

Circulation Research Compendium on Stroke

Introduction to the Stroke Compendium

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Global Burden of Stroke

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Abstract: On the basis of the GBD (Global Burden of Disease) 2013 Study, this article provides an overview of the global, regional, and country-specific burden of stroke by sex and age groups, including trends in stroke burden from 1990 to 2013, and outlines recommended measures to reduce stroke burden. It shows that although stroke incidence, prevalence, mortality, and disability-adjusted life-years rates tend to decline from 1990 to 2013, the overall stroke burden in terms of absolute number of people affected by, or who remained disabled from, stroke has increased across the globe in both men and women of all ages. This provides a strong argument that “business as usual” for primary stroke prevention is not sufficiently effective. Although prevention of stroke is a complex medical and political issue, there is strong evidence that substantial prevention of stroke is feasible in practice. The need to scale-up the primary prevention actions is urgent. (*Circ Res.* 2017;120:439-448. DOI: 10.1161/CIRCRESAHA.116.308413.)

Key Words: burden ■ epidemiology ■ GBD ■ prevention ■ stroke

Evidence-based approaches to organization and planning of stroke care and services require accurate ongoing data on stroke incidence, prevalence, and outcomes. The best sources of such data are population-based studies that meet “gold-standard” criteria and are continuously repeated over time,¹ as stroke epidemiology is changing rapidly.² However, such studies are expensive and require expertise for their proper design and execution. That is why no such studies have been done in most countries, especially in the developing countries and over a long period

of time. From the public health perspective, there is also a need to monitor stroke burden on a global scale and compare burden between different countries and regions over time, including trends and projections relative to other major diseases. To address these issues and fill the gaps in disease burden estimates across all countries, the GBD (Global Burden of Disease) Study was set up in 1992 within the Institute for Health Metrics and Evaluation of the University of Washington.³ During the period of time from 1990 to present, the GBD Study has developed (and

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Nonstandard Abbreviations and Acronyms

DALYs	disability-adjusted life-years
GBD	Global Burden of Disease
HS	hemorrhagic stroke
IS	ischemic stroke
NCDs	noncommunicable diseases
UI	uncertainty intervals
UN	United Nations

continuously updated) a large database and advanced methodologies for modeling the burden of a wide range of diseases and their risk factors in 188 countries.^{4–6} This article summarizes GBD 2013 Study findings on stroke burden recently published in the special open access issue of the journal *Neuroepidemiology*⁷ and outlines recommended measures to reduce stroke burden. In these publications, stroke burden is reported in terms of incidence of first-ever stroke (ischemic stroke [IS] and hemorrhagic stroke [HS] separately, and total stroke), prevalence, mortality, and disability-adjusted life-years (DALYs) in children (0–19 years of age),⁸ young to middle-aged adults (20–64 years of age),⁹ and overall for all ages combined² and by sex¹⁰ from 1990 to 2013. All burden estimates were reported with corresponding 95% uncertainty intervals (UI). In lay terms, DALYs mean the number of years lost because of disability. The diagnostic criteria for stroke used in the GBD analyses are based on the World Health Organization (WHO) definition of stroke.¹¹ Details on the methodology of the GBD stroke burden estimates, including diagnostic criteria and data sources, have been published elsewhere.^{12,13}

Overall Overview of the Global, Regional, and Country-Specific Burden of Stroke, Including Trends in Stroke Burden From 1990 to 2013

In 2013, stroke was the second most common cause of deaths (11.8% of all deaths [95% UI, 10.9–13.0%]) worldwide, after ischemic heart disease (14.8% of all deaths [95% UI, 13.4–15.8%]), and the third most common cause of disability (4.5% of DALYs from all cause [95% UI, 4.1–5.2%]) after ischemic heart disease (6.1% [95% UI, 5.5–6.8%]). Overall, the GBD 2013 stroke burden estimates confirmed previous observations about the significant increase in stroke burden in the world over the last two and half decades,¹⁴ especially in developing countries,^{14,15} and substantial geographical variations in stroke burden.^{14,15} As shown in Figure 1, the highest stroke DALYs and mortality rates in 2013 were observed in Russia and Eastern European countries.

Although stroke mortality and DALYs rates have declined from 142/100,000 person-years (95% UI, 129–154) and 2431/100,000 person-years (95% UI, 2224–2631), respectively, in 1990 to 110/100,000 person-years (95% UI, 102–122) and 1807 person-years (95% UI, 1667–1992), in 2013 the absolute number of people who died from stroke, remained disabled from stroke (as measured by DALYs), affected by stroke (as measured by incidence of new strokes), or survived stroke has increased statistically significant (1.4- to 1.8-folds for IS and 1.2- to 1.9-folds for HS). Globally, in 2013 there

were almost 25.7 million stroke survivors (71% with IS), 6.5 million deaths from stroke (51% died from IS), 113 million DALYs due to stroke (58% due to IS), and 10.3 million new strokes (67% IS). Improved stroke care, aging, and growth of the population combined with the increased prevalence of many modifiable stroke risk factors¹⁶ are likely to be the main drivers in the increased number of stroke survivors and people affected by stroke.

Proportional (%) contribution of DALYs from stroke to DALYs from all other causes in 2013 (Figure 2) varied between different countries but was largest in developing countries, especially Russia, Eastern European countries, and East Asian countries, ranging from 11.6% to 12.7% in North Korea, Macedonia, Bulgaria, and Georgia to 8.4% to 9.7% in China and Indonesia. As also shown in Figure 2, proportional contribution of stroke-related DALYs compared with 10 other leading causes of DALYs in 2013 was the second highest and not statistically significantly different from ischemic heart disease, especially in developed countries.

The proportional contribution of stroke-related DALYs and deaths due to stroke compared with all diseases also increased from 1990 (3.5% [95% UI, 3.1–4.0] and 9.7% [95% UI, 8.5–10.7], respectively) to 2013 (4.6% [95% UI, 4.0–5.3] and 11.8% [95% UI, 10.5–13.3], respectively), but there was a diverging trend in developed and developing countries with a significant increase in DALYs and deaths in developing countries (from 0.9 [95% UI, 0.8–1.0] and 2.1 [95% UI, 1.9–2.4] for DALYs and 3.0 [95% UI, 2.6–3.4] and 5.2 [95% UI, 4.6–5.8] for deaths in 1990 to 1.7 [95% UI, 1.3–1.9], 2.8 [95% UI, 2.5–3.3] for DALYs and 5.2 [95% UI, 4.2–5.7], 6.4 [95% UI 5.8–7.5] for IS and HS deaths, respectively, in 2013). There was no measurable change in the proportional contribution of DALYs and deaths from stroke in developed countries over the 23-year study period.

This GBD and other reports^{17,18} indicate that stroke in the young and middle-aged adults are not decreasing or may even be increasing, likely because of increase in metabolic risk factors, including obesity and diabetes mellitus, among the young. The GBD findings also suggest that stroke should no longer be regarded as a disease of the elderly: two thirds of all strokes occur among persons <70 years of age.

Sex Differences in Stroke Burden in the World, Including Trends From 1990 to 2013

The GBD 2013 Study identified significant disparities in stroke burden between men and women, with men having consistently greater incidence of IS than women (133/100,000 person-years [95% UI, 125–143] and 99/100,000 person-years [95% UI, 92–107], respectively). Although incidence rates of both IS and HS in 2013 were lower than that in 1990 for both men and women, the number of incident and prevalent strokes was significantly greater in 2013 compared with 1990 for both men and women, IS and HS (Table). The risk (rate of stroke) and absolute number of IS and HS events (both incident and prevalent strokes) in 2013 were significantly greater in men than in women (except no statistically significant excess of incident IS events in men), suggesting changes in the sex distribution of stroke burden in the world. Age-adjusted incidence rates seemed

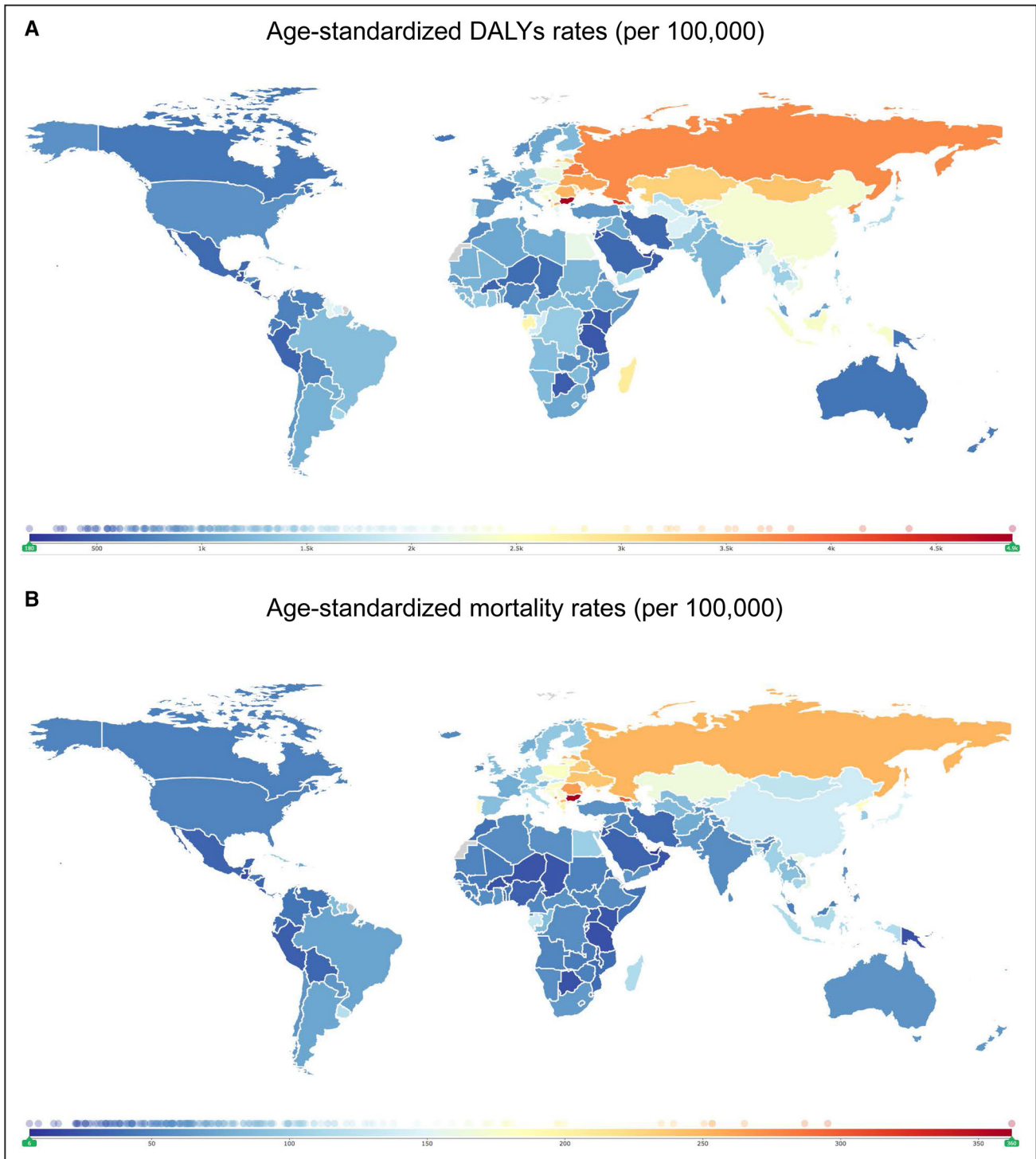


Figure 1. Age-standardized stroke disability-adjusted life-years (DALYs) and mortality rates per 100,000 person-years in various regions of the world in 2013 (both sexes, all ages)

to be declining worldwide at a faster rate in women than in men, but the reasons for that remain unclear.

In 2013, proportional (%) contribution of stroke-related deaths to deaths from all causes (Figure 3) in women was greater than in men and highest in Eastern European countries, Asia East, and North Africa, where it ranged from 35% (95% UI, 29–38) in Macedonia and 32% (95% UI, 28–35) in Vietnam to 16% to 18% in North Africa (95% UI, 14–20), and

lowest in Sub-Saharan Africa (range from 3 to 11) and Papua New Guinea (2% [95% UI, 1–3]).

There were also noticeable sex differences in the proportional contribution of stroke-related DALYs to DALYs from all causes (Figure 4). Although in men it was highest in Bulgaria, Macedonia, Georgia, China, and North Korea (11%–12%), in women it was not high in China (9% [95% UI, 7–10]).

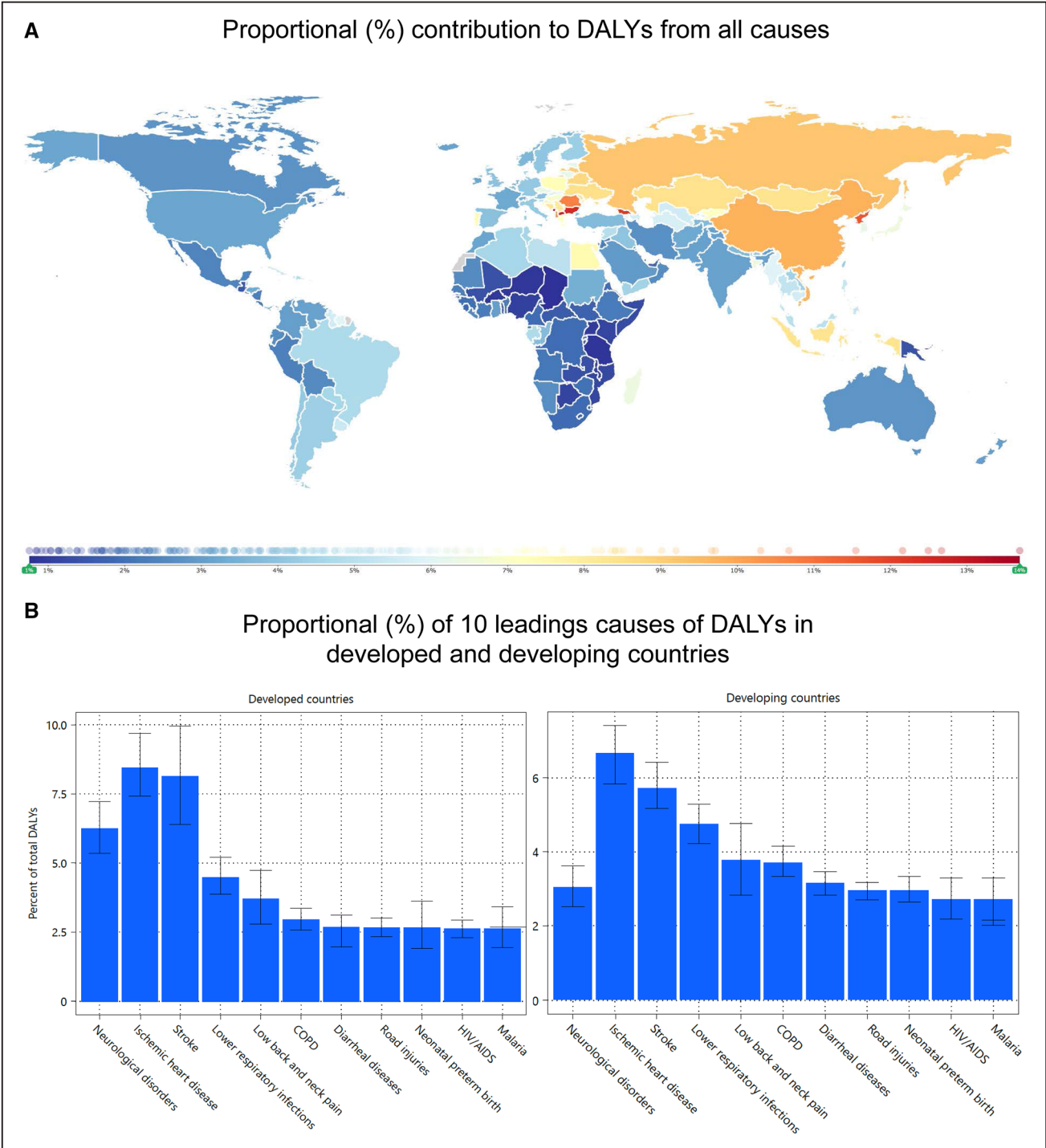


Figure 2. Proportional contribution (%) of age-standardized disability-adjusted life-years (DALYs) from stroke to DALYs in 2013. COPD indicates chronic obstructive pulmonary disease.

Overview of the Global, Regional, and Country-Specific Burden of Stroke in Adults, Including Trends in Stroke Burden From 1990 to 2013

Globally, between 1990 and 2013, there were significant increases in prevalent cases, total deaths, and DALYs because of HS and IS in younger adults aged 20 to 64 years. In 2013, in younger adults aged 20 to 64 years, the global prevalence of HS was 3.7 million cases [95% UI, 3.5–3.9] and IS was 7.3 million cases [95% UI, 7.0–7.6]. Globally, between 1990 and

2013, there were significant increases in absolute numbers and prevalence rates of both HS and IS for younger adults. There were 1.5 million [95% UI, 1.3–1.7] stroke deaths globally among younger adults, but the number of deaths from HS (1.0 [95% UI, 0.9–1.2]) was significantly higher than the number of deaths from IS (0.4 million [0.4–0.5]).

Death and DALY rates declined in both developed and developing countries, but a significant increase in absolute numbers of stroke deaths among younger adults was detected

Table. Absolute Number of Women and Men With Stroke (in Millions) in the World by Stroke Type in 1990 and 2013 (95% Uncertainty Limits Are in Brackets)

		Women		Men	
		1990	2013	1990	2013
Ischemic stroke	Incident	2.14 (1.96–2.33)	3.28 (3.06–3.52)	2.17 (2.05–2.33)	3.62 (3.43–3.85)
	Prevalent	4.86 (4.56–5.19)	8.66 (8.32–9.00)	5.18 (4.93–5.46)	9.65 (9.27–10.05)
Hemorrhagic stroke	Incident	0.86 (0.79–0.92)	1.53 (1.42–1.63)	1.03 (0.96–1.09)	1.84 (1.72–1.94)
	Prevalent	1.78 (1.67–1.87)	3.36 (3.23–3.51)	2.11 (2.02–2.22)	4.00 (3.81–4.17)

in developing countries, where most of the burden of stroke resided. There was a 20.1% [95% UI, –23.6 to 10.3] decline in the number of total stroke deaths among younger adults in developed countries, but a 36.7% [95% UI, 26.3–48.5] increase in developing countries. Percentage changes in deaths and DALYs in younger adults between 1990 and 2013 in developed and developing countries by 5-year age group also showed diverging trends (Figure 5), that is, increase of the percentage change toward greater burden with aging in developing countries and decrease of the percentage change toward the reduction of the burden with aging in developed countries. Death rates for all strokes among younger adults declined significantly in developing countries from 47/100,000 person-years [95% UI, 42.6–51.7] in 1990 to 39/100,000 person-years [95% UI, 35.0–43.8] in 2013. Death rates for all strokes among younger adults also declined significantly in developed countries from 33.3 [95% UI, 29.8–37.0] in 1990 to 23.5 [95% UI, 21.1–26.9] in 2013. Although the trends in declining death and DALY rates in developing countries are encouraging, these regions still fall far behind developed regions of the world.

In 2013, the greatest burden of stroke among younger adults was because of HS. A significant decrease in HS death rates for younger adults was seen only in developed countries between 1990 and 2013 (19.8 [95% UI, 16.9–22.6] and 13.7 [95% UI, 12.1–15.9] per 100,000). No significant change was detected in IS death rates among younger adults. The total DALYs from all strokes in 20 to 64 year olds were 51.0 million [95% UI, 46.6–57.3]. Globally, there was a 24.4% [95% UI, 16.6–33.8] increase in total DALYs for this age group, with a 20% [95% UI, 11.7–31.1] and 37.3% [95% UI, 23.4–52.2] increase in HS and IS numbers, respectively.

Overview of the Global, Regional, and Country-Specific Burden of Stroke in Children, Including Trends in Stroke Burden From 1990 to 2013

Globally, between 1990 and 2013, there was a significant increase in the absolute number of prevalent childhood strokes while absolute numbers and rates of both deaths and DALYs declined significantly. In 2013, there were almost 100,000 prevalent cases [95% UI, 91,000–106,000] of childhood IS and 68,000 [95% UI, 63,000–72,000] prevalent cases of childhood HS, reflecting an increase of ≈35% in the absolute numbers of prevalent childhood strokes since 1990. There were ≈33,000 [95% UI, 29,000–39,000] deaths and 2.6 million [95% UI, 2.3–3.1] DALYs because of childhood stroke in 2013 globally, reflecting ≈200% decrease in the absolute numbers of death and DALYs in childhood stroke since 1990.

Between 1990 and 2013, there were significant increases in the global prevalence rates of childhood IS, as well as significant decreases in the global death and DALY rates of all strokes in 0 to 19 year olds. Males showed a trend toward higher childhood stroke death rates (1.5/100,000 person-years [1.3–1.8]) than females (1.1/100,000 person-years [0.9–1.5] per 100,000) and higher childhood stroke DALYs rates (120.1/100,000 person-years [100.8–143.4]) than females (90.9/100,000 person-years [74.6–122.4]) globally in 2013.

Although the gap in childhood stroke burden between developed and developing countries is closing (Figure 6), the 2013 childhood stroke burden in terms of absolute numbers of prevalent strokes, deaths, and DALYs remained much higher in developing countries. Although prevalence rates for childhood IS and HS decreased significantly in developed countries, in developing countries, a decline was seen only in HS, with no change in IS prevalence rates. The childhood stroke DALY rates in 2013 were 13.3/100,000 person-years [95% UI, 10.6–17.1] for IS and 92.7/100,000 person-years [95% UI, 80.5–109.7] for HS. Although globally the prevalence of childhood IS compared with childhood HS was similar, the death rate and DALYs rate of HS was 6- to 7-fold higher than that of IS. In 2013, the prevalence rate of childhood IS and HS was significantly higher in developed countries than that in developing countries. Conversely, both death and DALY rates for all strokes were significantly lower in developed countries than in developing countries in 2013.

Call for Action

The patterns of the main categories of diseases have shifted considerably during the last few decades. The GBD project and other studies have shown a decline in infectious and nutritional disorders, and a rise in noncommunicable diseases (NCD), such as stroke, heart disease, cancer, diabetes mellitus, and chronic obstructive pulmonary disease.⁶ The most recent GBD estimates showed that during the last two and half decades, the number of stroke survivors and people with incident stroke have increased 50% to 100%, thus indicating that currently used primary stroke prevention strategies are not sufficiently effective and require a serious revision. Projections demonstrate that the NCDs will be increasingly prevalent in the next decades and will reach epidemic proportions, which will seriously influence global public health, and furthermore have substantial effects on social and economic development—unless urgent actions are undertaken. Fortunately, the core NCDs share one important element: they are all highly preventable. In the past, epidemiological global data on stroke have often

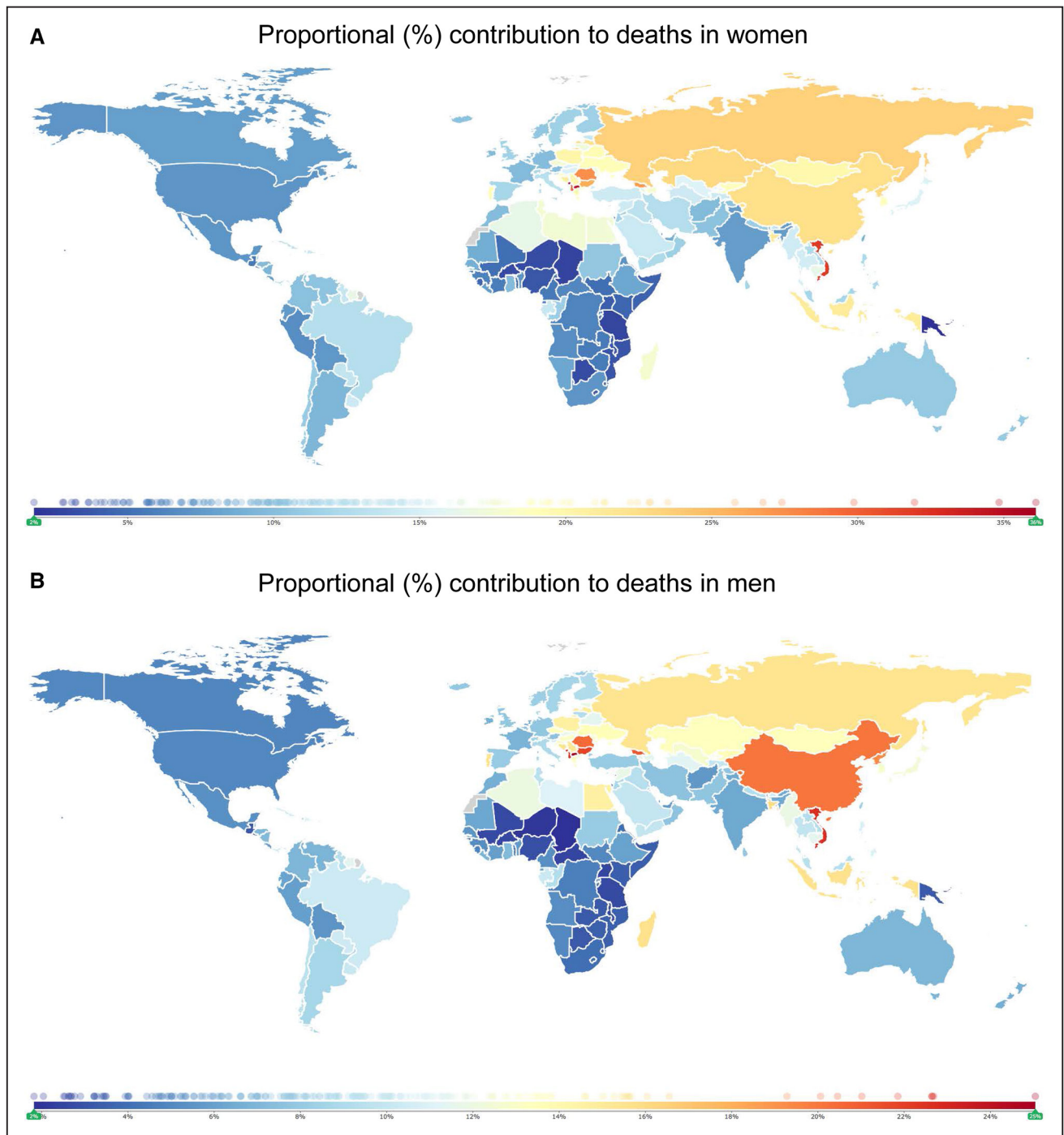


Figure 3. Proportional (%) contribution of stroke-related deaths to deaths from all causes in men and women in 2013.

been included under the term “cardiovascular disease” without further subdivision into the 2 main constituents, such as heart disease and stroke. The major implications of each of these disorders for global health warrant their recognition as stand-alone diseases that should be accounted for separately, rather than embedded under an umbrella term that is often not well understood.

A key to reducing the global burden of stroke is renewed emphasis on stroke prevention. Whereas each of the NCDs require specific management and treatment when they occur,

the prevention of NCDs share many common features because the main risk factors are mostly similar. For stroke, heart disease, diabetes mellitus, cancer, and pulmonary diseases, 4 modifiable lifestyle risk factors are of major importance: tobacco use, unhealthy diet, physical inactivity, and harmful use of alcohol. The WHO has established the “4 by 4” principle of 4 core NCDs (cardiovascular disease, cancer, diabetes mellitus, pulmonary diseases) and 4 major modifiable risk factors in their list of “best buys”: (mass actions on the lifestyle risk factors are the most cost-effective means

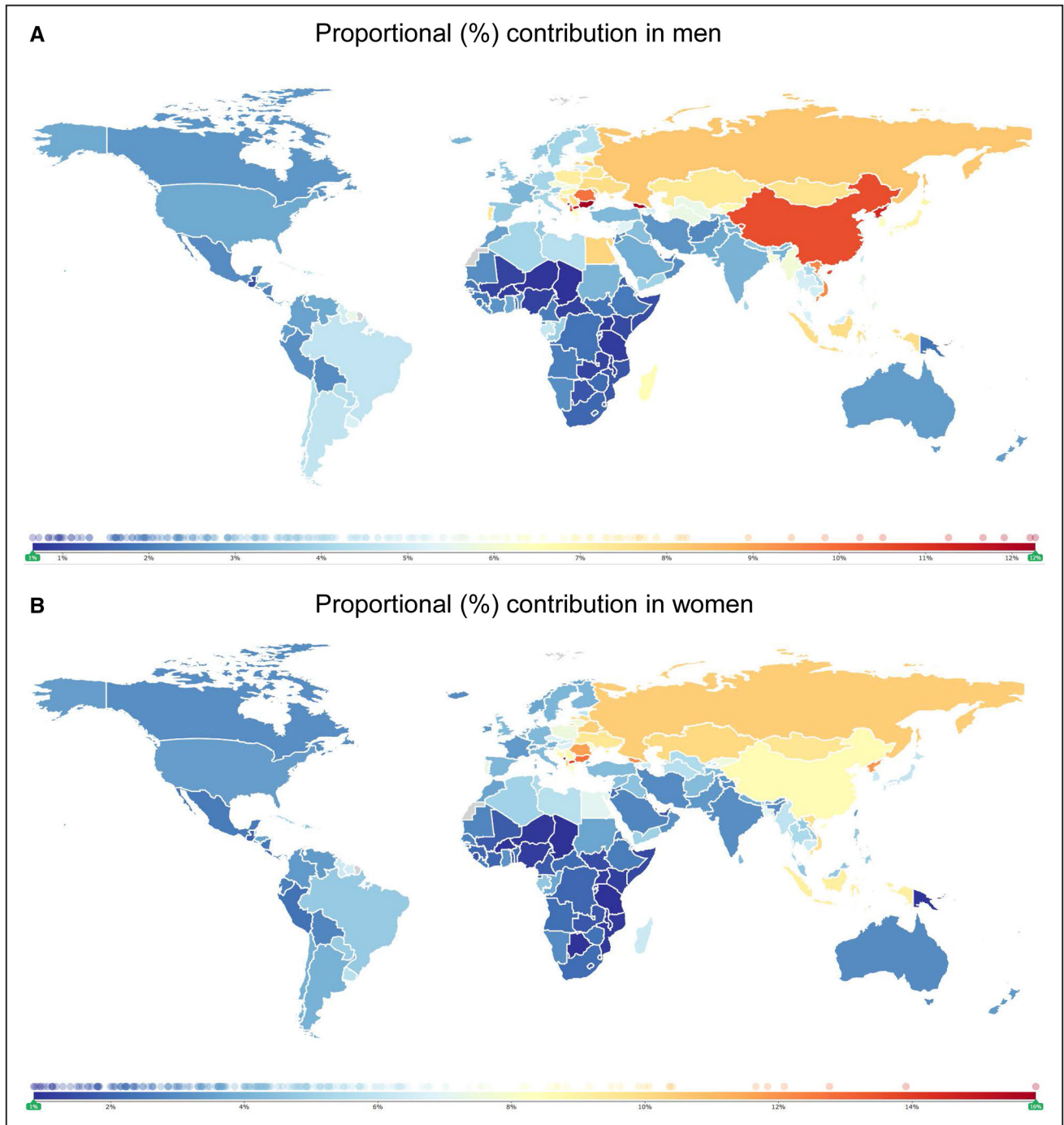


Figure 4. Proportional contribution (%) of age-standardized disability-adjusted life-years (DALYs) from stroke to DALYs from all causes in 2013 by sex.

of prevention).¹⁹ This cluster of diseases and risk factors are prioritized by the WHO in its Global Action Plan on NCDs.²⁰ For stroke, other major risk factors include hypertension, which is twice as important for stroke as for coronary heart disease²¹; and atrial fibrillation, which increases in importance with increasing age.

The major threat to global health and the implications for society was increasingly recognized from around the year 2000 onwards and lead to the landmark event of the adoption of the United Nations (UN) declaration on NCDs

in September 2011.²² This event clearly marked that stroke and NCDs not only constitute a medical but also a political and developmental issue of global importance. With the political declaration, the UN member states committed to take strong action on the NCDs. The task to lead the implementation and monitoring of the UN declaration was given to the WHO, who issued the WHO Global Action plan that included a set of global targets for lifestyle risk factors and health system improvements to achieve the overall goal of a 25% reduction in premature NCD mortality by the

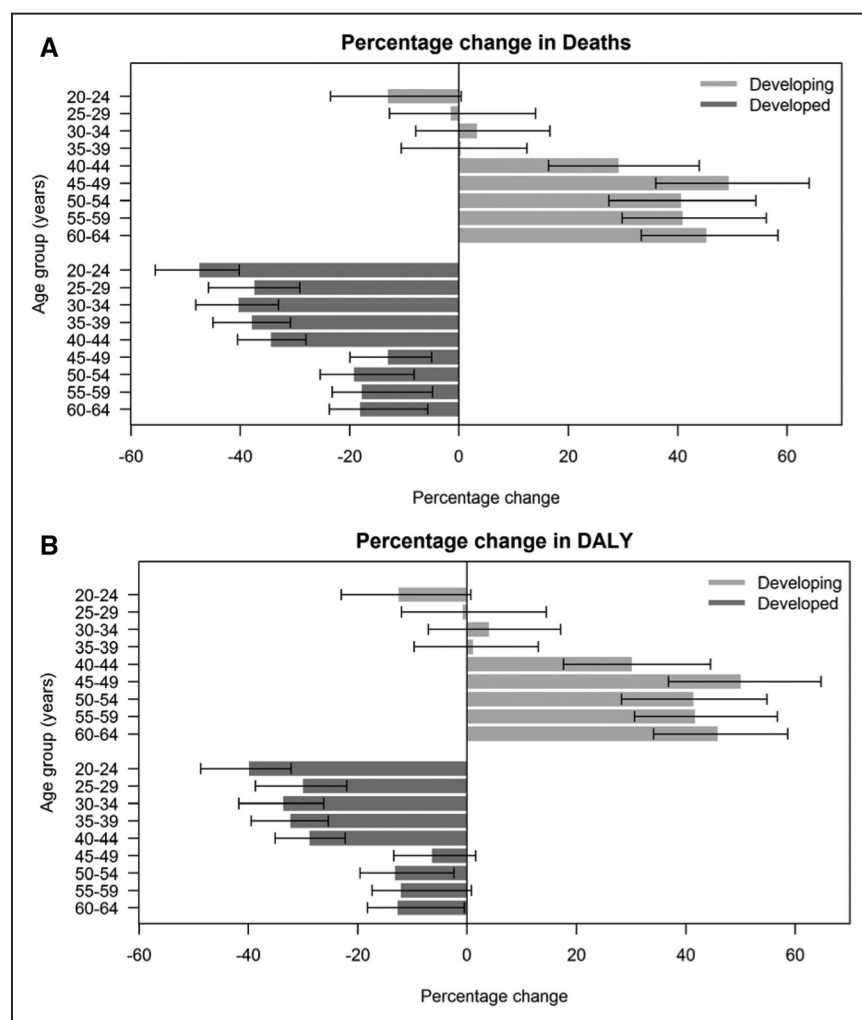


Figure 5. Percentage change in age-standardized death and disability-adjusted life-year rates in younger adults between 1990 and 2013 by 5-year age group in developed and developing countries.

year 2025. Stroke prevention should not be a stand-alone isolated issue, but be a part of the common actions now in progress on the major NCD risk factors. Only by joining forces with other initiatives for NCDs prevention will stroke prevention have its full impact. The major principles in prevention are similar for stroke and other types of cardiovascular disease.²³

The UN declaration called for a 25% relative reduction in premature mortality from NCDs, including stroke, by the year 2025. However, the other stroke epidemiological metrics should not be forgotten. The most important primary health goal for stroke is clearly a reduction in stroke incidence—prevention is always better than cure. However, the need for effective therapies in the acute phase (stroke unit management, thrombolytic, and other reperfusion therapies), as well as rehabilitation and long-term follow-up efforts to prevent stroke recurrence and improve functional outcomes should be recognized as important measures to substantially reduce the burden of stroke in people who have developed or survived stroke. As one-third of all strokes occur in persons who have had a previous cerebrovascular event, adequate attention should be paid to secondary stroke prevention. This should include measures to ensure adherence to the recommended (evidence based) poststroke and transient ischemic

attack surgical management (if indicated), medications, and lifestyle modifications. The world's first global stroke services guidelines (The World Stroke Organization Global Stroke Services Guidelines and Action Plan) have recently been published and provide a listing of essential components of care at different levels of services.²⁴ The document recognizes 3 levels of stroke care: minimal (stroke care delivery is based at a local clinic staffed predominantly by nonphysicians, and much of the emphasis is placed bedside clinical skills, on teaching, and prevention; there is a lack of diagnostics, such as computed tomographic scan, stroke units, thrombolytic therapies, basic secondary stroke prevention, and rehabilitation), essential (offers access to a computed tomographic scan, physicians, and the potential for acute thrombolytic therapy; however, stroke expertise may still be difficult to access; the bulk of evidence-based therapies for stroke is available at that level), and advanced (availability of multidisciplinary stroke expertise, multimodal imaging, and comprehensive therapies, eg, neurosurgical interventions and thrombectomy). The world map of stroke services is not precisely known at present, but a high proportion of populations is estimated to have access only to minimal stroke services. It is now urgent to change minimal services to essential services in all regions.

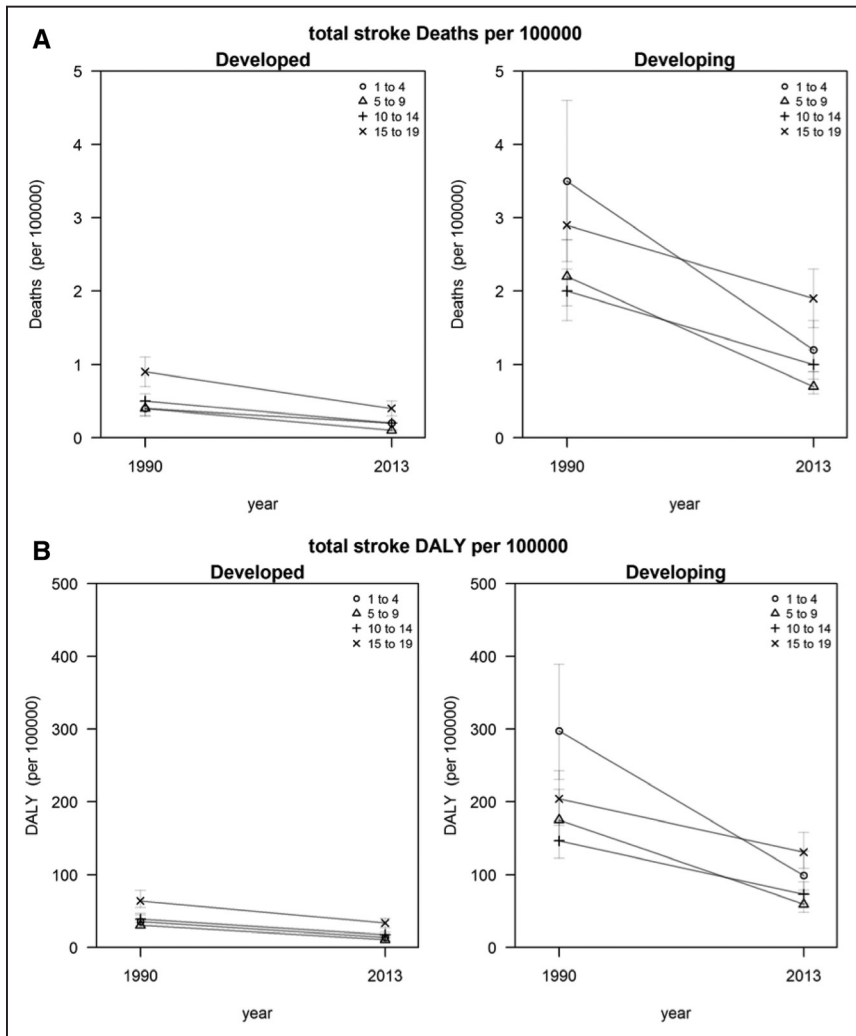


Figure 6. Trends in age-standardized death and disability-adjusted life-year (DALY) rates (per 100,000 people per year) in childhood stroke between 1990 and 2013 in developed and developing countries.

Several actors are responsible for ensuring that the call for action on stroke will be effective and lead to improvements in stroke metrics. Governments have the main responsibility and have the power to influence environmental (eg, air pollution), social (eg, poverty, racial/ethnic inequality in health care, education, employment, housing, etc.), medical (provision of adequate health services), and lifestyle factors (eg, smoking, nutrition, and physical activity) through legislation and taxation of tobacco, alcohol, and food contents (salt, sugar, and saturated fats). One still unmet need also within the responsibility of governments is adequate funding of stroke research, including primary stroke prevention research. However, in spite of stroke being a leading cause of death and disability, the volume of funding for stroke research (including primary stroke prevention research) is low in comparison with that spent on cancer or coronary heart disease.²⁵ Health systems have the responsibility to identify risk factors that require medical contacts for their detection and treatment (eg, elevated blood pressure, atrial fibrillation, and symptomatic carotid artery stenosis) to influence risk factors for the substantial part of the population that already have an NCD or a risk factor that requires regular medical contacts. Nongovernmental organizations, such as the World

Stroke Organisation and academia, have important responsibilities in providing adequate scientifically based advice on prevention, practices, management, and therapies. Academia also has the responsibility to develop technological advances, such as the Stroke Riskometer app,²⁶ to help individuals to recognize their own risk factors, calculate the future risk of stroke, and provide targeted advice on how to lower the risk.²⁷ Thus, the responsibilities to a decreased global burden of stroke are shared.

It has been estimated that with effective actions on common lifestyle factors, at least half of all strokes may be prevented.²⁸ Prevention of stroke is a complex medical and a political issue—but there is strong evidence that substantial prevention of stroke is feasible in practice. The need to scale-up the actions is urgent. Stroke prevention has entered a new era, with stroke being identified as one of the prioritized NCDs in the WHO and UN actions on NCDs.

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Disclosures

None.

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