility and preliminary efficacy of a stroke instructional and educational DVD in a multinational context: a randomized controlled pilot study. *Clin Rehabil*. 2018;32:1086-1097
210. Shiggins C, Ryan B, O'Halloran R, Power E, Bernhardt J, Lindley RI, McGurk G, Hankey GJ, Rose ML. Towards the Consistent Inclusion of People With Aphasia in Stroke Research Irrespective of Discipline. *Archives of Physical Medicine and Rehabilitation*. 2022;103:2256-2263
211. Owolabi MO, Leonardi M, Bassetti C, Jaarsma J, Hawrot T, Makanjuola AI, Dhamija RK, Feng W, Straub V, Camaradou J et al. The neurology revolution. *The Lancet Neurology*. 2022;21:960-961
212. GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet Neurology*. 2019;18:459-480

213. Feigin VL, Vos T, Nichols E, Owolabi MO, Carroll WM, Dichgans M, Deuschl G, Parmar P, Brainin M, Murray C. The global burden of neurological disorders: translating evidence into policy. *The Lancet Neurology*. 2020;19:255-265
214. The Lancet N. A decisive year for the neurological community. *The Lancet Neurology*. 2022;21:103
215. Guekht A, Brodie M, Secco M, Li S, Volkers N, Wiebe S. The road to a World Health Organization global action plan on epilepsy and other neurological disorders. *Epilepsia*. 2021;62:1057-1063
216. Wiebers DO, Feigin VL, Winkler AS. Brain Health, One Health, and COVID-19. *Neuroepidemiology*. 2021;55:425-426
217. Wiebers DO, Feigin VL, Winkler AS. All Life Protection and Our Collective Future. *Neuroepidemiology*. 2022 https://doi.org/10.1159/000525021
218. World Health Organization. Rehabilitation 2030. https://www.who.int/initiatives/rehabilitation-2030 Accessed 14 November 2022.
219. World Health Organization. Invisible numbers: the true extent of noncommunicable diseases and what to do about them. Geneva: World Health Organization; 2022 https://apps.who.int/iris/handle/10665/362800 Accessed 14 November 2022.
220. World Health Organization. One Health. https://www.who.int/news-room/questions-and-answers/item/one-health Accessed 13 January 2023.
221. UN Environment Programme. One Health Joint Plan of Action to address health threats to humans, animals, plants and environment. https://www.unep.org/news-and-stories/press-release/one-health-joint-plan-action-address-health-threats-humans-animals Accessed 13 January 2023.
222. UN Environment Programme. One Health Joint Plan of Action (2022 - 2026). 17 October 2022. https://www.unep.org/resources/publication/one-health-joint-plan-action-2022-2026 Accessed 13 January 2023.
223. World Health Organization. Optimizing brain health across the life course: WHO position paper [Internet]. Geneva: World Health Organization; 2022. https://apps.who.int/iris/handle/10665/361251 Accessed 14 November 2022.
224. Stroke Action Plan for Europe (SAP-E), https://actionplan.eso-stroke.org Accessesd 14 November 2022.
225. Jones KM, Bhattacharjee R, Krishnamurthi R, Blanton S, Theadom A, Barker-Collo S, Thrift A, Parmar P, Maujean A, Ranta A et al. Methodology of the Stroke Self-Management Rehabilitation Trial: an international, multisite pilot trial. *J Stroke Cerebrovasc Dis*. 2015;24:297-303
226. Pires DS, Boasquevisque DDS, Speciali DS, Silva GS, Conforto AB, Pires DS, et al. Success of promotion strategies for a stroke rehabilitation protocol. Revista da Associação Médica Brasileira. 2018 May;64(5):443–7.
227. Stuifbergen AK, Gordon D, Clark AP. Health Promotion: A Complementary Strategy for Stroke Rehabilitation. *Topics in Stroke Rehabilitation*. 1998;5:11-18
228. Allen LN, Pullar J, Wickramasinghe KK, Williams J, Roberts N, Mikkelsen B, Varghese C, Townsend N. Evaluation of research on interventions aligned to WHO 'Best Buys' for NCDs in low-income and lower-middle-income countries: a systematic review from 1990 to 2015. *BMJ Global Health*. 2018;3:e000535
229. Akinyemi R, Sarfo F, Abd-Allah F, Ogun Y, Belo M, Francis P, Mateus MB, Bateman K, Naidoo P, Charway-Felli A et al. Conceptual framework for establishing the African Stroke Organization. *Int J Stroke*. 2021;16:93-99
230. Owolabi M, Sarfo F, Akinyemi R, Gebreyohanns M, Ovbiagele B. The Sub-Saharan Africa Conference on Stroke (SSACS): An idea whose time has come. *Journal of the Neurological Sciences*. 2019;400

231. Urimubenshi G, Langhorne P, Cadilhac DA, Kagwiza JN, Wu O. Association between patient outcomes and key performance indicators of stroke care quality: A systematic review and meta-analysis. *Eur Stroke J*. 2017;2:287-307
232. Grube MM, Dohle C, Djouchadar D, Rech P, Bienek K, Dietz-Fricke U, Jöbges M, Kohler M, Missala I, Schönherr B et al. Evidence-based quality indicators for stroke rehabilitation. *Stroke*. 2012;43:142-146
233. Hubbard IJ, Harris D, Kilkenny MF, Faux SG, Pollack MR, Cadilhac DA. Adherence to clinical guidelines improves patient outcomes in Australian audit of stroke rehabilitation practice. *Arch Phys Med Rehabil*. 2012;93:965-971
234. Ntsiea MV. Current stroke rehabilitation services and physiotherapy research in South Africa. *S Afr J Physiother*. 2019;75:475
235. WHO report on the global tobacco epidemic, 2015: raising taxes on tobacco. World Health Organization, Geneva. 2015
236. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D et al. Grading quality of evidence and strength of recommendations. *BMJ*. 2004;328:1490
237. United Nations General Assembly, Seventy-second session. Progress on the prevention and control of non-communicable diseases. Report of the Secretary-General. 21 December 2017. A/72/662 https://ncdalliance.org/sites/default/files/resource_files/UNSG%20Report%20on%20NCDs%20December%202017%20A.72.662%20SG%20report.pdf Accessed on 9 March 2018.
238. Pearson TA, Palaniappan LP, Artinian NT, Carnethon MR, Criqui MH, Daniels SR, Fonarow GC, Fortmann SP, Franklin BA, Galloway JM et al. American Heart Association Guide for Improving Cardiovascular Health at the Community Level, 2013 update: a scientific statement for public health practitioners, healthcare providers, and health policy makers. *Circulation*. 2013;127:1730-1753
239. Goodchild M, Perucic A-M, Nargis N. Modelling the impact of raising tobacco taxes on public health and finance. *Bulletin of the World Health Organization*. 2016;94:250-257
240. Hopkins DP, Briss PA, Ricard CJ, Husten CG, Carande-Kulis VG, Fielding JE, Alao MO, McKenna JW, Sharp DJ, Harris JR et al. Reviews of evidence regarding interventions to reduce tobacco use and exposure to environmental tobacco smoke. *American Journal of Preventive Medicine*. 2001;20:16-66
241. Asaria P, Chisholm D, Mathers C, Ezzati M, Beaglehole R. Chronic disease prevention: health effects and financial costs of strategies to reduce salt intake and control tobacco use. *Lancet*. 2007;370:2044-2053
242. Wilson N. Salt tax could reduce population's salt intake. *British Medical Journal*. 2004;329:918
243. Chaloupka FJ, Grossman M, Saffer H. The effects of price on alcohol consumption and alcohol-related problems. *Alcohol Research and Health*. 2002;26:22-34
244. Delcher C, Maldonado-Molina MM, Wagenaar AC. Effects of alcohol taxes on alcohol-related disease mortality in New York State from 1969 to 2006. *Addictive Behaviors*. 2012;37:783-789
245. Elder RW, Lawrence B, Ferguson A, Naimi TS, Brewer RD, Chattopadhyay SK, Toomey TL, Fielding JE, Task Force on Community Preventive S. The effectiveness of tax policy interventions for reducing excessive alcohol consumption and related harms. *American Journal of Preventive Medicine*. 2010;38:217-229
246. Meier PS, Holmes J, Angus C, Ally AK, Meng Y, Brennan A. Estimated Effects of Different Alcohol Taxation and Price Policies on Health Inequalities: A Mathematical Modelling Study. *PLoS Medicine*. 2016;13(2): e1001963. doi: 10.1371/journal.pmed.1001963
247. Wagenaar AC, Tobler AL, Komro KA. Effects of alcohol tax and price policies on morbidity and mortality: A systematic review. *American Journal of Public Health*. 2010;100:2270-2278
248. Miura K. Epidemiology and prevention of hypertension in Japanese: How could Japan get longevity? *EPMA Journal*. 2011;2:59-64

249. Puska P. Successful prevention of non-communicable diseases: 25 year experiences with North Karelia Project in Finland. *Public Health Med*. 2001;4: https://www.julkari.fi/handle/10024/87423
250. Record NB, Onion DK, Prior RE, Dixon DC, Record SS, Fowler FL, Cayer GR, Amos CI, Pearson TA. Community-wide cardiovascular disease prevention programs and health outcomes in a rural county, 1970-2010. *JAMA - Journal of the American Medical Association*. 2015;313:147-155
251. Bertram MY, Sweeny K, Lauer JA, Chisholm D, Sheehan P, Rasmussen B, Upreti SR, Dixit LP, George K, Deane S. Investing in non-communicable diseases: an estimation of the return on investment for prevention and treatment services. *Lancet*. 2018;391:2071-2078
252. World Health Organization. Saving lives, spending less: a strategic response to noncommunicable diseases. Geneva, Switzerland 2018 (WHO/NMH/NVI/18.8). Licence: CC BY-NC-SA 3.0 IGO. https://www.who.int/ncds/management/ncds-strategic-response/en/ Accessed 26 May 2022.
253. Grundy Scott M, Stone Neil J, Bailey Alison L, Beam C, Birtcher Kim K, Blumenthal Roger S, Braun Lynne T, de Ferranti S, Faiella-Tommasino J, Forman Daniel E et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139:e1082-e1143
254. Guideline for the pharmacological treatment of hypertension in adults. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO https://apps.who.int/iris/bitstream/handle/10665/344424/9789240033986-eng.pdf Accessed 10 Oct 2022.
255. Cadilhac DA, Carter R, Thrift AG, Dewey HM. Organized Blood Pressure Control Programs to Prevent Stroke in Australia. *Stroke*. 2012;43:1370-1375
256. World Health Organization. One Health. September 2017 https://www.who.int/features/qa/one-health/en/ Accessed 27 December 2022.
257. Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, Creager MA, Eckel RH, Elkind MSV, Fornage M et al. Guidelines for the primary prevention of stroke: A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:3754-3832
258. Feigin VL, Roth GA, Naghavi M, Parmar P, Krishnamurthi R, Chugh S, Mensah GA, Norrving B, Shiue I, Ng M et al. Global burden of stroke and risk factors in 188 countries, during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet Neurology*. 2016;15:913-924
259. D'Agostino RB, Wolf PA, Belanger AJ, Kannel WB. Stroke risk profile: adjustment for antihypertensive medication. The Framingham Study. *Stroke*. 1994;25:40-43
260. Wolf PA, D'Agostino RB, Belanger AJ, Kannel WB. Probability of stroke: A risk profile from the Framingham Study. *Stroke*. 1991;22:312-318
261. Driving Sustainable action for Circulatory Health. White Paper on Circulatory Health. Geneva, Switzerland. Global Coalition for Circulatory Health. 2018. https://world-heart-federation.org/resource/white-paper-for-circulatory-health/ Accessed 24 November 2021.
262. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney M-T, Corrà U, Cosyns B, Deaton C et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *European Heart Journal*. 2016;37:2315-2381

263. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, Fang MC, Fisher M, Furie KL, Heck DV et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:2160-2236
264. Roshandel G, Khoshnia M, Poustchi H, Hemming K, Kamangar F, Gharavi A, Ostovaneh MR, Nateghi A, Majed M, Navabakhsh B et al. Effectiveness of polypill for primary and secondary prevention of cardiovascular diseases (PolyIran): a pragmatic, cluster-randomised trial. *The Lancet*. 2019;394:672-683
265. Muñoz D, Uzoije P, Reynolds C, Miller R, Walkley D, Pappalardo S, Tousey P, Munro H, Gonzales H, Song W et al. Polypill for Cardiovascular Disease Prevention in an Underserved Population. *New England Journal of Medicine*. 2019;381:1114-1123
266. Amarenco P, Labreuche J. Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention. *The Lancet Neurology*. 2009;8:453-463
267. Baigent C, Blackwell L, Collins R, Emberson J, Godwin J, Peto R, Buring J, Hennekens C, Kearney P, Meade T et al. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet*. 2009;373:1849-1860
268. Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, Bhala N, Peto R, Barnes EH, Keech A, Simes J et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376:1670-1681
269. Commitee CS. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet*. 1996;348:1329-1339
270. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: Meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ (Online)*. 2009;338:1245
271. Minhas JS, Chithiramohan T, Wang X, Barnes SC, Clough RH, Kadicheeni M, Beishon LC, Robinson T. Oral antiplatelet therapy for acute ischaemic stroke. *Cochrane Database of Systematic Reviews*. 2022:Art. No.: CD000029
272. Mortensen MB, Tybjærg-Hansen A, Nordestgaard BG. Statin Eligibility for Primary Prevention of Cardiovascular Disease According to 2021 European Prevention Guidelines Compared With Other International Guidelines. *JAMA Cardiol*. 2022;7:836-843
273. Paciaroni M, Agnelli G, Micheli S, Caso V. Efficacy and Safety of Anticoagulant Treatment in Acute Cardioembolic Stroke. *Stroke*. 2007;38:423-430
274. Sandercock PA, Counsell C, Kane EJ. Anticoagulants for acute ischaemic stroke. *Cochrane Database Syst Rev*. 2015;2015:Cd000024
275. Saxena R, Koudstaal PJ. Anticoagulants for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischaemic attack. *Cochrane Database of Systematic Reviews*. 2004:CD000185
276. Verro P, Gorelick PB, Nguyen D. Aspirin Plus Dipyridamole Versus Aspirin for Prevention of Vascular Events After Stroke or TIA. *Stroke*. 2008;39:1358-1363
277. Whiteley WN, Adams HP, Jr., Bath PM, Berge E, Sandset PM, Dennis M, Murray GD, Wong KS, Sandercock PA. Targeted use of heparin, heparinoids, or low-molecular-weight heparin to improve outcome after acute ischaemic stroke: an individual patient data meta-analysis of randomised controlled trials. *Lancet Neurol*. 2013;12:539-545
278. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev*. 2013;2013:Cd009329
279. Kim J, Gall SL, Dewey HM, Macdonell RA, Sturm JW, Thrift AG. Baseline smoking status and the long-term risk of death or nonfatal vascular event in people with stroke: a 10-year survival analysis. *Stroke*. 2012;43:3173-3178
280. Spence JD. Nutrition and Risk of Stroke. *Nutrients*. 2019;11:647

281. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, Rangarajan S, Islam S, Pais P, McQueen MJ et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *The Lancet*. 2010;376:112-123
282. Neal B, Wu Y, Feng X, Zhang R, Zhang Y, Shi J, Zhang J, Tian M, Huang L, Li Z et al. Effect of Salt Substitution on Cardiovascular Events and Death. *New England Journal of Medicine*. 2021;385:1067-1077
283. Bond DS, Thomas JG, Raynor HA, Moon J, Sieling J, Trautvetter J, Leblond T, Wing RR. B-MOBILE - A smartphone-based intervention to reduce sedentary time in overweight/obese individuals: A within-subjects experimental trial. *PLoS ONE*. 2014;9
284. Glynn LG, Hayes PS, Casey M, Glynn F, Alvarez-Iglesias A, Newell J, Ólaighin G, Heaney D, O'Donnell M, Murphy AW. Effectiveness of a smartphone application to promote physical activity in primary care: The SMART MOVE randomised controlled trial. *British Journal of General Practice*. 2014;64:e384-e391
285. Spring B, Schneider K, McFadden HG, Vaughn J, Kozak AT, Smith M, Moller AC, Epstein LH, DeMott A, Hedeker D et al. Multiple behavior changes in diet and activity: A randomized controlled trial using mobile technology. *Archives of Internal Medicine*. 2012;172:789-796
286. Wardlaw JM, Bath PM. Stroke research in 2018: extended time windows, refined benefit, and lifestyle prevention targets. *The Lancet Neurology*. 2019;18:2-3
287. Acting on Stroke and NCDs: Preventing and Responding to stroke to work towards Universal Health Coverage 2022. Policy brief co-authored by NCD Alliance, World Stroke Organization and American Stroke Association (Mia Grupper, Sarah Belson, Anita Wiseman, Bo Norrving, Valery Feigin, Diana Vaca McGhie, Stephanie Mohl). https://ncdalliance.org/sites/default/files/Acting%20on%20Stroke%20and%20NCDs_2022_PolicyBrief_Final%20for%20web.pdf Accessed 9 November 2022.
288. Wolters FJ, Paul NL, Li L, Rothwell PM. Sustained impact of UK FAST-test public education on response to stroke: a population-based time-series study. *Int J Stroke*. 2015;10:1108-1114
289. Lehtisalo J, Rusanen M, Solomon A, Antikainen R, Laatikainen T, Peltonen M, Strandberg T, Tuomilehto J, Soininen H, Kivipelto M et al. Effect of a multi-domain lifestyle intervention on cardiovascular risk in older people: the FINGER trial. *European Heart Journal*. 2022;43:2054-2061
290. Charlton KE, Corso B, Ware L, Schutte AE, Wepener L, Minicuci N, Naidoo N, Kowal P. Effect of South Africa's interim mandatory salt reduction programme on urinary sodium excretion and blood pressure. *Preventive Medicine Reports*. 2021;23:101469
291. Greenberg SM, Ziai WC, Cordonnier C, Dowlatshahi D, Francis B, Goldstein JN, Hemphill JC, Johnson R, Keigher KM, Mack WJ et al. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. *Stroke*.0:10.1161/STR.0000000000000407
292. Berge E, Whiteley W, Audebert H, De Marchis GM, Fonseca AC, Padiglioni C, de la Ossa NP, Strbian D, Tsivgoulis G, Turc G. European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. *Eur Stroke J*. 2021;6:I-lxii
293. Mayberg MR, Batjer HH, Dacey R, Diringer M, Haley EC, Heros RC, Sternau LL, Torner J, Adams HP, Jr., Feinberg W. Guidelines for the management of aneurysmal subarachnoid hemorrhage. A statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. *Circulation*. 1994;90:2592-2605
294. Maher M, Schweizer TA, Macdonald RL. Treatment of Spontaneous Subarachnoid Hemorrhage. *Stroke*. 2020;51:1326-1332