Journal of the American Heart Association

ORIGINAL RESEARCH

Projections of the Stroke Burden at the Global, Regional, and National Levels up to 2050 Based on the Global Burden of Disease Study 2021

Yiran Cheng, BS; Yongqi Lin, BE; Hujuan Shi, BE; Mingmei Cheng, PhD; Baoliang Zhang, PhD; Xiaofeng Liu, PhD; Chuan Shi, PhD; Yanzhong Wang, PhD; Chunhua Xia, PhD; Wanqing Xie, PhD

BACKGROUND: Stroke is a pressing public health issue worldwide. This study aimed to forecast the future temporal trends and distribution characteristics of the global stroke burden.

METHODS AND RESULTS: Global data on stroke incidence, prevalence, deaths, and disability-adjusted life years between 1990 and 2021 were obtained from the GBD (Global Burden of Disease) Study 2021. The temporal trends of stroke burden were estimated using various regression models. Gross domestic product per capita was adopted as a predictor in the model to consider the impact of economic development on stroke burden. Projections of stroke burden up to 2050 were generated using the optimal model selected based on the Akaike information criterion, encompassing global, World Bank income levels, national levels, and sex-age groups. In 2050, we projected 21.43 million stroke cases, 159.31 million survivors, 12.05 million deaths, and 224.86 million disability-adjusted life years due to stroke globally. From 2021 to 2050, there was a declining trend in the global age-adjusted stroke rates, with –7% in incidence, –4% in prevalence, –28% in deaths, and –28% in disability-adjusted life years. Upper-middle-income countries were projected to have the most severe stroke burden, followed by lower-middle-income countries, low-income countries, and high-income countries. The stroke burden in over half of the 204 countries and territories was expected to be alleviated from 2022 to 2050. Men and older women worldwide bear higher burden.

CONCLUSIONS: Stroke remains a serious global health challenge, especially in low-income and middle-income countries. Targeted implementation of prevention and interventions is imperative across diverse demographic groups.

Key Words: epidemiology ■ Global Burden of Disease ■ gross domestic product ■ projections ■ stroke

Stroke is a serious global health problem.[1,2] As the fourth-leading Level 3 cause of disability-adjusted life years (DALYs) in 2021,[3] stroke is resulting in long-term disability in most survivors.[4] Due to remarkable advances in the treatment of stroke, age-standardized DALY rates decreased by 16.9% (11.7–21.9) between 2010 and 2021. However, the absolute burden of stroke continues to escalate rather than diminish within the rapidly aging population. According to the GBD (Global Burden of Disease) 2021 study, the global DALYs of stroke increased from 144.0 million (137.0–150.0) in 2010 to 160.4 million (148.0–171.7) in 2021.[3] This increase was primarily due to an increase in population size and life expectancy.

Correspondence to: Chunhua Xia, PhD, Medical Image Center, The Third Affiliated Hospital of Anhui Medical University/Hefei No1. People's Hospital (Binhu Campus), Hefei, China. Email: xiachunhua3775@sina.com and Wanqing Xie, PhD, Department of Psychology, School of Mental Health and Psychological Sciences, Department of Intelligent Medical Engineering, School of Biomedical Engineering, Anhui Medical University, 81 Meishan Road, Hefei 230011, China. Email: xiewanqing17@gmail.com

This article was sent to Michelle H. Leppert, MD, MBA, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.124.036142

For Sources of Funding and Disclosures, see page 11.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Using gross domestic product per capita as a predictor, the global burden of stroke was predicted to increase continuously.
- Economic levels and demographics among countries influenced the inequalities of stroke burden.

What Are the Clinical Implications?

- The absolute burden of strokes was predicted to increase globally between 2022 and 2050 despite a downward trend in age-adjusted rates.
- The burden of stroke has remained a heavy issue, especially among men and older women worldwide.
- Optimizing stroke prevention and intervention strategies, as well as mitigating population aging, are crucial for countries to alleviate the burden of stroke.

Nonstandard Abbreviations and Acronyms

GBD	Global Burden of Disease Study
GDP	gross domestic product
GNI	gross national income
HICs	high-income countries
LICs	low-income countries
LMICs	lower-middle-income countries
UI	uncertainty interval
UMICs	upper-middle-income countries
WHO	World Health Organization

Moreover, the long-term outcomes of stroke and the corresponding rise in rehabilitation costs will lead to vast macroeconomic losses worldwide.[5] Previous study has demonstrated that the value of lost welfare caused by stroke was 2059.67 billion US dollars, accounting for 1.66% of the global gross domestic product (GDP) in 2019.[6] This trend will continue to increase the burden of disease and economic pressure on individuals and society.[5,7] To effectively alleviate these pressures, we need to increase the attention to the research on stroke epidemiological surveillance, prevention, and treatment.

Reducing the growing global burden of stroke in the future requires concerted efforts of countries at different development stages and economic levels. Geographical differences in future stroke burden have been demonstrated in previous studies that predict future stroke burden trends in several developed countries,[8–10] within specific regions,[11,12] and globally.[13] These significant geographical differences in stroke burden are related to different levels of economic development.[11] Economic development indicators, such as GDP per capita, have been proven to be proxies for indicating the impact of economic development on health levels. Therefore, it is imperative to consider the influence of economic development and demographic changes when predicting future trends in stroke burden over time. Comprehensive epidemiological projections of global stroke can facilitate a profound understanding of the future distribution of stroke burden. Additionally, these projections can provide key information for the development of policies to manage and mitigate the public health impacts of stroke in the coming years.

Using GDP as a key predictor, this study aimed to provide more reliable predictions of the stroke burden and its future patterns from 2022 to 2050. We provided epidemiological projections of the stroke burden globally, regionally, nationally, and sex-age groups. To fit the model, we estimated GBD data according to the GDP per capita and population projections. The predictions were based on comprehensive stroke data encompassing all epidemiological indicators from 1990 to 2021 in the GBD 2021 database.

METHODS

Study Data

The stroke burden data used in this study were sourced from the GBD 2021. The GBD 2021 database is provided by the Institute for Health Metrics and Evaluation at the University of Washington as a public resource.[14] The Global Health Data Exchange data page catalogs metadata and primary data sets, if publicly available.[15] The GBD 2021 study offers a comprehensive evaluation of health outcomes associated with 371 diseases and injuries,[3] and 88 risk factors.[16] This assessment encompasses 204 nations and territories, as well as uses the latest epidemiological data and enhanced standardized methodologies. Detailed information about the methodology of the GBD 2021 can be found in the article and appendix of a comprehensive analysis conducted by the GBD 2021 Diseases and Injuries Collaborators. We estimated temporal trends in stroke incidence, prevalence, deaths, and DALYs from 1990 to 2021 by age, sex, and country subgroups from GBD 2021. All data are available by using the GBD results tool (https://ghdx.healthdata.org/gbd-results-tool).[17]

The World Bank classifies the world's economies into four income groups: low, lower-middle, upper-middle, and high income.[18] This economic classification for the fiscal year 2021 was based on gross national income (GNI) per capita in current United States dollars

(using the Atlas method exchange rates) of the previous year. The classifications are as follows: low-income countries (LICs) have a GNI per capita of 1045 or less; lower-middle-income countries (LMICs) have a GNI per capita between 1046 and 4095; upper-middle-income countries (UMICs) have a GNI per capita between 4096 and 12 695; and high-income countries (HICs) have a GNI per capita of 12 696 or more.

Population estimations and projections for each country were obtained by World Population Prospects 2022 from the United Nations Department of Economic and Social Affairs/Population Division.[19] The predictions considered 3 demographic change components: fertility, death, and international migration. Our analysis followed the medium-variant assumption, which assumes a decrease in fertility in countries with a high prevalence of large families and a continuous decline in death rates across all age groups.[20] The historical and predicted data for GDP per capita, the economic indicator, were sourced from research conducted by the GBD Health Financing Collaborator Network.[21] Estimates were reported as GDP per capita in constant 2021 purchasing-power parity-adjusted dollars.

No ethics approval was required because all data were identified and publicly available. Interactive online tools were also available to search all data sources in detail. The reporting of the present study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting.[22]

Projection Methods

Separate projection models based on sex and 5-year age groups were used to estimate global temporal trends in 4 measures, including incidence, prevalence, deaths, and DALYs. Each measure was modeled as a rate (per 100 000 population) using observed data between 1990 and 2021. Our model predicted the global epidemiological trends of stroke by building a model with calendar year and GDP per capita as independent variables.[11] As a temporal variable, calendar years reflect the impact of stroke knowledge accumulation and optimization of treatment guidelines on stroke burden. As an economic indicator, GDP per capita may indirectly reflect the impact of economic development on medical levels and health status.[23,24]

Three regression models—linear, Poisson, and log-linear—were made use of to fit the data. The Akaike information criterion was used to evaluate and compare the error of these models in the model selection process (Tables S1 and S2). Compared with other models, the log-linear model consistently had lower Akaike information criterion values for the 4 measures across nearly all age-sex groups. As a result, log-linear regression provided the best fit and was used to build the final models. The final regression equations were as follows:

$$\ln R_{a,k,i} = C_{a,k,i} + \beta_1 \ln Y + \beta_2 t$$

where a represents age groups (0–19, 20–24, 25–29, …, 90–94, or 95+); k represents sex groups (female or male); i represents country groups; $R_{a,k,i}$ is the outcome rate corresponding to age group a, sex k, country i; $C_{a,k,i}$ is the constant term for the age-sex-country specific model; Y denotes GDP per capita; t stands for time in years. These age-sex-country specific models used GDP inputs from 2022 to 2050 provided by the GBD Health Financing Collaborative Network to generate forecasts of rates beyond the reference year (2021). The methods used a systematic procedure for model selection and inputted updated stroke-specific data for incidence, prevalence, deaths, and DALYs.

Model Validation

This study used internal model validation to compare stroke outcomes forecasted by our model with the actual observed data. The internal model validation predictions for the test period (2012–2021) used only data between 1990 and 2011 to fit our model. The out-of-sample validation predictions for the same period were compared with the Lee–Carter model, a widely used demographic approach.[25] The root mean square error was used to evaluate model performance during the test period. The study's results indicated that our model outperformed the widely used demographic method in predicting future stroke epidemiology with lower error (Figure 1). In addition, we have also carried out more detailed model validation for different age groups, and corresponding results can be seen in the appendix (Figures S1 through S4).

In 2021, the top 3 Level 2 risk factors for stroke in the GBD database were high systolic blood pressure, air pollution, and tobacco. Because of the scarcity of risk factors data, the additional models were fitted with data among people aged 25 years and older. This risk factors model exclusively incorporates the deaths and DALYs rate of stroke attributed to high systolic blood pressure, air pollution, and tobacco as direct predictors of stroke outcomes. Subsequently, models were fitted to data from 1990 to 2011, and then information on demography and risk factors from 2012 to 2021 was used to guide the forecasts during the same period. Results were then compared with our models' using GDP as a distant predictor of stroke outcomes at the global level and World Bank income levels (Figures S5 and S6). The comparative results indicated that our model exhibited lower errors in predicting global stroke epidemiology, particularly in HICs, LMICs, and LICs.

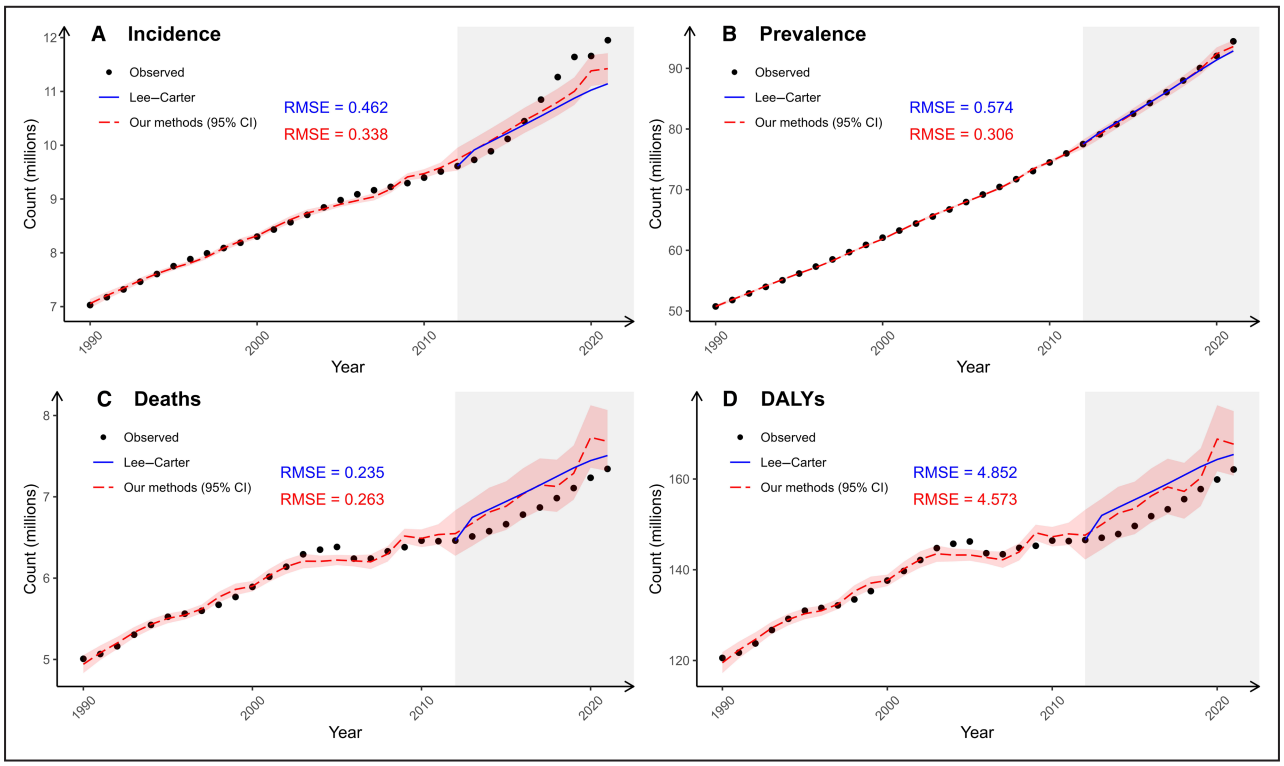

Figure 1. The predictive performance of various models worldwide was evaluated during the testing period (2012–2021): incidence (A), prevalence (B), deaths (C), and DALYs (D).
The RMSE reflects the average deviation between the predicted and observed values in the evaluation years (2012–2021). DALYs indicate disability-adjusted life years; and RMSE, root mean square error.

Statistical Analysis

The projected absolute numbers for each measure from 2022 to 2050 were calculated by multiplying the age-sex-country-specific projection rates for each year by the population projections for the corresponding subgroups in the same year. Estimates were aggregated to present the results at the global, World Bank income levels, and country levels. The direct standardization method, using the World Health Organization standard population as a reference, was exploited to calculate the age-adjusted rates for incidence, prevalence, deaths, and DALYs.[26] Finally, the average annual percentage change and its accompanying 95% CI for each measure from 2022 to 2050 was calculated to evaluate the change in the global age-adjusted rates of stroke. All analyses were performed using the statistical software R version 4.2.1.

RESULTS

Global Projected Trends in Stroke

Globally, the incidence of stroke was projected to increase from 11.81 million [95% uncertainty interval (UI): 9.05–15.18] in 2021 to 21.43 million (95% UI, 18.62–24.70) in 2050, reflecting a substantial 81% rise (Figure 2, Table). Similarly, the prevalence of stroke cases was anticipated to grow by 71%, from 93.18 million (95% UI, 82.95–104.15) in 2021 to 159.31 million (95% UI, 151.66–167.38) in 2050 (Figure 2, Table). The age-adjusted rates of incidence and prevalence were expected to show decline trends over this period, with relative changes of –7% (95% CI, –19% to 8%) and –4% (95% CI, –8% to 1%), respectively (Table).

In 2050, the worldwide number of deaths and DALYs due to stroke were 12.05 million (95% UI, 9.29–15.81) and 224.86 million (95% UI, 178.87–284.84), respectively (Figure 2, Table). These represent an increase of 67% and 41% from 2021 to 2050, correspondingly. However, the age-adjusted rates of deaths and DALYs were anticipated to show a decreasing trend. In 2050, the global age-adjusted rate of deaths and DALYs were projected to be 56.11 per 100 000 (relative change, –28% [95% CI, –44% to –7%]) and 1307.34 per 100 000 (relative change, –28% [95% CI, –42% to –9%]), respectively (Table).

World Bank Income Levels

The disease burden of stroke varies by World Bank income level groups. In 2050, this burden was highest in UMICs, with age-adjusted rates of incidence, prevalence, deaths, and DALYs reaching 184.85 per 100 000 (95% UI, 157.09–218.06), 1124.08 per 100 000 (95% UI,

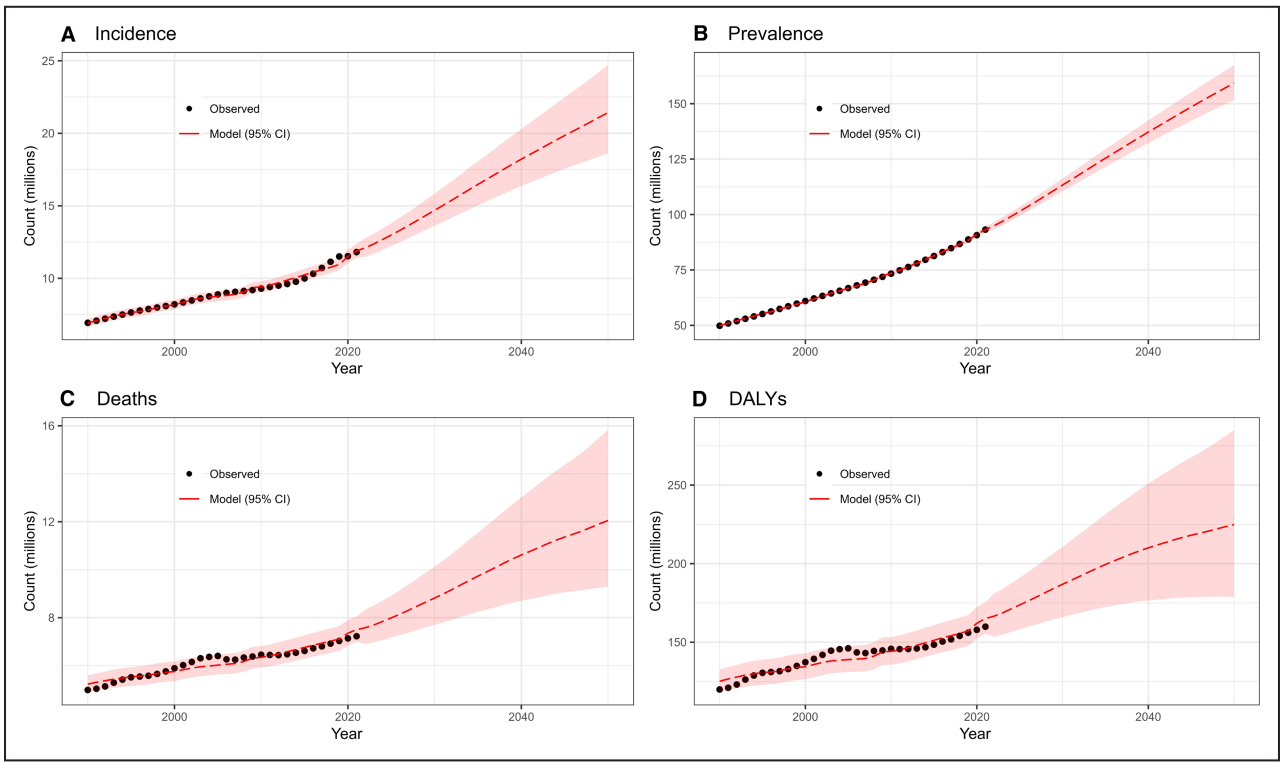

Figure 2. The historical trends and future projections of global stroke from 1990 to 2050: incidence (A), prevalence (B), deaths (C), and DALYs (D).
DALYs indicate disability-adjusted life years.

1023.43–1237.12), 114.13 per 100 000 (95% UI: 73.07–182.28) and 2151.49 per 100 000 (95% UI, 1475.4–3186.49), respectively (Figure 3). In contrast, HICs were expected to have the lowest stroke burden, with age-adjusted rates of incidence, prevalence, deaths and DALYs at 55.34 per 100 000 (95% UI, 46.64–65.73), 710.06 per 100 000 (95% UI, 654.85–770.29), 10.78 per 100 000 (95% UI, 8.66–13.51) and 300.97 per 100 000 (95% UI, 247.72–367.72), separately (Figure 3).

From 2021 to 2050, the burden of stroke was anticipated to decrease in the 3 regions defined by World Bank income levels, with the exception of UMICs. In this region, the age-adjusted rates of incidence, deaths, and DALYs were projected to show an upward trend, with relative changes estimated at 11% (95% CI, −6% to 31%), 12% (95% CI, −28% to 8%), and 2% (95% CI, −30% to 50%), separately. However, the age-adjusted prevalence rate in UMICs will have a downward trend over this period, with relative changes at −4% (95% CI, −13% to 6%) (Figure 3). The most significant reduction in stroke burden was anticipated in HICs, where the relative changes of age-adjusted rates of incidence, prevalence, deaths, and DALYs were projected at −33% (95% CI, −43% to −20%), −29% (95% CI, −35% to −23%), −61% (95% CI, −69% to −51%), and −55% (95% CI, −63% to −45%), respectively. Projections in LMICs indicated that by 2050, the absolute number of stroke burden will rise despite a decline in the age-adjusted rate (Figure 3, Figure S7).

National and Territorial Levels

Age-adjusted rates were expected to decline in more than half of 204 countries and territories. In 2050, our models predicted age-adjusted rates of stroke ranging from 15.4/100 000 (Ireland) to 439.38/100 000 (Philippines) for incidence, from 208.37/100 000 (Portugal) to 2170.21/100 000 (Lithuania) for prevalence, from1.10/100 000 (Singapore) to 1377.19/100 000 (North Macedonia) for deaths, and from 85.38/100 000 (Singapore) to 14062.8/100 000 (North Macedonia) for DALYs loss (Figure S8).

Nationally, the estimated range of the average annual percentage change of age-adjusted incidence rates was predicted to vary from 1.86 (95% CI, 2.08–3.48) to −0.75 (95% CI, −0.77 to −0.55) (Figure 4A). From 2021 to 2050, the largest increases of incidence were in the Philippines (1.86 [95% CI, 2.08–3.48]) and Uzbekistan (0.85, [95% CI, 0.88–1.93]). The most significant decreases were expected in Portugal (−0.75, [95% CI, −0.77 to −0.55]), Mauritius (−0.75 [95% CI, −0.79 to −0.49]), and Ireland (−0.72 [95% CI, −0.73 to −0.45]). From 2021 to 2050, the top 3 countries with a growth of age-adjusted prevalence rate will be Lithuania (1.12

Table. Changes in Global Stroke Incidence, Prevalence, Deaths, and Disability-Adjusted Life Years Between 1990 and 2050.

ID	1990	2021	2030	2050	Relative change (2021 vs 2050)
Incidence					
Count	6.93 (5.22–9.04)	11.81 (9.05–15.18)	14.69 (13.63–15.84)	21.43 (18.62–24.70)	1.81 (1.58–2.09)
Crude rate*	130.67 (98.35–170.39)	149.57 (114.64–192.24)	172.2 (159.75–185.7)	221.03 (192.04–254.77)	1.48 (1.28–1.7)
Adjusted rate*	170.73 (129.02–221.65)	133.48 (102.1–171.91)	131.72 (122.19–142.06)	124.79 (108.43–143.82)	0.93 (0.81–1.08)
Prevalence					
Count	49.81 (43.97–56.09)	93.18 (82.95–104.15)	113.3 (110.45–116.24)	159.31 (151.66–167.38)	1.71 (1.63–1.8)
Crude rate*	938.92 (828.73–1057.34)	1180.27 (1050.73–1319.25)	1328.1 (1294.63–1362.51)	1643.29 (1564.39–1726.55)	1.39 (1.33–1.46)
Adjusted rate*	1184.3 (1044.93–1334.02)	1077.62 (960.19–1203.54)	1066.2 (1039.81–1093.33)	1037.83 (990.13–1088.05)	0.96 (0.92–1.01)
Deaths					
Count	4.98 (4.15–5.84)	7.23 (5.66–8.91)	8.82 (7.7–10.13)	12.05 (9.29–15.81)	1.67 (1.28–2.19)
Crude rate*	93.94 (78.29–110.17)	91.52 (71.63–112.91)	103.38 (90.27–118.69)	124.3 (95.8–163.07)	1.36 (1.05–1.78)
Adjusted rate*	129.21 (107.78–150.96)	78.21 (61.18–96.75)	72.43 (63.35–83.02)	56.11 (43.59–72.9)	0.72 (0.56–0.93)
Disability-adjusted life years					
Count	119.89 (99.16–143.22)	159.86 (126.4–198.06)	186.88 (166.01–210.75)	224.86 (178.87–284.84)	1.41 (1.12–1.78)
Crude rate*	2259.92 (1869.06–2699.59)	2024.83 (1600.99–2508.66)	2190.54 (1945.89–2470.32)	2319.45 (1845.12–2938.23)	1.15 (0.91–1.45)
Adjusted rate*	2936.9 (2441.33–3481.16)	1804.99 (1425.01–2242.32)	1670.23 (1487.84–1878.17)	1307.34 (1051.82–1635.15)	0.72 (0.58–0.91)

Count data are in millions.
*Per 100 000 person-years.

[95% CI, 0.25–6.08]), the Philippines (0.51 [95% CI, 0.6–0.87]), and Mongolia (0.27 [95% CI, 0.17–0.61]) (Figure 4B). Over the same period, the age-adjusted rate of deaths and DALYs were projected to increase significantly in the United Arab Emirates, North Macedonia, and Lesotho. Conversely, Portugal, Qatar, and Singapore were expected to have the largest decreases (Figure 4C and 4D).

Age and Sex Patterns

The global burden of stroke in men was higher than in women. In 2021, the DALYs attributed to stroke in men 862.90 million [95% UI, 685.42–1070.56]) were significantly higher compared with those in women [735.69 million [95% UI, 578.56–910.02]). Similarly, stroke incident cases among men were 60.98 million (95% UI, 46.76–78.13), higher than the 57.11 million cases (95% UI, 43.74–73.64) in women (Table S3). According to projections, men will continue to bear a heavier burden of stroke. However, the number of stroke incidences in women was predicted to be 107.95 million (95% UI, 91.37–127.59) in 2050, which will exceed that of men 106.28 million [95% UI, 94.83–119.26]). From 2021 to 2050, global deaths and DALY loss caused by stroke will substantially surge, primarily among individuals aged ≥85 years. The increase in incidents and prevalent cases was projected to primarily affect women aged 80 years and above, as well as men aged 75 to 79 years. Conversely, the burden of stroke in people under 59 years of age was predicted to remain stable in the same period (Figure 5).

Percentage changes in the burden of stroke from 2021 to 2050 varied by age group across the 4 World Bank income levels (Figure 6). Generally, regions with higher income levels tend to have an older population affected by this disease. In HICs, the projected increase in deaths and DALYs due to stroke will be exclusive to those aged ≥85 years, whereas a reduction will be observed in the younger age groups. In UMICs, a substantial increase in the burden of stroke was projected among individuals aged ≥60 years, particularly those aged ≥85 years. Nevertheless, the increasing trend of stroke prevalent cases encompasses all age groups in LICs.

DISCUSSION

This study forecasted epidemiological trends in the global burden of stroke between 2022 and 2050, considering demographic structure and economic development. The absolute number of strokes was predicted to increase globally during this period despite a downward

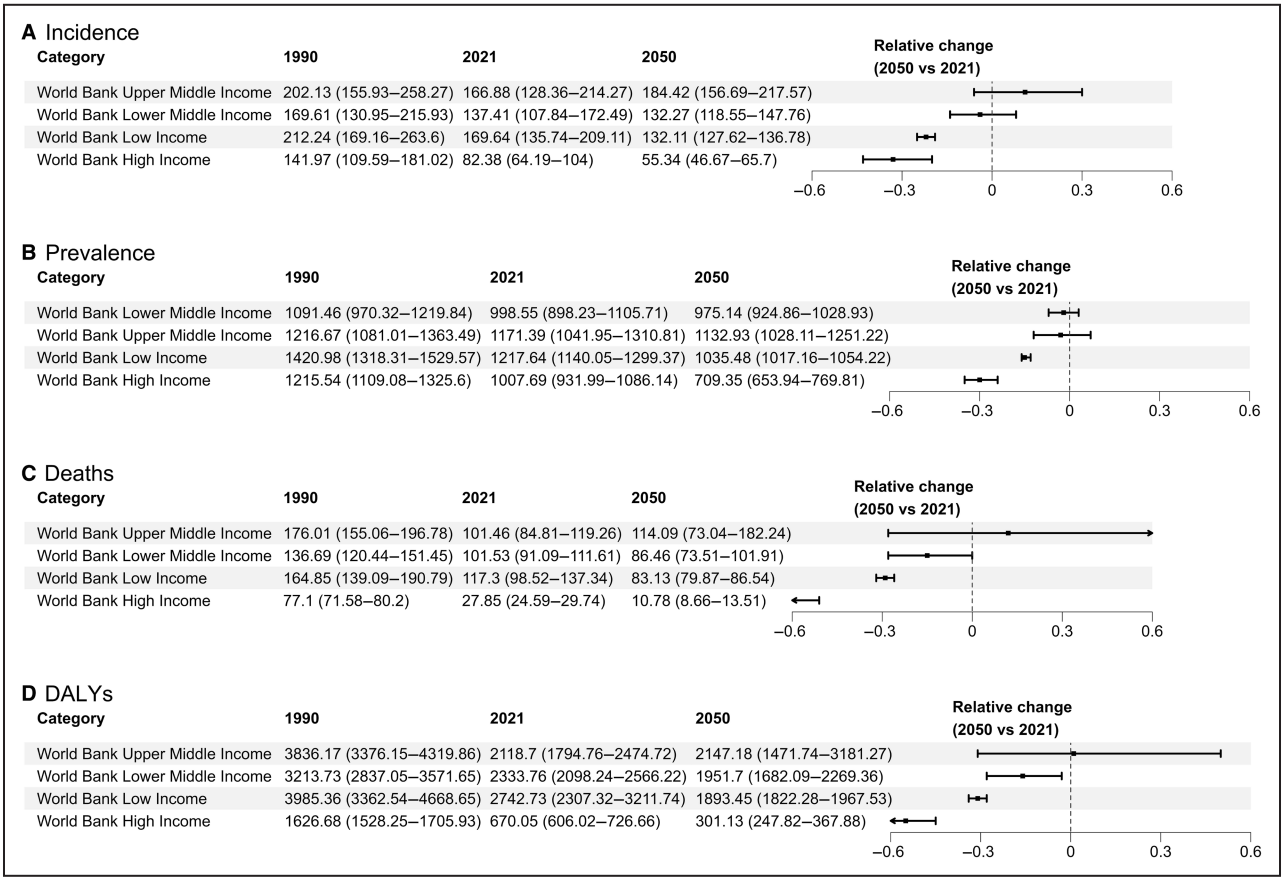

Figure 3. Age-adjusted stroke rates and corresponding relative changes in 4 regions with World Bank income levels from 2021 to 2050: incidence (A), prevalence (B), deaths (C), and DALYs (D).
DALYs indicate disability-adjusted life years.

trend in age-adjusted rates. Our projections highlighted significant disparities in the stroke burden across different income levels, country categories, and sex-age groups. Individuals in low- and middle-income countries face a heavier burden than those in HICs. Additionally, the burden of stroke remains exceptionally high among men and older womenworldwide. The in-depth study of future temporal trends in stroke provides an important reference for stroke prevention and promotes sustainable global health. The findings can guide the formulation of stroke prevention policies, facilitate the exchange of successful strategies, and strengthen international cooperation in stroke prevention and control.

The absolute number of stroke incidence and prevalence worldwide was projected to increase steadily despite a slight decrease in the age-adjusted rates from 2021 to 2050. The number of stroke incident cases was expected to increase by 81%, corresponding to a rise of 9.62 million first-ever strokes. This trend is primarily due to shifting demographics, particularly the aging population. The latest estimates from the United Nations showed that the global population of elderly individuals will increase continuously in the foreseeable future, and it is improbable the trend of population aging will be reversed.[27] Hence, there is an urgent need for investment in geriatric care facilities and specialized medical services tailored to meet the unique needs of an increasingly elderly population. Concurrently, owing to the rapid progress in acute stroke treatment, an escalating proportion of patients with stroke are now able to survive.[28] However, survivors of stroke are still facing severe challenges, including limited access to long-term rehabilitation resources and the high cost of stroke care.[29] These challenges may negatively affect prognosis and even increase the risk of death for survivors of stroke.[30] The good news is that the age-adjusted rates of stroke will trend downward globally. On the one hand, the implementation of primary prevention effectively reduces the risk of stroke in the general population.[31] On the other hand, the recurrence rate of stroke in patients can be reduced due to the widespread use of secondary prevention drugs such as statins and antihypertensive medications.[32] Furthermore, although COVID-19 is associated with elevated stroke risk,[33] the pandemic may have facilitated enhancements in stroke care systems,[34] potentially contributing to a reduction in the long-term impact of stroke.

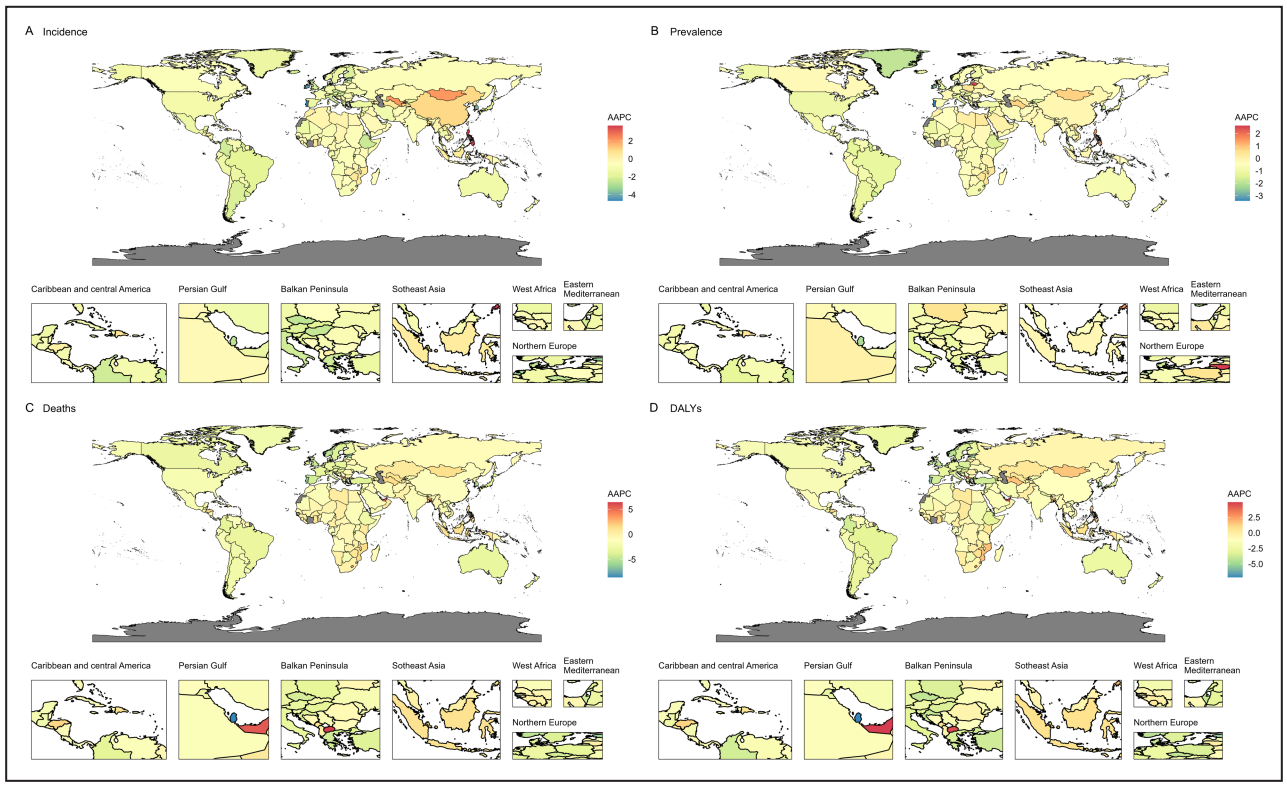

Figure 4. Projected average annual percentage change in the age-adjusted rates of stroke in 204 countries from 2021 to 2050: incidence (A), prevalence (B), deaths (C), and DALYs (D).
AAPC indicates average annual percentage change; and DALYs, disability-adjusted life years.

Residents of low-income and middle-income countries face a heavier burden than those in HICs. In UMICs, the burden of stroke-related death and disability was projected to increase substantially from 2021 to 2050. The short- and long-term prognoses following stroke insufficiently improved within UMICs despite advances in medical technology.[35] Additionally, improvements in health care systems and the availability of medical care in UMICs may prolong the survival of patients with stroke, leading to a higher number of individuals living with long-term disabilities from stroke-related complications. By 2050, the absolute number of stroke cases in LMICs will rise despite a decline in the age-adjusted stroke rate. In LMICs, the lack of primary prevention and early intervention has the potential to exacerbate the burden of stroke in this region.[36] Population growth may offset the improvements in stroke prevention and treatment. In LICs, health services frequently lack the necessary resources for prompt diagnosis and effective treatment of acute stroke.[29] A meta-analysis comparing the use of tissue plasminogen activators in treating acute stroke revealed that only 3% of LICs administer tissue plasminogen activator, far less than MICs and HICs.[37] Instead, the favorable trends in HICs can be attributed to advanced health care systems and sufficient medical resources, including monitoring, prevention, emergency care, and rehabilitation, which effectively reducing the stroke burden.[38,39]

Predicted changes across different age groups at different World Bank income levels showed that regions with higher income levels tend to have an older population affected by stroke. In HICs, the stroke burden is projected to increase only for individuals ≥80 due to the effective implementation of primary and secondary stroke prevention.[38] However, individuals aged 60 years and older in UMICs confronted the increase in stroke burden. The short- and long-term prognoses following stroke insufficiently improved within UMICs despite advances in medical technology.[40] Enhancing stroke treatment and rehabilitation services are crucial for reducing the recurrent risk of stroke and improving stroke outcomes in the elderly population. Conversely, in LMICs and LICs, the overall increase in stroke burden across all age groups suggests challenges in health care access and limited resources for preventive care. These disparities indicate the importance of considering the specific health care systems and developmental stages in the formulation of stroke prevention strategies for countries at varying economic levels.

The study also explored differences in stroke incidence, prevalence, deaths, and DALYs across 204 countries from 2021 to 2050. The countries with the

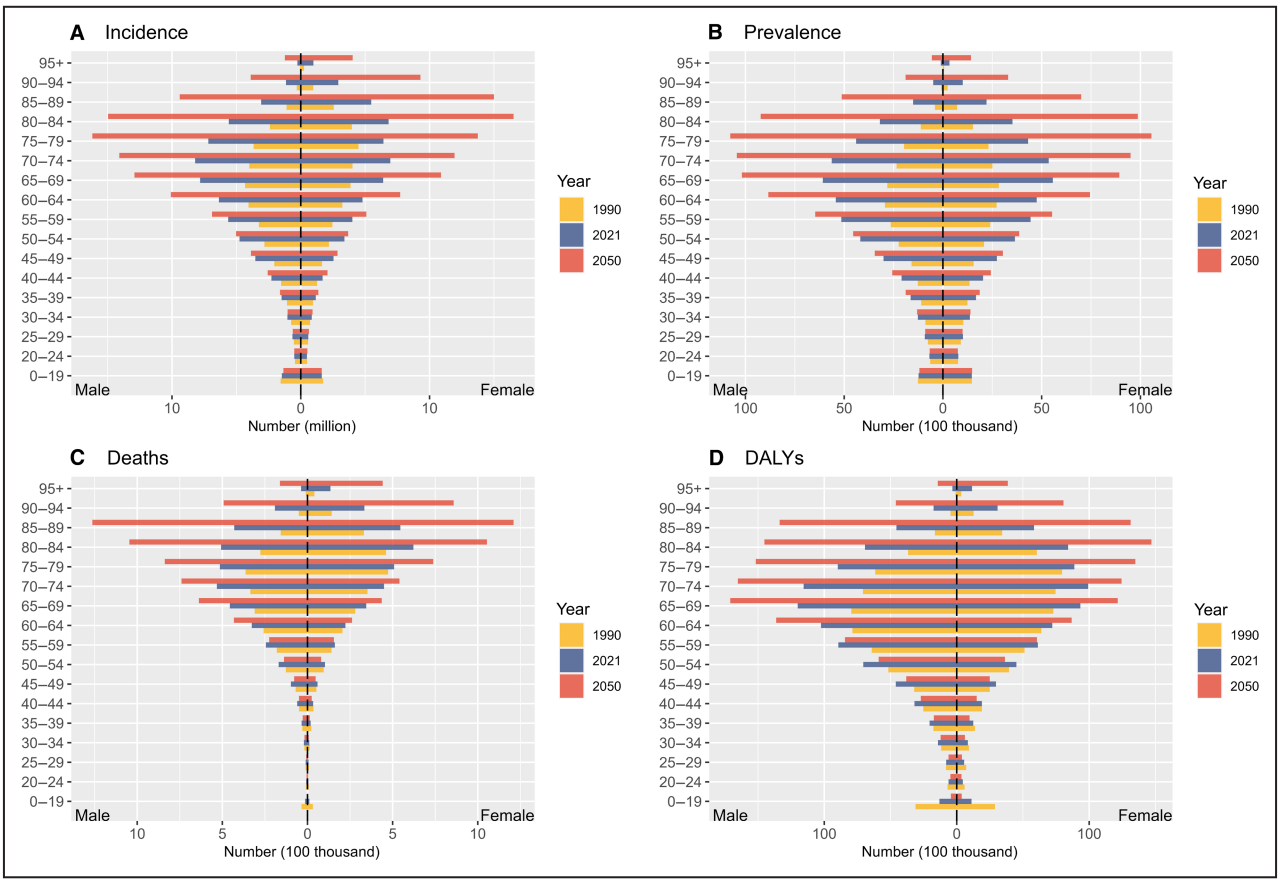

Figure 5. Absolute number of stroke by age and sex groups in 1990, 2021, and 2050 reference forecast: incidence (A), prevalence (B), deaths (C), and DALYs (D).
DALYs indicates disability-adjusted life years.

largest increases in age-adjusted incidence rates of stroke were the Philippines and Uzbekistan, which can be primarily attributed to a higher prevalence of cardiovascular disease risk factors, including hypertension, smoking, obesity, and heavy alcohol consumption in these countries.[41] Therefore, enhancing follow-up procedures and using more existing primary and secondary prevention measures is imperative to reduce the stroke burden effectively. On the contrary, Portugal, Mauritius, and Ireland are among the countries with the largest projected reductions in age-adjusted incidence. The reduction in the number and prevalence of patients with stroke may be attributed to the effective intervention of stroke risk factors and complete stroke rehabilitation guidelines in these countries.[42] In addition, extensive acute, convalescent, and long-term health care systems have been established to provide comprehensive and continuous medical support for each patient.[43] The first 3 countries projected to rise in age-adjusted deaths and age-adjusted DALYs were the United Arab Emirates, North Macedonia, and Lesotho. These countries generally have a deficiency in advanced stroke screening equipment such as high-resolution computed tomography scans, magnetic resonance imaging, and cerebral angiography.[44] Assisting less developed areas in establishing stroke monitoring centers can contribute to the early detection and treatment of patients with stroke, potentially leading to a reduction in mortality and disability rates.

With the continuous growth of population size and life expectancy, the global burden of stroke was projected to show an upward trend, particularly among the older population. The worldwide aging demographic causes a rising number of elderly individuals with cardiovascular disease, including stroke.[45] Given age-related physiological changes, individuals may experience a natural decline in cardiovascular health, including changes in vascular elasticity and the development of atherosclerosis.[46] These age-associated changes can further heighten the susceptibility to cardiovascular disease in the elderly population. The global patient cases, deaths, and disability numbers of stroke are higher in men than those in women, and the difference is probably widening. Men tend to have a higher prevalence of

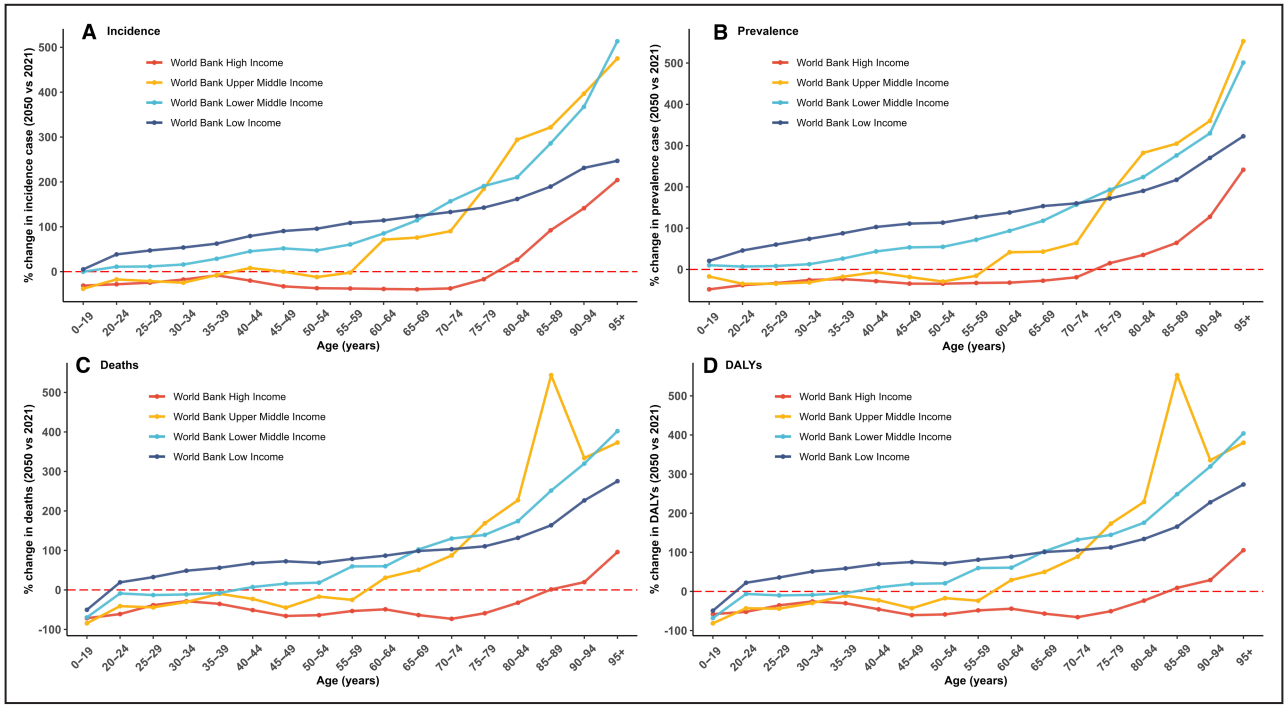

Figure 6. Projected change in absolute number of stroke by age group in four regions with World Bank income levels (2050 vs 2021): incidence (A), prevalence (B), deaths (C), and DALYs (D).
DALYs indicates disability-adjusted life years.

adverse lifestyle factors compared with women, such as tobacco use and alcohol abuse.[47] These negative factors significantly increase the risk of cardiovascular disease, including coronary heart disease, myocardial infarction, and peripheral arterial disease, which often serve as precursors for stroke occurrence in men.[48] However, women over the age of 85 years are more susceptible to stroke compared with men of the same age group globally. This discrepancy is partly due to the fact that women have a longer life expectancy than men.[49] In addition, sex-specific risk factors also play a role in increasing the risk of stroke for women.[50] For instance, peri- and postmenopausal periods present unique challenges, as the drop in estrogen levels can lead to increased blood pressure and a thickening of the carotid artery wall, both of which can increase the risk of stroke.[51] Therefore, relevant studies on stroke should be conducted to explore the variations in incidence, severity, treatment outcomes, and prognosis based on sex and age. This will facilitate the development of more precise treatment strategies and targeted prevention measures for stroke.

To the best of our knowledge, this is a comprehensive projection of the long-term pattern of the global stroke burden based on considerations of global demographic and economic development from 2022 to 2050. The unequal distribution of the stroke burden at the World Bank income levels, national levels, and sex-age groups found in this study may assist in the development of stroke prevention strategies and enhance the screening of targeted high-risk populations. However, our study has certain limitations. First, the limitations of the GBD database primarily stem from significant disparities in data availability and quality across different regions. These variations can lead to unavoidable errors when predicting future trends, which are reflected in the large UIs of projections. Although improvements in data processing and modeling methodologies have been observed in the GBD 2021 study, there is still room to improve data collection. Second, data on the stroke burden attributable to risk factors did not comprehensively cover all age groups and regions in the GBD 2021 study. Based on the lack of data availability, GDP was used instead of risk factors as a predictor variable in our stroke epidemiologic projections. More comprehensive predictive models that consider both economic factors and these risk factors may be valuable.

CONCLUSIONS

Globally, stroke remains a significant cause of both mortality and disability, with the burden of stroke projected to increase by 81% in stroke incidents and 71% in prevalent cases from 2021 to 2050. The rising stroke incident cases will also lead to increasing loss of life, with the absolute burden of deaths and DALYs caused by stroke projected to increase by 67% and

41%, respectively. Furthermore, the male population and elderly women bear a higher burden associated with stroke. Unequal distributions of stroke burden are evident across various World Bank income levels, with LICs and MICs experiencing a more significant burden compared with HICs. Therefore, public health initiatives must adopt target interventions that consider the specific needs of different demographic groups in order to mitigate the risk of stroke and alleviate the disparities of burden.

ARTICLE INFORMATION

Received April 23, 2024; accepted October 8, 2024.

Affiliations

Department of Psychology, School of Mental Health and Psychological Sciences (Y.C., W.X.) and , Department of Intelligent Medical Engineering, School of Biomedical Engineering (Y.L., H.S., M.C., B.Z., W.X.), Anhui Medical University, Hefei, China, Department of Radiology & Biomedical Imaging and Biomedical Informatics & Data Science, Yale University, New Haven, CT (X.L.); Peking University Sixth Hospital, Beijing, China (C.S.); Peking University Institute of Mental Health, Beijing, China (C.S.); National Clinical Research Center for Mental Disorders, Peking University Sixth Hospital, Beijing, China (C.S.); NHC Key Laboratory of Mental Health, Peking University, Beijing, China (C.S.); School of Life Course and Population Health Sciences, King's College London, London, United Kingdom (Y.W.); National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care (CLAHRC) South London, London, United Kingdom (Y.W.); Medical Image Center, The Third Affiliated Hospital of Anhui Medical University/ Hefei No1. People's Hospital (Binhu Campus), Hefei, China (C.X.); and Fubian Medical Technology Company, Ltd, Suzhou, China (W.X.).

Acknowledgments

The authors express their gratitude to the creators of the Global Burden of Disease database, the United Nations database, and the World Bank database for their invaluable contributions and generous provision of these data to facilitate public access.

Sources of Funding

This work is supported by the Young Scientists Fund of the National Natural Science Foundation of China (number 62306012), the Doctoral Program of Anhui Medical University (number 1401020201, 1401038201, and 1401046201), University Natural Science Research Project of Anhui Province (number 2022AH050696), Science Foundation for Youths of Anhui Medical University (number 2022xkj012), and Research Funds of Center for Xin'an Medicine and Modernization of Traditional Chinese Medicine of IHM (number 2024CXMMTCM003).

Disclosures

None.

Supplemental Material

Tables S1–S3
Figures S1–S8

REFERENCES

1. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, Abbasi-Kangevari M, Abbastabar H, Abd-Allah F, Abdelalim AJTL. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019. *Lancet*. 2020;396:1204–1222. doi: 10.1016/S0140-6736(20)30925-9
2. Zhang L, Lu H, Yang C. Global, regional, and national burden of stroke from 1990 to 2019: a temporal trend analysis based on the Global Burden of Disease study 2019. *Int J Stroke*. 2024;19:686–694. doi: 10.1177/17474930241246955
3. Ferrari AJ, Santomauro DF, Aali A, Abate YH, Abbafati C, Abbastabar H, Abd ElHafeez S, Abdelmasseh M, Abd-Elsalam S, Abdollahi A. 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;403:2133–2161. doi: 10.1016/S0140-6736(24)00757-8
4. Martin SS, Aday AW, Almarzooq ZI, Anderson CA, Arora P, Avery CL, Baker-Smith CM, Barone Gibbs B, Beaton AZ, Boehme AK. 2024 Heart disease and stroke statistics: a report of US and global data from the American Heart Association. *Circulation*. 2024;149:e347–e913. doi: 10.1161/CIR.0000000000001209
5. Feigin VL, Brainin M, Norrving B, Martins S, Sacco RL, Hacke W, Fisher M, Pandian J, Lindsay P. World Stroke Organization (WSO): global stroke fact sheet 2022. *Int J Stroke*. 2022;17:18–29. doi: 10.1177/17474930211065917
6. Gerstl JV, Blitz SE, Qu QR, Yearley AG, Lassarén P, Lindberg R, Gupta S, Kappel AD, Vicenty-Padilla JC, Gaude E. Global, regional, and national economic consequences of stroke. *Stroke*. 2023;54:2380–2389. doi: 10.1161/STROKEAHA.123.043131
7. Kaufman BG, Shah S, Hellkamp AS, Lytle BL, Fonarow GC, Schwamm LH, Lesén E, Hedberg J, Tank A, Fita E. Disease burden following non-cardioembolic minor ischemic stroke or high-risk TIA: a GWTG-stroke study. *J Stroke Cerebrovasc Dis*. 2020;29:105399. doi: 10.1016/j.jstrokecerebrovasdis.2020.105399
8. Sivenius J, Torppa J, Tuomilehto J, Immonen-Räihä P, Salomaa V. Modelling the burden of stroke in Finland until 2030. *Int J Stroke*. 2010;4:340–345. doi: 10.1111/j.1747-4949.2009.00330.x
9. Foerch C, Misselwitz B, Sitzer M, Steinmetz H, Neumann-Haefelin T. The projected burden of stroke in the German federal state of hesse up to the year 2050. *Deutsches Rzteblatt Int*. 2008;105:467–473. doi: 10.3238/arztebl.2008.0467
10. Struijs JN, van Genugten ML, Evers SM, Ament AJ, Baan CA, van den Bos GA. Modeling the future burden of stroke in the Netherlands: impact of aging, smoking, and hypertension. *Stroke*. 2005;36:1648–1655. doi: 10.1161/01.STR.0000173221.37568.d2
11. Wafa HA, Wolfe CD, Emmett E, Roth GA, Johnson CO, Wang Y. Burden of stroke in Europe: thirty-year projections of incidence, prevalence, deaths, and disability-adjusted life years. *Stroke*. 2020;51:2418–2427. doi: 10.1161/STROKEAHA.120.029606
12. Wafa HA, Marshall I, Wolfe CD, Xie W, Johnson CO, Veltkamp R, Wang Y, Harvey KH, Korompoki E, D'Anna L. Burden of intracerebral haemorrhage in Europe: forecasting incidence and mortality between 2019 and 2050. *Lancet Regional Health–Europe*. 2024;38:100842. doi: 10.1016/j.lanepe.2024.100842
13. Foreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, Pletcher MA, Smith AE, Tang K, Yuan C-W. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. *Lancet*. 2018;392:2052–2090. doi: 10.1016/S0140-6736(18)31694-5
14. *Global Health Data Exchange*. Institute for Health Metrics and Evaluation. 2024. Accessed June 26, 2024. https://ghdx.healthdata.org/gbd-2021
15. *How we Collect Data*. Institute for Health Metrics and Evaluation. 2024. Accessed June 26, 2024. https://www.healthdata.org/data-tools-practices/data-collection
16. Brauer M, Roth GA, Aravkin AY, Zheng P, Abate KH, Abate YH, Abbafati C, Abbasgholizadeh R, Abbasi MA, Abbasian M. 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;403:2162–2203. doi: 10.1016/S0140-6736(24)00933-4
17. *GBD Results*. Institute for Health Metrics and Evaluation. 2024. Accessed June 5, 2024. https://vizhub.healthdata.org/gbd-results/
18. World Bank Historic Income Levels. The World Bank. Accessed June 5, 2024. http://databank.worldbank.org/data/download/site-content/OGHIST.xls
19. World population prospects. United Nations, department of economic and social affairs, population division. 2022. Accessed August 21, 2023. https://population.un.org/wpp/.

20. Projecting age-sex-specific mortality: a comparison of the modified Lee-Carter and pattern of mortality decline methods. Accessed October 9, 2023. https://population.un.org/wpp/Publications/Files/WPP2017_TechnicalPaperNo6.pdf.
21. *Gross Domestic Product Per Capita 1960–2050—FGH*. Institute for Health Metrics and Evaluation (IHME); 2021. Accessed September 26, 2023. https://ghdx.healthdata.org/record/ihme-data/global-gdp-per-capita-1960-2050-fgh-2021
22. Stevens GA, Alkema L, Black RE, Boerma JT, Collins GS, Ezzati M, Grove JT, Hogan DR, Hogan MC, Horton R. Guidelines for accurate and transparent health estimates reporting: the GATHER statement. *Lancet*. 2016;388:e19–e23. doi: 10.1016/S0140-6736(16)30388-9
23. Rajsic S, Gothe H, Borba H, Sroczynski G, Vujicic J, Toell T, Siebert U. Economic burden of stroke: a systematic review on post-stroke care. *Eur J Health Econ*. 2019;20:107–134. doi: 10.1007/s10198-018-0984-0
24. Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. *Lancet Neurol*. 2009;8:345–354. doi: 10.1016/S1474-4422(09)70023-7
25. Lee RD, Carter LR. Modeling and forecasting US mortality. *J Am Stat Assoc*. 1992;87:659–671. doi: 10.1080/01621459.1992.10475265
26. Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJL, Lozano R, Inoue M. Age standardization of rates: a new WHO standard. 2000.
27. Pandian JD, Srivastava MVP, Aaron S, Ranawaka UK, Venketasubramanian N, Sebastian IA, Injety RJ, Gandhi DB, Chawla NS, Vijayanand PJ. The burden, risk factors and unique etiologies of stroke in South-East Asia Region (SEAR). *Lancet Regional Health-Southeast Asia*. 2023;17:100290. doi: 10.1016/j.lansea.2023.100290
28. Xiong Y, Wakhloo AK, Fisher M. Advances in acute ischemic stroke therapy. *Circ Res*. 2022;130:1230–1251. doi: 10.1161/CIRCRESAHA.121.319948
29. Pandian JD, Kalkonde Y, Sebastian IA, Felix C, Urimubenshi G, Bosch J. Stroke systems of care in low-income and middle-income countries: challenges and opportunities. *Lancet*. 2020;396:1443–1451. doi: 10.1016/S0140-6736(20)31374-X
30. Lindsay LR, Thompson DA, O'Dell MW. Updated approach to stroke rehabilitation. *Med Clin*. 2020;104:199–211. doi: 10.1016/j.mcna.2019.11.002
31. Owolabi MO, Thrift AG, Mahal A, Ishida M, Martins S, Johnson WD, Pandian J, Abd-Allah F, Yaria J, Phan HT. Primary stroke prevention worldwide: translating evidence into action. *Lancet Public Health*. 2022;7:e74–e85. doi: 10.1016/S2468-2667(21)00230-9
32. Diener H-C, Hankey GJ. Primary and secondary prevention of ischemic stroke and cerebral hemorrhage: JACC focus seminar. *J Am Coll Cardiol*. 2020;75:1804–1818. doi: 10.1016/j.jacc.2019.12.072
33. Siegler J, Heslin M, Thau L, Smith A, Jovin T. Falling stroke rates during COVID-19 pandemic at a comprehensive stroke center. *J Stroke Cerebrovasc Dis*. 2020;29:104953. doi: 10.1016/j.jstrokecerebrovasdis.2020.104953
34. Zhao J, Rudd A, Liu R. Challenges and potential solutions of stroke care during the coronavirus disease 2019 (COVID-19) outbreak. *Stroke*. 2020;51:1356–1357. doi: 10.1161/STROKEAHA.120.029701
35. Chen Y, Wright N, Guo Y, Turnbull I, Kartsonaki C, Yang L, Bian Z, Pei P, Pan D, Zhang Y. Mortality and recurrent vascular events after first incident stroke: a 9-year community-based study of 0.5 million Chinese adults. *Lancet Global Health*. 2020;8:e580–e590. doi: 10.1016/S2214-109X(20)30069-3
36. Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, Abbasifard M, Abbasi-Kangevari M, Abd-Allah F, Abedi V. 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;20:795–820. doi: 10.1016/S1474-4422(21)00252-0
37. Berkowitz AL, Mittal MK, McLane HC, Shen GC, Muralidharan R, Lyons JL, Shinohara RT, Shuaib A, Mateen FJ. Worldwide reported use of IV tissue plasminogen activator for acute ischemic stroke. *Int J Stroke*. 2014;9:349–355. doi: 10.1111/ijs.12205
38. Langhorne P, Audebert HJ, Cadilhac DA, Kim J, Lindsay P. Stroke systems of care in high-income countries: what is optimal? *Lancet*. 2020;396:1433–1442. doi: 10.1016/S0140-6736(20)31363-5
39. Feigin VL, Owolabi MO, Abd-Allah F, Akinyemi RO, Bhattacharjee NV, Brainin M, Cao J, Caso V, Dalton B, Davis A. Pragmatic solutions to reduce the global burden of stroke: a World Stroke Organization–Lancet Neurology Commission. *Lancet Neurol*. 2023;22:1160–1206. doi: 10.1016/S1474-4422(23)00277-6
40. Lin S, Wang C, Wang Q, Xie S, Tu Q, Zhang H, Peng M, Zhou J, Redfern J. The experience of stroke survivors and caregivers during hospital-to-home transitional care: a qualitative longitudinal study. *Int J Nurs Stud*. 2022;130:104213. doi: 10.1016/j.ijnurstu.2022.104213
41. Mercado-Asis LB, Ona DID, Bonzon D, Vilela GA, Diaz AF, Balmores BA, Co M, Mina AB, Atilano AA, Cabral EI. Socioeconomic impact and burden of hypertension in the Philippines projected in 2050. *Hypertens Res*. 2023;46:244–252. doi: 10.1038/s41440-022-01052-6
42. Khan F, Amatya B, De Groote W, Owolabi M, Syed IM, Hajjoui A, Babur MN, Sayed TM, Frizzell Y, Naicker AS. Capacity-building in clinical skills of rehabilitation workforce in low-and middle-income countries. *J Rehabil Med*. 2018;50:472–479. doi: 10.2340/16501977-2313
43. Gonçalves FB, Pedro LM. Centralisation of vascular care in Portugal. *Eur J Vasc Endovasc Surg*. 2024;67:370–372. doi: 10.1016/j.ejvs.2024.01.068
44. Prust ML, Forman R, Ovbiagele B. Addressing disparities in the global epidemiology of stroke. *Nat Rev Neurol*. 2024;20:207–221. doi: 10.1038/s41582-023-00921-z
45. Li R, Cheng X, Yang Y, Schwebel DC, Ning P, Li L, Rao Z, Cheng P, Zhao M, Hu G. Global deaths associated with population aging—1990–2019. *China CDC Weekly*. 2023;5:1150–1154. doi: 10.46234/ccdcw2023.216
46. Arnold M, Schweizer J, Nakas CT, Schütz V, Westphal LP, Inauen C, Pokorny T, Luft A, Leichtle A, Arnold M. Lipoprotein (a) is associated with large artery atherosclerosis stroke aetiology and stroke recurrence among patients below the age of 60 years: results from the biosignal study. *Eur Heart J*. 2021;42:2186–2196. doi: 10.1093/eurheartj/ehab081
47. Peters SA, Carcel C, Millett ER, Woodward M. Sex differences in the association between major risk factors and the risk of stroke in the UK biobank cohort study. *Neurology*. 2020;95:e2715–e2726. doi: 10.1212/WNL.0000000000010982
48. Yusuf S, Joseph P, Rangarajan S, Islam S, Mente A, Hystad P, Brauer M, Kutty VR, Gupta R, Wielgosz A. Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. *Lancet*. 2020;395:795–808. doi: 10.1016/S0140-6736(19)32008-2
49. Ryu W-S, Chung J, Schellingerhout D, Jeong S-W, Kim H-R, Park JE, Kim BJ, Kim J-T, Hong K-S, Lee K. Biological mechanism of sex difference in stroke manifestation and outcomes. *Neurology*. 2023;100:e2490–e2503. doi: 10.1212/WNL.0000000000207346
50. Yoon CW, Bushnell CD. Stroke in women: a review focused on epidemiology, risk factors, and outcomes. *J Stroke*. 2023;25:2–15. doi: 10.5853/jos.2022.03468
51. Bushnell CD, Kapral MK. Stroke in women and unique risk factors. *Stroke*. 2023;54:587–590. doi: 10.1161/STROKEAHA.122.041734