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Comparative analysis of stroke burden between ages 20–54 and over 55 years: based on the global burden of disease study 2019

Zhuoxi Wang^{1,2†}, Yiqing Liu^{1†}, Rui Qie³ and Yanhong Hu^{1*}

Abstract

Background Stroke remains one of the major diseases threatening human health and life worldwide. Therefore, it is urgent to investigate the stroke burden in different age groups.

Methods We described the disease burden of three subtypes of stroke, namely intracranial haemorrhage (ICH), subarachnoid haemorrhage (SAH), and ischaemic stroke (IS), among people aged 20–54 years and > 55 years from 1990 to 2019, based on data from Global Burden of Disease Study 2019 and calculated the estimated annual percentage changes (EAPC) for age-specific incidence, disability-adjusted life-years (DALYs), mortality and prevalence rates. Joinpoint regression analyzes showed the critical years of trend inflexion points. Decomposition and health inequality analyses determined the impact of different epidemiological factors on stroke burden. Population-attributable fractions were calculated for deaths and DALYs due to risk factors.

Results From 1990 to 2019, the incidence of ICH and SAH decreased by 11.32% and 10.45%, respectively, in the 20–54 age group globally, while the incidence of IS increased by 14.95%. Meanwhile, the incidence of stroke in the > 55 years group showed an overall decreasing trend. The burden of adverse outcomes, including death and DALYs, varied by stroke subtype, with the rates of mortality and DALYs decreasing significantly less in IS than in ICH and SAH. In addition, the decline in mortality and DALYs rates was consistently greater in the over 55 years age group than in the 20–54 years age group. Notably, the prevalence of ICH, SAH, and IS increased by 20.55%, 11.50%, and 7.38% in the 20–54 years age group, respectively, whereas in the elderly group, there was only a mild increase of IS in the over 55 years group. What is more, stroke burden showed a negative correlation with regional development. Furthermore, high systolic blood pressure was a common contributor to stroke burden in both age groups. The difference is that a high body mass index affects people aged 20–54 years more, while abnormal fasting blood glucose affects older people more.

Conclusion The stroke burden in people 20–54 years of age is increasingly becoming a global health problem, particularly the incidence of IS in lower economic development areas.

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Clinical trial number Not applicable.

Keywords Global disease burden, Intracranial haemorrhage, Subarachnoid haemorrhage, Ischemic stroke

Background

To date, stroke has had a huge impact worldwide. Still, its epidemiological assessment and reporting have always been incomplete due to inconsistencies in its definition in clinical practice, scientific research or public health systems. However, thanks to advances in neuropathology and imaging, there has been an improved understanding of ischemia, haemorrhage and infarction in the central nervous system, which has led to a clear definition of stroke. Therefore, this study describes trends in the burden of common stroke subtypes, including intracranial haemorrhage (ICH), subarachnoid haemorrhage (SAH), and ischemic stroke (IS), respectively, based on the 2009 consensus document issued by the American Heart Association (AHA)/American Stroke Association Stroke Council and in conjunction with the Global Burden of Disease Study (GBD) database [1]. Neurological deficits typically characterize them due to acute focal injury to the central nervous system of vascular origin and are a leading cause of disability and death worldwide [1].

It is well known that the burden of stroke comes mainly from the elderly population. However, the 40% increase in the incidence of stroke in young people worldwide in recent decades is of increasing concern, possibly due to the increasing prevalence of traditional vascular risk factors such as hypertension, hypercholesterolaemia, diabetes, obesity and smoking in the younger population [2, 3]. On the one hand, younger people have a longer life expectancy than older people, so the burden of care after a stroke is greater for younger people [4]. On the other hand, younger people have more socially productive tasks than older people, so stroke in younger people may have a greater impact on economic development [5].

Controlling risk factors is crucial to alleviating the burden of stroke, as they not only affect the incidence of stroke but also have a profound impact on its prognosis, recurrence and even mortality [6]. Studies have shown that in people with an average age of 63, every 1.0 mmol/L decrease in LDL cholesterol can reduce the risk of a major vascular event by one-fifth [7]. In addition, as society and the economy develop, risk factors also change. For example, new risk factors such as illicit and recreational drug use and increased mental and psychological stress are magnifying the impact of stroke [8, 9], which also relates to some extent to regional developmental imbalances. Much evidence suggests that the burden of stroke is significantly higher in developing countries than in economically wealthier areas, which may be related to race, ethnicity, population density, and ability to access and pay for healthcare services [4, 6]. It

is worth noting that different genders are susceptible to different risk factors. For example, compared to men of all ages, diabetes mellitus increases the risk of stroke in women by more than two times, while metabolic syndrome doubles the risk of IS in women [10, 11]. The most common explanation for the gender difference in stroke is related to sex steroid hormones, especially estrogen. Studies have found that estradiol promotes vasodilation and has anti-inflammatory effects [12]. Therefore, identifying age, gender, and regional differences in risk factors has far-reaching implications for developing stroke prevention and control strategies.

Although there have been studies reporting trends in stroke burden over the last 30 years, these studies have either only reported the burden of disease in specific age groups or only reported disease trends in a specific subtype of stroke [13, 14]. Given these gaps, we first age-grouped the stroke population based on age groupings from previous stroke epidemiologic studies, and, in conjunction with the GBD database, we broadly defined those aged 20–54 as the young group and those aged 55 years and older as the old group. Next, we characterized the epidemiology of stroke in each of the two cohorts from 1990 to 2019 and compared trends in the burden of disease between the two, exploring potential risk factors that may account for the differences. Second, another difference of this study is that we calculated and described the prevalence, morbidity, and mortality of common subtypes of stroke, including ICH, SAH, and IS, separately in different age groups and sexes, which is because the severity and prognosis of the different subtypes are also different in terms of the burden they impose on the patients and society.

Materials and methods

Study data

The current study was conducted based on the GBD 2019 (<https://vizhub.healthdat.org/gbd-results/>), a public database providing the burden and risk factors of multiple diseases in 204 countries and territories around the world, which aims to quantify global trends in health and burden of disease, where data were obtained through a variety of censuses, household surveys, civil registration, vital statistics, disease registries, and other sources [15]. In addition, to better analyze the disease burden in different regions, the GBD study divides the world into 21 super-regions based on epidemiological similarity and geographic proximity or into five regions based on the Socio-demographic Index (SDI) [16, 17].

SDI is a summary indicator that assesses the development of a society based on a combination of per capita income, average years of schooling and the total fertility rate of women under the age of 25, with a higher SDI value implying a higher level of development [18]. GBD2019 categorizes the SDI values of 204 countries and territories into five groups based on the numerical rankings, including High SDI, High-Middle SDI, Middle SDI, Low-Middle SDI and Low SDI. The current study analyzed whether different socioeconomic levels impact stroke burden based on the SDI subgroups.

As ICH, SAH, and IS are the predominant forms of stroke onset, we analyzed the annual data for these three stroke subtypes. Based on the age ranges delineated by the 2019 GBD database, we selected the young group (aged 20–54 years) and the old group (aged > 55 years) as the primary study populations. Additionally, we analyzed the data of all age groups to have a more comprehensive view of the disease burden of stroke in the whole population. We retrieved data on the incidence, disability-adjusted life years (DALYs), mortality and prevalence rates of ICH, SAH and IS based on sex, global regions, countries and territories from the 2019 GBD database.

Statistical analysis

We separately described the global and regional burden of stroke in the 20–54 years group and the over 55 years group and compared the number of cases and rates per 100,000 population of incidence, DALYs, mortality and prevalence in 1990 and 2019. We applied the estimated annual percentage change (EAPC) to quantify the disease burden trends, which was calculated with a generalized linear model conforming to the Gaussian distribution, describing the age-specific rate trend over time [19, 20]. Disease burden is considered to show an upward trend when both the estimate of the EAPC and the lower limit of its 95% confidence interval (CI) are greater than 0, and conversely, a downward trend if both the forecast of the EAPC and the lower limit of its 95% CI are less than 0.

In this study, we performed the joinpoint regression analysis using Joinpoint software version 5.1.0 to obtain annual percentage change (APC), a practical model describing disease prevalence trends with junction point regression [21]. This approach is not only able to identify statistically significant turning points within a particular time frame but also to demonstrate the overall trend within that time frame. Furthermore, we calculated the slope index and concentration indices of the stroke DALYs for different SDI regions from 1990 to 2019 using linear regression models and heteroscedasticity analysis methods, which visualize the inequalities in the burden of disease over time and, in particular, how unequal regional development affects health outcomes.

In addition, we performed a decomposition analysis to investigate the separate contributions of population age structure, population growth, and epidemiological changes to the incidence of stroke at different SDI levels. This statistical approach is commonly used to describe how specific factors influence epidemiological trends [22].

To further elucidate whether regional development imbalances also lead to inequalities in disease burden over time, we conducted a health inequality analysis to understand the relationship between regional development and health outcomes by calculating the slope index and concentration index of the DALYs for stroke over the last 30 years. First, the slope index was obtained by constructing a linear regression model and calculating heteroskedasticity. Then, it was weighted using repeated iterations of robust regression to obtain the coefficients and intercepts of the slope index. As for the concentration index, the absolute concentration index was mainly obtained by fitting the Lorenz curve with a cubic spline function [23].

Finally, considering that environmental pollution, dietary habits, alcohol consumption, smoking, blood pressure, and multiple metabolic factors are common attributable risk factors for stroke, we calculated population attributable fractions (PAFs) for stroke death and DALYs due to the aforementioned risk factors. In addition, to see whether different risk factors are associated with clinical subtypes and individual differences in stroke, we calculated PAFs for different age groups and sexes for ICH, SAH, and IS in 1990 and 2019, respectively. The percentage of stroke deaths and DALYs were obtained in the GBD database. R software version 4.3.3 and Joinpoint software version 5.2.0 were applied to perform all the statistics and visualizations, and $p < 0.05$ was deemed statistically significant.

Result

Global incidence, mortality, and dalys and prevalence burden for stroke

The case numbers and rates of incidence, DALYs, deaths, and prevalence for IS, ICH, and SAH in 1990 and 2019 at global levels are presented in Table 1 and Additional file: Table S1–S3, along with the EAPC from 1990 to 2019. In 2019, there was an estimated total of 1,102,113 and 449,169 incident cases of ICH and SAH in the 20–54 years age group, respectively. The corresponding incident rates decreased by 11.32% from 33.12 (95% CI: 27.15 to 39.98 per 100,000 population) to 29.37 (95% CI: 23.98 to 35.47 per 100,000 population) and 10.45% from 13.37 (95% CI: 10.6 to 16.46 per 100,000 population) to 11.97 (95% CI: 9.38 to 14.81 per 100,000 population). While there were 1,338,867 incident cases of IS in the 20–54 years age group, and the incidence rate increased by

Table 1 Global incidence burden for stroke

1990			2019			1990–2019		
20–54 years			55+ years			20–54 years		
	Number	Rate		Number	Rate		Number	Rate
ICH	Male	447,197 (366497,539120)	36.72 (30.09,44.27)	751,511 (612231,917578)	241.55 (196.79,294.93)	644,175 (526854,778998)	34.09 (27.88,41.23)	1,136,376 (943016,1367631)
	Female	349,493 (287158,421852)	29.44 (24.19,35.53)	738,963 (611082,886353)	205.28 (169.76,246.22)	457,938 (374279,554127)	24.58 (20.09,29.75)	1,062,452 (886559,1263542)
	Both	796,690 (653051,961612)	33.12 (27.15,39.98)	1,490,474 (1232899,1794797)	222.1 (183.71,267.44)	1,102,113 (899971,1331097)	29.37 (23.98,35.47)	2,198,828 (1828667,2634027)
SAH	Male	152,293 (120578,188292)	12.5 (9.9,15.46)	150,979 (117695,189656)	48.53 (37.83,60.96)	218,425 (171799,270380)	11.56 (9.09,14.31)	275,766 (218904,340524)
	Female	169,392 (134641,207726)	14.27 (11.34,17.5)	233,344 (184904,287839)	64.82 (51.37,79.96)	230,744 (180542,287250)	12.39 (9.69,15.42)	427,571 (341937,521967)
	Both	321,685 (254882,395947)	13.37 (10.6,16.46)	384,323 (302815,476930)	57.27 (45.12,71.07)	449,169 (351968,555734)	11.97 (9.38,14.81)	703,337 (561867,858766)
IS	Male	365,631 (285620,469117)	30.02 (23.45,38.52)	1,258,341 (1037505,1539271)	404.46 (333.48,494.76)	672,114 (521596,861052)	35.57 (27.64,55.7)	2,639,741 (2188613,3201282)
	Female	380,992 (297152,487241)	32.09 (25.03,41.04)	1,798,348 (1505373,2178796)	499.57 (418.18,605.26)	666,753 (513635,853969)	35.79 (27.57,45.84)	3,333,464 (2791095,4014725)
	Both	746,623 (582050,950777)	31.04 (24.2,39.53)	3,056,688 (2559002,3703900)	455.48 (381.32,551.92)	1,338,867 (1038751,1713556)	35.68 (27.68,45.67)	5,973,205 (4969053,7190692)

Note: ICH: Intracranial haemorrhage. SAH: Subarachnoid haemorrhage. IS: Ischaemic stroke. EAPC: Estimated annual percentage changes

14.95% from 31.04 (95% CI: 24.2 to 39.53 per 100,000 population) to 35.68 (95% CI: 27.68 to 45.67 per 100,000 population).

Regarding incidence burden in the over 55 age group, there was an estimated total of 2,198,828, 703,337, and 5,973,205 incidence cases of ICH, SAH, and IS, respectively. The corresponding incidence rate decreased by 29.58% from 222.1 (95% CI: 183.71 to 267.44 per 100,000 population) to 156.41 (95% CI: 130.08 to 187.37 per 100,000 population), 12.64% from 57.27 (95% CI: 45.12 to 71.07 per 100,000 population) to 50.03 (95% CI: 39.97 to 61.09 per 100,000 population), and 6.7% from 455.48 (95% CI: 381.32 to 551.92 per 100,000 population) to 424.9 (95% CI: 353.47 to 511.5 per 100,000 population).

Regarding mortality rate in the 20–54 years age group, ICH accounted for the highest number of stroke-related mortality with 425,798 deaths in 2019, followed by IS with 102,260 deaths and SAH with 90,441 deaths. From 1990 to 2019, the mortality rate of ICH, SAH, and IS decreased by 22.10% (from 14.57 to 11.35 per 100,000 population), 41.79% (from 4.14 to 2.41 per 100,000 population) and 8.49% (from 2.98 to 2.73 per 100,000 population), respectively, with a decreased EAPC of -1.58% (-1.81, -1.36), -3.52% (-3.83, -3.2) and -1.63% (-1.72, -1.54). Meanwhile, the global mortality rates of ICH, SAH, and IS in old individuals decreased by 31.92%, 57.29%, and 22.8%, respectively (Additional file: Table S1).

Globally, the number of stroke DALYs in the 20–54 years age group significantly decreased from 1990 to 2019; ICH represented a reduction of 22.19% (from 677.09 to 526.81 per 100,000 population), SAH 39.33% (from 205.04 to 124.4 per 100,000 population), and IS 2.89% (from 193.24 to 187.85 per 100,000 population). The DALYS rate also exhibited a decline, with an EAPC of -1.64% (-1.82, -1.46), -3.13% (-3.39, -2.88) and -1.34% (-1.42, -1.26), respectively. Notably, the decrease in DALYs among females also showed a greater EAPC than males. Meanwhile, the global DALYS rates of ICH, SAH, and IS in individuals aged over 55 years decreased by 38.78%, 58.83%, and 27.07%, respectively (Additional file: Table S2).

It was estimated that the global prevalence rates of ICH, SAH, and IS in the 20–54 years age group increased by 20.55% (from 694.74 to 837.49 per 100,000 population), 11.50% (from 439.48 to 490.03 per 100,000 population), and 7.38% (from 384.24 to 412.59 per 100,000 population) across 1990–2019, respectively. Meanwhile, the global prevalence rates of ICH, SAH, and IS in the over 55 age group decreased by 22.66% and 10.04%, respectively, but that of IS increased by 0.13%. From 1990 to 2019, for the burden of stroke, mortality and DALYS rates in the older age group were the most significant declines, followed by mortality

and DALYS rates in the 20–54 years age group, and the declines or increases in incidence and prevalence were relatively flat. The trends for men and women were almost parallel (Additional file: Table S3).

Regional incidence, mortality, and dalys and prevalence burden for stroke

The case numbers and rates of incidence, DALYs, deaths, and prevalence for IS, ICH, and SAH in 1990 and 2019 at regional levels are presented in the Additional file: Table S4–S6. The incidence of SAH showed a significant decline in all regions except high-income Asia Pacific, at 1.88% (95% CI: 1.52 to 2.24), where it increased. For IS, the incidence was decreasing in most areas, however, East Asia 1.03% (95% CI: 0.94 to 1.12), North Africa and Middle East 0.38% (95% CI: 0.33, 0.43), Southeast Asia 0.12% (95% CI: 0.09 to 0.14) showed a significant increase and Southern Sub-Saharan Africa 0.18% (95% CI: -0.02 to 0.37) a slight increase.

ICH mortality rates declined in all regions, with the high-income Asia Pacific region having the most significant decline, followed by Central Europe and Latin America. As for SAH, all regions significantly declined mortality except Central Asia at 0.58% (95% CI: 0.45 to 0.71). Most regions showed a decline in IS mortality, with Western Europe -4.01% (95% CI: -4.22 to -3.8) being the most significant decline, but Eastern Sub-Saharan Africa 0.36% (95% CI: 0.32 to 0.4), Southeast Asia 0.36% (95% CI: 0.23 to 0.49) and Southern Sub-Saharan Africa 0.64% (95% CI: 0.2 to 1.09) showed a mild upward trend in mortality.

Similar to the incidence and mortality rates, DALYS rates of ICH and SAH significantly declined in all regions. Except for Eastern Sub-Saharan Africa 0.15% (95% CI: 0.13 to 0.17), Southern Sub-Saharan Africa 0.4% (95% CI: 0 to 0.81), and Southeast Asia 0.28% (95% CI: 0.19 to 0.37), which has experienced a rise in the last 30 years, the remaining regions showed a decreasing trend. East Asia demonstrated the largest decrease with an EAPC of -6.17 (95% CI: -6.76 to -5.57).

The prevalence of stroke is increasing in several regions; for example, the prevalence of ICH in High-income North America 0.6% (95% CI: 0.35 to 0.85), SAH in High-income Asia Pacific 1.07% (95% CI: 0.92 to 1.23) and High-income North America 0.18% (95% CI: -0.15 to 0.51), and in particular the prevalence of IS has risen significantly in several Asian regions such as East Asia, South Asia and Southeast Asia and North Africa and Middle East and Oceania, and also in North Africa and Middle East. Overall, the disease burden in the High-income Asia Pacific region experienced the most significant decline from 1990 to 2019, particularly in mortality and DALYS, followed by East Asia and Central Europe.

Trends for stroke burden

The changing trends of the global disease burden of stroke in the past 30 years are shown in Figs. 1, 2 and 3. For ICH, the overall disease burden in the young and elderly groups shows a downward trend, but the disease burden in men is always higher than that in women. As for SAH and IS, although the overall burden rate in young and elderly groups shows a downward trend, the

incidence and prevalence are still increasing year by year. Furthermore, although the burden of incidence and prevalence of SAH and IS is higher in women than in men, men have higher mortality and DALYs than women, and this trend does not appear to be related to age. All age groups also showed similar trend changes (Additional file: Figure S1).

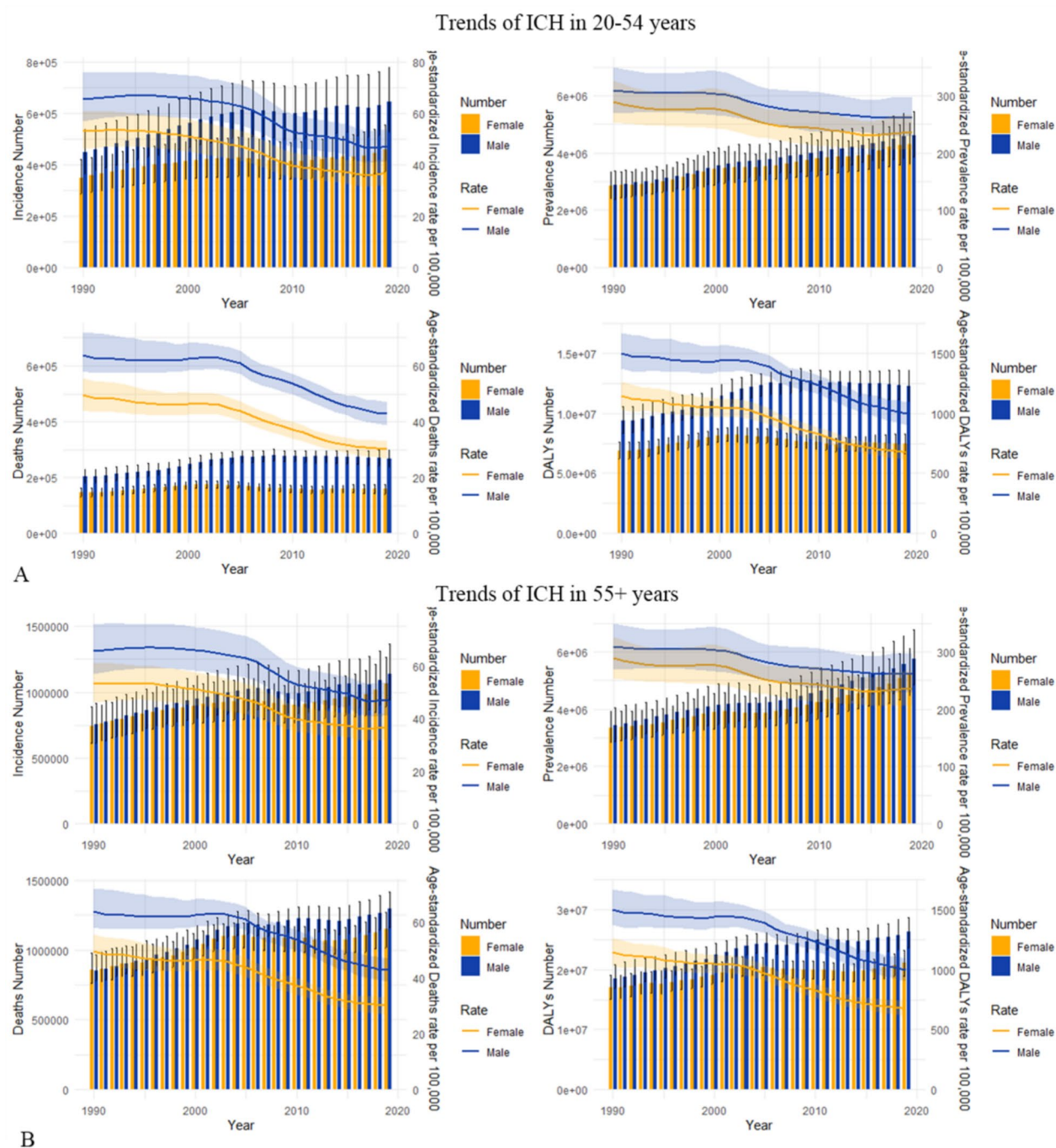


Fig. 1 Bar and line charts for the global burden of ICH from 1990 to 2019 in different age groups. **A.** Disease burden trends of ICH in the 20–54 years group. **B.** Disease burden trends of ICH in the over 55 years group. DALYs: Disability-adjusted life years. ICH: Intracranial haemorrhage

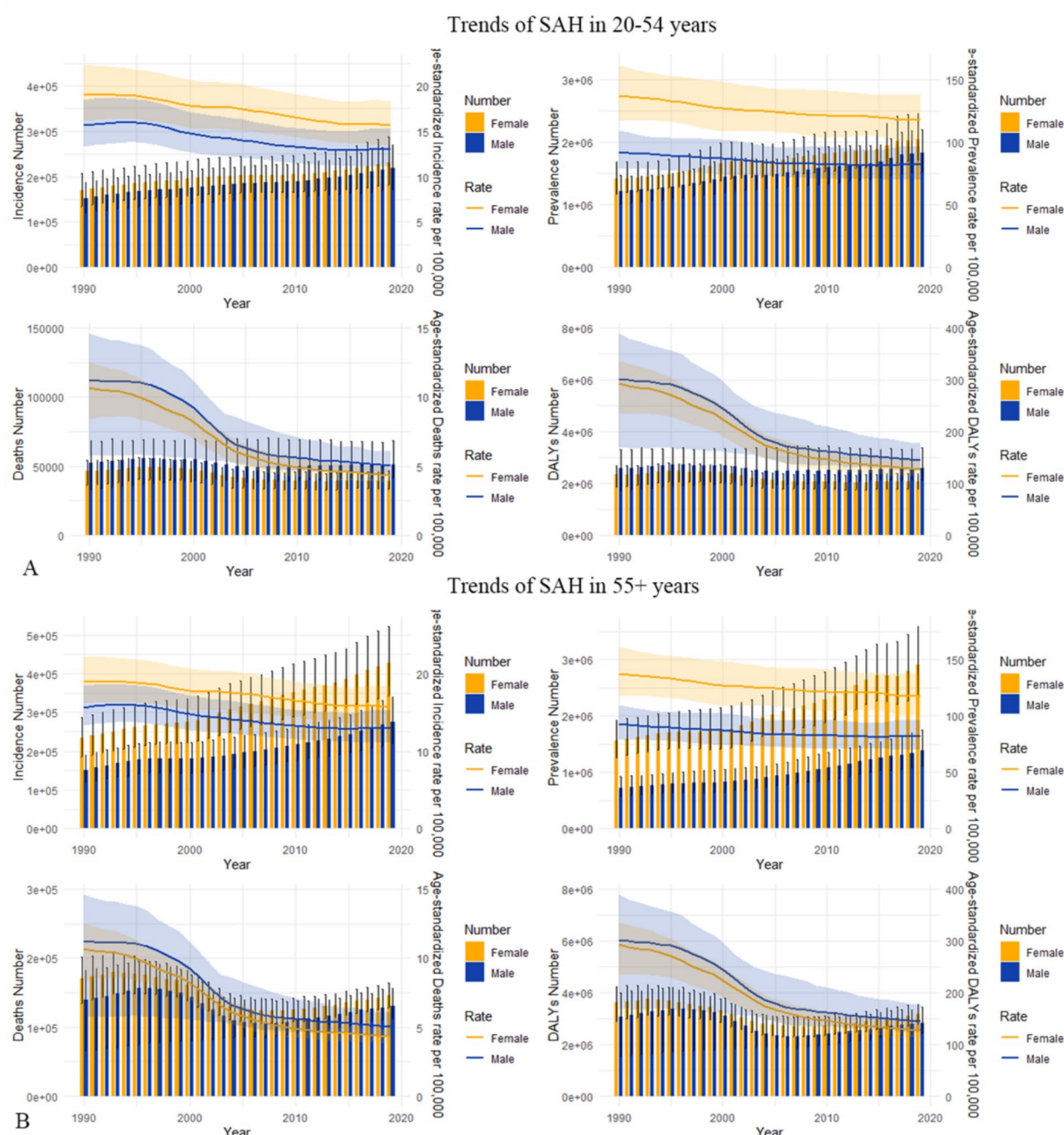


Fig. 2 Bar and line charts for the global burden of SAH from 1990 to 2019 in different age groups. **A.** Disease burden trends of SAH in the 20–54 years group. **B.** Disease burden trends of SAH in the over 55 years group. DALYs: Disability-adjusted life years. SAH: Subarachnoid haemorrhage

Joinpoint regression analysis

At the global level, the incidence of ICH and SAH has shown an overall downward trend, as shown in Fig. 4. Although the incidence in the elderly group has not increased significantly, the disease burden of ICH and SAH in the 20–54 years group has increased after 2017 and 2015, respectively. Although the incidence of IS shows an overall downward trend in all age groups and the elderly group, the disease burden in all age groups has

begun to increase since 2014, and the upward trend in the elderly group has started earlier, showing an upward trend since 2001. In addition, what is worrying is that the incidence of IS in people aged 20–54 years has increased year by year in the past 30 years. In different SDI areas, the incidence of ICH showed an overall downward trend, but SAH showed an upward trend in high SDI areas. Similarly, the disease burden for IS has shown a significant upward trend in moderate and low-moderate SDI

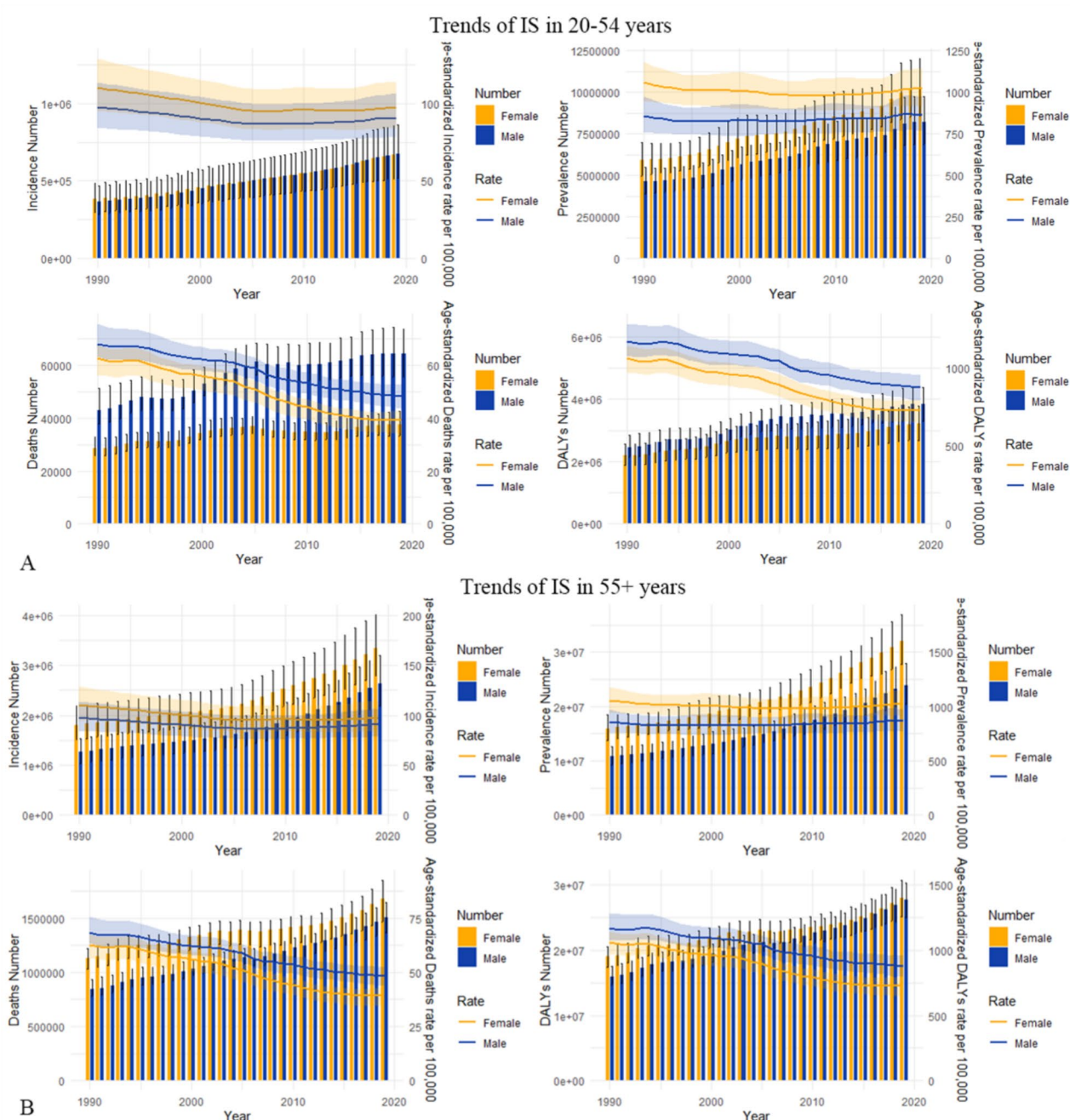


Fig. 3 Bar and line charts for the global burden of IS from 1990 to 2019 in different age groups. **A.** Disease burden trends of IS in the 20–54 years group. **B.** Disease burden trends of IS in the over 55 years group. DALYs: Disability-adjusted life years. IS: Ischemic stroke

areas. In conclusion, although the incidence of stroke in most SDI areas has been decreasing overall, this trend has reversed over the past five years, suggesting that the burden of stroke may increase in the short term.

In addition, to study whether there are gender differences in the incidence burden of stroke, we visually compared the incidence trends of “females” and “males” through subgroup joinpoint regression (Additional file: Figure S2–S3). The results showed that the incidence of

ICH in men was higher than that in women, both globally and in different SDI regions, while for SAH and IS, the incidence in women was higher than that in men.

Distribution for stroke across countries and territories

The incidence of SAH and IS shows different incidence trends in different SDI areas, suggesting that the severity of the disease burden may be intrinsically related to the local socio-economic development status. We mapped

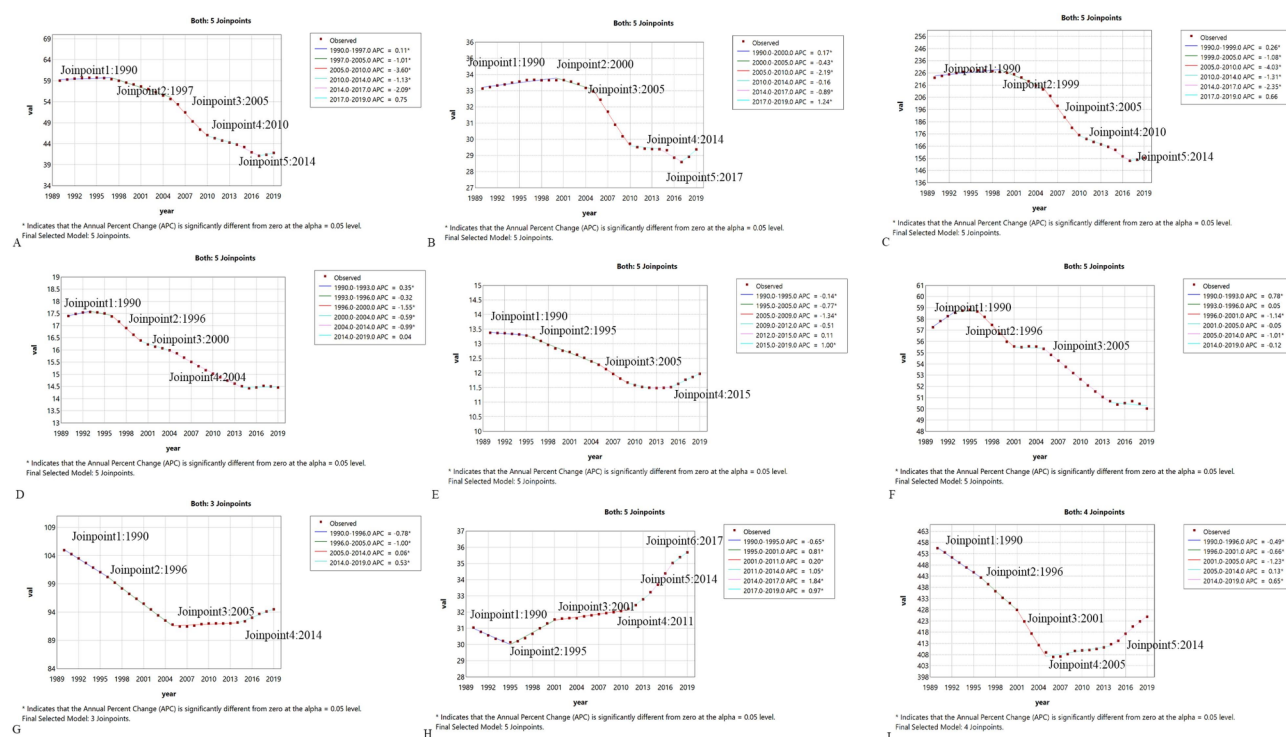


Fig. 4 Trends for global incidence of stroke from 1990 to 2019 based on joinpoint regression model in different age groups. **A.** Trends for ICH in age-standardised group. **B.** Trends for ICH in the 20–54 years age group. **C.** Trends for ICH in the over 55 years age group. **D.** Trends for SAH in age-standardised group. **E.** Trends for SAH in the 20–54 years age group. **F.** Trends for SAH in the over 55 years age group. **G.** Trends for IS in age-standardised group. **H.** Trends for IS in the 20–54 years age group. **I.** Trends for IS in the over 55 years age group. ICH: Intracranial haemorrhage. SAH: Subarachnoid haemorrhage. IS: Ischemic stroke

the distribution for 204 countries and regions in 1990 and 2019 to explore these results further (Figs. 5, 6 and 7). Overall, the disease burden of ICH and SAH, including prevalence, incidence, and mortality, has not changed significantly in the past 30 years. DALYs have declined considerably, especially in Asia, Africa, and South America. Prevalence and DALYs have declined in the Americas due to the disease burden of IS, but this decline is not obvious in East Asia and Africa. Even in China, the prevalence of IS in 2019 was higher than in 1990. Therefore, China should prioritize the management of IS and reduce the burden of IS on its citizens.

In detail, ICH has a larger disease burden in Africa, followed by the Americas, while Asia and Europe have a lighter disease burden. SAH also shows a similar worldwide incidence burden. IS exhibited a higher incidence in Asia, especially China, followed by the Americas. At the same time, the Nordic region has no obvious incidence burden, suggesting that although the burden of stroke is well managed globally, Africa and the Americas still need to pay more attention to ICH and SAH. At the same time, East Asia, represented by China, should focus more on IS superior. Next, we drew a visualization of EAPC for 204 countries and regions. During the period from 1990 to 2019, the most noticeable growth in the disease burden

of stroke was in Asian and African countries, especially the incidence of IS, while most European countries showed negative growth, which may be closely related to socioeconomic factors and living habits.

In addition, we plotted bar graphs of the incidence proportion of stroke by sex in each age group from 20 to 95 years and above across different SDI regions (Fig. 8). The results showed that the incidence of ICH was higher among young and middle-aged men. This trend was more evident in areas with high SDI. Both SAH and IS have a higher incidence rate in middle-aged and older women, especially in mid-to-high SDI areas with better economic development levels. The above incidence rates have not changed significantly over time.

Health inequality analysis

Given the apparent correlation between the incidence of stroke and SDI, we further conducted a health inequality analysis, as shown in Fig. 9. The slope index of DALYs for ICH has slightly improved from -429.48 (95% CI: -621.04 to -237.93) in 1990 to -408.19 (95% CI: -581.57 to -234.82) in 2019, while the concentration index has decreased from 0.15 in 1990 to 0.10 in 2019. The SAH slope index of DALYs slightly reduced from 97.50 (95% CI: 61.96 to 133.04) in 1990 to 79.39 (95% CI: 48.66 to

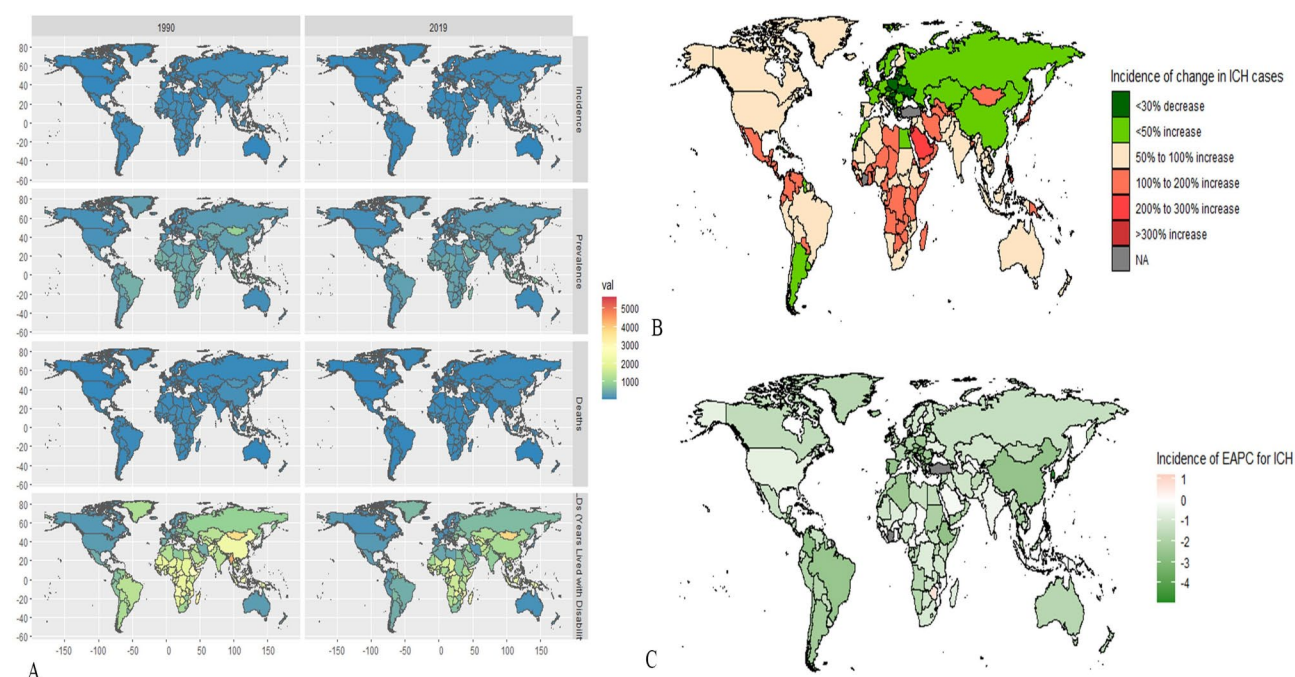


Fig. 5 Disease burden of ICH in 1990 and 2019 in 204 countries and territories worldwide. ICH: intracranial haemorrhage. EAPC: Estimated annual percentage changes

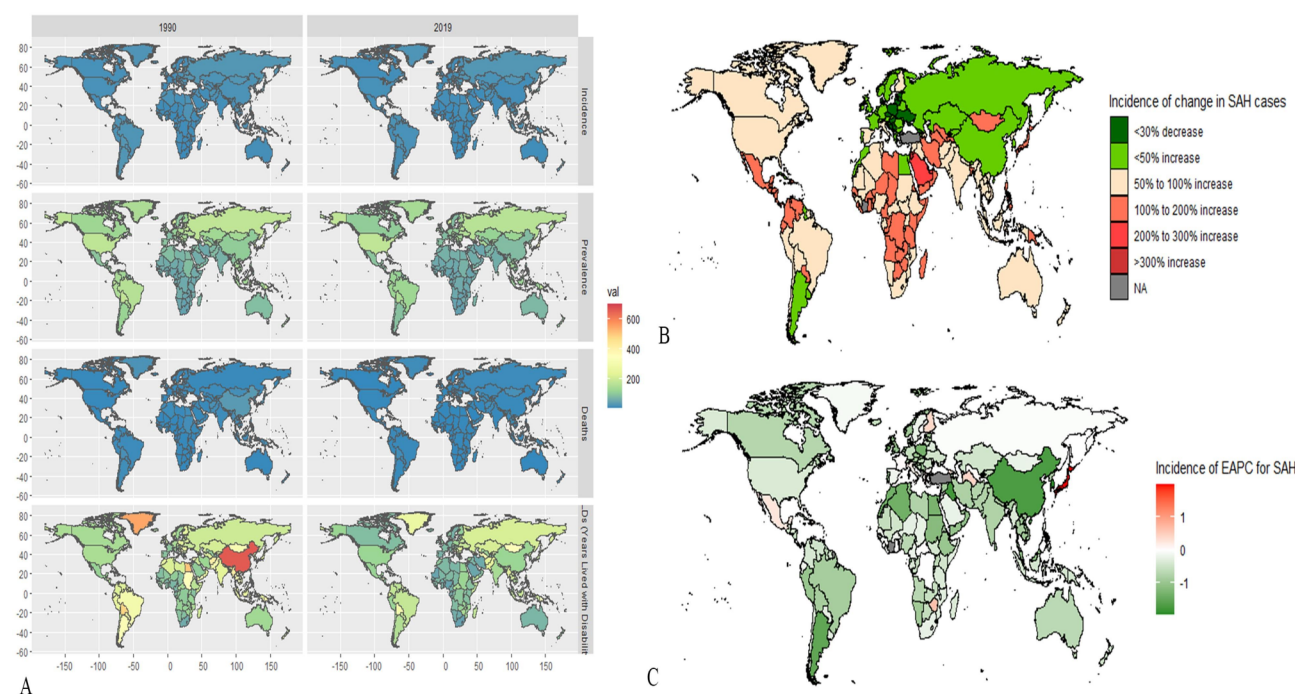


Fig. 6 Disease burden of SAH in 1990 and 2019 in 204 countries and territories worldwide. SAH: subarachnoid haemorrhage. EAPC: Estimated annual percentage changes

110.11) in 2019, and the concentration index also showed a downward trend, from 0.07 in 1990 to -0.02 in 2019. The DALYs of IS dropped significantly from 709.45 (95% CI: 544.47 to 874.43) in 1990 to 530.78 (95% CI: 398.90 to 662.66) in 2019, while the concentration index increased

slightly from -0.19 in 1990 to -0.10 in 2019. Across countries and regions, there are relative social development inequalities in DALYs caused by stroke, but the extent of these inequalities gradually decreases over time. It is worth noting that the DALYs burden of ICH is mainly

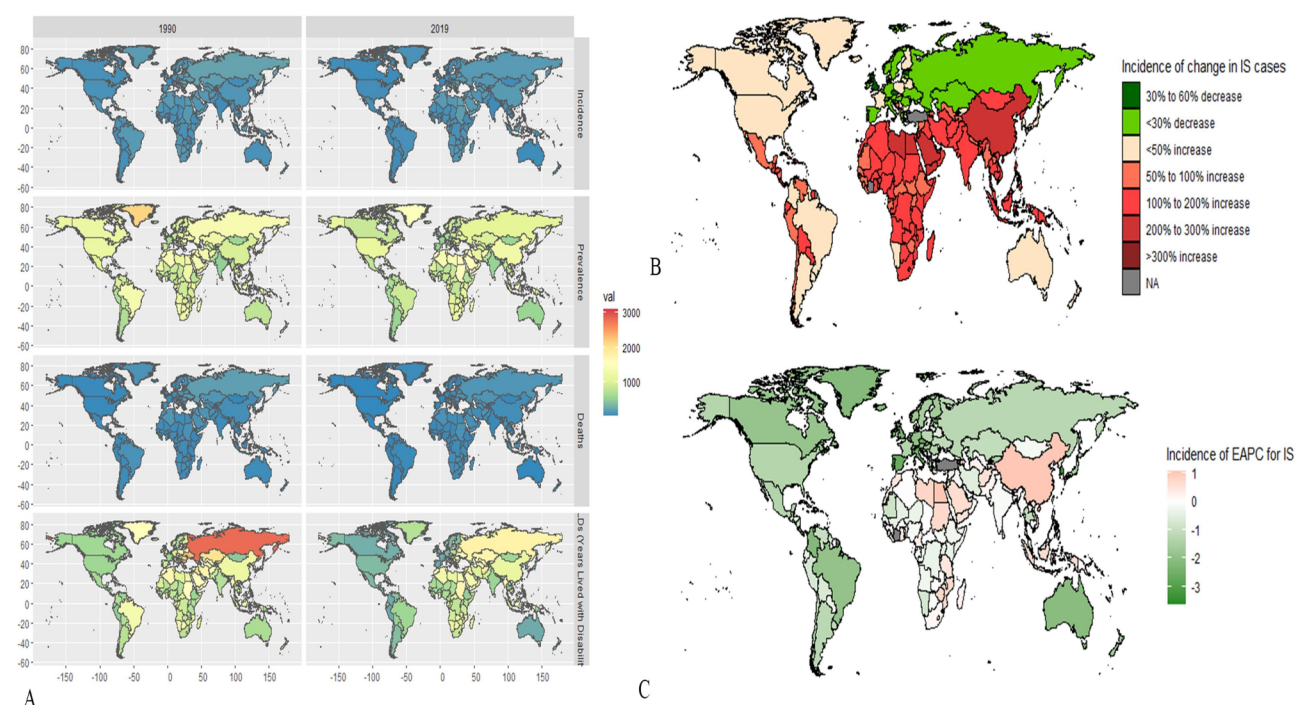


Fig. 7 Disease burden of IS in 1990 and 2019 in 204 countries and territories worldwide. IS: ischemic stroke. EAPC: Estimated annual percentage changes

concentrated in richer countries, while IS is primarily concentrated in poorer countries. In addition, the DALYs for SAH tended to focus toward lower SDI regions over time.

Decomposition analysis

To investigate the impact of population growth, ageing, and epidemiological changes on trends in the incidence of stroke from 1990 to 2019, we performed a decomposition analysis, as shown in Fig. 10. The results show that the incidence of ICH is mainly affected by demographic changes and epidemiological changes, in which demographic changes increase the incidence, while epidemiological changes reduce the incidence. This impact is particularly obvious in the mid-SDI region, although the direction of this impact is quite the opposite, almost to the same degree. The incidence of SAH also shows a similar impact trend. The difference is that population ageing positively impacts the incidence of ICH, especially in the mid-SDI region, while negatively impacting SAH. In particular, epidemiological changes increase the incidence of SAH in high-SDI areas and decrease the incidence in other areas. No matter which SDI region, IS is positively affected by demographic changes but also slightly affected by population ageing. Epidemiological changes have played a role in reducing the incidence of IS in areas with high SDI and high SDI. In short, the incidence of stroke is mainly affected by demographic and epidemiological changes, and the demographic effects are almost always positive but have little to do with ageing.

Association between stroke burden and SDI

To explore the relationship between SDI and the incidence of stroke, we performed a Pearson correlation analysis. At the national and regional levels, the incidence of ICH is significantly negatively correlated with SDI in both the young and elderly groups; the higher the economic level of a country or region, the lower the incidence of ICH (Fig. 11). However, the incidence of SAH is positively correlated with SDI (Fig. 12). Similarly, the incidence of IS is also positively correlated with SDI at the global and regional levels. Still, this correlation is insignificant at the national and regional levels, and the above correlations have little to do with age, as the young and over 55 years groups showed similar correlations (Fig. 13).

Attributable risk factors for dalys of stroke in individuals aged 20–54 and over 55 years

Overall, from 1990 to 2019, mainly air pollution, smoking, and metabolic factors drove the changes in the mortality and DALYs burden of stroke (Additional file: Figure S7–S9). Specifically, for the DALYs of ICH, SAH and IS, except for fasting blood glucose, which had a greater effect on the elderly than on the young, and systolic blood pressure, which has a similar impact on the two age groups, the remaining risk factors were more pronounced in the young, especially body mass index. In addition, LDL cholesterol significantly increases the risk of stroke in young people compared to older people. Risk factors did not display obvious discrepancies between

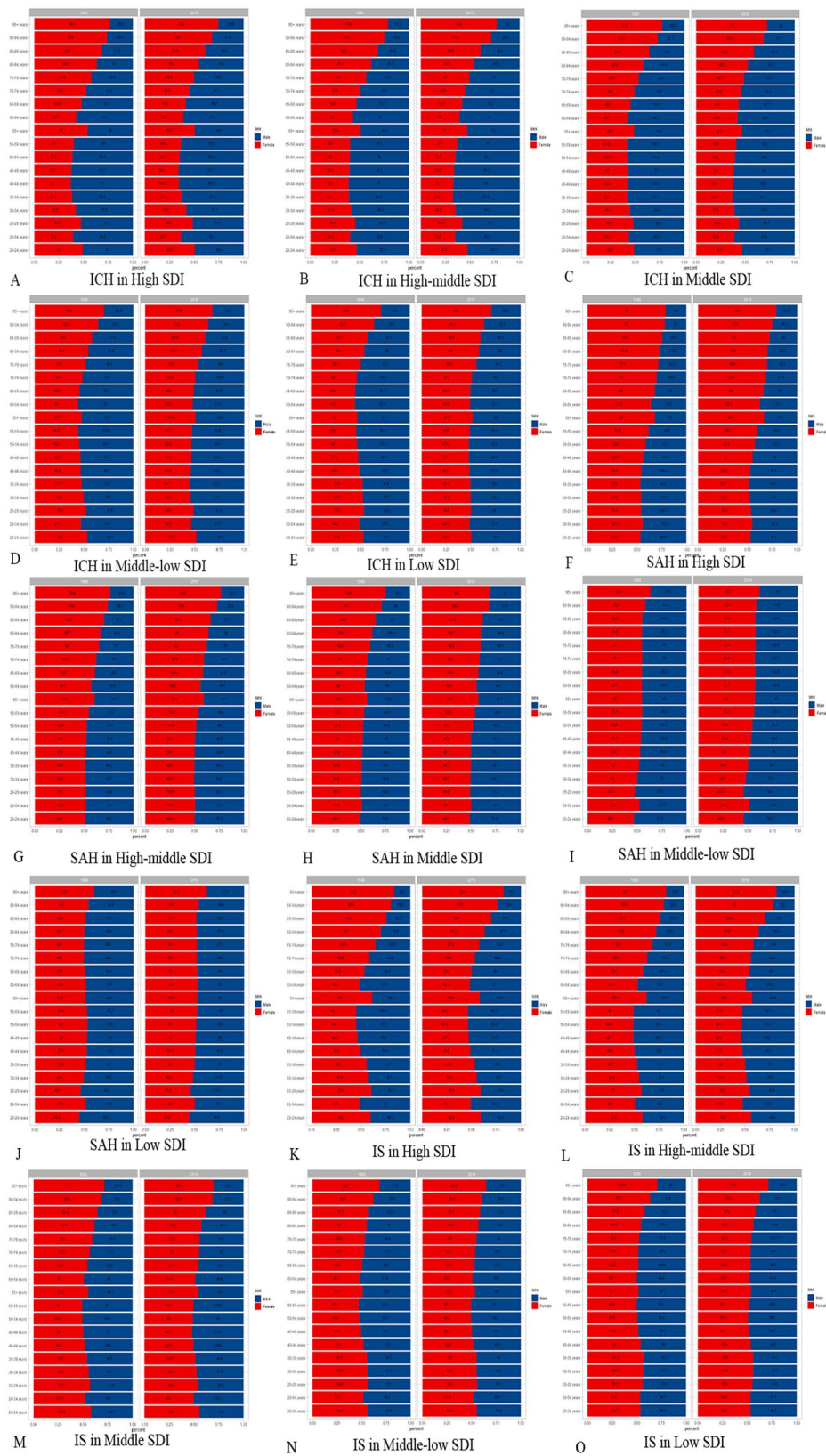


Fig. 8 Comparison for proportion of stroke incidence in different age groups between male and female across SDI regions. SDI: Socio-demographic index. ICH: Intracranial haemorrhage. SAH: Subarachnoid haemorrhage. IS: Ischemic stroke

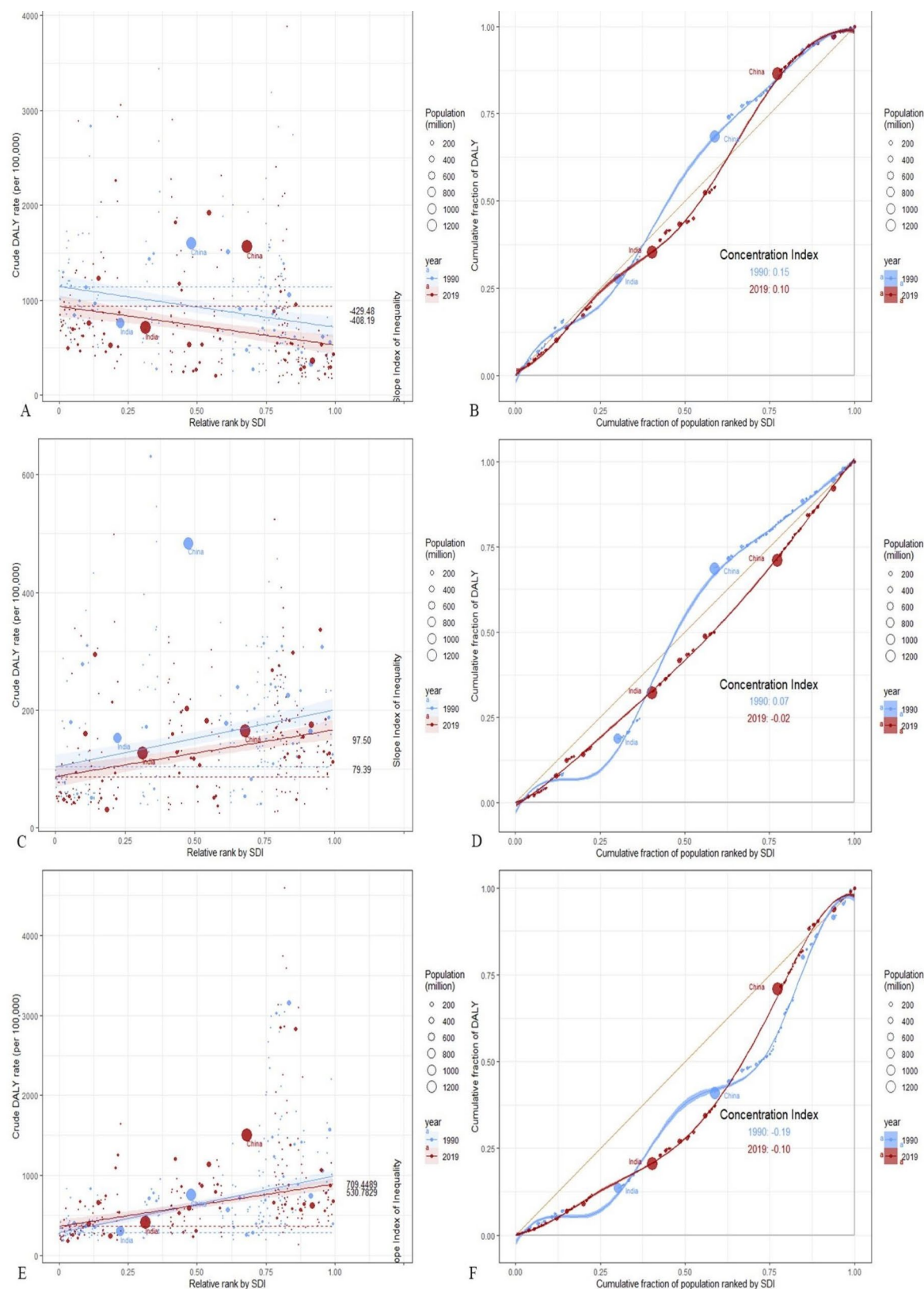


Fig. 9 Slope indexes and concentration indexes for stroke DALYs from 1990 to 2019 worldwide. **(A)** Slope indexes for ICH. **(B)** Concentration indexes for ICH. **(C)** Slope indexes for SAH. **(D)** Concentration indexes for SAH. **(E)** Slope indexes for IS. **(F)** Concentration indexes for IS. DALYs: Disability-adjusted life years. ICH: Intracranial haemorrhage. SAH: Subarachnoid haemorrhage. IS: Ischemic stroke

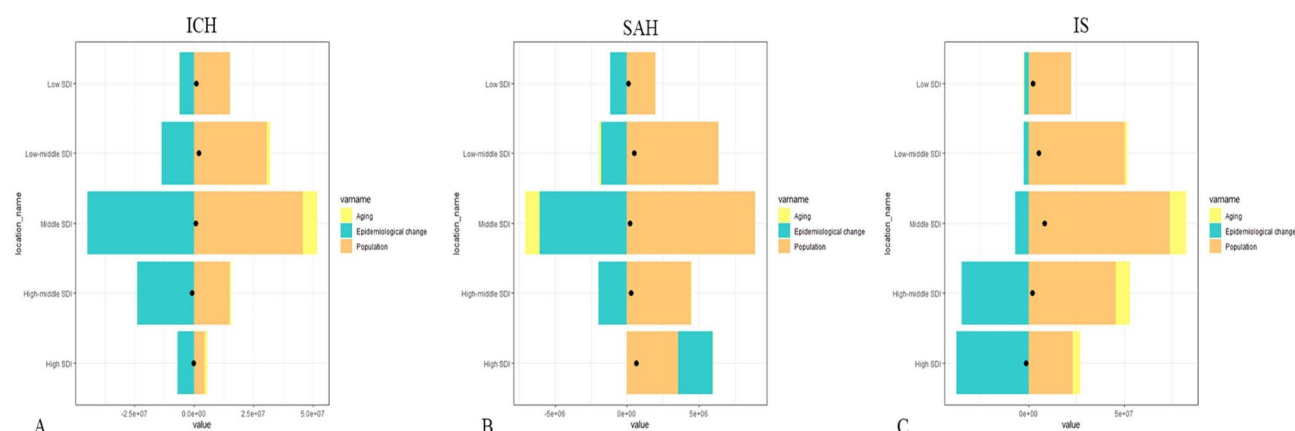


Fig. 10 Decomposition analysis of the trends in stroke incidence from 1990 to 2019. **(A)** Decomposition analysis for ICH. **(B)** Decomposition analysis for SAH. **(C)** Decomposition analysis for IS. ICH: Intracranial haemorrhage. SAH: Subarachnoid haemorrhage. IS: Ischemic stroke

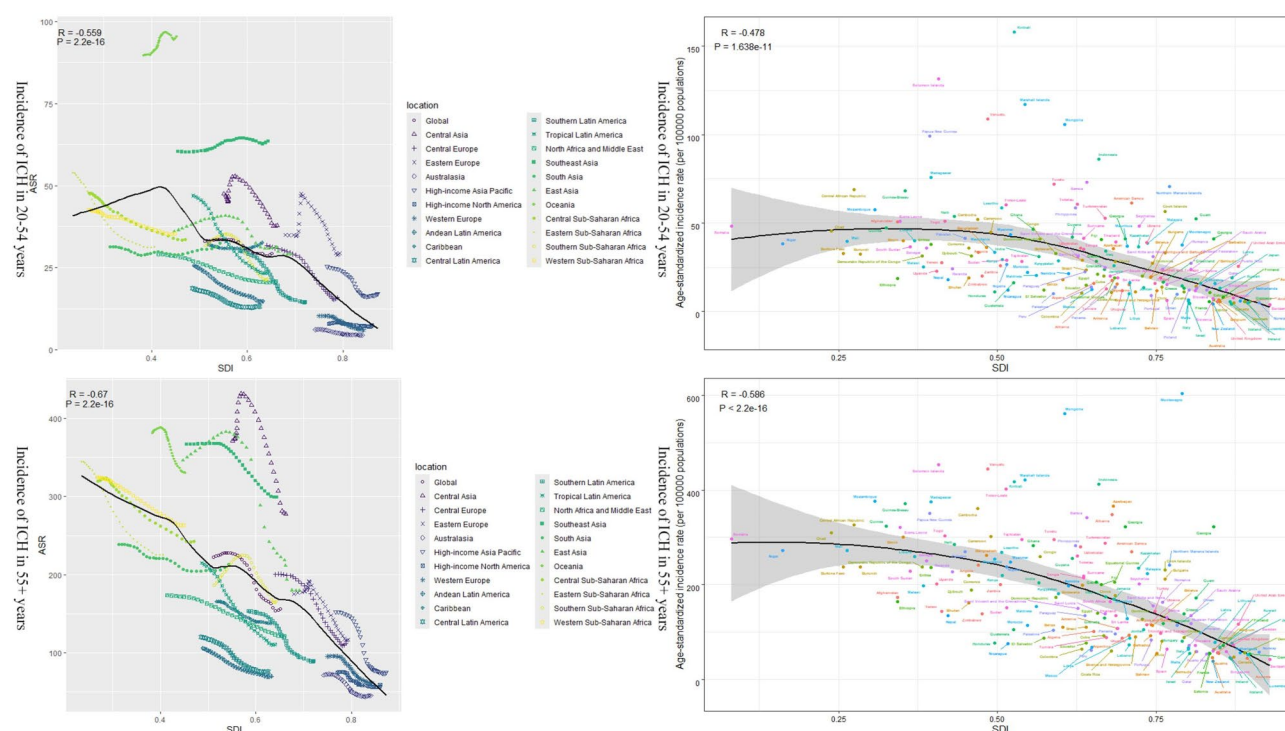


Fig. 11 Association between ICH incidence and SDI. **A–B.** Global, regions and countries or territories incidence in the 20–54 years age group. **C–D.** Global, regions and countries or territories incidence in the over 55 years age group. SDI: Socio-demographic index. ICH: Intracranial haemorrhage

genders. However, the contribution of some risk factors varies between the sexes rather than between age groups. For example, smoking and drinking affect men much more than women (Fig. 14).

Discussion

Over the past 30 years, the focus on stroke and the corresponding public health policies have led to significant changes in the global burden of stroke. Although strokes mostly occur in older people, with changes in traditional risk factors and the emergence of new risk factors, the

burden of stroke in young people is increasingly a cause for concern. Epidemiological evidence reports that more than 2 million young people aged 18 to 50 years worldwide suffer from ischaemic stroke each year, accounting for one-tenth of all stroke patients, and this proportion is increasing, which is a very worrying trend [24, 25].

Our work is the first study to analyze and compare the disease burden of different stroke subtypes in young and old age groups globally and across regions. Our study found that as of 2019, although the incidence and mortality for ICH, SAH, and IS are still increasing, the disease

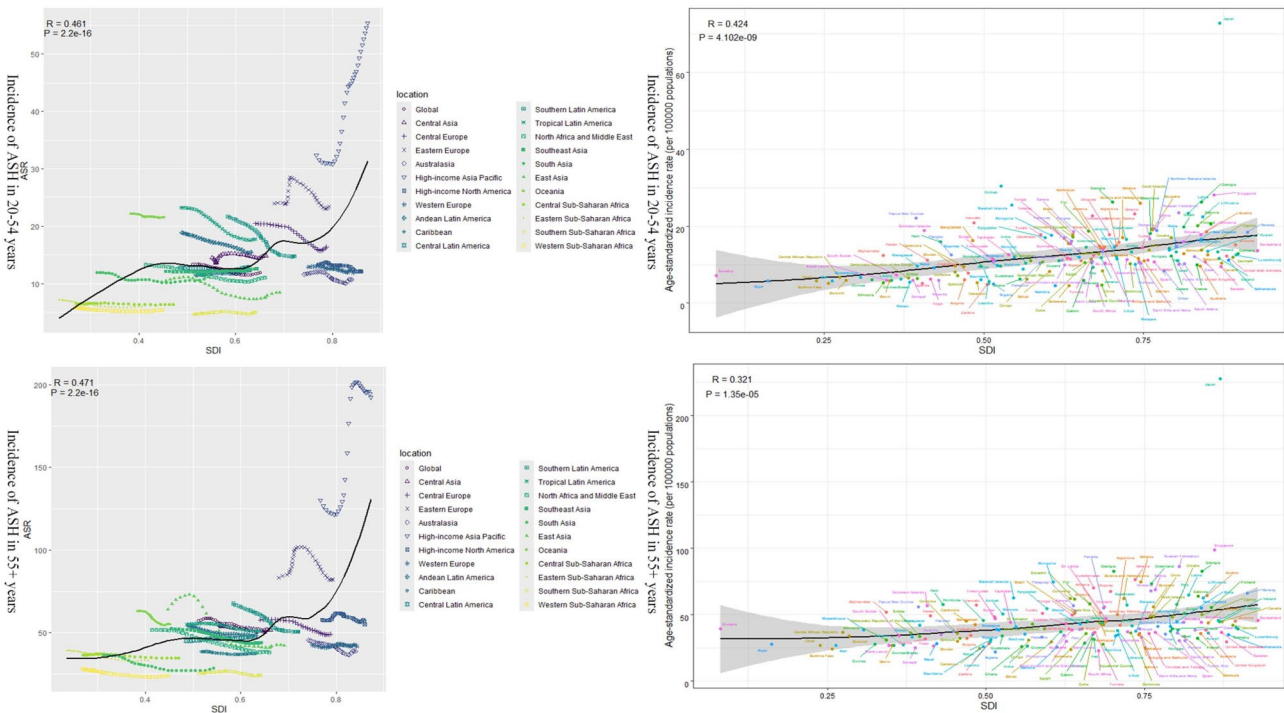


Fig. 12 Association between SAH incidence and SDI. **A-B** Global, regions and countries or territories incidence in the 20–54 years age group. **C-D** Global, regions and countries or territories incidence in the over 55 years age group. SDI: Socio-demographic index. SAH: Subarachnoid haemorrhage

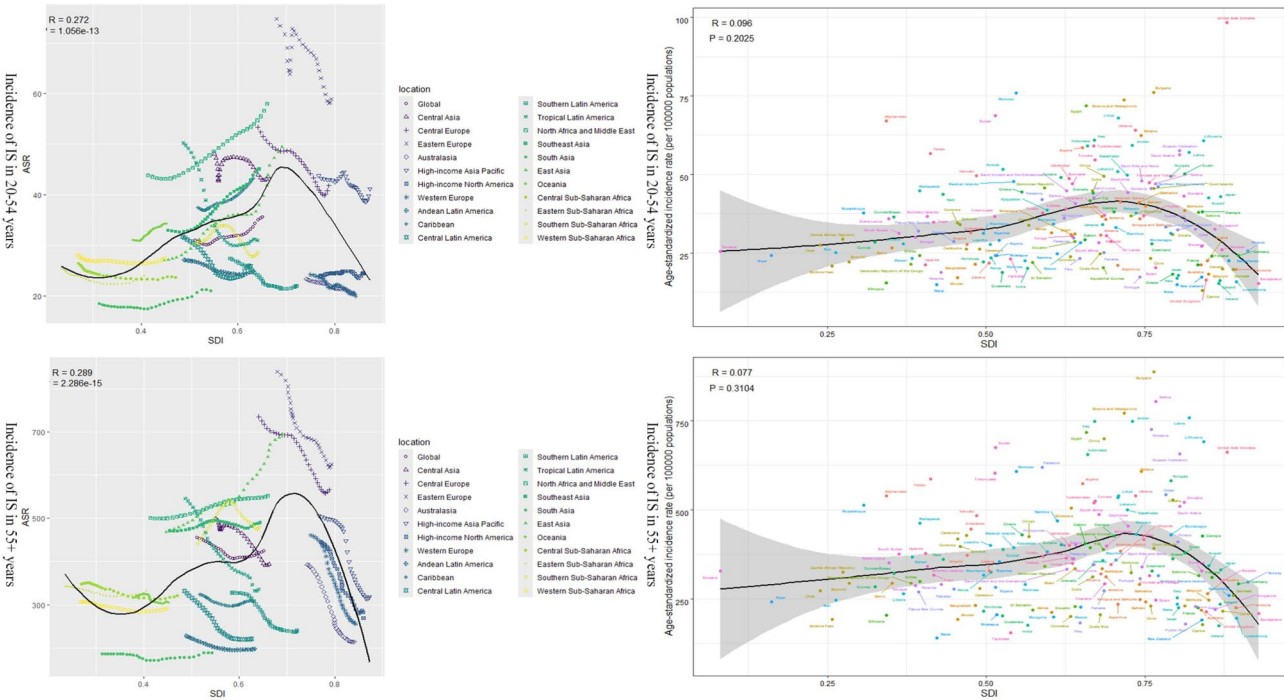


Fig. 13 Association between IS incidence and SDI. **A-B** Global, regions and countries or territories incidence in the 20–54 years age group. **C-D** Global, regions and countries or territories incidence in the over 55 years age group. SDI: Socio-demographic index. IS: Ischemic stroke

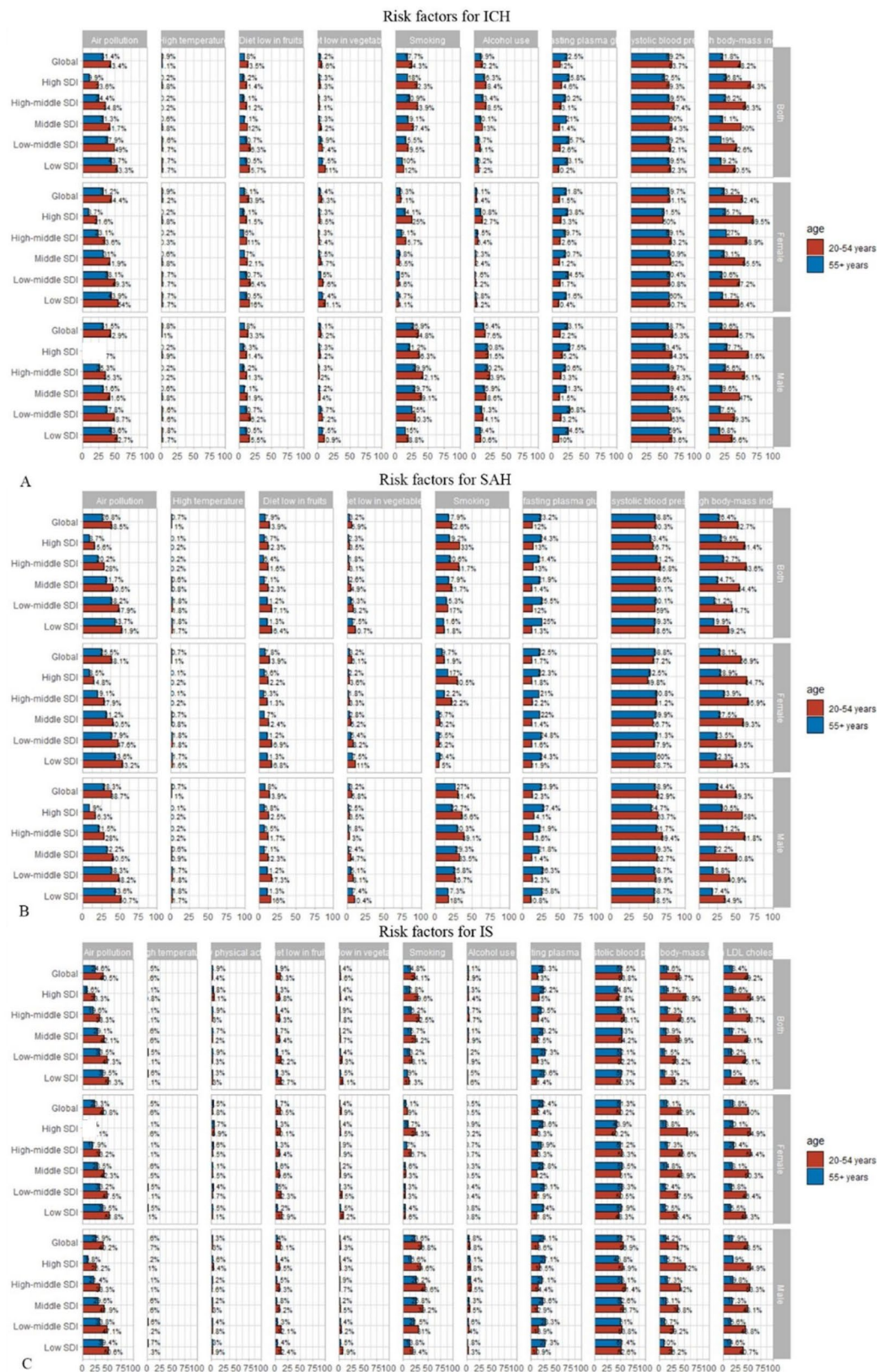


Fig. 14 PAF of risk factors for stroke DALYs for different genders in both age groups. **(A)** Risk factors for ICH. **(B)** Risk factors for SAH. **(C)** Risk factors for IS. ICH: Intracranial haemorrhage. SAH: Subarachnoid haemorrhage. IS: Ischemic stroke. PAF: Population attribution fractions. DALYs: Disability-adjusted life years

burden is generally trending downward except for IS, and the burden is decreasing more significantly in older individuals than in younger individuals. Compared with 1990, the burden of IS in young people has increased significantly, and the burden of IS in the elderly population has also increased year by year since 2005. In addition, the burden of stroke is closely related to the local level of economic development. We found that the proportion of the burden of ICH is significantly negatively correlated with the level of economic development; that is, in areas with a higher SDI, the burden of ICH is smaller. However, the burden of SAH is significantly positively correlated with SDI. There is a striking reversal in the correlation between the incidence of stroke and SDI: in regions with medium and low SDI, the higher the economic level, the higher the incidence of stroke; however, in areas with high SDI, the incidence of stroke is lower. We speculate that increasing diagnostic techniques have led to increasing detection and reporting of stroke in low and middle-income areas, and thus, we observe a rising incidence rate. In contrast, in economically developed regions, people may have healthier dietary and lifestyle habits and pay more attention to disease prevention, resulting in a lower disease burden. In addition, the trend in the burden of stroke in a single region is parallel in the young and old age groups. In conclusion, reducing stroke cases remains a long-term task, especially in regions with underdeveloped socioeconomic levels, and the unequal burden ratios between these regions above are largely consistent with other published literature [26].

The burden of disease regarding stroke has been a hot topic of research. However, some studies have focused only on the burden of stroke in young people and neglected the elderly population [24, 27], and some studies, although complete reporting of the burden of total stroke, ICH, SAH, and IS in all age groups, have lacked comparisons of the differences between genders [28, 29]; therefore, we attempted to summarize and fill in these gaps. Our study analyzes and compares the burden of ICH, SAH, and IS disease by gender in young and elderly populations horizontally and vertically, respectively, focusing on inequalities between regions, key time points at which the turnaround occurs, and the major risk factors contributing to these differences, to provide a more comprehensive basis for the development and implementation of prevention and management policies. We found that, possibly due to the increased global emphasis on the health status of the elderly, the decline in the burden of ICH and SAH in the elderly was more pronounced than in the young, especially in incidence and mortality. In addition, although the stroke burden has shown an upward trend in recent years in both age groups, the increase is greater in the younger group than in the older group, especially in less economically developed

regions. It is worth noting that although the trend in disease burden is generally decreasing, the number of both cases and deaths from stroke in 2019 was higher than in 1990, which can be explained in the following ways. First, it may be due to global demographic changes, which is also the main reason for the increase in the number of cases, and this reason is also verified in our decomposition analysis. Second, it may be due to increased detection rates due to advances in imaging technology, such as diffusion-weighted MRI, and the diagnosis of rare causes, including arterial dissection and patent foramen ovale [27, 30]. Last but not least, there has been an increase in traditional risk factors [31], as well as the emergence of new risk factors such as illegal and recreational drugs [8].

The analysis of risk factors may explain to some extent why there is a trend difference in the burden of stroke between young people and older people. It is well known that metabolic risk factors are increasingly becoming an essential contributor to the global burden of disease caused by stroke. We found that over time, fasting blood sugar and body mass index, which are difficult to control, have gradually become the main factors contributing to the burden of stroke. The difference is that older people are more susceptible to fasting blood sugar, while young people are more sensitive to body mass index. A retrospective cohort study found that higher fasting glucose variability significantly increased the risk of stroke, myocardial infarction, and all-cause mortality, especially in the elderly and those with a long history of diabetes [32]. Another larger prospective study found that diabetes, independent of other traditional risk factors, increases the risk of multiple vascular diseases, including hemorrhagic and ischaemic strokes, by about two times and that there is also a non-linear relationship between fasting blood glucose concentration and the risk of vascular disease in people without diabetes [33], which may be related to complex mechanisms such as oxidative stress during aging [34].

In addition, a high body mass index (BMI) is considered to be closely related to many cardiovascular and cerebrovascular diseases, which profoundly affect their morbidity and mortality [35]. We found that BMI has an increasing impact on the burden of stroke over time. In addition, the proportion of BMI on increasing the burden of death and DALYs from stroke in young people is significantly higher than that in the elderly. It is comparable between men and women, with no obvious regional differences, suggesting that we should pay more attention to weight management in young people and invest more in their lives, diet, activity, and mental health, as all of the above are considered to be closely related to adolescent BMI [36–38]. Furthermore, systolic blood pressure is another major risk factor for stroke. It reflects the stiffness and health of the arteries to a certain extent, directly

affecting the functions of the brain, heart, and kidneys. It is an important indicator for observing the occurrence, prognosis, and death of stroke and is of great significance for the recurrence of stroke [39, 40]. We found that systolic blood pressure has been the leading cause of stroke for the past 30 years. The effect of systolic blood pressure on stroke does not vary significantly with age or sex, and there is no apparent correlation with the level of economic development worldwide. In addition, we found that the above common risk factors contributed almost equally to the different subtypes of stroke, especially to the risk of ICH and SAH, with the difference that BMI did not seem to have as great an effect on IS as it did on ICH and SAH. Conversely, several studies have shown that obesity is associated with a higher risk of total stroke and IS than hemorrhagic stroke [41]. However, our findings were confirmed by another large retrospective study showing that obesity and overweight were associated with a higher risk of hemorrhagic stroke, especially in men, which may be related to the choice of regression model, control of covariates, and whether sensitivity analyses were performed [42].

It is worth noting that with the emphasis on environmental factors, air pollution has gradually become one of the leading causes of increased stroke burden, and young people are more likely to be affected than older people, regardless of gender. Growing evidence has demonstrated that air pollution is among the most common causes of health problems worldwide, especially in low- and middle-income countries [43]. A significant and strong temporal association exists between gaseous and particulate air pollutants and hospital admissions or mortality due to stroke [44], suggesting that in areas with a low level of development, emphasis should be placed on the management of healthcare and the control of environmental pollution, especially the control of fine particles such as PM_{2.5} that are easy to inhale [45]. Compared with 30 years ago, the contribution of the current air pollution burden of disease has slightly decreased in all regions, possibly due to the public and managers' attention to environmental issues. In addition, compared with 1990, in 2019, smoking as a primary risk factor has also been effectively managed and controlled, which may be related to the implementation of the smoking ban and the improvement of public awareness [37]. Moreover, dietary habits have traditionally been considered a risk factor that can lead to many diseases. Therefore, we explored the impact of fruits that may cause blood sugar to rise and vegetables that increase dietary fiber on the burden of stroke. Surprisingly, this contribution is smaller than we previously thought, indicating that nutritional habits may indirectly affect the occurrence of stroke through metabolic factors such as blood sugar and lipids.

In terms of gender rather than age, the burden of stroke differs between men and women. Both globally and in different SDI regions, from 1990 to 2019, the incidence and prevalence of ICH were consistently higher in men than in women, while the incidence and prevalence of SAH and IS were higher in women. However, the mortality and DALY burden of ICH, SAH, and IS were higher in men than in women, which may be related to the protective effect of estrogen. Studies have found that estrogen can induce the upregulation of transferrin, which in turn leads to a hypercoagulable state by enhancing FXIIa/thrombin and blocking the antithrombin-thrombomodulin interaction, causing women to be more prone to stroke than men [46]. Moreover, the above differences seem to be independent of age. We speculate that smoking and drinking behaviours may be the main reasons for the differences in mortality and DALY burden between the sexes. Men are more susceptible to the effects of smoking and drinking than women, and it is important to note that this effect is more pronounced in younger people than in older people. In addition, we found an interesting phenomenon. In terms of the DALYs burden of stroke, smoking behaviour among young women in high-SDI and upper-middle-SDI regions is significantly higher than in the other regions, accounting for more than a quarter of the many risk factors that contribute to the disease, which may be related to young people's greater participation in social activities such as bars, cinemas, and clubs. Areas with a higher level of socioeconomic development may have more similar places for activities and be safer, all of which may increase young women's exposure to smoking [47–50].

Globally, in contrast to the trends for ICH and SAH, the burden of disease for IS, including incidence, DALYs rate, and prevalence, has increased significantly over the past 30 years, both in younger and older age groups, with a more significant increase in the younger group, regardless of gender. Furthermore, the number of deaths from IS has increased despite a decline in mortality. A multi-centre cohort study found that traditional vascular risk factors, such as atherosclerosis in large and small blood vessels, have a more significant effect on stroke than ICH and SAH and are the main cause of stroke in young people [4]. In addition, in terms of IS itself, there are huge regional and socioeconomic differences in its disease burden, which are manifested in a significant increase in regions with medium and low SDI, especially in Asia and Africa. This may be related to various factors, including differences in the equity of access to healthcare among different races and ethnicities, differences in the financial distribution of medical insurance [31] and their inherent lifestyles [51]. Moreover, Young people are always more susceptible to the effects of air pollution, especially in areas with a medium to low level of economic

development. As people pay more attention to the relationship between environmental factors and diseases, this may also be one of the reasons for the younger age of stroke onset in low- and middle-income countries [25, 52]. Therefore, we need to pay more attention to the awareness and management of IS, especially for young people living in areas with an average or even poor level of socioeconomic development, to implement timely and effective prevention and treatment measures.

Limitation

The current work is the first study to comprehensively assess the differences in stroke burden between young and older adults. However, this study has some limitations. First of all, the GBD database covers the burden of disease information of almost all countries and regions in the world, which is affected by many factors such as economic, scientific, geographical and demographic factors. Therefore, the recorded data may be biased in different countries, mainly reflected in underestimating disease burden in regions with lower development index. Secondly, given the period of this database, disease-related information, including diagnostic criteria, reporting criteria, diagnostic tools, and health systems, may be constantly updated, affecting the consistency of data for the same disease. For example, in the current study, with the increasing accuracy of diagnostic techniques, ischemic stroke was defined as infarction of central nervous system tissue according to the revised definition of the AHA in 2002, so there are inevitable biases and gaps in the calculation of stroke disease burden [53]. Finally, because of the inherent limitations of the GBD database, we collected only three common subtypes of stroke; other broad definitions of stroke, such as central nervous system infarction and stroke due to cerebral venous thrombosis, were not recorded; thus, we may have overestimated the burden of stroke. As the GBD database continues to improve, we hope to describe the pressure caused by more stroke subtypes in more detail [1].

Conclusion

Overall, the burden of stroke declined from 1990 to 2019. Still, in recent years, there has been a potential upward trend, especially among young people, where the burden of stroke has continued to increase significantly. Air pollution, smoking, and metabolic factors may be the main risk factors that continue to affect stroke, and young people are more sensitive to these risk factors. In addition, the burden of stroke also shows significant gender differences, such as the burden of SAH. It is significantly higher in women than men, while ICH is lower than in men. We hope the above evidence can provide a basis for formulating public health policies on stroke for different populations.

Abbreviations

AHA	American Heart Association
EAPC	Estimated annual percentage changes
DALYs	Disability-adjusted life-years
PAF	Population-attributable fractions
ICH	Intracranial haemorrhage
SAH	Subarachnoid haemorrhage
IS	Ischaemic stroke
GBD	Global Burden of Disease Study
SDI	Socio-demographic Index

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12889-025-22460-6>.

Supplementary Material 1

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Not applicable.

Author contributions

Q.R. and H.Y. conceived, designed, and supervised the project. W. Z. and L.Y. collected data and performed statistical analyses, and wrote the first draft. H. Y. offered the funder. All authors read and approved the final manuscript.

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Data availability

All the data were available from GHDx platform (<https://vizhub.healthdata.org/gbd-results/>).

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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