

Stroke 3



Prevention of stroke: a global perspective

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Along with the rising global burden of disability attributed to stroke, costs of stroke care are rising, providing the impetus to direct our research focus towards effective measures of stroke prevention. In this Series paper, we discuss strategies for reducing the risk of the emergence of disease (primordial prevention), preventing the onset of disease (primary prevention), and preventing the recurrence of disease (secondary prevention). Our focus includes global strategies and campaigns, and measurements of the effectiveness of worldwide preventive interventions, with an emphasis on low-income and middle-income countries. Our findings reveal that effective tobacco control, adequate nutrition, and development of healthy cities are important strategies for primordial prevention, whereas polypill strategies, use of mobile technology (mHealth), along with salt reduction and other dietary interventions, are effective in the primary prevention of stroke. An effective collaboration between various health-care sectors, government policies, and campaigns can successfully implement secondary prevention strategies, through surveillance and registries, such as the WHO's non-communicable diseases programmes, across high-income and low-income countries.

Introduction

Globally, there is a huge burden of stroke, with 10·3 million new strokes and 113 million disability-adjusted life years (DALYs) per year.¹ The disparities in the burden of stroke between low-income and middle-income countries (LMICs) and high-income countries has been growing, with about 75% of deaths from stroke and more than 80% of DALYs now occurring in LMICs.^{2,3} Disparities in the incidence of stroke are also growing, with a 42% decrease in stroke incidence in high-income countries and a 100% increase in LMICs in the past four decades.⁴ The increasing burden and costs associated with stroke care all point towards the pressing need for effective measures of stroke prevention.

According to the Global Burden of Disease (GBD) 2013 study, potentially modifiable risk factors cause more than 90% of the stroke burden,² and more than 75% of this burden could be reduced by controlling metabolic and behavioural risk factors.¹ In this Series paper, we review the major and emerging strategies for the prevention of stroke globally, including, first, activities that prevent the emergence of risk factors via the establishment of environmental, economic, sociobehavioural, and cultural patterns of living (primordial prevention); second, reducing the incidence of stroke (primary prevention); and third, preventing the recurrence of stroke (secondary prevention). Given the growing burden of stroke in LMICs, we have specifically emphasised strategies in these regions (figure 1).

Risk factors for stroke

Risk factors associated with stroke can be classified as either non-modifiable or potentially modifiable. With our overall aim of reviewing the evidence for prevention, herein we focus on potentially modifiable risk factors.

Hypertension

Hypertension is the single most important potentially modifiable risk factor for stroke, accounting for 65·1% of the DALYs lost due to stroke in LMICs and 59·8% in high-income countries.² Over the past two decades the population attributable risk associated with hypertension has increased by 59% in LMICs and reduced by 18% in high-income countries.²

Poor dietary and physical activity habits

Diets that are low in fruits, vegetables, and whole grain, and high in sodium and sugar-sweetened beverages are

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Search strategy and selection criteria

We searched various databases using the PRISMA guidelines, including PubMed, Medline, and Google Scholar. We used the following search terms: "diet", "dietary patterns", "nutrition", "food", "Mediterranean", "DASH diet", "avocados", or "plant-based" in combination with "prevention", "stroke", "cerebrovascular disease", and "cardiovascular disease"; "stroke" in combination with "prevention", "guidelines", and "low to middle income countries"; "smoking uptake" OR "smoking initiation" in combination with "tax" OR "price" OR "mass media"; "salt" AND "policy" AND "diet"; "primordial" AND "diet" AND "cardiovascular"; "child" AND "school" AND "physical activity"; "built environment" AND "physical activity" in combination with "developing country" OR "low income" OR "middle income"; "physical activity"[title] OR "transport"[title] AND "policy" OR "legislation" in combination with "developing country" OR "low income" OR "middle income" OR "low and middle income"; "primordial" AND "cardiovascular" in combination with "developing country" OR "low income" OR "middle income" OR "low and middle income"; "task shifting" OR "task-shifting" OR "eHealth" OR "mHealth" OR "polypill" OR "salt reduction" in combination with "clinical trial" AND "random"; "behaviour change" OR "healthy cities"; "WHO PEN and Secondary prevention" OR "WSO roadmap AND stroke" OR "NCD targets AND stroke" OR "stroke registries AND prevention", OR "surveillance" AND "stroke prevention". We identified articles published between Jan 1, 2000, and Jan 31, 2018, with a focus on the past 5 years. Review articles and book chapters were also cited to enable readers to identify references other than those we could cite here. Our reference list was also modified based on comments from the reviewers.

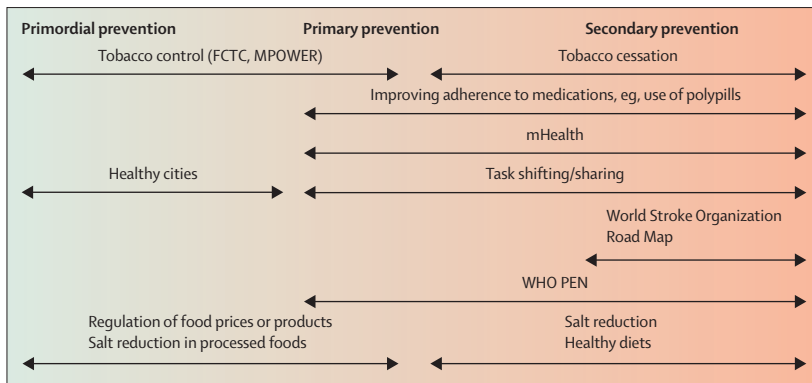


Figure 1: Summary of various measures for primordial, primary, and secondary prevention of stroke

FCTC=Framework Convention on Tobacco Control. mHealth=mobile technology devised to support health. MPOWER=monitoring tobacco use and policies, protecting people from tobacco, offering help to quit, warning about the dangers of tobacco, and enforcing bans on advertising, promotion, and sponsorship. WHO PEN=World Health Organization Package of Essential Non-Communicable Disease Interventions.

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associated with an increased risk of stroke.² Although diets that are low in vegetables account for a similar proportion of DALYs lost due to stroke in LMICs and high-income countries (around 20%), low fruit intake and high salt intake account for a much greater proportion of DALYs lost due to stroke in LMICs (38·3% because of fruit, 23·7% because of salt) than they do in high-income countries (24·3% because of fruit, 17·8% because of salt).² Sugar-sweetened beverages account for only a small proportion of DALYs lost due to stroke (0·3%); however, the contribution of sugar-sweetened beverages to DALYs lost due to stroke has considerably increased between 1990 and 2013, by 83·9% in high-income countries and 58% in LMICs.² Low physical activity is also associated with an increased risk of stroke,² with the percentage change in DALYs lost due to physical inactivity increasing by 68% in LMICs but reducing by 9·2% in high-income countries over this same period.²

Tobacco

Smoking accounts for a similar proportion of DALYs lost due to stroke in LMICs and high-income countries.² However, the proportion of DALYs lost due to stroke in high-income countries declined by approximately 25% between 1990 and 2013, but increased by almost 20% in LMICs.

Alcohol

Alcohol use is responsible for about 6·4% of DALYs lost due to stroke in LMICs, and about 50% more in high-income countries (9·6%).² A major concern is that these figures increased by 49% in LMICs between 1990 and 2013, but reduced by almost 7% in high-income countries. If this trend continues, the contribution of alcohol to DALYs lost due to stroke in LMICs will soon surpass that of high-income countries.

Diabetes, obesity, and dyslipidaemia

High concentrations of fasting plasma glucose (>5·4 mmol/L) and a high body-mass index (>23 kg/m²) are both associated with a substantial proportion of DALYs lost due to stroke, with both factors increasing in LMICs (fasting plasma glucose increasing by 60% and BMI increasing by 69%) and decreasing in high-income countries (fasting plasma glucose decreasing by 7–8% and BMI decreasing by 5%) between 1990 and 2013.² A similar pattern is observed for high total cholesterol.²

Cardiac causes

The major cardiac causes of ischaemic stroke include non-valvular atrial fibrillation or flutter, rheumatic heart disease, prosthetic valves, and previous myocardial infarction.⁵ These factors combined are associated with a 3·49-times increased risk of ischaemic stroke.⁵ The risk of ischaemic stroke caused by cardiac factors is greater in southeast Asia (odds ratio [OR] 9·70, 95% CI 3·32–28·3) and south Asia (9·70, 3·96–23·7) than in western Europe, North America, and Australasia (2·92, 2·12–4·01). However, the population attributable risk is lower in these Asian regions, largely because of the lesser prevalence of such cardiac conditions.⁵

Psychosocial stress

Psychosocial stress, which combines home and work stress, life events, and depression, is associated with a 2·2-times increased risk of stroke and approximately 17% of the population attributable risk of stroke.⁵ The influence of these factors appears to be greater in China (OR 5·79, 95% CI 3·39–9·87) and south Asia (3·49, 1·90–6·35) than it is in southeast Asia (1·63, 0·57–4·65) and western Europe, North America, and Australasia (1·19, 0·72–1·96).

Socioeconomic status

In LMICs, poverty might compound the effect of poorly controlled risk factors and increase the risk of stroke.⁶ Poverty affects not only the risk factors of stroke through lifestyle changes but also the delivery of stroke care services, knowledge and awareness of available resources, and accessibility to stroke care.⁶ In preliminary results from the INSPIRE study, a hospital-based multicentre prospective registry of causes, clinical management, and outcomes for acute strokes done in India, 82% of the patients with stroke were from either a lower-middle income or low-income group.⁷

Air pollution and rapid weather changes

According to the GBD 2013 study, 33·7% of DALYs lost due to stroke in LMICs are caused by household and ambient air pollution, compared with 10·2% in high-income countries.² Between 1990 and 2013, this figure rose by 18% in LMICs, but reduced by 31% in high-income countries. Exposure to smoke from solid fuels contributed to household air pollution in LMICs (19·4%), but not in high-income countries.² Rapid weather changes

increase the risk of ischaemic and haemorrhagic stroke at a population level.⁸ For each degree Celsius decrease in temperature over 2–4 days the incidence of intracerebral haemorrhage can increase by 11%, and for every degree Celsius increase in temperature in a single day the risk of ischaemic stroke can increase by up to 2·1%.⁹

Assessing the risk of stroke

Risk assessment tools can be used to identify prevention strategies for stroke at the community, physician, health worker, and individual level. Many tools for the assessment of the risk of stroke are available for physicians and also for personal use (appendix).^{10–15} The charts for predicting risk developed by WHO and the International Society of Hypertension for WHO epidemiological sub-regions are helping local governments frame their cardiovascular disease prevention policies.¹⁰ The non-laboratory INTERHEART risk score is easy to use and has been validated in high-income and low-income countries to predict the risk of cardiovascular disease.¹¹ However, most of the tools that have been developed have only moderate predictive powers, and serve as tools to increase awareness of risk factors among physicians and patients.¹² A locally validated cardiovascular risk assessment tool should be present in physicians' offices, on community health workers' mobile phones, used in national health awareness campaigns, and freely available to the public to assess their own risk. Early assessment of risk leading to a change in lifestyle might reduce stroke-related morbidity and mortality.

Prevention

New and effective approaches to stroke prevention include population-based approaches (eg, smoking bans, healthy cities), individual-based approaches (eg, polypills), and combinations of these approaches, such as the use of mobile technology (mHealth), task shifting (the process of transferring tasks from highly trained health professionals to health-care workers with less training, qualifications, and education), and salt reduction. Depending on the stage of epidemiological transition, some of these approaches might be considered primordial prevention and others as primary prevention. Global partnerships, such as those fostered within the projects funded by the Global Alliance for Chronic Diseases,¹⁶ promote the implementation of these new strategies. Generally, highly prevalent risk factors that have large absolute risk reductions are the best targets because eliminating or reducing these risk factors will have the largest effect on stroke prevention. These risk factors include hypertension and diabetes, and lifestyle factors that contribute to these conditions.

Primordial prevention

Primordial prevention strategies prevent the emergence of risk factors, ideally taking a life-course perspective that incorporates analysing and improving social and

Panel 1: Summary of the WHO Framework Convention on Tobacco Control and associated MPOWER policy package

Framework Convention on Tobacco Control¹⁷

- Reducing demand
 - Protection from exposure to tobacco smoke
 - Addressing tobacco dependence and cessation
 - Education and public awareness
 - Advertising, promotion, and sponsorship
 - Price and tax measures
 - Non-price measures
 - Regulation of tobacco contents
 - Regulation of tobacco product disclosures
 - Packaging and labelling of tobacco
- Reducing supply
 - Illicit trade
 - Sales to and by minors
 - Provision of economically viable alternative activities
- Protection of the environment
- Liability

MPOWER policy package¹⁸

- Monitoring tobacco use and policies
- Protecting people from tobacco
- Offering help to quit
- Warning about the dangers of tobacco
- Enforcing bans on advertising, promotion, and sponsorship
- Raising taxes

See Online for appendix

biological conditions throughout the life of individuals. We discuss various strategies in this Series paper.

Tobacco control

WHO's Framework Convention on Tobacco Control (FCTC)¹⁷ and MPOWER policy package (the package to help monitor and prevent the use of tobacco and help smokers to quit)¹⁸ provide comprehensive guidance on tobacco control (panel 1). Approximately 172 countries have adopted the FCTC framework and achieved encouraging results.¹⁹ It has been estimated that among 88 countries (69% of which are LMICs) that implemented at least one MPOWER policy, the number of smokers was reduced by about 53 million, averting around 22 million deaths.²⁰ Of these measures, raising the cost of tobacco is the most effective. Initiation of smoking is most strongly associated with the cost of tobacco products in LMICs and so should be prioritised.²¹ There is not much evidence that comprehensive smoke-free area legislation²² or mass media campaigns can prevent smoking uptake in LMICs,²³ but these methods are reasonably effective in high-income countries. According to WHO's 2017 report, comprehensive smoke-free legislation is in place in 39 LMICs and 16 high-income countries, covering almost 20% of the world's population, but only 40% (n=22) of countries have high compliance.²⁴ Bans on advertising, promotion, and sponsorship of tobacco products are poorly adopted, covering only 15% of the world's

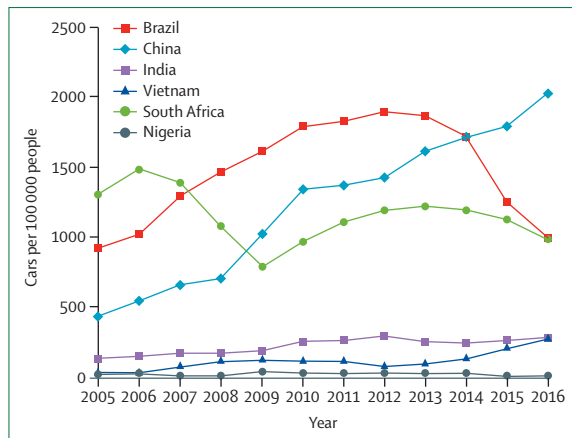


Figure 2: New passenger car sales by country between 2005 and 2016
Adapted from the Organisation Internationale des Constructeurs d'Automobiles (OICA).³⁷ OICA defines passenger cars as anything other than a motorbike used for non-commercial purposes. Data are displayed as sales of new cars per 100 000 people using population data from the World Bank for each country.³⁸

population, so should be addressed.²⁴ In contrast, warning labels that increase knowledge about the consequences of smoking are cost-effective²⁵ and are widely adopted (covering 47% of the world's population).²⁴ Strategies to end the tobacco epidemic have been discussed, including increasing the legal age of smoking to 21 or 25 years²⁶ or banning the sale of tobacco to people born after a certain year.²⁷ As a substantial cause of the burden of stroke and other chronic conditions in LMICs, tobacco should be controlled as a priority for primordial and primary stroke prevention strategies.

Nutrition

Common primordial prevention strategies relating to nutrition focus on price or product regulation. Taxes on foods associated with overnutrition, such as sugar-sweetened beverages, have been implemented in several countries. The introduction of a tax on Jan 1, 2014, equivalent to an approximate 10% increase in the sale price of sugar-sweetened beverages, reduced sales by 6% in the following year in Mexico²⁸ but had minimal effect on purchasing in Barbados.²⁹ The health effects of reduced consumption are uncertain, but a simulation study in Mexico provided evidence that a 10% reduction in consumption of sugar-sweetened beverages would result in 20 000 fewer strokes and myocardial infarctions and 19 000 fewer deaths per year.³⁰ Intensive individual-level dietary interventions also seem to be effective in the primordial prevention of cardiovascular risk factors. In the Special Turku Coronary Risk Factor Intervention Project (STRIP), a biannual dietary intervention that was begun in infants reduced the number and severity of cardiovascular and metabolic risk factors at 20 years old.³¹ LMICs should consider population-level as well as individual-level interventions that target nutrition for the primordial prevention of stroke.

Healthy cities

The rapid development of many LMICs is affecting levels of physical activity through the transition from active (eg, bicycles) to passive (eg, motorbikes) transport³² and shifts from manual to clerical occupations.³³ Primordial prevention strategies can target active transport, built environment, and schools. The aim of the WHO Healthy Cities project is to provide a policy approach to improve health equity and ensure that cities are planned according to a population's health requirements. Interventions that contribute most to preventing stroke relate to design that encourages walking and cycling, reduces exposure to pollution and second-hand smoke, provides incentives to ensure access to fresh and healthy food,³⁴ and provides equitable access to education and health care.³⁵

Walking and cycling can be encouraged by providing walking and cycling paths separate from the road, more green spaces, and changing the zoning of land from residential alone to support mixed-use (ie, residential and business) walkable neighbourhoods,³⁴ which include bicycle-sharing schemes and public transport infrastructure.³⁶ The ownership of private cars has risen steadily over the past decade (figure 2), but increasing the number of public transport options reduces prolonged sitting time, by decreasing the amount of time spent in private vehicles.³⁴ Aspects of the built environment that are associated with increased physical activity include a high population density and mixed-use developments. In a study modelling a compact city, potential health gains were reported, with 337–765 DALYs gained from a reduction in cardiovascular disease, and 27–94 DALYs gained for type 2 diabetes.³⁹ The finding that physical activity increases with population density might be true for some LMICs, such as Brazil, where the likelihood of leisure-time walking was greater among those living within 500 m of a square, bicycle path, or two or more destinations (square, bicycle path, or park) than those living further away.⁴⁰ However, in Chennai, India, increased population density and greater mixed use was associated with a reduction in physical activity.⁴¹ This might suggest that there is a tipping point, whereby high density and mixed use becomes prohibitive to physical activity, cautioning the application of evidence from high-income countries to LMICs. There is also some evidence, mostly from high-income countries, that long-term school-based interventions can have a sustained, positive effect on physical activity,⁴² such as the implementation of at least 1 hour or more of physical activity per day in schools by the Chinese government.⁴³

Primordial prevention strategies are effective at targeting the major risk factors for stroke. The mounting evidence for the role of childhood risk factors on adult cardiovascular diseases provides a strong rationale for investment in these strategies.⁴⁴ WHO's FCTC, which is the world's first public health treaty, serves as a model for primordial risk factor prevention, with its multi-level approach.

Primary prevention

Primary prevention strategies are mainly targeted towards those who are at risk of stroke because of the presence of risk factors. These can be individual-based or population-based strategies.

Polypill strategy: affordable combination therapy

Polypills are fixed-dose combination pills that combine several medications into a single pill. The medications combined for cardiovascular prevention are based on clinical effectiveness and interactions between medications and usually comprise a statin, aspirin, and at least one antihypertensive agent. The principal aim in prescribing a polypill is to improve control of risk factors by simplifying prescription, reducing costs, and improving adherence.

Large clinical trials of polypill use have shown improved adherence to medication (figure 3), with consequent improvements in blood pressure and serum cholesterol,⁴⁷ as well as reductions in ethnic inequities in the use of prevention medications.⁴⁸ In the Heart Outcomes Prevention Evaluation (HOPE-3) study, done in people with a moderate risk of cardiovascular disease, use of a combination therapy consisting of an angiotensin receptor blocker and a diuretic resulted in a reduction in combined fatal and non-fatal cardiovascular events (hazard ratio 0.73, 95% CI 0.56–0.94), but this was only evident in the group with hypertension at baseline (systolic blood pressure >143.5 mm Hg).⁴⁹ In a further analysis of individuals randomised to both lipid-lowering therapy and combined blood pressure lowering therapy, there was a significant reduction in overall cardiovascular events (0.71, 0.56–0.90), as well as in fatal and non-fatal stroke (0.56, 0.36–0.87) when compared with dual placebo (placebo for lipid-lowering and placebo for blood pressure-lowering treatment).⁵⁰ In the UMPIRE randomised controlled clinical trial, those randomly allocated to the fixed-dose group had improved adherence (relative risk [RR] 1.33, 95% CI 1.26–1.41, $p < 0.001$) compared with those who received usual care at an average follow-up of 15 months.⁴⁶ Systolic blood pressure was also reduced more in the fixed-dose group than those receiving usual care (–2.6 mm Hg, 95% CI, –4.0 to –1.1 mm Hg, $p < 0.001$) as was LDL cholesterol (–4.2 mg/dL, –6.6 to –1.9 mg/dL, $p < 0.001$). Importantly, effects were consistent between Europe and India and there was evidence of greater benefits in patients with poor adherence at baseline than in those with good adherence.

Studies are underway to assess the efficacy of various polypills in people without cardiovascular disease but who are at high risk (eg, the International Polycap Study 3 [NCT01646437]), and the effectiveness of polypills in those residing in LMICs (eg, the HOPE-4 study [NCT01826019] and others).^{51,52} The studies being undertaken in LMICs are being done in real-life clinical settings and will therefore better inform the potential for scalability than those done in highly regulated and constrained clinical trials.

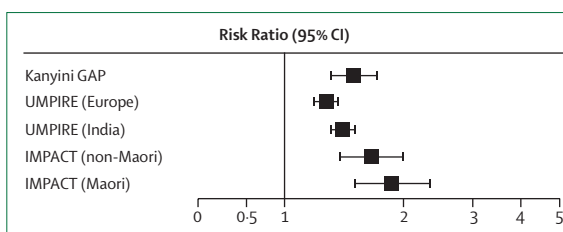


Figure 3: Adherence to medications in various polypill trials
The studies included are the Kanyini GAP (Guidelines Adherence with the Polypill) study,⁴⁶ the UMPIRE study,⁴⁶ and the IMPACT study.⁴⁷

mHealth

mHealth refers to the use of mobile phones to provide patients and health-care workers with support to improve health. Although most studies of mHealth interventions have been done in high-income countries,⁵³ there are emerging reports of potential benefits in LMICs,^{54,55} with other studies in LMICs underway.⁴⁷

Because of the growing ownership of mobile phones worldwide,⁵⁶ there is great potential to use mHealth in LMICs, particularly in regions with poor access to health care. Existing gaps in knowledge include identifying the characteristics of populations that might derive the most benefit from mHealth interventions, when and how mHealth systems can be adapted to patient characteristics and changing circumstances to enable patient-centred messaging, and how best to mobilise social networks to change behaviour.⁵³

In Ghana, Sarfo and colleagues did a two-arm cluster pilot randomised controlled trial of 60 stroke survivors to assess the feasibility and preliminary efficacy of using a bluetooth device with a smartphone for monitoring and reporting blood pressure measurements and medication intake for 3 months.⁵⁷ Control of systolic blood pressure (<140 mm Hg) at 3 months was 66.7% in the intervention group and 46.7% in the control group ($p = 0.12$). The medication possession ratio, a measure of adherence to medications, was larger in the intervention group (0.88 [SD 0.40]) than in the control group (0.64 [SD 0.45], $p = 0.03$).⁵⁷

Task shifting and sharing

Task shifting enables the reorganisation of health tasks to improve access and minimise costs,⁵⁸ and can include activities such as screening, patient education, prescription and delivery of medications, and follow-up to assess adherence to lifestyle modifications and use of medications. Task shifting has been shown to be effective in several settings,⁵⁸ including in hypertension management programmes in high-income countries,⁵⁹ and is an important initiative in containing the rapidly rising prevalence and burden of risk factors for stroke.⁶⁰

Despite promising findings from trials of task shifting to improve the management of hypertension and diabetes,⁶⁰ studies that include process evaluation are still required to better understand the specific aspects of the

interventions that are effective and cost-effective, while assessment of scalability and context will help in the translation of positive findings into routine delivery of health care.

Salt reduction

Reducing salt intake lowers systolic and diastolic blood pressure, a mechanism for preventing stroke.⁶¹ WHO recommends a sodium intake of less than 2 g per day (5 g of salt, or about one teaspoon),⁶² although the evidence for an optimum dose is still somewhat unclear. The strategy for reducing salt intake is contextual. For example, in many high-income countries, processed foods contribute to the majority of salt consumed, particularly from bread and breakfast cereals,⁶³ ready-made meals, and meals consumed away from home,⁶⁴ but in some Asian countries the majority of sodium consumed is added during cooking or at the table, with substantial sources from miso, soy sauce, and salted fish.⁶³

At the 66th World Health Assembly in 2013, one of nine global targets for preventing and controlling non-communicable diseases adopted by WHO member states was a 30% reduction in the mean population intake of salt by 2025;⁶⁵ 84 countries either have strategies in place for achieving this target or are planning strategies.⁶⁶ One approach involves engagement with industry to reformulate foods and reduce the salt content of foods. In the UK, collaboration with industry to achieve voluntary targets for sodium in more than 80 foods resulted in a 9.5% reduction in sodium intake between 2000 and 2008.⁶⁷ Other approaches include consumer education, labelling schemes for packaged foods, introducing standards for the sodium content of foods for consumption in public institutions, and taxation.

Salt substitution, whereby sodium chloride is partially replaced by other salts such as potassium chloride or magnesium sulphate, is also effective in reducing blood pressure. In a 2014 meta-analysis comparing various combinations of salt substitutes with sodium chloride, use of salt substitutes led to significant reductions in both systolic (−4.9 mm Hg, 95% CI −7.3 to −2.5) and diastolic (−1.5 mm Hg, −2.7 to −0.3) blood pressure.⁶⁸ Similar findings were reported in another study from rural China⁶⁹ and other trials are underway.^{70,71}

Other dietary interventions

Adherence to dietary patterns rather than consumption of particular foods or nutrients has been increasingly associated with cardiovascular health, particularly with stroke risk.^{72–75} The use of seasonal, healthy, regional foods and taxes and subsidies on specific foods could be a means to decrease cardiometabolic diseases and stroke at a population level (appendix).^{76–83}

Secondary prevention

Smoking cessation, antihypertensive therapy, glycaemia control, cholesterol reduction with statins, antiplatelet

agents, treatment of atrial fibrillation with oral anti-coagulants, and endarterectomy for symptomatic carotid stenosis are all examples of evidence-based secondary prevention interventions.⁸⁴ The simple combination of the use of aspirin, smoking cessation, antihypertensive drugs, and statins reduces the risk of recurrence of ischaemic events by about 75%.⁸⁴

WHO PEN approach

The package of essential non-communicable disease interventions, developed by WHO, comprises prioritised interventions to strengthen the efficiency and equity of primary health care in low-resource settings.⁸⁵ Technologies, medicines, and risk prediction tools are identified and recommended in panel 2.

World Stroke Organization roadmap

To guide the treatment of acute stroke in different socioeconomic settings, the World Stroke Organization developed the Road Map for Quality Stroke Care.⁸⁷ The document contains a guide to standardise the selection of appropriate therapies in a consistent manner, with suggestions for how to measure the success of therapies to create an environment of continuous quality improvement. The roadmap can be used in the implementation, monitoring, and evaluation of stroke services globally.⁸⁷

According to this roadmap, strategies for secondary stroke prevention that are considered universal include assessment of the presence of risk factors, advice on lifestyle modification strategies, and regular blood pressure assessments. A 2-month intervention involving periodic prescription reminders and health information through personalised text messages improved adherence to medications and appeared to improve diastolic blood pressure ($p=0.06$) in resource-poor settings in Pakistan.⁸⁸

Medications

Drugs such as aspirin, thiazide diuretics,⁸⁹ and oral anticoagulants⁹⁰ are inexpensive yet are not consistently available in most hospitals or health-care centres in LMICs.⁹¹ These medications should be made available at all times to all hospitals and ambulatory care centres and patients should be made aware of the need to carry their medication with them even during travel.

Global strategies for implementation of preventive programmes

WHO's non-communicable diseases campaign

WHO's non-communicable diseases campaign lists several targets, including a 25% RR reduction in the overall mortality from cardiovascular diseases, at least a 10% RR reduction in the harmful use of alcohol, a 10% RR reduction in prevalence of insufficient physical activity, a 30% RR reduction in mean population intake of salt or sodium, and a 30% RR reduction in the prevalence of tobacco use among people aged over 15 years.⁹² WHO's

Global Strategy on Diet, Physical Activity, and Health and its Global Adult Tobacco Survey are examples of national-level strategies being implemented to control stroke and other non-communicable diseases.⁸⁶ The Million Hearts initiative and the Mind Your Risks campaign, led by the US National Institute of Neurological Disorders and Stroke, are programmes to educate millions of people about the dangers of uncontrolled hypertension. Resolve, a multi-stakeholder, non-profit global health organisation, is working towards the vision of saving 100 million lives from cardiovascular diseases, including stroke.

Measuring and monitoring impact of any interventions to prevent stroke

Surveillance through registries

WHO's STEPwise approach to surveillance (STEPS) has been implemented in more than 40 countries, involving different socioeconomic settings.⁹³ The method aims to provide flexible options for assessing the burden of existing chronic diseases and its risk factors, using indicators that vary according to the technical and financial capacity of each country. There are options for surveillance via hospitals alone or in conjunction with community-based surveillance. STEPS provides software for data analysis in addition to the basic data for the programme implementation and tools for measuring the burden of disease and risk factors.⁹³ WHO's MONICA project (multinational monitoring of trends and determinants of cardiovascular disease)⁹⁴ is a registry that is helpful in policy making by providing information to understand the necessity for diverting human resources and finances, etc, to the aspects of a programme that are most in need of resources. The registry's upper age limit of 65 years does somewhat limit its usefulness for stroke in regions where strokes occur in older age groups, such as in high-income countries.

The American Stroke Association's Get With The Guidelines-Stroke registry, the US Paul Coverdell National Acute Stroke Program, Canada's Ontario Stroke Registry, the Chinese National Stroke Registry, India's Ludhiana Stroke Registry,⁹⁵ and STEPS-Stroke (used to collect intra-hospital data)⁹⁶ are a few examples of registries collecting information on hospital processes, care, and outcomes with an aim to improve quality of care, including secondary prevention of stroke.

Recently, there has been a strong effort to strengthen health systems to reach the top public health priorities, rather than focusing on specific diseases. Assessments of health-care systems are important to identify a country's real capacity to provide health care to its citizens, to assess the effectiveness of health programmes, and to identify health systems models that have been successfully implemented in other countries or localities.⁹⁷ Early steps to standardise the metrics of health-care systems that can be used globally include the UN Inter-agency and Expert Group on Millennium Development Goal Indicators.

Panel 2: WHO package of essential non-communicable diseases interventions

Components

Primary prevention

- Smoking cessation
- Regular physical activity at least 30 min per day
- Reduced intake of salt (<5 g per day), adequate intake of fruits and vegetables (at least 400 g per day)
- Availability of aspirin, statins, and antihypertensives for people with 10-year risk of developing cardiovascular disease >30%
- Antihypertensives for people with persistent blood pressure >140/90 mm Hg and 10-year risk of developing cardiovascular disease >20% who are unable to reduce blood pressure through lifestyle modifications

Secondary prevention

- Tobacco cessation, healthy diet, and regular physical activity
- Aspirin, antihypertensives (low dose thiazide, angiotensin-converting enzyme inhibitor), and statins

Tools, equipment, and drugs

- Blood pressure measurement device, measurement tape, weighing machine, glucometer, and blood glucose test strips
- When resources are available, electrocardiograph and lipid profile estimation
- WHO cardiovascular disease risk prediction charts, stroke warning symptoms and signs, evidence based clinical protocols, flow charts with referral criteria, and patient clinical record
- Aspirin, thiazide diuretic, calcium channel blocker (amlodipine), β -blockers (atenolol), angiotensin inhibitors (enalapril), statin (simvastatin), insulin, metformin, glibenclamide, isosorbide dinitrate, glyceryl trinitrate, frusemide

Adapted from Pandian et al.⁸⁶

For more on **Million Hearts** see <https://millionhearts.hhs.gov/>

For more on **Mind Your Risks** see <https://mindyourrisks.nih.gov/>

For more on **Resolve** see <https://www.resolve2osavelives.org>

Guidelines

Implementation of stroke prevention guidelines that are context-appropriate, evidence-based, and expert-recommended is particularly important for LMICs.⁹⁸ However, there is a paucity of hypertension guidelines in these countries.⁹⁹ Of the few hypertension guidelines available, recommendations are not unique to this setting, do not specify the level of evidence, and do not address hypertension treatment in special situations such as chronic kidney disease, coronary heart disease, heart failure, diabetes mellitus, and stroke.⁹⁹ A comparison of important quality characteristics of stroke prevention guidelines that are issued in LMICs and high-income countries revealed that guidelines issued in LMICs were less likely to identify the source of their recommendations, involve high quality systematic reviews, have good dissemination channels, or to consider patients' views

and preferences.¹⁰⁰ Renewed efforts should be made to routinely develop high quality, context-appropriate, pragmatic, practice guidelines for stroke prevention in LMICs that incorporate the perspectives of important stakeholders.⁹⁸

Conclusion

Effective implementation of tobacco control, adequate nutrition, development of healthy cities (with walkable neighbourhoods, access to healthy foods, and public transport), polypill strategies, use of mHealth programmes, along with salt reduction and dietary interventions, can substantially reduce the risk of stroke. These strategies require collaborations between various sectors of health care, government policies, and campaigns for dissemination of evidence-based strategies to enable implementation across low-income and high-income countries.

Contributors

JDP, SLG, MPK, GSS, ROA, BIO, PML, DBCG, and AGT contributed to the literature search. JDP, SLG, ROA, BIO, and AGT contributed to data interpretation. JDP, SLG, MPK, GSS, PML, DBCG and AGT contributed to the editing of the manuscript. SLG, ROA, and DBCG contributed to data collection. GSS approved the final version of the manuscript and BIO and AGT prepared the figures. All authors contributed to the writing of the manuscript.

Declaration of interests

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