Risk and impact of stroke across 38 countries and territories of the Americas from 1990 to 2021: a population-based trends analysis from the Global Burden of Disease Study 2021

Ramón Martinez,[a] Paula Muñoz-Venturelli,[b,] Pedro Ordunez,[a] Felipe Fregni,[c] Carlos Abanto,[d] Matias Alet,[e,f] Tony Fabián Alvarez,[g] Pablo Amaya,[h] Sebastian Ameriso,[e] Antonio Arauz,[i] Miguel A. Barboza,[j] Hernán Bayona,[k,l] Antonio Bernabé-Ortiz,[m] Juan Calleja,[i] Vanessa Cano-Nigenda,[i] Leonardo Augusto Carbonera,[n] Rodrigo M. Carrillo-Larco,[o] Angel Corredor,[p] Ana Cláudia de Souza,[n] Claudio Jimenez,[l] Fernando Lanas,[q] Sheila Martins,[n,r,s] Victor Navia,[t,u] Nelson Novarro-Escudero,[v] Verónica Olavarría,[t] Bruce Ovbiagele,[w] Kevin Pacheco-Barrios,[x] Octavio Pontes-Neto,[y] Virginia Pujol,[e] Alejandro Rabinstein,[z] Julieta Rosales,[e] Andrés Rosende,[a] Gisele Sampaio Silva,[aa] Gustavo Saposnik,[ab] Souvik Sen,[ac] Fernando D. Testai,[ad] Victor Urrutia,[ae] Craig S. Anderson,[af,ag] and Pablo M. Lavados[t]*

[a]Pan American Health Organization, Washington, DC, USA
[b]Centro de Estudios Clínicos, ICIM, Facultad de Medicina Clínica Alemana Universidad del Desarrollo, Santiago, Chile
[c]Harvard T.H. Chan School of Public Health, Harvard University, Massachusetts, USA
[d]The Cerebrovascular Disease Research Center, National Institute of Neurological Sciences, Lima, Peru
[e]Departamento de Neurología Vascular, Centro Integral de Neurología Vascular, Fleni, Ciudad Autónoma de Buenos Aires, Argentina
[f]Hospital General de Agudos J. M. Ramos Mejía. Ciudad Autónoma Buenos Aires, Argentina
[g]Centro de Excelencia en ACV, Instituto Neurológico, Hospital Internacional de Colombia-FCV
[h]Stroke Program, Neurology Department, Fundación Valle del Lili, Cali, Colombia
[i]Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suarez, Mexico City, Mexico
[j]Departamento de Neurociencias, Hospital Dr. Rafael A. Calderón Guardia, Universidad de Costa Rica, San José, Costa Rica
[k]Universidad de los Andes School of Medicine, Fundación Santa Fe de Bogotá, Department of Neurology, Stroke Center, Bogotá, Colombia
[l]Stroke Center, Hospital Simón Bolívar, Subred Norte, Bogotá, Colombia
[m]Faculty of Health Sciences, Universidad Científica del Sur, Lima, Peru
[n]Department of Neurology and Neurosurgery, Hospital Moinhos de Vento, Porto Alegre, Brazil
[o]Emory Global Diabetes Research Center and Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, USA
[p]Department of Neurology, Stroke Center, Clínica Central del Quindío, Armenia, Colombia
[q]Department of Internal Medicine, Faculty of Medicine, Universidad de la Frontera, Temuco, Chile
[r]Neurology Department, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
[s]Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil
[t]Servicio de Neurología, Departamento de Neurología y Psiquiatría, Clínica Alemana de Santiago, Facultad de Medicina Clínica Alemana Universidad del Desarrollo, Santiago, Chile
[u]Unidad de Neurología, Hospital Padre Hurtado, Santiago, Chile
[v]Primary Stroke Center, Pacífica Salud, Hospital Punta Pacífica, Panamá, Panama
[w]Department of Neurology, University of California San Francisco Weill Institute for Neurosciences, San Francisco, CA, USA
[x]Neuromodulation Center and Center for Clinical Research Learning Spaulding Rehabilitation Hospital and Massachusetts General Hospital, Boston, MA, USA
[y]Department of Neuroscience and Behavioral Sciences, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil
[z]Department of Neurology, Mayo Clinic, Rochester, MN, USA
[aa]Neurology Department, Universidade Federal de São Paulo (UNIFESP) and Albert Einstein Hospital, São Paulo, Brazil
[ab]Stroke Outcomes & Decision Neuroscience Research Unit, Department of Medicine, University of Toronto, Toronto, Canada
[ac]Department of Neurology, University of South Carolina School of Medicine, Prisma Health Medical Group Midlands, Columbia, SC, USA
[ad]Department of Neurology and Rehabilitation, University of Illinois Chicago College of Medicine, Chicago, IL, USA
[ae]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA
[af]The George Institute for Global Health, Faculty of Medicine, University of New South Wales, Sydney, Australia
[ag]Institute for Science and Technology for Brain-inspired Intelligence, Fudan University, China

*Corresponding author. Centro de Estudios Clínicos, ICIM, Facultad de Medicina Clínica Alemana Universidad del Desarrollo, Av Plaza 680, Las Condes, Santiago, Chile.
E-mail address: paumunoz@udd.cl (P. Muñoz-Venturelli).

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Summary

Background Despite substantial declines in burden over time, stroke remains a public health threat in the Americas. This study aimed to assess the current magnitude, trends, and disparities in the estimates of stroke burden by sex and age in the Americas from 1990 to 2021.

Methods Estimates from the Global Burden of Disease, Injuries and Risk Factors Study 2021 were used to analyze incidence, prevalence, mortality, years of life lost due to premature death, years lived with disabilities, and disability-adjusted life years (DALYs) caused by stroke and its major subtypes stratified by age, and sex in the Americas from 1990 to 2021. We used Joinpoint regression analysis to estimate the average annual percent change (AAPC) of stroke mortality and disease burden outcomes and assessed trends.

Findings In 2021, there were 1.1 million (95% uncertainty interval: 1.0–1.2) new cases, 12.9 million (12.3–13.7) prevalent cases, 0.5 million (0.5–0.6) deaths, and 11.4 million (10.6–12.1) DALYs due to stroke in the Americas. The absolute number of stroke burden outcomes increased from 1990 to 2021, but their corresponding age-standardized rates significantly declined. A deceleration in reduction rates of burden outcomes for all strokes and most stroke subtypes occurred over the last decade, with pronounced difference between sexes mainly in incidence among younger groups. From 2015 to 2021, trends in incidence rates from all stroke and stroke subtypes reversed to increase in most age groups, and strikingly, trends in mortality and DALY rates from ischemic stroke among younger populations reversed to upward with AAPC over 1.4%. A substantial number of countries contributed to these increasing trends.

Interpretation Regionally, the annual number of stroke cases and deaths significantly increased from 1990 to 2021, despite reductions in age-standardized rates. The declining pace in age-standardized stroke rates has decelerated in recent years, while trends in incidence, and ischemic stroke mortality and DALY among middle-aged adults and adults, reversed towards upward in the period 2015–2021. Further studies are needed to understand the determinants of this recent pattern and identify the most cost-effective interventions to stem this alarming trend.

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Keywords: Stroke; Ischemic stroke; Intracerebral hemorrhage; Subarachnoid hemorrhage; Burden of diseases; Americas

Introduction

In the Americas, stroke mortality has been substantially declining since the mid-1960s. The United States of America first, and Canada later, are two of the most notable global examples of reductions in stroke burden. Despite this remarkable trend, stroke has remained the second leading cause of death, accounting for 526.4 thousand deaths, and the sixth leading cause of disability-adjusted life years (DALYs), accounting for 11.1 million DALYs in 2019.[1] Indeed, with an estimated 1.2 million new stroke cases each year and a prevalence of 14.9 million people living with a history of cerebrovascular diseases,[1] stroke remains a major health issue for countries and territories of the Americas.

Being a largely avoidable condition from effective population-based interventions, and individual access to high-quality care[2] principally hypertension control, stroke has been recognized as a global priority in the United Nations' Sustainable Development Goals,[3] and the World Health Organization's (WHO) global action plan for the prevention and control of non-communicable diseases,[4,5] which set a target of reducing premature death due to noncommunicable diseases by one-third by 2030. In this context, monitoring the magnitude, trends, and disparity patterns of the stroke burden across countries and regions can provide important feedback on efforts to reduce the avoidable burden of stroke.

Several studies have examined the burden of stroke and its attributable risk factors.[1,6–15] However, only one of them,[13] with data up to 2017, assessed the level, trends, and disparities in stroke in the Region of the Americas. Notably, none of the studies have provided most recent estimates in relation to the COVID-19 pandemic period, which severely disrupted national noncommunicable disease-related health services.[16] A comprehensive and updated assessment of the regional and national burden of stroke and stroke subtypes in the Americas is needed to evaluate the current situation and to guide efforts on the prevention and control of cerebrovascular diseases. The Global Burden of Disease Study 2021 (GBD 2021), which provides comparable estimates of morbidity, mortality, and disease burden caused by diseases and injuries, from 1990 to 2021,[17–19]

Research in context

Evidence before this study

Stroke is a prominent cause of mortality and disability worldwide. Being largely preventable and treatable through effective public health and health services interventions, stroke has gained recognition as a priority in the United Nations' Sustainable Development Goals. We reviewed the available evidence on the regional and national burdens of stroke and its major subtypes in the Americas by performing a literature search in Medline, Scopus, Google Scholar, and PubMed without language restrictions, considering articles published from January 2000 to May 2024 using the following terms (stroke OR "isch(a)emic stroke" OR intracerebral h(a)emorrhage" OR "subarachnoid h(a) emorrhage") AND (incidence OR prevalence OR deaths OR mortality OR "burden of disease") AND (Americas OR "Region of the Americas"). Population-level estimates for stroke incidence, mortality, and disability-adjusted life years (DALYS) have been produced regularly by the WHO's Global Health Estimates (GHE) and the Global Burden of Disease Study (GBD). Numerous studies have explored the impact of stroke and its associated risk factors; however, our literature review did not yield any previous study that exclusively focused on the burden of stroke and its major subtypes in the Americas or that examined contemporary trends, including the COVID-19 pandemic period. There is an urgent need for a thorough and updated assessment of stroke burden, including stroke subtypes, at both regional and national levels in the Americas.

Added value of this study

This study shows that despite a substantial reduction in the age-standardized stroke incidence, mortality, and DALY rates since 1990, stroke remains a leading cause of mortality and disability in the region, ranking among the top three causes of death alongside COVID-19 and ischemic heart disease in 2021. Overall, stroke mortality during the pandemic remained stable compared to the pre-pandemic period. Despite significant advancements in managing stroke burden over the last three decades and regional declines in age-standardized stroke incidence, prevalence, mortality, and DALYs from 1990 to 2021, there has been an increase in absolute numbers of stroke cases and associated YLDs, underscoring critical priorities for healthcare services. Temporal trends analyses reveal a recent deceleration in the trajectory of stroke burden outcomes. Notably, there has been a rise in stroke incidence among middle-aged adults, and adults over the past decade, with a disproportionately negative impact on females. Ischemic stroke mortality and DALY rates among middle-aged adults have risen since 2010, more notably from 2015 to 2021, driven by increasing occurrences in highly populated and both high- and upper-middle-income countries.

Implications of all the available evidence

The findings of this study are an urgent call to the scientific and public health communities to understand the determinants of these recent untoward patterns, and promptly identify interventions to reverse these trends and re-accelerate previous trajectories. Population epidemiological surveillance and monitoring are crucial to facilitate targeted interventions aimed at halting this increase. Given the anticipated growth in the disease burden of stroke and its societal impact, it is imperative to integrate these findings into the development of effective strategies for stroke prevention and care.

becomes a key resource and opportunity to fill such needs.

This study aimed to assess current levels, temporal trends, and disparities in incidence, prevalence, mortality, and DALYs, years lived with disabilities (YLD), and years of life lost (YLL) caused by stroke and its major subtypes by sex and age in the Americas from 1990 to 2021.

Methods

Study design, setting, and data sources

This is a population-based study that investigates the incidence, prevalence, mortality, disease burden due to stroke, and the stroke subtypes by sex and age across 38 countries and territories of the Region of the Americas from 1990 to 2021, using estimates from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021. It is reported according to the STROBE statement (STROBE statement check list, section 3 in the Supplementary Material).

The Region of the Americas is a continent encompassing two large subregions: North America, and Latin America and the Caribbean (LAC) which is also subdivided into Central America, Latin Caribbean, Non-Latin Caribbean, Andean Area, and Southern Cone. The region comprises 35 countries and 10 territories (list of countries and territories in the Supplementary Material, pp 22–23) of which 21 are high-income economies, 20 are upper-middle-income countries, and 4 are lower-middle-income economies.[20] The region is home to over 1 billion people (12.5% of the global population), representing a rich tapestry of ethnicities, languages, and cultures, with an estimated mean life expectancy of 77.2 years, and an estimated 7.2 million deaths occurring in 2019.[21]

Using the GBD Results Tool (https://vizhub.healthdata.org/gbd-results/), we extracted estimates for incidence, prevalence, deaths, DALYs, YLLs, and YLDs in absolute numbers and rates per 100 000 population caused by stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage for male, female and both sexes combined, and age groups (<1, 2–4, the five year-intervals of age until 95+, all-ages, age-standardized, and the custom age groups Under 5 years, 5–14 years, 15–49 years, 50–74 years, and 75+ years) for the Region of the Americas, and 38 countries and territories of the Americas with available information. Additionally, we extracted annual estimates of the population size by sex, age, and country, as well as the socio-demographic index for each country from 1990 to 2021.

Overview of the GBD study

Full details of the data sources and methods used by GBD to estimate stroke fatal and non-fatal health outcomes have been described elsewhere.[1,18,19,22] GBD quantifies the magnitude of all major diseases, risk factors, and intermediate clinical outcomes in a highly standardized way, to allow for comparisons over time, and across populations and health problems.[23] GBD produces annual estimates of key health metrics for 371 diseases and injuries, and 88 risk factors over time and across 204 countries and territories by age and sex from 1990 to 2021. GBD produces epidemiological measures such as incidence, prevalence, deaths, and summary measures of disease burden, such as DALY, YLL, and YLD.[17,24] DALY represents the sum of YLL and YLD.

GDB organizes 371 diseases and injuries into hierarchically nested categories in four levels of aggregation, called the GBD cause list (https://ghdx.healthdata.org/record/ihme-data/gbd-2021-cause-icd-code-mappings).

The GBD study is performed in compliance with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).[25] All results are publicly available via the online GBD Results Tool [https://vizhub.healthdata.org/gbd-results/] and the GBD Compare [https://vizhub.healthdata.org/gbd-compare/], and all data input sources are identified via the GBD 2021 Sources Tool [https://ghdx.healthdata.org/gbd-2021/sources].

Definition of stroke and stroke subtypes

In the GBD study, stroke was defined by WHO clinical criteria[26] as rapidly developing clinical signs of (usually focal) disturbance of cerebral function lasting more than 24 h or leading to death with no apparent cause other than that of vascular origin. Ischemic stroke was defined as an episode of neurological dysfunction due to focal cerebral, spinal, or retinal infarction. Intracerebral hemorrhage was defined as stroke with a focal collection of blood in the brain, not due to trauma. Subarachnoid hemorrhage was defined as non-traumatic stroke due to bleeding into the subarachnoid space of the brain. These definitions were coded according to the International Classification of Diseases, 10th revision (ICD-10)[27] and detailed in the Supplementary Material, pp 8. In the GBD cause list, Stroke is a level 3 category under CVD,[28] which includes the major stroke subtypes: ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage as level 4 categories.

Estimation process for fatal and non-fatal stroke

For fatal estimates, the GBD study used vital registration, verbal autopsy, registry, survey, police, or surveillance data across all countries and territories as inputs into the Cause of Death Ensemble modeling (CODEm) framework to estimate deaths due to overall stroke and stroke subtypes. Deaths from vital registration systems coded to impossible or intermediate causes of death or unspecified stroke were reassigned by using statistical methods. For non-fatal estimates, sources came from scientific literature, household survey data, epidemiological surveillance data, disease registry data, clinical informatics data, and other sources. Estimates of the incidence and prevalence of stroke were generated with the DisMod-MR 2.1 (disease-model-Bayesian meta-regression) modeling tool[29] that uses data on various disease parameters and the epidemiological relationships between these parameters.[1] All available high-quality data on incidence, prevalence, and mortality were used to estimate non-fatal stroke burden. GBD modeled ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage from the day of incidence through 28 days and separately modeled survival beyond 28 days. All estimates are reported with their 95% uncertainty intervals, which are obtained from the 2.5th and 97.5th percentiles of 500 values generated for each measure in each step of the estimation process. Sample size for such estimates can be judged based on the width of the uncertainty intervals (Details of the GBD 2021 methods for stroke burden are in Supplementary Material section 1, pp 9).

Analytic strategies

We compared the number, age- and sex-specific rates, all-ages and age-standardized rates of incidence, prevalence, deaths, DALY, YLL, and YLD from stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage across 38 countries and territories of the Americas from 1990 to 2021, stratified by the socio-demographic index. Rates were age-standardized by direct method using the GBD world standard population. The socio-demographic index is a composite measure of lag-distributed income per capita, average years of education for those aged ≥15 years, and fertility rates among females <25 years. Socio-demographic index represents the national level of economic, social, and demographic development.

Temporal trends analysis

We assessed temporal trends of incidence, prevalence, mortality, DALY, YLL and YLD caused by stroke and stroke subtypes using the average annual percent change (AAPC), a summary measure of trends over years for a set full period. We applied Joinpoint regression method[30,31] for estimating AAPC and its 95% confidence interval (CI) for each measure of stroke and stroke type burden by sex and location (region, country) for periods 1990–2021, 2010–2021, and 2015–2021. The Joinpoint regression model was configured with the grid search on a log-linear function of the age-standardized and age-specific outcome rates per 100 000 population against years, to detect a maximum of 4 joinpoints and avoiding time segments comprising only two data points to ensure rate changes in outcome measures were due to consistent changes over time and not year-to-year variations. A Monte Carlo method[30] with 4499 randomly permuted data sets was used to estimate the P-value of each permutation test and the AAPC 95% CI, while the overall asymptotic level of P-value is maintained through a Bonferroni adjustment. We assessed the homoscedasticity/heteroscedasticity by computing the first difference of rates over the year of each cohort time series, which resulted on constant variance (homoscedasticity) in rates over time. We assessed the autocorrelation of each cohort times series by computing the autocorrelation function at lags from 1 to 10 years (one-third of the total number of years), and examining the resulting correlogram, which informed no autocorrelation. We selected the Weighted Bayesian Information Criterion for final model selection, as it is the most flexible in adapting to different situations, and it performs better when working with large datasets and data cohorts with a variety of characteristics.[32] AAPC is considered significant when it is different from "zero" at alpha = 0.05. A constant trend is considered when AAPC is not significant (P-value > 0.05), an increasing trend when AAPC is significant (P-value ≤ 0.05) and positive, and a decreasing trend when AAPC is significant (P-value ≤ 0.05) and negative. Details in section 2 Supplementary Methods.

Ethical considerations

This study used publicly available data from the GBD study, which the Institutional Review Board ethically approves at the University of Washington. No personal identifying information was used in the analysis.

Results

The regional burden of stroke in 2021

Regionwide in 2021, 1.1 million (95% UI: 1.0–1.2) new stroke cases were estimated, of which 70% (0.8 million [0.7–0.9]) were ischemic stroke. There were 12.9 million (12.3–13.7) prevalent stroke patients, higher in females (6.7 million [6.4–7.1]) than males (6.2 million [5.9–6.6]). Stroke accounted for 0.5 million (0.5–0.6) deaths, 55% (0.3 million [0.3–0.3]) from ischemic stroke, 34% (0.2 million [0.2–0.2]) from intracerebral hemorrhage, and 11% (0.1 million [0.1–0.1]) million from subarachnoid hemorrhage. Stroke accounted for 11.4 million (10.6–12.1) DALYs, the most of them (83%) due to ischemic stroke and intracerebral hemorrhage. DALYs were dominated by YLLs (86.1% of total DALYs) (Supplementary Table S1). These numbers resulted in the age-standardized incidence rate of 84.5 cases (76.4–93.6) per 100 000 population, prevalence of 1006.1 patients (955.4–1061.6) per 100 000, mortality of 38.1 deaths (33.9–40.5) per 100 000, and DALY rate of 869.2 years (807.8–924.1) per 100 000 population. All age-standardized stroke rates were slightly higher in males than females, except stroke YLD rates (Table 1). The regional levels of age-standardized rates of stroke and stroke subtypes burden in the Americas were consistently lower than the World during the study period except for prevalence and YLDs (Supplementary Material Section 3).

The distribution of incidence, prevalence, mortality, DALYs, YLLs, and YLDS rates due to stroke, breakdown for stroke subtypes by age and sex in 2021 is shown in Supplementary Fig.S1.

Temporal trends in the stroke burden in the region from 1990 to 2021

Stroke consistently ranked as the second-leading cause of death regionwide in the period 1990–2019, after ischemic heart disease (IHD). However, during the COVID-19 pandemic period (2020–2021), stroke moved down to the third position given that COVID-19 emerged as the first cause of death (Fig. 1). Stroke ranked the sixth leading cause of DALYs in 2019, moving down to the seventh position in 2020 and 2021 as COVID-19 emerged to the first position (Supplementary Fig. S2).

The absolute number of stroke incident cases, prevalent cases, and deaths, as well as the number of DALYs, YLDs, and YLLs due to stroke, showed an upward trend from 1990 to 2021. However, their corresponding age-standardized rates per 100 000 population declined at an average annual percent change of −1.4% (−1.5 to −1.4), −0.6% (−0.6 to −0.6), −1.8% (−1.9 to −1.8), −1.8% (−1.9 to −1.8), −0.7% (−0.7 to −0.7) and −2.0% (−2.0 to −1.9) respectively in that period. This pattern was observed for males and females and across stroke subtypes (Table 1, Fig. 2, Supplementary Fig. S3). The long-term decline trends shifted during the COVID-19 pandemic period for some outcomes and stroke subtypes.

Comparing the AAPC across stroke type burden outcomes in the period 1990–2021, the highest level of decline was observed in YLLs from stroke, ischemic stroke, and intracerebral hemorrhage for both males and females, whilst the lowest level of decline was observed in all measures for subarachnoid hemorrhage (Table 1). The reduction rate of mortality and YLLs from stroke and ischemic stroke decelerated in the last decade. Importantly, during 2015–2021, the trends in age-standardized incidence rates from stroke in females, and subarachnoid hemorrhage in males and females reversed to increase with an AAPC of 0.1% (0.0–0.2), 0.9% (0.8–1.0), and 0.9% (0.7–1.0), respectively. In this period, the age-standardized prevalence rates from

Outcome measure	Sex	Age-standardized rates per 100 000 population		Average annual percent change					
		1990	2021	1990–2021		2010–2021		2015–2021	
		Estimate (95% uncertainty interval)	Estimate (95% uncertainty interval)	Estimate (95% confidence interval)	P-value	Estimate (95% confidence interval)	P-value	Estimate (95% confidence interval)	P-value
Stroke									
Incidence	Both	133.19 (117.67–150.75)	84.49 (76.38–93.61)	−1.4 (−1.5 to −1.4)	<0.0001	−0.5 (−0.5 to −0.4)	<0.0001	−0.1 (−0.2 to −0.1)	0.01
	Male	146.25 (128.16–167.16)	91.84 (81.8–102.37)	−1.5 (−1.5 to −1.5)	<0.0001	−0.6 (−0.6 to −0.5)	<0.0001	−0.4 (−0.4 to −0.3)	<0.0001
	Female	122.37 (109.2–137.61)	78.13 (70.48–86.08)	−1.4 (−1.4 to −1.4)	<0.0001	−0.4 (−0.4 to −0.3)	<0.0001	0.1 (0.0–0.2)	0.04
Prevalence	Both	1209.17 (1135.64–1281.85)	1006.24 (955.4–1061.55)	−0.6 (−0.6 to −0.6)	<0.0001	−0.6 (−0.7 to −0.5)	<0.0001	−0.4 (−0.6 to −0.4)	<0.0001
	Male	1259.98 (1174.95–1341.53)	1050.37 (992.04–1110.61)	−0.6 (−0.6 to −0.6)	<0.0001	−0.6 (−0.7 to −0.5)	<0.0001	−0.4 (−0.5 to −0.3)	<0.0001
	Female	1174.21 (1109.27–1244.68)	973.56 (926.63–1026.03)	−0.6 (−0.6 to −0.6)	<0.0001	−0.6 (−0.7 to −0.6)	<0.0001	−0.5 (−0.6 to −0.4)	<0.0001
Deaths	Both	68.32 (62.85–71.05)	38.12 (33.89–40.53)	−1.8 (−1.9 to −1.8)	<0.0001	−1.4 (−1.5 to −1.3)	<0.0001	−1.2 (−1.4 to −1)	<0.0001
	Male	75.12 (71.13–77.33)	41.28 (38.06–43.67)	−1.9 (−1.9 to −1.8)	<0.0001	−1.3 (−1.4 to −1.2)	<0.0001	−1.1 (−1.2 to −0.9)	<0.0001
	Female	62.66 (56.5–65.74)	35.15 (30.31–37.74)	−1.8 (−1.9 to −1.8)	<0.0001	−1.4 (−1.6 to −1.3)	<0.0001	−1.4 (−1.6 to −1.1)	<0.0001
DALYs (Disability-Adjusted Life Years)	Both	1552.52 (1478.65–1611.84)	869.15 (807.8–924.13)	−1.8 (−1.9 to −1.8)	<0.0001	−1.3 (−1.4 to −1.2)	<0.0001	−1.1 (−1.3 to −0.9)	<0.0001
	Male	1714.89 (1652.32–1769.7)	956.14 (898.97–1010.43)	−1.8 (−1.9 to −1.8)	<0.0001	−1.2 (−1.3 to −1.1)	<0.0001	−0.9 (−1.1 to −0.7)	<0.0001
	Female	1415.25 (1334.96–1480.55)	790.94 (724.75–846.98)	−1.8 (−1.9 to −1.8)	<0.0001	−1.5 (−1.5 to −1.4)	<0.0001	−1.3 (−1.4 to −1.1)	<0.0001
YLDs (Years Lived with Disability)	Both	148.31 (106.56–188.42)	120.38 (87.52–153.71)	−0.7 (−0.7 to −0.7)	<0.0001	−0.8 (−0.9 to −0.7)	<0.0001	−0.6 (−0.8 to −0.6)	<0.0001
	Male	144.59 (104.6–183.99)	118.36 (85.61–150.78)	−0.6 (−0.7 to −0.6)	<0.0001	−0.7 (−0.8 to −0.7)	<0.0001	−0.6 (−0.7 to −0.5)	<0.0001
	Female	152.28 (109.16–194.42)	122.89 (89.53–157.37)	−0.7 (−0.7 to −0.7)	<0.0001	−0.8 (−0.9 to −0.8)	<0.0001	−0.7 (−0.9 to −0.6)	<0.0001
YLLs (Years of Life Lost)	Both	1404.21 (1332.78–1441.32)	748.76 (692.97–792.27)	−2 (−2 to −1.9)	<0.0001	−1.4 (−1.5 to −1.3)	<0.0001	−1.2 (−1.3 to −0.9)	<0.0001
	Male	1570.3 (1514.72–1607.79)	837.78 (787.03–886.27)	−2 (−2 to −1.9)	<0.0001	−1.3 (−1.4 to −1.2)	<0.0001	−0.9 (−1.1 to −0.7)	<0.0001
	Female	1262.97 (1182.24–1305.79)	668.05 (608.34–713.49)	−2 (−2.1 to −2)	<0.0001	−1.6 (−1.6 to −1.4)	<0.0001	−1.3 (−1.5 to −1.1)	<0.0001
Ischemic stroke									
Incidence	Both	92.31 (77.74–108.94)	57.55 (49.51–66.13)	−1.5 (−1.5 to −1.5)	<0.0001	−0.5 (−0.5 to −0.4)	<0.0001	−0.3 (−0.3 to −0.2)	<0.0001
	Male	102.65 (86.06–122.16)	63.27 (54.48–73.11)	−1.5 (−1.5 to −1.5)	<0.0001	−0.6 (−0.7 to −0.6)	<0.0001	−0.5 (−0.6 to −0.4)	<0.0001
	Female	83.44 (70.12–98.08)	52.49 (45.28–60.13)	−1.5 (−1.5 to −1.5)	<0.0001	−0.4 (−0.4 to −0.3)	<0.0001	0 (−0.1 to 0.1)	0.38
Prevalence	Both	897.77 (826.53–969.89)	749.17 (698.63–803.09)	−0.6 (−0.6 to −0.6)	<0.0001	−0.5 (−0.6 to −0.5)	<0.0001	−0.4 (−0.6 to −0.3)	<0.0001
	Male	966.05 (886.37–1044.85)	807.29 (748.71–866.58)	−0.6 (−0.6 to −0.6)	<0.0001	−0.5 (−0.6 to −0.5)	<0.0001	−0.3 (−0.5 to −0.3)	<0.0001
	Female	846.07 (779.08–914.76)	703.05 (657.48–754.07)	−0.6 (−0.6 to −0.6)	<0.0001	−0.6 (−0.7 to −0.5)	<0.0001	−0.5 (−0.6 to −0.4)	<0.0001
Deaths	Both	39.62 (35.41–41.66)	20.63 (17.86–22.12)	−2 (−2.1 to −1.9)	<0.0001	−1.2 (−1.3 to −1)	<0.0001	−0.9 (−1.2 to −0.6)	<0.0001
	Male	43.58 (40.52–45.13)	21.89 (19.8–23.24)	−2.1 (−2.2 to −2.1)	<0.0001	−1.1 (−1.2 to −0.9)	<0.0001	−0.8 (−1 to −0.5)	<0.0001
	Female	36.33 (31.51–38.67)	19.34 (16.07–20.98)	−2 (−2 to −1.9)	<0.0001	−1.2 (−1.4 to −1)	<0.0001	−1.2 (−1.4 to −0.8)	<0.0001
DALYs (Disability-Adjusted Life Years)	Both	720.4 (667.73–761.36)	392.96 (355.49–427.51)	−1.9 (−1.9 to −1.8)	<0.0001	−1 (−1.1 to −0.9)	<0.0001	−0.7 (−0.9 to −0.5)	<0.0001
	Male	812.97 (769.42–854.06)	431.11 (397.44–463.1)	−2 (−2 to −1.9)	<0.0001	−1 (−1.1 to −0.8)	<0.0001	−0.5 (−0.7 to −0.1)	0.01
	Female	643.63 (584.58–685.81)	358.58 (318.71–393.71)	−1.8 (−1.9 to −1.8)	<0.0001	−1.1 (−1.2 to −1)	<0.0001	−0.8 (−1 to −0.6)	<0.0001
YLDs (Years Lived with Disability)	Both	111.88 (80.78–142.79)	90.26 (65.85–114.76)	−0.7 (−0.7 to −0.7)	<0.0001	−0.7 (−0.8 to −0.7)	<0.0001	−0.6 (−0.8 to −0.5)	<0.0001
	Male	112.81 (82.32–143.45)	91.81 (66.81–116.46)	−0.7 (−0.7 to −0.7)	<0.0001	−0.6 (−0.7 to −0.6)	<0.0001	−0.5 (−0.6 to −0.4)	<0.0001
	Female	111.59 (79.93–142.36)	89.44 (65.25–113.99)	−0.7 (−0.8 to −0.7)	<0.0001	−0.8 (−0.9 to −0.8)	<0.0001	−0.8 (−0.9 to −0.8)	<0.0001
YLLs (Years of Life Lost)	Both	608.52 (560.31–631.81)	302.7 (270.78–321.61)	−2.2 (−2.2 to −2.1)	<0.0001	−1.1 (−1.3 to −0.9)	<0.0001	−0.6 (−0.9 to −0.2)	0.003
	Male	700.16 (663.8–721.22)	339.3 (313.78–358.83)	−2.2 (−2.3 to −2.2)	<0.0001	−1 (−1.1 to −0.8)	<0.0001	−0.5 (−0.8 to 0)	0.03
	Female	532.04 (476.16–559.65)	269.14 (233.08–288.63)	−2.1 (−2.2 to −2)	<0.0001	−1.2 (−1.3 to −1)	<0.0001	−0.8 (−1.1 to −0.5)	<0.0001
Intracerebral hemorrhage									
Incidence	Both	30.36 (26.59–33.89)	17.88 (15.85–19.77)	−1.7 (−1.7 to −1.7)	<0.0001	−0.7 (−0.8 to −0.7)	<0.0001	−0.3 (−0.4 to −0.1)	0.01
	Male	34.98 (30.62–39.28)	20.72 (18.35–22.99)	−1.7 (−1.7 to −1.7)	<0.0001	−0.8 (−0.9 to −0.7)	<0.0001	−0.4 (−0.5 to −0.2)	<0.0001
	Female	26.62 (23.31–29.84)	15.43 (13.64–17.22)	−1.7 (−1.8 to −1.7)	<0.0001	−0.7 (−0.8 to −0.7)	<0.0001	−0.1 (−0.3 to 0.1)	0.16

(Table 1 continues on next page)

Outcome measure	Sex	Age-standardized rates per 100 000 population		Average annual percent change					
		1990	2021	1990–2021		2010–2021		2015–2021	
		Estimate (95% uncertainty interval)	Estimate (95% uncertainty interval)	Estimate (95% confidence interval)	P-value	Estimate (95% confidence interval)	P-value	Estimate (95% confidence interval)	P-value
(Continued from previous page)									
Prevalence	Both	193.42 (177.3–210.61)	145.63 (134.12–157.21)	−0.9 (−1 to −0.9)	<0.0001	−1.4 (−1.5 to −1.3)	<0.0001	−1 (−1.1 to −0.8)	<0.0001
	Male	203.15 (185.72–221.94)	155.14 (142.76–168.18)	−0.9 (−0.9 to −0.9)	<0.0001	−1.4 (−1.5 to −1.3)	<0.0001	−1.1 (−1.2 to −1)	<0.0001
	Female	185.89 (169.59–202.1)	137.92 (127.31–149.01)	−1 (−1 to −1)	<0.0001	−1.4 (−1.5 to −1.3)	<0.0001	−0.9 (−1.1 to −0.7)	<0.0001
Deaths	Both	23.38 (22.25–24.06)	13.22 (12.13–14.03)	−1.8 (−1.9 to −1.8)	<0.0001	−1.8 (−1.9 to −1.7)	<0.0001	−1.7 (−1.9 to −1.5)	<0.0001
	Male	26.98 (25.96–27.73)	15.52 (14.54–16.46)	−1.8 (−1.8 to −1.8)	<0.0001	−1.6 (−1.7 to −1.5)	<0.0001	−1.5 (−1.7 to −1.3)	<0.0001
	Female	20.4 (19.19–21.09)	11.2 (10.04–12.01)	−1.9 (−2 to −1.9)	<0.0001	−2.1 (−2.2 to −1.9)	<0.0001	−1.9 (−2.2 to −1.7)	<0.0001
DALYs (Disability-Adjusted Life Years)	Both	638.16 (620.32–655.77)	336.56 (317.61–355.77)	−2.1 (−2.1 to −2)	<0.0001	−1.8 (−1.9 to −1.7)	<0.0001	−1.6 (−1.8 to −1.4)	<0.0001
	Male	733.43 (715.25–752.29)	399.77 (376.99–422.67)	−1.9 (−2 to −1.9)	<0.0001	−1.6 (−1.7 to −1.5)	<0.0001	−1.4 (−1.6 to −1.2)	<0.0001
	Female	554.96 (534.89–573.96)	279.85 (261.38–299.54)	−2.2 (−2.2 to −2.1)	<0.0001	−2.1 (−2.2 to −2)	<0.0001	−1.8 (−2 to −1.5)	<0.0001
YLDs (Years Lived with Disability)	Both	22.22 (16.13–28.45)	17.19 (12.56–22.01)	−0.8 (−0.9 to −0.8)	<0.0001	−1.4 (−1.5 to −1.4)	<0.0001	−1.2 (−1.4 to −1.1)	<0.0001
	Male	21.72 (15.88–27.85)	17.15 (12.46–21.9)	−0.8 (−0.8 to −0.7)	<0.0001	−1.4 (−1.5 to −1.4)	<0.0001	−1.3 (−1.4 to −1.2)	<0.0001
	Female	22.81 (16.43–29.26)	17.35 (12.64–22.36)	−0.9 (−0.9 to −0.9)	<0.0001	−1.6 (−1.7 to −1.5)	<0.0001	−1.2 (−1.3 to −1)	<0.0001
YLLs (Years of Life Lost)	Both	615.94 (598.63–631.36)	319.37 (300.69–338.41)	−2.1 (−2.1 to −2.1)	<0.0001	−1.8 (−1.9 to −1.7)	<0.0001	−1.6 (−1.8 to −1.4)	<0.0001
	Male	711.71 (692.25–730.45)	382.62 (360.86–405.55)	−2 (−2 to −1.9)	<0.0001	−1.6 (−1.7 to −1.5)	<0.0001	−1.4 (−1.6 to −1.1)	<0.0001
	Female	532.15 (512.12–550.15)	262.51 (244.42–280.44)	−2.3 (−2.3 to −2.2)	<0.0001	−2.1 (−2.2 to −2)	<0.0001	−1.8 (−2 to −1.5)	<0.0001
Subarachnoid hemorrhage									
Incidence	Both	10.52 (9.22–12.13)	9.06 (8–10.24)	−0.5 (−0.5 to −0.5)	<0.0001	0.5 (0.4–0.5)	<0.0001	0.8 (0.7–0.9)	<0.0001
	Male	8.62 (7.49–9.88)	7.86 (6.97–8.88)	−0.3 (−0.3 to −0.3)	<0.0001	0.6 (0.5–0.6)	<0.0001	0.9 (0.8–1)	<0.0001
	Female	12.31 (10.77–14.24)	10.21 (8.99–11.6)	−0.6 (−0.6 to −0.6)	<0.0001	0.4 (0.3–0.4)	<0.0001	0.9 (0.7–1)	<0.0001
Prevalence	Both	125.7 (114.72–138.29)	117.37 (108.31–127.18)	−0.2 (−0.3 to −0.2)	<0.0001	−0.1 (−0.1 to 0)	<0.0001	0 (−0.1 to 0.1)	0.24
	Male	99.02 (90.11–109.05)	94.3 (87.08–102.1)	−0.2 (−0.2 to −0.2)	<0.0001	0 (−0.1 to 0)	0.63	0.1 (0–0.2)	0.02
	Female	149.62 (136.42–164.4)	138.18 (127.56–149.54)	−0.3 (−0.3 to −0.2)	<0.0001	−0.1 (−0.2 to −0.1)	<0.0001	0 (−0.1 to 0)	0.41
Deaths	Both	5.31 (5.09–5.49)	4.27 (3.98–4.52)	−0.7 (−0.7 to −0.7)	<0.0001	−0.9 (−1.1 to −0.8)	<0.0002	−1.2 (−1.4 to −1)	<0.0001
	Male	4.57 (4.38–4.79)	3.87 (3.62–4.12)	−0.5 (−0.6 to −0.5)	<0.0001	−0.6 (−0.8 to −0.5)	<0.0003	−0.9 (−1.2 to −0.7)	<0.0001
	Female	5.93 (5.61–6.17)	4.61 (4.26–4.9)	−0.8 (−0.9 to −0.8)	<0.0001	−1.1 (−1.3 to −1)	<0.0004	−1.4 (−1.6 to −1.1)	<0.0001
DALYs (Disability-Adjusted Life Years)	Both	193.96 (187.32–200.34)	139.62 (132.07–148.28)	−1 (−1.1 to −1)	<0.0001	−1 (−1.1 to −0.9)	<0.0005	−1 (−1.1 to −0.9)	<0.0001
	Male	168.49 (162.26–175.66)	125.26 (118.06–133.51)	−0.9 (−1 to −0.9)	<0.0001	−0.8 (−0.9 to −0.7)	<0.0006	−1 (−1.2 to −0.8)	<0.0001
	Female	216.67 (205.72–225.58)	152.51 (143.1–163.23)	−1.1 (−1.2 to −1.1)	<0.0001	−1.2 (−1.3 to −1.1)	<0.0007	−1.2 (−1.3 to −1.1)	<0.0001
YLDs (Years Lived with Disability)	Both	14.21 (10.21–18.33)	12.93 (9.24–16.57)	−0.3 (−0.3 to −0.3)	<0.0001	−0.2 (−0.3 to −0.2)	<0.0008	−0.2 (−0.3 to −0.1)	<0.0001
	Male	10.06 (7.23–12.9)	9.4 (6.77–12.01)	−0.2 (−0.3 to −0.2)	<0.0001	−0.1 (−0.2 to −0.1)	<0.0009	0 (−0.1 to 0)	0.55
	Female	17.88 (12.9–23.1)	16.11 (11.43–20.59)	−0.3 (−0.4 to −0.3)	<0.0001	−0.3 (−0.4 to −0.3)	<0.0010	−0.2 (−0.4 to −0.2)	<0.0001
YLLs (Years of Life Lost)	Both	179.75 (173.94–184.97)	126.7 (119.08–134.1)	−1.1 (−1.1 to −1.1)	<0.0001	−1.1 (−1.1 to −1)	<0.0011	−1.1 (−1.1 to −1)	<0.0001
	Male	158.43 (152.31–165.31)	115.86 (108.76–123.86)	−1 (−1.1 to −1)	<0.0001	−0.9 (−1 to −0.7)	<0.0012	−1.1 (−1.3 to −0.8)	<0.0001
	Female	198.78 (188.04–206.38)	136.4 (127.68–145.48)	−1.2 (−1.2 to −1.2)	<0.0001	−1.3 (−1.3 to −1.1)	<0.0013	−1.3 (−1.4 to −1.1)	<0.0001

Table 1: **Age-standardized incidence, prevalence, mortality, and disability-adjusted life years rates (per 100,000 persons) from stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage in the region of the Americas in 1990, 2010, 2015, and 2021 and the average annual percent change for 1990–2021, 2010–2021, and 2015–2021.**

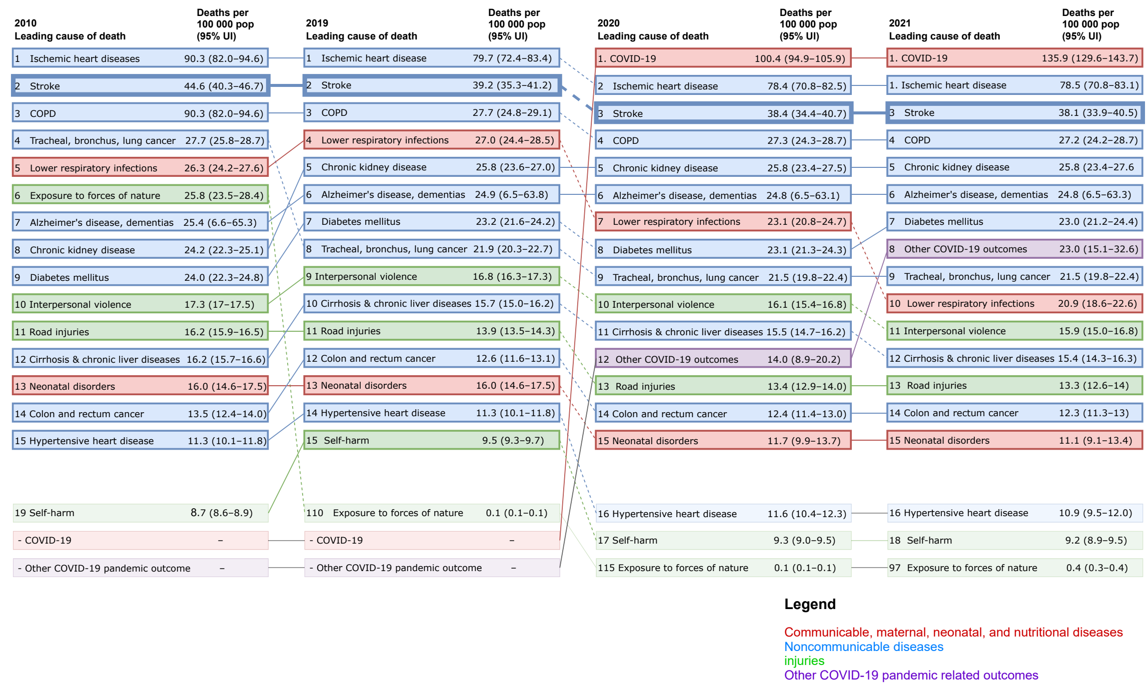

Fig. 1: Leading 15 Level 3 causes of death ranked by age-standardized death rates per 100 000 population for both sexes combined in the Region of the Americas 2010, 2019, 2020, and 2021. Footnotes: Among the 15 leading Level 3 causes of death, stroke is highlighted by the thicker border in the text box. Each cause is color coded by the corresponding GBD Level 1 groups of causes as informed in the legend. GBD = Global Burden of Disease study.

subarachnoid hemorrhage increased for males (0.1% [0.0–0.2]) and stagnated for females (0.0% [–0.1 to 0.0]) (Table 1).

Temporal trends in the stroke burden by age and sex in the region

During 1990–2021, the age-specific incidence, prevalence, mortality, and DALYs rates from stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage by sex in the region had downward trends in most age groups, except for subarachnoid hemorrhage among older adults (75+ years), intracerebral hemorrhage prevalence in males 75+ years, and subarachnoid hemorrhage prevalence in males aged 15–49 years (Fig. 3). In contrast, during 2015–2021, trends in incidence rates from stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage reversed to increasing in most age groups. Importantly, those increasing incidence trends were worse for females than males, specifically in stroke for females aged 15 years and over, in ischemic stroke for middle-aged adults (15–49 years) and adults (50–74 years), and in intracerebral hemorrhage for 50–74 years and +75 years. Furthermore, trends in mortality and DALY from ischemic stroke among young and middle-aged adults and adults for males and females reversed toward upward with an AAPC over 1.4% (Fig. 4).

National burden of stroke and stroke subtypes

The age-standardized incidence, prevalence, mortality, DALYs, YLLs, and YLDs rates per 100 000 population due to stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage in 2021, and their AAPC for periods 1990–2021, and 2015–2021 varied substantially across countries and territories of the Americas (Supplementary Fig. S5 and Table S2). Significant decreasing trends were observed in most countries from 1990 to 2021, but trends shifted to stagnant or increasing in several countries from 2015 to 2021. Detailed findings are in Supplementary Section 3.

Key findings from examining the incidence, mortality, and DALYs rates from stroke and stroke subtypes in 2021 and their trends latest years (2015–2021) are as follows.

Stroke

The highest incidence (≥107.7 cases per 100,000) was observed in eleven countries, notably Guyana and Haiti. Stroke incidence decreased in most countries from 1990 to 2021, but it stagnate or increased in fifteen countries from 2015 to 2021. Of them, Dominican Republic, Grenada, and Jamaica had high level and increasing trends. Mortality was high (≥82.9 deaths/100 000) mostly in Caribbean countries. Jamaica, Peru, Saint Lucia, and Venezuela experienced increasing trends

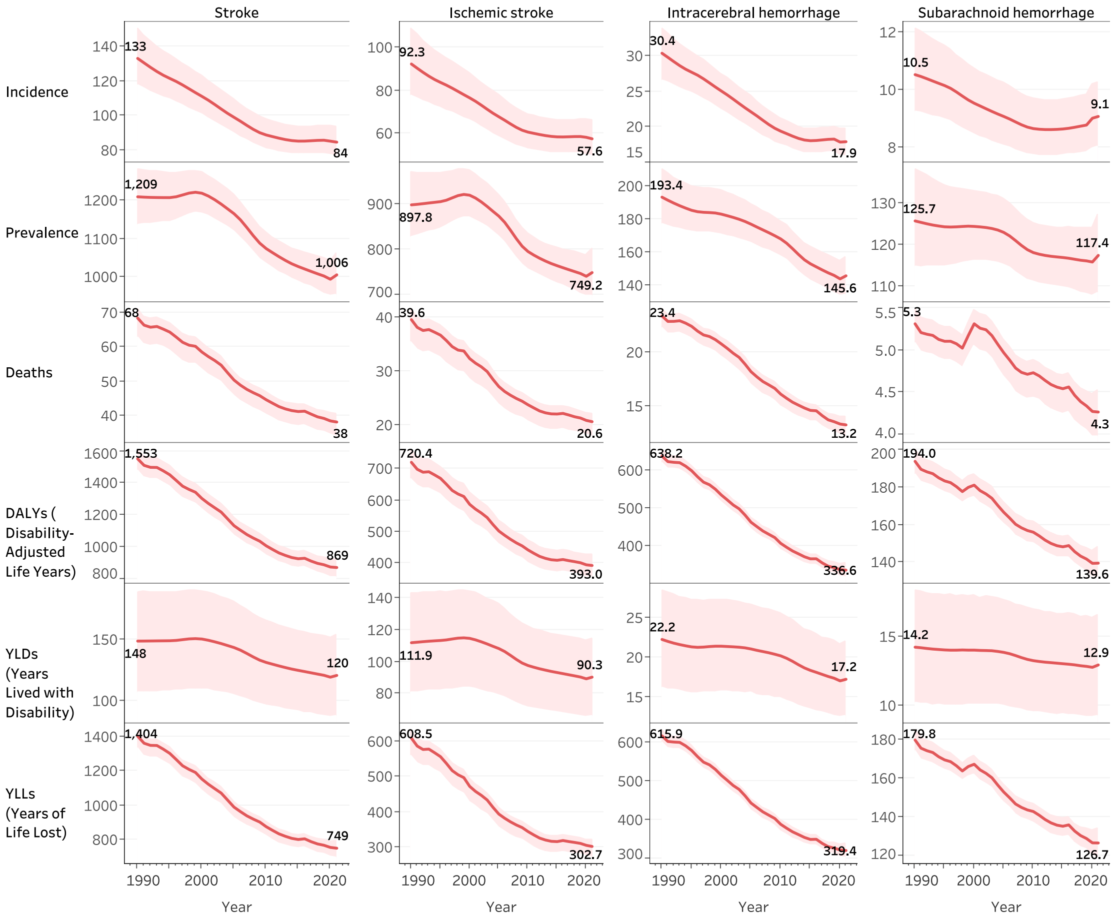

Fig. 2: Age-standardized rates of incidence, prevalence, deaths, DALYs, YLLs, and YLDs caused by stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage in both sexes combined in the Region of the Americas, 1990–2021. Footnotes: Red line represents the temporal trend of mean estimates, and the pink band represent the 95% uncertainty intervals of the mean estimate. DALYs = Disability-Adjusted Life Years, YLDs = Years Lived with Disability, YLLs = Years of Life Lost.

from 2015 to 2021, and of them, Jamaica, and Saint Lucia also had high mortality. During 2015–2021, trends in DALY reversed to increasing in three countries (Peru, Venezuela, and Jamaica), and shifted to constant in Saint Lucia, Trinidad and Tobago, Cuba, Suriname, Costa Rica, and Barbados. Only Jamaica had a high level and increasing trend (Fig. 5).

Ischemic stroke

The highest incidence was observed in Grenada, Guyana, Haiti, and Saint Kitts and Nevis. From 2015 to 2021, the trend shifted to increasing in nine countries, three of which (Dominican Republic, Grenada, and Saint Lucia) had also high incidence. Trends stagnated or reversed to increase in Costa Rica, Jamaica, Peru, Saint Lucia, Saint Vincent and the Grenadines, the United States of America (USA), and Venezuela. High DALY rates (≥732.0 years/100 000) occurred mostly in Caribbean countries. Trends in DALY rates reversed to increase in Peru, Saint Lucia, and Venezuela and it turned to constant in Colombia, Costa Rica, Jamaica, and the USA. Two countries (Jamaica, and Saint Lucia) had high levels and increasing trends (Fig. 5).

Intracerebral hemorrhage

High incidence rates (≥31.2 cases/100 000) were observed in the eight Caribbean countries. Dominica, Dominican Republic, Jamaica, and the USA had increasing trends from 2015 to 2021, and only Dominican Republic, and Jamaica had high levels and increasing trends. Mortality was high (≥31.4 deaths/ 100 000) in Caribbean countries and 2015–2021 trends shifted to increase in Jamaica, Peru, and Venezuela. Only Jamaica had high levels and increasing trends in incidence and mortality. The 2015–2021 DALY trends shifted to increasing in Jamaica, Peru, and Venezuela,

Fig. 3: Average annual percent change for period 1990–2021 of the age-specific incidence, prevalence, mortality and DALY rates per 100 000 population caused by stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage by age group and sex in the Region of the Americas. Footnotes: Short horizontal dashes represent the mean estimates of the average annual percent change (AAPC) for each outcome. The vertical line represents the 95% confidence interval of the estimated mean AAPC. The color in the marks informs the trend as red for increasing trends, gray for constant trends, and blue for decreasing trends.

while Jamaica had high level and increasing trend (Fig. 5).

Subarachnoid hemorrhage

During 2015–2021, trends reversed to increase in 22 (58%) countries and territories, including highly populated countries such as Brazil, Mexico, Venezuela, and the USA. Two countries (Jamaica, and Venezuela) had high incidence in 2021 and increasing trends during 2015–2021. In 2015–2021, increasing trends in mortality were observed in Peru, and Venezuela. Indeed, Venezuela had a high level and increasing trend in incidence and mortality. The trends in DALY rates varied across countries. Most countries, except Honduras, Guatemala, and Mexico, had decreasing trends from 1990 to 2021. Recently (2015–2021), the trend in DALY shifted to increasing in Venezuela, which level remained high in 2021 (Fig. 5).

National burden of stroke and stroke subtypes by age

Trends in stroke and stroke subtypes burden in each age group (5–14 years, 15–49 years, 50–74 years, and 75+ years) shifted from decreasing during 1990–2021 to increasing in the latest years (2015–2021) in several countries. Many countries experienced increasing incidence rates from each stroke type, notably ischemic stroke and subarachnoid hemorrhage in most ages, and increasing mortality from ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage in age groups 5–14, 15–49, and 50–74 years during 2015–2021 (Supplementary Fig. S6). Trends in stroke and stroke subtypes incidence, mortality, and DALY by age group varied across countries and territories, as illustrated in Supplementary Fig. S7–9. For example, during 2015–2021, trends in stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage incidence among children and adolescents aged 5–14 years reversed to increase in almost all countries. Among people aged 15–49 years, incidence rates from stroke increased in 22 countries, notably Venezuela, Mexico, Brazil and the USA (Supplementary Fig. S7A).

Stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage mortality decreased from 1990 to 2021 in most countries, with a few exceptions. Focusing on ischemic stroke mortality in age groups 15–49 and 50–74 years, where regional increasing trends during 2015–2021 were observed, we noted increasing trends in 13 (34%) countries in people aged 15–49 years, including highly populated middle socio-demographic index countries (Venezuela, Brazil, Mexico, Peru, and Colombia) and high socio-demographic index countries such as the USA, and Canada (Fig. 5). In adults aged 50–74 years, the ischemic stroke mortality rates increased

Fig. 4: Average annual percent change for period 2015–2021 of the age-specific incidence, prevalence, mortality and DALY rates per 100 000 population caused by stroke, ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage by age group and sex in the Region of the Americas. Footnotes: Short horizontal dashes represent the mean estimates of the average annual percent change (AAPC) for each outcome. The vertical line represents the 95% confidence interval of the estimated mean AAPC. The color in the marks informs the trend as red for increasing trends, gray for constant trends, and blue for decreasing trends.

in nine (24%) countries, including populated countries such as Venezuela, the USA, Peru, and Colombia, as well as Caribbean countries such as Saint Kitts and Nevis, Trinidad and Tobago, Barbados, Saint Lucia, and Dominican Republic (Fig. 6).

Comparing the trends in ischemic stroke mortality and incidence in age groups 15–49, and 50–74 years as illustrated in Supplementary Fig. S10, we observed that the AAPC in mortality rises with AAPC in incidence, suggesting a positive association. For the age group 15–49 years, 11 countries had increasing trends in both mortality and incidence, and for 50–74 years, 12 countries were in that category, including Brazil, Mexico, Peru, Trinidad and Tobago, the USA, and Venezuela. Diverging patterns emerged when these relationships were stratified by socio-demographic index quintile (Supplementary Fig. S11). For less developed socio-demographic countries (socio-demographic index quintile 1) increasing incidence leads to increasing mortality. In contrast, for highly developed socio-demographic countries, the increasing trend in incidence, does not lead to an increasing trend in mortality.

Discussion

Stroke continues to be among the foremost causes of mortality in the region, ranking in the top three alongside COVID-19 and IHD in 2021. The deceleration in the decline of most stroke and stroke subtype outcome measures is worrying and consistent with previous studies reporting the slowdown in the reduction of premature mortality from CVD, particularly IHD and stroke within this geographic area.[13] Notably, there has been a noticeable rise in stroke incidence among younger populations over the past decade, with marked differences between sexes.

The noticed shift in the regional incidence trends is due to a recent increase in stroke incidence in several countries, more evident during the period 2015–2021. This trend is significant for ischemic stroke and subarachnoid hemorrhage, and is most pronounced in younger age groups, which is consistent with previous reports.[14,33–35] Although traditional vascular risk factors, such as hypertension, diabetes mellitus, and overweight,[36–38] are increasingly prevalent and poorly controlled among younger patients, maybe they do not fully account for the observed increase in incidence in this group.[34] Emerging risk factors such as chronic inflammation,[39] air pollution and noise, psychosocial stress, as well as drug abuse among the younger may also play a role.[40–43] In addition, known social determinants of CVD as limited access to quality care, food and housing insecurity,[44] low education, as well as the rising prevalence of sedentary lifestyles[45] and poor

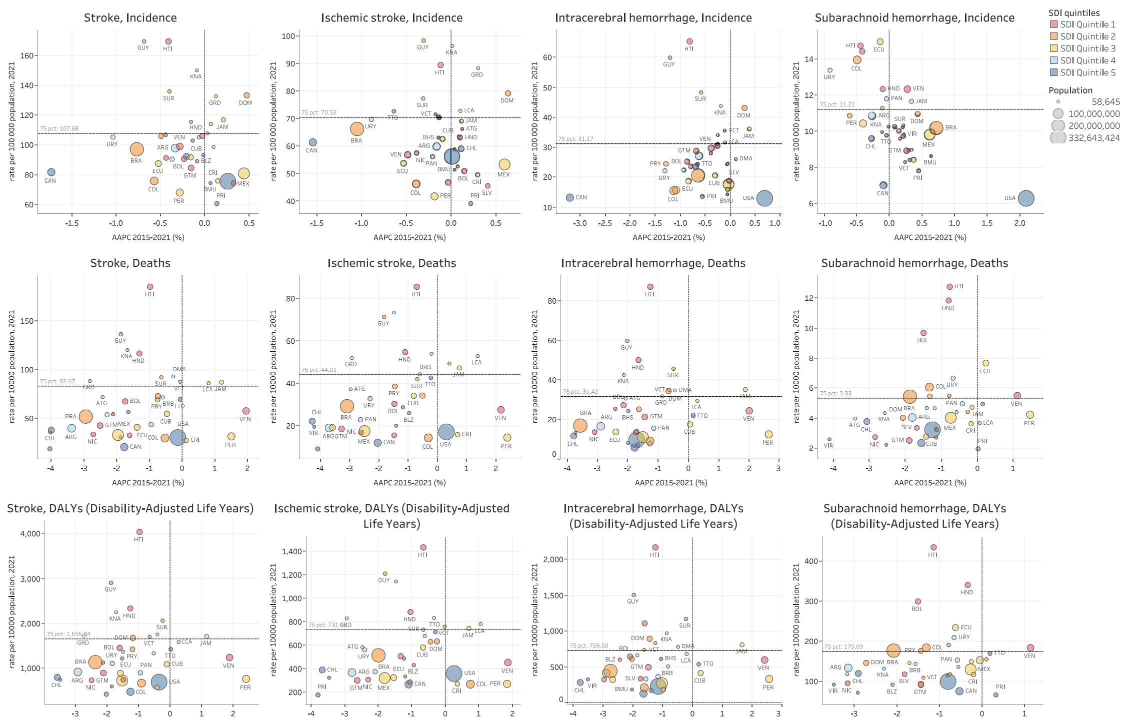

Fig. 5: Age-standardized incidence, mortality and DALY rates from stroke and stroke subtypes in 2021, and their average annual percentage change in the period 2015–2021 across 38 countries and territories of the Americas. Footnotes: Each circle represents a country, whose size is proportional to the country's total population in 2021, and the circle's color represents the country's socio-demographic index (SDI) quintile in 2021. Each country is labeled with the ISO 3166 three-letter (alpha-3) country code. The horizontal dashed line represents the 75th percentile or upper quartile of the outcome rate distribution, and the vertical dashed line represents the zero value of the average annual percentage change (AAPC).

dietary habits in younger populations are probably contributing to increased stroke risk in this age group.[35] Conversely, part of the observed increase may be attributed to progress in acute stroke management observed in North America[46] and in some Latin American countries[47] including improved detection and diagnosis of minor events and greater utilization of magnetic resonance imaging (MRI), potentially leading to a diagnostic shift from transient ischemic attack to stroke.[34]

Special mention to the detected broad increase in subarachnoid hemorrhage. Indeed, incidence rates for subarachnoid hemorrhage in both males and females have shown a reversal towards an increase from 2015 to 2021. This increase was observed in many (22 out of 38) countries and territories of the Americas. It is known that subarachnoid hemorrhage risk is particularly associated with hypertension, smoking, and excessive alcohol intake.[48] Being risk factors that are increasingly augmenting, these findings should be considered when planning stroke prevention programs specially in the most affected countries. Such increase might also be related to better case ascertainment, pre-hospital care, and diagnosis, including new imaging technologies, in the last decade.

Importantly, age-standardized incidence rates for stroke in females have shown a reversal towards an increase from 2015 to 2021. Specifically, there is a higher AAPC in females aged 15–49 and 50–74 years compared to males in this period. This is an unusual pattern, as premenopausal women have a lower risk of stroke than their male counterparts and the difference in stroke incidence between males and females narrows as stroke incidence increases in postmenopausal females.[49,50] The observed increase in younger females may be due to increasing exposure to risk factors specific to the female population, which might be changing over time and increasing in the latest decades, such as adverse pregnancy outcomes, exogenous estrogen, contraceptives, as well as increasing prevalence of common vascular risk factors such as hypertension, obesity, diabetes, and atrial fibrillation.[49,51] Part of this observed increasing incidence in females may be also attributed to improved detection.[52] A better understanding of determinants of

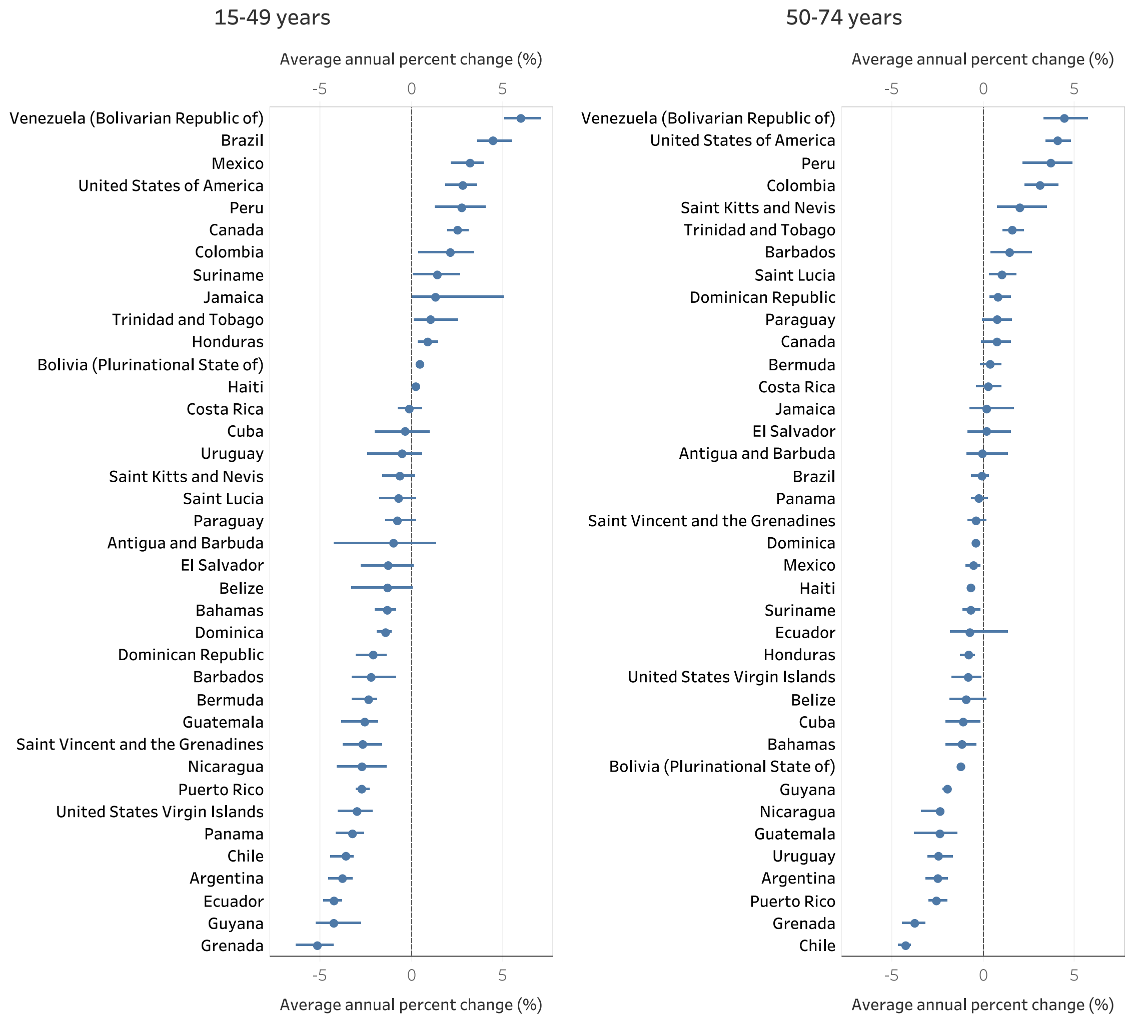

Fig. 6: Average annual percentage change during 2015–2021 of age-specific ischemic stroke mortality rates in people aged 15–49 years and 50–74 years across countries. Footnotes: Countries are sorted in descending order of the average annual percent change (AAPC) for the period 2015–2021 of the age-standardized mortality rate per 100 000 population. The dot represents the point estimates of the AAPC and the horizontal line represents the AAPC 95% credible interval. Footnotes: DALYs = Disability-adjusted life years, YLDs = Years lived with disability, YLLs = Years of life lost due to premature mortality. Figures marked in bold-red indicates an increasing trend, while those marked in bold-black indicates constant trend.

strokes in this population in the region is a priority for future research to inform prevention strategies and policy development.

An increase in mortality rates for certain stroke subgroups was observed in various countries in the region, particularly in ischemic stroke among younger populations, with over one-third of countries reporting elevated ischemic stroke mortality rates in the 15–49 age range. Notably, the AAPC in ischemic stroke mortality was directly associated with the AAPC in incidence in countries within the lowest quintile of the socio-demographic index. In contrast, higher socio-demographic index countries show an inverse association. These findings suggest inadequate access to high quality and effective medical interventions in lower socio-demographic index countries, resulting in high mortality rates. Conversely, in higher socio-demographic index countries, improved individual access to high quality healthcare systems may reduce mortality despite rising incidence, indicating a better performance of the stroke control program. The rising ischemic stroke mortality alongside incidence in lower socio-demographic development countries underscoring the urgent need for strengthened healthcare interventions to prevent mortality in these populations and the critical need to address healthcare disparities to enhance outcomes across different socioeconomic contexts.

There is a diversity of characteristics between the countries and territories contributing to these increasing trends and a scattered upward trend in both traditional and non-traditional risk factors in the region. Some countries have recently implemented strategies to control modifiable risk factors, particularly to improve hypertension control and CVD risk management,[53,54] while others had pre-existing measures that are now deemed insufficient and have a concurrent increase in other less recognized risk factors, including those specifically related to females, among others. Detailed and updated analyses of stroke risk factors[55] and available stroke policies[56] in the Region will be addressed in subsequent publication by this writing group. Close monitoring is essential to assess the need for improved preventive measures against this disease. Rising incidence rates may reflect insufficient public health interventions, high obesity prevalence, increasing diabetes, and poor hypertension control.[38,57]

The impact of the COVID-19 pandemic was devastating for society, the economy, and health, affecting all countries in the world, and especially this Region.[18] This study shows that COVID-19, the leading cause of death in the Americas (2020–2021), displaced stroke from the second cause of death for the first time in the last three decades (1990–2019). Furthermore, this study confirms that stroke mortality rates during the pandemic remained stable compared to the pre-pandemic period and maintained the decelerating trend observed since the mid-2010s.

Given the findings previously discussed, it is essential to review the initiatives that have been developed in the Region of the Americas. These initiatives can have a crucial impact on the stroke epidemiology, to expand the efforts to areas with limited resources. In the region, 33 countries and more than 6000 primary health facilities are implementing HEARTS,[53,54] the flagship program of WHO/PAHO for the prevention and control of CVD. HEARTS in the Americas is aimed to drive health services to change managerial and clinical practice in primary care settings to improve population-wide hypertension control. High systolic blood pressure is the primary modifiable risk factor for stroke. Population-based interventions, such as dietary salt reduction, and cost-effective hypertension management in primary care can significantly reduce stroke burden. In addition, HEARTS is also aimed at optimizing CVD primary and secondary prevention including stroke, an intervention underutilized in most countries globally.[58] Indeed, if the Americas improved population-based hypertension control from the current level of 36% to a target of 50%, over 400,000 CVD deaths could be avoided, including 120,000 stroke deaths and over half of a million of stroke events. Furthermore, if secondary CVD prevention efforts were expanded, many more deaths could be averted.[57]

In addition, several initiatives have been undertaken over recent decades aimed at improving stroke care and reduce stroke disparities in the Region. They include the Latin American Global Stroke Alliance (GSA) initiative to empower young medical stroke physicians (The Young Stroke Latin American Task Force [ALA-TAC]),[47,59] as well as the World Stroke Organization (WSO) Roadmap for Quality of Stroke Services implementation task force in Latin America, the WSO/Iberо-American Stroke Society Certification Program aimed at the continuously improvement of services and qualification of comprehensive care and the establishment of Stroke Centers Certification, and the implementation of acute stroke networks and care plans across Latin American countries.

This study has several strengths. First, it used the most comprehensive and recent estimates of the stroke burden, including major stroke subtypes, from the GBD study. Estimates of stroke outcomes have been produced using standardized and robust methods, aimed to overcome limitations or biases in the primary data sources, providing uncertainty information for each point estimates, and generating comparable estimates. Second, we applied Joinpoint regression methods[30,31] to estimate the AAPC, which allows us to assess and characterize the temporal trends through a summary and comparable measure of temporal trend. Importantly, this study explores and documented with data, the potential impact of the COVID-19 pandemic on stroke burden and care.

Some of the limitations of this study deserve specific attention: there are limitations inherent to the GBD Study, which are documented elsewhere.[17–19,60] In brief, limitations related to the accuracy of stroke outcomes ascertainment, which is determined by the data input sources. Administrative data or other sources that rely on ICD codes may be prone to misclassification and miscoding. Moreover, incompleteness and sparsity of data or unreliability of data from specific countries, years, or age groups can influence the accuracy of the estimates, particularly from countries with poor data quality and coverage, where estimates depend heavily on the modeling process. For example, Vital Registration is the main and most relevant input source for estimating mortality, and YLLs. While the quality of vital registration is high or medium for most countries of the region, vital registration is of low quality for some countries (Haiti, Bolivia, Honduras) in terms of completeness, and classification of causes of death. GBD study applied standard methods to overcome such data quality issues, specifically for low quality data, the estimates are mostly based on the modeling strategy, considering covariates and information from countries with similar epidemiological, social, economic, and geographical characteristics. Therefore, the estimates from countries with low quality or missing data input sources must be interpreted with caution. Second, model misspecifications could be a possible source of bias, so estimates and their 95% UI should be considered for judging, analyzing and interpreting results. Third, we lacked detailed information on stroke characteristics other than subtypes. Greater phenotypic detail can better inform the burden and trends in stroke-by-stroke etiology and severity. Fourth, although we reported on country, age, and sex disparities as well as trends in stroke burden, the use of GBD data precluded us from analyzing the data disaggregated at subnational levels (and thus comparing smaller regions/populations with higher burden within large countries, to those of small countries with high burden), race and ethnicity, or any other local Social Determinant of Health. Lastly, we did not include in our analysis information on access and quality of stroke health services in our analysis.

Stroke is a major public health problem in the Region of the Americas. Its societal and economic impact is massive and devastating, especially for low-resource settings and vulnerable people. Despite significant progress in prevention and care, recent trends in stroke burden confirm a deceleration in the decline pace for most stroke-related health outcomes. Indeed, there has been a noticeable rise in stroke incidence over the past decade starting in early middle age, with more negative impact on females. Stroke mortality during the pandemic remained stable compared to the pre-pandemic period, however, we must remain alert as it is premature to quantify the impact of COVID-19 on stroke burden and care. A regional shared technical and political agenda to strengthen the stroke surveillance, prevention and care is an imperative to address the current stroke burden and its demographics.

Contributors

PML, RM, PMV, PO and FF conceived the research idea and designed the study. RM extracted, verified, and processed all the underlying data, conducted the data analysis, and produced the tables and figures. RM and PMV drafted the manuscript with contributions from PO, and PML and CSA reviewed the final version of the manuscript. All authors reviewed the manuscript and contributed important intellectual content to the study and commented critically on the manuscript. All authors have full access to all the data in the study, accept accountability for the overall work, and the corresponding author had the final responsibility for submitting the manuscript for publication.

Data sharing statement

All results are publicly available via the online GBD Results Tool [https://vizhub.healthdata.org/gbd-results/] and the GBD Compare [https://vizhub.healthdata.org/gbd-compare/], and all data input sources are identified via the GBD 2021 Sources Tool [https://ghdx.healthdata.org/gbd-2021/sources]. There is no **individual de-identified participant data, and there are no additional, related documents to make available.** The database is already accessible on the specified websites and will remain available as determined by the project, in accordance with its access criteria**. The data that underlie the results reported in this article (text, tables, figures, and appendices) will be available immediately following publication until no end date, to anyone who wishes to access the data, for any purpose, upon written request to the corresponding author.**

Declaration of interests

CA: received honoraria as Speaker from Boehringer Ingelheim; TFA: received honoraria as Speaker from Boehringer Ingelheim; PA: received honoraria as Speaker from Boehringer Ingelheim, Abbott, Ipsen, Boston Scientific and Knigth therapeutics; CSA: Receives Grants and fellowship from the National Health and Medical Research Council (NHMRC) of Australia, Medical Research Foundation of the UK, Consulting fees as Advisory Board for AstraZeneca Australia, is the Vice-President of the World Stroke Organisation and the Editor-in-Chief of Cerebrovascular Diseases journal; MAB: received honoraria as Speaker from Roche and Boehringer Ingelheim; HB: Received payment or honoraria for lectures, presentations from Novartis and Adium Colombia; ACS: Received speaker fees from Boehringer Ingelheim; PML: Received Research grant from Boehringer-Ingelheim, payment as part of Steering Committee from Johnson & Johnson and Advisory Board from Bristol Meyer Squib and Pfizer, honoraria for lectures from Pfizer, Angels educational events from Boehringer Ingelheim, Support for attending meetings and/or travel from the Iberoamerican Stroke Society and Global Stroke Initiative, President of the Chilean Stroke Association (ACEVE) and Vice-president of the Iberoamerican stroke society (SIECV); BO: Editor-in-Chief, Journal of the American Heart Association, President, Society for Equity Neuroscience, Member, World Stroke Organization Board; OPN: Received speaker fees from Boehringer-Ingelheim and Astra-Zeneca; GSS: Received grant from the Brazilian Ministry of Health, Consulting fees from Astrazeneca and Bayer, Payment or honoraria for lectures from Astrazeneca, Bard, Support for attending meetings from Boehringer Ingelheim; SS: Received Grant from NIH Grant support; VU: Received Grant from Genentech, Inc; SA: Received payment or honoraria from Astra Zeneca and Silanes, Support for attending meetings from Astra Zeneca and Raffo, Participation on a Data Safety Monitoring Board from Astra Zeneca, VCN: Received payment or honoraria from Boehringer Ingelheim, AstraZeneca and Sanofi, Support for attending Meetings from Boehringer Ingelheim, LAC: Reveived grant from World Stroke Organization, Consulting fees from Allm Inc, IschemaView, AstraZeneca, Payment or honoraria for lectures from AstraZeneca, Boehringer Ingelheim, IschemaView, Support for attending Meetings from Boehringer Ingelheim, IschemaView, PMV: Received Research grants from ANID Fondecyt Regular 1221837 and Pfizer Research grant 76883481, Grant from Boehringer Ingelheim; AR: Participation on a Data Safety Monitoring Board or Advisory Board from Boston Scientific, Astra Zeneca, Shionogi, Brainomix, Chiesi.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2025.101017.

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