

Stroke Prevalence, Mortality and Disability-Adjusted Life Years in Adults Aged 20–64 Years in 1990–2013: Data from the Global Burden of Disease 2013 Study

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Key Words

Stroke · Ischemic · Hemorrhagic · Young adult · Global trends · Prevalence · Deaths · DALYs

Abstract

Background: Recent evidence suggests that stroke is increasing as a cause of morbidity and mortality in younger adults, where it carries particular significance for working individuals. Accurate and up-to-date estimates of stroke burden are important for planning stroke prevention and management in younger adults. **Objectives:** This study aims to estimate prevalence, mortality and disability-adjusted life years (DALYs) and their trends for total, ischemic stroke (IS) and hemorrhagic stroke (HS) in the world for 1990–2013 in adults aged 20–64 years. **Methodology:** Stroke prevalence, mortality and DALYs were estimated using the Global Burden of Disease (GBD) 2013 methods. All available data on rates of stroke incidence, excess mortality, prevalence and

death were collected. Statistical models were used along with country-level covariates to estimate country-specific stroke burden. Stroke-specific disability weights were used to compute years lived with disability and DALYs. Means and 95% uncertainty intervals (UIs) were calculated for prevalence, mortality and DALYs. The median of the percent change and 95% UI were determined for the period from 1990 to 2013. **Results:** In 2013, in younger adults aged 20–64 years, the global prevalence of HS was 3,725,085 cases (95% UI 3,548,098–3,871,018) and IS was 7,258,216 cases (95% UI 6,996,272–7,569,403). 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 1,483,707 (95% UI 1,340,579–1,658,929) stroke deaths globally among younger adults but the number of deaths

Members of the GBD 2013 Stroke Panel Experts Group are listed in the Appendix at the end of the paper.

from HS (1,047,735 (95% UI 945,087–1,184,192)) was significantly higher than the number of deaths from IS (435,972 (95% UI 354,018–504,656)). 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. Death rates for all strokes among younger adults declined significantly in developing countries from 47 (95% UI 42.6–51.7) in 1990 to 39 (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. 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 those aged 20–64 years was 51,429,440 (95% UI 46,561,382–57,320,085). Globally, there was a 24.4% (95% UI 16.6–33.8) increase in total DALY numbers 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. **Conclusions:** Between 1990 and 2013, there were significant increases in prevalent cases, total deaths and DALYs due to HS and IS in younger adults aged 20–64 years. 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 in developing countries. Most of the burden of stroke was in developing countries. In 2013, the greatest burden of stroke among younger adults was due to HS. While the trends in declining death and DALY rates in developing countries are encouraging, these regions still fall far behind those of developed regions of the world. A more aggressive approach toward primary prevention and increased access to adequate healthcare services for stroke is required to substantially narrow these disparities.

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Introduction

The burden of stroke in young adults aged 20–64 years has recently come to greater attention with studies showing an increase in the incidence of stroke in young adults over the last 3 decades [1–3]. While accurate comparisons are difficult between studies due to varying age ranges used for ‘young stroke’, approximately 5–10% of strokes are thought to occur in people under the age of 50 years [4]. According to the Global Burden of Disease (GBD) 2010 estimates, young adults aged 20–64 years constitut-

ed 31% of incident strokes globally [5]. A systematic review of literature on young stroke (between 20 and 44 years) suggests that stroke in those younger than 45 years is not as uncommon as previously perceived with standardized incidence rates ranging from 8.7 to 21.0 per 100,000 [6]. Evidence suggests that changes in unfavorable lifestyle factors such as unhealthy diets high in sugar, salt and processed foods, smoking, alcohol intake, drug use and reduced levels of physical activity have led to the increased exposure to stroke risk factors in the young [7, 8]. A population-based study in the United States found an increase in the number of young people aged 18–54 years with stroke, and that over half of these were current smokers and 1 in 5 abused illegal drugs [9]. The long-term impact of stroke is large in younger adults due to the impact of lost healthy life years among working-age adults, given their contributions and responsibilities as wage-earners and care-givers. Therefore, estimating the extent of the burden and temporal trends in younger adults with stroke is of critical importance for measuring societal impact and for data-driven public health planning and resource allocation.

Methods

Stroke modeling and methods used to estimate all-cause mortality, stroke-specific mortality, disability and prevalence have been previously described [10, 11]. In brief, all available data on mortality were corrected for non-specific codes and used to estimate mortality rates for GBD causes of death, including ischemic stroke (IS) and hemorrhagic stroke (HS). An ensemble modeling method was used to estimate death rates by age, sex, year and country [12]. Disease prevalence was estimated using the DisMod-MR disease modeling software [13]. We used all available estimates of stroke incidence, prevalence and case fatality from systematic reviews of the scientific literature, population surveys and stroke registries as well as GBD mortality estimates. Disability due to acute stroke was considered to last for 28–30 days while chronic stroke lasted from 30 days until death. Disability-adjusted life years (DALYs) were calculated as the sum of years of life lost prematurely due to stroke and years lived with disability due to stroke. Countries were defined as developing or developed according to GBD methods.

Results

Prevalence

GBD 2013. Among adults age 20–64 years, the global prevalence of HS in 2013 was 3,725,085 (95% uncertainty interval (UI) 3,548,098–3,871,018) and prevalence of IS was 7,258,216 (95% UI 6,996,272–7,569,403; table 1). The

Table 1. Prevalent cases, deaths and DALYs in those aged 20–64 years between 1990 and 2013

	Year	Prevalence	95% UI	Death	95% UI	DALYs	95% UI
<i>HS</i>							
Developing	1990	1,450,240	1,391,277–1,510,464	716,996	636,079–797,977	25,688,495	22,803,083–28,597,621
	2013	2,665,770	2,521,485–2,789,120	935,939	839,444–1,060,482	32,834,364	29,352,075–37,133,284
Developed	1990	530,589	490,269–574,953	140,931	119,814–160,849	4,839,572	4,165,098–5,492,067
	2013	1,059,315	983,851–1,138,970	111,795	98,625–129,473	3,861,930	3,426,825–4,432,344
Global	1990	1,980,830	1,918,964–2,056,065	857,927	761,615–955,263	30,528,067	27,119,019–33,944,576
	2013	3,725,085	3,548,098–3,871,018	1,047,735	945,087–1,184,192	36,696,295	33,011,678–41,372,106
<i>IS</i>							
Developing	1990	1,724,774	1,632,729–1,810,733	225,925	181,026–266,063	7,573,447	6,058,331–8,960,467
	2013	3,214,108	3,033,261–3,446,309	356,408	280,551–414,875	11,769,652	9,345,527–13,601,182
Developed	1990	2,076,621	1,954,109–2,206,981	95,635	78,800–112,305	3,157,115	2,664,748–3,664,830
	2013	4,044,107	3,869,281–4,238,562	79,564	68,651–96,978	2,963,492	2,551,752–3,520,588
Global	1990	3,801,396	3,660,560–3,957,700	321,560	259,801–370,056	10,730,563	8,685,007–12,392,179
	2013	7,258,216	6,996,272–7,569,403	435,972	354,018–504,656	14,733,144	12,209,576–17,011,339

global prevalence rates were 90.3 (95% UI 86.0–93.8) and 176 (95% UI 169.6–183.5) per 100,000 for HS and IS, respectively.

Developing vs. Developed Countries. In 2013, the prevalence rate of HS was significantly higher in developed countries (130.1 (95% UI 120.8–139.9)) than in developing countries (80.5 (95% UI 76.2–84.2)). The prevalence rate of IS was also significantly higher (by about 5-fold) in developed countries (496.7 (95% UI 475.3–520.6)) compared to that in developing countries (97.1 (95% UI 91.6–104.1)). In 2013, the absolute number of prevalent HS cases in developed countries (1,059,315 (95% UI 983,851–1,138,970)) was 5-fold higher than that of IS (2,665,770 (95% UI 2,521,485–2,789,120)), with greatest differences seen in those aged 50–59 years. In contrast, the number of prevalent HS cases was similar or lower than prevalent IS across age groups in developing countries (table 1).

By GBD Regions. The highest prevalence rates of both IS and HS were seen in high-income regions of Asia Pacific, North America, East and Southeast Asia, in those aged 50–64 years. The lowest prevalence of HS was seen in North Africa and the Middle East, while the lowest prevalence of IS was seen Central Latin America, with lowest rates in those of age 20–29 years.

Trends 1990–2013. Globally, there were significant increases in both numbers of cases (table 1) and prevalence rates of both HS and IS between 1990 and 2013 (fig. 1). The number of prevalent HS cases increased significantly

in developing countries between 1990 (1,450,240 (95% UI 1,391,277–1,510,464)) and 2013 (2,665,770 (95% UI 2,521,485–2,789,120)). Similarly, the absolute number of prevalent IS cases also increased significantly in developing countries between 1990 (1,724,774 (95% UI 1,632,729–1,810,733)) and 2013 (3,214,108 (95% UI 3,033,261–3,446,309)). In developed countries, the number of prevalent HS cases increased from 530,589 (95% UI 490,269–574,953) in 1990 to 1,059,315 (95% UI 983,851–1,138,970) in 2013 while the number of prevalent IS cases increased significantly from 2,076,621 (95% UI 1,954,109–2,206,981) in 1990 to 4,044,107 (95% UI 3,869,281–4,238,562) in 2013.

The global prevalence of HS increased almost 2-fold from 1,980,830 (95% UI 1,918,964–2,056,065) cases in 1990 to 3,725,085 (95% UI 3,548,098–3,871,018) in 2013. There was a similar nearly 2-fold increase in IS from 3,801,396 (95% UI 3,660,560–3,957,700) cases in 1990 to 7,258,216 (95% UI 6,996,272–7,569,403) in 2013. In developed countries, the prevalence rate of HS increased significantly by 1.7-fold between 1990 (74.6 (95% UI 69.0–80.9)) and 2013 (130.1 (95% UI 120.8–139.9)). In developing countries, there was a smaller (1.1-fold) but significant increase in the prevalence rate of HS between 1990 (72.3 (95% UI 69.4–75.3)) and 2013 (80.5 (95% UI 76.2–84.2; fig. 1). The prevalence rate of IS also increased significantly in developed countries between 1990 (292.1 per 100,000 (95% UI 274.8–310.4)) and 2013 (496.7 per 100,000 (95% UI 475.3–520.6)), while in developing

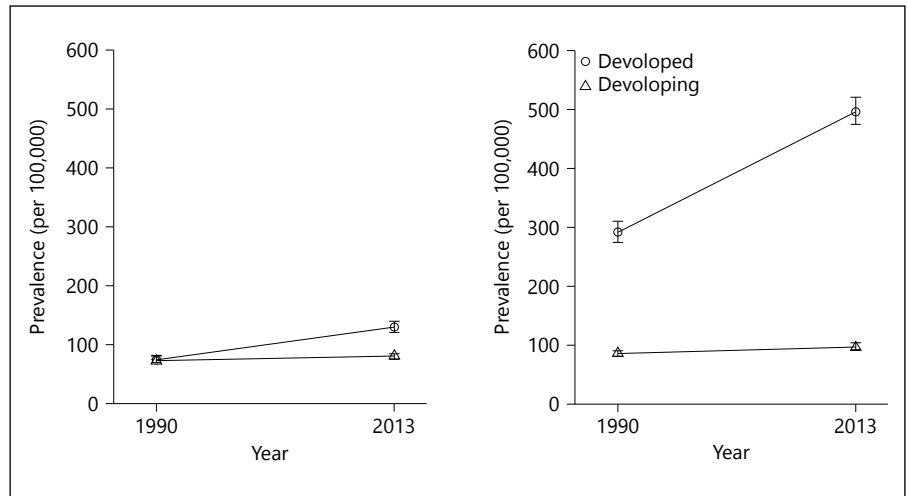


Fig. 1. Trends in prevalence rates for HS and IS between 1990 and 2013.

countries, the prevalence rate increased significantly from 86 (95% UI 81.4–90.3) in 1990 to 97.1 per 100,000 (95% UI 91.6–104.1) per 100,000 in 2013.

Deaths

GBD 2013. In 2013, there were 1,483,707 (95% UI 1,340,579–1,658,929) deaths due to stroke globally in those of age 20–64 years. The number of deaths from HS (1,047,735 (95% UI 945,087–1,184,192)) was significantly higher than the number of deaths from IS (435,972 (95% UI 354,018–504,656; table 1)).

Developing vs. Developed and by Region. The number of deaths as well the death rate was significantly higher in developing countries compared to developed countries (death rates 39 (95% UI 35.0–43.8) and 23.5 (95% UI 21.1–26.9) per 100,000) for developing and developed countries, respectively. The lowest death rates were in Australasia (Australia and New Zealand), and highest death rates were seen in South and East Asia, both for IS and HS, with the oldest individuals carrying the highest risk of stroke-related death.

Trends 1990–2013. Globally, there was a 25.6% (95% UI 17.7–35.2) increase in the number of prevalent stroke cases, with a 21.8 (95% UI 13.1–34.1) and 35.7% increase in HS and IS cases, respectively. However, there was a 20.1% (95% UI –23.6 to –10.3) decline in total stroke deaths in developed countries, particularly in the younger age groups (20–44 years) but a 36.7% (95% UI 26.3–48.5) increase in developing countries (fig. 2 and online suppl. appendix table 1; for all online suppl. material, see www.karger.com/doi/10.1159/000441098). Death rates for all strokes 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) per 100,000 in 2013. Death rates for all strokes showed a non-significant trend to decline in developing countries from 47 (95% UI 42.6–51.7) in 1990 to 39 (95% UI 35.0–43.8) per 100,000 in 2013 (fig. 3). A significant decrease in death rates was seen in HS and only in between 1990 (19.8 (95% UI 16.9–22.6)) and 2013 (13.7 (95% UI 12.1–15.9)) per 100,000. Increases in deaths in developing countries were seen particularly in those aged 45–64 years (fig. 3). Significant declines on mortality were seen in the high-income regions of Asia Pacific and other developed regions of the world, whereas increases in mortality were seen in African regions and Oceania across all age groups (fig. 4).

DALYs

GBD 2013. In 2013, total DALYs from all strokes in those aged 20–64 years was 51,429,440 (95% UI 46,561,382–57,320,085). The number of DALYs from HS (36,696,295 (95% UI 33,011,678–41,372,106)) was significantly higher than the number of DALYs from IS (14,733,144 (95% UI 12,209,576–17,011,339)).

Developing vs. Developed and by Region. Total DALYs were significantly higher by 6.5-fold in developing countries (44,604,017 (95% UI 40,099,464–49,788,189)) compared to developed countries (6,825,422 (95% UI 6,161,482–7,716,733; table 1)). DALY rates were also significantly higher in developing countries compared to developed countries. In developing countries, total DALYs and DALY rates were significantly higher for HS (991.8 (95% UI 886.6–1,121.6)) compared to IS (355.5 (95% UI 282.3–410.8)), while no significant difference was seen between HS and IS rates in developed countries. The lowest DALY rates were in Australasia and highest in East

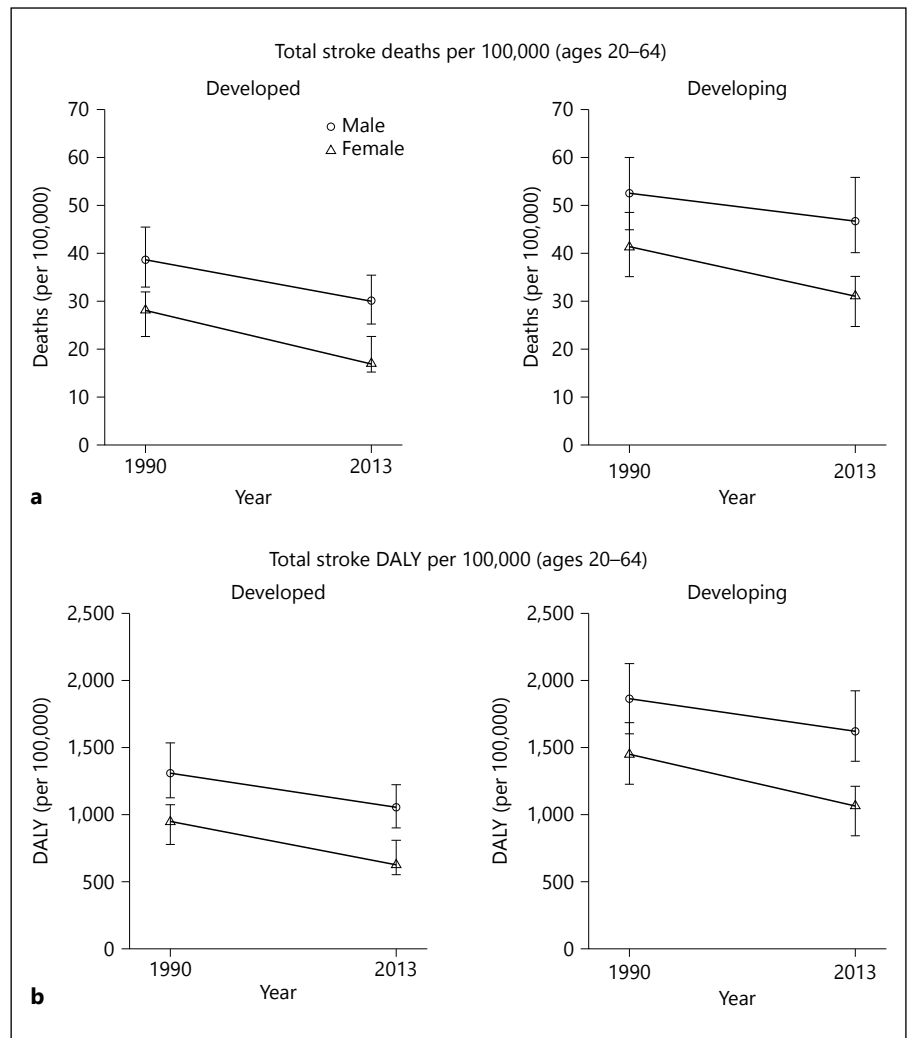


Fig. 2. Trends in death (a) and DALY (b) rates between 1990 and 2013.

Asia, both for IS and HS. The highest rates for both stroke types were in the age group of 60–64 years (fig. 4).

Trends 1990–2013. Globally, there was a 24.4% (95% UI 16.6–33.8) increase in total DALY numbers, 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. In developed countries, there was a 15.3% (95% UI –19.3 to –7.1) decline in total DALYs while there was a 33.9% (95% UI 23.8–45.4) increase in developing countries. DALY rates declined significantly in developed countries from 1,124.7 (95% UI 1,013.1–1,242.6) in 1990 to 838.4 (95% UI 756.8–947.9) in 2013 (fig. 2 and online suppl. appendix table 1). DALY rates also declined in developing countries but this change was not significant. HS and IS DALY rates decreased in developing countries by 27.6% (95% UI 17.6–40.8) and 56.2% (95% UI 33.5–77), respectively, while HS and IS DALY rates decreased by 20.6% (95% UI –26.5 to –10.6)

and 7% (95% UI –17.8 to 10.0), respectively, in developed countries. Increases in DALYs were seen particularly in those aged 45–64 years in developing countries (fig. 3).

Discussion

The risk of strokes in adults aged 20–64 years is lower than that in older adults, but the societal impact is high due to the greater number of years of life lost and the resulting loss in productivity [14]. This study provides global estimates of stroke burden in terms of prevalence, deaths and DALYs in those aged 20–64 years by stroke type. In 2013, the burden of stroke in adults aged 20–64 years was high, with almost 11 million living with stroke and almost 1.5 million deaths from stroke, contributing to over 51 million DALYs. This represents almost half of

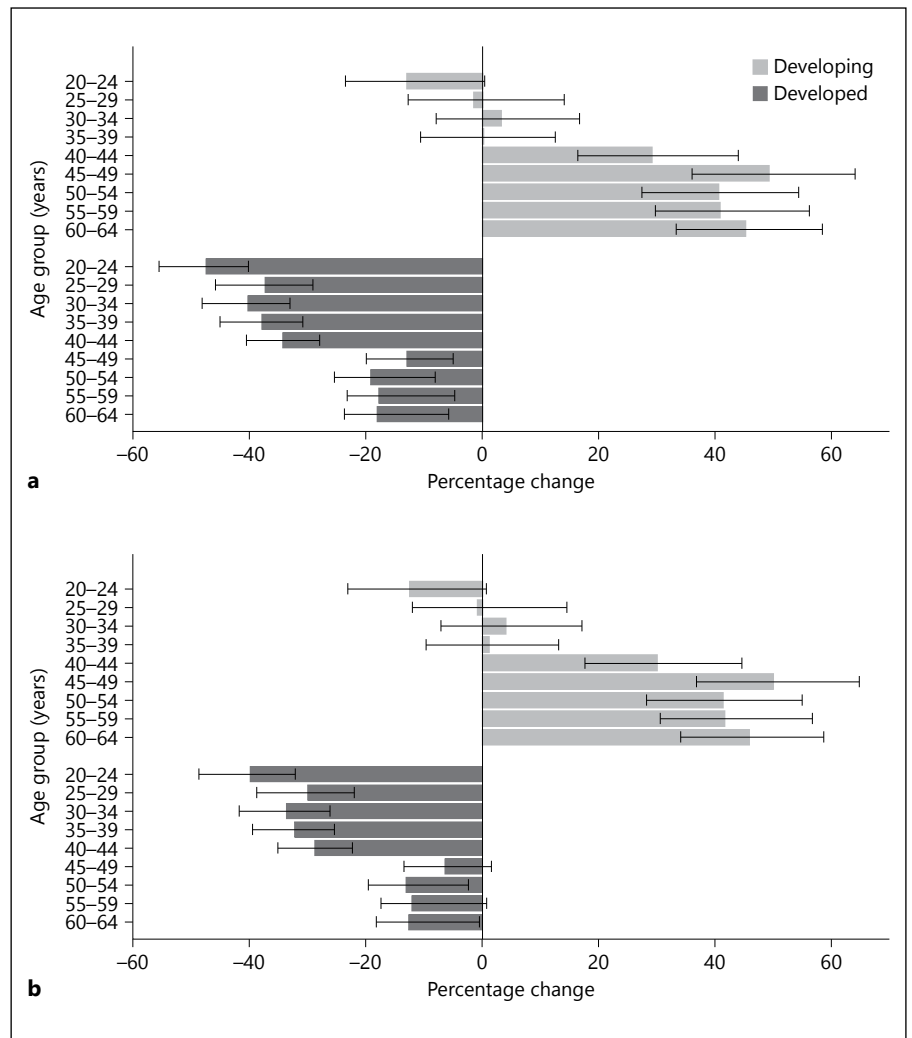


Fig. 3. Percentage change in death (a) and DALYS (b) between 1990 and 2013 by age group.

the total DALYS from stroke [10]. Significant increases were seen between 1990 and 2013 in the total numbers of prevalent HS and HS as well as total deaths and DALYS for this age group. Disparities were also found in trends of stroke burden between developing and developed countries, as death and DALY rates of stroke were significantly higher in developing countries than those in developed countries, and their rates declined significantly in developed countries but not in developing countries. Most of the burden of stroke was in developing countries, and due to HS in terms of the number of prevalent strokes, deaths and DALYS. The greater global burden of HS is likely due to greater burden of HS in developing countries where the burden of stroke is the largest.

There have been several reports of increasing stroke incidence in younger adults [1, 2, 15], although the differing age ranges used to define this age group make it dif-

ficult to compare studies [16]. Nonetheless, our data show that the overall burden of stroke in younger adults is increasing globally, with significant increases in absolute numbers of young people living with stroke and a disproportionate burden in developing countries. This has implications for healthcare and management resources, as well as plans for preventative measures to reduce this burden [17, 18].

It is also important to consider the etiological origins of stroke in young adults. The relative importance of modifiable risk factors may differ in young adults [19, 20] with cervical artery dissection [21] and cardioembolic [7] strokes known to be prominent causes of IS in younger adults and other less common etiologies such as patent foramen ovale, illicit drug use, migraine and oral contraceptives [8, 22] playing an important role in this age group. Antiphospholipid antibodies have also been

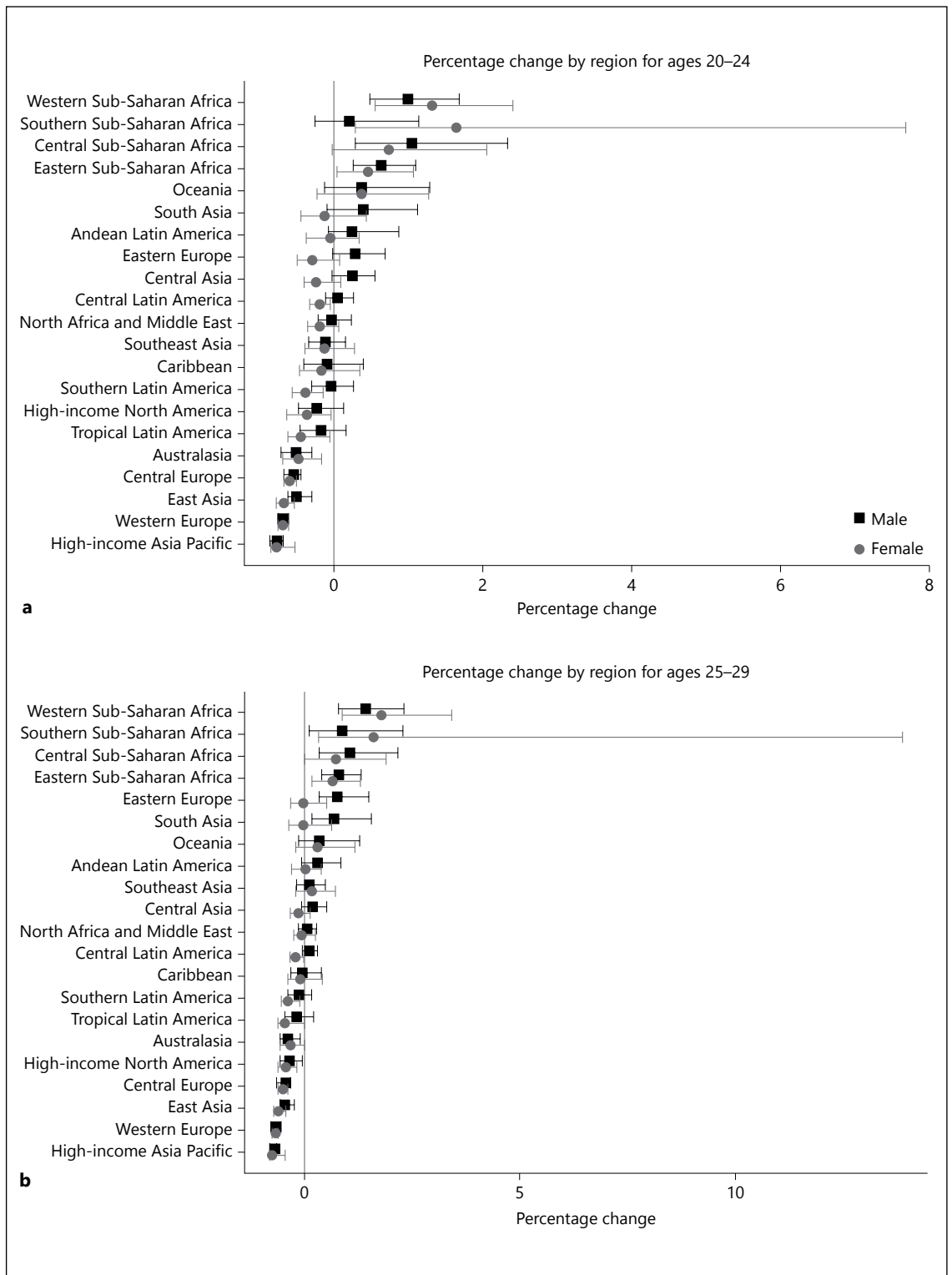
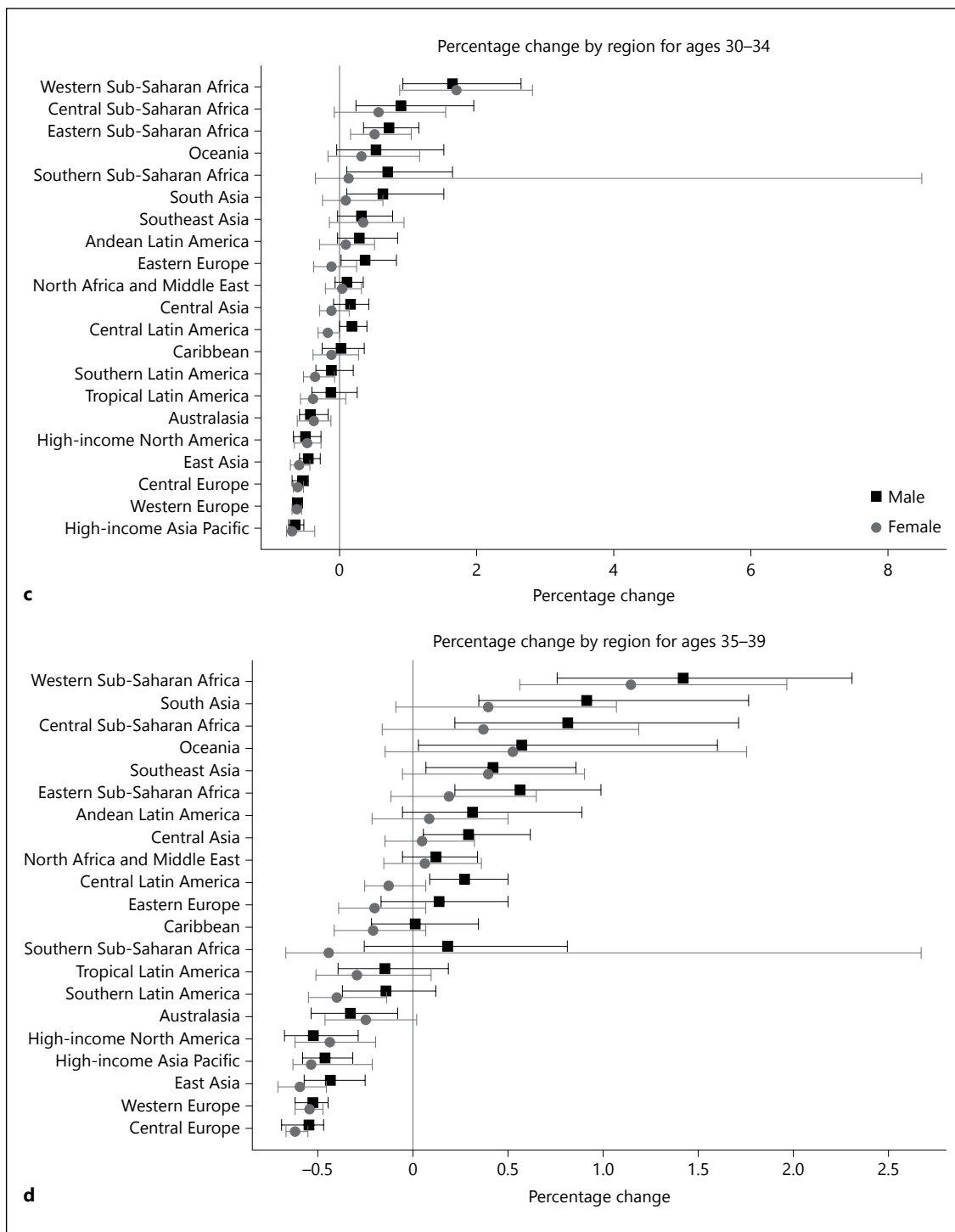


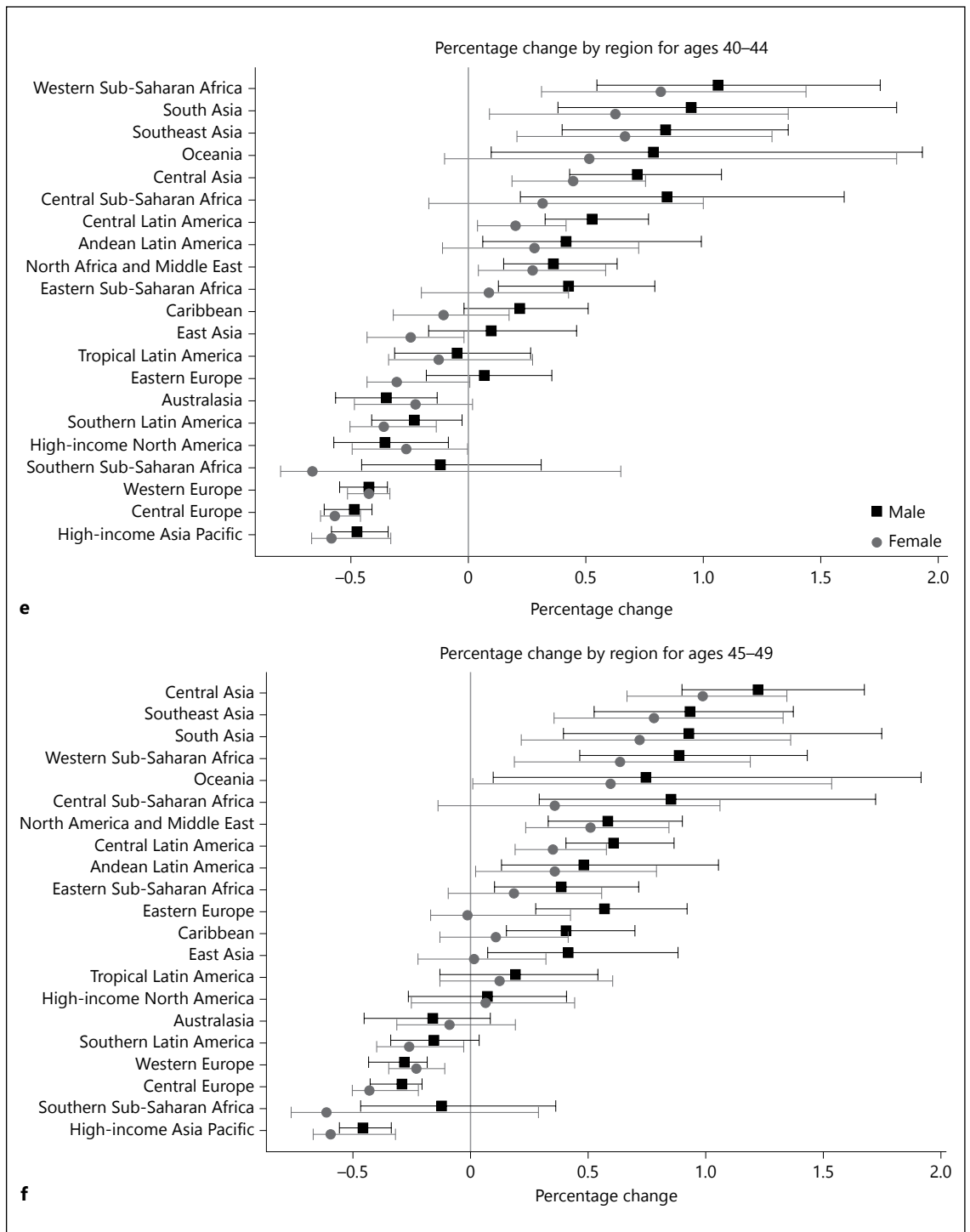
Fig. 4. a–i Percentage change in total stroke mortality by GBD region and age group.

(For figures 4c–i see next pages.)



shown to be an independent contributor to stroke [23], with evidence suggesting it may be a more important mechanism in young adult stroke than in the older stroke population [24]. The risk and outcomes of stroke are also likely to vary across regions of the world due to differing

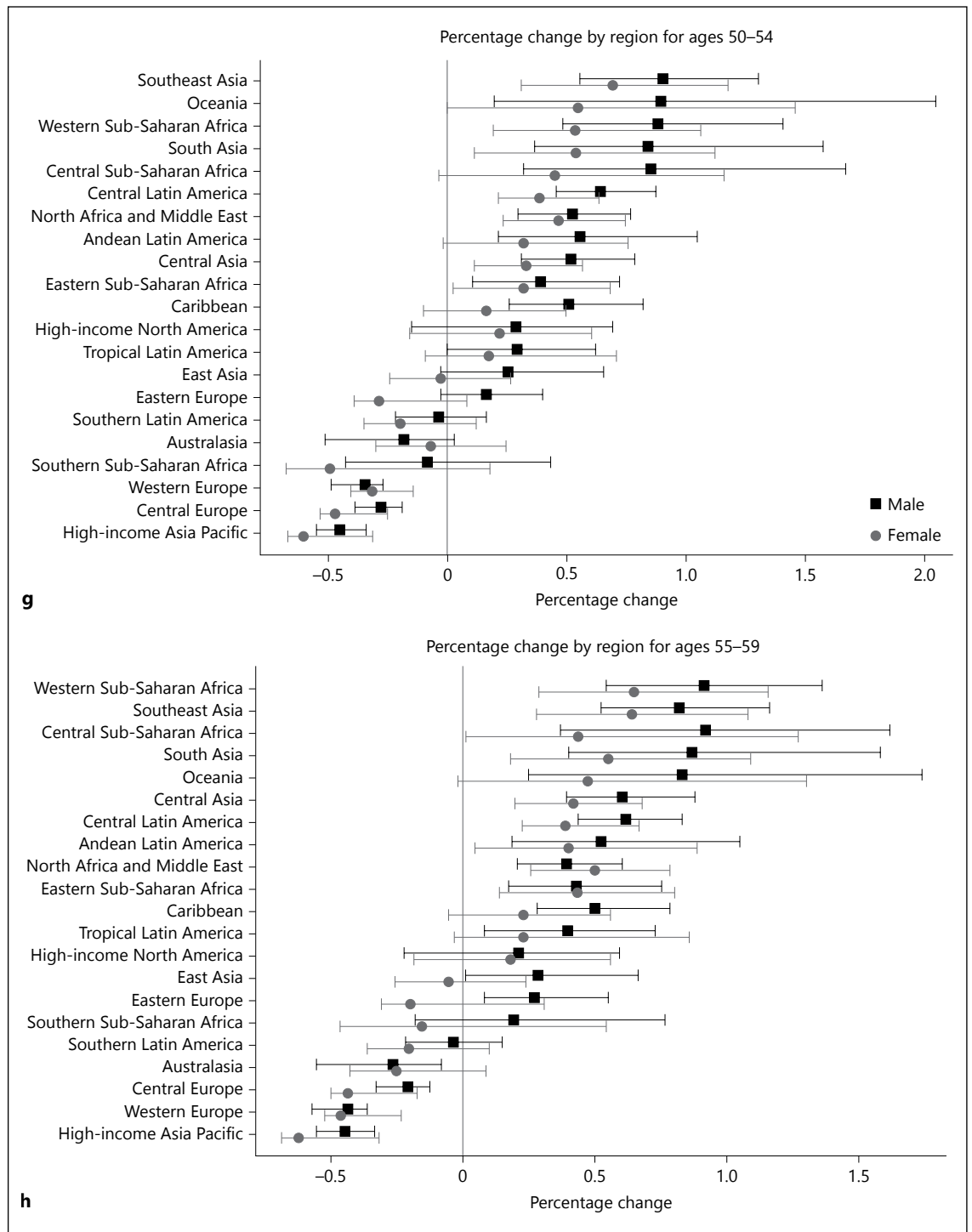
environmental and genetic factors as well as varying levels of access to healthcare services [8]. Ethnic and racial differences may be important in early-onset stroke, with studies in the United States showing higher incidence of stroke and higher stroke mortality in those of Black



race compared to White race aged 20–45 years [14]. The incidence of Moyamoya disease was shown to peak in a Chinese population at the age of 25–44 years [25].

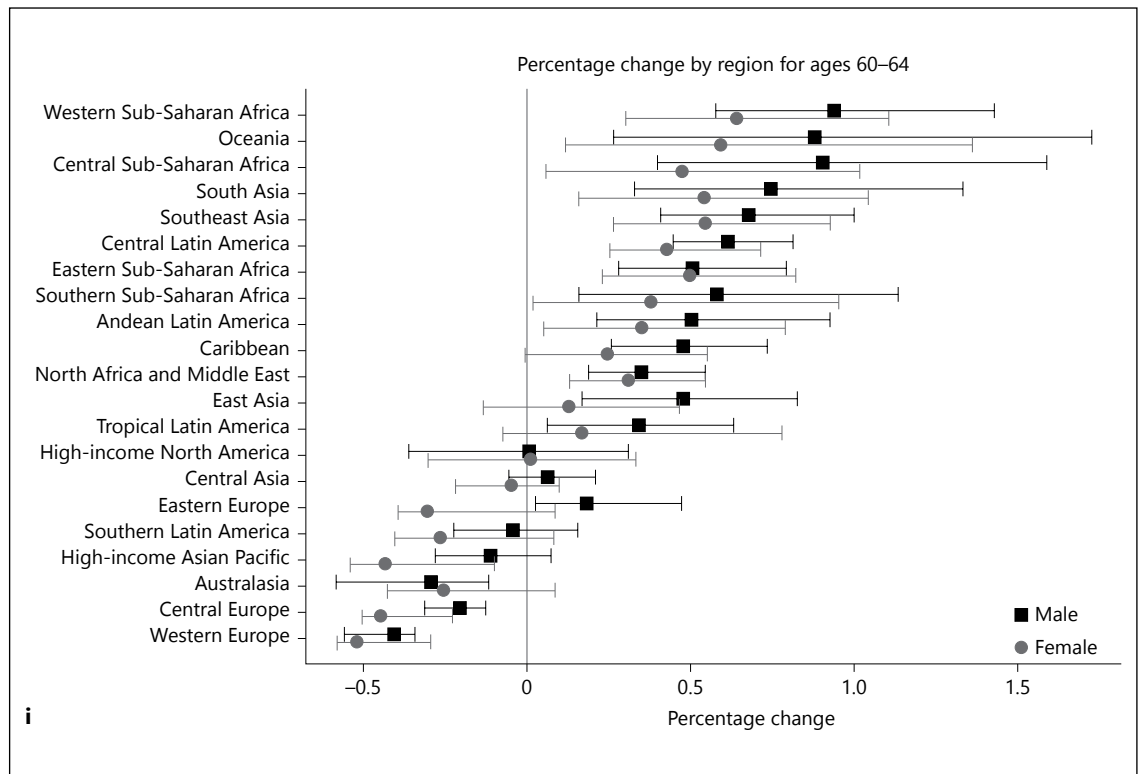
However, recent evidence suggests that there is also an increasing association of stroke in younger adults with

the prevalence of traditional vascular risk factors such as hypertension, diabetes and obesity [2]. The significant decline in death and DALY rates in developed countries may be the result of improved blood pressure control, acute care (e.g. stroke units, thrombolysis), increased



levels of neuroimaging leading to improved diagnosis and improvements in rehabilitation and chronic care [26–28]. For example, in a study of the safety and efficacy of thrombolysis in stroke patients of age 18–50 years, the prevalence of conventional stroke risk factors was high

–27% had hypertension, 6% had diabetes and 21% had hyperlipidemia [29]. In the multinational European Young Fabry Patients cohort of young adults aged 18–55 years, 55% were smokers, 48% were physically inactive, 46% had hypertension and 35% had dyslipidemia [30]. The



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prevalence of risk factors has also been shown to differ between regions and ethnic groups. For example, hyperlipidemia and smoking appear to be the most common risk factor in young Chinese adults [31], while hypertension and diabetes are more prevalent in Black Americans [14]. The increased prevalence of modifiable risk factors for stroke may be a contributing factor to the increase in the proportion of younger adults experiencing stroke.

There are limitations to this analysis, which have been described previously [10, 11]. Some country level data for young adult stroke was extrapolated from data from sub-national regions, particularly in developing countries. Low-income countries are more likely to have missing data, due to lack of population-based studies, particularly in this younger age group. More data are needed on estimates of first-ever in a lifetime and recurrent incidence of stroke to provide a more complete picture of stroke burden and adequately gauge the success of prevention strategies in different regions of the world. While estimates of incidence were not available in the current study, these will be important outputs planned for the GBD 2015 Study. A major strength of this study was the use of consistent methods to enable comparison between subtypes of stroke, both with global and regional estimates. The production of estimates for all 5-year age categories al-

lows us to report global estimates for the important category of younger adults with stroke.

The trend toward declining death and DALY rates developing countries is highly encouraging, but developing regions are still far behind compared to developed regions, in terms of gains in reducing overall stroke burden in the past 30 years. New strategies are needed to improve stroke surveillance efforts within lower income countries and support further efforts to estimate stroke burden for important subpopulations such as younger adults. These population-level estimates can encourage data-driven public health planning. Overall, improvements in acute and post-stroke care as well as continued investments in the reduction of traditional risk factors will be needed to reduce the burden of stroke in younger adults, particularly in developing countries.

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Contributions

R.K. wrote the first draft of the report. G.A.R. reviewed the first draft. V.L.F., G.A.R. and C.M. developed the study concept and oversaw the research. V.L.F., R.K. and G.A.R. undertook reviews of studies. M.H.F., M.N. and P.P. provided statistical analysis of the data and S.T. produced the graphs. M.H.F., M.N. and C.M. 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.

Disclosure Statement

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

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Disclaimer

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, National Institute of Mental Health, National Institutes of Health or the US Department of Health and Human Services.

Appendix

GBD Stroke Panel Experts Group (in Alphabetical Order by Country)

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