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GLOBAL, REGIONAL, AND COUNTRY-SPECIFIC LIFETIME RISK OF STROKE, 1990–2016

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Abstract

Background: Lifetime stroke risk has been calculated in a limited number of selected populations. We determined lifetime risk of stroke globally and at the regional and country level.

Methods: Using Global Burden of Disease Study estimates of stroke incidence and the competing risks of non-stroke mortality, we estimated the cumulative lifetime risk of ischemic stroke, hemorrhagic stroke, and total stroke (with 95% uncertainty intervals [UI]) for 195 countries among adults over 25 years) for the years 1990 and 2016 and according to the GBD Study Socio-Demographic Index (SDI).

Results: The global estimated lifetime risk of stroke from age 25 onward was 24.9% (95% UI: 23.5–26.2): 24.7% (23.3–26.0) in men and 25.1% (23.7–26.5) in women. The lifetime risk of ischemic stroke was 18.3% and of hemorrhagic stroke was 8.2%. The risk of stroke was 23.5% in high SDI countries, 31.1% in high-middle SDI countries, and 13.2% in low SDI countries with UIs not overlapping for these categories. The greatest estimated risk of stroke was in East Asia (38.8%) and Central and Eastern Europe (31.7 and 31.6 %%), and lowest in Eastern Sub-Saharan Africa (11.8%). From 1990 to 2016, there was a relative increase of 8.9% in global lifetime risk.

Conclusions: The global lifetime risk of stroke is approximately 25% starting at age 25 in both men and women. There is geographical variation in the lifetime risk of stroke, with particularly high risk in East Asia, Central and Eastern Europe.

Introduction

Stroke accounts for almost 5% of all disability-adjusted life years (DALYs)[1] and 10% of all deaths worldwide,[2] with the bulk of this burden (over 75% of deaths from stroke and 81% of DALYs) falling on low- and middle-income countries.[3] The total global burden of stroke is increasing[1-3] and prevention of stroke may require an improved understanding of risk among younger individuals. Stroke prevention strategies in low and middle income countries may differ from those adopted for high-income countries due to differences in access to health care, health technologies and relative rates of stroke risk factors.[4]

Estimates of lifetime risk, the cumulative probability of someone of a given age and sex developing a disease during their remaining lifespan after accounting for competing mortality, provide a measure of disease risk.[5] Lifetime stroke risk estimates may be useful for long-term health system planning.[6] In addition, estimates of the lifetime risk of stroke across the age spectrum on a national level may serve as a useful summary metric for gauging the impact of stroke prevention strategies.

There are limited data on trends in the lifetime risk of stroke. Prior estimates of lifetime stroke risk have been reported in a limited number of selected populations[6-12]. Diverging trends in stroke incidence and mortality rates have been observed between developed (decreasing) and developing countries (increasing),[13] against a background of increasing life expectancy for almost all countries.[14]

We used Global Burden of Disease (GBD) 2016 study estimates to provide global, regional, and country-specific lifetime risk of stroke in 1990 and 2016 by pathological subtype, age, sex and Socio-Demographic Index (SDI), accounting for competing risk of mortality due to all other non-stroke causes of death. The GBD is an ongoing global collaboration that uses all available epidemiological data to provide a comparative assessment of health loss across 328 causes for 195 countries and territories.

Methods

We used estimates from the GBD 2016 study[1, 2,] of first-ever-in-a-lifetime stroke, cause-specific mortality, and all-cause mortality at the global, regional (21 GBD regions nested within 7 GBD super-regions), and national (195 countries) levels by age and sex (see Supplement Table 1 and Supplement Table 2). Analysis was performed separately for ischemic stroke and hemorrhagic stroke (intracerebral hemorrhage and non-traumatic subarachnoid hemorrhage). The GBD 2016 study used all available representative population-based data on incidence, prevalence, case fatality and mortality to produce comparable estimates of disease burden for 195 countries, by sex and 5-year age categories. Mortality was estimated using the Cause of Death Ensemble Model, which produces cause-specific smoothed mortality cause fractions over time using vital registration and verbal autopsy data as well as country-specific covariates. Incidence was estimated using DisMod-MR, a Bayesian meta-regression disease modelling tool. Details of the methods used to estimate stroke incidence and mortality have been previously published and are summarized in the Supplement.

Countries were categorized by quintiles of the GBD SDI for the year 2016.[15] SDI is a composite indicator of development similar to the Human Development Index.[16] SDI uses as input country-level income per capita, average educational attainment among individuals over age 15, and total fertility rate.

We estimated lifetime risk at a given age as the cumulative risk of stroke occurrence during the remaining lifetime, assuming the rates of stroke incidence, prevalence, and stroke mortality in each following 5 year age category. In this way, risk at each age represents the risk of stroke from that age onwards, conditional on survival to that age without having died or having had a nonfatal stroke. Further details of this method are provided in the Supplement. To account for the competing risks of stroke and mortality within a specific age group, we calculated the probability of stroke-deleted mortality and experiencing a stroke, then scaled the separate event probabilities to match the combined probability of having either a stroke or dying in an age group.

We calculated the lifetime risk only for people aged 25 years and older because stroke incidence rates in younger people are low and are less dependent on the modifiable risks and health systems that determine stroke burden in older populations.

Uncertainty intervals were the 2.5th and 97.5th percentile of the distribution for each estimate. Significance was reported when uncertainty intervals did not overlap.

Results

Global, regional, and national lifetime risk of stroke in 2016

In 2016, the lifetime risk of stroke globally was 24.9% (95% UI: 23.5–26.2), with large regional and between-country differences (Table 1, Supplement Table S3). The highest risk was estimated in China (39.3% [37.5–41.1]) with similarly high levels in Latvia, Bosnia and Herzegovina, Romania, Montenegro, Russia, Macedonia, and Bulgaria. Among the 21 GBD regions, East Asia (38.8% [37.0–40.6]), Central and Eastern Europe (31.7% [95% UI: 30.0–33.3] and 31.6% [95% UI: 27.6–35.6], respectively) had the highest risk, and Eastern Sub-Saharan Africa (11.8% [95% UI: 10.9–12.8]) had the lowest risk. The risk was greatest in high-middle (31.1% [29.0–33.0]) and middle SDI countries (29.3% [27.8-30.8]), and lowest in low SDI countries (13.2% [12.3–14.2]).

Contribution of Non-Stroke Mortality to Lifetime Risk of Stroke

Supplement Figure S1A-C and Supplement Table S5 show the hypothetical national lifetime stroke risk if all countries experienced the average non-stroke mortality rate of high SDI countries. In such a counterfactual scenario, the lifetime risk of stroke is no longer lowest in sub-Saharan Africa. The largest increases in lifetime risk of stroke due to decreased non-stroke mortality in this hypothetical scenario were in Oceania (from 16% to 30%), sub-Saharan Africa (from 12 to 22%), and South Asia (from 15 to 21%). Smaller increases were seen for other low and middle-income countries, reflecting geographic variation in competing non-stroke mortality as a major determinant of lifetime stroke risk (Supplement Figures S9A-R).

Lifetime risk by sex, age, and stroke type

In 2016, the lifetime risk of stroke in men (24.7% [95% UI 23.3–26.0]) globally was not significantly different than in women (25.1% [23.7–26.5]) (Table 1), but there were regional (Table 1; Figure 1; Supplement Figures S10A and S10B) and between-country differences in sex-specific risk. The greatest risk in men was in China (41.1% [39.2–42.9]) where there was also the largest difference between men (41.1% [39.2-42.9]) and women (36.7% [35.0-38.6]). Latvia had the greatest risk in women (41.7% [37.7–45.4]) with similar levels in Russia, Montenegro, Romania, Bosnia and Herzegovina, Lithuania, Macedonia, Bulgaria, Ukraine,

Slovakia, Albania, Serbia and Belarus. Among 21 GBD regions, the highest lifetime risk in men (Table 1; Supplement Figure S2B) was in East Asia (40.6% [38.7-42.3]), while in women (Supplement Figure S2C) the highest risk was in both Eastern Europe (36.5% [31.2-41.9]) and East Asia (36.3% [34.5-38.1]).

The risk was significantly higher in women than men in Central Latin America, Southern and Western Sub-Saharan Africa, North Africa and Middle East, South Asia, and Central Europe. The lifetime risk of hemorrhagic stroke showed less variation by sex than ischemic stroke. The lifetime risk of ischemic stroke was about two times higher than the risk of hemorrhagic stroke in both men and women across different regions (Table 1) and SDI level quintiles (Supplement Table S6).

In 2016, the lifetime risk of total stroke was not significantly different between age 25 (24.7% [23.3-26.0]) and 70 years (22.6% [21.0-24.1]) in men, and women (25.1% [23.7-26.5] and 22.3% [20.6-23.9], respectively) (Supplement Figures S11A and S11B; Supplement Table S7). After age 70, the remaining lifetime risk decreased, reaching 13.4% (11.8–15.1) for adults aged 95 years (Figure 2).

Similar age patterns in lifetime risk were apparent for both ischemic and hemorrhagic strokes across all SDI geographies, with less decline with ageing for hemorrhagic stroke in low-middle and low SDI countries. (Supplement Figures S4-S8). The lifetime risks for ischemic and hemorrhagic separately add up to more than the total risk for all stroke because total risk is inclusive of both subtypes and represents the risk of getting either an ischemic or hemorrhagic stroke.

Differences for lifetime risk in 1990 and 2016

Globally from 1990 to 2016, there was a significant increase in the average lifetime risk of stroke from 22% to 24%, a relative increase of 9% (Table 1; Supplement Table S4). The relative increase in the risk was greater for men (15.4% [12.5-18.2]) than women (3.2% [0.2-6.1]), and for ischemic stroke (12.7% [8.9, 16.3]) than hemorrhagic stroke (4.0% [0.2, 7.6]). There was a significant increase in risk in Western and Eastern Sub-Saharan Africa, North Africa and Middle East, Central Europe, East Asia, South Asia and Southeast Asia. There was a significant reduction in risk in Central Asia, Southern and Tropical Latin America, high-income Asia Pacific, and Southern Sub-Saharan Africa. There were no significant changes estimated in the remaining GBD regions.

Discussion

The global lifetime risk of stroke from age 25 onward is estimated to have increased from 22% to 24% over the past three decades, with the risk of ischemic stroke exceeding the risk of hemorrhagic stroke (18% vs 8%, respectively). This increase in risk is the result of flat or increasing stroke incidence in many middle-SDI regions with simultaneous declines in the competing risks of non-stroke mortality.

The estimated global lifetime risk of stroke declined with age, due to age-related competing risks from other diseases. In low SDI countries with the youngest populations, such as Sub-Saharan Africa, estimated lower lifetime stroke risk is the result of high competing risk of mortality at both young and old ages and does not represent substantially lower stroke incidence or more effective prevention and treatment strategies.[17, 2,] In contrast, we estimated the highest estimated lifetime stroke risks are found in East Asia, Central and Eastern Europe.

Many of our national estimated lifetime stroke risks are similar or higher compared to what was observed for specific populations in the same country, including the Framingham Heart cohort (21.1% for women and 16.9% for men),[18] in a Japanese cohort (18.9% for men and 20.2% for women),[8] and in a Chinese cohort (18.0% for men and 14.7% for women).[7] Our estimates are lower than that for women in the Netherlands (29.8%) but similar to estimates there among men (22.8%).[9] We estimated ischemic stroke to be more frequent than hemorrhagic stroke which is comparable to the findings of other population-based studies.[6, 8, 12, 13. 19]

Regional variation in lifetime cardiovascular risk across subpopulations has been shown previously by the Cardiovascular Lifetime Risk Pooling Project, and support our finding of large geographic variation in total stroke risk.[10] The greater increase in the lifetime risk of ischemic stroke compared to hemorrhagic stroke from 1990 to 2016 may be related to reduction in the incidence of hemorrhagic stroke as opposed to minor increases in the incidence of ischemic stroke over the last two decades.[3] Although our findings of similar lifetime risk of stroke in men and women are in concordance with some other observations, there have been studies [8-10, 19] in which the risk was greater in women compared with that in men, and the reasons for these differences between studies is unclear. The Global Burden of Disease Study Comparative Risk Assessment [4, 20] estimated that elevated blood pressure was the leading attributable risk for stroke across all levels of the SDI, with greater attribution to

air pollution and low fruit intake in low-SDI countries and high body-mass index and high fasting plasma glucose in high-SDI countries.

Estimates of lifetime risk of a disease is new for the GBD study, which has previously published several other summary measures of health including years of life lost prematurely, years lives with disability,[3, 21] and stroke burden associated with various risk factors.[4] Lifetime risk may be useful for stroke prevention and public education. High estimates of lifetime risk of stroke suggest the possible value of intensive primary stroke prevention measures throughout the lifespan and suggest that strategies to reduce cardiovascular risk remain relevant for both younger and older adults.

The main strength of our study was that we systematically evaluated the lifetime risk of using data and methods that allow for comparable estimates between location and over time. We provided estimates of the lifetime risk of stroke for people aged 25 years and over (up to age 95) as opposed to stroke lifetime risk estimates from other studies, where the risk of stroke was estimated for people aged 45 or over.[6,8-10] Furthermore, our lifetime stroke risk estimates account for competing risk of mortality from other causes of death and represent whole populations, adding to the generalizability of these results.

Our approach has limitations. The accuracy of lifetime stroke risk estimates was limited by the accuracy and availability of epidemiological data from the countries studied. There was still lack of sufficient epidemiological data on stroke incidence and case fatality for most countries of the world. In countries without data on stroke incidence, estimates were dependent on geospatial statistical models incorporating data from neighboring countries and country-level risk exposure data, which is widely available. The ability to differentiate stroke from other acute neurological events and to differentiate ischemic from hemorrhagic strokes was impeded by the nature of health system in each country, by the technology available to diagnose strokes, and the customary manner of coding disease entities. We did not differentiate risk due to subarachnoid hemorrhage and intracerebral hemorrhage, which were combined as an estimate of total hemorrhagic stroke. There is significant subnational variation in stroke burden within large countries and our results represent only average national risk. Standard error was increased using a standard algorithm when data from subnational regions were used to represent an entire country. Finally, we analyzed only the lifetime risk of first-ever stroke and not recurrent stroke.

In conclusion, our study provides comprehensive global, regional, and country-specific estimates of the lifetime risk of stroke by sex, age, with imprecision introduced by limited data in many countries. The global lifetime risk of stroke is approximately 25% starting at age 25 in both men and women and there is large geographical variation, with particularly high lifetime risk in East Asia, Central and Eastern Europe.

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

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Disclosures

None of the other authors has competing financial interests.

Authors' contributions

VLF prepared the first draft. GN, GR and CJLM developed the lifetime stroke risk formula. GR analyzed data and reviewed and edited the first draft and final versions of the manuscript. KC analyzed data and prepared maps and figures. PP prepared tables. VLF, GR, and CJLM reviewed all drafts, finalized the draft, and approved the final version of the manuscript. All other authors provided key contributions to data, methods, or analysis, reviewed the manuscript, and approved the final version of the manuscript.

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Figure Legends

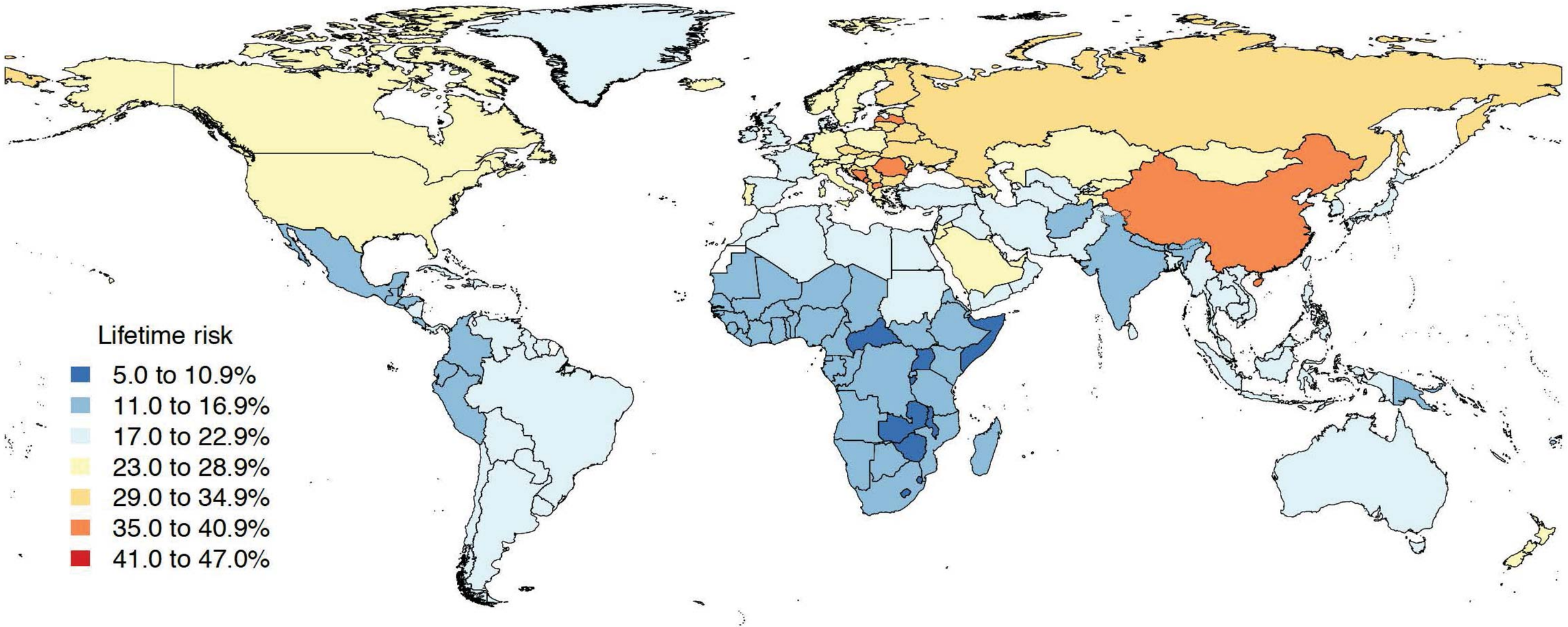
Figure 1: Global map showing lifetime risk of stroke occurrence (in %), both sexes combined, 2016.

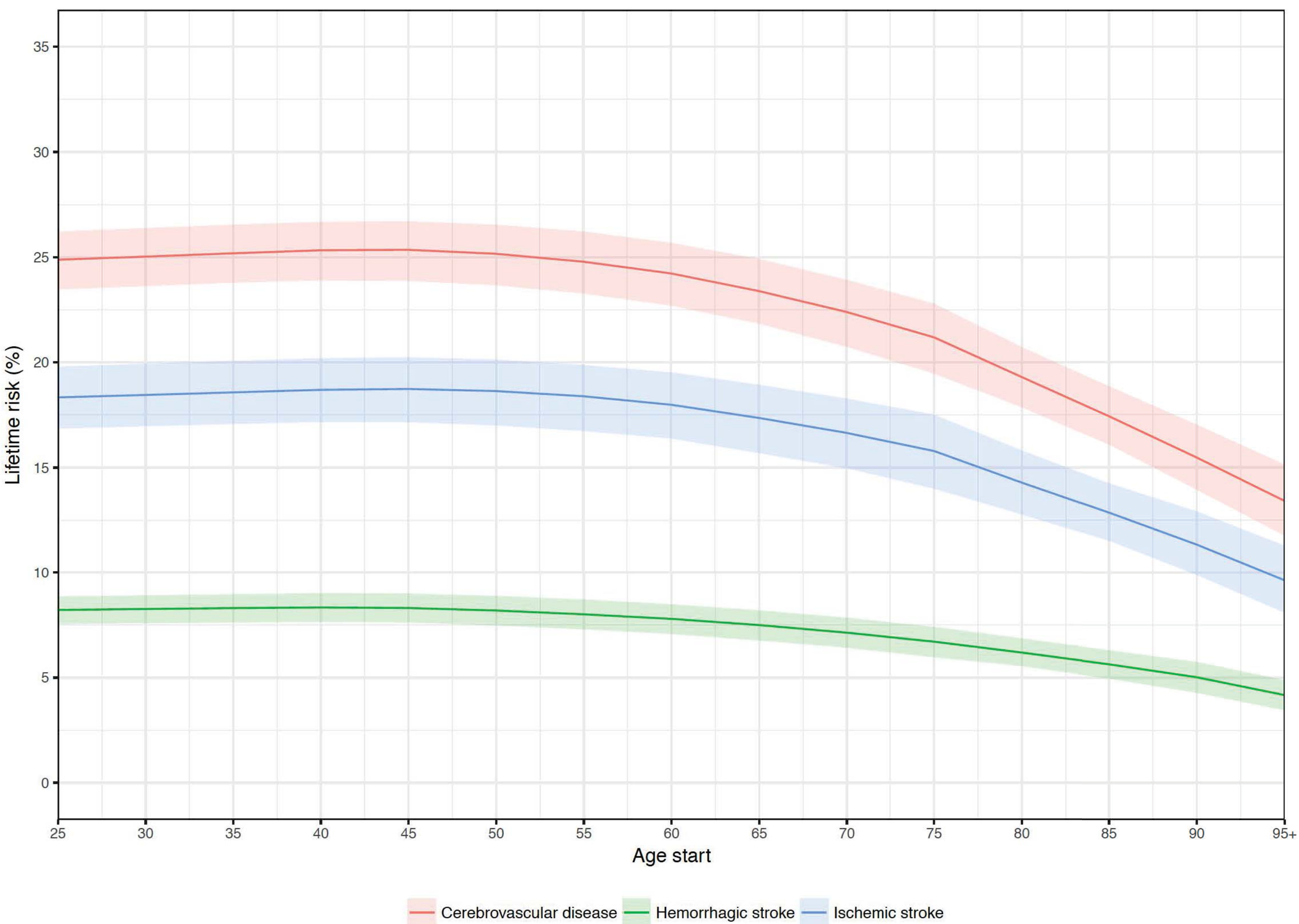
Figure 2. Global remaining lifetime risk of stroke occurrence (in % with 95% UI) by pathological types, age, and sex, 2016.

Relationship between lifetime risk of stroke and age. Each colored line represents a trend of the relationship for the specified pathological type. The 95% confidence interval is within the shaded region surrounding each line. Modeled age starts at 25.

Table 1. Lifetime risk of stroke (LTR in %) (with 95% UI) globally and regionally (21 GBD regions and 7 super regions) in 2016 and its percentage change (with 95% UI) from 1990 to 2016 by pathological type of stroke and sex

GBD super regions	GBD regions	Men		Women		Both sexes	
		LTR (95% UI)	Percentage change (95% CI) 1990-2015	LTR (95% UI)	Percentage change (95% CI) 1990-2015	LTR (95% UI)	Percentage change (95% CI) 1990-2015
Global		24.7 (23.3,26.0)	15.4 (12.5, 18.2)	25.1 (23.7, 26.5)	3.2 (0.2, 6.1)	24.9 (23.5, 26.2)	8.9 (6.2, 11.5)
High-income	Southern Latin America	17.8 (16.3, 19.3)	-14.2 (-20.4, -7.6)	20.6 (18.9, 22.3)	-14.5 (-20.7, -8.4)	19.2 (17.8, 20.5)	-14.1 (-19.0, -8.7)
	Western Europe	22.2 (20.9, 23.4)	4.2 (0.3, 8.2)	23.3 (21.9, 24.6)	-4.3 (-7.9, -0.4)	22.7 (21.4, 23.9)	-0.4 (-3.6, 3.1)
	High-income North America	22.4 (21.1, 23.7)	4.9 (1.7, 8.7)	25.1 (23.6, 26.4)	0.5 (-2.8, 3.8)	23.8 (22.4, 25.0)	2.7 (-0.3, 5.9)
	Australasia	20.9 (19.4, 22.4)	8.1 (1.1, 14.8)	23.0 (21.5, 24.7)	1.4 (-4.6, 7.9)	21.9 (20.6, 23.4)	4.7 (-0.5, 10.1)
	High-income Asia Pacific	22.2 (20.6, 23.8)	-11.4 (-16.3, -6.6)	23.5 (21.8, 25.2)	-15.1 (-19.7, -10.6)	22.8 (21.2, 24.3)	-13.5 (-17.4, -9.4)
Latin America and Caribbean	Caribbean	18.0 (16.6,19.3)	1.3 (-4.5, 6.8)	20.8 (19.3, 22.3)	-0.3 (-6.1, 5.9)	19.4 (18.0,20.7)	0.5 (-4.1, 5.4)
	Central Latin America	14.1 (13.1, 15.1)	0.0 (-4.3, 4.3)	16.4 (15.2, 17.6)	-2.4 (-6.4, 1.7)	15.2 (14.2, 16.4)	-1.3 (-4.8, 2.6)
	Tropical Latin America	18.9 (17.6, 20.2)	-10.4 (-13.9, -6.6)	19.5 (18.1, 20.9)	-15.1 (-18.8, -11.0)	19.1 (17.9,20.5)	-12.8 (-16.0, -9.2)
	Andean Latin America	15.5 (14.0, 17.0)	-0.9 (-9.0, 8.1)	17.9 (16.2, 19.6)	-0.1 (-7.8, 8.1)	16.7 (15.2,18.2)	-0.3 (-6.7, 6.5)
Sub-Saharan Africa	Central Sub-Saharan Africa	11.6 (10.6, 12.7)	12.4 (3.8, 20.8)	13.8 (12.6, 15.1)	1.4 (-6.9, 9.4)	12.8 (11.7, 13.8)	6.1 (-0.9, 12.9)
	Eastern Sub-Saharan Africa	11.2 (10.3, 12.3)	13.8 (5.4, 22.5)	12.5 (11.4, 13.6)	6.7 (-0.1, 13.9)	11.8 (10.9, 12.8)	9.8 (3.8, 16.1)
	Southern Sub-Saharan Africa	10.0 (9.2, 10.9)	-18.1 (-23.8, -12.3)	14.9 (13.7, 16.1)	-14.0 (-18.9, -9.0)	12.5 (11.6, 13.5)	-15.4 (-19.9, -11.1)
	Western Sub-Saharan Africa	13.0 (11.9, 14.2)	10.5 (2.3, 19.1)	15.8 (14.5, 17.3)	7.0 (-0.6, 15.8)	14.4 (13.3, 15.7)	7.9 (2.0, 14.4)
North Africa and Middle East	North Africa and Middle East	19.4 (17.8, 20.9)	10.2 (4.7, 15.7)	23.1 (21.4, 24.8)	3.7 (-0.8, 8.0)	21.2 (19.6, 22.8)	6.4 (2.5, 10.5)
South Asia	South Asia	13.5 (12.5, 14.5)	15.6 (11.0, 20.0)	15.9 (14.7, 17.1)	19.6 (14.5, 24.6)	14.6 (13.6, 15.7)	17.6 (13.6, 21.3)
Southeast Asia, East Asia, and Oceania	East Asia	40.6 (38.7, 42.3)	35.9 (31.9, 39.8)	36.3 (34.5, 38.1)	20.7 (16.6, 24.4)	38.8 (37.0, 40.6)	29.7 (26.1, 33.0)
	Southeast Asia	19.6 (18.3, 20.9)	6.9 (2.7, 11.5)	20.0 (18.8, 21.4)	14.2 (9.7, 18.9)	19.8 (18.6, 21.1)	10.4 (6.7, 14.2)
	Oceania	15.5 (13.8,17.2)	1.7 (-9.0, 13.0)	16.5 (14.6, 18.3)	1.6 (-9.2, 12.8)	16.0 (14.2, 17.6)	1.8 (-8.8, 12.7)
Central Europe, Eastern Europe, and Central Asia	Central Asia	22.7 (21.1, 24.4)	-2.4 (-8.1, 3.9)	26.1 (24.4, 27.9)	-10.8 (-15.2, -6.2)	24.4 (22.8, 25.9)	-7.7 (-11.7, -3.6)
	Eastern Europe	26.8 (22.0, 31.6)	-6.9 (-22.9, 11.0)	36.5 (31.2, 41.9)	-8.7 (-21.5, 3.7)	31.6 (27.6, 35.6)	-8.8 (-19.7, 2.7)
	Central Europe	29.8 (28.0, 31.5)	13.9 (9.2, 18.9)	33.7 (31.8, 35.5)	4.2 (-0.2, 8.7)	31.7 (30.0, 33.3)	8.7 (4.8, 12.8)


Lifetime risk
5.0 to 10.9%
11.0 to 16.9%
17.0 to 22.9%
23.0 to 28.9%
29.0 to 34.9%
35.0 to 40.9%
41.0 to 47.0%


Lifetime risk (%)
35
30
25
20
15
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0
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30
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40
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50
55
60
65
70
75
80
85
90
95+
Age start
Cerebrovascular disease
Hemorrhagic stroke
Ischemic stroke