Temporal trends in cross-country inequalities of stroke and subtypes burden from 1990 to 2021: a secondary analysis of the global burden of disease study 2021

Zeyu Luo,[a] Shiyi Shan,[a] Jin Cao,[a] Jiali Zhou,[a] Liying Zhou,[a] Denan Jiang,[b] Lingzi Yao,[a] Jing Wu,[a] Jiayao Ying,[a] Yajie Zhu,[c] Peige Song,[a,*] and Kazem Rahimi[d]

[a]Centre for Clinical Big Data and Statistics of the Second Affiliated Hospital Zhejiang University School of Medicine, School of Public Health Zhejiang University School of Medicine, Hangzhou, China
[b]The Fourth Affiliated Hospital of School of Medicine, and International School of Medicine, International Institutes of Medicine, Zhejiang University, Yiwu, China
[c]School of Information Science and Technology, Hangzhou Normal University, Hangzhou, Zhejiang, China
[d]Nuffield Department of Women's and Reproductive Health, Medical Science Division, University of Oxford, Oxford, UK

eClinicalMedicine 2024;76: 102829
Published Online xxx
https://doi.org/10.1016/j.eclinm.2024.102829

Summary

Background Stroke remains a significant global health challenge, with persistent disparities in burden across different countries and regions. This study aimed to assess the temporal trends in cross-country inequalities of stroke and its subtypes burden from 1990 to 2021.

Methods We conducted a secondary analysis of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021. The age-standardised disability-adjusted life years (DALYs) rate (ASDR) was used to assess the burden of stroke and its subtypes (ischemic stroke, intracerebral haemorrhage, and subarachnoid haemorrhage) across 21 GBD regions and 204 countries. The slope index of inequality (SII) and the concentration index were calculated to quantify the absolute and relative cross-country inequalities in the burden of stroke and its subtypes, with negative values indicating a higher burden in lower socio-demographic index (SDI) countries, and positive values indicating a higher burden in higher SDI countries. Estimated annual percentage change (EAPC) was used to illustrate temporal trends at global and regional levels from 1990 to 2021. The inequality changing patterns from 1990 to 2021 were classified as worsening, improving, and shifting to higher burdens among higher or lower SDI countries.

Findings From 1990 to 2021, the ASDR of total stroke decreased from 3078.95 (95% uncertainty interval [UI]: 2893.58, 3237.34) to 1886.20 (95% UI: 1738.99, 2017.90) per 100,000 population globally. While both absolute and relative inequalities increased, with a disproportionately higher burden shouldered by countries with lower SDI. The SII of total stroke exhibited a worsening inequality among lower SDI countries, increasing by 286.97 units from −2329.47 (95% confidence interval [CI]: −2857.50, −1801.43) in 1990 to −2616.44 (95% CI: −2987.33, −2245.56) in 2021. Similarly, the concentration index of total stroke increased by 0.03 from −0.0819 (95% CI: −0.1143, −0.0495) in 1990 to −0.1119 (95% CI: −0.1478, −0.0759) in 2021. The changing patterns from 1990 to 2021 were diverse across regions, yet most regions exhibited a worsening inequality among lower SDI countries in both SII and concentration index. Southern Sub-Saharan Africa showed the largest worsening inequality in SII (EAPC: −2.15, 95% CI: −2.71, −1.57) while Central Europe showed the largest worsening inequality in concentration index (EAPC: −0.51, 95% CI: −0.58, −0.44). In 2021, the highest negative SII was observed in Oceania and the highest negative concentration index was in the Caribbean. In terms of subtypes, ischemic stroke reported a worsening inequality among lower SDI countries in SII (EAPC: −2.13, 95% CI: −2.20, −2.05) while intracerebral haemorrhage showed an improving inequality in SII (EAPC: 0.44, 95% CI: 0.40, 0.47). SII in subarachnoid haemorrhage (EAPC: −0.18, 95% CI: −0.19, −0.17) and concentration index in ischemic stroke (EAPC: −0.25, 95% CI: −0.27, −0.23) presented a shift to higher burden among lower SDI countries from 1990 to 2021.

Interpretation Although the burden of stroke and its subtypes decreased from 1990 to 2021, inequalities have persisted and even widened in some regions. Timely and effective prevention and management strategies for stroke and its subtypes are needed in specific areas to reduce the stroke burden and achieve equity in health outcomes.

*Corresponding author. Centre for Clinical Big Data and Statistics of the Second Affiliated Hospital Zhejiang University School of Medicine, School of Public Health Zhejiang University School of Medicine, China.
E-mail address: peigesong@zju.edu.cn (P. Song).

Funding None.

Keywords: Stroke; Health inequalities; Global burden of disease; Temporal trends; Disability-adjusted life years

Research in context

Evidence before this study

We used the keywords "stroke", "global burden", "health inequality", and "temporal trends" to search PubMed and Web of Science from database inception to May 30th, 2024. Several studies have explored the global, regional, and national burden of stroke. However, these studies often focused on global trends, with less emphasis on cross-country inequalities at both the global and regional levels. Additionally, previous studies are limited to examining overall stroke without exploring its subtypes, or they focus exclusively on specific stroke risk factors. Furthermore, most of these studies extend up to 2019. To date, there has been no analysis of cross-country inequalities in the burden of stroke and its subtypes from 1990 to 2021.

Added value of this study

This study leverages the newly updated Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 data to explore the temporal trends in cross-country inequalities stroke and its subtypes from 1990 to 2021 at both the global and regional levels. We quantified both absolute and relative inequalities, employing the slope index of inequality (SII) and the concentration index, alongside the estimated annual percentage change (EAPC) to describe trends. This analysis revealed that although the burden of stroke and its subtypes decreased from 1990 to 2021, inequalities have persisted and even widened in some regions. Countries with lower socio-demographic index (SDI) have disproportionately shouldered a greater burden of stroke and its subtypes.

Implications of all the available evidence

The evidence presented in this study underscores the critical need for targeted public health interventions and policies that address the unequal distribution of stroke burden, especially in several specific regions. The increasing inequalities suggest that global health efforts must prioritize high-burden, low-SDI regions to mitigate the disparities in stroke outcomes. Furthermore, understanding the subtype-specific trends in stroke burden can lead to more tailored approaches to prevention and management strategies.

Introduction

Stroke is defined as an acute focal neurological deficit caused by a vascular lesion.[1,2] Globally, stroke remains one of the leading cause of disease burden (measured by Disability-Adjusted Life Years [DALYs]).[3] From 1990 to 2019, the age-standardised DALYs rate (ASDR) of stroke decreased by 36.0% globally, yet the absolute DALYs increased by 32.0%.[4] Furthermore, stroke was the greatest contributor to nervous system DALYs globally in 2021, placing a significant burden on global health systems.[5] Stroke mainly includes three subtypes: ischemic stroke (IS), intracerebral haemorrhage (ICH), and subarachnoid haemorrhage (SAH).[2] Notably, IS and ICH comprised the majority of total stroke DALYs, accounting for 44.32% and 47.87%, respectively.[4] Beyond the physiological symptoms, stroke profoundly impacts patients' psychological and social functioning, presenting significant demands and loads on their families and caregivers.[6–8] Stroke also incurred substantial economic costs, with global direct costs estimated at $891 billion in 2017, which accounts for approximately 1.12% of the global gross domestic product (GDP).[9] To address the significant healthcare burden posed by stroke and its subtypes, a thorough understanding of their temporal trends is needed.

Previous studies have demonstrated significant variations in the ASDR of stroke and its subtypes across different regions and countries. For instance, the ASDR of stroke in World Bank low-income countries was 3.7 times higher than that in high-income countries in 2019.[4] Furthermore, 89.0% of stroke-related DALYs occurred in lower-income, lower-middle-income, and upper-middle-income countries.[3] Additionally, World Bank low-income to upper-middle-income countries had nearly double the ASDR of ICH but a lower ASDR of SAH compared to high-income countries in 2019.[4] The World Health Organisation (WHO) has proposed a universal health coverage policy aimed at decreasing inequalities and achieving "health for all".[10] Emphasizing the inequalities of stroke across different regions and countries is crucial for optimizing resource allocation. However, there remains a lack of comprehensive analysis investigating global and regional cross-country inequalities in the burden of stroke and its subtypes. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 provides a useful tool for quantifying the epidemiology and burden of diseases, including stroke and its subtypes.[11] By extracting data on the burden of disease, population and sociodemographic development levels, indicators can be calculated to quantify cross-country inequalities.[12] This study could therefore guide targeted prevention and treatment strategies, facilitating the effective distribution of resources to enhance global health outcomes.

This study aimed to 1) describe the disease burden of stroke and its subtypes at global, regional, and national levels; 2) assess inequalities in the burden of stroke and its subtypes at global and regional levels; and 3) quantify temporal trends in the burden and inequalities of stroke and its subtypes at global and regional levels from 1990 to 2021.

Methods

Data source

We conducted a secondary analysis of the GBD 2021 (https://vizhub.healthdata.org/gbd-results/). The GBD 2021 includes nationally representative surveys, censuses, and meta-analysis results, and provides an accessible epidemiological assessment of 371 diseases and injuries as well as 88 risk factors, covering 21 GBD regions and 204 countries/territories from 1990 to 2021.[13,14] The GBD 2021 utilized data from a variety of sources including peer-reviewed literature, survey data, disease registers, and hospital inpatient records to ensure the quality and comprehensiveness of the stroke-related analysis.[15] Detailed descriptions of these data sources and their validation processes are systematically reviewed and accessible via the Global Health Data Exchange web tool (http://ghdx.healthdata.org/). We extracted gender- and location-specific estimates of ASDR along with their corresponding 95% uncertainty intervals (UIs) for stroke and its three subtypes (IS, ICH and SAH) from 1990 to 2021. We included data from 21 GBD regions and 204 countries and territories. Additionally, we utilized the socio-demographic index (SDI), a composite metric that measures development levels based on the geometric mean of three factors: fertility rates under 25, education levels for adults over 15, and income per capita.[16] These factors are normalized on a scale from zero (indicating minimal development relevant to health) to one (indicating maximal development). For specific information about SDI, see https://ghdx.healthdata.org/record/global-burden-disease-study-2021-gbd-2021-socio-demographic-index-sdi-1950%E2%80%932021.

This study adhered to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).[17] The study didn't involve any personal or sensitive information. Consequently, no ethical approval was required for the execution of this study.

Disease definitions

Following the WHO criteria, stroke is defined as rapidly developing clinical signs of focal disturbance of cerebral function, lasting 24 hours or longer or leading to death, with vascular origin as the sole apparent cause.[1] In GBD 2021, stroke is categorized into ischemic stroke and haemorrhagic stroke (comprising intracerebral haemorrhage and subarachnoid haemorrhage).[2] Ischemic stroke refers to vascular incidents that restrict blood flow to the brain, leading to infarction, thromboembolic, or atherosclerotic strokes. Haemorrhagic stroke is defined as either non-traumatic subarachnoid haemorrhage or intracerebral haemorrhage, with the former being non-traumatic bleeding into the brain's subarachnoid space and the latter as non-traumatic focal bleeding within the brain.

Statistical analysis

Burden description

We delineated the burden of total stroke, IS, ICH and SAH from 1990 to 2021 through the distribution of ASDR per 100,000 population across 21 GBD regions and 204 countries/territories. Global map plots provided a visual representation of the disparity in ASDR among countries/territories. The relationship between SDI and ASDR for total stroke, IS, ICH and SAH in 21 GBD regions was demonstrated via compound line graphs, which elucidated the disparities of stroke burden related to socioeconomic development.

Cross-country inequality analysis

The slope inequality index (SII) and concentration index were calculated as standardised metrics to quantify inequalities in stroke ASDR globally and across 21 GBD regions. The SII is a measure that quantifies the absolute inequality in a health indicator between the most advantaged and least advantaged subgroups within a population, taking into account the entire distribution of a socioeconomic factor such as education or wealth through a weighted regression model. In comparison, the concentration index is a measure that quantifies the relative inequality by indicating the extent to which a health indicator is concentrated among the disadvantaged or advantaged.[12] The SII quantified absolute inequality by regressing country-specific stroke ASDR against a relative position scale related to the SDI, defined as the midpoint of the population range ranked by cumulative SDI.[12] To account for heteroscedasticity, we used robust linear regression models. This method applies iteratively reweighted least squares, where observations with larger residuals receive smaller weights, thus minimizing the influence of outliers and ensuring more reliable and stable trend estimations.[18] The concentration index was calculated by numerical integration under the Lorenz curve, which plots the cumulative proportion of stroke ASDR against the cumulative population distribution, ranked by SDI, providing a measure of relative inequality.[19,20] A negative SII/concentration index represents that a higher SDI corresponds to a lower ASDR, and vice versa. A larger absolute value of the SII/concentration index indicates greater inequality.

Trend analysis

The estimated annual percentage change (EAPC) was applied to elucidate trends in burden and inequality of

stroke and its subtypes at global and regional levels. EAPC is an estimate of the annual percentage rate of change over a specific period, estimated through a linear regression model.[21] A negative EAPC indicates a downward trend, while a positive EAPC indicates an upward trend. The ranking graphs for SII and concentration index indicated the increases and decreases in rank as well as the percentage changes in values across the GBD regions from 1990 to 2021, elucidating the temporal trend of health inequalities among regions. The changing patterns of inequality from 1990 to 2021 were divided into six categories: Worsening inequality among lower SDI countries, Improving inequality among lower SDI countries, Worsening inequality among higher SDI countries, Improving inequality among higher SDI countries, Shift to higher burden among higher SDI countries, and Shift to higher burden among lower SDI countries. Their implications are exhibited in Table 1.

Statistical analysis

All statistical analyses were performed in R version 4.3.3 and Stata 17.0. The ASDR was reported per 100,000 population along with 95% UI. SII, concentration index, and EAPC were all presented with their respective 95% confidence intervals (CIs).

Role of the funding source

There was no funding source for this study. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication.

Results

Global burden of stroke, 1990–2021

Total stroke

From 1990 to 2021, the ASDR of total stroke decreased from 3078.95 (95% UI: 2893.58, 3237.34) to 1886.20 (95% UI: 1738.99, 2017.90) per 100,000 population globally, with an EAPC of –1.77 (95% CI: –1.86, –1.67) (Supplementary Table S1). Among GBD regions, Oceania showed the highest ASDR (3657.45 [95% UI: 3015.67, 4394.91]/100,000 population), while Australasia had the lowest ASDR (449.31 [95% UI: 402.92, 491.86]/100,000 population) in 2021. The top five countries with the highest ASDR of stroke in 2021 were Nauru, Solomon Islands, Mozambique, Guinea-Bissau, and Marshall Islands (Fig. 1A). The ASDR of total stroke generally decreased as the SDI value increased. However, regional variations were observed. For example, in Eastern Europe and Central Asia, the ASDR initially increased and then decreased remarkably with an increase in the SDI value (Supplementary Fig. S1A).

Ischemic stroke

Between 1990 and 2021, there was a decline in the ASDR for IS, falling from 1286.31 (95% UI: 1195.19, 1376.06) to 837.36 (95% UI: 763.73, 904.98) per 100,000 population globally. This decline was quantified by an EAPC of –1.59 (95% CI: –1.68, –1.50), as indicated in Supplementary Table S1. Across GBD regions, Eastern Europe showed the highest ASDR (1601.20 [95% UI: 1483.51, 1723.12]/100,000 population) and Australasia had the lowest ASDR (249.45 [95% UI: 216.51, 278.22]/100,000 population) in 2021. North Macedonia, Egypt, Afghanistan, Bulgaria and Yemen emerged as the top five countries with the highest ASDR of IS in 2021 (Fig. 1B). ASDR initially stabilized and then decreased with the increase of SDI. The trend of the GBD regions was similar to that of total stroke (Supplementary Fig. S1B).

Intracerebral haemorrhage

Between 1990 and 2021, the ASDR of ICH decreased from 1516.80 (95% UI: 1421.03, 1613.26) to 923.64 (95% UI: 844.83, 993.18) per 100,000 population globally, with an EAPC of –1.74 (95% CI: –1.88, –1.61) (Supplementary Table S1). Among GBD regions,

Pattern	Inequality values			Implication
	1990	2021	Trend	
Worsening inequality among lower SDI countries	Negative	Negative	Relative increasing	The inequality index was consistently negative, and its absolute value increased over time. It means the disease burden was consistently higher among countries with lower SDI, and this inequality has widened over time.
Improving inequality among lower SDI countries	Negative	Negative	Relative decreasing	The inequality index was consistently negative, but its absolute value decreased over time. It means the disease burden was consistently higher among countries with lower SDI, but this inequality has narrowed over time.
Worsening inequality among higher SDI countries	Positive	Positive	Relative increasing	The inequality index was consistently positive, and its absolute value increased over time. It means the disease burden was higher among countries with higher SDI, and this inequality has widened over time.
Improving inequality among higher SDI countries	Positive	Positive	Relative decreasing	The inequality index was consistently positive, but its absolute value decreased over time. It means the disease burden was higher among countries with higher SDI, but this inequality has narrowed over time.
Shift to higher burden among higher SDI countries	Negative	Positive	/	The inequality index was negative in 1990 but shifted to positive in 2021. It means the disease burden was higher among countries with lower SDI initially, but shifted to being higher among countries with higher SDI by 2021.
Shift to higher burden among lower SDI countries	Positive	Negative	/	The inequality index was positive in 1990 but shifted to negative in 2021. It means the disease burden was higher among countries with higher SDI initially, but shifted to being higher among countries with lower SDI by 2021.

SDI, socio-demographic index.

Table 1: **The changing patterns of inequalities from 1990 to 2021 and their implications.**

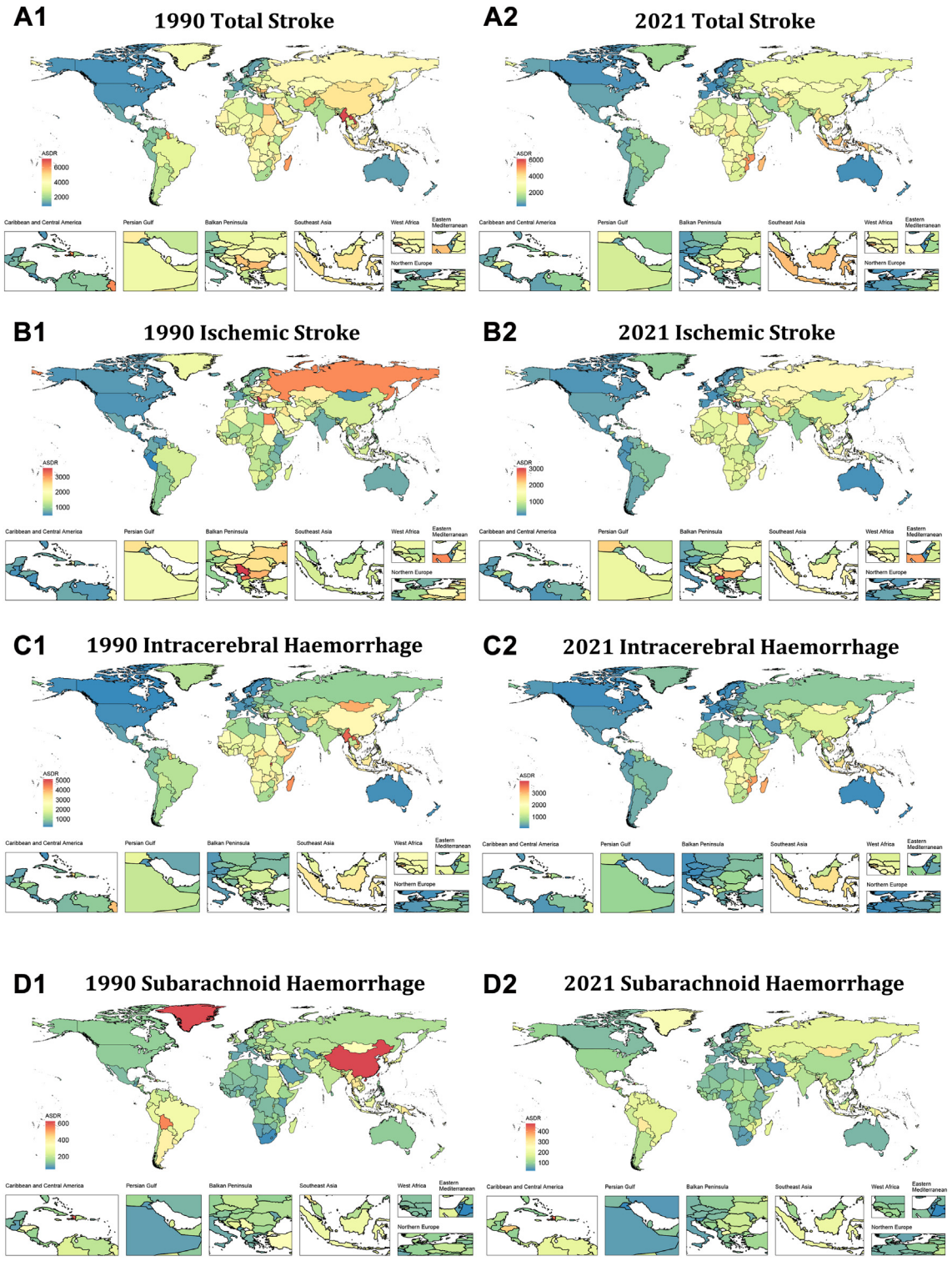


Fig. 1: **Global maps of ASDR per 100,000 population by stroke and subtypes in 1990 and 2021. Notes:** (A1) ASDR of total stroke in 1990. (A2) ASDR of total stroke in 2021. (B1) ASDR of ischemic stroke in 1990. (B2) ASDR of ischemic stroke in 2021. (C1) ASDR of intracerebral haemorrhage in 1990. (C2) ASDR of intracerebral haemorrhage in 2021. (D1) ASDR of subarachnoid haemorrhage in 1990. (D2) ASDR of subarachnoid haemorrhage in 2021. ASDR, age-standardised DALY rate. DALYs, disability-adjusted life years.

Oceania reported the highest ASDR (2582.46 [95% UI: 2058.74, 3157.50]/100,000) and Australasia the lowest (126.59 [95% UI: 115.89, 136.69]/100,000) in 2021. The highest ASDRs in 2021 were in Nauru, Solomon Islands, Marshall Islands, Micronesia (Federated States of), and Mozambique (Fig. 1C). SDI and ASDR of ICH correlated similarly to total stroke (Supplementary Fig. S1C).

Subarachnoid haemorrhage

From 1990 to 2021, the ASDR of SAH decreased from 275.85 (95% UI: 213.22, 335.43) to 125.20 (95% UI: 110.54, 142.61) per 100,000 population globally. The decrease was tracked by an EAPC of −2.88 (95% CI: −3.06, −2.70) (Supplementary Table S1). Oceania recorded the highest ASDR (285.62 [95% UI: 209.42, 379.65]/100,000), while Western Europe recorded the lowest (67.75 [95% UI: 63.56, 71.94]/100,000) in 2021. The highest ASDRs in 2021 were seen in Haiti, Nauru, Marshall Islands, Micronesia (Federated States of), and Solomon Islands (Fig. 1D). Generally, the ASDR remained stable as the SDI value increased. However, regional variations were observed. Notably, in Eastern Europe, the ASDR initially rose then sharply declined as the SDI increased. While in Southeast Asia, the ASDR showed an extreme decline as the SDI rose (Supplementary Fig. S1D).

Cross-country inequalities of stroke, 1990–2021

Total stroke

Globally, significant absolute and relative SDI-related inequalities in the ASDR of total stroke were observed, with a disproportionately higher burden shouldered by countries with lower SDI (Table 2, Fig. 2A). From 1990 to 2021, the SII of stroke ASDR exhibited a worsening inequality among lower SDI countries, rising from −2329.47 (95% CI: −2857.50, −1801.43) to −2616.44 (95% CI: −2987.33, −2245.56), with an EAPC of −0.22 (95% CI: −0.27, −0.16). Similarly, the concentration index of stroke ASDR increased from −0.0819 (95% CI: −0.1143, −0.0495) to −0.1119 (95% CI: −0.1478, −0.0759), with an EAPC of −0.09 (95% CI: −0.12, −0.06) (Table 2, Fig. 2B). From 1990 to 2021, most regions showed a worsening inequality among lower SDI countries in SII and concentration index, with Southern Sub-Saharan Africa showing the largest worsening inequality in SII (EAPC: −2.15, 95% CI: −2.71, −1.57) while Central Europe showed the largest worsening inequality in concentration index (EAPC: −0.51, 95% CI: −0.58, −0.44). Southern Latin America and Western Sub-Saharan Africa exhibited a shift to higher burden among lower SDI countries in SII and concentration index, while Central Asia and High-income Asia Pacific exhibited a shift to higher burden among higher SDI countries in SII and concentration index, respectively. Meanwhile, Central Asia presented a worsening inequality among higher SDI countries for concentration index. In 2021, the highest negative SII was observed in Oceania (−3605.30 [95% CI: −8109.66, 899.05]) and the highest negative concentration index in the Caribbean (−0.2941 [95% CI: −0.3732, −0.2150]). Conversely, Western Europe showed the lowest negative SII (−135.62 [95% CI: −301.44, 30.21]) and lowest negative concentration index (−0.0046 [95% CI: −0.0456, 0.0364]) in 2021 (Supplementary Table S2, Fig. 2C). From the perspective of temporal trend, the SII of Oceania showed an obvious trend of first increasing and then decreasing from 1995 to 2005, with 2000 as the turning point, indicating that the burden was continuously concentrated in lower SDI areas at the beginning, and improved after 2000. Detailed trends of SII for total stroke and its subtypes from 1990 to 2021 can be seen in Supplementary Figs. S2 and S3.

Ischemic stroke

The global ASDR burden of IS was mainly concentrated in lower SDI countries in both 1990 and 2021 (Table 2, Fig. 3A). Between 1990 and 2021, the SII of IS ASDR showed a worsening inequality among lower SDI countries with the value from −212.45 (95% CI: −433.72, 8.81) to −758.54 (95% CI: −920.64, −596.45), marked by an EAPC of −2.13 (95% CI: −2.20, −2.05). The concentration index of IS ASDR showed a shift to higher burden among lower SDI countries with the value shifted from 0.0262 (95% CI: −0.0107, 0.0632) to −0.0558 (95% CI: −0.0958, −0.0158), with an EAPC of −0.25 (95% CI: −0.27, −0.23) (Table 2, Fig. 3B). Regionally, the changing patterns of SII and concentration index were similar to total stroke, with Central Europe reporting the largest worsening inequality among lower SDI countries in SII (EAPC: −3.14, 95%CI: −4.76, −1.49). It is worth mentioning that Central Asia (EAPC: 0.00, 95% CI: −0.05, 0.05) and Oceania (EAPC: 0.04, 95% CI: 0.01, 0.07) exhibited a worsening inequality among higher SDI countries in the concentration index. In 2021, Central Europe reported the highest negative SII (−1278.64 [95% CI: −1953.83, −603.46]) and the Caribbean the highest negative concentration index (−0.2261 [95% CI: −0.2992, −0.1529]). Conversely, High-income Asia Pacific showed the lowest positive SII (6.28 [95% CI: −711.11, 723.68]), and Eastern Sub-Saharan Africa the lowest negative concentration index (−0.0058 [95% CI: −0.1226, 0.1110]) (Supplementary Table S3, Fig. 3C).

Intracerebral haemorrhage

Globally, the ASDR burden primarily concentrated in lower SDI areas (Table 2, Fig. 4A). From 1990 to 2021, the SII of ICH ASDR demonstrated an improving inequality among lower SDI countries, decreasing from −2183.78 (95% CI: −2534.42, −1833.13) to −1723.23 (95% CI: −1943.18, −1503.27), marked by an EAPC of 0.44 (95% CI: 0.40, 0.47). In contrast, the concentration index of ICH ASDR showed a stable trend, from −0.1693 (95% CI: −0.2086, −0.1301)

Global	Slope index of inequality			Concentration index		
	1990	2021	EAPC (%)	1990	2021	EAPC (%)
Total stroke						
Both	−2329.47	−2616.44	−0.22	−0.0819	−0.1119	−0.09
	(−2857.50, −1801.43)	(−2987.33, −2245.56)	(−0.27, −0.16)	(−0.1143, −0.0495)	(−0.1478, −0.0759)	(−0.12, −0.06)
Female	−2339.71	−2527.24	−0.18	−0.0964	−0.1433	−0.16
	(−2810.77, −1868.66)	(−2866.28, −2188.19)	(−0.23, −0.13)	(−0.1286, −0.0641)	(−0.1798, −0.1068)	(−0.20, −0.13)
Male	−2203.18	−2673.70	−0.30	−0.0618	−0.0819	−0.04
	(−2823.55, −1582.81)	(−3100.46, −2246.95)	(−0.38, −0.21)	(−0.0962, −0.0275)	(−0.1207, −0.043)	(−0.08, −0.01)
Ischemic stroke						
Both	−212.45	−758.54	−2.13	0.0262	−0.0558	−0.25
	(−433.72, 8.81)	(−920.64, −596.45)	(−2.20, −2.05)	(−0.0107, 0.0632)	(−0.0958, −0.0158)	(−0.27, −0.23)
Female	−235.16	−699.73	−1.79	0.0057	−0.0795	−0.29
	(−447.45, −22.87)	(−855.35, −544.11)	(−1.86, −1.72)	(−0.0337, 0.0451)	(−0.1242, −0.0348)	(−0.31, −0.26)
Male	−127.68	−806.23	−2.53	0.0538	−0.0301	−0.23
	(−380.20, 124.83)	(−994.97, −617.50)	(−2.60, −2.46)	(0.0157, 0.0918)	(−0.0715, 0.0112)	(−0.25, −0.22)
Intracerebral haemorrhage						
Both	−2183.78	−1723.23	0.44	−0.1693	−0.1698	0.01
	(−2534.42, −1833.13)	(−1943.18, −1503.27)	(0.40, 0.47)	(−0.2086, −0.1301)	(−0.213, −0.1266)	(−0.04, 0.06)
Female	−2192.57	−1741.52	0.38	−0.1903	−0.2188	−0.10
	(−2492.41, −1892.73)	(−1940.93, −1542.12)	(0.36, 0.41)	(−0.2293, −0.1514)	(−0.2617, −0.1760)	(−0.15, −0.04)
Male	−2089.95	−1694.60	0.43	−0.1459	−0.1287	0.08
	(−2502.85, −1677.04)	(−1948.77, −1440.44)	(0.37, 0.48)	(−0.1873, −0.1046)	(−0.1752, −0.0823)	(0.03, 0.13)
Subarachnoid haemorrhage						
Both	0.90	−47.27	−0.18	−0.0183	−0.0445	−0.09
	(−36.06, 37.85)	(−71.58, −22.97)	(−0.19, −0.17)	(−0.0705, 0.0338)	(−0.0739, −0.0150)	(−0.14, −0.05)
Female	38.57	−26.39	−0.25	0.0075	−0.0235	−0.12
	(0.61, 76.54)	(−50.63, −2.15)	(−0.27, −0.24)	(−0.0466, 0.0617)	(−0.0573, 0.0103)	(−0.16, −0.07)
Male	−39.33	−69.02	−0.10	−0.0413	−0.0635	−0.07
	(−77.53, −1.14)	(−95.24, −42.79)	(−0.11, −0.08)	(−0.0930, 0.0103)	(−0.0928, −0.0342)	(−0.12, −0.03)

ASDR, age-standardised DALY rate. DALYs, disability-adjusted life years. EAPC, estimated annual percentage change.

Table 2: **Slope index of inequality and concentration index in global ASDR of stroke and its subtypes in 2021 and percentage changes from 1990, by sex.**

to −0.1698 (95% CI: −0.213, −0.1266), with an EAPC of 0.01 (95% CI: −0.04, 0.06), reflecting a consistent burden concentration in lower SDI countries (Table 2, Fig. 4B). Regionally, the changing patterns of SII and concentration index were similar to total stroke, with East Asia presenting the largest worsening inequality among lower SDI countries in SII (EAPC: −1.24, 95% CI: −1.63, −0.84). The difference was that most regions presented an improving inequality among lower SDI countries in SII. In 2021, Oceania recorded the highest negative SII (−3144.92 [95% CI: −6470.96, 181.11]), while the Caribbean had the highest negative concentration index (−0.3409 [95% CI: −0.4246, −0.2572]). Central Asia reported the lowest negative SII (−10.56 [95% CI: −1180.53, 1159.41]) while Eastern Europe showed the lowest positive concentration index (0.0046 [95% CI: −0.0434, 0.0525]) (Supplementary Table S4, Fig. 4C).

Subarachnoid haemorrhage

Viewing from SII, the global ASDR burden showed a fairly uniform distribution in 1990, transitioning to concentrate in lower SDI countries by 2021 (Table 2, Fig. 5A). The SII of SAH ASDR transitioned from 0.90 (95% CI: −36.06, 37.85) to −47.27 (95% CI: −71.58, −22.97) between 1990 and 2021, marked by an EAPC of −0.18 (95% CI: −0.19, −0.17). Meanwhile, the concentration index of SAH ASDR revealed a worsening inequality among lower SDI countries, shifting from −0.0183 (95% CI: −0.0705, 0.0338) to −0.0445 (95% CI: −0.0739, −0.0150), with an EAPC of −0.09 (95% CI: −0.14, −0.05) (Table 2, Fig. 5B). Regionally, most regions showed an improving inequality among lower SDI countries in SII and a worsening inequality in concentration index. East Asia exhibited the largest improving inequality in SII (EAPC: 5.48, 95% CI: 3.14, 7.87), while Southern Sub-Saharan Africa exhibited the largest worsening inequality in concentration index (EAPC: −0.53, 95% CI: −0.60, −0.46). It is worth mentioning that Eastern Europe showed a worsening inequality among higher SDI countries in concentration index (EAPC: −0.02, 95% CI: −0.11, 0.06). Andean Latin America showed the highest negative SII (−226.45 [95% CI: −271.89, −181.01]) in 2021, while Western Europe had

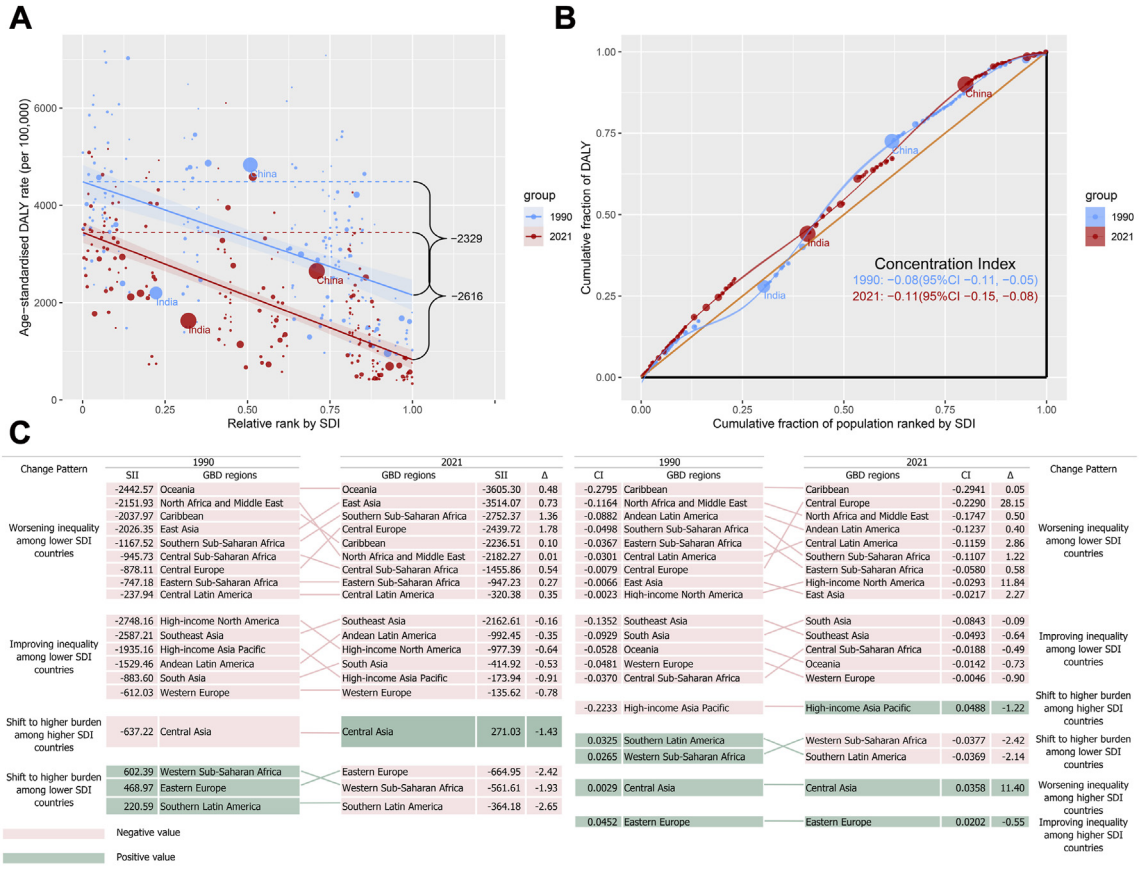


Fig. 2: **Absolute and relative cross-country inequality in ASDR and rankings of total stroke, 1990–2021. Notes**: (A) Health inequality regression curves for ASDR of total stroke. (B) Concentration curves for ASDR of total stroke. (C) Ranking graphs and change patterns for SII and CI of total stroke. Δ, the percentage change of inequality from 1990 to 2021. ASDR, age-standardised DALY rate. DALYs, disability-adjusted life years. SDI, socio-demographic index. SII, slope index of inequality. CI, concentration index. GBD, global burden of disease.

the lowest negative SII (–6.75 [95% CI: –30.81, 17.30]). The Caribbean exhibited the highest negative concentration index (–0.3257 [95% CI: –0.4258, –0.2256]), and Oceania the lowest negative concentration index (–0.0045 [95% CI: –0.0289, 0.0199]) in the same year (Supplementary Table S5, Fig. 5C).

Discussion

This study is the first to quantify the cross-country inequality in the burden of stroke and subtypes and its temporal trend from 1990 to 2021, by gender and region. Between 1990 and 2021, a decrease in ASDR of stroke and subtypes globally was demonstrated, with a disproportionately higher burden shouldered by regions or countries with lower SDI. Despite the decline in the global stroke burden, increasing inequality was revealed from 1990 to 2021. SII and concentration index showed a worsening inequality among lower SDI countries globally and in most regions. Southern Sub-Saharan Africa showed the largest worsening inequality in SII, while Central Europe showed the largest worsening inequality in the concentration index. By 2021, Oceania had the highest negative SII and the Caribbean had the highest negative concentration index, indicating that these regions experienced the most significant inequalities in stroke burden, with a disproportionately higher impact on countries with lower SDI. Among the three subtypes, there was a worsening inequality among lower SDI countries in the SII for IS and concentration index in SAH. Conversely, ICH showed an improving inequality in SII. The SII in SAH and concentration index in IS presented a shift to higher burden among lower SDI countries from 1990 to 2021. Additionally, the concentration index in ICH exhibited a stable trend. These findings underscore the imbalance of progress in stroke management and prevention across different subtypes and regions as well as highlight the importance of addressing disparities between countries.

At the global level, we found that regions or countries with lower SDI bore a disproportionately high burden of stroke. Inequality analysis revealed a

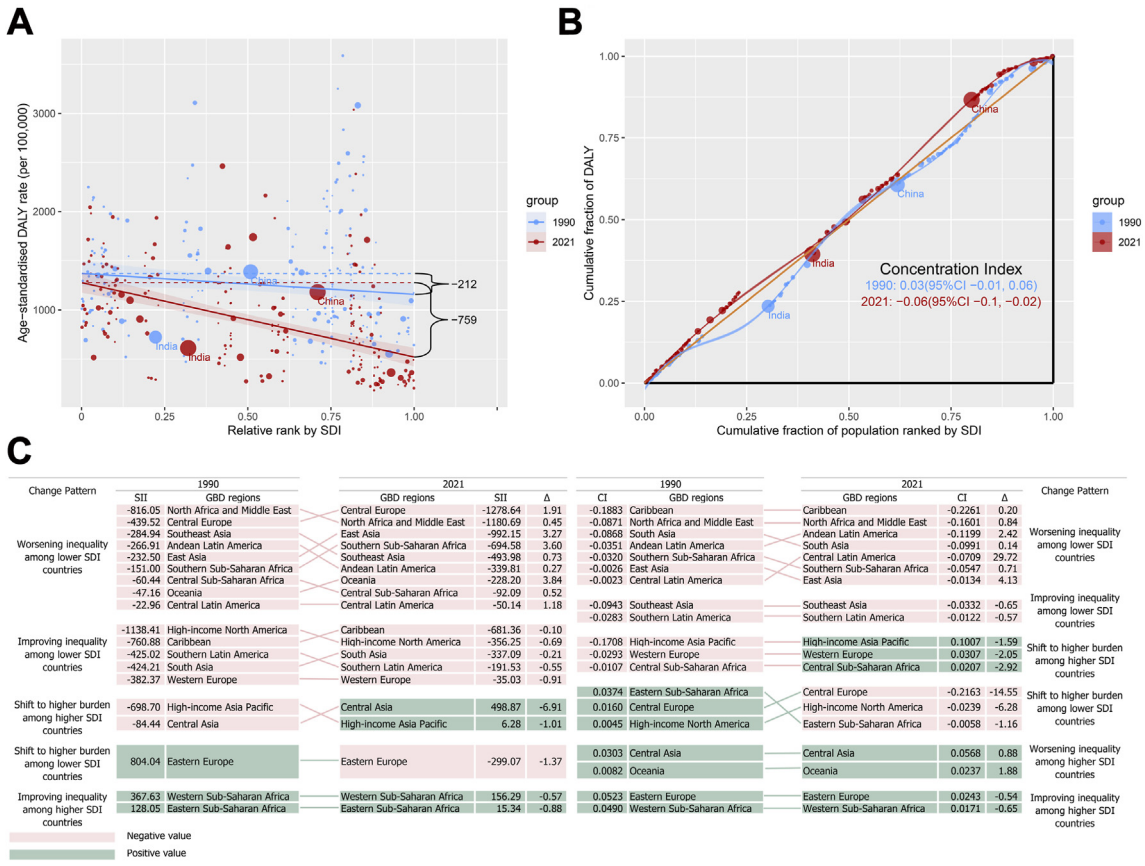


Fig. 3: **Absolute and relative cross-country inequality in ASDR and rankings of ischemic stroke, 1990–2021. Notes:** (A) Health inequality regression curves for ASDR of ischemic stroke. (B) Concentration curves for ASDR of ischemic stroke. (C) Ranking graphs and change patterns for SII and CI of ischemic stroke. Δ, the percentage change of inequality from 1990 to 2021. ASDR, age-standardised DALY rate. DALYs, disability-adjusted life years. SDI, socio-demographic index. SII, slope index of inequality. CI, concentration index. GBD, global burden of disease.

worsening inequality among lower SDI countries in both the SII and concentration index globally. This trend aligned with the broader understanding that higher levels of socioeconomic development correlated with better healthcare infrastructure, easier access to medical services, and higher overall health literacy, which were crucial for managing and preventing chronic diseases including stroke.[22] Therefore, enhancing economic development and improving healthcare resource allocation in countries with lower SDI are critical strategies for reducing these inequalities and improving public health outcomes. To achieve this, strengthening international cooperation to facilitate the sharing of best practices, provide technical assistance, and mobilize resources for healthcare infrastructure is essential.

Regional variations were observed. For instance, in Central Asia, ASDR initially increased and then significantly decreased as the SDI value increased, with a peak value in 1995. This pattern may relate to economic growth and the extent of urbanization completed by the late 20th century, where lifestyle-related stroke risk factors typically increased initially.[23] These include higher consumption of unhealthy diets and more common sedentary lifestyles in rapidly urbanizing areas.[24] Besides, improvements in healthcare accessibility and quality began to emerge over time, and ASDR decreased. In 2021, the highest ASDR of stroke was concentrated in Oceania island countries primarily inhabited by Melanesians and Micronesians.[25] These populations had genetic predispositions and metabolic characteristics that increase susceptibility to diseases like diabetes and cardiovascular disease, common precursors to stroke.[26] From 1990 to 2021, regions such as High-income Asia Pacific and Western Europe saw improvements in healthcare and effective public health policies, enhancing stroke prevention, early detection, and treatment, possibly contributing to a reduction in their ASDR.[27,28]

Disparity was also found in terms of cross-country inequalities at the regional level. Southern Sub-Saharan Africa showed the largest worsening

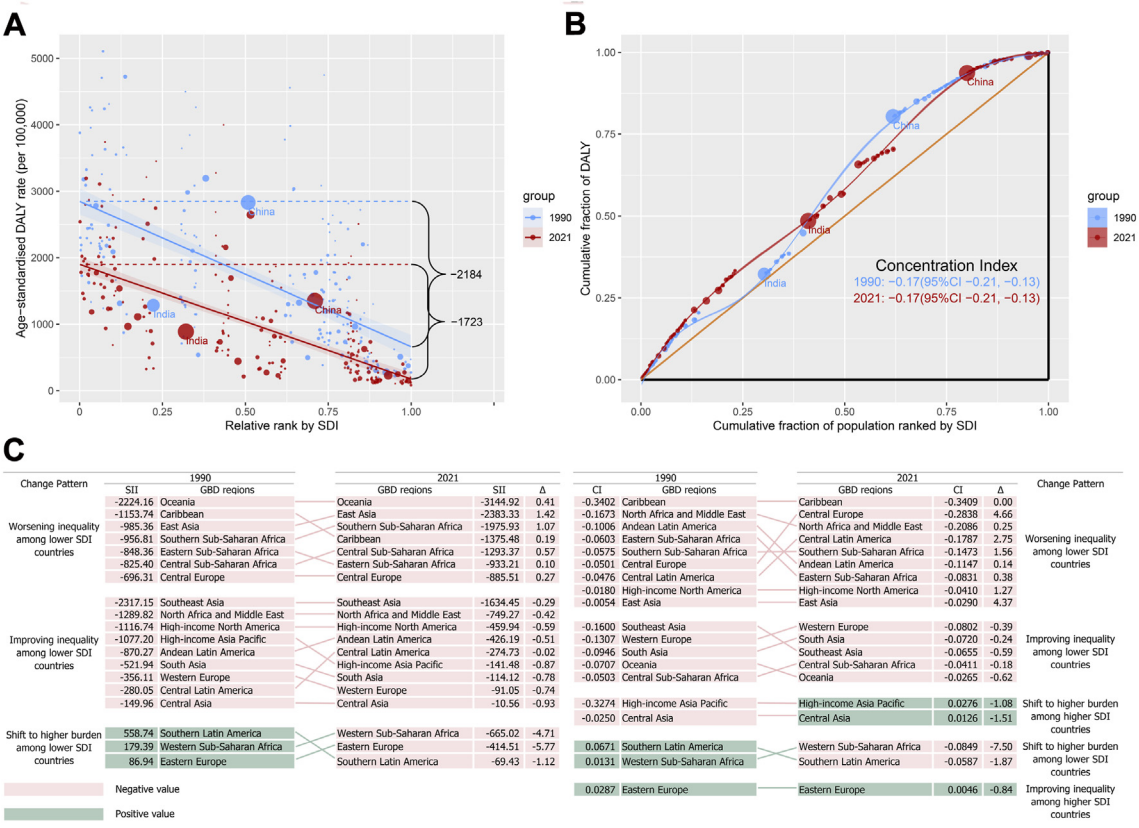
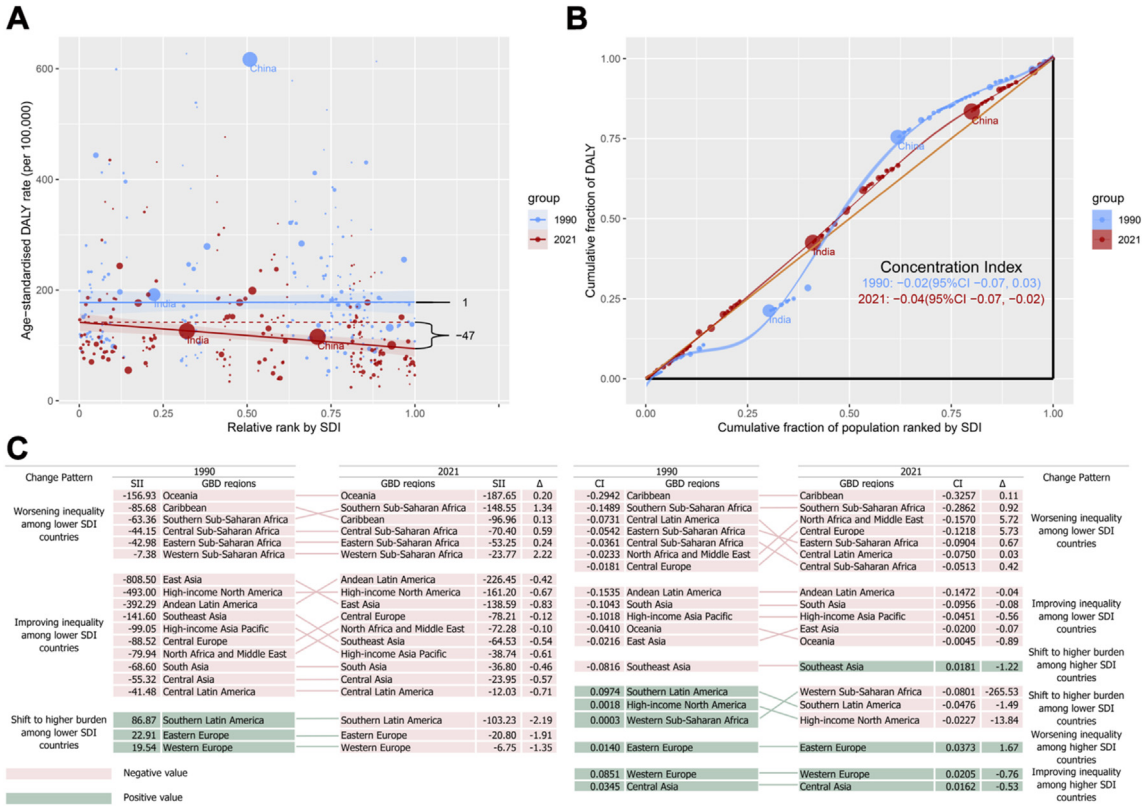


Fig. 4: **Absolute and relative cross-country inequality in ASDR and rankings of intracerebral haemorrhage, 1990–2021. Notes:** (A) Health inequality regression curves for ASDR of intracerebral haemorrhage. (B) Concentration curves for ASDR of intracerebral haemorrhage. (C) Ranking graphs and change patterns for SII and CI of intracerebral haemorrhage. Δ, the percentage change of inequality from 1990 to 2021. ASDR, age-standardised DALY rate. DALYs, disability-adjusted life years. SDI, socio-demographic index. SII, slope index of inequality. CI, concentration index. GBD, global burden of disease.

inequality among lower SDI countries in SII while High-income North America showed the largest improving inequality in SII. This indicated that while the burden of disease remained concentrated in lower SDI countries in both regions, the gap in Southern Sub-Saharan Africa is widening significantly, whereas it is closing in High-income North America. In 2020, influenced by the COVID-19 pandemic, the number of people in extreme poverty in Southern Sub-Saharan Africa increased by more than 32 million, widening the wealth gap,[29] which may lead to disparities in healthcare access between the rich and the poor. Central Europe displayed the most pronounced worsening inequality among lower SDI countries in the concentration index, indicating that the disparity in health burdens between lower and higher SDI regions was widening. This increasing relative inequality can be attributed to varying degrees of economic instability and policy effectiveness, which may impact government expenditures on health and public health initiatives.[30,31] In 2021, Oceania had the highest negative SII, demonstrating that it experienced the most significant inequalities in stroke burden. This was marked by a disproportionately higher impact on countries with lower SDI, highlighting disparities in healthcare quality and accessibility, particularly between different island nations.[32] The Caribbean experienced the highest negative relative inequality in 2021, suggesting the uneven distribution of health benefits among its low-income populations. Conversely, Western Europe exhibited the lowest absolute and relative inequality possibly due to uniformly effective healthcare and chronic disease management.[33,34] These findings highlight the need for region-specific public health measures to effectively reduce the inequalities in the burden of stroke.

Among the three subtypes of stroke analysed from 1990 to 2021, SAH showed the most significant decrease in ASDR, with the lowest ASDR by 2021. This substantial decrease can largely be attributed to advancements in medical technology, particularly improvements in neuroimaging techniques.[35] These



1990 SII	1990 GBD regions	2021 GBD regions	2021 SII	Δ
-156.93	Oceania	Oceania	-187.65	0.20
-85.68	Caribbean	Southern Sub-Saharan Africa	-148.55	1.34
-63.36	Southern Sub-Saharan Africa	Caribbean	-96.96	0.13
-44.15	Central Sub-Saharan Africa	Central Sub-Saharan Africa	-70.40	0.59
-42.98	Eastern Sub-Saharan Africa	Eastern Sub-Saharan Africa	-53.25	0.24
-7.38	Western Sub-Saharan Africa	Western Sub-Saharan Africa	-23.77	2.22
-808.50	East Asia	Andean Latin America	-226.45	-0.42
-493.00	High-income North America	High-income North America	-161.20	-0.67
-392.29	Andean Latin America	East Asia	-138.59	-0.83
-141.60	Southeast Asia	Central Europe	-78.21	-0.12
-99.05	High-income Asia Pacific	North Africa and Middle East	-72.28	-0.10
-88.52	Central Europe	Southeast Asia	-64.53	-0.54
-79.94	North Africa and Middle East	High-income Asia Pacific	-38.74	-0.61
-68.60	South Asia	South Asia	-36.80	-0.46
-55.32	Central Asia	Central Asia	-23.95	-0.57
-41.48	Central Latin America	Central Latin America	-12.03	-0.71
86.87	Southern Latin America	Southern Latin America	-103.23	-2.19
22.91	Eastern Europe	Eastern Europe	-20.80	-1.91
19.54	Western Europe	Western Europe	-6.75	-1.35

1990 CI	1990 GBD regions	2021 GBD regions	2021 CI	Δ	Change Pattern
-0.2942	Caribbean	Caribbean	-0.3257	0.11	
-0.1489	Southern Sub-Saharan Africa	Southern Sub-Saharan Africa	-0.2862	0.92	
-0.0731	Central Latin America	North Africa and Middle East	-0.1570	5.72	Worsening inequality among lower SDI countries
-0.0542	Eastern Sub-Saharan Africa	Central Europe	-0.1218	5.73	
-0.0361	Central Sub-Saharan Africa	Eastern Sub-Saharan Africa	-0.0904	0.67	
-0.0233	North Africa and Middle East	Central Latin America	-0.0750	0.03	
-0.0181	Central Europe	Central Sub-Saharan Africa	-0.0513	0.42	
-0.1535	Andean Latin America	Andean Latin America	-0.1472	-0.04	
-0.1043	South Asia	South Asia	-0.0956	-0.08	Improving inequality among lower SDI countries
-0.1018	High-income Asia Pacific	High-income Asia Pacific	-0.0451	-0.56	
-0.0410	Oceania	East Asia	-0.0200	-0.07	
-0.0216	East Asia	Oceania	-0.0045	-0.89	
-0.0816	Southeast Asia	Southeast Asia	0.0181	-1.22	Shift to higher burden among higher SDI countries
0.0974	Southern Latin America	Western Sub-Saharan Africa	-0.0801	-265.53	Shift to higher burden among lower SDI countries
0.0018	High-income North America	Southern Latin America	-0.0476	-1.49	
0.0003	Western Sub-Saharan Africa	High-income North America	-0.0227	-13.84	
0.0140	Eastern Europe	Eastern Europe	0.0373	1.67	Worsening inequality among higher SDI countries
0.0851	Western Europe	Western Europe	0.0205	-0.76	Improving inequality among higher SDI countries
0.0345	Central Asia	Central Asia	0.0162	-0.53	

Fig. 5: **Absolute and relative cross-country inequality in ASDR and rankings of subarachnoid haemorrhage, 1990–2021. Notes:** (A) Health inequality regression curves for ASDR of subarachnoid haemorrhage. (B) Concentration curves for ASDR of subarachnoid haemorrhage. (C) Ranking graphs and change patterns for SII and CI of subarachnoid haemorrhage. Δ, the percentage change of inequality from 1990 to 2021. ASDR, age-standardised DALY rate. DALYs, disability-adjusted life years. SDI, socio-demographic index. SII, slope index of inequality. CI, concentration index. GBD, global burden of disease.

advancements enabled earlier and more accurate detection of SAH, leading to timely interventions that prevented complications and reduced mortality rates.[35] Furthermore, SAH often linked to detectable and treatable conditions like aneurysms and arteriovenous malformations, benefited more from these advancements compared to ICH.[36,37] Inequality analysis revealed a shift to higher burden among lower SDI countries in SII of SAH and concentration index of IS, with the burden being concentrated in higher SDI countries in 1990 to lower SDI countries by 2021. However, the persistent concentration of the ASDR of ICH in low SDI countries, alongside an improving inequality in SII, highlights a slighter burden on the poorest populations within these areas. Additionally, specific risk factors for stroke subtypes also influenced the distribution of the burden, such as high cholesterol and diabetes in IS and uncontrolled hypertension in ICH,[38,39] highlighting the need for targeted healthcare strategies to address these unique challenges in countries with lower SDI countries. Regionally, the Caribbean showed the largest negative relative inequalities among all subtypes, attributed to its geographical fragmentation of many small islands with unique cultural and demographic characteristics, complicating the standardisation and distribution of healthcare resources.[40] This led to significant relative inequalities as not all citizens had equal access to necessary care.

To address the global inequalities in stroke burden, region-specific policies are essential. Internationally, fostering economic development in low-SDI countries is crucial. A region like Africa, which continues to grapple with social inequalities, poverty, heavy disease burden, and inequitable healthcare services, can benefit from international collaborations that focus on equitable resource distribution and promoting healthcare equity to improve stroke prevention and healthcare.[41] High-income regions like North America may help by sharing advanced medical technologies and expertise, providing essential supplies, funding stroke-specific programmes, and ensuring affordable medications to improve stroke management.[42] These measures may reduce the inequalities in stroke burden and improve health outcomes globally.

This study has several strengths. Firstly, to our knowledge, this is the first study conducted to examine the cross-country inequalities of stroke and subtypes burden from 1990 to 2021. Identification of disparities among regions and subtypes that called for more attention and resources could guide global efforts to optimize care and resource allocation, potentially enhancing treatment outcomes and reducing health inequalities. Additionally, we used advanced tools GBD 2021, the latest release of the database, which had a robust design, a diverse sample size, and sophisticated statistical methods.

However, several limitations still warranted a mention. Firstly, the cases presented in underdeveloped countries in the GBD may be underestimated due to systemic and infrastructural deficiencies. These deficiencies include a lack of robust surveillance systems and a scarcity of qualified healthcare professionals relative to the population, which could contribute to potential missed diagnoses, documentation loss, and other related issues.[43,44] Additionally, in these regions, empirical data representative of the true stroke burden are not typically collected. As a result, the data presented are often based on extrapolations and models with wide UIs, which must be considered when interpreting these findings. Besides, for Australasia and Tropical Latin America, inequality analysis is not feasible since GBD only covers two countries in these regions. Lastly, GBD results heavily rely on modelled data, which inherently involves estimates of data completeness, healthcare access, and disease prevalence. These estimates may not reflect real-world conditions and can introduce systematic biases, affecting the accuracy and reliability of our findings.[45] Such limitations should be considered carefully when interpreting our results.

In conclusion, our study indicated that although the ASDR of stroke and subtypes decreased from 1990 to 2021, increasing inequalities in stroke and subtypes have become apparent at global and regional levels. Countries with lower SDI have disproportionately shouldered a greater burden of stroke and its subtypes. Timely and effective prevention and management strategies of stroke and subtypes are needed especially in high-burden regions to improve global health. Internationally, fostering economic development in low-SDI countries is crucial, and high-income regions may share advanced medical technologies and expertise as well as provide essential supplies to improve health outcomes. Future studies are warranted to explore the factors influencing the burden and inequalities of stroke and its subtypes.

Contributors

PS designed the study. ZL did data collection and data analysis as well as drafted the manuscript. SS, JC, JZ, LZ, DJ, LY, JW, JY, YZ, and KR reviewed and edited the manuscript, with comments from PS. PS and ZL have access to and verify the underlying study data. All authors gave final approval and agreed to be accountable for all aspects of the work ensuring integrity and accuracy.

Data sharing statement

Data used for the analyses can be accessed openly through the GBD 2021 online database (https://vizhub.healthdata.org/gbd-results/).

Editor note

The *Lancet* Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

Declaration of interests

All authors declare no competing interests.

Acknowledgements

There was no funding source for this study.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102829.

References

1 Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO collaborative study. *Bull World Health Organ*. 1980;58(1):113–130.
2 World Health Organization. *Guidelines for management of stroke*. 2012.
3 Feigin VL, Brainin M, Norrving B, et al. World stroke organization (WSO): global stroke fact sheet 2022. *Int J Stroke*. 2022;17(1):18–29. https://doi.org/10.1177/17474930211065917.
4 Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol*. 2021;20(10):795–820. https://doi.org/10.1016/s1474-4422(21)00252-0.
5 Global, regional, and National burden of disorders affecting the nervous system, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet Neurol*. 2024;23(4):344–381. https://doi.org/10.1016/s1474-4422(24)00038-3.
6 Centers for Disease Control and Prevention. Signs and symptoms of stroke. https://www.cdc.gov/stroke/signs-symptoms/index.html. Accessed August 19, 2024.
7 Kirkevold M, Kildal Bragstad L, Bronken BA, et al. Promoting psychosocial well-being following stroke: study protocol for a randomized, controlled trial. *BMC Psychol*. 2018;6(1):12. https://doi.org/10.1186/s40359-018-0223-6.
8 Suksatan W, Collins CJ, Koontalay A, Posai V. Burdens among familial caregivers of stroke survivors: a literature review. *Work Older People*. 2022;26:37–43. https://doi.org/10.1108/WWOP-02-2021-0007.
9 Owolabi MO, Thrift AG, Mahal A, et al. Primary stroke prevention worldwide: translating evidence into action. *Lancet Public Health*. 2022;7(1):e74–e85. https://doi.org/10.1016/s2468-2667(21)00230-9.
10 Verrecchia R, Thompson R, Yates R. Universal Health Coverage and public health: a truly sustainable approach. *Lancet Public Health*. 2019;4(1):e10–e11. https://doi.org/10.1016/s2468-2667(18)30264-0.
11 IHME | GHDx. Global burden of disease study 2021 (GBD 2021) data resources. https://ghdx.healthdata.org/gbd-2021. Accessed August 19, 2024.
12 World Health Organization. *Handbook on health inequality monitoring, with a special focus on low- and middle- income countries*. Geneva: World Health Organization; 2013.
13 Global burden and strength of evidence for 88 risk factors in 204 countries and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024;403(10440):2162–2203. https://doi.org/10.1016/s0140-6736(24)00933-4.
14 Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*.

2024;403(10440):2133–2161. https://doi.org/10.1016/s0140-6736(24)00757-8.
15 IHME | GHDx. Global burden of disease study 2021 (GBD 2021) years lived with disability, disability-adjusted life years, and healthy life expectancy 1990-2021. https://ghdx.healthdata.org/record/ihme-data/gbd-2021-yld-daly-hale-1990-2021. Accessed August 19, 2024.
16 IHME | GHDx. Global burden of disease study 2021 (GBD 2021) socio-demographic index (SDI) 1950–2021. https://ghdx.healthdata.org/record/global-burden-disease-study-2021-gbd-2021-socio-demographic-index-sdi-1950%E2%80%932021. Accessed August 19, 2024.
17 Stevens GA, Alkema L, Black RE, et al. Guidelines for accurate and transparent health estimates reporting: the GATHER statement. *Lancet*. 2016;388(10062):e19–e23. https://doi.org/10.1016/s0140-6736(16)30388-9.
18 Hampel F, Ronchetti E, Rousseeuw PJ, Stahel WA. *Robust statistics: the approach based on influence functions*. 1986.
19 Ordunez P, Martinez R, Soliz P, Giraldo G, Mujica OJ, Nordet P. Rheumatic heart disease burden, trends, and inequalities in the Americas, 1990-2017: a population-based study. *Lancet Global Health*. 2019;7(10):e1388–e1397. https://doi.org/10.1016/s2214-109x(19)30360-2.
20 Cao F, He YS, Wang Y, et al. Global burden and cross-country inequalities in autoimmune diseases from 1990 to 2019. *Autoimmun Rev*. 2023;22(6):103326. https://doi.org/10.1016/j.autrev.2023.103326.
21 Fay MP, Tiwari RC, Feuer EJ, Zou Z. Estimating average annual percent change for disease rates without assuming constant change. *Biometrics*. 2006;62(3):847–854. https://doi.org/10.1111/j.1541-0420.2006.00528.x.
22 Marshall IJ, Wang Y, Crichton S, McKevitt C, Rudd AG, Wolfe CD. The effects of socioeconomic status on stroke risk and outcomes. *Lancet Neurol*. 2015;14(12):1206–1218. https://doi.org/10.1016/s1474-4422(15)00200-8.
23 ESCAP. *Urbanization in central Asia: challenges, issues and prospects*. 2013.
24 CORINNA HAWKES JHASG. *Changing diets: urbanization and the nutrition transition*. 2017.
25 Infoplease. Pacific islands & Australia map: regions, geography, facts & figures. https://www.infoplease.com/atlas/pacific-islands. Accessed August 19, 2024.
26 Horwood PF, Tarantola A, Goarant C, et al. Health challenges of the pacific region: insights from history, geography, social determinants, genetics, and the microbiome. *Front Immunol*. 2019;10:2184. https://doi.org/10.3389/fimmu.2019.02184.
27 Centers for Disease Control and Prevention. CDC grand rounds: public health strategies to prevent and treat strokes. https://www.cdc.gov/mmwr/volumes/66/wr/mm6618a5.htm. Accessed August 19, 2024.
28 Thomson K, Hillier-Brown F, Todd A, McNamara C, Huijts T, Bambra C. The effects of public health policies on health inequalities in high-income countries: an umbrella review. *BMC Publ Health*. 2018;18(1):869. https://doi.org/10.1186/s12889-018-5677-1.
29 Abebe Aemro Selassie HF. Seven charts that show sub-saharan Africa at a crucial point. International Monetary Fund. https://www.imf.org/en/News/Articles/2021/10/20/na102021-seven-charts-that-show-sub-saharan-africa-at-a-crucial-point. Accessed August 19, 2024.
30 OECD. *Economic insecurity in Europe and potential policy responses*. 2023.
31 Saw D. Global instability and the challenge for Europe. https://euro-sd.com/2022/01/articles/exclusive/25129/global-instability-and-the-challenge-for-europe/. Accessed August 19, 2024.
32 National Geographic. Australia and Oceania: resources. https://education.nationalgeographic.org/resource/oceania-resources/. Accessed August 19, 2024.
33 The Lancet N. A unified European action plan on stroke. *Lancet Neurol*. 2020;19(12):963. https://doi.org/10.1016/s1474-4422(20)30409-9.
34 Seychell M. Towards better prevention and management of chronic diseases. https://ec.europa.eu/health/newsletter/169/focus_newsletter_en.htm. Accessed August 19, 2024.
35 Obenaus A, Barnes S. Neuroimaging assessment of subarachnoid hemorrhage. In: Chen J, Xu X-M, Xu ZC, Zhang JH, eds. *Animal models of acute neurological injuries II: injury and mechanistic assessments*1.
36 Rammos S, Gardenghi B, Bortolotti C, Cloft HJ, Lanzino G. Aneurysms associated with brain arteriovenous malformations. *AJNR Am J Neuroradiol*. 2016;37:1966–1971.
37 Westerlaan HE, van Dijk JM, Jansen-van der Weide MC, et al. Intracranial aneurysms in patients with subarachnoid hemorrhage: CT angiography as a primary examination tool for diagnosis–systematic review and meta-analysis. *Radiology*. 2011;258(1):134–145. https://doi.org/10.1148/radiol.10092373.
38 Maida CD, Daidone M, Pacinella G, Norrito RL, Pinto A, Tuttolomondo A. Diabetes and ischemic stroke: an old and new relationship an overview of the close interaction between these diseases. *Int J Mol Sci*. 2022;23(4):2397. https://doi.org/10.3390/ijms23042397.
39 Alessandro Biffi KCT, Pablo Castello Juan, Abramson Jessica R, et al. Impact of uncontrolled hypertension at 3 Months after intracerebral hemorrhage. *J Am Heart Assoc*. 2021. https://doi.org/10.1161/JAHA.120.020392.
40 OECD. *Health at a glance: Latin America and the caribbean 2023*. 2023.
41 de Villiers K. Bridging the health inequality gap: an examination of South Africa's social innovation in health landscape. *Infect Dis Poverty*. 2021;10(1):19. https://doi.org/10.1186/s40249-021-00804-9.
42 World Health Organization. Global health partnerships. https://www.who.int/europe/about-us/partnerships/partners/global-health-partnerships. Accessed August 19, 2024.
43 Davis A, Lembo T, Laurie E, et al. How public health crises expose systemic, day-to-day health inequalities in low- and-middle income countries: an example from East Africa. *Antimicrob Resist Infect Control*. 2022;11(1):34. https://doi.org/10.1186/s13756-022-01071-5.
44 Jayatilleke K. Challenges in implementing surveillance tools of high-income countries (HICs) in low middle income countries (LMICs). *Curr Treat Options Infect Dis*. 2020;12(3):191–201. https://doi.org/10.1007/s40506-020-00229-2.
45 Muñoz Laguna J, Puhan MA, Rodríguez Artalejo F, et al. Certainty of the global burden of disease 2019 modelled prevalence estimates for musculoskeletal conditions: a meta-epidemiological study. Review. *Int J Publ Health*. 2023;68:1605763. https://doi.org/10.3389/ijph.2023.1605763.