Global, regional, and national burden of ischemic stroke, 1990–2021: an analysis of data from the global burden of disease study 2021

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Summary

Background Ischemic stroke remains a major contributor to global mortality and morbidity. This study aims to provide an updated assessment of rates in ischemic stroke prevalence, incidence, mortality, and disability-adjusted life-years (DALYs) from 1990 to 2021, specifically focusing on including prevalence investigation alongside other measures. The analysis is stratified by sex, age, and socio-demographic index (SDI) at global, regional, and national levels.

Methods Data for this study was obtained from the 2021 Global Burden of Diseases, Injuries, and Risk Factors Study (GBD). To quantify temporal patterns and assess trends in age-standardized rates of ischemic stroke prevalence (ASPR), incidence (ASIR), mortality (ASDR), and DALYs, estimated annual percentage changes (EAPCs) were computed over the study period. The analyses were disaggregated by gender, 20 age categories, 21 GBD regions, 204 nations/territories, and 5 SDI quintiles. R statistical package V 4.4.2 was performed for statistical analyses and plot illustrations.

Findings In 2021, the global burden of ischemic stroke remained substantial, with a total of 69,944,884.8 cases with an ASPR of 819.5 cases per 100,000 individuals (95% UI: 760.3–878.7). The ASIR was 92.4 per 100,000 people (95% UI: 79.8–105.8), while the ASDR was 44.2 per 100,000 persons (95% UI: 39.3–47.8). Additionally, the age-standardized DALY rate was 837.4 per 100,000 individuals (95% UI: 763.7–905). Regionally, areas with high-middle SDI exhibited the greatest ASPR, ASIR, ASDR, and age-standardized DALY rates, whereas high SDI regions had the lowest rates. Geospatially, Southern Sub-Saharan Africa had the highest ASPR, while Eastern Europe showed the highest ASIR. The greatest ASDR and age-standardized DALY rates were observed in Eastern Europe, Central Asia, as well as North Africa, and the Middle East. Among countries, Ghana had the highest ASPR, and North Macedonia had both the highest ASIR and ASDR. Furthermore, North Macedonia also exhibited the highest age-standardized DALY rate.

Interpretation Regions with high-middle and middle SDI continued to experience elevated ASPR, ASIR, ASDR and age-standardized DALY rates. The highest ischemic stroke burden was observed in Southern Sub-Saharan Africa, Central Asia, Eastern Europe, and the Middle East.

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Keywords: Ischemic stroke; Global burden of disease; Disability-adjusted life years; Incidence; Prevalence

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Research in context

Evidence before this study

The GBD studies provide the most comprehensive estimates of ischemic stroke burden at global, regional, and country-specific levels. We searched PubMed databases from their inception to May 31, 2024, for papers published in English, using the terms "global burden", "ischemic stroke", "GBD". Our search yielded 112 results. These studies have highlighted high prevalence and incidence rates in Eastern Europe, Central Asia, and parts of Southeast Asia while noting that population aging, lifestyle changes, and healthcare improvements are reshaping its global distribution. Despite these insights, there remains an urgent need for up-to-date, comprehensive data on the global burden of ischemic stroke to inform current health policies and interventions effectively.

Added value of this study

This study provides the most up-to-date and comprehensive analysis of the global ischemic stroke burden using the latest GBD 2021 data. It extends previous research by including prevalence alongside incidence, mortality, and DALYs, offering a more complete picture of the disease burden. The analysis is stratified by sex, age, and SDI at global, regional, and national levels, allowing for a nuanced understanding of how ischemic stroke affects different populations.

Implications of all the available evidence

The findings of this study, combined with previous evidence, underscore the persistent global burden of ischemic stroke, particularly in regions with high-middle and middle SDI. The highest ischemic stroke burden was observed in Southern Sub-Saharan Africa, Central Asia, Eastern Europe, and the Middle East, highlighting the need for targeted interventions in these areas. The study also reveals a shift in the age distribution of ischemic stroke cases, with an increasing burden among older adults, especially in high SDI regions.

Introduction

Stroke is the second leading cause of death globally and a significant contributor to disability.[1] In 2019, it accounted for 6.55 million deaths and 143 million disability-adjusted life-years (DALYs) worldwide.[2] In addition, the estimated direct and indirect costs of stroke are $73.7 billion annually.[3] Ischemic stroke, which results from a blockage in a cerebral artery, represents about 85% of all stroke cases.[4] Despite significant progress in prevention, diagnosis, and treatment, the global burden of ischemic stroke remains substantial, with notable disparities across different regions and socioeconomic groups.[5,6]

Prior studies have explored the worldwide epidemiology of ischemic stroke utilizing data from the GBD. The GBD 2013 analysis revealed a substantial decrease in age-standardized rates of ischemic stroke incidence, deaths, and DALYs between 1990 and 2013.[7] Nevertheless, the total number of incident cases, deaths, and DALYs rose during this period, primarily due to population growth and aging. The GBD 2016 study revealed a persistent increase in the global burden of ischemic stroke, with low- and middle-income countries experiencing the highest age-standardized incidence and mortality rates.[8] More recently, the GBD 2019 study provided an updated assessment of the global, regional, and national burden of ischemic stroke from 1990 to 2019.[9]

Although the findings corroborated the overall declining trends in age-standardized rates, they also emphasized the enduring disparities across geographical regions and sociodemographic index (SDI) quintiles.[9] Nonetheless, a comprehensive analysis of the global ischemic stroke burden utilizing the latest GBD 2021 data has not been performed to date.

To bridge this knowledge gap, we aimed to present an updated evaluation of the trends in ischemic stroke prevalence, incidence, mortality, and DALYs from 1990 to 2021 at the global, regional, and national levels. Our analyses were disaggregated by sex, age, and SDI to pinpoint the populations most affected by ischemic stroke and to guide targeted prevention and treatment strategies.

Methods

Data acquisition

The GBD 2021 study offers a comprehensive evaluation of health loss linked to 369 diseases, injuries, and impairments, along with 88 risk factors, across 204 nations and territories, employing the latest epidemiological data and refined standardized methods.[1] The GBD database employs sophisticated methods to address missing data and adjust for confounding factors. Details about the study design and methods of GBD studies have been extensively described in existing GBD literature.[1] Furthermore, the University of Washington Institutional Review Board waived the requirement for informed consent to access the GBD data.[10] This research adhered to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).[11]

Estimation framework

The GBD study employed sophisticated modeling techniques to estimate the burden of ischemic stroke. The DisMod-MR 2.1 (disease-model-Bayesian meta-regression) tool was utilized to calculate incidence and prevalence. This Bayesian geospatial software integrates diverse disease parameters, epidemiological relationships, and geospatial data to generate robust estimates.[1]

For mortality estimation, the Cause of Death Ensemble modeling (CODEm) framework was applied. This method incorporates vital registration and verbal autopsy data, including those with non-specific codes. The data underwent rigorous adjustment to ensure accuracy before analysis.[1] CODEm combines multiple models to estimate death rates with improved precision. These models were applied to the 2021 database, producing comprehensive estimates of ischemic stroke burden. The approach accounts for differences in study design and methodology across multiple data sources, ensuring consistent and accurate estimates of ischemic stroke incidence, prevalence, and mortality. To calculate the DALYs due to ischemic stroke, we summed two components: the Years Lived with Disability (YLD), which quantifies the burden of living with the effects of stroke, and the Years of Life Lost (YLL), which measures the impact of premature death. The detailed methodology for these calculations is provided in the Supplementary Methods section.

Sociodemographic index

The SDI quantifies a country's or region's development level using fertility rate, education level, and per capita income data. Ranging from 0 to 1, a higher SDI indicates greater socioeconomic development.[1,2] The SDI is known to correlate with disease incidence and mortality rates. In this study, we classified countries and regions into five SDI categories (low, low-medium, medium, medium–high, and high) to examine the relationship between ischemic stroke burden and socioeconomic development.

Risk factors

In addition to the primary metrics of prevalence, incidence, mortality, and DALYs, this study also examined the impact of specific risk factors on ischemic stroke burden. We focused on four key risk factors identified in the GBD 2021 study: high body mass index, high alcohol use, low physical activity, and tobacco use. Our analysis included data on ischemic stroke-related DALYs and deaths attributable to these factors, with additional stratification by region to elucidate geographical variations in their impact.

To quantify the influence of these risk factors, we employed sophisticated methodologies, including DisMod-MR 2.1 and spatiotemporal Gaussian process regression.[12] These approaches enabled us to model exposure distributions for each risk factor across various demographics and locations. We then established the theoretical minimum risk exposure level (TMREL) for each factor, based on epidemiological evidence, representing the optimal exposure level for minimizing ischemic stroke risk.[13] By integrating exposure data, relative risk estimates, and TMRELs, we calculated population attributable fractions (PAFs) for each risk factor. These PAFs, stratified by location, age, sex, and year, quantify the potential reduction in ischemic stroke burden if exposure to a given risk factor were reduced to its TMREL.[13] To translate these fractions into meaningful health outcomes, we multiplied the PAFs by DALYs. This calculation provided estimates of the risk-attributable burden, offering valuable insights into how modifying these risk factors could potentially impact ischemic stroke outcomes across different populations. This comprehensive approach not only highlights the direct burden of ischemic stroke but also illuminates the contribution of modifiable risk factors, providing a more nuanced understanding of the disease's impact and potential avenues for intervention.

Statistical analyses

To assess the trends in age-standardized rates (ASR) of ischemic stroke incidence, mortality, DALYs, and prevalence, the study utilized the Estimated Annual Percentage Change (EAPC). The ASR was computed per 100,000 individuals utilizing the subsequent formula:

$$ASR = \frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} w_i} \times 100,000$$

(a_i: the age-specific rate in *i*th the age group; w: the number of people in the corresponding *i*th age group among the standard population; *A*: the number of age groups).

The calculation of EAPCs was based on a regression model that characterizes the pattern of age-standardized rates during a specified period.[13] The equation employed was: Y = α + βX + e, where Y represents the natural logarithm of the ASR, X indicates the calendar year, α is the intercept term, β denotes the slope or trend, and e is the error term. The EAPC is calculated as 100 × [exp(β)–1], representing the annual percentage change. The linear regression model was used to compute the 95% confidence interval (CI) for the EAPC. An ASR is deemed to have an increasing trend if both the EAPC and the lower bound of its 95% CI are positive. In contrast, if both the EAPC and the upper bound of its 95% CI are negative, the ASR is considered to have a decreasing trend. If neither condition is satisfied, the age-standardized rate is regarded as stable. Spearman correlation was used to assess associations between the SDI and the age-standardized rates of ischemic stroke. In this study, we utilized a Bayesian age-period-cohort (BAPC) model incorporating integrated nested Laplace approximations to project future trends in ischemic stroke burden. Previous research has demonstrated that BAPC offers superior coverage and precision compared to alternative prediction methods.[14–17] The computational process was implemented using the R-package BAPC, following established protocols from prior studies.[14] All analyses and visualizations were carried out using the World Health Organization's Health

Equity Assessment Toolkit and the R statistical computing software (Version 4.2.2).

Informed consent
Informed consent was not needed.

Ethics
The institutional review board granted an exemption for this study, as it utilized publicly accessible data that contained no confidential or personally identifiable patient information.

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results
Global level
In 2021, the global burden of ischemic stroke remained substantial, with a total of 69,944,884.8 cases (95% UI: 64,788,695.1–75,009,602.8), representing a staggering 101.8% increase from 1990. Despite this significant rise in the absolute number of cases, the ASPR demonstrated a slight decrease from 849.5 per 100,000 persons (95% UI: 785.9–913.2) in 1990 to 819.5 per 100,000 persons (95% UI: 760.3–878.7) in 2021. The EAPC for ASPR was −0.18 (95% CI: −0.21 to −0.16) (Table 1, Fig. 1). The global incidence of ischemic stroke reached 7,804,449.4 cases (95% UI: 6,719,760.4–8,943,692.1) in 2021, marking an 87.69% increase from 1990. The ASIR of ischemic stroke exhibited a decline from 109.8 per 100,000 persons (95% UI: 93.6–127.6) in 1990 to 92.4 per 100,000 persons (95% UI: 79.8–105.8) in 2021. Over the study period, the EAPC in ASIR was −0.67 (95% CI: −0.76 to −0.58), indicating a consistent decrease in the incidence rate of ischemic stroke (Table 1, Fig. 1). Mortality due to ischemic stroke was estimated at 3,591,498.6 deaths (95% UI: 3,213,281.3–3,888,326.8), with an ASDR of 44.2 per 100,000 persons (95% UI: 39.3–47.8) and an EAPC of −1.83 (95% CI: −1.92 to −1.74) (Table 1, Fig. 1). The global DALYs for ischemic stroke in 2021 were 70,357,911.9 (95% UI: 64,329,575.6–76,007,063), with an age-standardized DALY rate of 837.4 per 100,000 persons (95% UI: 763.7–905) and an EAPC of −1.59 (95% CI: −1.68 to −1.5) (Table 1, Fig. 1).

Regional level
The global burden of ischemic stroke exhibits significant regional variations, closely tied to SDI levels. The ASPR demonstrated notable disparities, with High-middle SDI regions experiencing the highest rate at 893.3 per 100,000 people (95% UI: 824–960), while Low-middle SDI regions reported the lowest at 669.3 per 100,000 (95% UI: 616.3–720.6) (Table 1, Fig. 1). Temporal trends in ASPR reveal divergent patterns across SDI levels, potentially indicative of varying stages of epidemiological transition. High SDI regions exhibited the most substantial decline, with an EAPC of −0.57 (95% CI: −0.64 to −0.5). In these regions, the ASPR decreased from 892.7 per 100,000 (95% UI: 845.1–947.8) in 1990 to 813.9 per 100,000 (95% UI: 768.6–864.1) in 2021, suggesting effective prevention and management strategies (Table 1, Fig. 1). In contrast, Middle SDI regions experienced the highest increase, with an EAPC of 0.27 (95% CI: 0.24–0.30), indicating a growing burden of ischemic stroke in these areas (Table 1, Supplementary Fig. S1A). This trend may reflect a complex interplay of factors, including improving diagnostic capabilities leading to higher detection rates, increasing life expectancy expanding the at-risk population, and growing exposure to risk factors associated with rapid urbanization and lifestyle changes. The adoption of more sedentary behaviors, shifts in dietary patterns, increased stress levels, and rising prevalence of obesity and metabolic disorders in these transitioning economies could all contribute to this observed increase in ischemic stroke burden. The ASIR and ASDR further underscore these regional disparities. High-middle SDI regions reported the highest ASIR and ASDR, while High SDI regions had the lowest for both measures. Specifically, the ASIR in High-middle SDI regions was 116 per 100,000 people (95% UI: 99.2–133.9), compared to 66.1 per 100,000 (95% UI: 58.2–74.7) in High SDI regions. Similarly, the ASDR in High-middle SDI regions was 59.7 per 100,000 people (95% UI: 53.0–65.4), whereas High SDI regions reported a considerably lower rate of 19.4 per 100,000 (95% UI: 16.5–21.0) (Table 1, Fig. 1, Fig. 2C). This stark contrast highlights not only differences in risk factor prevalence but also in acute care quality and secondary prevention efforts. The burden of disease, quantified by the age-standardized DALY rate, further emphasized these regional disparities. High-middle SDI regions bore the highest burden with a DALY rate of 1076.5 per 100,000 people (95% UI: 973.4–1176.2), while High SDI regions had the lowest at 395.6 per 100,000 (95% UI: 352.2–434.8) (Table 1, Fig. 1, Fig. 2D). These findings collectively highlight the complex relationship between socio-demographic factors and ischemic stroke outcomes. They suggest that while High SDI regions have made significant progress in reducing the prevalence and impact of ischemic stroke, Middle and High-middle SDI regions face growing challenges.

Our findings indicate that Sub-Saharan African regions bear the highest burden of ischemic stroke prevalence globally. Specifically, the ASPR were most elevated in Southern Sub-Saharan Africa, reaching 1122 per 100,000 population (95% UI: 1019.9–1224.9), followed closely by Western Sub-Saharan Africa at 1046 per 100,000 population (95% UI: 977.7–1112.6) (Table 1, Fig. 2A). East Asia also demonstrated a high ASPR, with

Location	1990		2021		EAPC_95%CI
	Number	ASR	Number	ASR	
Prevalence					
Global	34668041.4 (32153636.8–37171587.5)	849.5 (785.9–913.2)	69944884.8 (64788695.1–75009602.8)	819.5 (760.3–878.7)	−0.18 (−0.21 to 0.16)
High SDI	10141955.7 (9487690–10833007.6)	933.8 (874.5–998)	15864865.5 (14925797.9–16872854.7)	813.9 (768.6–864.1)	−0.57 (−0.64 to 0.5)
High-middle SDI	9,174,385 (8429846.2–9882568)	906.2 (834.7–975)	17110640.3 (15738888.3–18478803.4)	893.3 (824–960)	−0.09 (−0.14 to 0.04)
Middle SDI	8555789.7 (7763206.5–9309792.2)	765.9 (693–837.5)	22230670.7 (20239639.4–24119856)	838.4 (764.8–911)	0.27 (0.24–0.3)
Low-middle SDI	4631395.2 (4229093.5–5023596.6)	680.8 (620.6–741.7)	10234283.1 (9418964.3–11004022.1)	669.3 (616.3–720.6)	−0.09 (−0.11 to 0.06)
Low SDI	2124875.9 (1976569.5–2270871.1)	838.1 (776.3–901.2)	4447699.2 (4174214.7–4699709.5)	755.7 (707.7–800.1)	−0.39 (−0.43 to 0.36)
Andean Latin America	138242.8 (131026.6–145937.1)	604.9 (573.4–638.1)	312484.9 (297506.2–327199.8)	515.1 (490.6–539)	−0.6 (−0.64 to 0.57)
Australasia	176175.4 (169750.4–183601.5)	751.3 (724.3–783.4)	296950.7 (286363–308252.3)	581.9 (560.2–603.2)	−0.93 (−0.98 to 0.89)
Caribbean	178810 (169859.7–188128.7)	649.1 (616.1–684.1)	327164.5 (312540.5–341547.6)	616.9 (589.7–643.6)	−0.18 (−0.2 to 0.16)
Central Asia	550460.5 (523473.4–577216.8)	1107.9 (1052.3–1164.9)	866712.4 (829519.2–902763)	1014.9 (969.9–1063.6)	−0.31 (−0.33 to 0.29)
Central Europe	1418231.7 (1324818.4–1513619.6)	959.6 (897.8–1022.4)	1631106.1 (1537835–1733826.7)	776.1 (733.5–820.8)	−0.77 (−0.82 to 0.72)
Central Latin America	678691.9 (630061.6–725121)	725.2 (673.9–777.8)	1387551.7 (1296756.3–1484316)	552.6 (516.9–591.3)	−1.03 (−1.09 to 0.96)
Central Sub-Saharan Africa	266923.7 (253028.2–281576.5)	1113.6 (1052.2–1178.4)	596223.3 (568897.8–624228.7)	995.7 (947.7–1046.3)	−0.41 (−0.43 to 0.38)
East Asia	6921707.7 (6208387–7617523.8)	774.2 (691.5–863.7)	21503822.8 (19292836.5–23714701.3)	1018 (920–1120.1)	0.95 (0.89–1)
Eastern Europe	2869099.4 (2565924.6–3174157)	1028 (921.9–1132.8)	3049360.5 (2763322.4–3340261.4)	920.4 (835.8–1005.3)	−0.38 (−0.41 to 0.35)
Eastern Sub-Saharan Africa	867800.8 (811693.6–925063.4)	1066.6 (996.2–1139.8)	1869299.3 (1761941.3–1973402.3)	992.1 (934.2–1049.9)	−0.27 (−0.29 to 0.25)
High-income Asia Pacific	2058456.1 (1893145.5–2220222.2)	1030.5 (947.1–1109.2)	3295961.7 (3048492.7–3555085.8)	775.6 (723–832.2)	−1.04 (−1.09 to 0.98)
High-income North America	3403854.6 (3107281.7–3724886.2)	991.5 (904.5–1081.9)	5699097.6 (5260863.2–6152298.3)	950 (880.6–1024.5)	−0.39 (−0.57 to 0.21)
North Africa and Middle East	1847829.4 (1741882.4–1963338.4)	909.3 (852.4–967.6)	4366507.3 (4157817.8–4571157.7)	866.3 (823.7–909.4)	−0.18 (−0.2 to 0.17)
Oceania	26485.1 (25138.3–27927.3)	809.7 (767.7–855)	59506.3 (57089.1–62156.1)	741.4 (711.4–772)	−0.31 (−0.31 to 0.3)
South Asia	3441863 (3041705–3832962.8)	526 (462.2–586.9)	7828397.3 (6997064.5–8621267.5)	497.7 (445.7–549)	−0.21 (−0.25 to 0.18)
Southeast Asia	2557635.5 (2350464.3–2762167)	921.2 (846.8–999.6)	6104966 (5651318.6–6562857)	919 (851.9–986.3)	−0.03 (−0.04 to 0.02)
Southern Latin America	399118 (380518.4–419432.1)	859.4 (819.6–903.1)	546568.7 (524188.8–570536.2)	640.6 (614.8–668.1)	−1.05 (−1.1 to 1)
Southern Sub-Saharan Africa	364210.1 (330935.5–399540.5)	1274.6 (1149.8–1404.1)	640169.7 (583548.5–694855.4)	1122 (1019.9–1224.9)	−0.49 (−0.54 to 0.44)
Tropical Latin America	827663.7 (739294.2–917728.8)	850 (757.8–943.6)	1543559.5 (1392394.6–1692607.6)	605.7 (546.6–663.9)	−1.24 (−1.3 to 1.18)
Western Europe	4563751.4 (4343952.8–4819225.2)	806.9 (768.4–850.6)	5540066.3 (5333481.7–5752361.9)	625.7 (600.1–649.9)	−0.86 (−0.89 to 0.83)
Western Sub-Saharan Africa	1111030.5 (1034246.3–1188453)	1109.4 (1026.9–1194.5)	2479408.3 (2331911–2621732.8)	1046 (977.7–1112.6)	−0.23 (−0.24 to 0.21)
Incidence					
Global	4151978.1 (3536772.4–4868149.6)	109.8 (93.6–127.6)	7804449.4 (6719760.4–8943692.1)	92.4 (79.8–105.8)	−0.67 (−0.76 to 0.58)
High SDI	1153374.2 (992806–1333283.4)	105.5 (91.2–121.2)	1351912.5 (1179761–1535709.8)	66.1 (58.2–74.7)	−1.75 (−1.86 to 1.64)
High-middle SDI	1306276.5 (1096265.3–1547833.2)	141.4 (119.9–164.1)	2243339.9 (1899825.1–2614462.6)	116 (99.2–133.9)	−0.74 (−0.85 to 0.63)
Middle SDI	953540.6 (800911.7–1134826.9)	97.5 (81.4–115.6)	2648524.6 (2240569.1–3082587)	103.5 (88–120)	0.12 (0.07–0.16)
Low-middle SDI	516850.9 (439585.9–603885.2)	87.3 (74.1–102.4)	1120427.2 (971629.9–1273722.5)	80.7 (70–91.7)	−0.34 (−0.38 to 0.3)
Low SDI	216493.5 (183974.3–252019)	94.4 (80.4–110.8)	433298.4 (374564.8–494218)	82.2 (71–93.1)	−0.51 (−0.56 to 0.46)
Andean Latin America	13562.9 (11785.2–15387)	63.5 (55.4–71.9)	27415.5 (24041.9–31116.2)	46.3 (40.6–52.4)	−1.13 (−1.24 to 1.02)
Australasia	20989.3 (19362.1–22541)	91.1 (84.1–97.8)	28159.6 (25187.7–31109)	52.8 (47.3–58.5)	−2.05 (−2.2 to 1.91)
Caribbean	19577.4 (17215.7–21952.6)	76.2 (67.5–85.7)	36042.3 (32142.5–39960.6)	67.3 (60–74.7)	−0.42 (−0.46 to 0.37)
Central Asia	65958.6 (58343.7–73949.5)	141.9 (124.6–159.1)	102572.6 (91018.4–114462.7)	132.9 (118.2–148.1)	−0.2 (−0.29 to 0.11)
Central Europe	222510.3 (193304.8–251309.2)	158 (138.4–177.7)	238905.2 (209922.3–266603.5)	107 (95.3–118.4)	−1.35 (−1.4 to 1.3)
Central Latin America	68642.9 (58878.8–78850.5)	80.5 (69–93.2)	127074.9 (110155–144196.4)	52 (45.1–58.8)	−1.67 (−1.82 to 1.51)
Central Sub-Saharan Africa	27144.3 (23222–32004.7)	122.7 (104.3–142.6)	59172.9 (51496.2–68041.3)	109 (95–124.8)	−0.41 (−0.45 to 0.38)

(Table 1 continues on next page)

Location	1990		2021		EAPC_95%CI
	Number	ASR	Number	ASR	
(Continued from previous page)					
East Asia	800330.3 (656281.1–982072.7)	101.3 (83–121.9)	2850089.7 (2363157.7–3405882.5)	134.8 (112.6–158.4)	0.86 (0.8–0.92)
Eastern Europe	515846.2 (425258.3–623600.8)	197.9 (164.9–232.4)	490197.1 (415356.1–571450.5)	142.6 (122.1–164.7)	−1.13 (−1.24 to 1.02)
Eastern Sub-Saharan Africa	85161.6 (72719–99207.2)	110.9 (94.2–130.1)	179317.5 (154965.6–204334.2)	103.6 (89.2–118.4)	−0.21 (−0.26 to 0.17)
High-income Asia Pacific	234946.3 (193848–280991)	121 (100.7–144)	284444.7 (249282.5–322677.8)	64.6 (56.4–73.7)	−2.53 (−2.73 to 2.33)
High-income North America	315394.2 (259208–383545.1)	90 (74.4–108.3)	352963.3 (299100–413294.4)	56.9 (48.6–66.1)	−1.58 (−1.73 to 1.43)
North Africa and Middle East	199912.2 (175527.7–229003.4)	117.5 (102.6–133.5)	461145.6 (409815.1–516836.6)	103.6 (91.6–116.1)	−0.43 (−0.47 to 0.39)
Oceania	2342.9 (2016.9–2728.2)	81.5 (70–94.3)	5311.5 (4624.9–6003.2)	73.2 (63.7–82.9)	−0.43 (−0.47 to 0.39)
South Asia	398076.4 (331671.9–474038.3)	72.6 (60.6–86.5)	853370.3 (727638.3–990208.9)	61.2 (52.3–70.7)	−0.74 (−0.82 to 0.66)
Southeast Asia	265778.9 (228020.3–310151.1)	107.3 (91.5–125.6)	667263 (582280.6–763034.9)	107.3 (93.7–122.7)	−0.04 (−0.07 to 0)
Southern Latin America	44172.3 (38720–49910.2)	97.8 (86.3–109.9)	52069.9 (46168.9–58185)	60.3 (53.5–67.6)	−1.77 (−1.93 to 1.62)
Southern Sub-Saharan Africa	33295 (28141.1–39224.7)	122.3 (101.9–146.7)	64729.4 (54456.2–74990.5)	121.9 (102.5–142.2)	−0.11 (−0.36 to 0.15)
Tropical Latin America	106000 (88155.9–125886.1)	119.2 (98.3–142.3)	166748.8 (140997.7–194698.4)	66.4 (56–77.5)	−2.04 (−2.16 to 1.92)
Western Europe	613766.1 (538423.5–692797.7)	106 (94–118)	549190.6 (496801.9–601605.6)	58.1 (52.9–63.7)	−2.12 (−2.21 to 2.03)
Western Sub-Saharan Africa	98569.9 (83977.2–114606.6)	104.1 (88.2–122.1)	208264.8 (181390.6–236453.6)	94.7 (82.1–106.9)	−0.29 (−0.33 to 0.25)
Deaths					
Global	2317112.3 (2131459.6–2475545.5)	73.1 (66.4–77.9)	3591498.6 (3213281.3–3888326.8)	44.2 (39.3–47.8)	−1.83 (−1.92 to 1.74)
High SDI	595527.7 (535846.6–623760.2)	53.8 (48.2–56.6)	507950.1 (426776.9–553062.1)	19.4 (16.5–21)	−3.58 (−3.71 to 3.44)
High-middle SDI	887525.1 (831446.7–925960.5)	112.1 (103.4–117)	1151654.6 (1025972.1–1263429.3)	59.7 (53–65.4)	−2.4 (−2.6 to 2.2)
Middle SDI	484058.8 (438722.6–543562.9)	66.6 (59.5–74.6)	1171548.3 (1037070.4–1296280)	51.6 (45.4–57.1)	−0.86 (−0.95 to 0.76)
Low-middle SDI	258770.9 (227017.4–300181.6)	59 (51.6–67.7)	581649.1 (517710.7–657998.2)	50.9 (45.4–57)	−0.49 (−0.53 to 0.44)
Low SDI	87274.6 (72465–110945.7)	57.1 (47.5–72)	174655.2 (149332.8–216890.5)	49.4 (42.1–60.4)	−0.48 (−0.54 to 0.42)
Andean Latin America	5509.9 (4929.9–6092.1)	31.7 (28.5–35)	9794 (8202.4–11613.6)	17.7 (14.8–21)	−2.11 (−2.31 to 1.92)
Australasia	9883.4 (8879.5–10632.7)	45.7 (40.5–49.3)	9400.2 (7587.5–10374.5)	14.1 (11.4–15.5)	−4.01 (−4.11 to 3.9)
Caribbean	11986.1 (11099.1–12742.1)	53 (48.9–56.1)	19947.9 (17601.2–22402.6)	36.4 (32.1–40.9)	−1.16 (−1.24 to 1.09)
Central Asia	32985.7 (30490.8–35153.2)	81.7 (74.9–87.2)	44870 (40632.4–48966)	71 (64.3–77.3)	−0.87 (−1.11 to 0.63)
Central Europe	181353.2 (171926.6–186859.2)	141 (132.2–145.9)	160199.8 (144922.2–171305.8)	65.6 (59.3–70.1)	−2.79 (−2.92 to 2.65)
Central Latin America	24285.3 (22792.7–25098.5)	37.5 (34.9–38.9)	43026.9 (37956.3–47739.9)	18.7 (16.5–20.7)	−2.39 (−2.56 to 2.23)
Central Sub-Saharan Africa	8561.3 (6432–10967.9)	64.7 (50–81.8)	18858.6 (13939.7–25744.9)	59.6 (44.2–81.5)	−0.41 (−0.46 to 0.36)
East Asia	442486.3 (376804.2–522373.7)	74.6 (64.1–87.4)	1202218.5 (1010916.2–1397915.2)	63.2 (52.9–73.1)	−0.52 (−0.76 to 0.27)
Eastern Europe	405262.3 (383950–415283.8)	168.1 (157.8–173)	329291.2 (299910.8–356034.7)	91 (82.8–98.5)	−2.78 (−3.24 to 2.32)
Eastern Sub-Saharan Africa	24975.3 (20418.5–31170.8)	51.9 (42.8–64.3)	51922.8 (43067–61814.2)	46.3 (38.3–55.3)	−0.44 (−0.48 to 0.41)
High-income Asia Pacific	105658.8 (93890.9–112114.1)	62.9 (54.9–67.2)	112784.6 (87154.9–127258)	15.8 (12.5–17.5)	−4.76 (−4.91 to 4.6)
High-income North America	110126.6 (96139.9–117560.5)	29.6 (25.8–31.6)	126352.9 (103455–138349.4)	16.8 (13.8–18.3)	−2.38 (−2.68 to 2.08)
North Africa and Middle East	131134.7 (114693.3–148486.9)	106.6 (92.3–120.8)	253284 (220811.7–283440.7)	73.7 (64–82.1)	−1.17 (−1.23 to 1.11)
Oceania	805.7 (627.1–1041.5)	48.7 (39.3–62.1)	1843 (1487.9–2388.7)	40.7 (33.3–52.3)	−0.69 (−0.76 to 0.63)
South Asia	172616.6 (142119.9–218916.2)	43.3 (35.7–54.1)	441295.8 (382997.1–539466.9)	38 (33.1–45.8)	−0.57 (−0.68 to 0.45)
Southeast Asia	131563 (114807.7–147288.5)	72.6 (62.9–81.6)	341541 (293259–391952.9)	68.1 (58.7–77.5)	−0.13 (−0.28 to 0.02)
Southern Latin America	23300 (21541–24643.9)	57.5 (52.7–60.9)	19658 (17471.5–21165.2)	21.1 (18.8–22.8)	−2.87 (−3.02 to 2.73)

(Table 1 continues on next page)

Location	1990		2021		EAPC_95%CI
	Number	ASR	Number	ASR	
(Continued from previous page)					
Southern Sub-Saharan Africa	9795.3 (8049.9–11101)	47.3 (38.5–53.9)	24959.1 (22677.4–27158.1)	60.3 (54.6–65.5)	0.94 (0.47–1.42)
Tropical Latin America	55341.3 (50934–57540.9)	80.4 (72.6–84.3)	71582.3 (63128.3–76435)	29.6 (26–31.7)	−3.02 (−3.14 to 2.91)
Western Europe	380194.8 (341008–399352.9)	62.8 (56–66.1)	215655.9 (175954.9–236145.9)	16.7 (13.9–18.2)	−4.43 (−4.57 to 4.29)
Western Sub-Saharan Africa	49286.9 (38585.3–64037.9)	76.5 (60.2–98.5)	93012.1 (77667.9–111241)	68.2 (58.2–81)	−0.36 (−0.45 to 0.27)
Disability-adjusted life years					
Global	46176240.2 (42961948.4–49414586.1)	1286.3 (1195.2–1376.1)	70357911.9 (64329575.6–76007063)	837.4 (763.7–905)	−1.59 (−1.68 to 1.5)
High SDI	10239251.7 (9461539.4–10819068.1)	916.4 (845.1–969.3)	8975176.2 (7913834.9–9812024.1)	395.6 (352.2–434.8)	−2.98 (−3.11 to 2.85)
High-middle SDI	16876354.8 (15868635.1–17770724.4)	1885.8 (1768.1–1980.9)	21054343.3 (19044777.9–23026603)	1076.5 (973.4–1176.2)	−2.19 (−2.39 to 1.99)
Middle SDI	10950853.7 (9944439.6–12298162.2)	1221.8 (1103.2–1364.8)	23896856.7 (21522553.1–26137544.5)	960.7 (864–1047.8)	−0.83 (−0.89 to 0.76)
Low-middle SDI	5912050.1 (5266484–6751650.2)	1094.9 (975.4–1254.6)	12300861.9 (11013179–13998937.3)	942.3 (846.1–1065.9)	−0.52 (−0.55 to 0.48)
Low SDI	2126088.5 (1791117.4–2645820)	1074.9 (910.4–1345.2)	4059454.6 (3492447.5–4963611.5)	914.3 (789.8–1116.6)	−0.58 (−0.63 to 0.53)
Andean Latin America	113706.9 (101757.8–126128.5)	574.2 (516.6–631.3)	183295.9 (154621.1–214987.2)	320.1 (270.1–375.3)	−2.11 (−2.31 to 1.91)
Australasia	162897.7 (149973.8–174032.1)	714.1 (655.9–763.6)	149125.4 (129769–166038.6)	249.5 (216.5–278.2)	−3.61 (−3.75 to 3.48)
Caribbean	224864.3 (209623.5–241939.4)	904.3 (839.8–969)	353682.3 (313628.5–399100.7)	656.5 (582.4–742)	−0.97 (−1.04 to 0.9)
Central Asia	719855.9 (669625.7–766900.1)	1625.4 (1511.2–1730.1)	985308.7 (892228.7–1076484.2)	1356.1 (1234.2–1474.8)	−1.04 (−1.3 to 0.78)
Central Europe	3203847.5 (3074576.6–3318844)	2300.3 (2201.6–2386.8)	2593397.6 (2385308.7–2776479.6)	1101.6 (1014.2–1180.5)	−2.7 (−2.83 to 2.57)
Central Latin America	487685.4 (464997.7–508604.3)	642.8 (610.1–669.7)	804658.5 (727628.1–889436.1)	336.6 (304.4–372)	−2.29 (−2.46 to 2.11)
Central Sub-Saharan Africa	225423.7 (175336.9–276839.1)	1219.9 (970.3–1523.6)	447160.6 (347101.5–579987.1)	1076.3 (830.8–1416.6)	−0.54 (−0.59 to 0.49)
East Asia	10279514.2 (8853619.5–12005870.4)	1382.7 (1191.1–1606.7)	24021156 (20420316–27562228.9)	1165.9 (998.2–1336.6)	−0.53 (−0.71 to 0.35)
Eastern Europe	7422389.7 (7152141.6–7643097.8)	2826 (2711.2–2913.4)	5713718.3 (5294961.4–6142848.3)	1601.2 (1483.5–1723.1)	−2.61 (−3.06 to 2.16)
Eastern Sub-Saharan Africa	616225 (510230.3–758430.1)	981.7 (824.1–1188.9)	1231675.4 (1050098.8–1440686.2)	873.5 (749–1018.6)	−0.47 (−0.51 to 0.44)
High-income Asia Pacific	1927882.9 (1766027.7–2055873)	1047.1 (954.8–1117.8)	1862336.8 (1582664.1–2083583)	335.4 (287.8–378.9)	−3.99 (−4.14 to 3.83)
High-income North America	2017603.2 (1818785.7–2187490.4)	554.8 (500–602.5)	2384648.5 (2094174.1–2640685.5)	352.6 (309.3–392.7)	−1.94 (−2.17 to 1.7)
North Africa and Middle East	3002344.4 (2668214.5–3383384.5)	1940.2 (1715.2–2180.5)	5405417.4 (4711954.4–6041794.4)	1329.4 (1165.6–1483)	−1.23 (−1.27 to 1.2)
Oceania	22713.6 (18479.8–28041.1)	937.3 (770.9–1171.1)	48691.5 (40674.8–59299.1)	789.4 (663.2–980)	−0.65 (−0.71 to 0.6)
South Asia	4009489.4 (3328354.2–5033258.3)	809.3 (676–1013.2)	9193296.6 (8004944.1–11543775)	690.1 (604–851.2)	−0.67 (−0.76 to 0.58)
Southeast Asia	3004177.4 (2687919–3310660.4)	1355.4 (1203.6–1499.1)	7318327.8 (6238954.4–8317299.8)	1266.5 (1088.1–1430.1)	−0.17 (−0.28 to 0.06)
Southern Latin America	424811.3 (394539.8–451983.7)	974.1 (900.6–1035.8)	352924.8 (323073.8–382286.2)	391.3 (357.8–424.2)	−2.72 (−2.84 to 2.59)
Southern Sub-Saharan Africa	224900.3 (194622.1–249787.3)	917.3 (782.6–1023.4)	523152.9 (480110.1–569334)	1073.7 (979–1165.9)	0.64 (0.22–1.06)
Tropical Latin America	1095135.7 (1036359.2–1137132)	1368.1 (1271–1425.6)	1292888 (1180665.7–1372019)	520.4 (473.3–553.1)	−3.05 (−3.18 to 2.92)
Western Europe	5852489.4 (5397741.8–6160459.2)	964 (888.1–1017.4)	3307777 (2903214.4–3626266.1)	297.7 (262.8–327.9)	−3.95 (−4.1 to 3.79)
Western Sub-Saharan Africa	1138282.3 (925815.7–1442064.5)	1420.2 (1161.3–1810.1)	2185272 (1840339.5–2608225.5)	1256.2 (1075.9–1478.5)	−0.39 (−0.49 to 0.29)

Table 1: **Global and regional trends in ischemic stroke burden: prevalence, incidence, mortality, and disability-adjusted life years (1990–2021).**

1018 per 100,000 population (95% UI: 920–1120.1), ranking third among the regions studied. Sub-Saharan African regions bear the highest burden of ischemic stroke prevalence globally. This could be attributed to a combination of genetic predisposition, increasing prevalence of hypertension and diabetes, limited access to quality healthcare, and inadequate awareness of stroke risk factors. The high ASPR in East Asia might be linked to dietary habits, high salt intake, and rapid urbanization.

Our analysis reveals that the incidence of ischemic stroke in Asian regions warrants significant attention.

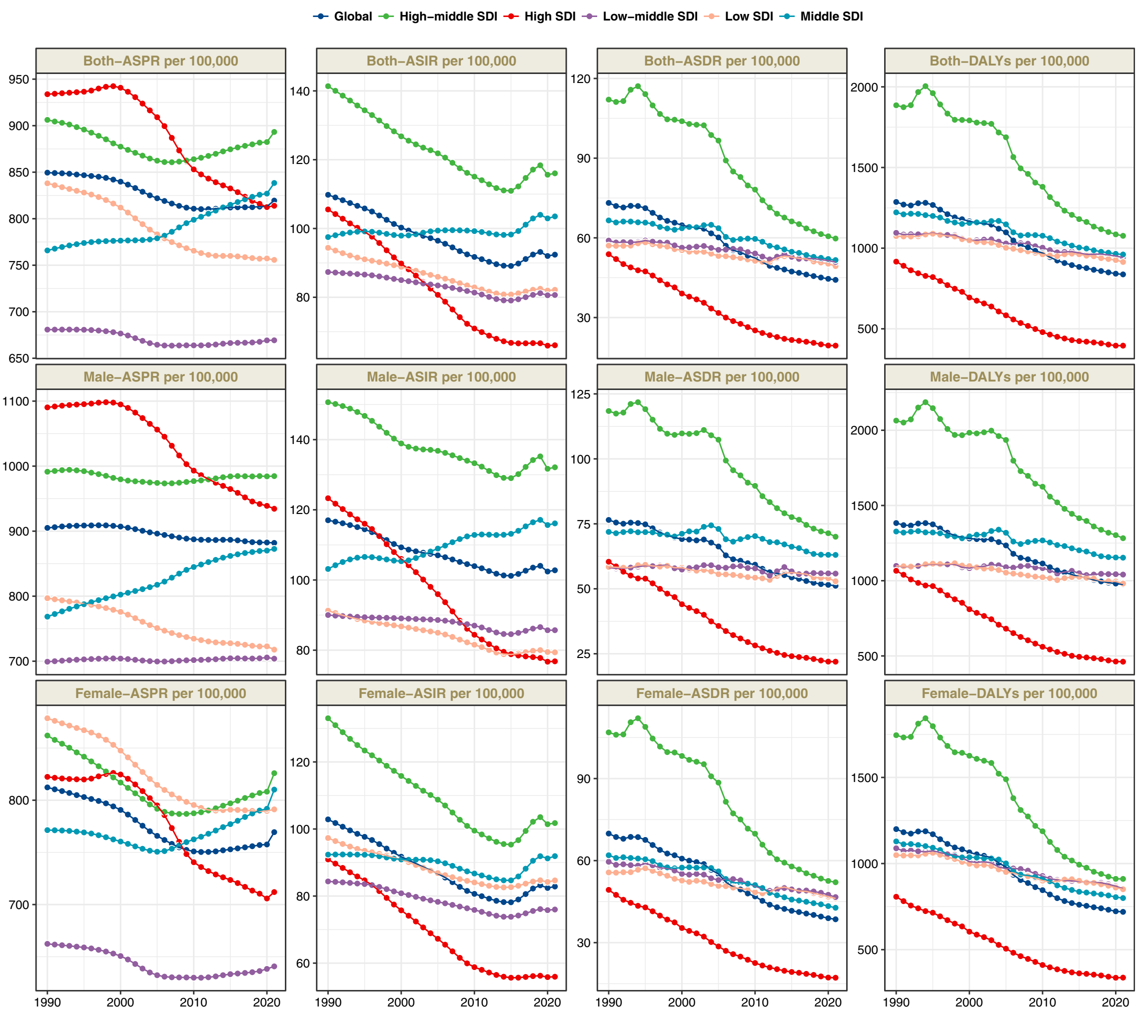

Fig. 1: Trends in ischemic stroke prevalence, incidence, deathes and disability-adjusted life-years from 1990 to 2021.

The findings show that East Asia and Central Asia are among the regions with the high ASIR globally. Specifically, East Asia reported an ASIR of 134.8 per 100,000 people (95% UI: 112.6–158.4), while Central Asia had an ASIR of 132.9 per 100,000 people (95% UI: 118.2–148.1). These rates were second and third highest respectively, surpassed only by Eastern Europe with an ASIR of 142.6 per 100,000 people (95% UI: 122.1–164.7). In contrast, Andean Latin America exhibited the lowest ASIR at 46.3 per 100,000 people (95% UI: 40.6–52.4) (Table 1, Fig. 2B). Moreover, temporal trends from 1990 to 2021 indicate divergent patterns within Asia. East Asia experienced the most substantial increase in ASIR with an EAPC of 0.86 (95% CI: 0.80–0.92). Conversely, High-income Asia Pacific showed the most significant decrease, with an EAPC of −2.53 (95% CI: −2.73 to −2.33) (Table 1, Supplementary Fig. S1B). These contrasting trends underscore the complex and varying dynamics of ischemic stroke incidence across different Asian regions, highlighting the need for targeted interventions and further research to address these disparities.

Eastern Europe, North Africa and Middle East, and Central Asia exhibited notably high ASDR for ischemic stroke, each surpassing 70 per 100,000 people. From 1990 to 2021, the ASDR of ischemic stroke increased the most in Southern Sub-Saharan Africa (EAPC 0.94, 95% CI: 0.47–1.42) and decreased the most in High-income Asia Pacific (EAPC −4.76, 95% CI: −4.91 to −4.60) (Table 1, Supplementary Fig. S1C). Conversely, the regions with the highest age standardized DALYs rates were Eastern Europe at 1601.2 per 100,000 persons (95% UI: 1483.5–1723.1), Central Asia at 1356.10 per 100,000 persons (95% UI: 1234.2–1474.8), North Africa and the Middle East at 1329.4 per 100,000 persons (95% UI: 1165.6–1483) (Table 1, Fig. 2D). From 1990 to 2021, the age-standardized DALYs rates of ischemic stroke increased the most in Southern Sub-Saharan Africa (EAPC 0.64, 95% CI 0.22–1.06) and decreased the most in High-income Asia Pacific (EAPC −3.99, 95% CI −4.14

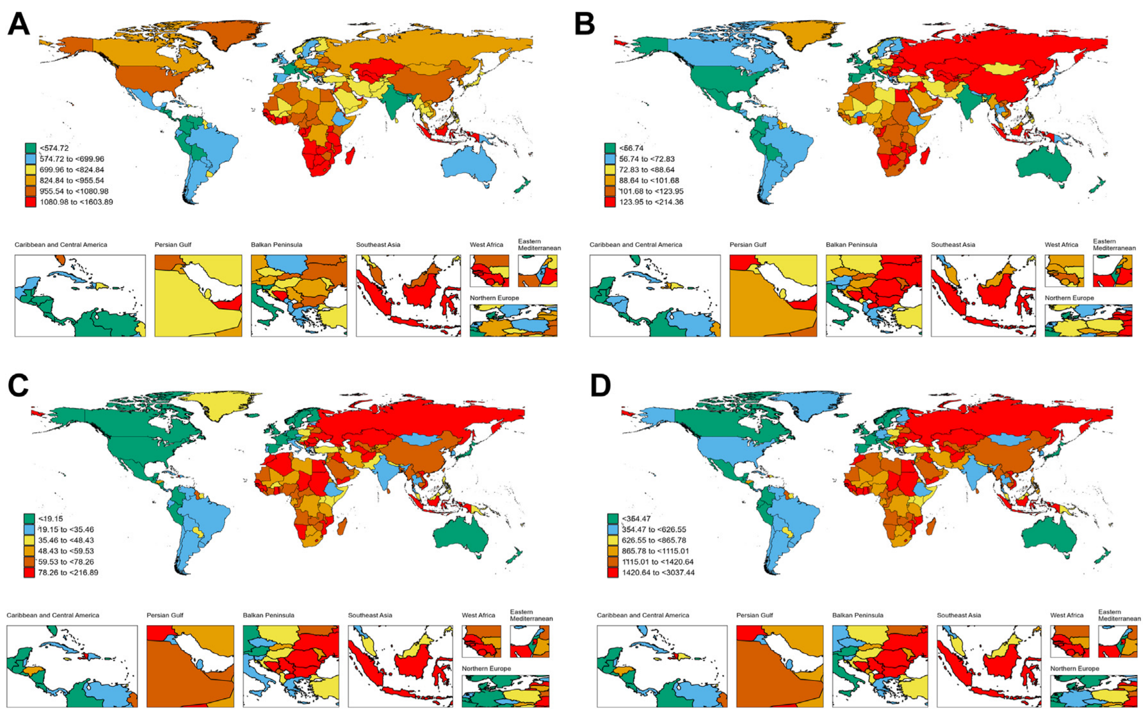

Fig. 2: The global disease burden of ischemic stroke for both sexes in 204 countries and territories. (A) Prevalence rate. (B) Incidence rate. (C) Death rate. (D) DALYs rate.

to −3.83) (Table 1, Supplementary Fig. S1D). Negative correlations were found between the age-standardized DALYs rates and the SDI (Supplementary Fig. S2). It was also noted that regions with a higher SDI had a lower proportion of ischemic stroke cases among younger individuals, while those with a higher SDI in both 1990 and 2021 exhibited a higher proportion of cases among older adults (Fig. 3). However, from 1990 to 2019, the incidence of ischemic stroke increased with age, particularly in those aged 50–69 years and older. The incidence rate of ischemic stroke in elderly individuals was significantly higher than in younger populations across all SDI regions (Supplementary Fig. S3).

National level

The ASPR of ischemic stroke varies from approximately 1603.9 to 312.3 per 100,000 people. Among all countries, Ghana (1603.9 per 100,000 persons; 95% UI: 1542–1675.7), Sao Tome and Principe (1422.2 per 100,000 persons; 95% UI: 1361.8–1485.1), and Nauru (1369 per 100,000 persons; 95% UI: 1315.8–1425) exhibit the highest ASPR (Fig. 2A, Supplementary Table S1). Notably, two of the three countries with the highest ASPR are located in Africa–Ghana in West Africa and Sao Tome and Principe off the western coast of Central Africa. This finding aligns with our regional analysis, which identified Sub-Saharan African regions as bearing the highest burden of ischemic stroke prevalence globally. The consistency between country-level and regional data underscores the significant challenge posed by ischemic stroke in African nations.

The most significant increases in the ASPR of ischemic stroke were observed in Lithuania (EAPC 1.59, 95% CI 0.95–2.23) (Supplementary Fig. S1A and Table S1). The country-specific distribution of ASIR is presented in Fig. 2B and Supplementary Table S2. North Macedonia had the highest ASIR of ischemic stroke (214.4 per 100,000 persons; 95% UI: 190.5–239.9), while Malta had the lowest (38.9 per 100,000 persons; 95% UI: 33.9–44.5). These findings underscore the complex and varied landscape of ischemic stroke epidemiology across different nations. The wide range of incidence rates and the notable increase in prevalence in certain countries like Lithuania suggest that risk factors, healthcare systems, and prevention strategies may vary significantly between nations. Analyzing the data for ASDR and DALYs due to ischemic stroke in 2021, we observe a notable consistency in the countries most severely affected. North Macedonia, Bulgaria, and Egypt appear prominently in both metrics. North Macedonia leads in both categories with the highest ASDR (216.9 per 100,000 persons; 95% UI: 184–249.4) and the highest DALYs rate (3037.4 per 100,000 persons; 95% UI: 2559–3507.5). Bulgaria ranks second in ASDR (147.6 per 100,000 persons; 95% UI:

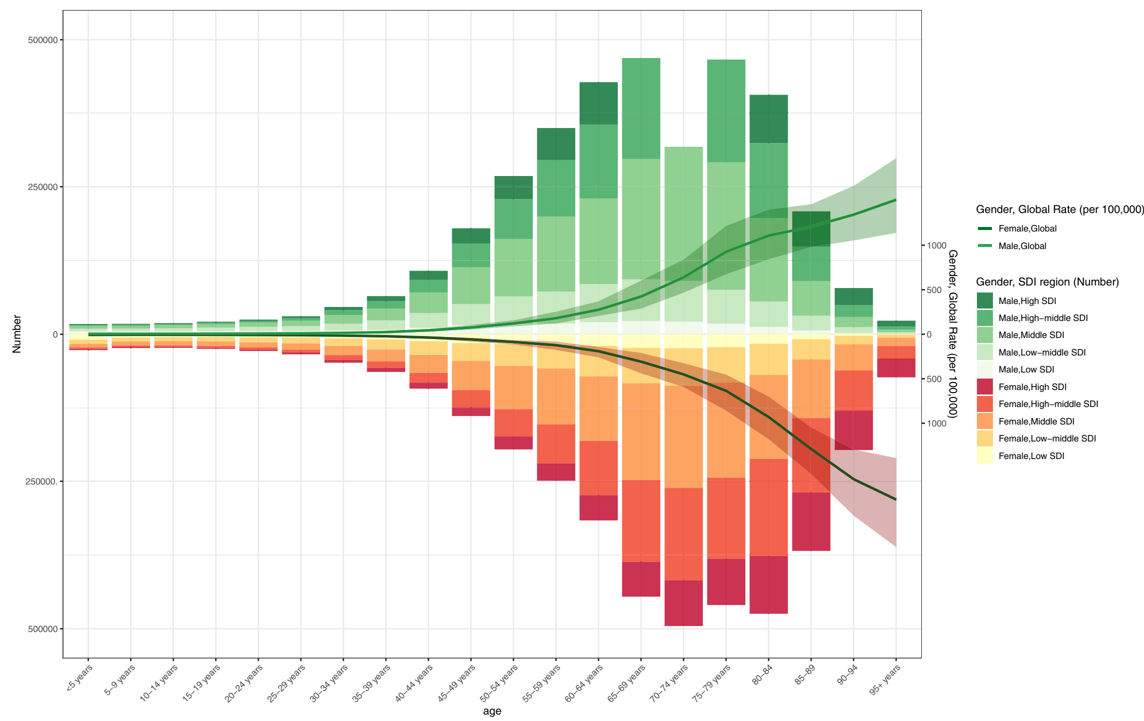

Fig. 3: The age-specific numbers and ASIRs of ischemic stroke by SDI regions in 2021.

130.3–164.6) and third in DALYs (2383.6 per 100,000 persons; 95% UI: 2105.1–2689.8), while Egypt ranks third in ASDR (139.8 per 100,000 persons; 95% UI: 113.6–167.3) and second in DALYs (2462.6 per 100,000 persons; 95% UI: 1969.1–3002.4) (Fig. 2D, Supplementary Table S4). This overlap suggests that these countries face a particularly high burden of ischemic stroke, impacting both mortality and overall health-related quality of life among their populations. The number of age-standardized DALYs due to ischemic stroke decreased most in Estonia (EAPC -6.3, 95% CI -6.84 to –5.77), Portugal (EAPC -6.2, 95% CI -6.42 to –5.98), and Singapore (EAPC -5.61, 95% CI -5.81 to –5.4) (Supplementary Fig. S1D and Table S4).

The United Arab Emirates experienced the most dramatic increase in prevalence cases, with an astounding 677 percent growth, while Portugal saw a 33 percent reduction (Fig. 4A). Likewise, the United Arab Emirates also had the highest increase in incidence cases, with a 652 percent rise, while Estonia witnessed a 44 percent decline (Fig. 4B). In terms of the number of death cases, Djibouti faced the most substantial increase, with a 373 percent rise, whereas Estonia had a 67 percent decrease (Fig. 4C). Finally, Djibouti also experienced the most significant increase in the number of DALYs, with a 349 percent rise, while Estonia saw a 68 percent decrease (Fig. 4D).

Age and sex patterns

In 2021, the ASPR of ischemic stroke demonstrated a progressive increase with advancing age, peaking at 80–95 years (Fig. 5). At ages 45 to 49, the ASPR ratios for men and women were similar; however, with increasing age, the ASPR was consistently higher in men compared to women within the same age group. Similarly, the ASIR of ischemic stroke in 2021 exhibited a gradual rise with age, reaching its zenith in individuals aged 95 years and older (Supplementary Fig. S4). Among the population aged 40 years and older, the incidence in males progressively surpassed that in females, although the disparity between genders diminished in those over 85 years of age. In comparison to 1990, the ASDR for ischemic stroke in 2021 showed a decline in both men and women, yet continued to escalate with age, with men experiencing higher ASDRs than women at most ages (Supplementary Fig. S5). DALYs also indicated a downward trend in 2021 relative to 1990, with ASR being greater in men than in women after the age of 40 (Supplementary Fig. S6).

Risk factors for ischemic stroke

The study collected data on ischemic stroke-related deaths and DALYs attributable to four risk factors: High body-mass index, High alcohol use, Low physical activity, and Tobacco, as categorized in GBD 2021, and

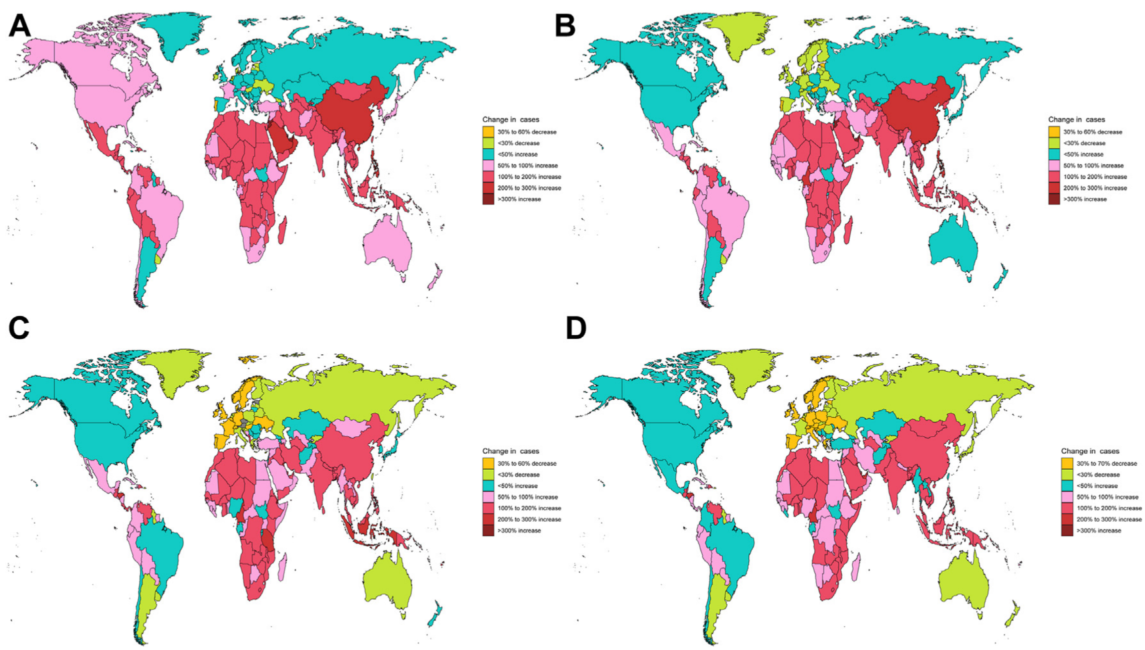

Fig. 4: Change cases of ischemic stroke for both sexes in 204 countries and territories. (A) Change prevalence cases. (B) Change incidence cases. (C) Change deaths cases. (D) Change DALYs.

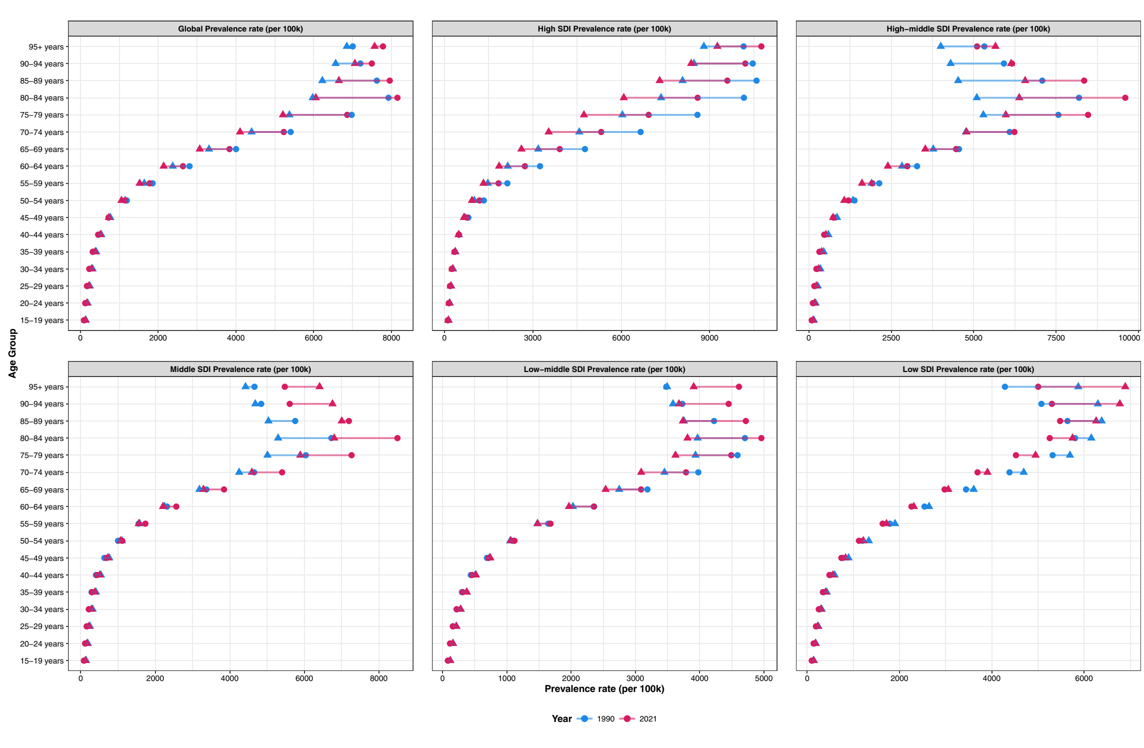

Fig. 5: Age-standardized prevalence rates of ischemic stroke by sex, age group, and socio-demographic index, 1990 and 2021.

further stratified the data by region (Supplementary Fig. S7). On a global scale, Tobacco was the most significant contributor to deaths and DALYs due to ischemic stroke in 2021. Specifically, tobacco use accounted for 12.6% of all deaths worldwide. Among the geographical regions, East Asia had the highest proportion of tobacco-attributable deaths at 18%, while Australasia had the lowest at 4.4%. High body-mass index also played a crucial role, with the highest proportion in North Africa and the Middle East at 10.2% and the lowest in High-income Asia Pacific at 1.9%. High alcohol use had a substantial impact, with the highest proportion in Australasia at 10.1% and the lowest in North Africa and the Middle East at 0.4%. Low physical activity also contributed to deaths, with the highest proportion in North Africa and the Middle East at 5.7% and the lowest in Eastern Sub-Saharan Africa at 2.1%. The contribution of these risk factors to deaths varied across SDI regions, with High-middle SDI regions having higher proportions of deaths attributable to high body-mass index and high alcohol use compared to Low SDI regions.

Globally, tobacco use was the primary risk factor, contributing to 15.5% of all DALYs. Among the geographical regions, East Asia had the highest proportion of tobacco-attributable DALYs at 20.9%, while Western Sub-Saharan Africa had the lowest at 5.9%. High body-mass index significantly contributed to DALYs, with the highest proportion in Central Asia at 10.5% and the lowest in High-income Asia Pacific at 2.6%. High alcohol use played a notable role, with the highest proportion in Australasia at 10.9% and the lowest in Oceania at 1.3%. Low physical activity also contributed to DALYs, with the highest proportion in Oceania at 6.1% and the lowest in Central Asia at 3.4%. When considering the five SDI regions, the Middle SDI region had the highest proportion of tobacco-attributable DALYs at 17.4%, while the Low SDI region had the lowest at 8.8%. The contribution of other risk factors to DALYs also varied across SDI regions, emphasizing the complex interplay of these factors in the global burden of ischemic stroke.

Future forecasts of global burden of ischemic stroke

The global burden of ischemic stroke is projected to evolve significantly from 2021 to 2040, with varying trends across different measures. The ASPR of ischemic stroke is expected to increase globally for both sexes combined, rising from approximately 820 per 100,000 population in 2021 to about 900 per 100,000 by 2040, representing a roughly 10% increase over two decades (Fig. 6). For males, the prevalence is expected to remain relatively stable, with a slight increase from about 882 per 100,000 in 2021 to 910 per 100,000 in 2040. In contrast, females are projected to experience a more pronounced increase, from approximately 769 per 100,000 in 2021 to 898 per 100,000 in 2040, indicating a steeper upward trend. The global incidence of ischemic stroke shows a slight upward trend for both sexes combined, with the ASIR projected to increase from about 110 per 100,000 population in 2021 to approximately 120 per 100,000 by 2040. The ASDR for ischemic stroke is projected to decrease slightly for both sexes combined, from about 50 per 100,000 population in 2021 to approximately 37 per 100,000 by 2040, suggesting a potential improvement in acute care and

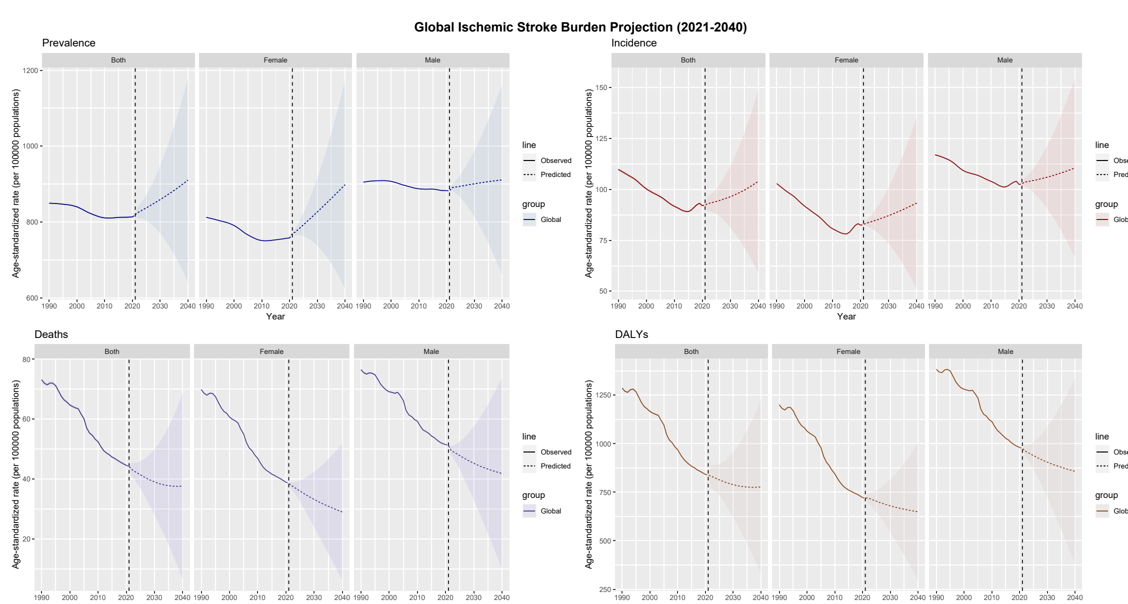

Fig. 6: Future forecasts of global burden of ischemic stroke.

management of ischemic stroke. The age-standardized DALY rate for ischemic stroke is expected to remain relatively stable for both sexes combined, with a slight decrease from 837.4 per 100,000 population in 2021 to approximately 777 per 100,000 by 2040. Across all four measures, males consistently show higher rates compared to females, although the gap between males and females appears to narrow over time, particularly for prevalence.

Discussion

Our comprehensive analysis of the global burden of ischemic stroke from 1990 to 2021 reveals a complex landscape of disparities and trends across regions and sociodemographic indices. On a global scale, the ASPR, ASIR, ASDR, and age-standardized DALY rate of ischemic stroke decreased from 1990 to 2021. These findings align with previous GBD studies, which have also reported a decline in age-standardized rates of ischemic stroke over time.[18–20] At the regional level, the highest ASPR, ASIR, ASDR, and age-standardized DALY rates were observed in regions with high-middle SDI, while the lowest rates were found in high SDI regions. This finding highlights the persistent socioeconomic disparities in the global burden of ischemic stroke.[21,22] The higher burden in high-middle SDI regions may be due to a combination of factors, including limited access to healthcare, suboptimal management of risk factors, and inadequate secondary prevention strategies.[23,24] In contrast, high SDI regions may have benefited from well-established healthcare systems, effective public health interventions, and greater awareness of stroke risk factors and symptoms.[25] The high prevalence and incidence rates in Sub-Saharan Africa and parts of Asia, for instance, likely stem from a combination of genetic predisposition, increasing prevalence of risk factors, and healthcare system limitations.[26] In Sub-Saharan Africa, the high burden of ischemic stroke may be partly explained by the increasing prevalence of hypertension,[27] which has been linked to rapid urbanization, dietary changes, and physical inactivity. Moreover, the region faces significant challenges in healthcare access and quality, with limited resources for both prevention and acute stroke care.[28,29] The genetic factors, such as the high prevalence of sickle cell trait in some African populations, may also contribute to the elevated stroke risk.[30] The high incidence rates observed in Eastern Europe and Central Asia could be attributed to a combination of factors, including high rates of smoking, excessive alcohol consumption, and suboptimal management of cardiovascular risk factors. The economic transition in these regions has been associated with lifestyle changes that have increased the prevalence of obesity and metabolic disorders, further contributing to stroke risk. The contrasting trends observed within Asia, particularly the increasing incidence in East Asia versus the decreasing rates in High-income Asia Pacific, underscore the impact of socioeconomic development and healthcare policies. The rapid economic growth and urbanization in East Asia have led to lifestyle changes that increase stroke risk factors, while High-income Asia Pacific countries have implemented effective prevention strategies and improved acute stroke care. The lower burden observed in high SDI regions, particularly in terms of mortality and DALYs, likely reflects the success of primary prevention strategies, improved acute stroke care, and better secondary prevention measures. These regions typically have better control of traditional risk factors, more widespread use of anticoagulation for atrial fibrillation, and more advanced systems for acute stroke treatment, including wider access to thrombolysis and thrombectomy.[19–21]

Despite the decrease in age-standardized rates, the absolute number of prevalent cases, incident cases, deaths, and DALYs due to ischemic stroke increased from 1990 to 2021, especially in low- and middle-income countries. This increase can be primarily attributed to population growth and aging, as well as the epidemiological transition occurring in these regions, which is characterized by a shift from communicable to non-communicable diseases.[9] As populations grow and age, the number of individuals at risk of ischemic stroke increases, leading to a higher absolute burden of the disease. Moreover, the rising prevalence of risk factors such as obesity, physical inactivity, and unhealthy diets in low- and middle-income countries may also contribute to the increasing burden of ischemic stroke. As these countries undergo economic development and adopt more sedentary lifestyles and westernized diets, the prevalence of these risk factors tends to increase, leading to a higher incidence of ischemic stroke and other non-communicable diseases.[31,32] Furthermore, limited access to quality healthcare, including acute stroke services and rehabilitation facilities, may exacerbate the burden of ischemic stroke in resource-constrained settings.[33]

The study also found that the burden of ischemic stroke increases with age, with the highest ASPR, ASIR, ASDR, and age-standardized DALY rates observed in older age groups. This aligns with the well-established association between aging and the risk of ischemic stroke.[34] The increased burden in older populations may be attributed to the cumulative effect of risk factors over time, as well as age-related changes in the cerebrovascular system, such as arterial stiffness and endothelial dysfunction.[35,36] Furthermore, the burden of ischemic stroke was higher in men than in women, particularly in older age groups. This gender disparity may be explained by the higher prevalence of risk factors such as smoking and alcohol consumption among men,[37] as well as potential differences in the pathophysiology and presentation of ischemic stroke between men and women.[38,39]

The analysis of risk factors revealed that tobacco use, high body mass index, high alcohol consumption, and low physical activity are significant contributors to the global burden of ischemic stroke. The impact of these risk factors varies across regions and SDI quintiles, underscoring the need for tailored prevention strategies that consider the specific risk factor profiles of different populations. For instance, in high-income countries, where smoking rates have declined, greater emphasis might be placed on promoting physical activity and healthy diets to mitigate the burden of obesity-related stroke. Conversely, in low- and middle-income countries, where smoking and air pollution are major risk factors, interventions targeting these exposures could significantly reduce the burden of ischemic stroke.[40,41] To address these varied risk factors and reduce the global burden of ischemic stroke, a multi-faceted approach is necessary. In high-income countries, strategies could include implementing workplace wellness programs that encourage regular physical activity and provide healthier food options.[42] Developing urban planning policies that promote walkability and access to green spaces could facilitate increased physical activity.[43] Enhancing public education campaigns about the risks of excessive alcohol consumption and its link to stroke could also be effective. For low- and middle-income countries, effective measures might include strengthening tobacco control policies, such as increasing tobacco taxes, implementing comprehensive smoke-free laws, and expanding cessation services. Improving air quality through stricter emissions standards, promoting clean energy sources, and enhancing public transportation systems could address the issue of air pollution. Implementing community-based hypertension screening and management programs, particularly in rural areas with limited healthcare access, could help manage a key risk factor. Developing culturally appropriate dietary guidelines and promoting traditional, healthier eating patterns might combat the rise of obesity. Across all settings, additional strategies to reduce the burden of ischemic stroke could include integrating stroke risk assessment into primary care visits, with a focus on early identification and management of modifiable risk factors.[5]

The COVID-19 pandemic, which emerged in late 2019 and continued through 2021, likely influenced the trends observed in our study of the global burden of ischemic stroke. Our findings of persistent high stroke burden in certain regions may be partially attributed to the pandemic's impact. COVID-19 has been associated with an increased risk of thrombotic events, including ischemic stroke,[44] which could contribute to the elevated incidence rates observed in some areas. Moreover, the pandemic-induced disruptions to healthcare systems worldwide[44] may have exacerbated existing disparities in stroke care, potentially explaining the continued high mortality and DALY rates in regions with middle and high-middle SDI. Interestingly, our observed trends in risk factors such as high body-mass index and low physical activity could be linked to lifestyle changes during lockdowns.[45] The persistence of high stroke burden in regions like Eastern Europe and Central Asia, as shown in our results, aligns with reports of these areas being significantly affected by COVID-19. These interconnections underscore the complex relationship between the pandemic and global ischemic stroke patterns, reinforcing the need for adaptive stroke prevention and management strategies in the post-COVID era.

However, the study also has some limitations that should be considered when interpreting the results. First, the accuracy of the estimates may be affected by the quality and availability of data sources across countries and regions. In some low- and middle-income countries, the lack of reliable epidemiological data and the underreporting of stroke cases may lead to an underestimation of the true burden. Second, the GBD methodology relies on various assumptions and modeling techniques, which may introduce some uncertainty in the estimates. While the GBD study employs rigorous statistical methods to address these uncertainties, the results should be interpreted as the best available estimates based on the current evidence.

In conclusion, despite a decrease in age-standardized rates, the absolute burden of ischemic stroke remains high, with significant variations across regions, countries, and SDI regions. The findings underscore the need for targeted prevention and treatment strategies that address the specific needs of different populations, particularly in low- and middle-income countries. Strengthening healthcare systems, promoting healthy lifestyles, and reducing socioeconomic disparities are crucial steps to mitigate the global burden of ischemic stroke. Future research should prioritize identifying and implementing the most effective interventions and policies for ischemic stroke prevention and management, especially in high-burden regions. Additionally, efforts should focus on elucidating the complex interplay between genetic, environmental, and lifestyle factors contributing to ischemic stroke development.

Contributors
All authors have made substantial contributions to this study. Xin-yu Li, Xiang-meng Kong, and Cheng-hao Yang were responsible for the conceptualization and methodology of the research. Zhi-feng Cheng, Jia-jie Lv, and Hong Guo conducted the investigation and data curation. Xiao-hong Liu contributed to both aspects of the study. All authors were involved in (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the version to be submitted. Xin-yu Li and Xiang-meng Kong accessed and verified the underlying data. The authors declare that this manuscript, including related data, figures, and tables, has not been previously published and is not under consideration elsewhere.

Data sharing statement

GBD study 2021 data resources were available online from the Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool).

Editor note

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Declaration of interests

No competing interests declared.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102758.

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