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UPDATE ON THE GLOBAL BURDEN OF ISCHAEMIC AND HAEMORRHAGIC STROKE IN 1990–2013: THE GBD 2013 STUDY

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Abstract

Background—Global stroke epidemiology is changing rapidly. Although age-standardised rates of stroke mortality have decreased worldwide in the past two decades, the absolute numbers of people who have a stroke every year, live with the consequences of stroke, and die from their stroke are increasing. Regular updates on the current level of stroke burden are important for advancing our knowledge on stroke epidemiology and facilitate organization and planning of evidence-based stroke care.

Objectives—To estimate incidence, prevalence, mortality, disability-adjusted life-years (DALYs) and years lived with disability (YLDs), and their trends for ischaemic stroke (IS) and haemorrhagic stroke (HS) for 188 countries from 1990–2013.

Methodology—Stroke incidence, prevalence, mortality, DALYs and YLDs were estimated using all available data on mortality and stroke incidence, prevalence and excess mortality. Statistical models and country-level covariate data were employed and all rates were age-standardised to a global population. All estimated were produced with 95% uncertainty intervals (UI).

Results—In 2013, there were globally 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). Over the 1990–2013 period, there was a significant increase in the absolute number of DALYs due to IS, and of deaths from IS and HS, survivors and incident events for both IS and HS. The preponderance of the burden of stroke continued to reside in developing countries, comprising 75.2% of deaths from stroke and 81.0% of stroke-related DALYs. Globally, the proportional contribution of stroke-related DALYs and deaths due to stroke

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Contributions

VLF, GAR and CM developed the study concept and oversaw the research. VLF, RK, GAR undertook reviews of studies. MHF, MN and PP provided statistical analysis of the data and produced graphs. VLF wrote the first draft of the report. MHF, MN and CM developed the statistical model and wrote a section on statistical analysis. All authors contributed to the critical revision of the manuscript for important intellectual content.

Conflict of interest

All the authors declare that they have no conflict of interest.

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compared to all diseases increased from 1990 (3.54% [95% UI 3.11–4.00%] and 9.66% [95% UI 8.47–10.70%]) to 2013 (4.62% [95% UI 4.01–5.30%] and 11.75% [95% UI 10.45–13.31%], respectively), but there was a diverging trend in developed and developing countries with a significant increase in DALYs and deaths in developing countries, and no measurable change in the proportional contribution of DALYs and deaths from stroke in developed countries.

Conclusion—Global stroke burden continues to increase globally. More efficient stroke prevention and management strategies are urgently needed to halt and eventually reverse the stroke pandemic, while universal access to organized stroke services should be a priority.

Keywords

stroke; ischaemic stroke; haemorrhagic stroke; global burden; GBD 2013

Introduction

Stroke remains a major global health problem[1,2] and its significance is likely to increase in the future due to ongoing demographic changes, including ageing of the population and health transitions observed in developing countries.[3] The Global Burden of Disease (GBD) 2010 Study showed that while age-standardised rates of stroke mortality have decreased worldwide in the past two decades, the absolute number of people who have a stroke every year, live with the consequences of stroke, and die from their stroke is increasing. New epidemiological papers on stroke published since 2010 and updated death records are now included in the GBD 2013 Study dataset. Important advances and refinements have been made to the methodology for deriving the GBD estimates. Therefore, this updated report on the current level of stroke burden is important for advancing our knowledge on stroke epidemiology and planning for adequate evidence-based stroke systems of care. In the GBD 2013 study, we use new DisMod[4,5] methodology in order to provide new estimates of incidence, prevalence, disability-adjusted life-years (DALYs) and years lived with disability (YLDs) for ischaemic strokes (IS) and haemorrhagic and other non-ischaemic strokes combined (HS) separately for 1990 and 2013 at regional and global levels.

Methodology

Methods to estimate all-cause mortality and cause-specific mortality been previously described.[6] Stroke modeling and methodology used to estimate GBD 2013 stroke burden (including an updated list of publications included in this analysis) has also been described in detail.[7] In brief, we used all available estimates of stroke incidence, prevalence and case fatality from systematic reviews of the scientific literature, population surveys, and stroke registries. Stroke was defined based on the WHO clinical criteria.[8] All available national mortality data were compiled. Non-specific cause codes were redistributed based on expert opinion and statistical methods.[7] The total for all cause-specific deaths was fitted within an envelope for all-cause mortality. Deaths were compiled into 240 causes, including IS and HS. For stroke death estimates, GBD defined stroke ICD-10 codes as IS, HS, or nonspecific as to type. The parent category of cerebrovascular disease was based on the mapping of the detailed causes. Deaths coded as due to G45 (transient ischaemic attack) were coded as IS

and deaths coded as due to nonruptured aneurysms (ICD code I67.0) were coded as HS. Nonspecific codes, including I64, I67.9, I68.8, I69.4–I69.9, were redistributed to IS or HS using a regression model.

An ensemble model was used to estimate a continuous time-series for mortality by age, sex, country (developed or developing), and year. Country-level covariates associated with stroke were used in the model and out-of-sample validity testing was used to assess model performance. 95% uncertainty intervals (UI) were estimated using 1000 draws from the posterior distribution for each age-sex-country group. Disease prevalence was estimated using DisMod state-transition disease modeling software[9] and Bayesian statistical models. IS and HS were modelled separately. Adjustments were made to account for incidence estimates specifying first-ever or any stroke. Disability due to acute stroke was considered to last for 28–30 days and for chronic stroke from 31st day until death. Five disability weights derived from large-scale studies while SF-12 scores from the U.S. Medical Expenditures Panel Survey for stroke patients supplied the distribution of these severity levels plus the proportion asymptomatic.[10] YLDs were calculated as the product of a disability weight and prevalent cases of stroke. DALYs were calculated as the sum of years of life lost prematurely, based on maximum observed global longevity, and YLDs. Countries were stratified into two groups (developed countries [high-income countries] and developing countries [low- and middle-income countries]). We report age-standardised incidence and mortality rates per 100 000 person-years, and prevalence and DALYs estimates per 100 000 people with the direct method of standardisation and GBD estimates of population as a reference.

Results

Globally from 1990 to 2013 there were statistically significant reductions in the incidence, mortality and DALY rates of IS. For HS there were statistically non-significant increases in the incidence and prevalence, and decreases in the mortality and DALY rates (Fig. 1, Table 1). In 2013, the DALYs and mortality rates of IS and HS combined in developing countries (2,189/100,000 per year [95% UI 1,995–2,416/100,000 per year] and 137/100,000 per year [95% UI 125–150/100,000 per year], respectively) were statistically significantly greater than that in developed countries (1,022/100,000 [95% UI 941–1,159/100,000] and 67/100,000 [95% UI 62–78/100,000], respectively) due to the higher rate for HS (Table 1), while the absolute number of people affected by both IS and HS in the world over that time period had increased significantly (Table 2). While mortality rates from IS and HS combined in developed countries were almost halved from 1990 to 2013 (112.9/100,000 and 67.2/100,000), in developing countries IS and HS mortality rates were reduced by only approximately 15% (from 160.9/100,000 in 1990 to 136.9/100,000 in 2013). As shown in Table 2, 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% were IS). Over the 1990 to 2013 period, there was a statistically significant increase in the absolute number of DALYs due to IS, and deaths from, survivors and incident events of both IS and HS. The prevalence nearly doubled for both IS and HS from 1990 to 2013. Globally, from 1990 to 2013 there was a statistically non-significant increase in the prevalence rates of IS (statistically significant increase in the

prevalence of IS from 1990 to 2005 was followed by statistically significant decrease from 2005 to 2013; Figure 1) and a statistically significant increase in HS prevalence rates (Figure 1). However, in developed countries the increase in the prevalence rates was statistically significant for both IS and HS (Table 3).

Analysis of age-specific patterns of incidence, prevalence and mortality rates by country development status in 2013 (Figures 2 and 3) showed that IS incidence and prevalence rates in developed countries were statistically significantly greater and demonstrated a steeper increase with age than that in developing countries after the age of 49 and 39 years respectively. However, IS mortality rates after the age of 49 years were greater in developing countries. The age-related patterns of increase in IS mortality rates were similar in developed and developing countries. Age-specific incidence and mortality rates of HS were statistically significantly greater in developing countries after the age of 39 (Figure 3). There was no statistically significant difference in the age-specific prevalence rates between developed and developing countries after age 54 (Figure 3). However, the prevalence rates of HS in younger age groups were significantly greater in developed countries.

Analysis of the percentage contribution of IS and HS to all diseases (Table 4) showed that the relative burden of strokes in the world increased from 1990 to 2013, particularly for the burden due to IS in which the increase in DALYs and in deaths reached a statistically significant level. In developing countries, statistically significant increases in DALYs and deaths due to stroke were present for both IS and HS, while there was little change in YLDs. In developed countries, we observed a decrease in the proportional contribution of DALYs and deaths from IS and HS to all diseases but an increase in the proportional contribution of YLDs due to stroke. In comparison to other causes of DALYs in the world (Figure 4), stroke was the second largest contributor after ischaemic heart disease globally and in developing countries, and the third largest contributor to DALYs in developed countries (after ischaemic heart disease and lower back and neck pain), with significant regional variation in disease burden across both developed and low to middle-income countries.

There were large inter- and intra-regional variations in IS and HS age-adjusted incidence, prevalence and mortality rates (Figures 5 and 6; Supplementary Tables). The highest prevalence rate of IS (1,015–1,184/100,000) was shown in developed countries (particularly USA), the lowest (up to 339/100,000) in overall developing countries. The highest IS mortality rates (124–174/100,000 person-years) were observed in Russia and Kazakhstan, and the lowest (at or below 25/100,000) in – Western Europe, North and Central America, Turkmenistan and Papua New Guinea. Prevalence rates of HS were highest (232–270/100,000) in the USA, and lowest (up to 78/100,000) in Latin America, Africa, Middle East, France, Eastern Europe, Northern part of Asia and Russia. HS mortality rates were highest (159–222/100,000 person-years) in Mongolia and Madagascar, and lowest (up to 32/100,000) in North America, most parts of Western Europe, Russia, Iran, Saudi Arabia, Morocco, Japan, Australia and New Zealand (Figure 6).

Discussion

The GBD 2013 stroke study supersedes all previous GBD stroke estimates. These new data confirm the previous GBD observations[1] about the significant increase in stroke burden in the world over the last two decades and substantial geographical differences in stroke burden and the directions of the changes by country income level.[1,11] We observed a greater than 3-fold increase in burden due to stroke with 4.85 million stroke deaths and 91.4 million DALYs in developing countries compared with 1.6 million deaths and 21.5 million DALYs in high- income countries. We demonstrated that 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 of people with new strokes (67% were IS). Over the 23 years study period (1990–2013), there was a much greater reduction in stroke mortality rates in developed countries than that in developing countries, thus further deepening the disparities in the global stroke burden.

We showed that the HS incidence and mortality are very high in developing countries. The YLD did not change due to HS mainly because of high mortality rate in developing countries. We demonstrated that globally, from 1990 to 2013, there was a statistically significant increase in HS prevalence rates and in developed countries the increase in the prevalence rates was statistically significant for both IS and HS, although the prevalence of IS after 2005 decreased. While the increase in the prevalence of HS in developing countries may be related to the high rate of undetected and/or poorly controlled arterial hypertension, [12–15] stroke incidence increase[11] or even better detection of stroke in those countries, the increase in the prevalence of IS and HS in developed countries could be related to the improvements in acute stroke care, or more effective secondary prevention and greater identification of minor stroke cases (including wider use of advanced neuroimaging),[16] which is highly dependent on universal access to primary care.[17,18]

We also found that proportional contribution of DALYs and deaths due to stroke to all diseases has increased from 1990 (3.54% [95% UI 3.11–4.00] and 9.66% [95% UI 8.47–10.70%]) to 2013 (4.62% [95% UI 4.01–5.30] and 11.75% [95% UI 10.45–13.31%], respectively) with a diverging trend in developed and developing countries: a statistically significant increase of the proportional contribution of stroke-related DALYs and stroke-related deaths in developing countries, and a trend, though not statistically significant, towards reduction of the proportional contribution of stroke-related DALYs and stroke-related deaths in developed countries. Apart from health transition in developing nations, this may also be explained by the widening gap in stroke prevention and management between developed and developing countries.[19–21] It may emphasize the pressing need for improving stroke prevention and treatment across the world.[22] The results of GBD 2013 showed the rise in the number of people with multi-morbidity and sequelae driven by longevity. Multi-morbidity has major implications for health systems and research, including stroke community.[23,24]

Although this research was based on the most comprehensive stroke epidemiological data relevant to the 1990–2013 study period and utilised the latest advances in DISMOD-MR stroke modeling techniques, it was not free from some limitations. Because death data were

not available for all countries, mortality estimates relied on geospatial statistical models based on country-specific information. There was still lack of sufficient epidemiological data on stroke in most countries of the world, particularly in developing nations. To address this limitation, we used country-level covariate data and applied out-of-sample validity testing to assess mortality model performance. Statistical models of stroke incidence and prevalence also relied on Bayesian methods and all available data on incidence and prevalence for each type of stroke. In particular, data from subnational regions were often assumed to represent an entire country. Although data were borrowed across time which may blunt actual trends in disease epidemiology, the initial findings were reviewed by a global network of stroke experts to assess plausibility and then subsequent refinements were made to data sources and modeling strategies based on their comments and suggestions. It should also be noted that current estimates combine intracerebral haemorrhage with other more rare stroke types (such as subarachnoid haemorrhage) to better reflect the burden due to HS. To accurately reflect total disease burden, analysis was not limited to first-ever-in-a-lifetime strokes but also reflects all recurrent events. We were not able to report country-level incidence data because modeling at this level of detail is still under development. The GBD 2015 Study estimates will also include estimates of total stroke incidence (IS and HS combined) that we were not able to provide for this paper. Strengths of the study include the utilisation of the latest advances in DisMod stroke modeling techniques and a more comprehensive dataset available for the analysis after 2010.

Stroke is currently the second largest contributor to DALYs after ischaemic heart disease globally in developing countries, and it is third largest contributor to DALYs in developed countries (after ischaemic heart disease and low back and neck pain). This emphasizes 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. If the current trend in stroke burden continues, the UN Global Targets to reduce premature mortality from NCDs[22] (including stroke) by 25% by 2025 will not be met. More efficient stroke prevention strategies and improved organization of stroke systems of care are urgently needed to halt and eventually reverse the stroke pandemic. Although there were improvements in the rates of DALYs, mortality and incidence rates from 1990 to 2013, the magnitude of the differences between these changes in developed and developing countries increased over time, suggesting disparities in the access to and quality of primary and secondary prevention and acute care between these countries. Therefore, there is an urgent need for action to negate these disparities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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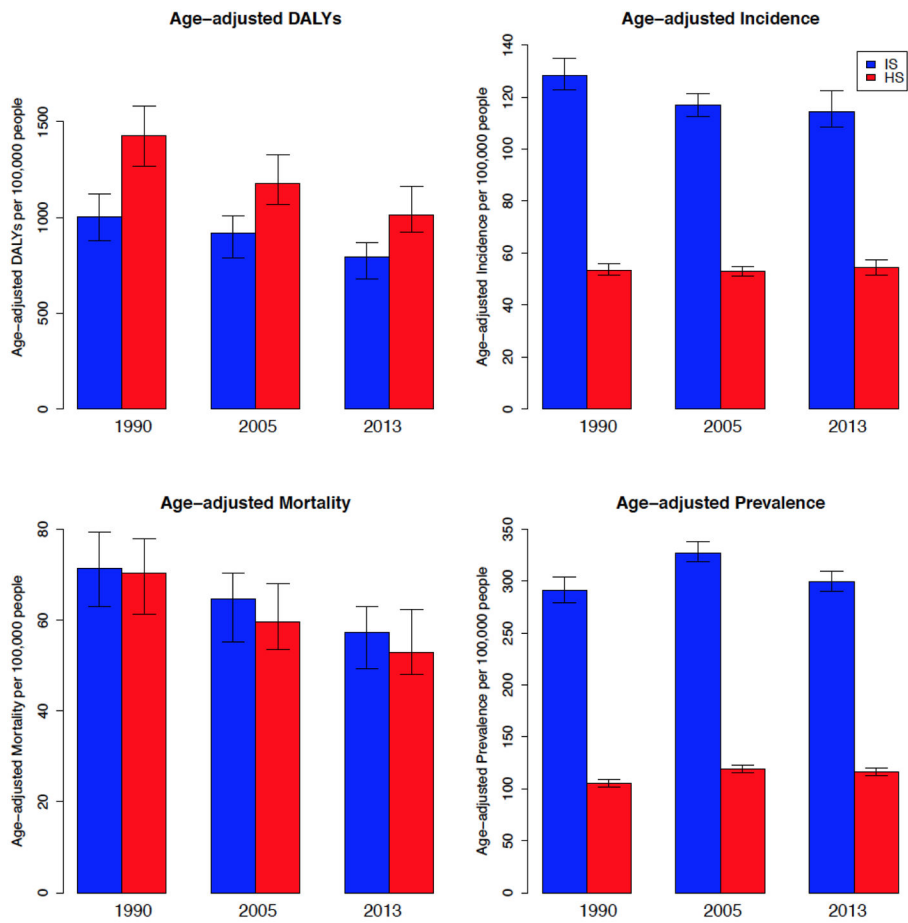
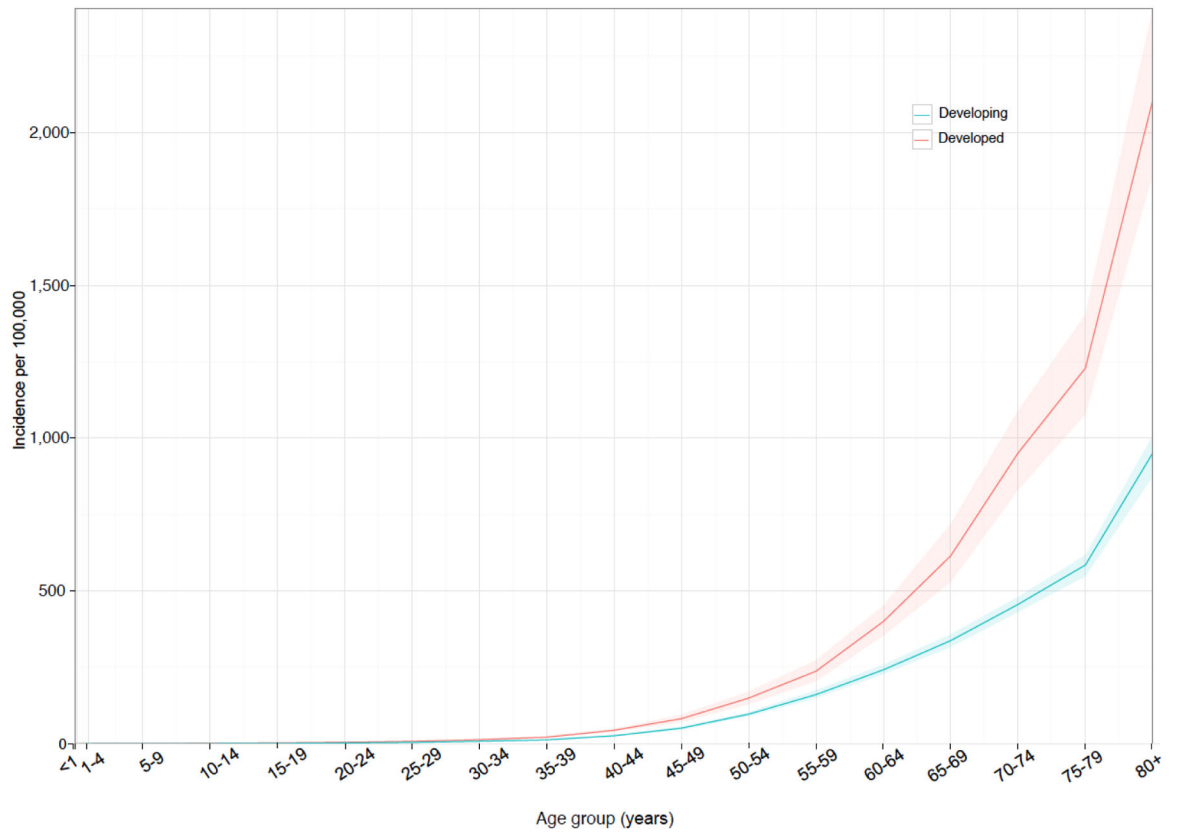


Figure 1. Age-adjusted DALYs, mortality, incidence and prevalence rates of ischaemic and haemorrhagic strokes per 100,000 people (with 95% uncertainty intervals [UI]) in 1990, 2005 and 2013

Ischaemic stroke incidence by age and development status, 2013



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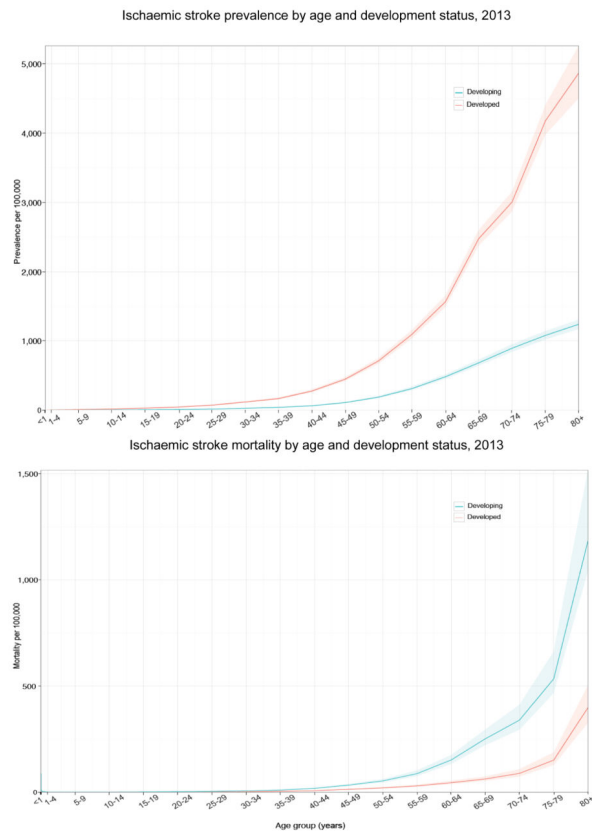
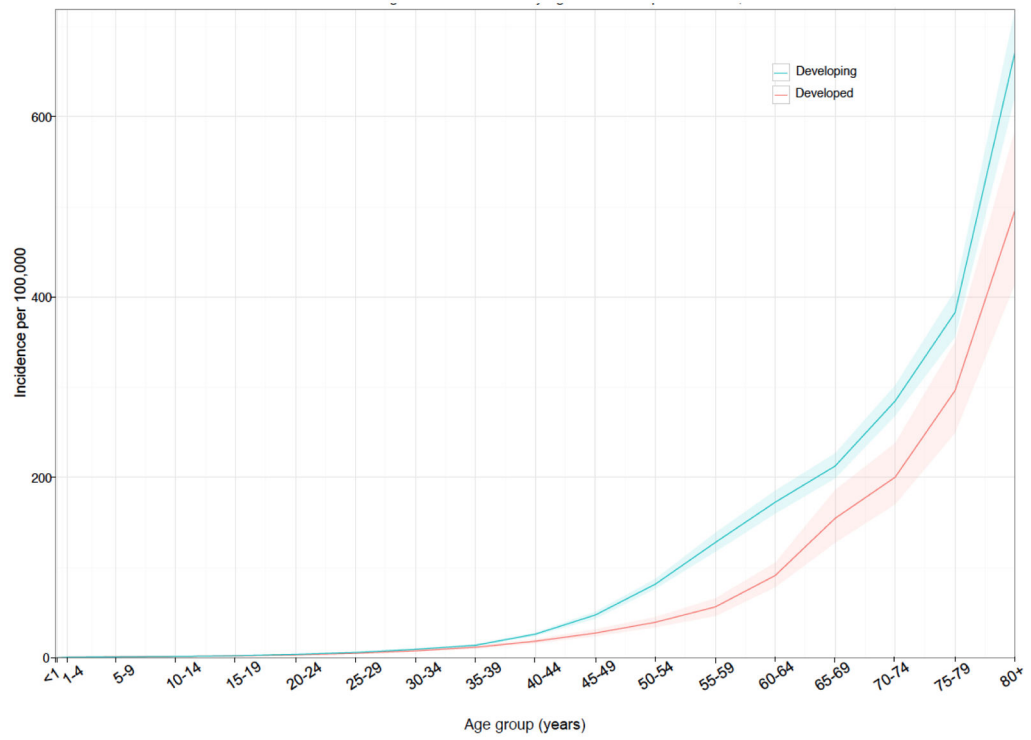


Figure 2. Age-specific incidence, prevalence and mortality rates of ischaemic stroke per 100,000 people per year by country development status in 2013 (shaded area around solid lines represents 95% uncertainty intervals).

Haemorrhagic stroke incidence by age and development status, 2013



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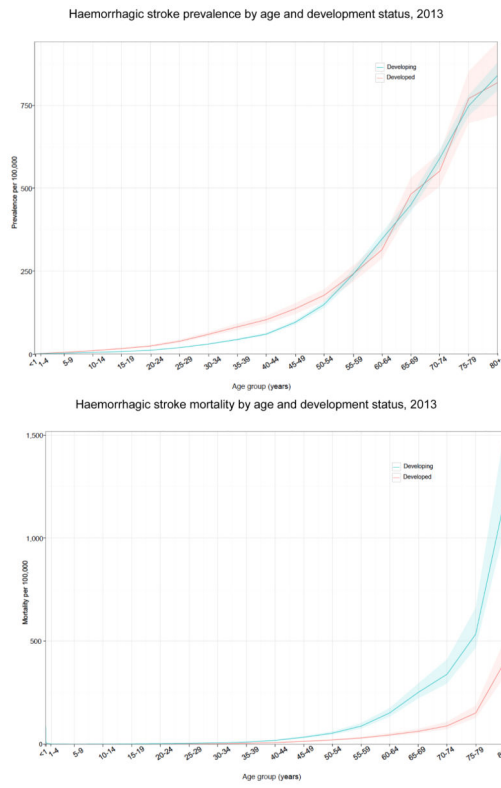
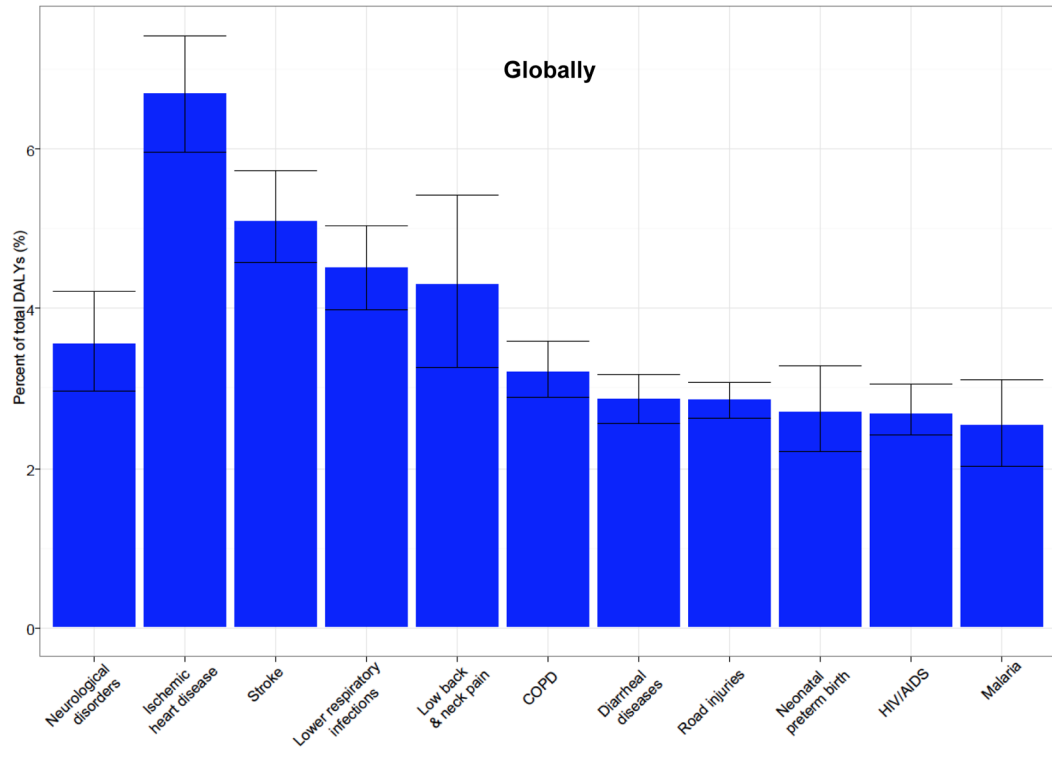


Figure 3. Age-specific incidence, prevalence and mortality rates of haemorrhagic stroke per 100,000 people per year by country development status in 2013 (shaded area around solid lines represents 95% uncertainty intervals).



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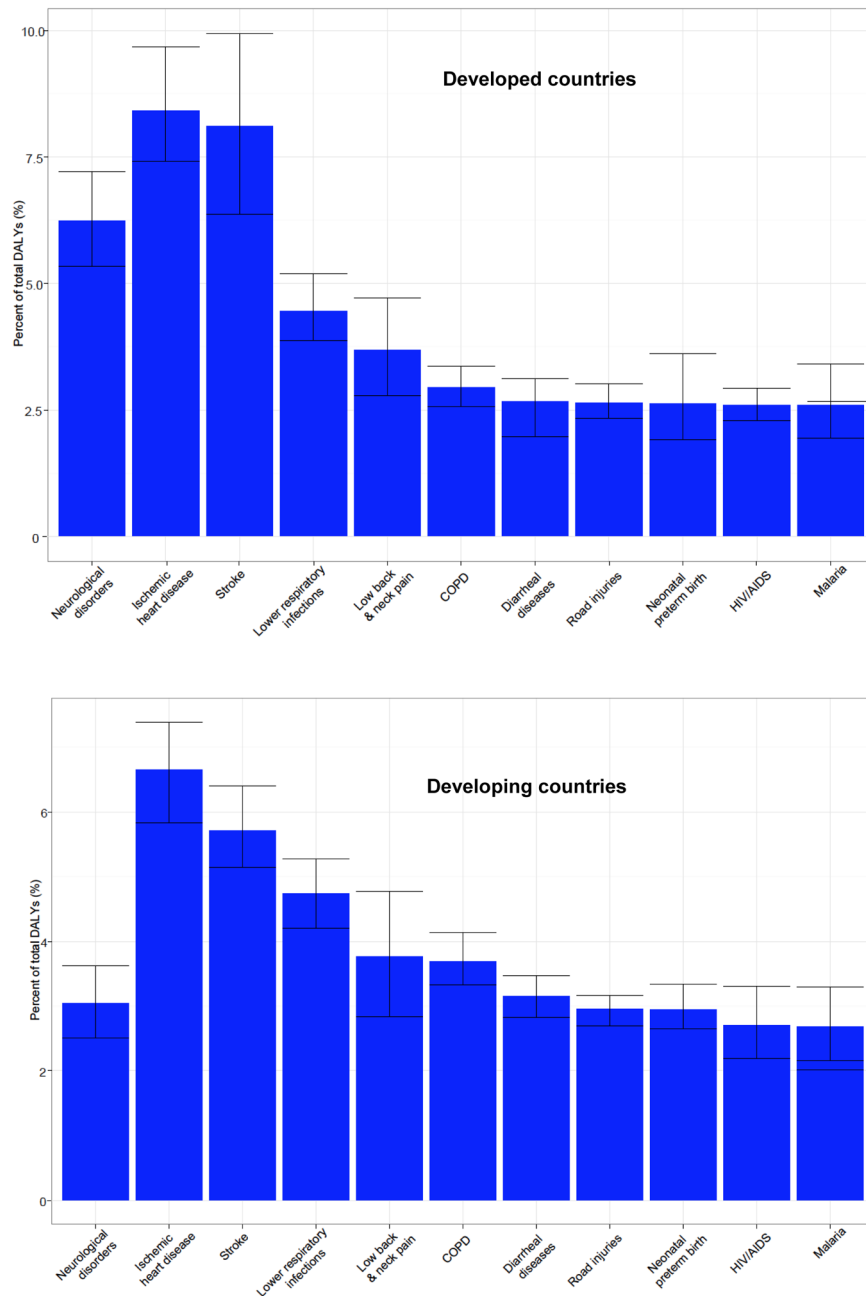


Figure 4. Proportion contribution (%) of age-standardised DALYs from stroke in comparison to 10 other leading causes of DALYs, Global, 2013

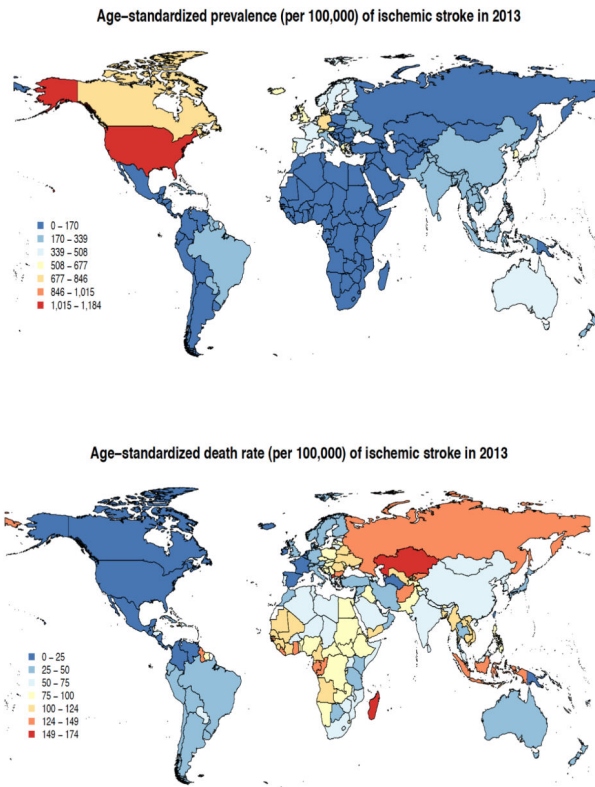
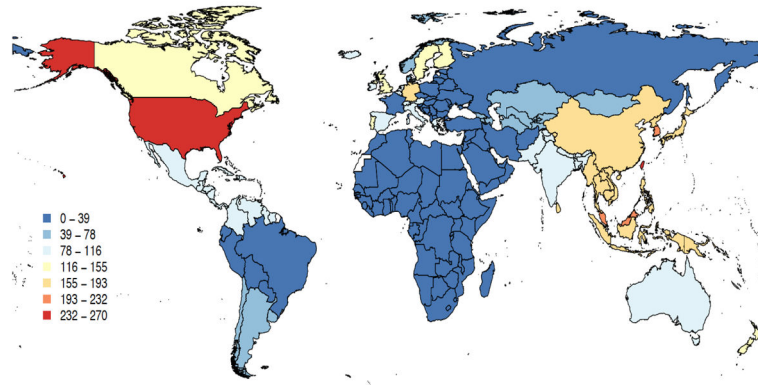


Figure 5. Age-standardised prevalence and mortality of ischaemic stroke per 100,000 person-years in various regions in 2013

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



Age-standardized death rate (per 100,000) of hemorrhagic stroke in 2013

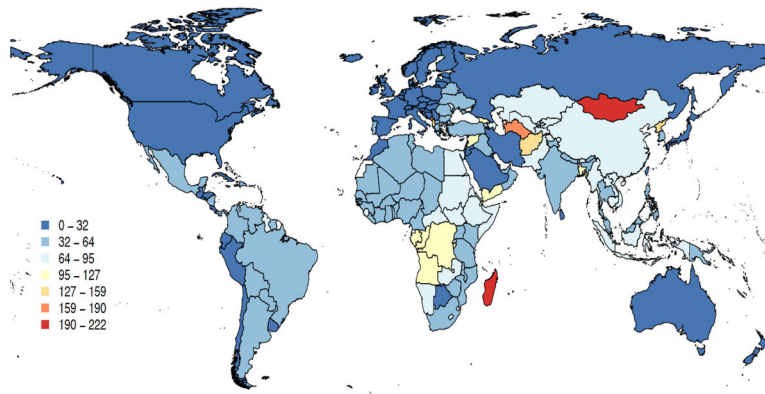


Figure 6. Age-standardised prevalence and mortality of haemorrhagic stroke per 100,000 person-years in various regions in 2013

Table 1

Age-adjusted DALYs and mortality rates of ischaemic and haemorrhagic strokes combined per 100,000 people (with 95% uncertainty intervals [UI]) in developed and developing countries in 1990 and 2013

Year and stroke type	Metric	Developed countries	Developing countries	Globally
1990: ischaemic and haemorrhagic strokes combined	DALYs	1,721.4 (1,564.3–1,866.5)	2,818.2 (2,578.3–3,064.0)	2,430.8 (2,224.0–2,631.4)
	Mortality	112.9 (100.6–121.8)	160.9 (146.8–174.8)	141.6 (128.5–153.9)
Ischaemic stroke	DALYs	1,023.7 (906.4–1,120.3)	950.6 (807.6–1,096.6)	1,004 (877.6–1,222.4)
	Mortality	76.8 (67.3–84.1)	63.7 (54.9–73.8)	71.3 (63.0–79.3)
Haemorrhagic stroke	DALYs	697.7 (598.4–789.4)	1,867.6 (1,657.9–2,069.3)	1,426.0 (1,269.9–1,579.9)
	Mortality	36.1 (30.1–41.2)	97.2 (84.8–108.6)	70.3 (61.2–77.9)
	Mortality	27.9 (25.1–33.2)	80.9 (72.5–93.0)	59.5 (53.5–68.1)
2013: ischaemic and haemorrhagic strokes combined	DALYs	1,022.2 (940.9–1,158.6)	2,189.3 (1,995.4–2,416.0)	1,806.9 (1,667.4–1,991.7)
	Mortality	67.2 (61.9–78.2)	136.9 (125.2–150.4)	110.1 (101.8–122.2)
Ischaemic stroke	DALYs	609.8 (553.0–707.1)	889.4 (718.1–989.8)	791.3 (678.0–868.8)
	Mortality	44.9 (40.9–53.5)	65.1 (52.1–72.0)	57.3 (49.3–62.9)
Haemorrhagic stroke	DALYs	412.4 (369.1–473.3)	1,299.9 (1,178.2–1,495.9)	1,015.6 (923.2–1,163.2)
	Mortality	22.2 (19.6–26.1)	71.8 (64.6–85.6)	52.8 (48.0–62.3)

Table 2

Absolute number of DALYs, deaths, incident and prevalent cases of ischaemic and haemorrhagic stroke (with 95% uncertainty intervals [UI]) in the world in 1990 and 2013

	Metric	1990	2013
Ischaemic stroke	DALYs	34,155,606 (29,592,196 – 38,325,866)	47,424,681 (40,537,540 – 52,211,800)
	Deaths	2,182,865 (1,923,290 – 2,430,872)	3,272,924 (2,812,654 – 3,592,562)
	Incidence	4,309,356 (4,118,103 – 4,531,909)	6,892,857 (6,549,814 – 7,352,226)
	Prevalence	10,045,202 (9,643,525 – 10,453,439)	18,305,491 (17,767,372 – 18,920,736)
Haemorrhagic stroke	DALYs	55,953,376 (49,881,127 – 62,161,971)	65,454,194 (59,497,415 – 74,654,738)
	Deaths	2,401,930.40 (2,109,380.2 – 2,669,117.5)	3,173,951 (2,885,717 – 3,719,684)
	Incidence	1,886,345 (1,816,991 – 1,976,659)	3,366,175 (3,199,978 – 3,543,213)
	Prevalence	3,891,158 (3,769,541 – 4,019,014)	7,363,457 (7,139,691 – 7,616,146)

Age-adjusted prevalence rates of ischaemic and haemorrhagic strokes per 100,000 people and median percentage change with 95% uncertainty intervals (UI) in developed and developing countries in 1990 and 2013

Table 3

	Years	Ischaemic stroke		Haemorrhagic stroke	
		Rate (95% UI)	Median % change 1990–2013 (95% UI)	Rate (95% UI)	Median % change 1990–2013 (95% UI)
Developing countries	1990	155.4 (148.6–161.5)	0.001 (–0.051; 0.065)	113.8 (110.0–117.8)	0.003 (–0.040; 0.049)
	2013	156.0 (149.3–164.6)		114.3 (110.3–118.0)	
Developed countries	1990	472.7 (446.0–500.1)	0.214 (0.140; 0.317)	93.3 (86.4–99.7)	0.372 (0.253; 0.521)
	2013	577.6 (558.7–600.4)		128.3 (121.1–135.9)	
Globally	1990	291.2 (278.7–303.8)	0.024 (–0.028; 0.091)	105.6 (102.0–109.2)	0.102 (0.054; 0.161)
	2013	299.1 (290.2–309.2)		116.6 (113.1–120.5)	

Table 4

Proportional (%) contribution of ischaemic and haemorrhagic strokes burden (with 95% uncertainty intervals [UI]) to all health conditions by year and country development status

	Metrics	Developing countries	
		1990	2013
Ischaemic stroke	DALYs	0.90 (0.75 – 1.04)	1.65 (1.32 – 1.87)
	Deaths	2.97 (2.55 – 3.42)	5.19 (4.20 – 5.72)
	YLDs	0.13 (0.10 – 0.16)	0.16 (0.12 – 0.21)
Haemorrhagic stroke	DALYs	2.14 (1.90 – 2.40)	2.79 (2.48 – 3.25)
	Deaths	5.22 (4.62 – 5.76)	6.40 (5.82 – 7.53)
	YLDs	0.10 (0.08 – 0.13)	0.13 (0.10 – 0.16)

	Metrics	Developed countries	
		1990	2013
Ischaemic stroke	DALYs	3.96 (3.42 – 4.48)	3.49 (3.06 – 4.12)
	Deaths	9.87 (8.64 – 10.82)	8.42 (7.65 – 10.03)
	YLDs	0.67 (0.51 – 0.84)	0.97 (0.75 – 1.22)
Haemorrhagic stroke	DALYs	2.59 (2.17 – 3.05)	2.07 (1.79 – 2.49)
	Deaths	4.55 (3.79 – 5.21)	3.82 (3.33 – 4.53)
	YLDs	0.13 (0.10 – 0.17)	0.21 (0.16 – 0.26)

	Metrics	Globally	
		1990	2013
Ischaemic stroke	DALYs	1.34 (1.16 – 1.52)	1.94 (1.64 – 2.18)
	Deaths	4.60 (4.02 – 5.12)	5.97 (5.16 – 6.52)
	YLDs	0.27 (0.20 – 0.34)	0.35 (0.26 – 0.44)
Haemorrhagic stroke	DALYs	2.20 (1.95 – 2.48)	2.68 (2.37 – 3.12)
	Deaths	5.06 (4.45 – 5.58)	5.78 (5.29 – 6.79)
	YLDs	0.11 (0.08 – 0.14)	0.14 (0.11 – 0.18)