

Prevention of stroke: a strategic global imperative

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Abstract | The increasing global stroke burden strongly suggests that currently implemented primary stroke prevention strategies are not sufficiently effective, and new primary prevention strategies with larger effect sizes are needed. Here, we review the latest stroke epidemiology literature, with an emphasis on the recently published Global Burden of Disease 2013 Study estimates; highlight the problems with current primary stroke and cardiovascular disease (CVD) prevention strategies; and outline new developments in primary stroke and CVD prevention. We also suggest key priorities for the future, including comprehensive prevention strategies that target people at all levels of CVD risk; implementation of an integrated approach to promote healthy behaviours and reduce health disparities; capitalizing on information technology to advance prevention approaches and techniques; and incorporation of culturally appropriate education about healthy lifestyles into standard education curricula early in life. Given the already immense and fast-increasing burden of stroke and other major noncommunicable diseases (NCDs), which threatens worldwide sustainability, governments of all countries should develop and implement an emergency action plan addressing the primary prevention of NCDs, possibly including taxation strategies to tackle unhealthy behaviours that increase the risk of stroke and other NCDs.

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doi:10.1038/nrneuro.2016.107
Published online 22 Jul 2016

Stroke remains a major global health problem¹, and its impact is likely to increase in the future due to ongoing demographic changes, including ageing of the population and health transitions observed in developing countries^{2,3}. The Global Burden of Disease (GBD) study provides the most comprehensive assessments of the state of health in the world since 1990 (REF. 4). The most recent assessment of the global, regional and country-specific burden of stroke is the 2013 study (GBD 2013), which provides results for 1990, 2005 and 2013. Data from the GBD 2013 study showed that although age-standardized rates of stroke mortality have decreased worldwide over the past two decades, the absolute number of people affected by stroke worldwide increased significantly between 1990 and 2013 (REF. 3). Virtually no country in the world has seen a reduction in stroke burden in terms of absolute numbers of incident and fatal strokes, stroke survivors and disability-adjusted life years (DALYs). The increasing global stroke burden strongly implies that the current high-risk and population-wide primary stroke prevention strategies are not sufficiently effective, and we need to develop strategies that have larger effect sizes.

In this article, we provide an overview of the most recent literature on stroke epidemiology, with an

emphasis on the main results of the GBD 2013 study concerning ischaemic and haemorrhagic stroke burden in 1990 and 2013. Drawing on these data, we highlight problems with current primary stroke and cardiovascular disease (CVD) prevention strategies, outline several new developments in primary stroke and CVD prevention, and suggest key priorities for action.

The global burden of stroke

The GBD 2013 stroke burden estimates were published in a special free-access issue of *Neuroepidemiology* in October 2015 (REFS 3, 5–11). Globally in 2013, there were almost 25.7 million stroke survivors (71% with ischaemic stroke), 6.5 million deaths from stroke (51% from ischaemic stroke), 113 million DALYs due to stroke (58% due to ischaemic stroke), and 10.3 million new strokes (67% ischaemic)³.

Large geographical variations in age-adjusted incidence, prevalence and mortality were reported for both ischaemic and haemorrhagic stroke (FIGS 1,2). The highest prevalence of ischaemic stroke (1,015–1,184 per 100,000) was observed in developed countries (particularly the USA), and the lowest prevalence (up to 339 per 100,000) was observed in developing countries.

Key points

- Although global stroke incidence and mortality declined from 1990 to 2013, the stroke burden, in terms of absolute numbers of people affected by stroke, continues to increase rapidly throughout the world
- The ever-increasing burden of stroke suggests that current primary prevention strategies for stroke and cardiovascular disease (CVD) are not sufficiently effective
- To improve primary stroke prevention strategies, we need to shift the emphasis from a high-risk approach to a more comprehensive approach targeting people at all levels of CVD risk
- To be cost-effective, primary stroke prevention strategies must be integrated with prevention strategies for other major noncommunicable diseases that share common risk factors with stroke, including CVD, vascular dementia and diabetes
- Resources for the development and implementation of culturally appropriate and population-specific primary stroke prevention strategies could be taken from revenue resulting from taxation on tobacco, salt, sugar and alcohol
- Given the already immense and fast-increasing burden of stroke and other major NCDs, which threatens global sustainability, failure to act on primary prevention of these diseases is unacceptable

The highest mortality from ischaemic stroke (124–174 per 100,000 person-years) was observed in Russia and Kazakhstan, and the lowest (≤ 25 per 100,000 person-years) in Western Europe, North and Central America, Turkmenistan, and Papua New Guinea.

Prevalence of haemorrhagic stroke was highest (232–270 per 100,000) in the USA, and lowest (≤ 78 per 100,000) in Latin America, Africa, the Middle East, France, Eastern Europe, North Asia, and Russia. Mortality from haemorrhagic stroke was highest (159–222 per 100,000 person-years) in Mongolia and Madagascar, and lowest (≤ 32 per 100,000 person-years) in North America, most parts of Western Europe, Russia, Iran, Saudi Arabia, Morocco, Japan, Australia, and New Zealand (FIG. 2). These geographical variations in stroke burden emphasize the need for a region-specific approach to stroke prevention and care.

Over the past few decades, the global stroke burden, in terms of absolute number of people affected by and/or dying from stroke, has increased dramatically^{1,3}, largely due to ageing of the population and population growth in most regions², and no country in the world has experienced a decline in this burden¹². From 1990 to 2013, the absolute number of DALYs due to ischaemic stroke increased significantly, as did deaths from ischaemic and haemorrhagic stroke, and numbers of survivors and incident events for ischaemic and haemorrhagic stroke (TABLE 1) in both men and women^{1,3,9,10,13}. The bulk of the burden of stroke — 75.2% of global deaths from stroke and 81.0% of global stroke-related DALYs — continued to reside in developing countries (FIG. 3). Globally, the proportional contribution of DALYs and deaths due to stroke compared with all diseases increased by 20–25% from 1990 (3.5% and 9.66%, respectively) to 2013 (4.6% and 11.8%, respectively). However, developed and developing countries exhibited divergent trends. For example, DALYs and deaths from stroke, in proportion to all causes, increased significantly in developing countries, but showed no measurable change in developed countries. In 2013, the proportional contribution of ischaemic stroke-related DALYs and deaths was

greatest in developed countries, whereas for haemorrhagic stroke, the contribution was greatest in developing countries (FIG. 4).

The increase in the incidence of haemorrhagic stroke in developing countries may be related to a high rate of undetected and/or poorly controlled arterial hypertension^{14–17}, but could also reflect better detection of stroke in those countries. The rising prevalence of ischaemic and haemorrhagic stroke in developed countries could be related to improvements in acute stroke care, or more-effective secondary prevention and greater identification of minor stroke cases (including wider use of advanced neuroimaging)¹⁸, which is highly dependent on universal access to primary care^{19,20}.

Of additional concern is a significant increase in the numbers of younger adults (aged <65 years) affected by stroke^{1,21,22}. In 2013, 97,800 prevalent cases of childhood (0–19 years of age) ischaemic stroke and 67,621 prevalent cases of childhood haemorrhagic stroke were recorded, reflecting an increase of approximately 35% in the absolute numbers of prevalent childhood strokes since 1990 (REF. 8). Between 1990 and 2013, there were significant increases in the global prevalence of childhood ischaemic stroke, as well as significant decreases in global mortality and DALYs from all strokes in 0–19 year olds. The prevalence of childhood ischaemic and haemorrhagic stroke increased significantly in developed countries over this period, whereas in developing countries, a statistically significant increase was only seen for ischaemic stroke, with some — albeit not statistically significant — increase in haemorrhagic stroke. In 2013, the prevalence of both ischaemic and haemorrhagic stroke in children was significantly higher in developed than in developing countries. However, both mortality and DALYs from all strokes in children were significantly lower in developed than in developing countries. Also, between 1990 and 2013, there were significant increases in prevalent cases, total deaths, and DALYs due to haemorrhagic and ischaemic stroke in younger adults (aged 20–64 years)⁹.

If these trends continue, the burden of stroke will increase even faster²³, and the United Nations (UN) global target²⁴ of a 25% reduction in premature mortality from noncommunicable diseases (NCDs), including stroke, by the year 2025 will not be met. However, for stroke in particular, mortality reduction should not be the only health goal¹², because about three-quarters of stroke survivors remain disabled, and reduced mortality will inevitably lead to a greater number of people with stroke-related disabilities. Focus on acute-phase treatment and rehabilitation alone will not significantly reduce the burden of stroke¹². An urgent need exists to address the regional disparities in stroke burden in children and young adults (taking into account some specific causes of childhood stroke)²⁵, with both global and country-level initiatives targeting prevention early in life, as well as improving access to acute and chronic stroke care⁸.

The GBD 2013 Study also demonstrated important sex-related differences in stroke burden¹⁰. In 2013, males had a higher age-specific (FIG. 5) and age-standardized incidence of ischaemic stroke and haemorrhagic stroke than did females: the age-standardized

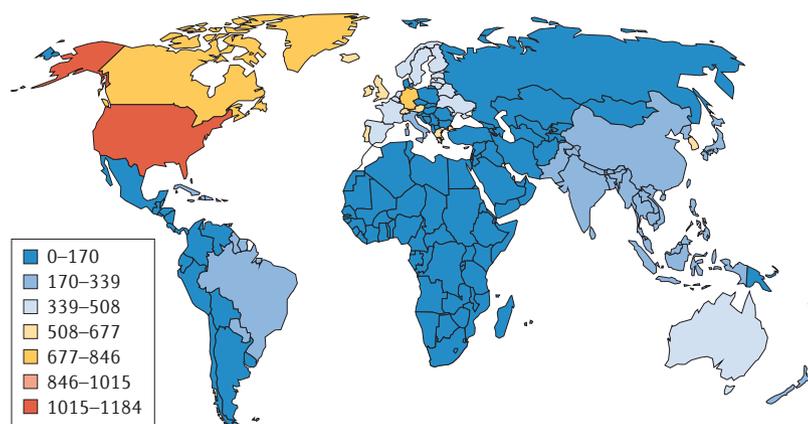
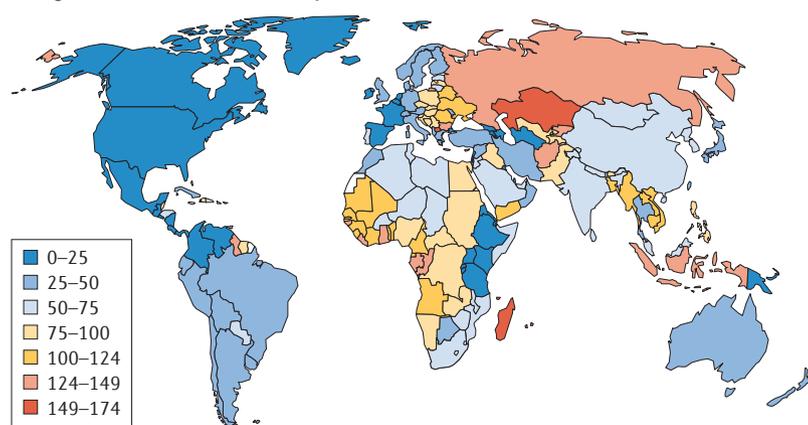
a Age-standardized prevalence (per 100,000) of ischaemic stroke in 2013**b Age-standardized death rate (per 100,000) from ischaemic stroke in 2013**

Figure 1 | Ischaemic stroke prevalence and mortality. The maps show age-standardized prevalence and mortality figures for ischaemic stroke per 100,000 person-years in various regions in 2013. The highest prevalence of ischaemic stroke was observed in developed countries (particularly the USA), and the lowest prevalence was reported in developing countries. The highest mortality from ischaemic stroke was observed in Russia and Kazakhstan, and the lowest was observed in Western Europe, North and Central America, Turkmenistan, and Papua New Guinea. Permission obtained from S. Karger AG, Basel © Feigin, V. L. *et al. Neuroepidemiology* **45**, 161–176 (2015).

incidence of ischaemic stroke was 132.8 per 100,000 person-years in males versus 98.9 per 100,000 person-years in females, and the incidence of haemorrhagic stroke was 64.9 per 100,000 person-years in males versus 45.9 per 100,000 person-years in females. Total age-standardized DALYs for both stroke subtypes were also greater in males, although for DALYs associated with ischaemic stroke, the sex differences did not reach a significant level. Between 1990 and 2013, both ischaemic and haemorrhagic stroke DALYs showed an upward trend for both men and women, which was statistically significant only for ischaemic stroke among men. These findings show a clear need for additional research into factors that potentially contribute to sex-related differences in stroke risk and outcomes. In addition, the evidence for differences in stroke incidence and burden between the sexes is sufficient to warrant well-designed stroke intervention trials,

equally powered for men and women, to examine the effectiveness of primary care, risk factor management strategies, and hospital services¹⁰.

Approaches to stroke prevention

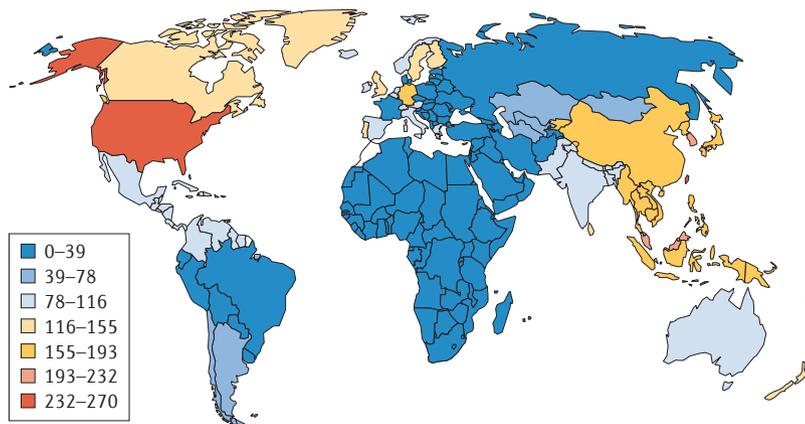
As highlighted by the GBD 2013 data, stroke is currently the third largest contributor to DALYs in both developed and developing countries²⁶. These findings emphasize the importance of stroke as a leading global health problem that requires urgent and sustained attention from governments, health-care policy makers, international agencies, clinicians, public health specialists, and individual citizens.

Prevention of new strokes is the core solution to the problem of the growing stroke burden. Although mainstream preventive strategies should be similar in developed and developing countries, differences in the epidemiology of stroke (including prevalence and relative importance of risk factors), as well as availability of resources for stroke prevention, should be taken into account when setting realistic goals and priorities. For example, given the much greater burden from haemorrhagic stroke in developing countries than in developed countries, a strong emphasis on early detection and management of elevated blood pressure, and on reduction of exposure to air pollution²⁷, should be a priority in developing countries. By contrast, in developed countries, where the burden associated with ischaemic stroke is noticeably higher than in developing countries, it seems reasonable to focus more heavily on reduction of behavioural risks (in particular, diet, physical inactivity and obesity), and management of medical conditions that lead to atherosclerosis. The prevalence of behavioural and other modifiable risk factors for CVD²⁸, including stroke, has reached epidemic proportions worldwide^{29,30}, and evidence indicates that modification of health behaviours is feasible, improves health outcomes, reduces health-care costs³¹, can, arguably, reduce stroke burden²⁷ and an individual's risk of stroke by about 80%^{32,33}, and can reduce stroke incidence by about 50% (REF. 34). There is also evidence that aggressive lowering of systolic blood pressure to <130 mm Hg is a reasonable target for stroke prevention, even in people with borderline hypertension and without diabetes^{35,36}.

Another very important and prevalent risk factor for stroke is atrial fibrillation, the management of which has recently changed dramatically³⁷. As the incidence and prevalence of atrial fibrillation (including paroxysmal atrial fibrillation) is increasing^{38–40}, an urgent need exists for better detection and wider implementation of modern treatment for this condition.

The ever-increasing burden of stroke across the globe, large sex and racial/ethnic disparities, and a trend towards more strokes in younger people in both developed and developing countries, all indicate deficiencies in current stroke prevention strategies. More-efficient stroke prevention strategies are urgently needed to halt and eventually reverse the stroke pandemic³. However, before discussing new approaches to stroke prevention, it is important to untangle the deficiencies of the currently used strategies.

a Age-standardized prevalence (per 100,000) of haemorrhagic stroke in 2013



b Age-standardized death rate (per 100,000) from haemorrhagic stroke in 2013

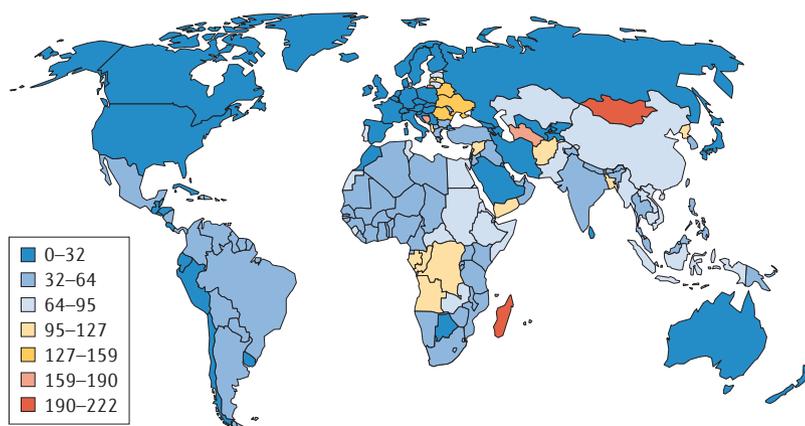


Figure 2 | Haemorrhagic stroke prevalence and mortality. The maps show age-standardized prevalence and mortality figures for haemorrhagic stroke per 100,000 person-years in various regions in 2013. The prevalence of haemorrhagic stroke was highest in the USA, and lowest in Latin America, Africa, the Middle East, France, Eastern Europe, North Asia, and Russia. Mortality from haemorrhagic stroke was highest in Mongolia and Madagascar, and lowest in North America, most parts of Western Europe, Russia, Iran, Saudi Arabia, Morocco, Japan, Australia, and New Zealand. Permission obtained from S. Karger AG, Basel © Feigin, V. L. et al. *Neuroepidemiology* 45, 161-176 (2015).

Population-wide strategies. The current WHO guidelines⁴¹ advocate a combination of population-wide and high-risk approaches to prevent stroke and other types of CVD. Population-wide strategies are essential, because even small changes in the distribution of risk factors could lead to major reductions in stroke and CVD incidence in the population^{42,43} (FIG. 6).

The population-wide prevention strategy was suggested by Sir Geoffrey Rose in 1985 as the most effective approach to primary CVD prevention⁴³. As this strategy targets several behavioural and lifestyle risk factors — including tobacco use, unhealthy diet, physical inactivity, overweight, and the harmful use of alcohol — that are common for a range of major NCDs, this strategy should positively influence the risk not only of stroke, but also of NCDs such as heart disease, diabetes, cancer, dementia and pulmonary heart disease.

Over the past 15–20 years, the population-wide approach has been included in all major CVD prevention guidelines^{33,44}, often in combination with a high-risk approach, and several anecdotal reports support its effectiveness in selected populations^{45–47}. Nevertheless, no country in the world has yet implemented this strategy in full at the national level, possibly owing to costs — for example, of increasing the availability of physical activity facilities and healthy food outlets — and the need for policy and legislative changes that are often not supported by major industries, such as salt reduction in processed food, and reduction of exposure to smoking, alcohol and fast food²³.

An additional important benefit of population-wide prevention approaches that target the entire population, rather than just those at high risk, is that promoting maintenance of health might be easier and more effective than reversing existing damage. Changes in health practices are likely to have the greatest impact early in life, before subclinical risk factors have emerged.

High-risk strategies. Worldwide, intensive clinical care for high-risk individuals remains the dominant paradigm for prevention of stroke⁴⁸. However, although management strategies for primary stroke prevention in individuals at high risk of CVD are well established³³, they are underutilized^{33,49–51}, and existing methods of primary stroke prevention are not sufficiently effective^{52–54}. Health-care systems have been largely unsuccessful in providing relevant meaningful information to assist people in adhering to recommended lifestyle changes and medications^{33,52,53,55–57}. Uptake of primary prevention recommendations is particularly low in people with a moderately increased risk of stroke who would benefit from lifestyle modifications^{52,57,58}, possibly owing partly to a lack of effective communication between health professionals and patients and their families^{52,59–61}.

The high-risk prevention strategy requires calculation of absolute risk of CVD over the next 5 or 10 years with the aim of identifying people at high risk of development of acute CVD. High risk is usually defined as a risk of $\geq 15\%$ over the next 5 years or $\geq 30\%$ over the next 10 years, or having an established CVD, for example, stroke, ischaemic heart disease, transient ischaemic attack (TIA), or peripheral artery disease⁶².

Although assessment of people for absolute stroke or CVD risk is important for matching the intensity of prevention efforts with the individual's absolute risk⁶³, and for monitoring success or failure of primary stroke or CVD prevention, the high-risk approach has several major drawbacks. A prevention strategy that is aimed primarily at high-risk individuals fails to engage the majority of the population in active prevention^{64,65}, and it also diminishes personal motivation to control risk factors by people who are at low or moderate risk of CVD events. Other limitations of this strategy include costs associated with laboratory tests and doctors' visits to determine the risk, and lack of population-specific algorithms for stroke and CVD prevention²³. Evidence suggests that even effective population-wide use of high-risk prevention strategies with aggressive pharmacological

Table 1 | Global stroke burden in 1990 and 2013

Metric	Ischaemic stroke			Haemorrhagic stroke		
	1990 (millions)	2013 (millions)	Increase (%)	1990 (millions)	2013 (millions)	Increase (%)
Disability-adjusted life years	34.2	47.4	38.6	56.0	65.5	17.0
Deaths	2.2	3.3	50.0	2.4	3.2	33.3
Incident cases	4.3	6.9	60.5	1.9	3.4	78.9
Prevalent cases	10.0	18.3	83.0	3.9	7.4	89.7

Data from Feigin *et al.* (2015)³.

treatment in individuals with a 10-year Framingham event risk of $\geq 30\%$ (6% of the population) would have reduced the incidence of major CVD by, at most, 11%, and if high-risk strategies are to have a major impact on CVD in the population, they need to be more widely used than previously envisaged⁴⁸. In addition, the use of high-risk prevention strategies is limited by access to medical professionals⁶⁶ and, even when care is available, adherence to recommended medications and lifestyle modifications⁶⁷ is often poor for multiple reasons⁶⁸, including limited health literacy⁶⁹ and comorbidities⁷⁰.

Screening for CVD risk is generally accepted as a reliable guide for making clinical decisions on the intensity and effectiveness of preventive interventions^{41,71}, and screening of the population for CVD risk in order to provide intensive medical care to high-risk individuals continues to be considered an important health target by many governments⁷². However, compelling evidence from 15 large randomized controlled trials (totalling over 240,000 patients)^{73,74}, indicates that screening for high CVD risk, even in combination with counselling⁷⁴, is not effective for reducing CVD incidence and mortality.

The lack of effectiveness of population screening for high CVD risk, and ethical concerns about promotion of screening without linkage to diagnosis and management, has led some governments to explore additional ways to improve CVD prevention. For example, the use of CVD prediction algorithms, in combination with incentivization of clinicians for effective CVD prevention, is being trialled in the USA^{75–77}, and the most recent evidence suggests that incentivization of both clinicians and patients works⁷⁸. The shared financial incentives that were shown to be effective for reducing LDL cholesterol levels — US\$512 per patient for physicians and \$355 for each patient enrolled in the trial⁷⁸ — may not be feasible in less-affluent societies. However, the finding that motivation of both physicians and their patients is important for effective CVD prevention should not be underestimated, and more-affordable incentives can and should be trialled in other populations.

A combined approach. Primary prevention of stroke and other major NCDs is regarded by the UN as the most cost-effective strategy to reduce burden from these diseases⁷⁹. For example, one study showed that by reducing salt intake by 15% and implementing four key WHO elements of reduction in tobacco use — taxation, enforcement of smoke-free workplaces, packaging and

labelling requirements, and awareness campaigns — 13.8 million deaths over 10 years could be averted at a cost of less than \$0.4 per person per year in low-income and lower middle-income countries, and only \$0.50–1.00 per person per year in upper middle-income countries⁸⁰.

In our view, it is essential for stroke prevention strategies aimed at specific high-risk populations (for example, people with stroke or TIA, atrial fibrillation, or sickle cell disease) to be accompanied by population-wide prevention strategies targeted at behavioural, lifestyle and environmental risks, in which responsibilities are shared between the health sector, non-governmental organizations and government bodies. Certain governmental bodies have the power to inform or influence lifestyle, socioeconomic and environmental factors (including tobacco control, healthy nutrition, cycle lanes, availability of fruits and vegetables at corner stores, and improvements in air quality), as well as to provide adequate health services to ensure universal implementation of preventive strategies. In turn, the health system has the responsibility to identify and manage risk factors at the individual level^{81,82}. These integrative, cross-sectoral approaches, combined with behavioural modifications (including stroke preparedness and lifestyle modifications) and other strategies, have recently been identified as the key strategies for stroke and CVD prevention^{57,83,84}, but some

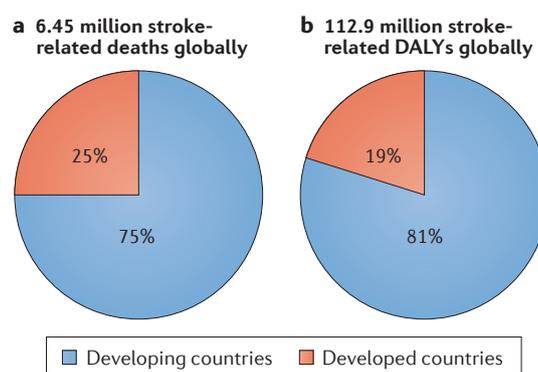


Figure 3 | Stroke-related deaths and DALYs by country development status. The charts show absolute numbers and proportions of stroke-related deaths and disability-adjusted life years (DALYs) by country development status in 2013. These figures illustrate that the bulk of the global burden of stroke continues to reside in developing countries, despite a comparatively low prevalence of stroke in these countries.

difficult questions remain. Specifically, what could make stroke prevention work, and how can population-wide and high-risk prevention strategies best be combined? In the section that follows, we suggest four major strategies to improve primary stroke prevention (BOX 1).

Improving primary stroke prevention

Shifting the emphasis. We propose that the emphasis in primary stroke prevention should be shifted from a high absolute risk approach to a more comprehensive approach that includes primary stroke prevention strategies in people at all levels of CVD risk. In addition to more-aggressive control of elevated blood pressure and other metabolic and physiological risk factors (including atrial fibrillation), primary stroke prevention needs to focus on behavioural and lifestyle risk factors (including tobacco use, unhealthy diet, physical inactivity, and the harmful use of alcohol), thereby allowing an integrative approach that also targets other major NCDs, such as heart disease, diabetes, cancer, dementia and pulmonary heart disease. This cluster of diseases and risk factors was prioritized by WHO in its Global Action Plan on NCDs⁸⁵, and was also included in the 2011 UN NCD Declaration, and the UN Post-2015 Sustainable Development Goals¹².

When using data from predictive algorithms to communicate stroke and CVD risk to patients, health professionals should avoid categorizing people into low, moderate and high absolute risk, as this this approach reduces the motivation of people with low and moderate risk of CVD to reduce their risk and engage in primary prevention programmes²³. To illustrate the increased risk for the benefit of people with low absolute CVD risk, use of relative risk charts, lifetime risk^{23,86,87}, and various risk visualization techniques⁸⁷⁻⁸⁹ has been recommended.

Such an approach should empower people with a 10-year absolute CVD risk of <30% to control their modifiable risk factors, improve CVD health, and reduce their risk of stroke and CVD to as low a level as possible. In addition to healthy lifestyle modifications⁹⁰ and better adherence to recommended medications^{91,92}, multidrug regimens — for example, polypills⁹³ — could enable cost-effective prevention of stroke in all developing regions, potentially halving the risk of death from CVD and increasing life expectancy⁹⁴.

An integrated approach. An integrated approach would incorporate community–clinical linkages that coordinate clinical strategies for high-risk individuals and community-based strategies to promote healthy behaviours and reduce health disparities^{95,96}. Coordinated interventions allow community-wide prevention and management approaches that link efforts to improve health across the care continuum, and across settings and strategies. Community–clinical linkages help ensure that people who already have or are at high risk of chronic diseases have access to community resources and support to prevent, delay or manage these conditions⁹⁷. This support includes interventions such as clinician referral, community delivery and payment coverage for effective programmes that increase the likelihood that people with heart disease, diabetes or prediabetes will be able to ‘follow the doctor’s orders’ and take charge of their health⁹⁷. Examples include clinical strategies to promote individual smoking cessation along with smoke-free laws that reduce secondary exposure, or the use of community health workers and community pharmacists who can extend the work of the clinical provider into the community and the broader population⁹⁸.

In view of the limited resources available for stroke and CVD prevention, even in developed countries, a logical approach would be to place the emphasis on effective population-wide interventions to control or reduce exposure to leading risk factors in the region. For example, population-wide efforts to reduce salt intake and smoking through multiple economic and educational policies and programmes have been suggested as cost-effective primary stroke and CVD prevention strategies in developing countries⁹⁹⁻¹⁰³. With the UN 2011 Declaration on NCDs¹², all UN-member governments have the mandate, power and responsibility to undertake actions to reduce the burden from NCDs, including stroke. The practical question is, how should resources be gathered and deployed to enable these actions? We believe that revenue from tobacco and salt taxation, as well as taxation on sugar and alcohol — reduced consumption of which has been shown to be beneficial for cardiovascular and overall health at the population level^{104,105} — can and should be used to fund primary prevention strategies and primary prevention research for stroke and other major NCDs. Such uses of the tax revenue would also be important to ensure public acceptability of these taxes¹⁰⁶. Compelling evidence indicates that tobacco¹⁰⁷⁻¹⁰⁹, salt^{80,106}, sugar¹¹⁰⁻¹¹² and alcohol¹¹³⁻¹¹⁷ taxation is a valuable strategy to improve

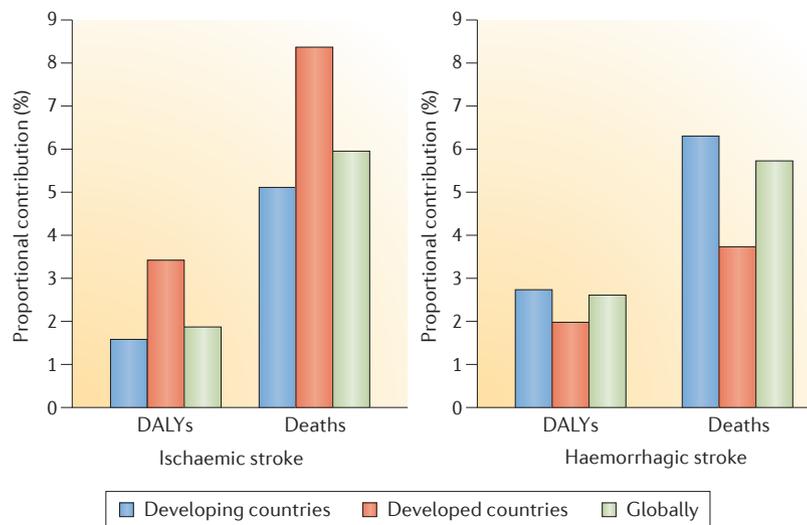


Figure 4 | **Burden of stroke in proportion to all health conditions.** The graphs show proportional (percentage) contribution of ischaemic and haemorrhagic stroke burden to the burden of all health conditions by country development status in 2013. For ischaemic stroke, the proportional contribution of disability-adjusted life years (DALYs) and deaths was greatest in developed countries, whereas for haemorrhagic stroke, the contribution was greatest in developing countries.

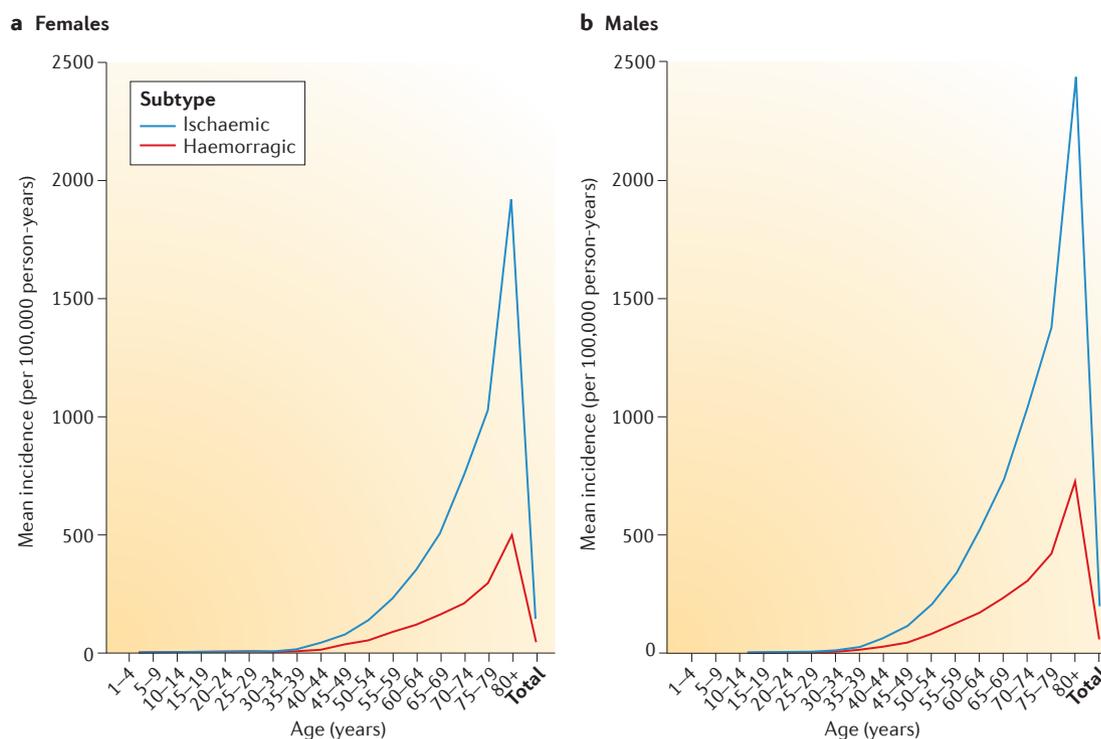


Figure 5 | **Sex-related differences in stroke burden.** The graphs show the incidence of ischaemic and haemorrhagic stroke in females and males by 5-year age bands in 2013 (REF. 10). Males had a higher age-specific incidence of ischaemic and haemorrhagic stroke than did females, but there were no overall age-standardized sex differences in the incidence of either stroke type.

health, especially when combined with other preventive interventions in the population, while generating considerable revenue for governments^{111,118–120}.

Given the already immense and fast-increasing global burden of stroke and other major NCDs, which threatens the sustainability of our whole society, failure to instigate effective strategies for primary prevention of these diseases is not acceptable. Governments should develop and implement emergency action plans to address the primary prevention of NCDs. It is also important to work on the broader implementation of proven primary stroke and NCD prevention strategies in many developed countries.

Using information technology. The impact of stroke and other NCDs with similar risk factors, such as ischaemic heart disease, dementia and type 2 diabetes mellitus, is huge and continues to increase^{121–123}. The burden of NCDs is likely to burgeon given the ageing of the world's population and the epidemiological transitions currently being observed in low-income to middle-income countries¹²⁴. However, awareness about these NCDs and their risk factors is low, particularly in developing countries. These factors, coupled with underutilization of strategies for primary prevention of NCDs at the individual level and a lack of accurate data on the frequency and relevance of risk factors in different countries and populations, have been implicated in the ever-increasing worldwide burden of NCDs.

Recent advances in mobile (smartphone) technologies and their worldwide use (~1.7 billion users) offer unique opportunities to utilize these technologies to

improve health awareness and research capabilities. Empowerment of people to self-manage their risk factors through mobile health apps is one potential application of these technologies, and might be particularly appealing to less-affluent populations and communities with limited access to health services (for example, rural communities). A number of stroke and other NCD apps are currently available in App Store and Google Play, and promising results are emerging from clinical trials of several smartphone-based technologies and apps designed to aid the management of particular medical conditions and risk factors, including smoking, depression, weight problems and asthma^{125–129}.

Primary stroke prevention should capitalize on information technology to advance prevention approaches and techniques. Electronic health information can be useful to support patients, providers and population health, for example, through improved public health surveillance activities¹³⁰. Importantly, accumulating evidence demonstrates the feasibility and effectiveness of mobile technologies for promoting healthy lifestyles^{131–137} and improving some medical conditions that predispose to stroke^{138–143}. Supported by WHO¹⁴⁴, these technologies are evolving fast¹⁴⁵, and have shown unprecedented uptake among lay consumers and professionals alike¹⁴⁶. Widely accessible, affordable and validated technological advances¹⁴⁵, such as the Stroke Riskometer app^{23,147}, can provide targeted advice to enable a person to recognize and control their own risk level and risk factors, as well as educating about the warning signs of stroke, and measuring the effectiveness of primary prevention of NCDs.

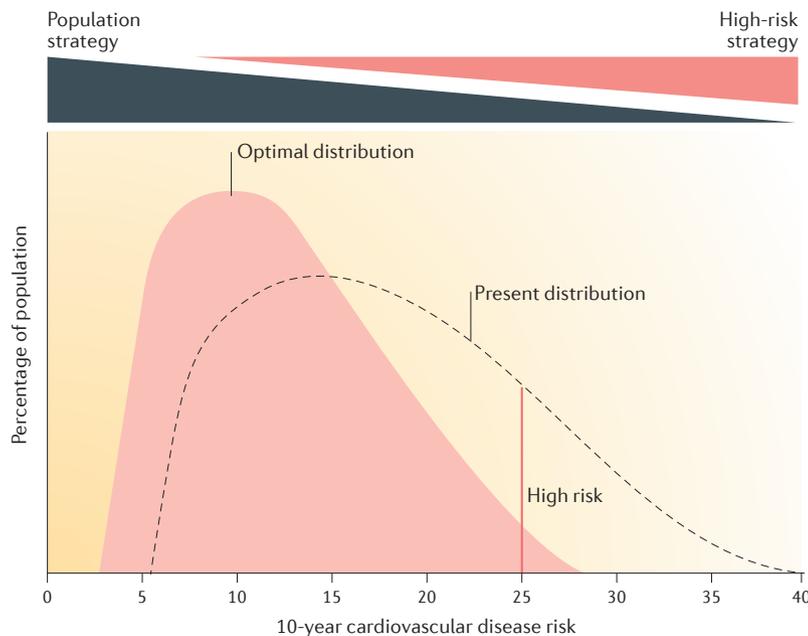


Figure 6 | **Combining population-wide and high-risk strategies.** Optimal shift in the distribution of cardiovascular disease risk through a combination of population-wide and high-risk prevention strategies. Reprinted from World Health Organization. Cardiovascular disease prevention and control. Translating evidence into action. http://apps.who.int/iris/bitstream/10665/43235/1/9241593253_eng.pdf © 2015 (REF. 178).

Such apps represent an important approach for stroke prevention that should be incorporated into the health system and used by both health professionals and lay people. These mobile technologies are particularly useful for developing countries, where availability and affordability of health care and access to health professionals are limited. Self-care programmes are seen by WHO¹⁴⁸ as a vital form of prevention in individuals at high risk, and for improving outcomes in people with NCDs.

Culturally appropriate health education. Given the substantial disparities in the risk and burden of stroke among various racial and ethnic groups^{149–153} and the fact that many lifestyle habits are set early in life, culturally appropriate education about healthy lifestyles should be incorporated into standard education curricula and started early in life, with reinforcement across the lifespan. Evidence suggests that school-based stroke education is effective in middle-school children¹⁵⁴, and trained children and community leaders might be valuable healthy lifestyle educators for other children.

Stroke knowledge is a sociocultural construct that can limit the utility of universal primary prevention strategies for at-risk groups^{8–10}. Therefore, it is essential to understand the views, values, norms and beliefs of peoples of various races and ethnicities who are at risk of stroke, so as to determine what approach is most likely to work for them in terms of understanding stroke and its associated risk factors, and using this information to modify their daily practices. Evidence suggests that even if an intervention is effective, adherence to its recommendations remains poor unless it is meaningful, acceptable and takes into account the factors that make

up the patients' health-care environment¹⁵⁵. In addition, research has shown that people's beliefs are important predictors of the extent to which they will engage in behaviours to reduce the risk of secondary stroke⁶⁸. Stroke prevention strategies must take these factors into account to have optimal impact. This information might also be used to inform culturally appropriate preventive strategies for other major NCDs that share common risk factors with stroke, such as CVD, dementia and diabetes.

Linguistic, cultural and subcultural differences between people of different races and ethnicities, in relation to social interactions, family values, and sex and gender roles, should be taken into consideration when developing culturally competent health education programmes¹⁵⁶. For example, healthy diet recommendations that are successful for stroke and CVD prevention in people of European origin may not be successful for people from the Asia-Pacific region, because their food habits and traditions are very different. Racial and ethnic differences in the relative importance of various determinants of stroke occurrence are also evident¹⁵⁰, and should be taken into account when developing culturally specific health education programmes. Generic guidelines for making a health education programme more culturally appropriate have been suggested¹⁵⁶. Development of consensus statements and national stroke prevention guidelines by recognized experts from the region to address local and cultural issues on the basis of the best available evidence, along with effective strategies to improve stroke awareness (including campaigns to remove stigma associated with stroke), should be encouraged⁹⁹.

Maternal health and lifestyle, normal birth weight, and adequate nutrition from the first days of life are important determinants of health, including risk of stroke and other major NCDs, later in life. Healthy lifestyle habits, adequate physical activity and maintenance of a healthy weight should be established at a young age¹⁵⁷ and reinforced throughout the lifespan (for healthy diet habits, probably during the first year of life)¹⁵⁸, and can be successfully incorporated in preschool, school, day-care and other interventions in early-life settings¹⁵⁹.

Recent studies in other countries have shown that knowledge of stroke risk factors and warning signs is deficient in older adults (aged ≥ 65 years)^{160,161}, minority ethnic groups^{161–164}, people with low levels of education¹⁶¹, and rural dwellers¹⁶⁵. Consistent, culturally sensitive and motivational stroke education campaigns throughout the year (not only at national or global stroke awareness days) should be prioritized. Such campaigns are unlikely to be funded by industry, but the public sector has the opportunity to promote stroke awareness alongside other educational campaigns. Compelling evidence indicates that increasing population-specific and country-specific knowledge about stroke warning signs and risk factors can reduce stroke burden in the population^{83,166–170}.

Future research directions

More good-quality research is urgently needed on stroke risk factors and prevention in various countries and populations, including research to untangle

Box 1 | Key priorities for effective primary stroke prevention**Lifestyle factors**

- Shift the emphasis in primary stroke prevention to a more comprehensive approach that includes primary stroke prevention strategies targeting people at all levels cardiovascular disease (CVD) risk
- Focus on behavioural and lifestyle risk factors, including tobacco use, unhealthy diet, physical inactivity, and harmful use of alcohol
- Partnering across sectors
- Health sector, non-governmental organizations and government bodies to share responsibility for the development and implementation of population-wide and high-risk prevention strategies to control stroke and other noncommunicable diseases (NCDs)
- Implement an integrated approach that incorporates community–clinical linkages to coordinate clinical strategies for high-risk individuals with community-based strategies that promote healthy behaviours and reduce health disparities
- Incentivize health professionals and patients for effective prevention of stroke and other NCDs
- Electronic health information technology
- Incorporate widely accessible, affordable and validated mobile technologies for primary prevention into health systems for use by health professionals and lay people
- Reframe risk categories. In communicating absolute stroke and CVD risk, categorization of people into low, moderate and high risk should be abandoned. People with 10-year absolute CVD risk of <30% should be motivated and taught by their health professional to control their modifiable risk factors and reduce their risk of to as low a level as possible

Early-life interventions

- Implement culturally appropriate education about healthy lifestyles in standard education curricula early in life, with reinforcement across the lifespan

the causes of the increasing burden of stroke in developing countries, and the causes of changes in trends and projections of stroke burden in men and women of different ages, races and ethnicities. In particular, we need research to investigate interventions for the ageing population, and strategies for implementation that can remain cost-effective in a growing population. Although mortality from stroke has declined substantially in developed countries, the use of proven strategies for stroke and CVD prevention, even in wealthy countries, is far from optimal.

Stroke and CVD rates could be further reduced in future not only with more-widespread implementation of proven strategies, but also with greatly improved understanding of regional and ethnic variations in the causes of stroke²⁸. Population-wide strategies for primary prevention of NCDs have proved to be feasible and effective^{45–47}, but more research is warranted on the most culturally appropriate and cost-effective ways of implementing these strategies, including their combination with high-risk strategies, self-management and knowledge transfer. Digital health research and randomized controlled trials that are sufficiently powered to address differences related to sex, race, ethnicity and age are required to enable the development of behavioural and educational interventions to specifically prevent stroke. However, primary prevention research is expensive, commonly not supported by industry, and often regarded as ‘non-sexy’ by research funding agencies, and there is an obvious lack of funding for such

research, even in affluent countries¹⁷¹. Therefore, the question of how to fund and manage primary prevention research remains.

For the prevention of cardiovascular disease, including stroke, the World Heart Federation recommends conducting “large population studies in different regions of the world as the types and patterns of diet, activity, alcohol consumption, and tobacco use vary by region” (REF. 84). This recommendation recognizes the importance of region-specific and country-specific data on stroke risk and causative factors. In 2012, the Stroke Progress Review Group of the NIH National Institute of Neurological Disorders and Stroke recommended three top priorities for future stroke epidemiological research: first, improving the understanding of the role of race and ethnicity in stroke disparities; second, evaluation of the usefulness of health information technology as a tool for epidemiology research; and third, translating knowledge from epidemiological studies into improved health¹⁷². Cultural contexts are essential to capture contributory factors to stroke risk, such as language barriers, and access to health care and education. A study that compared CVD events in low-income and high-income countries, for example, showed that although the prevalence of conventional risk factors was relatively low in the low-income countries, better control of these factors and more-frequent use of proven therapies seemed to have mitigated the burden of stroke in the high-income countries¹⁷³. Exploration of promising indigenous medicines (including supplements) that carry claims of CVD preventive properties might also be beneficial.

Given the limited resources for conducting national and international epidemiological studies, especially in developing countries, the use of mobile technologies to explore new strategies seems appropriate. Recent advances in smartphone technologies, including high processing power, increased storage capacity, constant Internet connection, personalized notification methods, growing worldwide uptake, and proximity to users, offer unique opportunities to utilize these technologies to improve health and enhance research capabilities²³. Numerous smartphone apps for stroke and other NCDs are currently available in Apple Store and Google Play. In addition, as highlighted above, several smartphone-based technologies and apps are being used with some success in clinical trials for the management of specific medical conditions and risk factors^{125–129}. In recognition of the importance of digital technologies for health, in 2013 the UN Economic and Social Council, the International Telecommunication Union and WHO launched a new mHealth initiative to improve NCD prevention, treatment and policy enforcement¹⁷⁴. RIBURST (Reducing the International Burden of Stroke Using Mobile Technology Study) is a good example of an affordable, large-scale, smartphone-based worldwide study on stroke risk factors²³.

New discoveries in stroke risk factors can be expected when the interplay between genetic, environmental, behavioural, and medical and physiological determinants is considered, with the involvement of a multidisciplinary team of experts, including clinicians, epidemiologists, geneticists, biostatisticians,

mathematicians and computer scientists. In its top three priorities for future directions in stroke research, the 2012 Stroke Progress Review Group report makes the following recommendation: “focus future biomarker development on markers of small vessel disease severity and location, integrating these into multimodal studies of existing imaging markers, biochemical and genetic risks, and epidemiological factors (including variations related to racial/ethnic/demographic group), aimed ultimately at unravelling the precise connections between vascular pathology, neurodegenerative pathology, and neurological impairment”¹⁷². Further research is also required to advance the precision medicine approach for stroke prevention that was recently introduced in the USA¹⁷⁵.

Conclusions

Stroke has been identified as one of the prioritized NCDs by WHO and the UN and, as a consequence, primary stroke prevention is entering a new era in which these organizations must work together with government bodies, medical systems and non-governmental organizations. Our hope is that the promotion and endorsement of new, more-effective approaches for the prevention of stroke and CVD, in combination with previously endorsed high-risk and population-wide prevention strategies, will change current practice worldwide, thereby saving millions of lives. By complementing cost-effective individual health-care interventions with population-wide prevention strategies, we could make a substantial impact on the global NCD epidemic^{148,176}.

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Competing interests statement

V.L.F. declares that Stroke Riskometer app is copyrighted by the Auckland University of Technology, and funds resulting from the sale of the professional version of this app will be used for further research and education for stroke prevention. The other authors declare no competing interests.

Acknowledgements

V.L.F. was partly funded by the Health Council of New Zealand, the Brain Research New Zealand Centre of Research Excellence, the “Ageing Well” Programme of the National Science Challenge, and the Ministry of Business, Innovation and Employment of New Zealand. G.A.R. has grant funding from the US National Institute on Ageing and Medtronic Philanthropy. We would like to thank Barbara Bowman at the Centers for Disease Control and Prevention for her valuable comments on early version of the manuscript. The views expressed in this article are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; NIH; Centers for Disease Control and Prevention; or the U.S. Department of Health and Human Services.

Author contributions

All authors researched data for the article, made substantial contributions to discussions of the content and reviewed and/or edited the manuscript before submission. V.L.F. wrote the article.