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The Global Burden of Disease Brain Summit

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Abstracts

Guest Editors

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Global Burden of Disease Study 2017: Key Findings and Implications for Neurological Disorders

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The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) is the largest and most comprehensive effort to date to measure epidemiological levels and trends worldwide. The results show both major progress for example in combating infectious disease, and also significant gaps, for example in tackling causes of death and disability that could be reduced with increased coverage of drugs, vaccines, and greater access to primary health care. The GBD is a valuable resource allowing users to better understand the disease profile of a given population, and thus understand what resources are needed to target and ultimately reduce the causes of death and disability in that population.

The latest update, GBD 2017, uses and expands upon the infrastructure of methodology, datasets, and tools that were presented in GBD 2010, 2013, 2015, and 2016, and presents estimates of population and fertility, all-cause mortality, deaths by cause, years of life lost, years lived with disability, and disability-adjusted life years by geography, age, and sex from 1990 to 2017. This project draws upon the efforts of a multitude of people, including more than 3,585 experts from 143 countries and 2 territories. This presentation will highlight results from the GBD 2017 study, focusing on neurological disorders in the context of the other diseases and risk factors studied, to demonstrate global impact of these conditions over the past two decades.

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The Burden of Neurological Disorders 1990 to 2016

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In 2016, diseases that are largely cared for by neurologists made up 16.5% of global deaths and 11.6% of global disability adjusted life years (DALYs) a composite measure of years of life lost due to premature mortality and the disability associated with a disease and its consequences. Grouping stroke with neurological disorders rather than with cardiovascular diseases made neurological disease the leading cause group of DALYs and the second ranked cause group of deaths, globally, in 2016. Stroke was the largest of these neurological disorders (42.2% of neurological DALYs in 2016) followed by migraine (16.3%), Alzheimer's disease and other dementias (10.4%) and meningitis (7.9%). Since 1990, the burden of these

combined disorders increased by 15% despite significant decreases in the age-standardized rates of stroke, meningitis and tetanus. Age by age, the prevalence and incidence of the other neurological disorders has shown little change since 1990 and with ageing populations this means a large increase in the number of patients requiring neurological care. Up-to-date estimates of these numbers is essential to plan for adequate resources to provide neurological services.

The state of knowledge of risk factors that determine the levels and outcomes of neurological disorders is rather poor. Stroke is the exception for which we have abundant evidence on risk factors and can explain almost 90% of the disease burden. The lack of predictive covariates makes the estimation of the other neurological disorders more difficult as our statistical models have to rely on geographical proximity to predict values for countries with sparse or absent data. Variations in case definitions and study methods are a further challenge. To deal with this disease by disease, we set a reference case definition and study method and adjust data from alternative methods if we detect a systematic bias. This is easier for diseases with a longer history of standardized data collection methods. The heterogeneity in survey methods used for dementia stands out making it more difficult to determine if the variation in prevalence between countries is true variation or a reflection of measurement bias. An additional challenge is the measurement of death rates from dementia and Parkinson's disease which have increased in high quality vital registration systems like those in the US and Scandinavian countries by a far greater amount than plausibly can be explained in comparison to stable or marginally changing prevalence. Rather, this comes from a change in coding practices that has occurred over time in some countries but not in others. We correct for these large differences assuming the more recent coding practice in the US and selected other countries is the 'correct' level of deaths with dementia as the underlying cause. While this method solves the spurious time trend in dementia death rates, it relies on prevalence data to make this correction and thus propagates the measurement error of survey data onto the mortality rates.

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The Global Burden of Stroke: Where Do We Go Next?

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Stroke is a leading cause of death and, in 2016, accounted for 10% of all deaths globally. The Global Burden of Disease (GBD) Study 2016 estimated that these deaths were split almost equally between ischemic and hemorrhagic strokes. There were approximately 13.7 million new strokes in 2016, with slightly more occurring among men than women. These strokes occurred predomi-

nantly among older adults, however we estimated approximately 50,000 strokes annually for each 5-year age group starting at birth, doubling to more than 100,000 strokes for adults age 30–35, peaking at between 3–4 million strokes annually for adults between the ages of 60 and 70. There were approximately 80 million prevalent cases of stroke in 2016. The majority of these people, almost 30 million stroke survivors, were living in middle SDI countries.

Based on estimates of levels of established risk factors and their relative risks, globally, 85% of strokes can be attributed to known, modifiable risk factors. This is true even for adults as young as age 30. The largest fraction of stroke can be attributed to elevated systolic blood pressure, with almost twice as many DALYs attributed as the next leading modifiable risk factor, dietary risks. Low dietary fruits, vegetables, and whole grains are major dietary risk factors for stroke along with high dietary sodium. Other contributing risks include tobacco smoking and second-hand smoke, high body-mass index, ambient and household air pollution, high fasting plasma glucose, alcohol use, high plasma cholesterol, impaired kidney function, and low physical activity.

There are significant challenges to measuring the impact of stroke globally. Pediatric stroke remains particularly challenging to measure. The etiology of stroke among children is strikingly different that for even younger adults and includes a wide range of rare conditions of the brain, blood vessels, and blood as well as cancers and trauma.

Even among adults, stroke is, itself, a downstream event for a range of conditions, including thromboembolism due to atrial fibrillation, left-sided valve disease, left ventricular dysfunction, and paradoxical emboli from venous thrombosis, as well as atherosclerotic extracranial and cranial arterial diseases. Epidemiologic studies have done a good job of collecting the causes of stroke for a limited number of locations but this data has not been integrated into a single picture of what causes stroke for all regions of the world.

It is vitally important to consider the degree of disability due to stroke. The GBD study has collected a great deal of data on Rankin scores among stroke survivors and uses this data to inform our understanding of how stroke disability varies by age and sex. A better understanding of stroke disability within countries might improve our ability to target resources and improve the quality of care.

Most recently has been the development of a new method for using the results of the GBD Study to estimate the lifetime risk of stroke for every country. The global average lifetime risk of stroke at age 25 is approximately 25%, highlighting the important role that early and sustained primary prevention could have on population health.

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Dementia Estimation for the Global Burden of Disease Study 2016

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The number of individuals both living with and affected by dementia is increasing, putting more stress on health systems, communities and caregivers. In order to address this growing chal-

lenge, it is important to have a thorough understanding of the global landscape of dementia disease burden. The Global Burden of Disease Study 2016 (GBD 2016) aimed to synthesize evidence on dementia through the collation and analysis of all available data from vital registration systems, published literature, surveys and health service encounters databases. There are a number of methodological challenges to the global estimation of dementia mortality and prevalence, driven primarily by changes over time in disease reporting and a lack of consistency in case ascertainment methods. To correct for differences in cause of death coding across time and locations, mortality due to dementia was modelled using prevalence data and estimates of excess mortality derived from selected countries most likely to code deaths to dementia relative to prevalence. However, our prevalence data were heterogeneous, with 230 different diagnostic procedures used across 237 literature sources. While the vast majority of data ultimately classify dementia cases using the DSM or ICD definitions, many protocols differed in the screening tests utilized, the cut-off scores used, the diagnostic tests used in clinical evaluation and use of supplemental clinical records.

Despite these limitations, the GBD 2016 estimate of 43.8 (37.8–51.0) million people living with dementia in 2016 is on par with other global estimates, including those from the World Alzheimer Report 2015. This number represents an increase of 117% (114–121) from the 20.2 (17.4–23.5) million prevalent cases globally in 1990. The number of deaths also increased by 148% (140–157) globally over the same time period. Additionally, dementia was the fifth leading cause of death in 2016. These increasing trends are only expected to continue with increases in population growth and aging.

Future iterations of GBD will aim to improve these estimates and address some of the methodological challenges in dementia estimation. Using multiple cause of death data and linkages between administrative data sets and death certificates, we will improve our method for the correction of bias in cause of death coding over time. Furthermore, we are developing a method to predict formal dementia diagnoses from less detailed survey data on cognition, which will allow us to drastically increase data availability and global data coverage. These improvements and the annual release of new estimates will facilitate the use of GBD dementia results as an important tool for policy makers planning for the effects of population aging.

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The Burden of Epilepsy. Practice/Research Implications

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Epilepsy is a neurological condition in which health loss is caused by recurrent seizures. We assessed frequency and trends of epilepsy for 195 countries and territories from 1990 to 2016 quantifying health loss by disease, age, sex, year, socio-demographic context and geographical location. A PubMed search was made of epidemiological studies on epilepsy without language restrictions

through December 31, 2016. Epilepsy was defined by recurrent unprovoked seizures and active epilepsy by 1+ seizures in the past five years. Severity was assessed based on seizure frequency. Most estimates refer to idiopathic epilepsy, i.e., epilepsy of genetic origin or with no documented etiology.

In 2016, 45.9 million persons (95% uncertainty interval, UI 39.9–54.6) had epilepsy (age-standardized prevalence 621.5/100,000; 540.1–737.0). 24.0 million (20.4–27.7) had active idiopathic epilepsy, giving a prevalence of 324.1/100,000 (276.0–375.2) with peaks at 5–9 years and 80+ years. Rates were similar in men and women and among countries based on socio-demographic index (SDI). Age-standardized DALYs rates were 182.6/100,000 (149.0–223.5), 163.6 (130.6–204.3) for women and 201.2 (166.9–241.4) for men. The higher rates in men were due to premature mortality. Between 1990 and 2016 there was a significant decrease in age-standardized mortality rates (24.5%; 10.8–31.8) and in age-standardized DALY rates (19.4%; 9.0–27.6). One-third of the difference was due to the greater severity of epilepsy in low-income settings and two-thirds by higher case fatality.

On this background, epilepsy is an important cause of disability and mortality. Sizeable gains can be expected from improved access to treatments.

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The Burden of Traumatic Brain Injury and Spinal Cord Injury from 1990 to 2016: Estimates from the Global Burden of Disease Study 2016

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Traumatic brain injury (TBI) and spinal cord injury (SCI) can cause considerable health loss and suffering, and previous research has characterized how different injuries such as road injuries and falls lead to TBI and SCI in all areas of the world. However, to date, there are no comprehensive estimates of the burden of TBI and SCI in every country, from every cause of injury, and for every demographic group through recent years. In this study, we aimed to estimate the incidence, prevalence, and years lived with disability (YLDs) of TBI and SCI from all causes of injury in every country, to measure these trends over time, and to derive the proportions of TBI and SCI caused by every different cause of injury. Our study used the Global Burden of Disease (GBD) 2016 framework to estimate this burden. We first used survey, surveillance, and clinical data to measure the incidence of each cause of injury requiring medical care. Second, we used clinical record data with ICD-9 and ICD-10 diagnosis coding to estimate the proportion of each cause of injury that would result in TBI or SCI being the most disabling injury among all injuries sustained. Third, we used a meta-analysis of long-term injury outcomes to convert incidence to prevalence of long-term disability. Fourth, we applied GBD disability weights to health states associated with TBI and SCI to estimate years lived with disability. We conducted each of these steps for 195 countries, for all age groups, for males and females, and for the time period from 1990 to 2016.

Using this framework, we estimated that in 2016, there were 27 million (95% uncertainty interval [UI] 24–30) new cases of TBI,

and 930 thousand (780 thousand – 1.16 million) new cases of SCI from all injuries combined. Age-standardized incidence rates increased by 3.6% (1.8–5.5%) from 1990 to 2016 for TBI, while for SCI, age-standardized incidence rates did not change significantly (–3.6% [–7.4–4.0%]). In general, falls and road injuries were the leading causes of TBI and SCI. Central Europe, Eastern Europe, and Central Asia had higher incidence rates of TBI than most other regions of the world, though among countries, Syria had the highest incidence rate of TBI in the world. For SCI, High-income North America and Western Europe were the regions with the highest incidence rate, though Syria, Yemen, and Iraq were the countries with the highest age-standardized incidence rates. Overall, we found that TBI and SCI are important outcomes among the global injury burden with a distinctive epidemiological pattern that highlights considerable burden in areas with high rates of falls, road injuries, and conflict. It is concerning that rates of TBI are increasing over time, given that many injuries are preventable, and it is additionally concerning that incidence of SCI is not improving since SCI cases can require substantial medical resources and specialty care.

8

EU Support for Research, Coordination of European National Programmes and International Cooperation

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Alzheimer's disease is a longstanding priority for the EU, both at policy and research levels. Over the last 10 years, the EU Framework Programmes have devoted €5.24 billion to brain research, of which a total amount of 853 million have been devoted to dementia research and €544 million specifically awarded to Alzheimer's disease research.

EU funding spans basic research (ERC), as well as clinical and implementation research, and is very open to international collaboration with the participation of non-European research institutions.

The EU also fosters the coordination of national research programmes in Europe through public-public partnerships and the development of networks. The prime example is the EU Joint Programme – Neurodegenerative Disease Research (JPND), which is the largest global research initiative. It includes some 30 countries, including three non-EU countries (Australia, Canada and Switzerland), while discussions are ongoing with the US. www.neurodegenerationresearch.eu/

JPND aims to increase coordinated research investment between participating countries, the ultimate goal being to find cures for neurodegenerative diseases and to enable early diagnosis for early, targeted treatments. Through its Research and Innovation Strategy, JPND has identified common research goals for joint action between countries to accelerate progress to alleviate the symptoms and lessen the social and economic impact for patients, families and health care systems. Some €150 million have been mobilised through JPND. An example of a JPND funded project is

BRIDGET, which is identifying individuals with early alterations of the brain.

The EU also supports the establishment of research infrastructures, such as the Human Brain Project, and build capacity, as well as public-private partnerships, such as the Innovative Medicines Initiative (IMI). Projects supported by IMI include EPAD, the European prevention of Alzheimer's dementia consortium, with an EU grant of € 25.9 million, to investigate pre-symptomatic dementia, thus opening up new avenues for prevention. The PHAGO project is investigating the role of neuro-inflammation on AD in order to pave the way for future therapies. AMYPAD for earlier AD detection through Amyloid imaging to prevent Alzheimer's disease, and MOPEAD – Models Of Patient Engagement for Alzheimer's Disease.

The European Commission is also currently exploring other areas where there is potential for international collaboration with like-minded funding agencies. To facilitate this, the EC is also launching a new initiative – the European Brain Research Area (EBRA) – to coordinate brain research in Europe and develop global initiatives. EBRA will facilitate the emergence of large-scale international research collaborations. It is led by the European Brain Council (EBC) working in close collaboration with the EC and includes JPND and HBP.

Furthermore, in order to address the pressing socioeconomic challenges of caring for and assisting European citizens faced with dementia, the EU funds research to develop ICT solutions for independent living and their potential implementation in health systems.

The EU will continue to prioritise Alzheimer's disease and other neurodegenerative diseases in its next framework programme – Horizon Europe (2021–2027).

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GBD 2016 Publications in *The Lancet Neurology*: The Best Science for Better Lives

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Since its foundation in 1823, *The Lancet* has been committed to increasing the social impact of medical science. *The Lancet* journals strive to achieve this aim by contextualising the best scientific evidence and by disseminating it broadly so that research findings can inform debate and transform society. In 1997, a series of four articles in *The Lancet* marked the inception of a close collaboration between the journal and investigators of the Global Burden of Disease (GBD) Study. Over the past 20 years, as the GBD Study has progressed, that collaboration has led to the publication of scores of articles in *The Lancet* journals that have proved to be a useful resource for research funders and health organisations.

The methods of the GBD 2016 Study involve global collaboration, with hundreds of investigators contributing data and revising the manuscripts. Because of the increased granularity of the 2016 analysis, compared with analyses reported in the 1997 publications, the detail and complexity of the findings reported in these articles have also increased. The statistical methods in the analyses have also evolved, and the GBD Study now uses cutting-edge mod-

elling of estimates. These changes have added complexity not only to the Study and its analyses, but also to the editorial procedures involved in their publication.

In 2018 and 2019, *The Lancet Neurology* will publish the findings on neurological disorders from the GBD 2016 Study. For the peer review of these papers, the editors sought input from many expert clinical reviewers. All the papers were also assessed by experts in statistics and epidemiology. The recommendations from the reviewers and the editors have been considered by a large group of authors, who have had to revise their manuscripts several times during a necessarily-long peer review process. Even after the final manuscripts were accepted, they have required extensive, time-consuming editing owing to the sheer amount of data presented in each article. To contextualise the findings, every article will be accompanied by a linked Comment, written by a neurological expert. And to facilitate their dissemination, all these publications will be open access.

Epidemiological findings are an essential source of evidence in guiding public-health policies and decision-making in health-care systems across the globe. The GBD 2016 Study provides the best available epidemiological evidence for neurological diseases. These papers should prove useful for research-funding agencies, health-care institutions, and policy makers as they set up their priorities on brain health.

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Epidemiology and Burden of Stroke in China

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Stroke has been the first leading cause of death in China in recent years. It is a serious threat to human health that often leads to severe complications. However, little is known about the prevalence, incidence, and mortality of stroke on the country level in China and reliable data on stroke burden in China are lacking. A large-scale epidemiological survey of stroke in China was carried out in 2013.

A multistage stratified cluster sampling method, based on 2010 national census data, was conducted in 155 urban and rural sites in 31 provinces across China in 2013. Investigators screened for a history of symptoms of stroke using a door-to-door survey with a questionnaire. Subjects with positive symptoms were re-interviewed and examined by neurologists to confirm the diagnosis. Neurologists also re-checked all available information on study participants who died between January 1, 2012 and September 1, 2013. We used inter-regional comparative study in order to obtain regular burden related characteristics of stroke in China, as measured by years of life lost (YLLs), years lived with disability (YLDs) and disability-adjusted life-years (DALYs).

Of the 480,687 adult participants, 7,672 (4,217 men [55.0%], 3,455 women) were considered by the neurologists as having had a first-ever stroke, yielding a crude prevalence of stroke 1596.0 per 100,000 people (95% CI 1560.6–1631.5) and age-adjusted prevalence per 100,000 people of 1114.8 (95% CI 997.7–1231.9). The crude incidence of the first-ever stroke was 345.1 (95% CI 328.4–

361.7) per 100,000 person-years and the age-adjusted incidence was 246.8 (95% CI 211.2–282.5) per 100,000 person-years. The crude stroke mortality rate was 159.2 (95% CI 147.9–170.5) per 100,000 person-years and the age-adjusted mortality rate was 114.8 (95% CI 96.3–133.3) per 100,000 person-years.

The prevalence and incidence of stroke in rural areas had increased by 155% and 31.6% respectively in the past 30 years. Among the nationwide populations of all ages, the YLLs per 100,000 people for stroke was 1748, the YLDs was 262, and the DALYs was 2010 (2171 for male and 1848 for female). With reference to differences between urban and rural areas, the YLLs, YLDs and DALYs in rural areas were higher compared to urban areas. For the age stratification on burden of stroke, among all age groups, the highest YLLs was observed in ≥ 80 age-group.

Calculated according to the results of the nationwide survey, there were over 11.1 million stroke survivors, 2.5 million first-ever stroke and over 1.1 million people died of stroke per year in China. Our study revealed that the burden of stroke in China appears to be increasing particularly in rural areas in the past 30 years. There is north-to-south gradient in stroke in China, with the greatest stroke burden observed in the northern and central regions.

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NINDS and the Global Burden of Neurological Disorders

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The mission of the National Institute of Neurological Disorders and Stroke is to seek fundamental knowledge about the brain and nervous system and use that knowledge to reduce the burden of neurological disease. According to data from the World Health Organization, stroke continues to be the second leading cause of death globally and since 2000 the rise of Alzheimer's-related deaths has substantially increased. Given the extent of the burden of illness a major barrier is the scarcity of neurological expertise in much of the underdeveloped countries. An important feature of NINDS' activities in global health is to build capacity to conduct neurological research through investments in research training. Such efforts overlap with the need to build neurological expertise to improve health. We do this in part through the NIH Medical Education Partnership Initiative (MEPI) program which funds foreign institutions in sub-Saharan African countries that receive PEPFAR support and their partners to develop or expand and enhance models of medical education.

In 2017, NINDS invested almost \$7 million in global health initiatives around the world on research focused on a spectrum of diseases including epilepsy, neurocysticercosis, Parkinson's Disease, Essential Tremor, pediatric TBI, cerebral malaria, HIV/AIDS-related meningitis, cerebral ischemia, and stroke in children with SCD. In concert with the development of a clinical neuroscience workforce another opportunity to reduce the global burden of neurological disorders lies in the development of affordable technologies to aid in the prevention, diagnosis and treatment of these disorders in low resource settings. Effective tools that lever-

age inexpensive technologies will help fill gaps in the treatment of chronic conditions in the United States and abroad. These tools require care in implementation, as a lack of expertise remains the greatest problem and could contribute to the misuse of technology. Future research opportunities will likely emerge in the areas of telemedicine, imaging technologies, point-of-care diagnostics and screening tools, monitoring and tracking devices, digital health records, and accessible neurosurgical procedures and devices. New tools must be readily transportable, light-weight, with good sensitivity/specificity, minimally invasive, sustainable and low cost. Their development and adoption can come from collaborative partnerships between investigators in the US and LMICs, training on how to use them, and phased awards to allow for preliminary studies and data collection to inform larger projects and avoid premature adoption without appropriate evidence.

12

New Trends in Multiple Sclerosis Epidemiology

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Multiple sclerosis (MS) prevalence and incidence have been regularly assessed and reviewed across many regions of the world. Unfortunately, most reports have covered relatively small areas, many areas of the world have not been assessed and methods are disparate. We propose a new method for the assessment of MS morbidity at the country level. In addition, the Global Burden of Disease (GBD) approach for modeling data across countries and regions is highlighted.

A validated algorithm was used to identify adult MS cases in private, military, and public health care datasets between 2008 and 2010 in the United States (US) and estimate prevalence. We applied insurance-specific and stratum-specific estimates to the 2010 US census data and pooled the findings to calculate the 2010 prevalence of MS in the US cumulated over three years. GBD methodological tools were used to assess MS neurological progression and other morbidity outcomes both in the US and world-wide between 1990 and 2016. Epidemiologic outcomes for MS were modelled using DisMod-MR 2.1, a Bayesian meta-regression framework widely used in GBD epidemiologic modelling. There were 123 unique studies on prevalence and 65 unique studies on incidence. MS cause of death modelling is based on 13,110 site-years of vital registration data analyzed in GBD's cause of death ensemble module, CODEm.

The estimated 2010 prevalence of MS in the US adult population cumulated over 10 years was 309.2 per 100,000 (95% confidence interval (CI): 308.1–310.1), representing 727,344 cases. A US north-south decreasing prevalence gradient was identified. In 2016, there were an estimated 2,221,188 prevalent cases (95% CI: 2,033,866 to 2,436,858) of MS globally, which corresponded to a 10.4% (95% CI: 9.1–11.8) increase in the age-standardized prevalence between 1990 and 2016. In 2016, MS ranked 14th among major neurological conditions as a cause of Disability-adjusted-life-years (DALYs). MS also contributed 0.42% (95% CI: 0.37 to 0.46) of total DALYs and 0.21% (95% CI: 0.18 to 0.23) of all total

deaths in 2016. Globally, age-standardized death rates decreased significantly by 11.5% (95% CI: -35.4 to -4.7) while the change in age-standardized DALY rates was not significant. The impact of MS on years lost to premature death and disability was greatest in the sixth decade of life.

MS is the most common progressive neurological condition of young adults. The disease has become significantly more prevalent in many world regions since 1990. The use of a validated MS algorithm within large administrative datasets is an efficient and cost-effective way to improve the surveillance of MS, especially in countries without data. Use of the GBD methodology and metrics allows for consistency and comparability of epidemiological estimates between regions of the world. These findings will be useful for resource allocation and health services planning.

13

Inequities of Access to Neurological Care

William Carroll

Sir Charles Gairdner Hospital, Perth, Australia and President, World Federation of Neurology

Neurological or brain health disorders are now ranked as second in mortality and first in morbidity by DALYs. In addition to the Global Burden of Disease study, the second edition of the Neurology Atlas lists the manpower and resources available in each of 132 countries. By implication and comparison with measures considered normal the deficits can be estimated. To combat these deficiencies of care and threats to brain health there needs to be a reasonably accurate perspective of the problem, identified causes to target with modifiable strategies and coordination in the overall approach.

The Global Burden of Disease study quantitates to a greater degree the threat to the world as a consequence of a range of diseases. The threat is unevenly distributed for many reasons. Some are readily identifiable not least the economic divide between high, middle- and low-income countries. Other reasons relate to variable prioritisation in some, to inertia of action of democracies in others and a lack of recognition of the magnitude of such problems by some.

The WFN recognises the need for quantification and education in the struggle against the inequities of access to neurological care. It is developing its regional needs-based registry which in concert with the European Academy of Neurology, the American Academy of Neurology and hopefully the World Health Organisation, as well as combining with the disease specific groups such as the Multiple Sclerosis International Federation, will provide the platform for the redress of access inequalities. It is also attempting to strengthen the relationship with all neurological and neuroscience groups by the development of the Global Neurology Alliance which it currently convenes.

By such initiatives the WFN plans to be able to engage in global advocacy initiatives, in initiatives at regional and national levels and in partnership with disease-specific organisations and their lay counterparts.

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Using GBD Stroke Estimates to Inform Policy of the World Stroke Organisation

Michael Brainin

Danube University Krems, Austria, and President, World Stroke Organisation

Stroke is already the second leading cause of death and disability in the world. It is one of the most fearful disorders placing a huge physical, psychological and financial burden on the patients, their families and society. About half of stroke survivors have some level of disability and about one third of them develop cognitive impairment and/or dementia. The estimated global direct (health care) and indirect (mainly due to lost productivity) costs of all circulatory diseases including heart disease and stroke is estimated at USD 957 billion in 2015. On current projections, this figure is set to rise to USD 1004 billion by 2030, according to the White Paper on Circulatory Health.

The World Stroke Organisation was established in 2006 and has 4000+ individual members, 38 scientific and more than 50 patient organisational members. It is the global voice of stroke and has UN and WHO Consultative Status. It is a partner member of the NCD Alliance and Founding Partner of the Global Coalition for Circulatory Health. The WSO has a strong role in advocacy and develops and supports a Global Stroke Policy Agenda, Global Stroke Guidelines, a World Stroke Campaign as well as the World Stroke Day. It edits the *International Journal of Stroke* and organises bi-annual congresses and many other regional and educational meetings around the world.

For promoting action, fostering education, and drafting public statements and news releases the WSO leans heavily on the comprehensive work of the Global Burden of Disease group. Their research has over the years provided invaluable data about the incidence, prevalence, mortality as well as time trends on stroke that help us to clarify and visualise stroke as a leading health problem around the world. We can now reliably state that there are over 13 million new strokes each year and almost 60 per cent of these occur in people under the age of 70 years and 8 per cent of all strokes in people younger than 44 years. There are over 80 million people currently living who have experienced a stroke globally, just over a half (51%) of these are women. Five and a half million people die of stroke annually and over 116 million years of productive life is lost each year due to stroke related disabilities. We can also stratify these numbers according to ischemic and haemorrhagic stroke. As for risk factors for stroke, there are almost 4 million new cases of atrial fibrillation diagnosed each year contributing to a prevalence of over 46 million people. We can also derive 2016 GBD estimates for stroke burden (as measured by DALYs) attributable to risk factors. Globally, high systolic blood pressure is the largest single risk for stroke, followed by dietary risk factors, high BMI, smoking, high fasting glucose, alcohol use, high total cholesterol, impaired kidney function and low physical activity. One of the most compelling results of the GBD group was to show that all risk factors combined account for 88.8% (86.5–90.9) of the global stroke burden.

Stroke Burden in Africa: Practical Aspects

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Africa appears to be the global capital of the stroke and cardiovascular syndemic. Every minute, at least 6 Africans develop stroke. Global estimates suggest that Africa has the highest incidence (age-standardized incidence 316 per 100,000 persons/yr), highest prevalence (age-adjusted prevalence of up to 14.6 /1000 people) and highest case fatality (up to 43% at 1 month and 84% at 3 years) from stroke. This is not surprising given the overwhelming and escalating burden of cardiovascular risk factors on the continent. Africa bears the highest global burden of hypertension with a prevalence rate of 46% (WHO, based on a threshold of 140/90 mm Hg). In a meta-analysis of those with hypertension in Africa, only 27% were aware of their hypertensive status; only 18% of individuals with hypertension were receiving treatment, and only 7% had controlled blood pressure. The high prevalence (93%) of uncontrolled hypertension and other vascular risk factors in Africa, highlights the need for implementation of timely, innovative and appropriate strategies for the control of stroke and its risk factors on the continent.

Within the context of the stroke and cardiovascular quadrangle, concerted effort is required for epidemiological surveillance, prevention, acute care and rehabilitation. This could be facilitated by following the principles of the implementation cycle which includes appropriate understanding of the barriers for control, and properly contextualized and communicated targeted interventions involving all stakeholder across all sectors: patients, providers, payers, policy makers, physicians and implementation partners.

These efforts can be greatly enhanced by the activities of the SIREN study (to unravel the risk factors) and the World Health Organization, World Stroke Organization, and Lancet Neurology Commission on Stroke. The Commission will be effective through the operation of the global Stroke Control, Observatory and Reduction Ecosystem (gSCORE) including >130 stroke commissioners globally.

Effective Coordination to Maximise the Impact of Brain Health and Brain Research

Frédéric Destrebecq, Giovanni Esposito, Vinciane Quoidbach

European Brain Council, Brussels, Belgium

Fragmentation in both research and health care practice is a particularly acute issue in the case of brain disorders, where the complexity of the brain and its dysfunction imposes a joint and coordinated effort to advance our understanding and to deliver optimal care for people living with brain conditions.

The brain is the most complex organ of the human being and disorders of the brain are generally more complicated to analyse, diagnose and treat than other diseases. This complexity has long hindered the analysis, diagnosis and treatment of brain disorders, as reflected by the heavy burden they impose on health services and

the increasing strain on society associated with the ageing of the European population. 179 million Europeans are living with a brain disorder, causing a total cost (direct and indirect, in 2010) of 800 billion euros for the European economy and national health budgets. Moreover, many brain disorders have an early-onset in life and, due to their chronic course, have an enormous health and socio-economic impact. While there is still no cure for most brain disorders, numerous needs of individuals at risk and patients remain unmet. An estimated 3 to 8 out of 10 people living with a brain disorder remain inadequately or not treated although effective treatment exists.

The EBC Value of Treatment study examined a range of mental and nervous system disorders and demonstrated the health gains and socio-economic impact resulting from optimum health interventions – pharmacological and psychosocial alike – in comparison with current care or, in some cases, with no treatment at all. Care pathways were mapped for specific disorders along the whole care process from prevention, prodromal, early diagnosis to disease management in order to identify major patient unmet needs and underlying reasons for treatment gaps. In all instances, case studies highlighted the need for research and knowledge on the disorders themselves as well as for better evidence to inform treatment decisions or better organization of services for the management of these conditions.

Against this backdrop, an increased effort to support research in the brain is necessary. Efficient coordination and cooperation also are crucial to achieve the full impact of brain research and to deliver effective care in order to improve the quality of life of those living with brain disorders in Europe.

The European Brain Council (EBC) is a non-profit organisation gathering patient associations, major brain-related societies as well as industries, whose mission is to promote brain research and health care in Europe. Through its expertise and network of experts and with the support of the European Commission, EBC is launching the “European Brain Research Area” (EBRA) which will serve as the focal point to coordinate and support brain research in Europe and, potentially, at the global level. EBRA will create the structure to bring research networks to maturity into clusters of cooperation and will also align strategies from the main actors and funders of brain research in Europe.

Global Disease Burden: Neurological Disorders in Africa

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Neurology first originated in Egypt, and Africa is the cradle of neurology. Africa has the least neurological services, and African neurologists cannot match the rapid progress in the developed world. Contributory socio-economic factors include inadequate

infrastructure and equipment, health-care personnel, lack of neurology training programs, research facilities, community health education and awareness, workforce inefficiency and very little funding.

Twenty African countries have between 1–4 neurologists, while 5 have between 5–10 neurologists. In 11 countries of a 26 m population, there are no neurologists. Neurologists trained in the developed world prefer to stay overseas, rather than return to their countries, partly because of inadequate remuneration (brain-drain).

Brain disorders affect 250 million people in LMIC, as a result of epidemiological transition (ageing, population growth, rapid urbanization, lifestyle changes).

Globalization of chronic diseases suggests that all populations are susceptible, and variation in rates exist because of differential exposures to environmental causes, including lifestyles, cultural practices, health seeking behaviours, inequalities in access to neurological care, inadequate resources and socio-economic differences. African ancestry sometimes demonstrates enhanced genetic predisposition, younger-age different subtypes, worse-severity and poorer outcomes.

Neurological services in Africa vary from no formal care to established neurological care with residency training, and ancillary equipment. Health care systems are liberal, private sector driven, with attempted inefficient models of universal health insurance coverage. High-cost-of care, poor community awareness, inadequate manpower development with limited local training, programs, resources, personnel centralized in and near big cities, gaps in data/knowledge/service/treatment, low priority in the political agenda, inadequate resource allocation of government funding to health, and lack of ICT are contributory factors.

The Lancet Neurology Commission on stroke in LMICs, constituted in collaboration with WHO/WSO, will organise a global pre-intervention survey of the current state of neurological services, a post-interventional evaluation and engagement/empowerment of stakeholders with ethical, legal and socio-economic considerations.

There is a need to establish on the African continent, regional training centers for brain disorders research, contributing to capacity building with and for Africa, as overseas training is not always adapted to the Africans local needs. In addition, the African continent needs to optimise patient care, improve GPs clinical skills, establish an effective 2-way referral national health insurance scheme to reduce social inequalities; create platforms for reflection, education, exchange of info between African/Western colleagues, and seek further collaborations and CME (Continuous Medical-Education). Policy-makers, members of government, civil society and patient associations should have their interactions and information sharing placed under the WFN umbrella to mitigate the suffering of Africans. Travel stipends should be granted to participate in international meetings, and cooperation with neuroscientists in the industrialized world is crucial to improve the African research infrastructure.

We need to convert brain-drain to brain-gain and provision of equipment, as well as attractive and better remuneration to encourage African neurologists to return home. Courses in Africa dispensed by different organizations are useful, but are short-term, one-shot missions; continuing programs over longer periods should be organized. Moreover, there is need for support, and increasing participation of service-users, including neurologists in policy-making and service planning.

Long-Term Costs of Acute Ischemic Stroke And the Impact of 3-Month Functional Outcome in Korea

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Stroke is one of the most devastating and costly health problems of today. However, there is a paucity of knowledge about how costly it is in a long-term perspective and how much long-term costs differ according to 3-month functional outcome, a major primary outcome variable of acute stroke intervention trials.

Acute ischemic stroke patients who were registered into the multicenter stroke registry (Clinical Research Collaboration for Stroke in Korea, CRCS-K) database in South Korea between 2011 and 2013 were matched to the National Health Insurance Service claim database. All the healthcare expenditure was extracted from the claim database and converted into daily cost of each individual. Yearly costs and cumulative costs up to 5 years were obtained and compared according to 3-month functional outcome (modified Rankin disability scale, mRS).

A total of 11,136 acute ischemic stroke patients (mean age, 68 years; men 58%) were analyzed. The median follow-up period was 1,418 days (4 years). The mean cumulative cost over 5 years was \$121,519 (standard deviation [SD], \$148,173) and showed a dramatic increment during the first month followed by a constant increase without a considerable change. The mean total cost during a year before stroke was \$8,718, which occupied 23% of cost of the first year after stroke.

The mean 5-year cumulative cost differed significantly according to 3-month functional outcome (Table, $P < 0.0001$); The cost for 3-month mRS score of 0 was \$56,506, and the cost for 3-month mRS score of 5 was \$263,096 which was 5 times greater. After adjusting for the selected potential confounders, the yearly costs and cumulative costs differed significantly according to 3-month mRS scores at each time point.

Table 1. Five-year cumulative and yearly costs of acute ischemic stroke patients by 3-month mRS (for Abstract No. 18)

Cost (USD)		Yearly cost						5-year cumulative cost
		During a year before stroke	1st year	2nd year	3rd year	4th year	5th year	
Total								
N		11,136	11,136	11,136	11,136	7,361	3,393	3,393
Mean (SD)		8,718 (18,472)	38,152 (40,772)	22,094 (35,577)	20,634 (36,130)	18,757 (34,759)	18,329 (34,985)	121,519 (148,173)
mRS at 3 month								
0	N	2,667	2,667	2,667	2,667	1,842	876	876
	Mean (SD)	4,702 (10,240)	16,117 (18,689)	8,962 (18,402)	9,108 (21,611)	9,223 (20,812)	9,364 (21,395)	56,506 (73,899)
1	N	2,456	2,456	2,456	2,456	1,636	777	777
	Mean (SD)	4,729 (9,995)	18,925 (20,447)	10,171 (19,709)	11,242 (23,396)	11,074 (23,301)	10,146 (23,158)	58,833 (72,125)
2	N	1,773	1,773	1,773	1,773	1,050	477	477
	Mean (SD)	6,886 (13,971)	31,365 (30,264)	19,040 (29,954)	19,798 (33,160)	18,463 (32,575)	20,556 (34,394)	113,365 (123,476)
3	N	1,339	1,339	1,339	1,339	881	390	390
	Mean (SD)	9,855 (18,905)	54,728 (40,774)	37,929 (42,085)	36,316 (43,396)	35,991 (44,339)	36,514 (46,790)	206,692 (167,792)
4	N	1,111	1,111	1,111	1,111	734	331	331
	Mean (SD)	14,941 (26,496)	88,033 (42,715)	58,407 (46,019)	49,767 (48,264)	41,466 (48,343)	39,088 (48,623)	286,852 (180,046)
5	N	738	738	738	738	480	228	228
	Mean (SD)	20,221 (31,362)	97,077 (44,220)	51,950 (49,518)	41,446 (51,380)	31,773 (48,355)	26,564 (45,929)	263,096 (193,086)
6	N	716	716					
	Mean (SD)	17,625 (27,557)	28,866 (27,050)					

This study shows that the impact of 3-month functional outcome on the long-term costs of stroke may be more than expected. The efforts for improving functional outcomes are urgent.

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Migraine: The Greatest Disability of All in Australia

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Migraine is the leading cause of adult disability in Australia beating stroke and dementia as second and third leading causes of adult disability [1]. The nature of invisible disability, lack of a bio-

marker, strong nonmedical lay model of headache and stress, headache and hormones, headache and poor work place (I misdiagnosis of migraine as stress related, hormone related etc.) lead this disabling disorder to be the most neglected, most underdiagnosed medical disorder worldwide [2].

The fascinating entity of late life migraine accompaniments (LLMA) is one of the critically important stroke mimics in neurological emergencies [3–7]. Difficulty in differentiation of migraine from vascular insults such as stroke, transient ischemic attacks and amyloid angiopathy make this an important public health problem.

Migraine is more than just a headache. The Deloitte Access Economics reports on “Migraine in Australia Whitepaper” reveals burden of migraine on 4.9 million Australians and \$35.7 billion cost to the economy annually [8]. Australian people with migraine and their families pay it themselves over \$2.2 billion of health system costs every year [8]. Australians suffering regular migraines often resort to hospital care with up to one third of these patients presenting to emergency departments at least once every three months [9]. Hospital admissions and emergency department visits together make up a very high proportion of health system expenditure at \$6.8 billion every year [8]. Nearly 90% of Australian people with migraine are of working age with significant impact on productiv-

Table 1. NHMRC funding for migraine research in Australia (for Abstract No. 19)

Year	Migraine expenditure	Total expenditure	Proportion
2008	\$946,680	\$621,736,983	0.15%
2009	\$1,304,666	\$708,331,331	0.18%
2010	\$1,105,145	\$727,402,210	0.15%
2011	\$620,214	\$778,111,355	0.08%
2012	\$266,989	\$826,681,371	0.03%
2013	\$386,234	\$775,507,598	0.05%
2014	\$599,051	\$844,184,184	0.07%
2015	\$921,966	\$889,830,964	0.10%
2016	\$477,543	\$817,085,049	0.06%
2017	\$746,844	\$809,049,937	0.09%
Total	\$7,375,333	\$7,797,920,982	0.09%

Migraine expenditure proportion from 2008 to 2017 (source NHMRC, Australia).

ity as a result of up to eight months of migraine days per year. In 2018, the total economic cost of migraine in Australia is estimated as \$35.7 billion (\$14.3 billion of health system costs, \$ 16.3 billion of productivity costs and \$5.1 billion of other financial costs such as reduced carer productivity, loss of wellbeing, loss of efficiency) [8].

Despite this huge tax hole in the budget, the amount of research funding for migraine remains low. The National Health and Medical Research Council (NHMRC) is Australia's leading expert body promoting the development and maintenance of public and individual health standards. The NHMRC has allocated less than 0.09% of its total funding towards research in migraine during the last ten years (Table 1).

It is critically important to address this gross injustice now. We make the strongest argument to raise funding for targeted migraine research as there are many unanswered questions about migraine, and little effective treatment for a disorder that causes personal, and societal havoc for millions [10].

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Stroke Care in Sri Lanka – The Past, the Present and the Future

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Sri Lanka is a South Asian country in the lower-middle income category. A combination of free education, free health and excellent primary health care coverage has enabled it to achieve impressive health and social indicators, notwithstanding the limited resources. The country is placed in the high human development category, with its Human Development Index (HDI) and Healthcare Access and Quality (HAQ) Index rankings being the highest among South Asian countries. Chronic non-communicable diseases (NCDs) are the main cause of death in Sri Lanka, accounting for 71% of all annual deaths, and stroke is an important cause of death and disability. Rapid demographic and epidemiological transitions are likely to lead to a large increase in the burden of stroke and other chronic NCDs.

Research data on stroke in Sri Lanka is limited. Previous studies have shown a high burden of stroke, significant gaps in the quality of available stroke care, and deficient stroke awareness among patients and in the community. Developments have been slow in the field of modern stroke care, and this is attributable to a lack of human resources and infrastructure facilities. A majority of the patients with acute stroke are treated in state-sector hospitals where

facilities for modern stroke care are limited. Neurologists are few in number, and general physicians provide acute stroke care for most of the patients.

A survey was conducted among neurologists attached to all the state-sector hospitals regarding the existing stroke services in Sri Lanka. Out of 22 hospitals with neurologists, a stroke unit was available in nine. Physiotherapy, occupational therapy, speech therapy, mental health services and social services support were available in 100%, 90.5%, 81%, 90.5% and 66.7% of these hospitals respectively. Only 12 hospitals had nurses trained in stroke care. CT scanning was available in 18 hospitals, and MRI was available in only four. Thrombolysis was provided in 14 hospitals, and mechanical thrombectomy in only one.

Recent trends in development of stroke care, however, are promising. Availability of stroke units, imaging facilities and modern treatment modalities is improving in many parts of the country. The National Stroke Association of Sri Lanka, established in 2000, is playing a key role in creating public awareness on stroke. There is a clear need to improve the existing facilities for acute care, rehabilitation and community support, and more research data is needed to guide strategies to minimise the burden of stroke of the country. Much more needs to be done to make Sri Lanka ready to face the challenges of stroke in the 21st century.

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2018 RES-Q Update – Current Results from the International Registry of Stroke Care Quality

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The Registry of Stroke Care Quality (RES-Q) was launched in November 2016 as an ESO program in order to provide a tool for monitoring the quality of stroke care in hospitals throughout Europe. RES-Q collects internationally recognized quality of care metrics, based on "Cross-national key performance measures of the quality of acute stroke care in Western Europe" (Norrving et al, 2015). After the first year of operation, feedback was gathered from all participating sites, and an updated version of the RES-Q questionnaire was decided on by both the ESO-EAST steering committee and national steering committees.

RES-Q was implemented as a single page, dynamic questionnaire and made accessible through the RES-Q website (qualityregistry.eu). Participation in the registry is free for all sites, with development and maintenance of the program supported by ESO. Collection of quality of care metrics has been promoted by both ESO programs as well as the Angels Initiative. Data is collected by all participating sites for a minimum of one month per year, with additional data collection periods being implemented at the discretion of national steering committees.

RES-Q has expanded beyond its initial European mandate and currently involves the participation of more than 500 hospitals in

50 countries globally. Reports are delivered quarterly to all participating hospitals and national societies providing an overview of current treatment delivery. More than 50,000 patients are enrolled in RES-Q, however national representation levels vary significantly by country. 45 of 45 stroke centres in the Czech Republic enroll patients annually, resulting in a nationally representative sample of quality of care in that country. The Romanian National Stroke Society has utilized RES-Q results data to motivate an increase from 11 existing stroke centres, to 41 approved stroke centres by January 1st, 2019. One of the busiest stroke centres in the world, located in Vietnam, uses RES-Q to track all stroke treatment data and has over 7000 patients enrolled to date.

RES-Q has demonstrated the viability of an accessible, web-based, international registry for monitoring standard stroke care quality metrics. The implementation of the questionnaire is crucial to improving participation while avoiding a selection bias based on adoption criteria. Effectively monitoring the implementation of internationally recognized guidelines is essential to motivating governments and health authorities to prioritize stroke treatment policies.

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Brain-Inspired AI for Personalised Predictive Modelling of Neurological Diseases

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The talk presents novel approaches of creating brain-inspired AI using spiking neural networks for modelling and prediction of neurological diseases, such as stroke and dementia. The methods are illustrated on large populations of stroke and dementia data to demonstrate that this approach can be used for accurate early onset disease prediction along with personalised profiling and knowledge extraction for a better understanding of the individual triggering factors. The talk discusses potential applications of the proposed approach for predictive modelling of the onset of other neurological diseases and the response to treatment at an individual level.

Primary Stroke Prevention Needs Overhaul

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An increasing number of people affected by stroke in each and every country of the world strongly suggests that currently used primary stroke prevention strategies are not sufficiently effective to cope with aging and population growth.

A critical appraisal of literature on primary prevention of stroke. Electronic medical databases and published literature were searched from 1970 to August 2018 using the terms: “stroke”, “cardiovascular disease” AND “prevention”.

Of the two currently existing primary stroke prevention strategies (population-wide and high absolute cardiovascular disease [CVD] risk strategies), population-wide strategy is undoubtedly the most cost-effective because it applies to the whole population regardless of the level of CVD risk and allows prevention of not only stroke but also other non-communicable diseases (NCDs). However, it often requires legislative changes and there is often opposition from the industry. That is why, although suggested almost 40 years ago, there is still no country in the world where this strategy has not been implemented in full on a national level. The high absolute CVD risk strategy is perfect for exercising a holistic

approach for CVD risk factors management and monitoring progress with CVD prevention on the individual level. However, this strategy misses out a population with low and moderate CVD risk where about 80% of strokes and myocardial infarctions arise, it does not motivate and educate people to reduce their risk of stroke, and does not include several important risk factors for stroke, such as diet, physical activity, stress etc. Even more importantly, recent evidence from large randomised controlled trials showed no efficacy of the high absolute CVD risk strategy to reduce incidence and mortality from stroke and myocardial infarction.

A very wide use of mobile technologies across the globe offers a unique opportunity to improve the health of smartphone users. Of all currently evaluable apps in stroke only the Stroke Riskometer app allows not only estimation of absolute and relative risk of stroke occurrence over the next 5 to 10 years, but also educates the user about stroke (including F.A.S.T. warning signs) and stroke risk factors and how to control risk factors. Evidence from a pilot RCT shows its high motivational ability and potential to reduce stroke incidence by about 3% per annum.

To be effective primary stroke prevention must include people at all levels of risk of stroke and CVD. The Stroke Riskometer app takes advantage of both population-wide and high absolute CVD risk strategies and offers a new, potentially highly effective and widely used motivational population-wide strategy for primary stroke and other NCDs prevention.

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