PRIMARY STROKE PREVENTION WORLDWIDE: TRANSLATING EVIDENCE INTO ACTION

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Word count: Abstract – 119; main text (without panels, tables and references) – 3988

References: 79
Panels: 2
Tables: 2
Figures: 5
Supplement materials

Abstract

Stroke is the second leading cause of death and third leading cause of disability worldwide and its burden is increasing rapidly in low- and middle-income countries (LMICs), many of which are unable to face the challenges it imposes. In this Policy View paper on primary stroke prevention, we provide an overview of the current situation regarding primary prevention services, cost of stroke and stroke prevention, and identify deficiencies in existing guidelines and gaps in primary prevention. We further offer a set of pragmatic solutions for implementation of primary stroke prevention, with an emphasis on population-wide strategies, including task shifting/sharing and health system re-engineering that includes patients, health professionals, funders, policymakers, implementation partners and the entire population along the life course.

Funding

World Stroke Organization.

Introduction

The burden of stroke remains a huge public health issue of growing importance. In 2019, stroke was the second leading cause of death (6.6 million) and disability (143 million disability-adjusted life years lost [DALYs]) worldwide, after neonatal disorders (in children) and ischaemic heart disease (in adults).[1] Over the past three decades, global stroke incidence increased by 70%, its prevalence by 85%, its mortality by 43%, and DALYs due to stroke by 32%, with a greater increase in stroke burden in low- and middle-income countries (LMICs) compared to high-income countries (HICs). Over a similar time frame, from 1990 to 2018, there was a 37% global increase in the total number of stroke-related DALYs due to risk factors, with LMICs disproportionately affected. Indeed, LMICs experienced a 48% increase in stroke-related DALYs attributable to risk factors, while in HICs there was a 25% decline.[1] In 2019, the five leading risk factors were high systolic blood pressure, high body-mass index, high fasting plasma glucose, ambient particulate matter ($PM_{2.5}$) pollution, and smoking (figure 1).[1]

In 2011, the United Nations (UN) resolution followed by the WHO Global Action plan 2013-2020 called upon all governments to give primary prevention of non-communicable diseases (NCDs), including stroke, the highest priority. The goal was to achieve a 25% reduction in their NCD-related burden by 2025.[2,3] However, as stated by the UN Secretary-General in 2017,[4] the current level of progress on the prevention and control of NCDs is insufficient to meet the goal. The already enormous and continuously growing burden of stroke presents several challenges. First, although LMICs bear most of the burden, they have only a small share of the global financial and health-care resources to combat it. Over 90% of the poorest billion people live in LICs and lower-MICs.[5] Secondly, strokes occur about 15 years earlier among individuals in LMICs than in HICs[6] leading to a marked negative impact on socio-economic development, as persons at the peak of their productive lives are most often affected.[7] Finally, despite the current available knowledge of evidence-based interventions for stroke prevention, this has not been translated into reduced stroke burden in LMICs due to barriers limiting implementation.[8]

The growing burden of stroke across the globe strongly suggests that current primary stroke and cardiovascular disease (CVD) prevention strategies are either not used widely enough or are insufficiently effective. A previous comprehensive review of primary and secondary prevention of stroke[9] was largely focused on individual risk factors and measurements of the effectiveness of preventative interventions. This Policy View paper is based on a more holistic approach including a critical review of existing primary prevention strategies and current guidelines, economic analysis, and identification of gaps in primary stroke prevention. This approach enabled us to provide evidence-based pragmatic solutions on strategies for primary stroke prevention within a cost framework that global, regional and national policymakers can use to reduce the burden of stroke across the globe, especially in LMICs (Panel 1). To derive these solutions (figure 2) the following four steps were carried out. Firstly, a situational evaluation was conducted by collecting and analysing data on the state of stroke-related

services and resources in LMICs compared to HICs.[10] Secondly, priority setting was conducted by extracting the highest grade of evidence-based recommendations using the stroke guidelines that best satisfied the criteria from the Institute of Medicine[11] as identified from a systematic review of all available stroke guidelines across the globe. Thirdly, the barriers and facilitators for implementing these recommendations in the context of LMICs were derived from the situational evaluation and relevant literature review (Tables 1 and 2). Finally, a roadmap for primary prevention was devised (Tables 1 and 2) and pragmatic solutions were proffered to implement evidence-based recommendations to reduce the burden of stroke in LMICs and other underserved settings.

The cost burden of stroke and the economic case for prevention

To develop an economic case for the pragmatic solutions we are proposing for the primary prevention of stroke, we performed an economic analysis based on simulation modelling. We estimated the global financial costs of providing acute care to patients with stroke in hospital including rehabilitation, as well as associated income losses due to premature death and disability as a result of stroke (supplementary materials section 1). In brief, data from the GBD study on the number of new stroke cases and deaths from stroke in 2017[12] were combined with best available estimates of the costs of stroke treatment and rehabilitation from a selected number of countries respresenting different income-levels (i.e. Germany, United States, United Kingdom, Japan, China, Brazil, Turkey and India). Our estimates suggest that stroke-related treatment and rehabilitation costs globally ranged from approximately US$66 billion to US$213 billion among new stroke cases in 2017. In addition to direct costs, there were large indirect costs associated with income losses from premature death and disability after stroke. We estimated that the discounted lifetime economic losses to households with incident stroke cases in 2017 amounted to US$576 billion globally. Roughly half of the global income losses from stroke occurred in HICs, and another 42% in upper-MICs. Income losses from stroke in LMICs and LICs accounted for only 8% of the global total, primarily because of their much lower income levels. Thus, based on our simulation modelling, the estimated treatment, rehabilitation, and indirect costs for stroke are more than US$700 billion annually. A linear interpolation shows that if the current trends in stroke burden continue, by 2030 the cost of stroke to the global economy will be over US$1 trillion. These estimates are likely to be conservative because they do not account for out-of-pocket costs and income losses arising from the added responsibilities falling upon caregivers who may have to give up paid work.

Even so, with the costs of stroke care, the economic gains from interventions that can help reduce stroke incidence and/or mortality by small numbers are potentially very large. There is a sufficient body of evidence to show that achieving the United Nations (UN) Sustainable Development Goals (SDGs)[13] (supplement section 2) and WHO health targets[3] with low costs, e.g. <US$1 a day (US$0.43-US$0.90) across low-income countries and <US$3 a day (US$0.54-US$2.93) across middle-income countries,[14,15] could reduce the mortality rate for ischaemic

heart disease and stroke by 10%. In turn, economic losses in LMICs would be reduced by an estimated US$25 billion per year.[15,16] Another promising strategy is to re-prioritise health investment streams towards population-wide primary prevention across the lifespan. It has been estimated that for every US$1 spent on prevention of stroke and CVD there is over US$10 return on investment, and that the preventative interventions focused on risk factors are the most cost-effective options.[17] Moreover, stroke primary prevention efforts are likely to yield large gains due to spill over effects in terms of reducing the risk of acquiring heart disease, type 2 diabetes mellitus, dementia and some types of cancer that share common risk factors, thus supporting achievements of a range of the UN SDGs.

Epidemiological evidence and situational analyses for improving primary prevention

Our recent World Stroke Organization (WSO) coordinated international survey on stroke[10,11] showed that only about one-third of the recommended primary prevention activities are being used in the 82 countries participating in the survey, and these activities were particularly poor in LICs. Although more than three quarters (81%) of countries reported that CVD risk stratification was offered at primary health care facilities, the availability reported within these countries varied widely. While nearly half of these countries reported that risk stratification was available in over 50% of health care facilities, 29% reported that it was available in fewer than 25% of facilities, and an additional 15% reported that it was available in between 25% and 50% of facilities. Moreover, just over half of the countries (53%) reported general availability of all six essential tests and procedures (measurement of height, weight, blood pressure, blood glucose, and total cholesterol, as well as urine strips for albumin assay). Marked disparities were evident across the income groups: 96% of HIC reported all six tests and procedures were generally available compared with 16% of low-income countries. Although many countries have a national strategy towards a healthy diet, reducing tobacco use and reducing diabetes, only 42% of countries have national strategies for all three issues, and less than 1 in 3 countries have smoke-free environments in all indoor workplaces, public transport and indoor public places.

There are two main primary stroke/CVD prevention strategies currently in use: population-wide and individual high CVD risk strategies. Conventional screening of the population for high CVD risk using various prediction algorithms (such as Atherosclerotic Cardiovascular Disease [ASCVD] Risk Evaluation[18] or PREDICT algorithms[19]), which categorise people into mild (moderate), low or high CVD risk. These have been shown to be ineffective to reduce stroke and ischaemic heart disease incidence and mortality rates in randomised trials in 107 421 persons (relative risk, 1.05 [95% CI, 0.95–1.17]; I^2=53%).[20-22] Because of the need for a blood lipid test, and associated costs, these prediction tools have low applicability in LMIC settings[23] (until low-cost point of care devices are available for blood lipid testing). Moreover, as stated by the World Heart Federation and WSO[24] these screening programmes may exacerbate socioeconomic inequalities,[25] have potential hazards of labelling people as 'low risk', giving them false reassurance that they are protected from stroke and heart attack and compromising any motivation to control risk factors.[23,25] Therefore, it has been suggested

that when communicating absolute CVD risk to patients, categorisation of people into low, moderate (mild) and high risk (including heat charts) should be abandoned.[24,26] Finally, "high-risk" prevention strategies are targeted rescue operations for high CVD risk individuals that are usually implemented by health care professionals. Whilst they may be adequate for conditions confined to an identifiable minority of people at high CVD risk, stroke/CVD is a disease of society,[27] and most cases (up to 80%) arise in "low risk" individuals,[28,29] not covered by the high-risk prevention strategies.[23] Issues for clinicians in primary stroke prevention at the individual level include the lack of digital decision-making tools,[30] and the lack of time to motivate, develop and give tailored primary prevention recommendations to the patient. An example of a digital decision-making tool that can help to solve all these issues is the desk-top multi-language PreventS© webapp for clinicians.[1] The PreventS© webapp can be integrated with electronic medical databases via a cloud-based agnostic system that clinicians can securely use on any computer (figure 3, supplement section 3).

As the mean (average) level of exposure to causal risk factors throughout the population correlates closely with the incidence of stroke/CVD in the population, the population-based strategy of prevention aims to reduce the mean level, and overall distribution, of exposure to causal risk factors throughout the population to reduce the incidence of CVD.[31] Preliminary calculations suggest that if population-wide strategies were implemented widely and effectively they could prevent up to 50-90% of stroke/CVD events over 5 years.[1,26,32,33] A motivational mass prevention strategy via eHealth technologies[34] in combination with polypill and task-shifting/sharing (or task-transfer)[26] could prevent up to 50% of stroke/CVD events. "High risk" strategies can potentially prevent about 11% of stroke/CVD events (figure 4),[35] with both strategies complementing each other[36,37] and priority given to population-wide strategies.[23,24]

Guidelines and pragmatic solutions

Population-wide strategies for primary stroke/CVD prevention are well established[3] (e.g. nation-wide measures to reduce exposure to smoking/vaping, sugary drinks, excessive salt and alcohol intake; promote adequate physical activity etc.). They are recommended in several international and WHO guidelines,[14,38-40] but their implementation in practice is unacceptably slow and far from universal.[11] As shown in a recent systematic review of stroke guidelines,[11] there are two main reasons for slow implementation of population-wide strategies. First, such strategies require policy and legislative changes that are often not supported by major industries (e.g., salt reduction in processed food, reduction of exposure to smoking, alcohol, fast food).[41] Second, implementation of a full range of population-wide prevention strategies requires substantial investments from governments and industry, preferably creation of the Universal Health Coverage, including setting up affordable and widely accessible health services, affordable facilities for adequate physical activities to integrate physical activity into our daily lives, reduction of air pollution and socio-economic inequalities. In addition, despite a special 2011 NCDs UN Declaration to have a NCD prevention plan in every country,[2] most countries still do not have such a plan.

The majority of the burden of stroke (60-70%) across all countries in the world is associated with elevated systolic blood pressure (SBP) and unhealthy lifestyle risk factors such as smoking, obesity, low physical activity and poor diet (including excessive salt, sugar and alcohol intake; low fruits/vegetables consumption).[1] Reducing exposure to these risk factors and treating hypertension should be the priority targets for both population-wide and individual-based preventative interventions for primary stroke prevention (panel 2). A good example of decisive actions to stop smoking is the recent suite of proposals of the New Zealand government aimed at creating a smoke free generation and moving the country closer to its goal of being smoke-free by 2025. Step-by-step action plans and online courses on Global Salt Reduction Strategies for policy makers, advocates, and programme managers have recently been developed to implement scalable sodium reduction interventions focusing mainly on LMICs, and are offered for free by Johns Hopkins University. The medical community must continue to lobby and advocate governments to implement evidence-based population-wide prevention strategies.

Based on the totality of evidence the WSO recently issued a Declaration[26] that recommends the use of the following four strategies for global primary prevention of stroke and dementia: (1) population-wide policy strategies to reduce exposure to risk factors for stroke, dementia, CVD and other NCDs (including environmental risk factors such as air pollution) across the lifespan of the entire population regardless of the level of individual CVD risk; (2) motivational population-wide strategy using health apps (an example is the free Stroke Riskometer app[22,34,42,43]) or similar mobile phone applications to reduce lifestyle and other risk factors in adults at any increased risk of stroke (supplementary section 3, figure 1); (3) targeted polypill (consisting of two low-dose generic blood pressure and one generic lipid lowering medication) strategy for middle-age and older adults at risk of CVD (at least two behavioural and/or metabolic CVD risk factors); and (4) preventative strategies to control behavioural risk factors (especially smoking, elevated blood pressure) and diabetes mellitus via community health workers (community health workers were also suggested to facilitate implementation of strategies 2 and 3).

As stated in the WSO Declaration,[26] policy makers and health providers must reduce exposure to risk factors at a population level regardless of the CVD risk through mass approaches (e.g. smoking cessation campaigns, reducing salt and sugar in processed food and restricting alcohol consumption) and more individual-focused motivational education about behavioural risks (poor diet, physical inactivity, alcohol and smoking) via the free Stroke Riskometer app or similar mobile phone applications would apply to the general population at any risk of CVD. In addition, simple inexpensive screening for vascular risks (elevated blood pressure, smoking and overweight/obesity)[22] by community health workers or people from stroke support organisations in resource poor settings or by medical professionals (including blood lipid tests) in more affluent countries, would identify individuals in need of prophylactic drug therapy, in conjunction with lifestyle and behavioural interventions.[23] There is also evidence of sex differences in the risk of stroke[1] and its risk factors[44] and that the intensity of primary

stroke prevention should not be reduced in older people.[45] These recommendations are summarised in the 2021-2030 Primary Stroke Prevention Roadmap (Table 1). With all these recommendations implemented into practice, a similar risk factor shift in the distribution of risk factors would occur as with the population-wide primary prevention strategy (figure 4, part A).

Joint efforts and establishment of a regional and national plans

Stroke is a complex medical and socioeconomic issue. Therefore the importance of global, international and national efforts and collaboration between various sectors of health care and decision-makers, government and non-government agencies (e.g. stroke and CVD/NCD organisations), industry, communities and individuals for effective reduction of stroke burden cannot be overemphasised (figure 5).[9,46] Government bodies have the power and responsibility to provide adequate health services to cover primary prevention, improve socioeconomic conditions, reduce inequities and influence environmental (e.g. reduction of air pollution, building healthy cities) and lifestyle factors (e.g. reducing salt, sugar in processed food and alcohol intake through legislation and taxation). In concert with this, health systems have responsibilities for identification and management of risk factors and people with cerebrovascular diseases, and government and non-government organisations have responsibilities for ongoing public (e.g., stroke awareness days) and professional education (e.g. teaching courses, conferences). In addition, intersectoral intervention is required to provide essential medicines for primary stroke prevention (e.g., affordable blood pressure and lipid lowering medications) and an enabling environment for healthy lifestyles, including reworking the food chain to make healthy food available and affordable for all, providing safe neighbourhoods conducive to walking, and ensuring access to care. Another approach would be to change public policy to enable community health workers to distribute medicines prescribed by doctors. This is particularly important in hard-to-reach regions where there is limited access to medical professionals. This type of coordinated intervention allows interlinking community-wide prevention and individual management approaches that improve health across the care continuum, and across settings and strategies (figure 5).[47]

The development and implementation of action plans for primary stroke prevention should be aimed towards achieving the internationally recommended goals and targets for reducing the burden from NCDs.[2,3] These country-specific and financially sustainable action plans and consensus statements need to be (i) developed by recognised local experts, (ii) evidence-based, (iii) endorsed by government agencies, and (iv) contain well-developed implementation plans including key performance indicators, steps, timelines, funding (including funding for implementation) and accountable people. These action plans must be facilitated by national, culturally appropriate, and up-to-date guidelines for primary stroke prevention. Unfortunately, there is a shortage of operational national plans aligned with the Global Action Plan on NCDs.[48] While there are a number of national guidelines for primary stroke prevention in HICs,[38,49] there is a paucity of such evidence-based, context-appropriate pragmatic guidelines in LMICs.[9]

Although mainstream preventative strategies should be similar in HICs and LMICs, differences in the population-attributable risks, lifetime risk of stroke, the distrubtuion of different risk factors and the availability of resources should be considered when setting goals and priorities. For example, given the much greater burden of smoking, air pollution and haemorrhagic stroke in LMIC than in HIC, a strong emphasis on early detection and management of elevated blood pressure, reduction of air pollution and anti-smoking campaigns should be a priority in LMICs. This should be facilitated by government-imposed measures to reduce sodium in processed food as well as education of individuals about reducing salt and tobacco intake.[50] In addition, in HICs, where smoking prevalence has reduced and the burden associated with ischaemic stroke is noticeably higher than in LMICs, it seems reasonable to focus more heavily on reduction of other behavioural risks (particularly on the reduction of sugar consumption and physical inactivity) as well as on the identification and pharmacological or surgical management of medical conditions that lead to stroke, including hypertension, diabetes mellitus and atrial fibrillation. Population-wide and individual primary stroke/CVD prevention strategies (including motivational mass individual strategy)[42] should be used regardless of the level of stroke/CVD risk, with priority given to population-wide strategies.

Actions to improve stroke prevention come at a cost. With already overstretched health budgets, even in HICs, one wonders where the funding could come from to support stroke prevention in a sustainable manner. One of the most promising strategies to secure such funding is to re-invest revenues from taxation on unhealthy products (e.g. tobacco, sugary drinks, alcohol, salt in processed food)[17,51-56] followed by adding savings from preventing stroke back into health services and preventative strategies.[47] This is important as reduced consumption of these unhealthy foods has been shown to be beneficial for stroke/CVD and overall health at the population level. Although it is widely acknowledged that prevention is better than cure, even high-income countries allocate less than 2-3% on average of their health spending to public health and prevention activities[57] and there is also evidence of significant underfunding of stroke-related research.[58] Governments have to be transparent about the proportion of health budgets that are focused on prevention.

Politicians and policy decision-makers must realise that without urgent improvement in primary prevention of stroke and other major NCDs, the sustainability of the whole health system will soon be in question. Only by joining forces with other interventions for NCD prevention will stroke prevention have its full impact.[46] The Global Alliance for Chronic Diseases[59] is a good example of such an integrative approach. There are several reports showing the effectiveness of population-wide primary prevention strategies in selected populations of Finland,[60] Japan[61] and the USA.[62]

Innovative dissemination for substantial implementation and impact

Beyond the publication of these key recommendations and evidence-based pragmatic solutions and advocacy tools, further steps will be taken immediately by the commissioners, the WHO and the WSO to spread the key messages of this Commission, through innovative

deployment via social media and other media platforms. This will include engagement of societal opinion-shapers via the establishment of the Global Stroke Control, Observatory and Reduction Ecosystem (gSCORE, supplement section 4, figure 2)[10,63] to: (i) address key environmental factors via policy change – social determinants of health, making default choices healthy; (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; and (iv) empower the stroke commissioners to be the champions and advocates ensuring rigorous implementation and evaluation across the globe.

The gSCORE, leveraging the WHO Global Action plan against NCDs, is planned to operate at country, regional and global levels in collaboration with relevant policy makers and implementation partners including national and regional stroke, neurology, CVD and NCD organisations and relevant alliances.

Conclusions and future directions

The proffered key solutions are targeted at reducing the occurrence of stroke and preventing economic losses from stroke through primary prevention across the life-course. As many lifestyle habits are set early in life, culturally appropriate education about healthy lifestyles should be incorporated into standard education curricula, started early in life with reinforcement across the lifespan and incorporate families. These preventative strategies should be complemented by adequate stroke education campaigns that consider cultural and subcultural differences and beliefs of people of various races and ethnicities but also significant geographical differences in the lifetime risk of stroke and its risk factors.

For an effective effort, there is a need for synergy between healthcare providers, government and non-government agencies, industry, academic organisations, societal opinion-leaders, and individuals. An approach which integrates strategies aimed at primary stroke prevention (population-wide and targeted strategies towards individuals with any level of increased stroke risk) with strategies aimed at prevention of other NCDs is most likely to be successful, as many risk factors are shared between stroke and other NCDs.

As many stroke risk factors are common to other major NCDs, such as ischaemic heart disease, type 2 diabetes mellitus, renal disease, dementia, and some types of cancer, it is expected that the worldwide implementation of the solutions will not only halve the burden of stroke but also significantly reduce the burden from other major NCDs. This would not only save millions of lives around the globe but would also have a dramatic economic impact. Developing primary stroke prevention guidelines for LMIC is urgently required. We must increase the target audience for future primary stroke prevention guidelines in both HIC and LMIC since many primary stroke prevention interventions require intersectoral funding and policy initiatives as well as population buy-in. Further research is required to develop integrative, culturally appropriate, and population-specific eHealth technologies for effective

primary stroke prevention, including digital decision-making tools for clinicians and community health workers, and to establish the best balance between various primary stroke prevention strategies to maximise cost effectiveness and minimise inequalities.

Role of the funding source

The funder had no role in the design, data collection, analysis and interpretation of the study results, writing of the report, or the decision to submit the study results for publication.

AUTHORS' CONTRIBUTIONS

MO, VLF, AGT, SM, and WJ conceptualised the structure and design of the manuscript. VLF and MO wrote the first draft of the manuscript. JY analysed and wrote on systematic review of stroke guidelines. AM developed economic analysis of stroke cost. All other co-authors provided critical intellectual contribution to the manuscript. All authors reviewed and approved the final version of the manuscript.

DECLARATIONS OF INTEREST

VLF declares that PreventS webapp and free Stroke Riskometer app are owned and copyrighted by Auckland University of Technology, New Zealand. 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 declares funding from the National Health & Medical Research Council (NHMRC, Australia: GNT1042600, GNT1122455, GNT1171966, GNT1143155, GNT1182017), Stroke Foundation Australia (SG1807), and Heart Foundation Australia (VG102282) outside the submitted work; and Board membership of the Stroke Foundation (Australia), outside of the submitted work. SLG is funded by the National Health Foundation of Australia (Future Leader Fellowship 102061) and the National Health and Medical Research Council (GNT1182071, GNT1143155, GNT1128373). SCOM declares Boehringer Ingelheim, honoraria for lectures from Medtronic, Bayer, Pfizer, Penumbra, outside of the submitted work. PB declares that he is Board of Directors and Chair of Industry Committee of the WSO, outside of the submitted work. SFA declares that he has received an unrestricted research grant for an epidemiological study (EstePA), outside of the submitted work. SFA also declares receiving travel support for the 2020 WSO-IASO meeting in Brazil and he is a member of the Steering Committees and principal investigator of the NAVIGATE-ESUS, AXIOMATIC and ENRICH trials conducted by PHRI (CANADA), outside of the submitted work. Dr. Inoue reports lecturer's fees from iSchemaView, Bayer, and Medico's Hirata, outside of the submitted work. BN declares honoraria from Astra Zeneca and Bayer for data monitoring and safety committee

work for the SOCRATES, THALES and NAVIGATE-ESUS trials, outside the submitted work. PML reports grants from FONDECYT-ANID, grants from The George Institute for Global Health, grants from Boehringer-Ingelheim, personal fees from ANGELS initiative, other from Clinica Alemana de Santiago, outside the submitted work. YK reports a grant from the Wellcome Trust/DBT India Alliance (IA/CPHI/14/1/501514), outside the submitted work. ME reports grants from Bayer and fees paid to the Charité (no personal fees) from Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Covidien, Daiichi Sankyo, GSK, Novartis, Pfizer, Sanofi, all outside the submitted work. RM is supported by the project No. CA18118 from the IRENE COST Action - Implementation Research Network in Stroke Care Quality of the COST (European Cooperation in Science and Technology) and by the IRIS-TEPUS project No. LTC20051 from the INTER-EXCELLENCE INTER-COST program of the Ministry of Education, Youth and Sports of the Czech Republic, outside of the submitted work. SK reports grants from Austrian Research Promotion Agency FFG, outside the submitted work. JK declares honoraria for lectures and payment for travel for attending meeting from Boehringer Ingelheim, and honoraria for lectures from Pfizer, outside the submitted work. RGN declares that Emory University has received a grant from Cerenovus to conduct the ENDOLOW trial, reports consulting fees for advisory roles with Anaconda, Biogen, Cerenovus, Genentech, Hybernia, Imperative Care, Medtronic, Phenox, Prolong Pharmaceuticals, Stryker Neurovascular, and Synchron; Legal consulting fees for expert testimony from Law Firms; participation in the Synchron SWITCH Trial Clinical Events Committee; and stock options for advisory roles with Astrocyte, Brainomix, Cerebrotech, Ceretrieve, Corindus Vascular Robotics, Vesalio, Viz-AI, and Perfuze, outside the submitted work. KWW declares that he has received funding from the National Health and Medical Research Council (Canberra) and Medical Research Council (London) as Nigeria Regional Coordinator for TRIDENT and INTERACT3 studies respectively, outside of the submitted work. He received honorarium from Servier Pharmaceutical Company for a lecture presented on behalf of the Company, outside of the submitted work. MSE reports Grants from BMS-Pfizer Alliance for Eliquis, Roche, royalties from UpToDate for chapters related to stroke, Officer (President) American Heart Association, outside of the submitted work. BN declares declares fees for DMC work for SOCRATES, THALES trials for Astra Zeneca and fee for DMC work for NAVIGATE-ESUS trial from Bayer, outside of the submitted work. HMR declares Scientific advisory board honoraria from Amgen, grant from Bangerter foundation, personal fees from Bayer, membership of the ESO Board of Directors and of the ESO Education Committee, outside of the submitted work. All other authors declare no competing interests.

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Acknowledgements

The stroke services survey reported in this publication was partly supported by the WSO; the Auckland University of Technology, New Zealand. VL Feigin and R Krishnamurthi were partly supported by the grants received from the Health Research Council of New Zealand. MO is supported by NIH grants SIREN U54 HG007479 under the H3Africa initiative and SIBS Genomics R01NS107900; SIBS Gen Gen R01NS107900-02S1; ARISES R01NS115944-01; H3Africa CVD Supplement 3U24HG009780-03S5, and CaNVAS 1R01NS114045-01. 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 and a National Health and Medical Research Council Synergy Grant.

We would like to acknowledge Arsovska A. *MD, PhD*, Bohara M. *MD, PhD* , Čerimagić D. *MD, PhD*, Correia M. *MD*, *PhD*, Cuervo D.L.M. *MD*, Członkowska A. *MD*, Ekeng G. *MSc*, Sargento-Freitas J. *MD, PhD*, Flomin Y. *MD, PhD*, Gebreyohanns M. *MD*, Gonçalves I.P. *MD*, Johnston S. C. *MD*, *PhD,* Jurjāns K. *PhD*, Kalani R. MD, Karaszewski B. *MD*, Kozera G. *MD*, Kutluk K. *MD*, Malojcic B. *MD, PhD*, Ocampo C. *MD*, Shaw L. *MBChB*, Thapa L. *MD, DM*, Wojtyniak B. *PhD*, Yang J. *MD, PhD*, and Zdrojewski T. *MD* for their comments on early draft of the manuscript.

The views expressed in this article are solely the responsibility of the authors and they do not necessarily reflect the views, decisions, or policies of the institution with which they are affiliated.

Panel 1. Aims of this Policy View

- To provide an understanding of the burden and cost of stroke, and evidence for cost and cost-effectiveness of the existing primary stroke prevention strategies
- To provide an overview of available primary stroke prevention strategies, services, guidelines, and identify deficiencies and gaps in primary stroke prevention
- To provide a set of pragmatic solutions for policy makers, funding organisations and other stakeholder for funding and implementation of primary stroke prevention strategies, with examples of successful translation of evidence into actions

Search and selection criteria

For covering the latest data, we searched MEDLINE, Embase, Google Scholar, and the Cochrane Library, as well as the internet (using Google and other search engines), for research published between January 1980 and 15 May 2021 using the following key words in title or abstract: “stroke”, “cerebrovascular disease”, “isch(a)emic stroke”, “intracerebral h(a)emorrhage”, “subarachnoid h(a)emorrhage” “transient isch(a)emic attack” or “cardiovascular disease AND “prevention”, “cost”, “guidelines”, “awareness”, “tax or taxation”, “trial”, “policy”, “legislation”, “mHealth”, “eHealth”, “polypill”, “roadmap”, “incidence”, “prevalence”, “mortality”, “burden” or “outcomes”. Also, websites of medical societies and stroke experts were approached for additional stroke prevention guidelines. We concentrated on population-based studies and guidelines related to primary stroke prevention since 2011. Additionally, we manually searched the reference lists of relevant publications and consulted with experts in stroke, CVD and other relevant stakeholders, to complement the electronic searches.

Panel 2. Key solutions for primary stroke prevention

- Effective stroke prevention must include both population-wide and individual-based strategies that cover all or most of the population, with priority given to population-wide strategies. Individual-based primary stroke prevention strategies can be best accomplished using:
    - Mobile technology (so-called motivational mass individual strategy for stroke prevention),[23] a simple, inexpensive screening for a history of CVD and presence of modifiable risk factors (particularly smoking/vaping, obesity, elevated blood pressure), linked to local, regional and/or national healthcare electronic databases.
    - Shifting/sharing of tasks from highly trained health professionals to health-care workers, particularly community-based health workers, with less training, qualifications, and education to facilitate stroke prevention interventions on the individual level.[26,64]

Practical example: Effectiveness of population-wide primary prevention strategies in selected populations of Finland,[60] Japan[61] and the USA.[62] The validated and free Stroke Riskometer app[34,42,43] which is being used in 19 languages in 78 countries, potentially covering 5.3 billion people; PreventS webapp for clinicians.[1] Transferring/sharing tasks from highly trained health professionals to health-care workers was implemented in several areas of India.[64,65]

- While governments should provide adequate health services, improve socioeconomic conditions, reduce inequities and influence environmental (e.g., air pollution) and lifestyle factors (e.g., smoking, vaping, reducing salt, sugar in processed foods and alcohol intake through legislation and taxation), health systems should identify, screen, and manage risk factors. Revenues from these taxations should be invested into the public health sector and health research to improve health of the taxpayers, including appropriate funding of primary prevention strategies for stroke/CVD and other NCDs. Governments have to be transparent about the proportion of health budgets that are focused on prevention.

Practical example: Effective smoking cessation campaigns in some countries,[66] taxation of sugary drinks in several countries, including the UK, Ireland, France, Canada, South Africa, UAE, Portugal, Mexico, Sri Lanka,[67] junk food taxes in Mexico and Hungary,[68] successful alcohol reduction in Russia,[69] successful air pollution campaign in China.[70]

- Effectiveness of the proposed primary stroke prevention measures should be regularly assessed by monitoring of stroke incidence, mortality, prevalence (rates and absolute numbers) and risk factors (prevalence, changes in absolute and relative risks of stroke/CVD) at the individual and population levels.

Practical example: WSO stroke survey,[11] WHO health survey,[71] GBD Study.[72]

Figure 1. Infographic: the global impact of stroke and stroke risk factors[1,45] (estimates of the stroke cost were derived from the current publication)

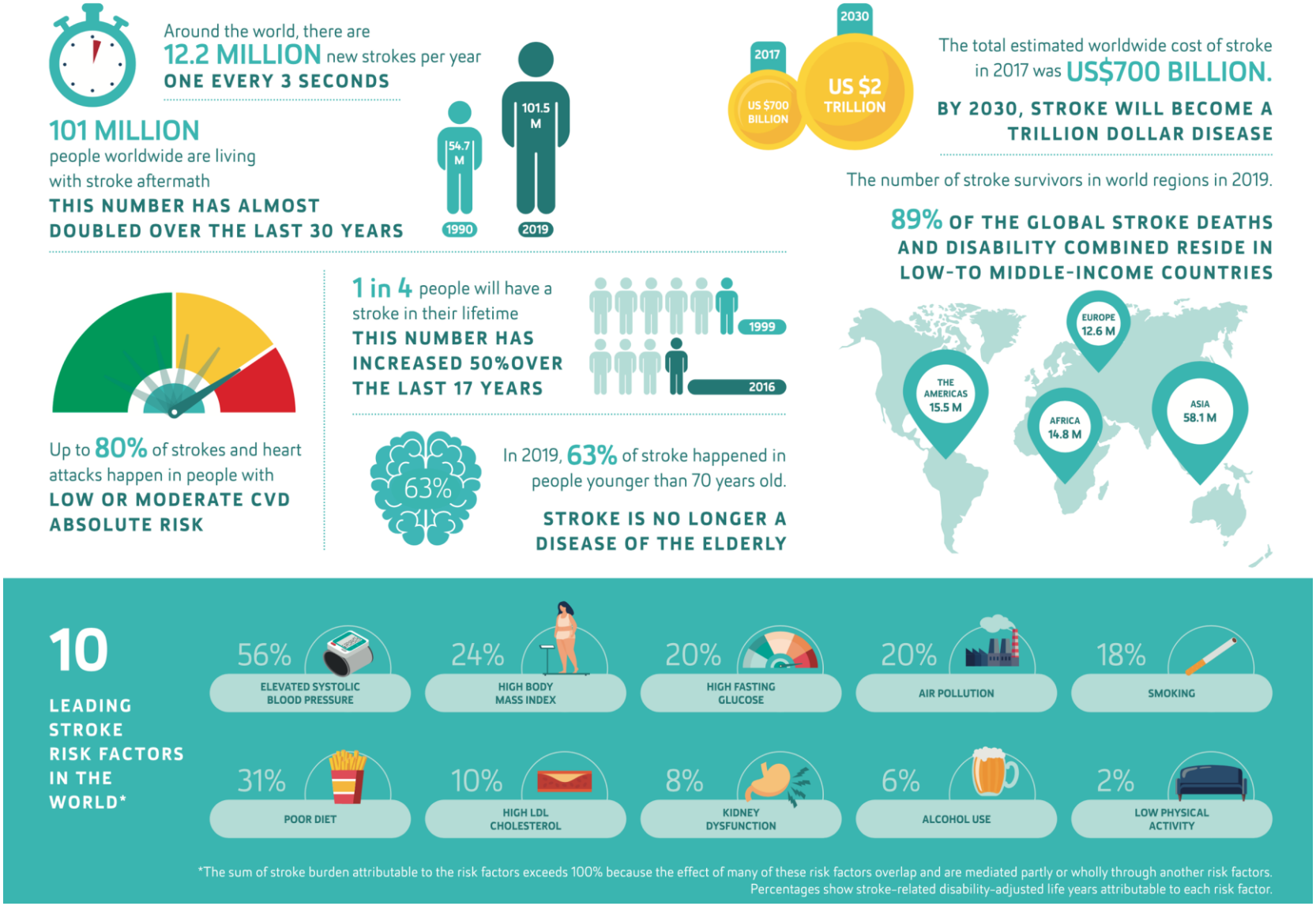

Figure 2. Methodological workflow for deriving pragmatic solutions for primary stroke prevention

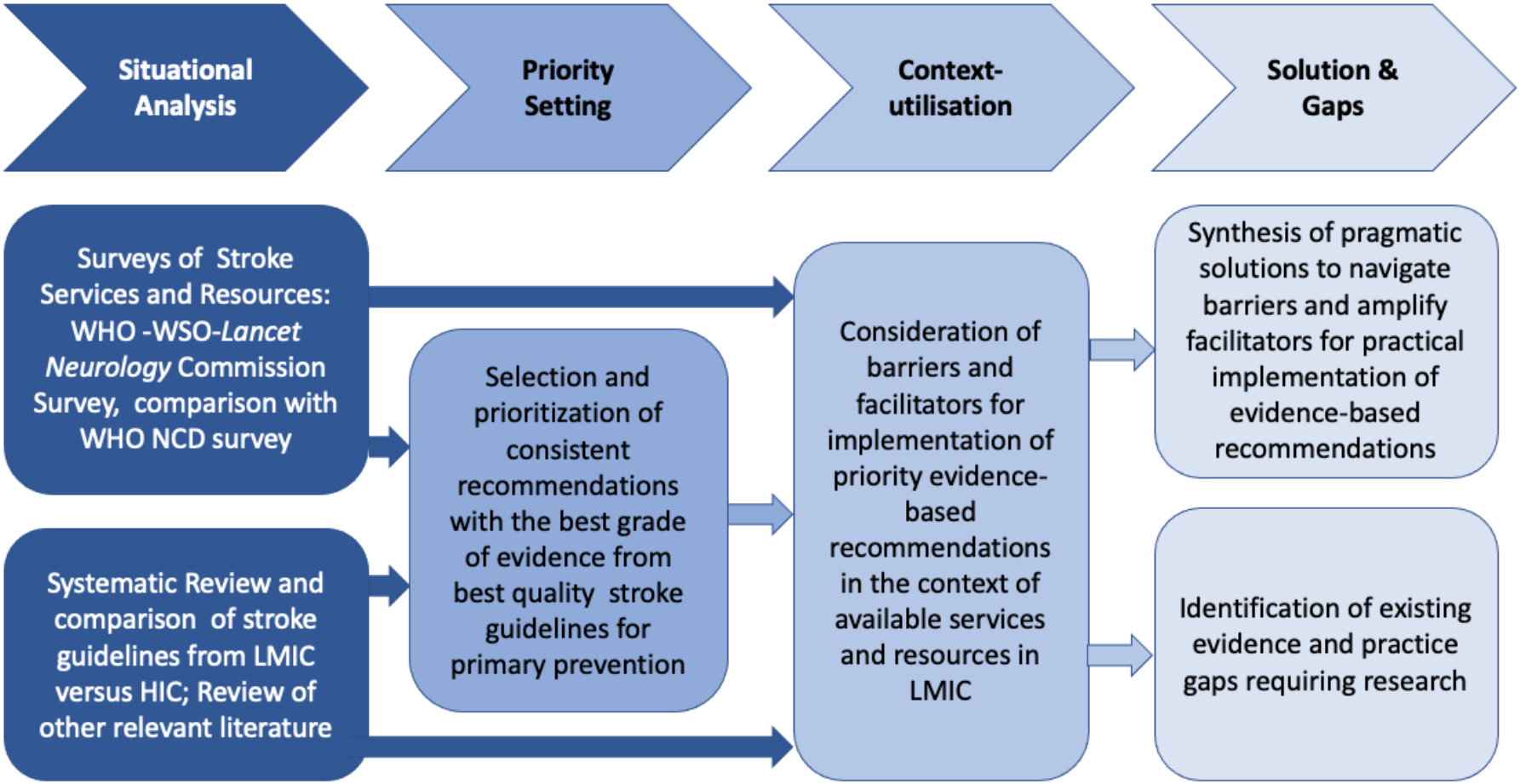

Figure 3. Outline of the PreventS© cloud-based platform for clinicians. PreventS© algorithm for calculation absolute and relative risks of stroke are based on the validated and internationally endorsed Stroke Riskometer app.[34,42,43]

Figure 4. Optimal shift in the distribution of cardiovascular disease (CVD) risks through a combination of population-wide (including motivational mass individual primary prevention) and high CVD risk prevention strategies. Modified from BMJ Glob Health,[42] with permission. Areas shadowed in grey show a theoretically possible proportion of the population that could benefit from (a) population-wide prevention strategy, (b) high CVD risk prevention strategy, and (c) motivational mass individual risk prevention strategy regardless of the CVD risk level (i.e., use of mobile applications to reduce lifestyle and other risk factors).

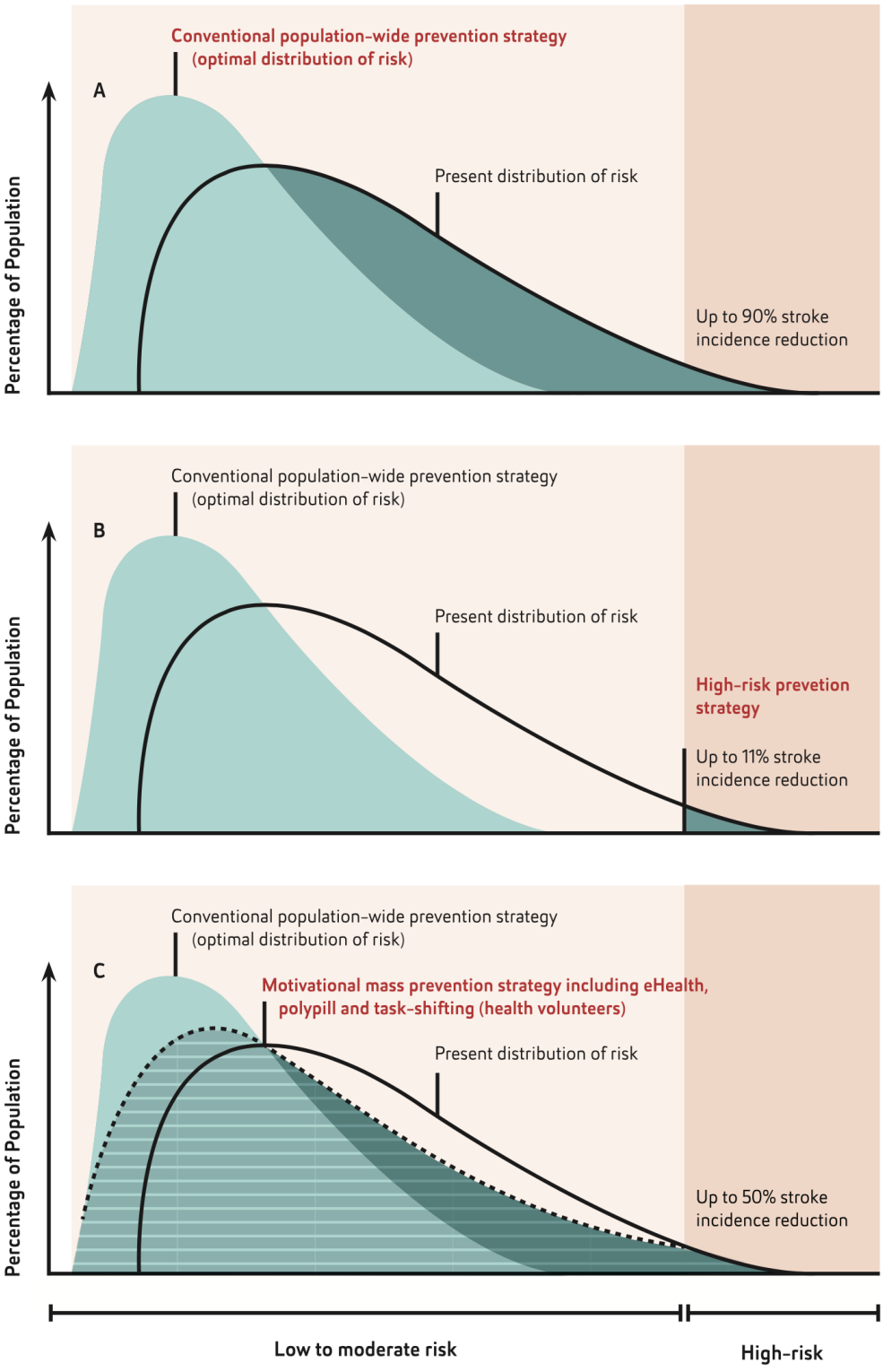

Figure 5. Action plan for governments and other policy makers for primary stroke prevention measures at the population (socio-economic, environmental, behavioural) and individual levels.

Table 1: 2021-2030 primary stroke prevention roadmap

Problems	Goals	Targets	Recommendations/Actions	Assessment methods
Lack of funding for primary stroke prevention across all countries, particularly in LMIC.	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 foods, aimed at reducing consumption) back to health services and preventative strategies All health care 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 stroke prevention.
Few countries or regions have established action plans for stroke prevention.	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 freely available and validated mobile apps for managing their risk factors (e.g., WSO/WHF/WFN/ESO recommended Stroke Riskometer app) Transferring/sharing tasks of primary stroke prevention from highly trained health professionals to health-care workers with less training, qualifications, and education, followed by appropriate training. Culturally appropriate education about healthy lifestyles should be incorporated into standard education curricula and started early in life, with reinforcement across the lifespan.	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.
Lack of integrative approach in primary stroke prevention, particularly in LMIC.	To establish collaboration between different national and international agencies and organisations involved in primary prevention of NCDs.	National and international agencies and organisations.	Include nationally and internationally recognised stroke experts in all relevant national and international agencies and organisations involved in primary prevention of NCDs. Prioritise primary stroke prevention strategies to reduce exposure to CVD risk factors in the whole population across the life course including intrauterine life, with a focus on optimal maternal and child health care, behavioural and lifestyle risk factors. This would enable an integrative approach that also targets other major NCDs, such as dementia, diabetes, cancer, and pulmonary diseases.	Checklist of representation of stroke experts in all relevant national and international agencies and organisations 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 organisations should conduct ongoing stroke awareness campaigns about stroke, its warning signs and prevention, coordinated by the WSO. Regular TV programmes is the preferred channel of media for such campaigns.	Stroke awareness surveys.
Lack of monitoring	To establish national and subnational (for	Whole population	All countries should have monitoring systems to evaluate the effects of primary and secondary prevention strategies.	Changes in the 5- or 10-year absolute risk of stroke/CVD of outpatients.

systems for evaluation of the effectiveness of preventative strategies.	large countries) monitoring frameworks.	and people at risk of stroke.	In the absence of sufficient quality country-specific epidemiological data on burden of stroke and risk factors, health care policy makers should be encouraged to use relevant Global Burden of Disease estimates. Regular use of accurate data to support decision-making.	Strengthening surveillance for key stroke risk factors (raised blood pressure, smoking, alcohol, obesity, excessive salt consumption) with employment of regular (e.g. once in 2-5 years) inexpensive population-based surveys (e.g. WHO STEPS Survey) would provide policy-makers with accurate estimates of prevalence of stroke risk factors to prioritise investments to reduce exposure to the risk factors and, consequently, reduce incidence and burden of stroke. Ongoing or regularly (e.g. once in 2-5 years) conducted registries of strokes morbidity and mortality.
Insufficient funding of stroke prevention research across all countries, particularly in LMIC.	To study determinants of stroke occurrence and outcomes and the best strategies to reduce stroke burden.	Health research funding agencies.	In consultation with recognised 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 prevention (compared to the total health research funding).

CVD, cardiovascular disease; LMICs, low- and middle-income countries; NCDs, non-communicable diseases; TIA, transient ischaemic attack; WHO, World Health Organization

Table 2: Evidence and pragmatic solutions for improving primary stroke prevention worldwide

Key recommendations and their sources (references)	**Level of evidence/ GRADE**	**Resources required for implementation**	**Ethical, Legal and Social Implications (ELSI)/Barriers/ Facilitators**	**Recommendation for contextualisation and implementation through policy makers and other activities**
Countries should have government endorsed policies for community-wide stroke prevention. Sources: UN/WHO/WSO,[3,73-75] Action Plan for Stroke in Europe,[76] AHA Guide for improving cardiovascular health at the Community Level[77]	Level B evidence that tobacco, salt, and alcohol taxation is an effective strategy to improve health. Level A evidence for population-wide primary stroke and other NCD prevention	Expertise in stroke and CVD epidemiology and public health.	Industry lobbing (e.g., for reducing salt content in processed food, reducing consumption of sugary drinks and alcohol). Major barriers also include lack of: (i) expertise to develop an efficient action plan. (ii) Community support for introducing taxation on salt, sugary drinks, alcohol, tobacco products. (iii) Government and health policy engagement; and (iv) Public resources for accessible and affordable healthy food outlets, physical activity facilities, healthy ecological environment.	Policy makers and health experts* to develop legislative changes for reducing salt content in processed food, reducing consumption of sugary drinks and alcohol, including the development of policies for community-wide stroke prevention activities, monitoring effectiveness of these activities, and workforce development. Reinvestment of taxation revenue into primary and secondary prevention, health service development and health research. Health Ministry order for public health services; developing and regularly (at least every 5 years) updating national primary stroke prevention guidelines. Reinvestment of taxation revenue into the development of accessible and affordable healthy food outlets, physical activity facilities, reducing air pollution (healthy city).
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 of sodium (>2.3 g/day; equivalent to 5.8 g/salt/day) intake, overweight (BMI ≥25 or waist-to-hip ratio ≥0.8 for women and ≥0.9 for men), tobacco use, cardiac causes (coronary heart disease, 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 (>2 standard drink a day in men and >1 standard drink a day in women), and diabetes mellitus.	Level B evidence. WHO 'One Health' initiative Level A evidence for control of risk factors for stroke prevention Level A evidence for use of polypill for BP and cholesterol reduction.	Expertise in development and maintenance of awareness campaigns; electronic patient management systems.	Major barriers include lack of: (i) engagement of stakeholders (patients, providers, and policymakers). (ii) collaboration between multiple sectors of society (e.g., government, public health, research/education).	Policy makers and health experts* to develop strategies and action plans for ongoing stroke awareness and primary prevention, with a strong emphasis in LMIC on early detection and management of elevated blood pressure, and on reduction of exposure to air pollution. Policy makers and health experts* should develop a plan for prioritising multisectoral and cost-effective accessible and affordable interventions, including the implementation of mobile technologies to promote a healthy lifestyle and primary

Polypill containing generic BP-lowering medications and statin can be recommended for SBP and LDL-C reduction in adults 40-75 years with elevated blood pressure (SBP 120-160 mmHg) and LDL-C <190 mg/dL (<4.9 mmol/L), and no contraindications to the medications. Pharmacological treatment of dyslipidaemia with statins should be considered in adults with LDL-C ≥190 mg/dL or at intermediate levels of CVD risk (≥7.5% 10-year estimated risk). Aspirin should not be routinely used for primary stroke prevention. Pharmacological treatment of elevated blood pressure for primary stroke prevention should be initiated in people with a 10-year CVD risk score ≥10% or an average BP ≥130/80 mmHg. For those requiring pharmacological therapy, the target blood pressure should generally be <130/80 mm Hg. Recreational drugs should be avoided. All adults should consume a healthy diet that emphasizes the intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, and fish and minimizes the intake of *trans* fats, red meat and processed red meats, refined carbohydrates, and sweetened beverages. For adults with overweight and obesity, counselling and caloric restriction are recommended for achieving and maintaining weight loss. Adults should engage in at least 150 minutes per week of accumulated moderate-intensity physical activity or 75 minutes per week of vigorous-intensity physical activity. Mental health and well-being strategies to optimize brain health should be implemented at both the individual and societal levels. A life-course approach for healthy lifestyle, initiated from maternal and child health, should be exercised. Sources: WSO,[78] WHO,[79] Action Plan for Stroke in Europe,[76] Stroke Riskometer app,[22,34,42,43] AHA stroke/CVD primary prevention guidelines,[38,39] European Guidelines on CVD prevention,[49] INTERSTROKE[32]				stroke prevention. For example, population-wide strategies recently recommended for implementation for stroke prevention in all Latin American countries (e.g., free Stroke Riskometer app), should be one of the priorities for funders and policy makers. Adequate education and regular antenatal care for pregnant women, balanced and adequate nutrition for pregnant women and infants are important primordial measures to reduce the risk of stroke.
Countries should have a nationwide and representative system for measuring and monitoring effects of primary prevention activities (e.g., absolute risk of stroke/CVD of the population, stroke incidence and mortality). Sources: Action Plan for Stroke in Europe[76]	Level B evidence	Expertise in epidemiology, data management and statistics to support ongoing monitoring of stroke.	Major barriers include lack of: (i) infrastructure to support a monitoring programme. (ii) expertise to develop an efficient programme. (iii) capacity to analyse the data collected and produce quality statistics; and (iv) use of data to drive decision-making.	Policy makers and health experts to develop, implement and monitor reliable, simple, and fit-for-purpose strategic action plan with all stakeholders to ensure the availability of a reliable monitoring of stroke and risk factors standardised surveillance systems in their countries and regions.

*An Ecosystem of all relevant stakeholders and experts for the implementation of the suggested recommendations on primary stroke prevention at the global, regional, and national levels is being created to maximise impact of this Policy View paper. AF, atrial fibrillation; AHA, American Heart Association; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; HDL-C, High density lipoprotein - cholesterol; LDL-C, Low density lipoprotein - cholesterol; NCDs, non-communicable diseases; SBP, Systolic blood pressure; UN, United Nations; WHO, World Health Organization; WSO, World Stroke Organisation

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