Global, regional and national stroke burden and disability-adjusted life-years lost attributable to risk factors in 204 countries, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021

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ABSTRACT

Background: Up-to-date estimates of stroke burden and attributable risks and their trends on global, regional and national levels are essential for evidence-based health care, prevention and resource allocation planning.

Methods: The results provided here are the most up-to-date (1990-2021) estimates of incidence, prevalence, death, and disability-adjusted life-years (DALY) counts and age-standardised rates per 100,000 per year for overall stroke, ischaemic stroke (IS), intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH). We also calculated attributable burden of stroke due to 20 risk factors and 6 risk clusters (with 95% uncertainty intervals [UI]) at the global and regional levels (21 GBD regions and socio-demographic index quintiles), using the standard GBD methodology.

Findings: At level 3 of GBD cause hierarchy, in 2021 stroke was the second most common cause of death (7.3 million deaths; 95% UI 6.6 to 7.8; 10.7% of all deaths [9.8 to 11.3]) and DALYs (160.4 million DALYs [148.0 to 171.7]; 5.6% of all DALYs [5.0 to 6.1]), after ischaemic heart disease. In 2021, there were 93.8 million (89.0 to 99.3) prevalent and 12.0 million (10.8 to 13.2) incident strokes. The study documented disparities in stroke burden and risk factors by GBD region, country, and SDI as well as a stagnation in the reduction of incidence rates from 2015 onwards, and even some increase in the stroke incidence, death, prevalence and DALY rates in Southeast Adia, East Asia, Oceania, countries with lower SDI and in people younger that 70 years. Globally, IS constituted 65.3% (62.4 to 67.7), ICH - 28.8% (28.3 to 28.8), and SAH – 5.8% (5.7 to 6.0) of all incident strokes. Although stroke is highly preventable (84.2%; 78.3 to 88.8), globally, the total number of stroke-related percent of DALYs due to risk factors increased from 1990 to 2021 by 35% (95% UI 24.0 to 46.0), with the most significant increase over that time period in the contribution of high body mass index (BMI; 88.2%; 53.4 to 117.7), high ambient temperature (72.4%; 51.1 to 179.5), ambient particulate matter pollution (46.0; 15.5 to 84.1), high fasting plasma glucose (32.1%; 26.7 to 38.1), and low physical activity (11.3%; 1.8 to 34.9).

Interpretation: Stroke burden - as measured by the number of people who develop new stroke, survived stroke or died and remained disabled (DALYs) - as well as the proportional significance of BMI, high ambient temperature, high fasting plasma glucose and diet high in sugar-sweetened beverages and stroke-related DALYs have significantly increased over the last three decades. The bulk of the stroke burden continues to reside in countries with lower SDI. Additionally, more effective pragmatic solutions recently suggested by the World Stroke Organization – *Lancet Neurology* Commission on Stroke to reduce stroke burden need to be urgently implemented across all countries.

INTRODUCTION

Evidence from the Global Burden of Disease (GBD) studies suggests that prevalent cases of total CVD (including stroke) nearly doubled from 271 million in 1990 (95% UI 257-285 million) to 523 million in 2019 (95% UI 497-550 million).[1] Moreover, despite a consistent decline in age-standardised CVD (including stroke) mortality rates globally in the last half of the 20th century,[1] there has been a subsequent deceleration in the decline, and now an overall flattening of the decline in the past few years.[2] Since 2010, age-standardised CVD (including stroke) mortality rates have even increased in many locations (e.g., USA, Mexico, UK)[1,3] and there has been a significant increase in the age-standardised incidence of stroke in young individuals (under 55) in high-income countries.[4,5] The last GBD study on stroke burden and risks covered the period 1990-2019 and identified stroke as the second leading cause of death in the world.[6] The most recent GBD Study stroke burden projects have demonstrated an almost doubling of the disability-adjusted life-years lost (DALYs), deaths and cost due to stroke from 2020 to 2050.[7] Globally, the age-standardised prevalence of stroke/CVD risk factors (including hypertension, overweight, and diabetes)[1] are also increasing.[8] These worrisome projections and fast increasing stroke burden over the last 30 years,[6] with a trend towards increasing incidence rates in younger people (<55 years old) and increased prevalence of major risk factors for stroke (elevated blood pressure, overweight, and diabetes) over the last 10-15 years, necessitate timely updated data on the most recent changes in stroke burden and risks across the globe to inform adequate health care planning, resource allocation and priority setting for stroke and to assess the success or failure of measures to reduce stroke burden.

The current GBD 2022 Study of stroke burden and risks covers the period from 1990 to 2021. It includes analysis of the additional data sources for 2019-2021 with corresponding re-calculation of all previous stroke burden and risks estimates, including stroke incidence, prevalence, death and disability-adjusted life-years lost (DALYs) for total stroke and its three main pathological types (ischaemic stroke [IS], intracerebral haemorrhage [ICH], and subarachnoid haemorrhage [SAH]). It also includes analysis of DALYs due to stroke and stroke pathological type attributable to 20 risk factors and six risk factor clusters at global, regional and national (204 countries) levels.

METHODS

Details of the GBD 2021 methods for stroke burden and risk factors estimates remained the same as for GBD 2019 estimates and were described elsewhere[9] (see also Appendix, Sections 1 and 2). In brief, stroke was defined according to the clinical WHO criteria[10] and categorised into three pathological types (IS, ICH, and SAH), as described previously.[11] In order to simplify the stroke modelling process and to ensure that all major pathological types were estimated correctly, vital registration and surveillance data were used to model each pathological type of stroke independently, resulting in separate acute and chronic stroke models for IS, ICH and SAH type separately (for details, see Appendix, Section 1). As in in previous GBD stroke burden estimates, we modelled first-ever-in-a-lifetime IS, ICH and SAH from the day of stroke onset through 28 days and separately modelled survival (prevalence) beyond 28 days.[6]

As in previous GBD stroke burden estimates, the Cause of Death Ensemble modelling (CODEm) was used to estimates deaths due to overall stroke and stroke pathological types for 1990-2021 period. For non-fatal disease modelling (incidence and prevalence of stroke) we used the DisMod-MR 2.1 tool,[12] a

Bayesian geospatial disease modelling software that uses data on various disease parameters, the epidemiological relationships between these parameters, and geospatial relationships.[6] It is important to note that in the GBD Study the incidence rate represents new events in a given year while the death rate represents those that occurred in that year regardless of when the stroke occurred.

To analyse the attributable burden of stroke and its three pathological types due to 20 risk factors currently available for such analysis in GBD 2021, we calculated population attributable fractions (PAFs) of DALYs (Appendix Section 2), using the exposure level for each risk factor and theoretical minimum risk exposure that minimises risk for each individual in the population (TMREL) as the reference variable. We analysed data on the prevalence of exposure to a risk and derived relative risks for any risk-outcome pair for which we found sufficient evidence of a causal relationship.[13] Relative risk data were pooled using meta-analysis of cohort, case-control, and/or intervention studies. From the prevalence and relative risk results, population attributable fractions were estimated relative to the TMREL. The PAF represents a proportion of the stroke DALYs that would be decreased if the exposure to the risk factor in the past had been reduced to the counterfactual level of the TMREL.

The risks included in the analysis were (1) ambient particulate matter pollution; (2) household air pollution from solid fuels; non-optimal temperature: (3) low temperature (daily temperatures below the TMREL) and (4) high temperature (daily temperatures above the TMREL); (5) lead exposure; (6) diet high in sodium; (7) diet high in red meat; (8) diet high in processed meat; (9) diet low in fruits; (10) diet low in vegetables; (11) diet low in whole grains; (12) high alcohol use (any alcohol dosage consumption); (13) low physical activity (only for IS burden); (14) smoking; (15) second-hand smoke; (16) high BMI; (17) high fasting plasma glucose; (18) high systolic blood pressure; (19) high LDL cholesterol (only for IS burden); and (20) kidney dysfunction, as measured by low glomerular filtration rate (GFR; not assessed for SAH burden). We set the TMREL to zero for all harmful dietary risk factors with monotonically increasing risk functions (e.g., processed meat intake); this excludes sodium. For protective risks with monotonically declining risk functions with exposure (e.g., fruit intake), we first determined the 85th percentile of exposure in the cohorts or trials used in the meta-regression of each outcome that was associated with the risk. Then, we determined the TMREL by weighting each risk-outcome pair by the relative global magnitude of each outcome.[6]

As with causes, GBD organises risk factors into four levels, from the broadest (Level 1: environmental risks, behavioural risks, and metabolic risks) to the most specific (Level 4; 20 individual risk factors available for the analysis). The PAFs of risk factor groups took into account interactions between risk factors included in the group, as explained elsewhere.[14] Percentages and number of DALYs are not mutually exclusive. The crude sum of the PAF of the risk factors might exceed 100% because the effects of many of these risk factors are mediated partly or wholly through another risk factor or risk factors.[6] Definitions of risk factors and risk groups and further details of risk factors are provided in Section 2 of the Appendix. Changes in the modelling of stroke for GBD 2021 are presented in Section 3 of the Appendix.

For this GBD 2021 analysis, we used data from 3736 vital registration sources, 147 verbal autopsy sources, 368 incidence sources, 117 prevalence sources, 229 excess mortality sources, 7753 risk factor exposure sources, and 2733 risk factor relative risk sources. Further details of the data sources used in this analysis are available on the Global Burden of Disease 2021 Sources Tool website.

Stroke incidence, mortality, prevalence, and DALY estimates are presented in absolute numbers and as age-standardised rates per 100 000 population (with 95% uncertainty intervals [UIs]) and are stratified by age, sex, 21 GBD regions, and seven GBD super-regions (Appendix Figure 6.1). Countries and territories were also grouped into quintiles of high, high-middle, middle, low-middle, and low socio-demographic Index (SDI; a summary indicator of geometric mean of normalised values of a location's income per capita, the average years of schooling in the population aged 15 and over, and the total fertility rate)[15] based on their 2021 values. Expressed on a scale from 0 to 1, a location with an SDI of 0 would have a theoretical minimum level of development relevant to health, while a location with an SDI of 1 would have a theoretical maximum level.

Count data are presented in tables to two decimal places (and rounded to one decimal place in the text), and percentage data (including percentage change) are presented to one decimal place. Uncertainty was propagated throughout all these calculations by creating 1,000 values for each incidence, prevalence, death, or DALY estimate and performing aggregations across causes and locations at the level of each of the 1,000 values for all intermediate steps in the calculation. The lower and upper bounds of the 95% uncertainty interval are the 25th and 975th values of the ordered 1,000 values.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or the writing of the report. All authors had full access to the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Stroke incidence, prevalence, death, and DALYs

In 2021, there were 93.5 million (95% UI 88.7, 99.1) stroke survivors, almost 12 million new stroke events (10.7 to 13.2), 7.3 million deaths from stroke (6.6 to 7.8) and 160.4 million DALYs from stroke (148.0 to 171.7), comprising 10.7% (9.8 to 11.3) and 5.6% (5.0 to 6.1) of all deaths and DALYs from all causes respectively, therefore the second leading cause of deaths and DALYs after ischaemic heart disease (Table 1, Appendix Figure 2). In 2021, there were 93.8 million (89.0 to 99.3) prevalent and 12.0 million (10.8 to 13.2) incident strokes. Although there was a non-significant 2.2% (-7.8 to 3.6) decrease in the absolute number of people who died from stroke from 1990 to 2021 and significant decrease in age-standardised incidence, prevalence, death, and DALY stroke rates (-22% [-24 to -20], -8% [-10 to -7], -39% [-44 to -35] and -39% [-43 to -34], respectively, the number of people who survived stroke, developed new stroke, and the number of people who died or remained disabled from stroke (as measured by DALYs) have increased significantly over that period: 26.8% (24.7 to 29.1), 16.8% (13.1 to 20.3), and 18.7% (9.6 to 27.0), respectively (Table 1, Appendix Figure 3).

Geographical variations in stroke incidence, prevalence, death, and DALYs

We also observed noticeable geographical differences in age-standardised stroke incidence (lowest in Luxemburg [57.7/100,000; 95% UI 53.5 to 62.1] and highest in the Solomon Islands [355/100,000; 332.7 to 378.1]), prevalence (lowest in Cyprus [521.5/100,000; 495.7 to 553.5] and highest in Ghana [245.8/100,000; 1997.3 to 20120.1], death (lowest in Singapore [14.2/100,000; 12.3 to 15.6] and highest in North Macedonia [277.4/100,000; 235.5 to 321.2]) and DALY rates (lowest in Switzerland

[333.3/100,000; 291.0 to 368.8] and highest in Nauru [6100.0/100,000; 4917.8 to 7576.1]). Overall, the highest stroke burden in 2021 was observed in East/Central Asian and Sub-Saharan regions and lowest in North America, Australasian, and Latin America regions (Figure 1, appendix Tables 1-6).

Although there was a trend towards reducing age-standardised stroke burden rates across all quintiles of the SDI, there was a stagnation in the reduction of incidence rates from 2015 onwards, and even some increase in the prevalence rates in high-middle SDI countries from 2020 to 2021 (Figure 2). Similar trend patterns were observed in 7 GBD super regions, with more prominent increases in age-standardised incidence and prevalence rates after 2015 in Southeast Adia, East Asia, and Oceania (Appendix Figure 4).

Burden by pathological type of stroke

IS constituted the largest proportion of all incident strokes (7.8 million [6.7 to 8.9] or 65.3% [62.4 to 67.7] of all strokes), followed by ICH (3.4 million incident events [3.1 to 3.8] or 28.8% [28.3 to 28.8] of all strokes). However, the absolute number of DALYs due to ICH (79.5 million [72.7 to 85.2] or 49.6% of total DALYs due to stroke) was greater, albeit not significantly, than the number of DALYs due to IS (70.3 million [64.1 to 76.1] or 43.8%). In 2021, SAH occurred in 0.7 million people (0.6 to 0.8; or 5.8% [5.7 to 6.0] of all strokes), and there were 10.6 million (9.4 to 12.1) DALYs due to SAH (6.6% of DALYs from all strokes combined). Similar to total stroke, risk patterns were observed for age-standardised rates for the three pathological types of stroke and their trends from 1990 to 2021 globally and by SDI (Appendix Figures 3, 5 and 6): highest rates of incident and fatal IS (92.4/100,000; 79.8 to 105.8 and 44.2/100,000; 39.5 to 47.8, respectively) followed by ICH (40.8/100,000; 36.2 to 45.2 and 39.1/100,000; 35.4 to 42.6, respectively) and SAH (8.3/100,000; 7.3 to 9.5 and 4.2/100,000; 3.7 to 4.8, respectively).

Trends in stroke burden and risks by age, sex and SDI

Among almost 12 million new strokes in 2021, there were 6.3 million males (5.6 to 7.0) and 5.7 females (5.1 to 6.3), or 52.6% and 47.4% respectively; the corresponding sex distribution of prevalent stroke, deaths from stroke and stroke-related DALYs were 51.0% (47.8 million [45.3 to 48.8]) and 49.0% (46.0 million [43.5 to 48.8]), 52.1% (3.8 million [3.4 to 4.2]) and 47.9% (3.5 million [3.1 to 3.8]), and 55.0% and 45.0% (72.2 million [65.5 to 78.3), respectively, with the majority of the stroke burden in middle SDI, high-middle and low-middle SDI regions (appendix Table 13). At level 1 of GBD risk factors hierarchy, the greatest contribution of metabolic and behavioural risks to stroke-related DALYs had regions with higher SDI, whereas environmental risks most prominently contributed to stroke-related DALYs in lower SDI countries (appendix Tables 13-16).

While incidence, prevalence, death and DALY rates significantly increased in people younger that 70 years (percentage change from 1990 to 2021: 5.7% [2.1 to 9.6], 15.9% [14.2 to 17.9], 9.7% [2.5 to 17.8], and 18.1% [8.6 to 29.0], respectively), stroke incidence, death and DALY rates significantly reduced in people older than 70 years (-22.5% [-25.5 to – 19.0], -27.6% [-31.5 to -23.7], and -27.7% [-31.7 to -24.2]), and prevalence rate in this age group did not significantly change over the last three decades (-1.0 [-3.1 to 1.2]) (Appendix Figures 6 and 7). Similar to that trend, patterns were observed for IS for both age groups, while incidence of and death from SAH was reduced in people younger than 70 years (-10.2% [-13.5 to -6.7] and 23.0% [-34.2 to -2.4]) as well as incidence rates of ICH (-9.9% [1-13.54 to -4.7]); death rate from ICH in people younger that 70 years also significantly increased from 1990 to 2021 (10.1% [2.0 to 19.5]).

Contribution of risk factors to the stroke-related DALYs

Globally, the total number of stroke-related DALYs due to risk factors increased substantially from 1990 (100.1 million [95% UI 92.3 to 107.5]) to 2021 (135.1 million; 122.1 to 148.2). In 2021, 84.2% (95% UI 78.3 to 88.8) of DALYs from stroke were attributed to the 20 risk factors analysed, with the largest proportions of attributable risks for total stroke, IS, ICH and SAH observed in Eastern Europe, Asia, and Sub-Saharan Africa (Figure 3). Stroke attributable to metabolic risks constituted 68.8% (57.6 to 77.5), environmental risks 36.7% (29.0 to 44.2), and behavioural risks 35.4% (23.4 to 47.5). While the proportion of stroke related DALYs from metabolic risks has increased from 1990 to 2021 by 6.7% (3.8 to 10.0; mainly because of the increase in high BMI [88.2%; 53.4 to 117.7], high ambient temperature [72.4%; 51.1 to 179.5], high fasting plasma glucose [32.1%; 26.7 to 38.1] and diet high in sugar-sweetened beverages [23.4%; 12.7 to 35.7]), proportions of stroke related DALYs from behavioural and environmental risks over the same period have decreased by 7.8% (-13.7 to -2.7; mainly because of the decrease in tobacco smoking [12.0%; -16.9 to -6.6] and dietary risks [10.8%; -25.2 to -1.4]) and 14.8% (-21.6 to – 8.7; mainly because of the decrease in ambient air pollution [20.4%; -27.3 to -12.9]), respectively.

Globally, of the 20 risk factors analysed, at level 4 GBD hierarchy of risk factors 14 individually significant risk factors for stroke (Figure 4, A) were: high SBP (56.8% attributable DALYs [42.5 to 68.0]), ambient particular matter (16.6%; 11.5 to 20.9), smoking (13.8%; 2.5 to 26.0), high LDL cholesterol (13.1%; 4.6 to 21.3), household air pollution (11.2%; 6.4 to 19.3), diet high in sodium (10.6%; 2.8 to 22.8), high fasting plasma glucose (10.3%; 8.1 to 12.6), kidney disfunction (9.3%; 6.8 to 11.8), diet low in fruits (5.9%; 0.4 to 10.4), high alcohol use (5.2%; 1.3 to 9.8), high BMI (4.7%; 0.4 to 9.8), second-hand smoking (4.4%; 1.0 to 7.9), low physical activity (2.1%; 0.5 to 3.9), and diet low in vegetables (1.6%; 0.4 to 2.6).

Similar to total stroke, risk factors were individually significant for IS and ICH, except for high alcohol use which was not independently significant associated with IS-related DALYs (Figure 4, B) and diet low in fruits and vegetables and high BMI that were not independently significant associated with ICH-related DALYs (Figure 4, C). Unlike IS and ICH, non-optimal ambient temperature appeared to be independently associated with the SAH-related DALYs, with the greater contribution of low ambient temperature (4.5%; 3.8 to 5.3) compared to high ambient temperature (1.1%; 0.2 to 2.5). Other independently significant risk factors for SAH (Figure 4, D) were second-had smoking (4.8%; 1.1 to 8.5), diet high in sodium (8.9%; 2.0 to 19.8), household air pollution from solid fuels (10.3%; 5.5 to 17.4), ambient particulate matter pollution (14.2%; 9.8 to 18.0), smoking (14.5%; 2.7 to 27.2), and high SBP (51.6%; 37.9 to 62.6).

From 1990 to 2021 (Appendix Figure 8), we observed an increase in the percentage of stroke-related DALYs attributable to ambient particulate matter (46.0% increase), high fasting plasma glucose (32.1% increase), high alcohol use (3.3% increase), high BMI (88.2% increase), and low physical activity (11.3% increase), but a reduction in the proportional change in household air pollution, kidney dysfunction, low ambient temperature, second-hand smoking, diet low in fibre, and diet low in vegetables (-52.5%, 0.5%, -20.8%, -12.6%, -25.1%, and -30.3%, respectively). While high SBP was the highest ranked risk factor across all 21 GBD regions (Figure 5), there were noticeable variations in the ranking of PAFs of other risk factors. For risk factors by pathological type of stroke, SDI, 21 GBD regions and 204 countries see Appendix Tables 7-16.

DISCUSSION

In 2021, at level 3 of GBD cause hierarchy, stroke was not only the second leading cause of death in the world, as in 2019,[6] but it also became the second leading cause of DALYs, evidencing the globally increased burden of stroke, with the bulk of the stroke burden residing in countries with lower SDI. Consistent with previous studies,[6,16] this study showed disparities in stroke burden and risk factors by GBD region, country, and SDI as well as a continuous trend towards reducing stroke incidence, prevalence, and DALY rates from 1990 to 2021. However, the current study documented a stagnation in the reduction of incidence rates from 2015 onwards, and even some increase in the stroke incidence, death, prevalence and DALY rates in Southeast Asia, East Asia, Oceania, countries with lower SDI and in people younger that 70 years. A trend towards increasing incidence and prevalence rate of CVDs (including stroke) in youth and young adults aged 15-39 years globally[17] and stroke incidence rates in people younger than 55 years[4] vs older people was also demonstrated in previous systematic reviews.

Apart from the population growth and aging,[1,18] other factors responsible for the increased burden of stroke in the world are likely to be related to the insufficient effectiveness of the currently used primary stroke and CVD prevention strategies[19,20] as well as the disparities and major gaps in stroke service provision/accessibility and workforce of stroke care providers in many countries (especially low- to middle-income countries).[16,21,22] Although stroke is highly preventable (PAF 84.2%; 78.3 to 88.8), globally, the total number of stroke-related DALYs due to risk factors increased by 35% (95% UI 24.0 to 46.0), with the most significant PAF increase of high BMI (88.2%; 53.4 to 117.7), high ambient temperature (72.4%; 51.1 to 179.5), high fasting plasma glucose (32.1%; 26.7 to 38.1) and diet high in sugar-sweetened beverages (23.4%; 12.7 to 35.7). While the increase in PAF of stroke-related DALYs due to the increase in BMI and high fasting plasma glucose were also observed in the previous GBD stroke burden report,[6] the high PAF due to high ambient temperature and diet high in sugar-sweetened beverages are the new findings, suggesting the growing role of these environmental and behavioural risks in the increased burden of stroke.

This study is the first to show the high contribution of ambient particulate matter pollution and household air pollution from solid fuels though the DALYs burden due to SAH are comparable to the contribution of smoking. A close relationship between ambient air pollution and SAH mortality was found in some studies.[23-25] Air pollution in 2021 appeared to be highly significant to other pathological types of stroke and also caused 11.9% (10.0 to 13.8) of total deaths making it the second highest cause of death globally (after high SBP) and 8.2% (6.9 to 9.6) of global DALYs making it the second cause of DALYs from all causes (after malnutrition)[26] As ambient air pollution is reciprocally associated with the ambient temperature and climate change all of which synergistically influence stroke/CVD occurrence[27-29] and overall health,[30,31] the importance of urgent climate actions and measures to reduce ambient and household air pollution outlined by the WHO cannot be overestimated.[30,31] It is also recommended for governments to increase implementation of a clean energy economy, promote unprocessed plant-based food choices[27] and global phaseout of factory (industrialised animal) farming, ending government subsidies for animal-based meat, dairy, and eggs, and initiating taxes on such products.[32]

Additional measures to reduce stroke burden were recently outlined by the World Stroke Organization – Lancet Neurology Commission on Stroke[22] and include evidence-based pragmatic recommendations to reduce the global stroke burden, including measures to improve stroke surveillance, prevention, acute care and rehabilitation. Key recommendations include: (1) Establishing low-cost surveillance systems to provide accurate epidemiological stroke data to guide prevention and treatment; (2) Raising public awareness and action to improve healthy lifestyles and prevent stroke through population-wide use of mobile and digital technologies, such as training and awareness-raising videos and apps; (3) Prioritising effective planning of acute stroke care services, capacity building, training, provision of appropriate equipment, treatment and affordable medicines, and adequate resource allocation at national and regional levels; (4) Adapting evidence-based recommendations to regional contexts, including training, support and supervision of community health workers to assist in long-term stroke care; and (5) Establishing local, national and regional ecosystems involving all relevant stakeholders to co-create, co-implement and monitor stroke surveillance, prevention, acute care and rehabilitation.

Every member State of the United Nations has committed to meeting the SDGs, but at present few countries are on target to achieve SDG 3.4. By implementing and monitoring the World Stroke Organization – Lancet Neurology Commission's recommendations, the global burden of stroke would be reduced drastically this decade and beyond. Not only will this enable us to meet SDG 3.4, as well as other key SDGs, it will improve brain health and the overall wellbeing of millions of people across the globe. One of the most common problems in implementing stroke prevention and care recommendations is the lack of funding. The Commission recommends introducing legislative regulations and taxations of unhealthy products (such as salt, alcohol, sugary drinks, unsaturated fatty acids) by each government in the world. Such taxation would not only reduce consumption of these products and, therefore, lead to the reduction of burden from stroke and major other non-communicable diseases but also generates a large revenue sufficient to fund not only prevention programmes and services for stroke and other major disorders, but also reduce poverty, inequality in health service provision and improve wellbeing of the population and boost local economies.

The main strength of this study is the extended number of data sources included in the analysis that allowed us to get more accurate and up-to-date stroke burden and risk factor estimates. This allows evidence-based health care planning and resource allocation by health policy makers on the national, regional, and global levels. However, as with all previous GBD analyses, our study is not free from limitations detailed elsewhere.[6,33] Specifically, there is still a lack of good-quality stroke epidemiological studies in most countries of the world. Unlike previous GBD estimates, the current GBD 2021 study does not present estimates by the World Bank country income levels, thus preventing us from comparing trends by country income levels. Race/ethnic disparities and race/ethnic-associated risk factors should also be incorporated into future GBD analyses.

In summary, our study findings continue to point out that currently used stroke prevention strategies are not sufficiently effective to hold, let alone reduce, the fast-growing stroke burden. Additional, more effective stroke prevention strategies (with the emphasis on population-wide measures, task shifting and the wider use of evidence-based mobile and telehealth platforms) and pragmatic solutions to address the critical gaps in stroke service delivery and development of context-appropriate workforce capacity building and epidemiological surveillance systems recently suggested by the World Stroke Organization – *Lancet Neurology* Commission on Stroke[22] need to be urgently implemented across all countries. Without scaling up these innovative evidence-based strategies and policies that target local, national, regional and global stroke prevention and care disparities, the burden of stroke continues to grow, thus threatening the sustainability of the health system in the whole world.

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For authors' contribution to the manuscript, please see appendix pp.5-10.

Declaration of interests

The authors declare no competing interests. XXX

Tables

Table 1. Absolute number (in millions) and age-standardised rates per 100,000 people per year, with 95% uncertainty intervals (UI), of incident and prevalent stroke, deaths from stroke and DALYs due to stroke in 2021 and percentage change in the metrics in the world for 1990-2021, by pathological type of stroke.

Table 2. Stroke related DALYs (absolute numbers [in millions with 95% UI] and percentage [with 95% UI]) associated with risk factors and their clusters in 2021, all ages, both sexes

Figures

Figure 1. Global age-standardised rates (per 100,000 people) of stroke incidence, prevalence, death, and DALYs in 2021 of stroke, both sexes.

Figure 2. Global trends in age-standardised stroke incidence, prevalence, death, and DALY rates per 100,000 per year for 1990-2021 by SDI, both sexes.

Figure 3. Age-standardised stroke-related DALYs attributable to all risk factors combined, for both sexes, 2021.

Figure 4. Most individually significant risk factors for total stroke, IS, ICH and SAH, as measured by the proportion of DALYs from stroke attributable to the risk factors.

Figure 5. Ranking of age-standardised stroke-related DALYs attributable to risk factors by 21 GBD regions, for both sexes, 2021.

Appendix

Table 1. Absolute number (in millions) and age-standardised rates per 100,000 people per year, with 95% uncertainty intervals (UI), of incident and prevalent stroke, deaths from stroke and DALYs due to stroke in 2021 and percentage change in the metrics in the world for 1990-2021, by pathological types of stroke

Pathological types of stroke		Incidence (95% UI)		Deaths (95% UI)		Prevalence (95% UI)		DALYs (95% UI)	
		Metric in 2021	Percentage change, 1990-2021	Metric in 2021	Percentage change, 1990-2021	Metric in 2021	Percentage change, 1990-2021	Metric in 2021	Percentage change, 1990-2021
Ischaemic stroke	Absolute number, millions	7.79 (6.70 - 8.94)	88% (81% to 95%)	3.59 (3.22 to 3.89)	55% (66% to 44%)	69.67 (64.48 to 74.77)	102% (98% to 106%)	70.31 (64.07 to 76.03)	52% (41% to 64%)
	Age-standardised rate (per 100,000)	92.2 (79.7 - 105.7)	-16% (-19% to -13%)	44.2 (39.5 to 47.8)	-40% (-35% to -44%)	816.2 (756.6 to 875.7)	-3% (-5% to -2%)	836.8 (762.5 to 905.1)	-35% (-39% to -30%)
Intracerebral haemorrhage	Absolute number, millions	3.44 (3.05 to 3.81)	46% (41% to 52%)	3.31 (3.01 to 3.60)	41% (57% to 28%)	16.59 (15.14 to 18.17)	49% (44% to 53%)	79.44 (72.66 to 85.52)	26% (14% to 38%)
	Age-standardised rate (per 100,000)	40.8 (36.2 to 45.2)	-31% (-34% to -29%)	39.1 (35.4 to 42.6)	-37% (-30% to -43%)	194.3 (177.8 to 212.4)	-22% (-24% to -21%)	923.5 (844.0 to 993.4)	-39% (-45% to -33%)
Subarachnoid haemorrhage	Absolute number, millions	0.70 (0.61 to 0.80)	37% (32% to 42%)	0.35 (0.31 to 0.40)	-6% (30% to -23%)	7.83 (7.14 to 8.56)	60% (57% to 63%)	10.64 (9.41 to 12.09)	-12% (-25% to 10%)
	Age-standardised rate (per 100,000)	8.3 (7.3 to 9.5)	-29% (-32% to -26%)	4.2 (3.7 to 4.8)	-56% (-39% to -65%)	91.9 (83.8 to 100.4)	-16% (-18% to -15%)	125.2 (110.7 to 142.3)	-55% (-62% to -43%)
Total stroke	Absolute number, millions	11.93 (10.76 to 13.20)	70% (66% to 75%)	7.25 (6.60 to 7.82)	44% (56% to 33%)	93.51 (88.69 to 99.07)	86% (83% to 90%)	160.40 (147.97 to 171.61)	32% (22% to 43%)
	Age-standardised rate (per 100,000)	141.4 (127.8 to 155.7)	-22% (-24% to -20%)	87.4 (79.5 to 94.4)	-39% (-35% to -44%)	1,095.6 (1,040.1 to 1,158.9)	-8% (-9% to -7%)	1,885.5 (1,739.6 to 2,016.7)	-39% (-43% to -34%)

Table 2. Stroke related DALYs (absolute numbers [in millions with 95% UI] and percentage [with 95% UI]) associated with risk factors and their clusters in 2021, all ages, both sexes

	Globally		**High SDI countries**		**High Middle SDI countries**		**Low Middle SDI countries**		**Low SDI countries**	
	Absolute number (in millions)	**Percentage (%)**	**Absolute number (in millions)**	**Percentage (%)**	**Absolute number (in millions)**	**Percentage (%)**	**Absolute number (in millions)**	**Percentage (%)**	**Absolute number (in millions)**	**Percentage (%)**
Air pollution and environmental risks										
Ambient $PM_{2.5}$ pollution	26.78 (18.08 to 34.22)	17% (12% to 21%)	1.62 (1.22 to 2.08)	11% (8% to 14%)	7.17 (5.10 to 9.08)	19% (14% to 23%)	4.63 (2.75 to 6.59)	14% (8% to 19%)	1.04 (0.66 to 1.53)	8% (5% to 11%)
Household air pollution from solid fuels	0.44 (0.10 to 0.78)	0% (0% to 0%)	0.16 (0.04 to 0.28)	1% (0% to 2%)	0.17 (0.04 to 0.31)	0% (0% to 1%)	0.04 (0.01 to 0.07)	0% (0% to 0%)	0.01 (0.00 to 0.02)	0% (0% to 0%)
Low ambient temperature	-5.16 (-21.85 to 7.27)	-3% (-13% to 5%)	-0.50 (-2.20 to 0.76)	-3% (-14% to 5%)	-1.53 (-6.62 to 2.20)	-4% (-17% to 6%)	-0.46 (-1.78 to 0.68)	-1% (-5% to 2%)	-0.19 (-0.72 to 0.30)	-1% (-6% to 2%)
High ambient temperature	17.40 (4.61 to 37.98)	11% (3% to 23%)	1.20 (0.19 to 2.97)	8% (1% to 20%)	5.19 (1.65 to 10.45)	13% (4% to 27%)	2.41 (0.30 to 6.26)	7% (1% to 19%)	0.61 (0.02 to 1.86)	5% (0% to 14%)
Lead exposure	9.63 (0.66 to 16.96)	6% (0% to 11%)	0.52 (0.05 to 0.93)	3% (0% to 6%)	1.40 (0.13 to 2.60)	4% (0% to 7%)	3.16 (0.23 to 5.38)	9% (1% to 16%)	1.19 (0.06 to 2.07)	9% (0% to 16%)
Dietary risks										
Diet high in sodium	2.54 (0.64 to 4.27)	2% (0% to 3%)	0.08 (0.02 to 0.14)	1% (0% to 1%)	0.11 (0.04 to 0.18)	0% (0% to 0%)	0.95 (0.22 to 1.61)	3% (1% to 5%)	0.87 (0.13 to 1.50)	7% (1% to 11%)
Diet high in red meat	3.13 (-3.18 to 8.78)	2% (-2% to 5%)	0.31 (-0.30 to 0.93)	2% (-2% to 6%)	1.00 (-0.99 to 2.78)	3% (-3% to 7%)	0.55 (-0.57 to 1.52)	2% (-2% to 4%)	0.23 (-0.23 to 0.63)	2% (-2% to 5%)
Diet high in processed meat	8.44 (2.06 to 16.10)	5% (1% to 10%)	1.21 (0.22 to 2.47)	8% (2% to 16%)	2.64 (0.59 to 5.25)	7% (1% to 14%)	0.96 (0.22 to 1.85)	3% (1% to 5%)	0.41 (0.09 to 0.82)	3% (1% to 6%)
Diet low in fruits	7.69 (0.62 to 15.86)	5% (0% to 10%)	1.05 (0.08 to 2.12)	7% (1% to 14%)	2.35 (0.19 to 4.87)	6% (1% to 12%)	1.34 (0.12 to 2.73)	4% (0% to 8%)	0.39 (0.03 to 0.85)	3% (0% to 6%)
Diet low in vegetables	16.47 (12.73 to 20.29)	10% (8% to 13%)	2.15 (1.68 to 2.63)	14% (11% to 17%)	4.52 (3.55 to 5.63)	12% (9% to 14%)	3.17 (2.39 to 3.99)	9% (7% to 12%)	0.91 (0.68 to 1.15)	7% (5% to 9%)
Diet low in whole grains	20.98 (7.41 to 34.67)	13% (5% to 21%)	2.66 (0.90 to 4.38)	17% (6% to 29%)	6.61 (2.32 to 10.84)	17% (6% to 28%)	3.46 (1.24 to 5.73)	10% (4% to 17%)	1.07 (0.38 to 1.80)	8% (3% to 13%)
Alcohol use	91.85 (69.07 to 112.22)	57% (43% to 68%)	8.14 (6.00 to 10.02)	53% (39% to 65%)	22.82 (16.77 to 28.10)	59% (45% to 71%)	19.29 (14.61 to 23.62)	57% (43% to 68%)	6.83 (5.10 to 8.52)	52% (38% to 63%)
Physical activity										
Low physical activity	1.80 (0.33 to 4.12)	1% (0% to 2%)	0.08 (-0.03 to 0.23)	1% (0% to 1%)	0.13 (-0.14 to 0.56)	0% (0% to 1%)	0.77 (0.23 to 1.52)	2% (1% to 4%)	0.24 (0.10 to 0.43)	2% (1% to 3%)
Tobacco smoking										
Smoking	18.18 (10.67 to 30.88)	11% (7% to 20%)	0.01 (0.00 to 0.07)	0% (0% to 0%)	0.63 (0.04 to 3.29)	2% (0% to 8%)	8.21 (5.34 to 11.52)	24% (16% to 34%)	4.80 (3.78 to 5.77)	37% (30% to 43%)
Second-hand smoking	15.01 (10.94 to 19.13)	9% (7% to 12%)	1.26 (0.84 to 1.72)	8% (6% to 11%)	3.25 (2.32 to 4.27)	8% (6% to 11%)	3.53 (2.60 to 4.49)	10% (8% to 13%)	1.22 (0.89 to 1.59)	9% (7% to 12%)
Physiological factors										
High Body Mass Index	12.02 (-1.59 to 26.56)	7% (-1% to 17%)	0.57 (-0.08 to 1.29)	4% (0% to 9%)	2.35 (-0.31 to 5.29)	6% (-1% to 14%)	3.18 (-0.43 to 6.93)	9% (-1% to 21%)	1.23 (-0.16 to 2.66)	9% (-1% to 21%)
High fasting plasma glucose	3.36 (0.91 to 6.30)	2% (1% to 4%)	0.37 (-0.03 to 0.83)	2% (0% to 5%)	0.94 (0.16 to 1.89)	2% (0% to 5%)	0.65 (0.24 to 1.13)	2% (1% to 3%)	0.16 (0.06 to 0.28)	1% (0% to 2%)
High systolic blood pressure	7.61 (6.48 to 9.01)	5% (4% to 6%)	0.97 (0.84 to 1.12)	6% (6% to 7%)	2.75 (2.33 to 3.23)	7% (6% to 8%)	0.78 (0.48 to 1.14)	2% (1% to 3%)	0.29 (0.22 to 0.39)	2% (2% to 3%)

High LDL cholesterol	7.17 (1.67 to 12.72)	4% (1% to 8%)	0.39 (0.09 to 0.71)	3% (1% to 5%)	1.80 (0.42 to 3.17)	5% (1% to 8%)	1.56 (0.36 to 2.82)	5% (1% to 8%)	0.41 (0.10 to 0.76)	3% (1% to 6%)
Kidney dysfunction	22.61 (4.00 to 41.84)	14% (3% to 27%)	1.88 (0.31 to 3.71)	12% (2% to 25%)	6.32 (1.20 to 11.65)	16% (3% to 31%)	4.02 (0.67 to 7.61)	12% (2% to 23%)	0.95 (0.14 to 1.91)	7% (1% to 15%)
Cluster of risk factors										
Air pollution*	44.96 (35.02 to 55.47)	28 (23 to 35)	1.63 (1.23 to 2.08)	11% (8% to 14%)	7.80 (5.93 to 10.19)	20% (16% to 26%)	12.84 (10.11 to 15.25)	38% (31% to 45%)	5.84 (4.66 to 6.93)	45% (37% to 52%)
Tobacco smoke†	28.80 (10.28 to 47.41)	18 (7 to 30)	2.21 (0.69 to 4.01)	15% (4% to 27%)	7.83 (2.76 to 12.88)	20% (7% to 34%)	5.40 (2.02 to 9.00)	16% (6% to 27%)	1.33 (0.50 to 2.29)	10% (4% to 18%)
Dietary risks‡	27.38 (13.00 to 45.75)	17 (8 to 28)	1.77 (0.67 to 3.47)	12% (4% to 22%)	6.35 (2.67 to 11.34)	17% (7% to 29%)	6.23 (1.91 to 10.10)	19% (6% to 31%)	2.51 (0.67 to 4.04)	19% (5% to 32%)
Behavioural risks§	57.75 (36.54 to 78.62)	36 (24 to 48)	4.78 (2.79 to 6.87)	31% (18% to 45%)	14.76 (9.35 to 20.23)	38% (25% to 52%)	11.52 (7.28 to 15.76)	34% (22% to 47%)	3.93 (2.27 to 5.39)	30% (17% to 42%)
Environmental/occupational risks¶	111.02 (91.92 to 127.72)	69 (58 to 78)	10.57 (8.79 to 12.29)	69% (59% to 78%)	27.85 (22.71 to 32.43)	73% (61% to 81%)	22.92 (19.07 to 26.50)	68% (57% to 77%)	8.08 (6.54 to 9.61)	62% (51% to 70%)
Metabolic risks¦	59.41 (45.89 to 72.10)	37 (29 to 45)	3.01 (2.27 to 3.79)	20% (15% to 24%)	11.77 (8.94 to 14.98)	31% (24% to 38%)	15.56 (12.22 to 18.54)	46% (37% to 55%)	6.74 (5.47 to 7.91)	51% (43% to 59%)
Combined risk factors										
All risk factors combined	135.05 (122.07 to 148.22)	84 (78 to 89)	12.21 (10.71 to 13.59)	80% (73% to 86%)	32.73 (29.06 to 36.72)	85% (79% to 90%)	28.73 (25.90 to 31.34)	85% (80% to 89%)	10.67 (9.37 to 11.88)	81% (76% to 85%)

Percentages and number of DALYs are not mutually exclusive. The sum of percentages and number of DALYs in the columns exceeds the totals for all risk factors combined because of overlap between various risk factors. 0% represents very low numbers. *Air pollution cluster includes ambient PM2.5 pollution and household air pollution. †Tobacco smoke includes smoking and second-hand smoking. ‡Dietary risks cluster includes diet high in sodium, diet high in sugar-sweetened beverages, diet low in fruits, diet low in vegetables, and diet low in whole grains. §Behavioural risks cluster includes smoking (including second-hand smoking), dietary risks (diet high in sodium, diet high in sugar-sweetened beverages, diet low in fruits, diet low in vegetables, diet low in whole grains, and alcohol use), and low physical activity. ¶Environmental risks cluster includes air pollution cluster, low ambient temperature, high ambient temperature and lead exposure. ¦Metabolic risks cluster includes high fasting plasma glucose, high LDL cholesterol, high systolic blood pressure, high body-mass index, and low glomerular filtration rate. **Age-standardised total percentage of DALYs due to all risk factors combined. The crude sum of PAF of the risk factors may exceed 100% because the effect of many of these risk factors are mediated partly or wholly through another risk factors.

Figure 1. Global age-standardised rates (per 100,000 people) of stroke incidence, prevalence, death, and DALYs in 2021 of stroke, both sexes.

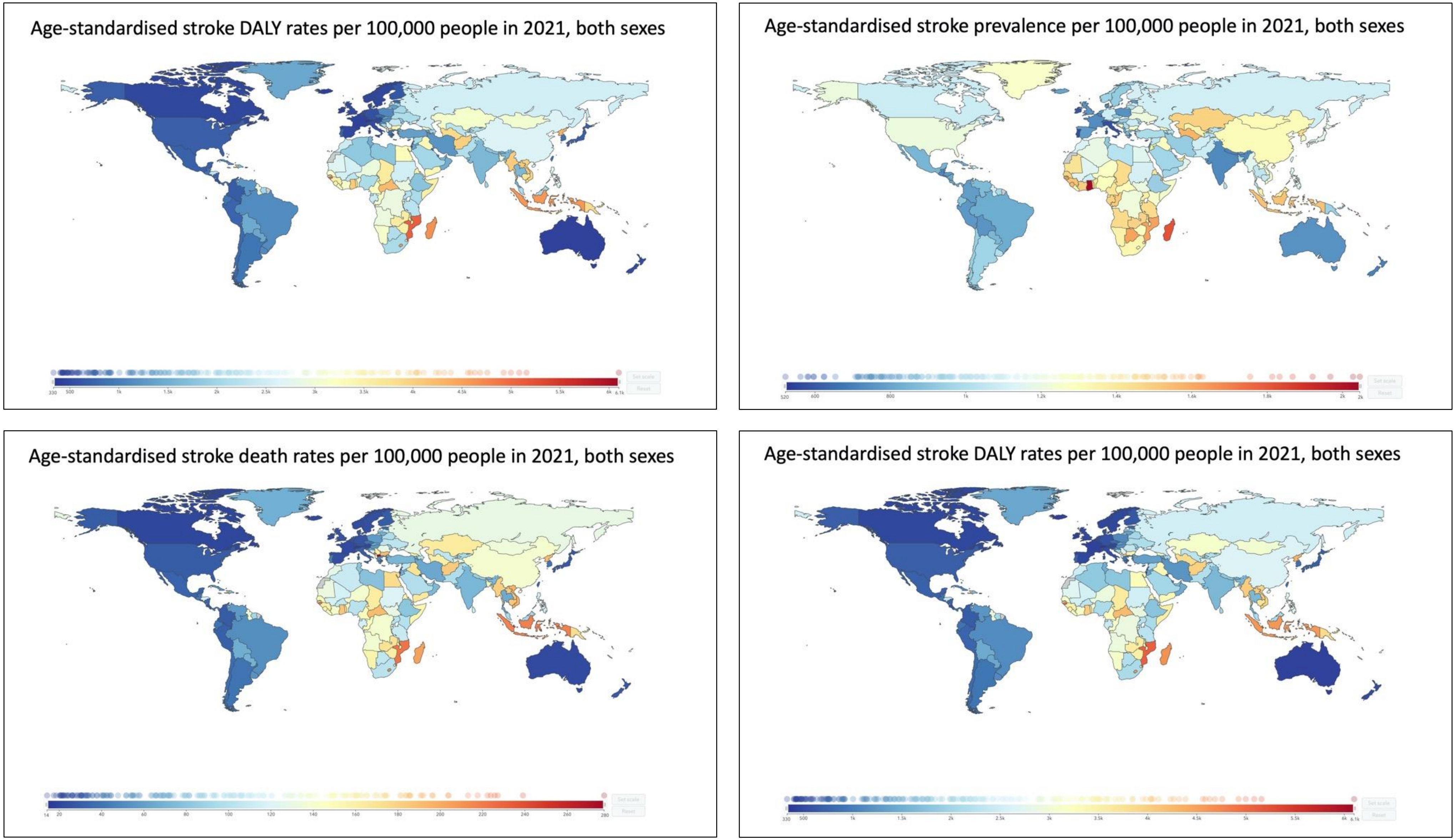


Figure 2. Global trends in age-standardised stroke incidence, prevalence, death, and DALY rates per 100,000 per year for 1990-2021 by SDI, both sexes

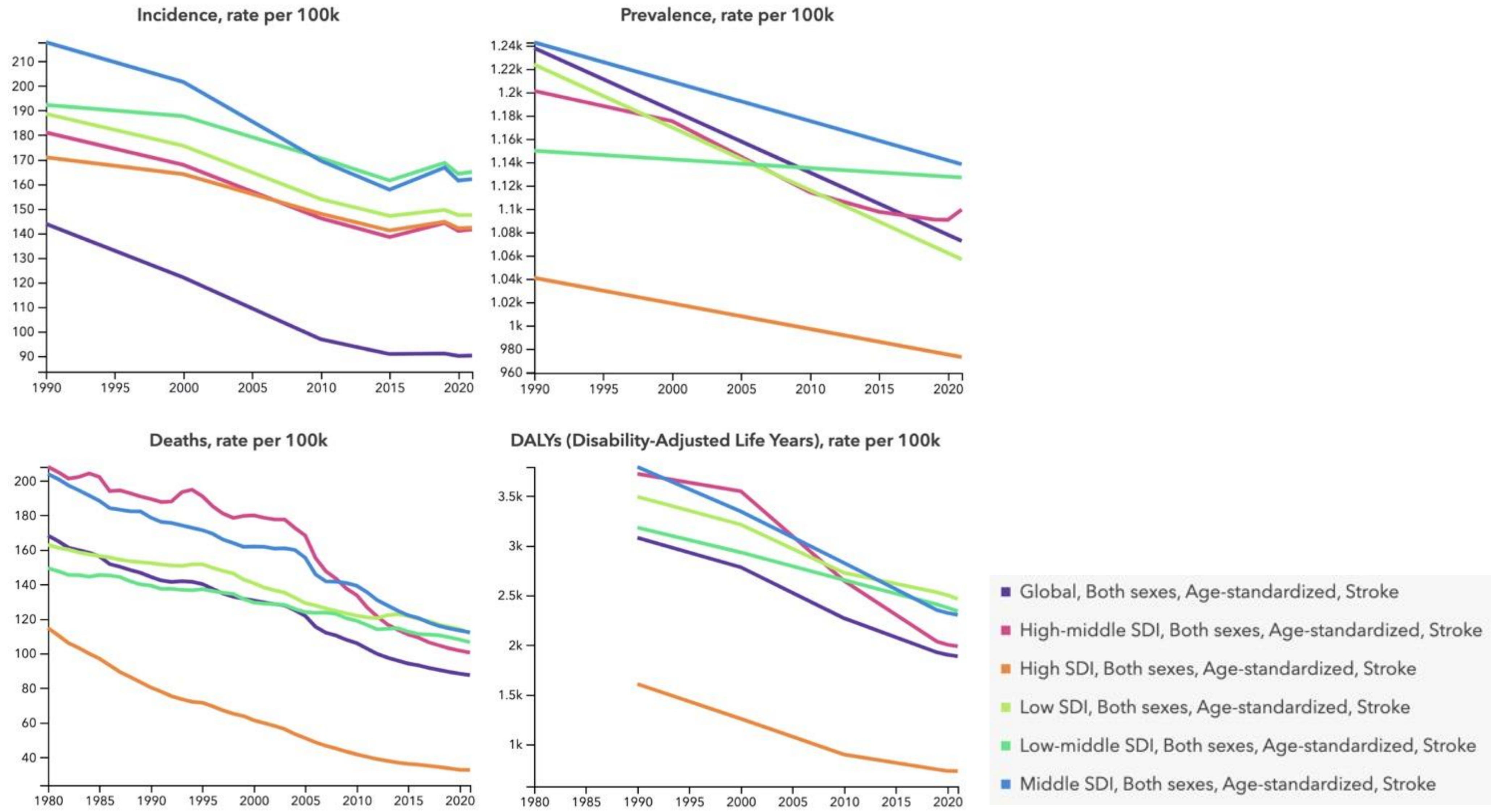


Figure 3. Age-standardised stroke-related DALYs attributable to all risk factors combined by pathological types of stroke, for both sexes, 2021

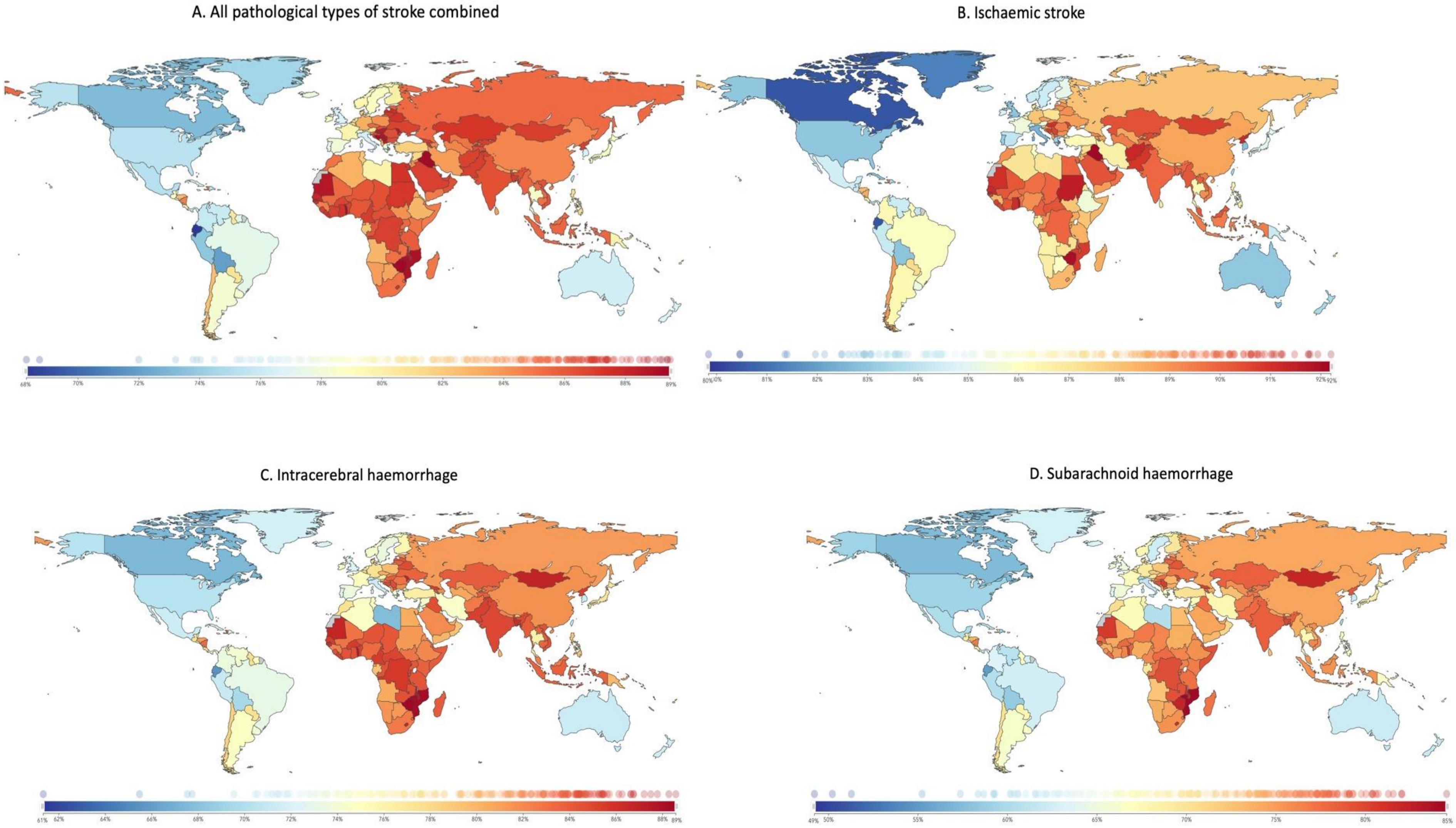
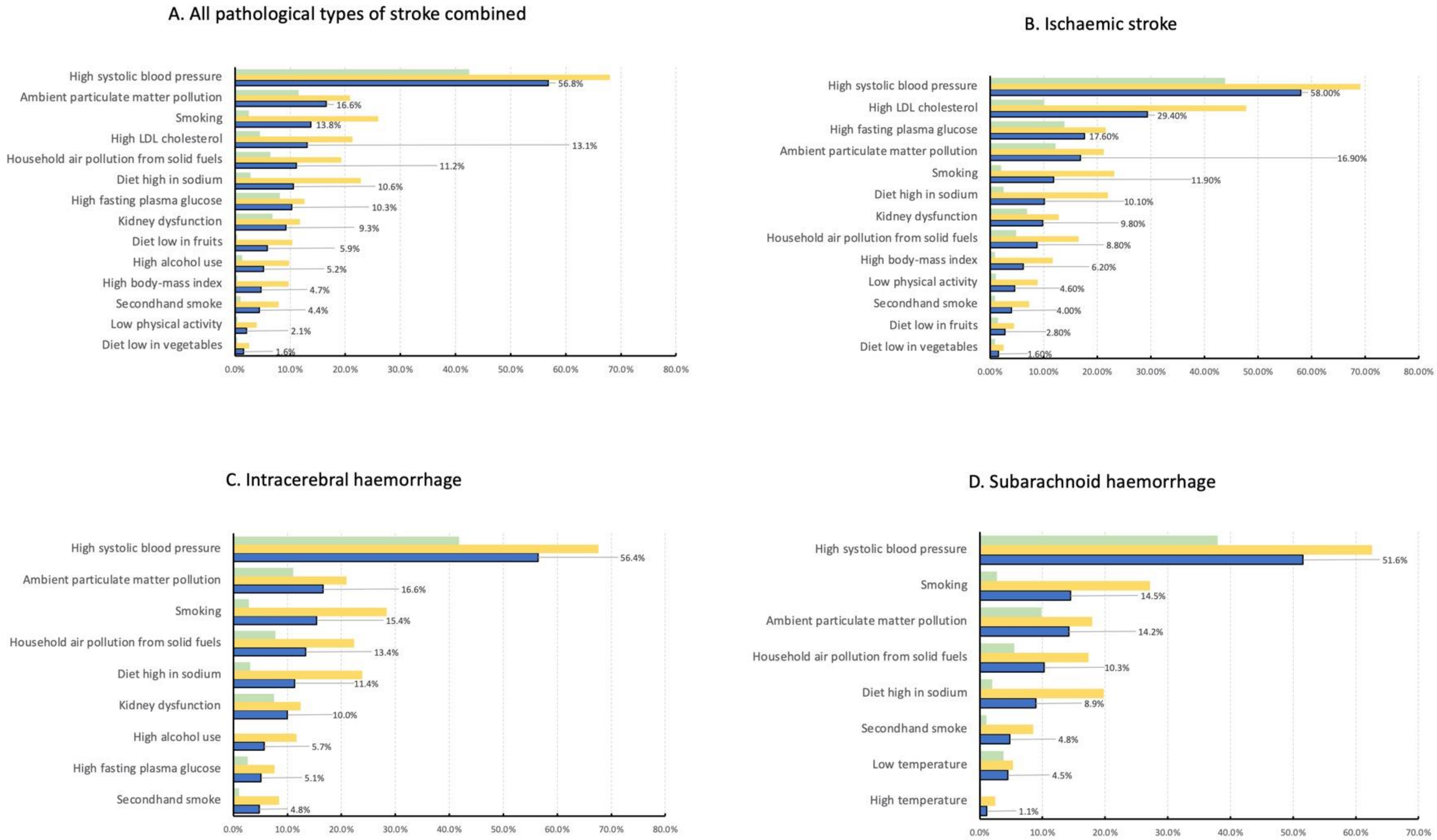
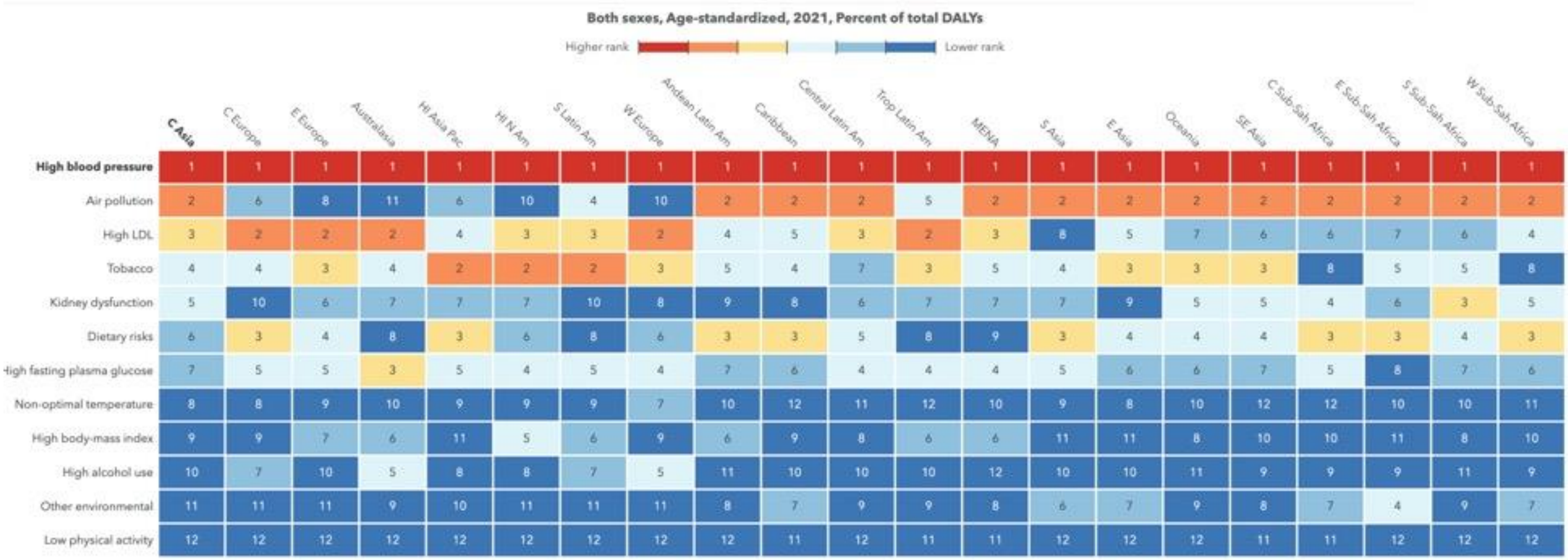

A. All pathological types of stroke combined
B. Ischaemic stroke
C. Intracerebral haemorrhage
D. Subarachnoid haemorrhage

Figure 4. Most individually significant risk factors for total stroke, IS, ICH and SAH, as measured by the proportion of DALYs from stroke attributable to the risk factors.



Dark blue bars show PAF point estimates. 95% UI are shown in green (low level) and yellow (upper level) colour bars.

Figure 5. Ranking of age-standardised stroke-related DALYs attributable to risk factors by 21 GBD regions, for both sexes, 2021



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