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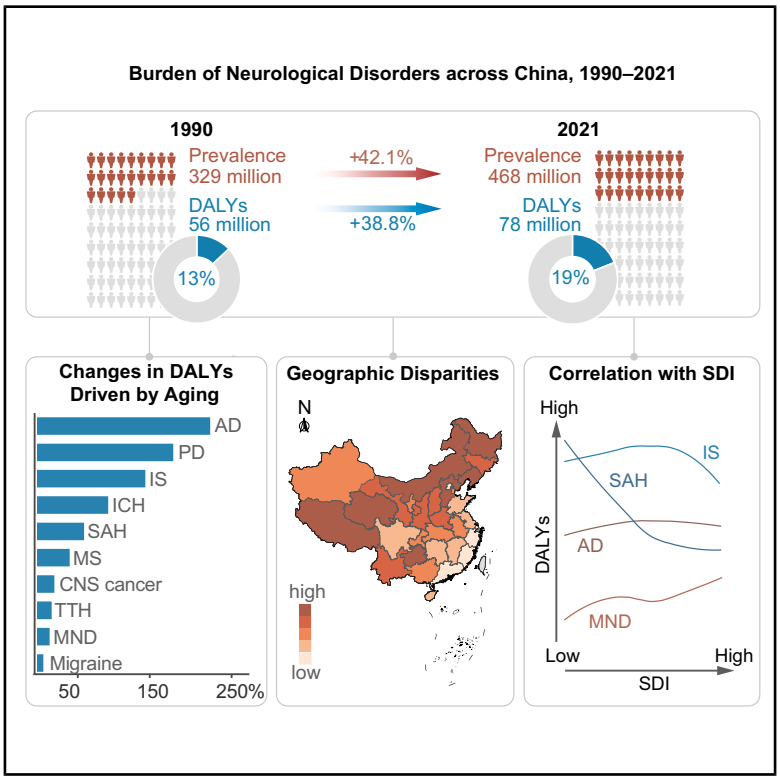
Burden of neurological disorders in China and its provinces, 1990–2021: Findings from the global burden of disease study 2021

Graphical abstract



Highlights

- Neurological disorders affected nearly one-third of China's population in 2021
- Population aging was a key driver of the increasing burden of neurological disorders
- Neurological burden varied between western and eastern provinces despite rising SDI
- Our findings could guide targeted strategies to improve neurological services

Authors

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In brief

GBD 2021 China Neurological Disorders Collaborators reveal a large and growing burden of neurological disorders in China, with demographic and regional disparities underscoring the need for targeted early intervention and optimized long-term management strategies.

Translation to Population Health

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Burden of neurological disorders in China and its provinces, 1990–2021: Findings from the global burden of disease study 2021

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CONTEXT AND SIGNIFICANCE Neurological disorders have been the leading cause of global health loss, yet the neurological burden in China remains poorly understood. Researchers in this study comprehensively examined the distribution and trends of burden due to neurological disorders in China and its provinces. They found that neurological disorders extensively affected the Chinese population across the lifespan, disproportionately impacting the elderly, with population aging being a major driver for the substantial increases in prevalence and health loss. The disparities in the neurological burden among provinces were correlated with socioeconomic development. These findings highlight the heavy burden of neurological disorders in China, underscoring the necessity for improved access to neurological services, early prevention, and standardized treatment to address this growing public health challenge.

SUMMARY

Background: The burden of neurological disorders in China has not been systematically analyzed. We aim to provide a comprehensive estimation of the national and subnational neurological burden across China from the Global Burden of Disease Study (GBD) 2021.

Methods: We assessed burden estimates for 16 neurological disorders by age, sex, and province from 1990 to 2021, with prevalence, death, disability-adjusted life years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs). We performed decomposition analysis to determine contributing factors for DALYs and used the socio-demographic index (SDI) to assess relations with development level.

Findings: In 2021, there were 468.29 million prevalent cases of neurological disorders in China, corresponding to 78.10 million DALYs. Intracerebral hemorrhage was the leading cause of DALYs, followed by ischemic stroke, dementias, and migraine. DALYs of neurological disorders were higher in males than females, peaking at 70–74 years. From 1990 to 2021, the number and age-standardized rate of DALYs significantly decreased for idiopathic epilepsy and subarachnoid hemorrhage, primarily attributed to the reduction in YLLs, while the number of DALYs disproportionately increased for dementias, Parkinson's disease, and ischemic stroke contributed by population aging. The age-standardized DALY rates of seven neurological disorders had more than 5-fold variation between western and eastern provinces, despite reduced burdens with rising SDI.

Conclusions: Neurological disorders pose a large and growing burden on public health, primarily driven by population aging. Our findings could inform priority setting and targeted strategies to optimize neurological service delivery.

Funding: The funding information is presented in the acknowledgments.

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INTRODUCTION

Neurological disorders have emerged as the leading cause of health loss, profoundly impacting people's health and well-being.[1] Based on the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) 2015 and 2016 estimates, researchers for the first time reported the global burden of 14–15 neurological disorders, revealing their substantial role in global disability and mortality.[2,3] Subsequent regional studies further elucidated the heterogeneity in burden distribution across areas like the US, Europe, and India.[4–6] Within the latest GBD 2021 framework, Steinmetz and colleagues expanded the analysis to include neurodevelopmental disorders and neurological complications from systemic conditions, assessing the global burden of 37 neurological disorders.[7] Their findings revealed that 43% of the global population experienced conditions affecting the nervous system in 2021, with an 18% increase in disability-adjusted life-years (DALYs) since 1990, primarily driven by shifts in demographic and disease patterns. Over 80% of the global neurological burden stems from low-income and middle-income countries, mainly due to the high prevalence of neonatal and infectious diseases. Aiming to reduce neurological burden, the World Health Organization (WHO) launched the Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders 2022–2031 with a range of proposed actions, necessitating more information on specific geographies to guide member states in setting their own national targets based on local circumstances and challenges.[1]

Over the past decades, China's health pattern has shifted from communicable and neonatal disorders to chronic non-communicable diseases, with stroke ranking as the leading cause of health loss, accompanied by notable increases in the burden of dementia and headache disorders.[8] However, the overall burden and trends of neurological disorders across China remain unclear. Most previous studies focused on morbidity and mortality of individual neurological diseases like stroke and dementia,[9,10] with scattered reports on rare conditions such as multiple sclerosis (MS) and myasthenia gravis.[11,12] A cross-sectional study in Shanghai[13] analyzed selected neurological disorders (not including stroke) and revealed significant upward trends in the rates of premature mortality from 1995 to 2018, particularly for neurodegenerative diseases. According to the 2020 population census, China has stepped into an aging society, with the population aged 65 years and older reaching 190.64 million (13.50% of the total population), and this aging population is projected to increase in the coming years.[14] Considering the increasing life expectancy, the disease burden of neurological disorders is expected to rise and may seriously challenge the health and social care system of China.[15] Therefore, a comprehensive understanding of the overall neurological burden is crucial for guiding health policy decisions, shaping preventive strategies, optimizing resource allocation, and enhancing healthcare services.

The GBD project provides updated, quantified, and comparable estimates of health loss due to diseases, injuries, and risk factors by demographic, geographic, and temporal variables in each iteration,[16] offering critical insights for global, national, and subnational health planning. Based on the latest GBD 2021, we aim to comprehensively assess the magnitude, distribution, and trends of the burden from neurological disorders in China and its provinces from 1990 to 2021 in terms of prevalence, mortality, DALYs, and its two components. The GBD study currently estimates the burden from specific neurological disorders. In this study, we defined neurological disorders as conditions primarily managed by neurologists in diagnosis, treatment, and care. Thus, we did not include pediatric neurodevelopmental disorders, neonatal conditions, neurological complications from systemic diseases and injuries, and infectious conditions with specific regional pathogen endemicity, as these are beyond the scope of this study. This manuscript was produced as part of the GBD Collaborator Network and in accordance with the GBD Protocol.[17]

RESULTS

Burden of combined neurological disorders in 2021

In 2021, the estimated number of prevalent cases of neurological disorders was 468.29 million in China, accounting for 32.91% of the total Chinese population and 34.35% of the total prevalence from all causes in China (Tables 1 and S1). The number of deaths caused by neurological disorders was 3.28 million in China, accounting for 28.04% of total deaths from all causes. The DALYs due to neurological disorders were 78.10 million in China, accounting for 19.41% of total DALYs from all causes. Notably, non-communicable neurological disorders contributed to more than 99% of all these burden measures due to neurological disorders in 2021.

Among neurological disorder categories in 2021, the five most prevalent diseases were tension-type headache (TTH) (283.81 [95% uncertainty interval [UI], 251.44 to 320.43] million cases), migraine (184.75 [160.84 to 213.63] million cases), ischemic stroke (20.80 [18.62 to 22.995] million cases), Alzheimer's disease (AD) and other dementias (16.99 [14.49 to 19.67] million cases), and Parkinson's disease (PD) (5.08 [4.28 to 6.05] million cases) (Table 1; Figure S1). The five leading causes of death were intracerebral hemorrhage (1.32 [1.11 to 1.57] million deaths), ischemic stroke (1.18 [0.99 to 1.37] million deaths), AD and other dementias (0.49 [0.12 to 1.33] million deaths), PD (92.04 [75.91 to 108.13] thousand deaths), and subarachnoid hemorrhage (91.80 [66.67 to 116.22] thousand deaths). The five most common causes of DALYs were intracerebral hemorrhage (27.46 [22.84 to 32.68] million DALYs), ischemic stroke (23.43 [19.92 to 26.93] million DALYs), AD and other dementias (10.07 [4.95 to 22.22] million DALYs), migraine (6.99 [1.13 to 15.19] million DALYs), and subarachnoid hemorrhage (2.297 [1.73 to 2.85] million DALYs), with the three stroke types accounting for 68% of the total neurological DALYs (Figures 1 and S2).

Age- and sex-specific burden of neurological disorder categories in 2021

In 2021, neurological disorders extensively affected people of all age groups (Figures S3 and S4; Tables S2, S6, and S7; Data S1). As the most common neurological disorders, headache disorders had the highest number and rate of prevalence in each age group except children under 5 years and elderly over 85 years, and the prevalence of migraine was significantly higher

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Table 1. The absolute number and age-standardized rates of DALYs, death, and prevalence by neurological disorder category in China, 1990–2021

		Absolute numbers (thousands)			Age-standardized rate (per 100,000)		
Neurological disorders	Measure	1990	2021	Percentage change, 1990–2021 (%)	1990	2021	Percentage change, 1990–2021 (%)
All neurological disorders	DALYs	56,274.97 (37,843.74 to 74,471.59)	78,097.64 (50,158.05 to 105,860.82)	38.78	6,760.93 (4,638.21 to 8,844.33)	4,149.61 (2,566.14 to 5,720.54)	−38.62
All neurological disorders	deaths	1,808.14 (1,322.79 to 2,280.48)	3,278.24 (2,163.54 to 4,375.77)	81.30	291.68 (203.9 to 376.6)	179.85 (115.52 to 242.91)	−38.34
All neurological disorders	prevalence	329,489.68 (287,221.99 to 373,386.09)	468,288.42 (416,897.48–525,576.93)	42.13	28,013.34 (24,661.94–31,500.26)	30,094.77 (26,635.73–33,813.77)	7.43
Ischemic stroke	DALYs	9,926.13 (8,510.1 to 11,656.22)	23,430.41 (19,918.95 to 26,933.91)	136.05 (89.69 to 190.97)	1,387.93 (1,188.74 to 1,621.4)	1,180.98 (1,009.7 to 1,356.67)	−14.91 (−30.9 to 4.19)
Ischemic stroke	deaths	427.97 (362.34 to 506.37)	1,176.95 (986.88 to 1,372.71)	175.01 (116.14 to 246.57)	75.22 (64.48 to 88.23)	64.47 (54.03 to 74.82)	−14.29 (−31.93 to 6.12)
Ischemic stroke	prevalence	6,577.2 (5,875.42 to 7,262.38)	20,803.93 (18,615.87 to 22,995.49)	216.3 (202.18 to 228.68)	759.2 (675.25 to 850.31)	1,018.82 (918.5 to 1,123.35)	34.2 (29.88 to 38.8)
Intracerebral hemorrhage	DALYs	22,779.12 (19,630.52 to 26,510.84)	27,463.75 (22,839.24 to 32,676.71)	20.57 (−2.98 to 50.66)	2,830.02 (2,441.76 to 3,281.07)	1,351.55 (1,129.11 to 1,600.86)	−52.24 (−61.24 to −41.1)
Intracerebral hemorrhage	deaths	913.02 (784.4 to 1,064.53)	1,322.89 (1,108.05 to 1,567.71)	44.89 (16.23 to 79.58)	139.67 (121.09 to 162.03)	68.84 (57.61 to 81.17)	−50.71 (−60.31 to −39.87)
Intracerebral hemorrhage	prevalence	3,115.04 (2,764.29 to 3,518.25)	4,385.24 (3,892.1 to 4,906.56)	40.78 (32.54 to 48.59)	308.41 (274.49 to 348.29)	222.11 (200.09 to 246.48)	−27.98 (−30.64 to −25.31)
Subarachnoid hemorrhage	DALYs	5,298.11 (2,791.02 to 6,806.26)	2,296.53 (1,727.44 to 2,847.37)	−56.65 (−70.18 to −28.03)	616.84 (315.45 to 799.17)	115.49 (86.86 to 142.5)	−81.28 (−87.24 to −68.37)
Subarachnoid hemorrhage	deaths	189.6 (90.81 to 249.02)	91.8 (66.67 to 116.22)	−51.58 (−68.15 to −13.71)	27.29 (12.81 to 36.07)	4.72 (3.45 to 5.95)	−82.71 (−88.71 to −67.93)
Subarachnoid hemorrhage	prevalence	1,104.54 (961.69 to 1,242.64)	1,323.29 (1,176.08 to 1,484.05)	19.8 (14.43 to 25.17)	107.89 (94.6 to 121.79)	68.88 (61.53 to 76.9)	−36.16 (−38.34 to −34.17)
Alzheimer's disease and other dementias	DALYs	2,702.48 (1,239.18 to 6,085.39)	10,072.48 (4,947.15 to 22,219.15)	272.71 (222.22 to 330.14)	534.47 (236.2 to 1,190.6)	562.39 (271.16 to 1,238.81)	5.22 (−9.08 to 21.94)
Alzheimer's disease and other dementias	deaths	119.81 (28.35 to 322.1)	491.77 (124.97 to 1,330.18)	310.47 (248.01 to 403.84)	31.39 (7.6 to 83.63)	30.82 (7.88 to 82.43)	−1.8 (−15.92 to 18.32)
Alzheimer's disease and other dementias	prevalence	4,024.54 (3,446.4 to 4,623.09)	16,990.83 (14,488.49 to 19,672.74)	322.18 (304.73 to 338.68)	703.14 (608.36 to 809.51)	900.82 (770.92 to 1,043.22)	28.11 (24.47 to 31.11)
Parkinson's disease	DALYs	685.01 (597.88 to 765.41)	2,159.51 (1,826.2 to 2,521.34)	215.25 (168.29 to 272.87)	105.26 (93.23 to 116.71)	107.96 (91.1 to 125.52)	2.57 (−12.92 to 20.92)

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Table 1. ***Continued***

Neurological disorders	Measure	Absolute numbers (thousands)			Age-standardized rate (per 100,000)		
		1990	2021	Percentage change, 1990–2021 (%)	1990	2021	Percentage change, 1990–2021 (%)
Parkinson's disease	deaths	32.58 (28.7 to 36.28)	92.04 (75.91 to 108.13)	182.48 (128.71 to 248.73)	6.11 (5.38 to 6.78)	5.03 (4.17 to 5.89)	−17.65 (−32.87 to 0.42)
Parkinson's disease	prevalence	651.83 (546.48 to 786.52)	5,077.06 (4,277.76 to 6,049.74)	678.89 (621.46 to 734.36)	91.77 (75.88 to 109.65)	245.73 (208.28 to 289.24)	167.77 (148.07 to 187.19)
Idiopathic epilepsy	DALYs	2,134.56 (1,717.52 to 2,651.18)	1,374.72 (969.52 to 1,888.68)	−35.6 (−51.33 to −14.5)	178.61 (143.44 to 220.63)	101.39 (72.51 to 139.41)	−43.23 (−56.91 to −25.48)
Idiopathic epilepsy	deaths	21.5 (18.26 to 25.96)	11.89 (9.81 to 14.77)	−44.71 (−54.88 to −31.48)	1.86 (1.6 to 2.25)	0.81 (0.68 to 1)	−56.6 (−63.97 to −47)
Idiopathic epilepsy	prevalence	2,178.53 (1,525.45 to 2,896.31)	3,086.32 (2,176.54 to 4,020.73)	41.67 (−1.18 to 99.25)	189.28 (132.48 to 252.96)	214.71 (150.11 to 278.57)	13.44 (−18.73 to 59.11)
Multiple sclerosis	DALYs	7.02 (5.08 to 9.8)	15.01 (11 to 19.59)	113.89 (80.29 to 147.05)	0.62 (0.46 to 0.87)	0.83 (0.61 to 1.09)	33.57 (11.5 to 54.02)
Multiple sclerosis	deaths	0.05 (0.03 to 0.07)	0.11 (0.09 to 0.14)	131.66 (36.76 to 296)	0.01 (0 to 0.01)	0.01 (0 to 0.01)	11.72 (−33.45 to 94.47)
Multiple sclerosis	prevalence	17.89 (13.4 to 23.69)	40.16 (31.81 to 50.04)	124.51 (105.73 to 143.46)	1.55 (1.19 to 2.01)	2.23 (1.74 to 2.83)	43.29 (37.03 to 50.23)
Motor neuron disease	DALYs	87.56 (50.25 to 111.67)	122.66 (81.01 to 167.33)	40.08 (−14.69 to 155.84)	7.99 (4.67 to 10.15)	7.67 (4.88 to 10.06)	−4.03 (−43.05 to 77.63)
Motor neuron disease	deaths	1.53 (0.85 to 1.95)	3.45 (2.22 to 4.79)	125.79 (38.03 to 302.24)	0.15 (0.09 to 0.19)	0.18 (0.11 to 0.25)	19.58 (−27.03 to 119.41)
Motor neuron disease	prevalence	25.69 (20.34 to 31.96)	33.34 (27.03 to 40.37)	29.78 (19.18 to 44.15)	2.13 (1.72 to 2.6)	2.3 (1.84 to 2.8)	7.84 (2.74 to 14.45)
Migraine	DALYs	5,028.79 (767.67 to 11,262.27)	6,988.2 (1,133.32 to 15,186.29)	38.96 (28.64 to 53.32)	412.97 (66.16 to 911.02)	443.65 (66.93 to 971.68)	7.43 (−0.24 to 11.47)
Migraine	prevalence	133,474.54 (114,199.44 to 153,482.6)	184,752.28 (160,836.52 to 213,633.96)	38.42 (29.87 to 48.03)	10,948.52 (9,428.76 to 12,586.13)	11,777.51 (10,137.56 to 13,538.56)	7.57 (3.53 to 11.42)
Tension-type headache	DALYs	489.46 (151.74 to 1,687.08)	716.16 (224.4 to 2,174.72)	46.32 (20.26 to 70.8)	41.79 (13.09 to 141.41)	43.5 (13.07 to 141.34)	4.08 (−3.25 to 19.16)
Tension-type headache	prevalence	204,064.31 (176,898.6 to 233,568.23)	283,814.15 (251,438.66 to 320,431.56)	39.08 (30.2 to 49.33)	17,174.48 (15,086.74 to 19,379.66)	18,525.07 (16,380.87 to 20,958.7)	7.86 (3.99 to 12.15)
Brain and central nervous system cancer	DALYs	1,884.41 (1,333.56 to 2,298.06)	2,247.66 (1,715.82 to 2,880.77)	19.28 (−8.2 to 55.34)	174.36 (123.93 to 213.51)	134.15 (102.9 to 171.51)	−23.06 (−40.41 to −0.62)

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Table 1. ***Continued***

Neurological disorders	Measure	Absolute numbers (thousands)			Age-standardized rate (per 100,000)		
		1990	2021	Percentage change, 1990–2021 (%)	1990	2021	Percentage change, 1990–2021 (%)
Brain and central nervous system cancer	deaths	39.16 (28.52 to 49.2)	68.91 (52.05 to 88.28)	75.97 (35.5 to 126.13)	4.05 (2.97 to 5.04)	3.63 (2.74 to 4.6)	−10.19 (−29.75 to 14.08)
Brain and central nervous system cancer	prevalence	108.12 (77.29 to 130.97)	305.06 (244.87 to 387.36)	182.16 (123.13 to 270.41)	9.68 (6.94 to 11.76)	21.23 (16.98 to 26.56)	119.29 (73.41 to 181.51)
Neuroblastoma and other peripheral nervous cell tumors	DALYs	22.02 (16.94 to 28.51)	42.34 (31.94 to 50.79)	92.29 (36.19 to 168.45)	1.99 (1.53 to 2.58)	3.31 (2.49 to 4)	66.51 (20.86 to 133.15)
Neuroblastoma and other peripheral nervous cell tumors	deaths	0.32 (0.25 to 0.41)	1.07 (0.79 to 1.3)	236.08 (129.45 to 352.1)	0.03 (0.02 to 0.04)	0.07 (0.05 to 0.08)	117.3 (52.96 to 184.66)
Neuroblastoma and other peripheral nervous cell tumors	prevalence	4.75 (3.07 to 7.23)	6.17 (4.35 to 8.08)	29.94 (−13.82 to 105.78)	0.43 (0.28 to 0.65)	0.71 (0.49 to 0.94)	65.35 (9.46 to 164.13)
Other neurological disorders	DALYs	168.12 (122.34 to 227.25)	582.63 (459.11 to 721.52)	246.56 (167.58 to 356.83)	15.18 (11.15 to 20.24)	38.75 (30.31 to 48.98)	155.23 (94.91 to 235.12)
Other neurological disorders	deaths	0.73 (0.59 to 0.91)	7.39 (5.65 to 9.26)	906.08 (542.77 to 1,393.21)	0.07 (0.06 to 0.09)	0.45 (0.35 to 0.56)	546.52 (320.94 to 854.48)
Other neurological disorders	prevalence	2.44 (1.53 to 3.52)	3.55 (2.29 to 4.88)	45.86 (23.51 to 75.45)	0.22 (0.14 to 0.31)	0.23 (0.15 to 0.33)	6.08 (−0.51 to 13.74)
Meningitis	DALYs	2,991.87 (2,360.96 to 3,648.77)	285.43 (247.41 to 320.68)	−90.46 (−92.6 to −87.66)	267.3 (210.39 to 326.38)	27.95 (23.73 to 32.23)	−89.54 (−91.98 to −86.84)
Meningitis	deaths	37.28 (30.28 to 45.37)	6.18 (5.28 to 7.11)	−83.43 (−87.01 to −78.17)	3.54 (2.9 to 4.27)	0.48 (0.41 to 0.54)	−86.56 (−89.35 to −82.92)
Meningitis	prevalence	1,646.6 (1,306.35 to 2,086.18)	256.23 (200.56 to 337.64)	−84.44 (−86.07 to −82.52)	140.1 (110.62 to 177.69)	16.62 (13.1 to 21.78)	−88.14 (−89.31 to −86.79)

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Table 1. *Continued*

Neurological disorders	Measure	Absolute numbers (thousands)			Age-standardized rate (per 100,000)		
		1990	2021	Percentage change, 1990–2021 (%)	1990	2021	Percentage change, 1990–2021 (%)
Encephalitis	DALYs	1,115.81 (788.11 to 1,368.67)	290.85 (240.18 to 364.97)	−73.93 (−79.93 to −60.45)	98.81 (69.34 to 121.76)	29.23 (23.72 to 38.84)	−70.42 (−78.11 to −51.8)
Encephalitis	deaths	12.15 (8.39 to 14.96)	3.53 (2.83 to 4.54)	−70.95 (−78.72 to −53.61)	1.11 (0.77 to 1.36)	0.33 (0.26 to 0.44)	−70.53 (−78.73 to −51)
Encephalitis	prevalence	1,281.75 (877.44 to 1,683.57)	914.19 (641.33 to 1,176.48)	−28.68 (−31.88 to −25.05)	108.14 (73.11 to 142.44)	59.94 (42.88 to 76.35)	−44.57 (−47.69 to −40.61)
Tetanus	DALYs	954.51 (398.94 to 1,378.94)	9.3 (3.15 to 21.04)	−99.03 (−99.48 to −97.55)	86.79 (36.33 to 125.26)	0.8 (0.27 to 1.75)	−99.08 (−99.48 to −97.78)
Tetanus	deaths	12.44 (5.39 to 17.39)	0.26 (0.08 to 0.62)	−97.92 (−98.94 to −94.61)	1.19 (0.52 to 1.65)	0.02 (0.01 to 0.04)	−98.59 (−99.2 to −96.57)
Tetanus	prevalence	20.4 (15.09 to 26.47)	2.69 (1.72 to 3.92)	−86.8 (−89.76 to −83.48)	1.74 (1.29 to 2.26)	0.19 (0.12 to 0.28)	−89.05 (−91.49 to −86.25)

Data in parentheses are 95% uncertainty intervals (UIs). DALYs, disability-adjusted life years.

in females than in males. The prevalence substantially increased with age for ischemic stroke, peaking at age 70–74 years, and the prevalence rate was higher in males than in females from the age groups of 45–49 years to 85–89 years. After the age of 50 years, a steep rise was observed in the prevalence of PD and AD and other dementias, with a notable male predominance for PD and a female predominance for the latter.

In China, the total number and age-standardized rate of DALYs were higher in males than in females, while the disease burden varied by age and sex in individual neurological disorders. In children younger than 5 years, the major contributors to the burden of neurological disorders were encephalitis, meningitis, idiopathic epilepsy, and brain and central nervous system (CNS) cancer (Figure 2A). In children older than 5 years and adolescents, both the number of DALYs and the DALY rates due to meningitis and encephalitis sharply decreased, in contrast to the major burden coming from migraine, idiopathic epilepsy, and brain and CNS cancer (Figure 2B). In young and middle-aged adults, migraine was the leading cause of DALYs, with a higher burden in females than in males, followed by intracerebral hemorrhage with a notably higher DALY burden in males than in females. After the age of 50 and over, the major contributors to the burden of neurological disorders were intracerebral hemorrhage and ischemic stroke, the DALY numbers of which increased sharply with age and peaked at 70–74 years. Correspondingly, DALY rates of these two conditions exhibited exponential growth by age and were significantly higher in males than in females. Likewise, the burden of AD and other dementias steeply increased with age, particularly after the age of 70, with the number of DALYs peaking at 80–84 years and female predominance in both the number of DALYs and the DALY rate (Figures S5 and S6; Tables S3, S8, and S9; Data S1).

Changes in neurological burden between 1990 and 2021

From 1990 to 2021, the prevalent cases and age-standardized prevalence rates significantly increased for most of the non-communicable neurological disorders (Figure 3A). PD, AD and other dementias, and ischemic stroke had more than a 3-fold increase in prevalence (678.89% [95% UI, 621.46 to 734.36], 322.18% [304.73 to 338.68], and 216.30% [202.18 to 228.68], respectively), with modest increases in age-standardized prevalence rates (167.77% [148.07 to 187.19], 28.11% [24.47 to 31.11], and 34.20% [29.88 to 38.80], respectively). Similarly, the prevalent cases of MS also more than doubled (124.51% [105.73 to 143.46]), with marginal increases in the age-standardized prevalence rate (43.29% [37.03 to 50.23]), while for brain and CNS cancer, both its prevalent cases and age-standardized prevalence rate showed more than a 2-fold increase (182.16% [123.13 to 270.41] and 119.29% [73.41 to 181.51]). Notably, despite mild increases in the prevalent cases of intracerebral hemorrhage and subarachnoid hemorrhage, the age-standardized prevalence rates for both conditions declined substantially. By contrast, both morbidity and mortality of the three communicable neurological disorders (meningitis, encephalitis, and tetanus) significantly decreased over the past 32 years.

As expected, the number of DALYs for AD and other dementias, PD, and ischemic stroke showed large increases

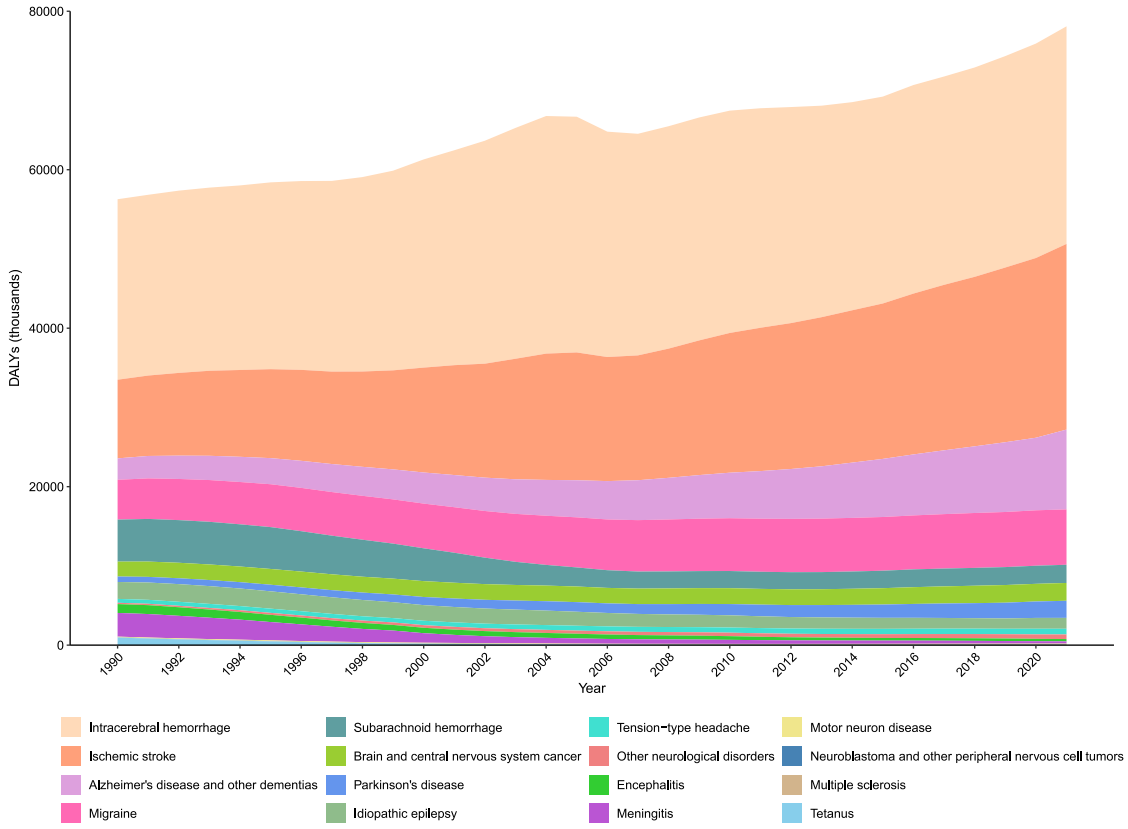

Figure 1. The composition of DALYs for neurological disorder categories in China from 1990 to 2021
Total number of DALYs for 16 neurological disorder categories in China from 1990 to 2021. DALYs, disability-adjusted life years.

(272.71% [222.22 to 330.14], 215.25% [168.29 to 272.87], and 136.05% [89.69 to 190.97], respectively), while the temporal changes of age-standardized DALY rates remained relatively stable (Figure 3B). Both the number of DALYs and the DALY rates for rare neurological disorders increased substantially, including neuroblastoma and other peripheral nervous cell

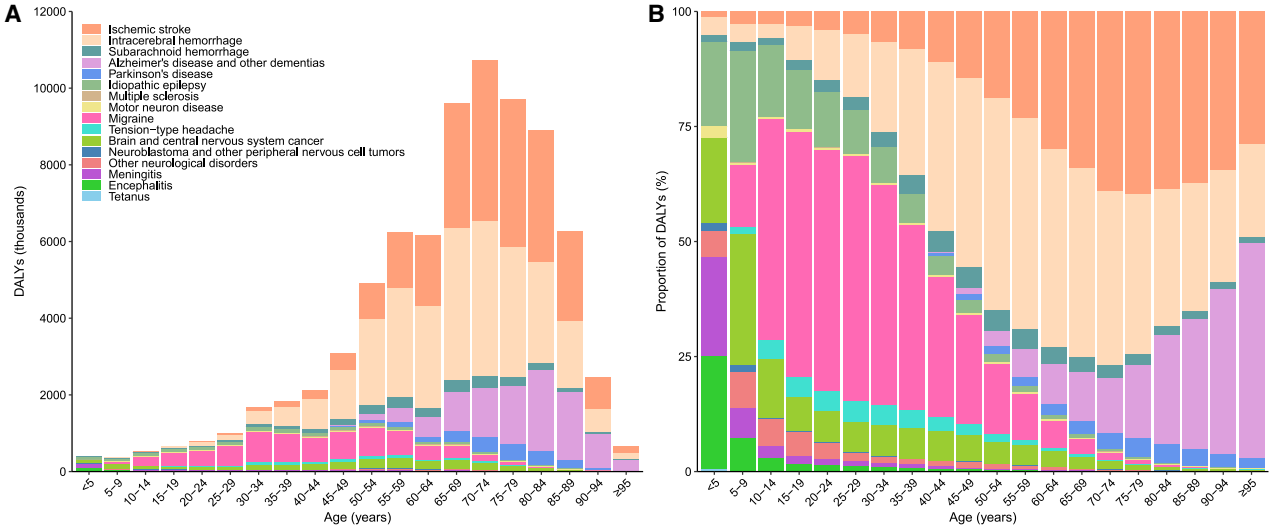

Figure 2. DALYs of neurological disorders by age in China, 2021
Total number of DALYs (A) and contribution (B) of individual neurological disorders by age group in 2021. DALYs, disability-adjusted life years.

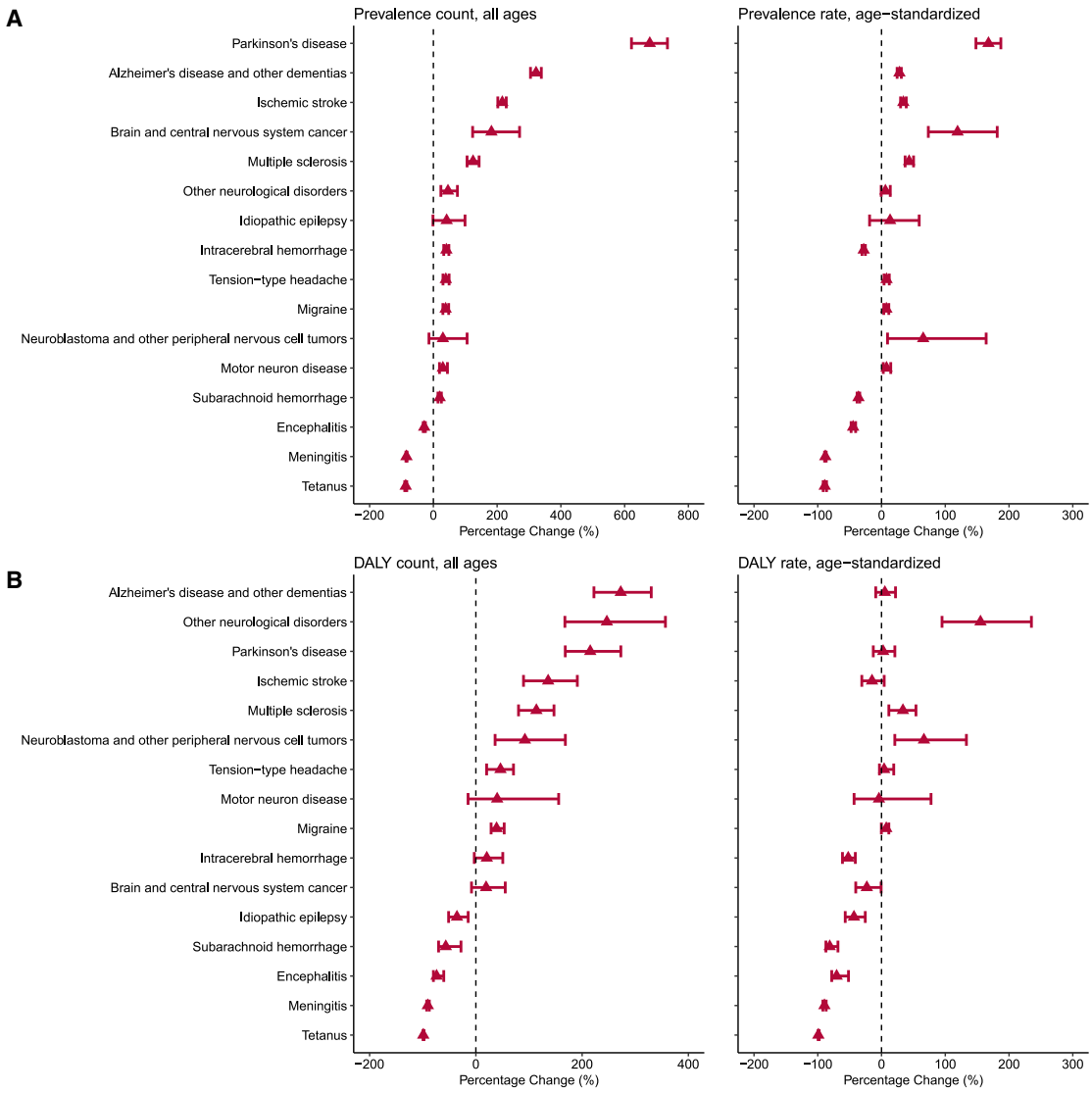

Figure 3. Changes in the number and rates of prevalence and DALYs by neurological disorder category between 1990 and 2021 in China

(A) Percentage changes in the number and age-standardized rate of prevalence by neurological disorder category between 1990 and 2021.

(B) Percentage changes in the number and age-standardized rate of DALYs by neurological disorder category between 1990 and 2021.

Error bars depict 95% uncertainty intervals. DALYs, disability-adjusted life years.

tumors, MS, and other neurological disorders. Conversely, idiopathic epilepsy and subarachnoid hemorrhage showed significant decreases for both the number of DALYs and the age-standardized DALY rate (−35.60% [−51.33 to −14.50] and −43.23% [−56.91 to −25.48] for idiopathic epilepsy and −56.65% [−70.18 to −28.03] and −81.28% [−87.24 to −68.37] for subarachnoid hemorrhage). While there was little change in DALY counts due to intracerebral hemorrhage, the age-standardized DALY rate experienced a marked reduction.

Years of life lost (YLLs) remain the dominant feature of DALYs among the 14 fatal neurological disorders, while the leading contributors to YLLs of neurological disorders have changed from intracerebral hemorrhage, ischemic stroke, and subarachnoid hemorrhage in 1990 to intracerebral hemorrhage, ischemic stroke, and AD and other dementias in 2021. Between 1990 and 2021, the notable decrease in DALYs of idiopathic epilepsy, subarachnoid hemorrhage, and intracerebral hemorrhage was mainly driven by the significant reduction in YLLs (Table S4; Figure S7). Notably, migraine, ischemic stroke, and AD and other dementias were the leading contributors to years lived with disability (YLDs) of neurological disorders in both 1990 and 2021.

Decomposition of neurological burden

The changes in the number of DALYs for individual neurological disorders between 1990 and 2021 were contributed variously by population growth, population aging, and changes in age-specific DALY rates (Figure 4). Population growth accounted for the increases in DALYs across all neurological disorders, with

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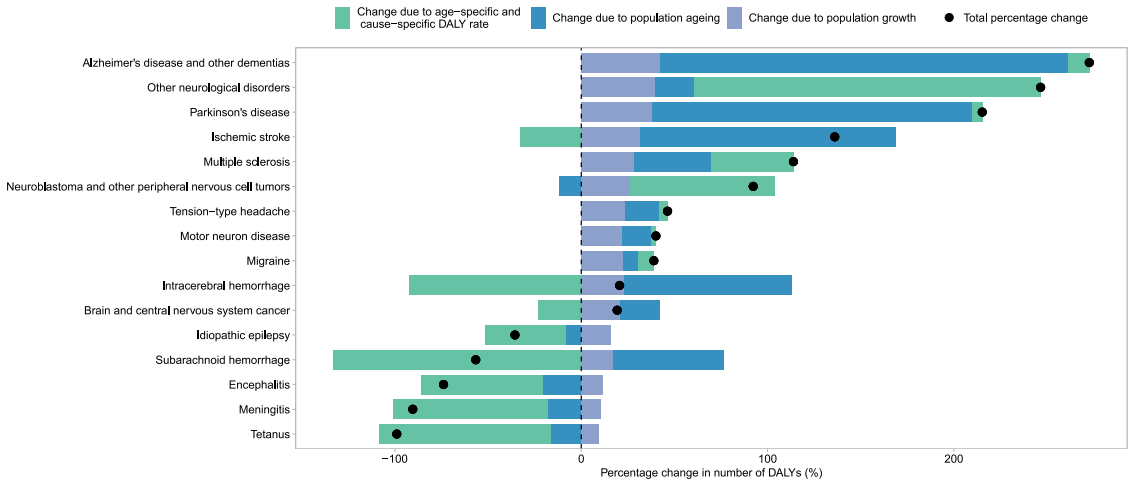

Figure 4. Decomposition of percentage changes in the number of DALYs due to individual neurological disorders between 1990 and 2021 in China

DALYs, disability-adjusted life years.

its contribution ranging from 9.46% for tetanus to 42.37% for AD and other dementias. Population aging led to substantial increases in DALYs of AD and other dementias (218.79%), PD (172.11%), ischemic stroke (136.99%), intracerebral hemorrhage (89.81%), subarachnoid hemorrhage (59.45%), and MS (41.31%). Conversely, population aging led to reductions in DALYs of idiopathic epilepsy (8.36%), neuroblastoma and other peripheral nervous (11.82%), and communicable neurological disorders (16.68%–20.63%). Shifts in age-specific DALY rates led to the declines in DALYs for half of the neurological disorders, ranging from 23.0% for brain and CNS cancer to 133.0% for subarachnoid hemorrhage. For subarachnoid hemorrhage, idiopathic epilepsy, and three infectious diseases, the declines in DALYs due to changes in age-specific DALY rates fully offset the rise in DALYs contributed by population growth and aging. In contrast, changes in age-specific DALY rates were the primary drivers for the increases in DALYs of other neurological disorders (186.22%), neuroblastoma and other peripheral nervous cell tumors (77.75%), and MS (44.21%).

Geographic distribution of neurological burden at the provincial level

The DALY burden attributed to the 16 neurological disorders varied across provinces in China's four major regions (northeastern, eastern, central, and western regions) (Table S5). The age-standardized DALY rates of seven neurological disorders had more than 5 times variation between the provinces in 2021, including tetanus, intracerebral hemorrhage, meningitis, subarachnoid hemorrhage, ischemic stroke, motor neuron disease (MND), and idiopathic epilepsy (Figure 5). For communicable neurological disorders, the age-standardized DALY rates were highest in western provinces and lowest in eastern provinces (Data S1: Figures S8–S10). A similar pattern was found for intracerebral hemorrhage and subarachnoid hemorrhage, whereas the age-standardized DALY rates of ischemic stroke were highest in northeastern provinces and lowest in Hong Kong and Macao SAR (Data S1: Figures S11–S13). The age-standardized DALY rates of idiopathic epilepsy were highest in the western provinces of Tibet and Qinghai; conversely, the DALY burden of MND was highest in the eastern provinces of Shanghai and Beijing and lowest in western provinces of Tibet and Guizhou (Data S1: Figures S14 and S15). Meanwhile, minimal variation between provinces was observed in headache disorders, AD and other dementias, and PD (Data S1: Figures S16–S23).

From 1990 to 2021, the patterns of DALYs for individual neurological disorders at the provincial level varied with socio-demographic index (SDI) (Figure 6). For ischemic stroke, the age-standardized DALY rates initially increased with SDI from low to middle levels and then steadily declined as SDI rose to higher levels, with the declines primarily occurring in northeastern and eastern provinces (Data S1: Figure S24). The DALY rates of intracerebral hemorrhage, subarachnoid hemorrhage, and infectious diseases across the provinces decreased sharply with increasing SDI. For idiopathic epilepsy, the DALY rates also noticeably declined as SDI increased, and among the 10 provinces experiencing significant declines, 8 were located in the western region. By contrast, some rare diseases, such as MND, showed a slight increase in DALY rates with rising SDI, but provincial variation exhibited considerable deviations from the expected pattern. While SDI increased, AD and other dementias, PD, and headache disorders showed minimal changes in their DALY rates.

DISCUSSION

Utilizing data from the latest GBD 2021, we conducted a comprehensive analysis of the prevalence and health loss due to the major neurological disorders in mainland China and its provinces in 2021 and examined the temporal changes of the neurological burden from 1990 to 2021. The findings revealed that neurological disorders collectively accounted for 28.04% of all deaths and 19.41% of all DALYs in China, affecting nearly one-third of the total Chinese population across the lifespan.

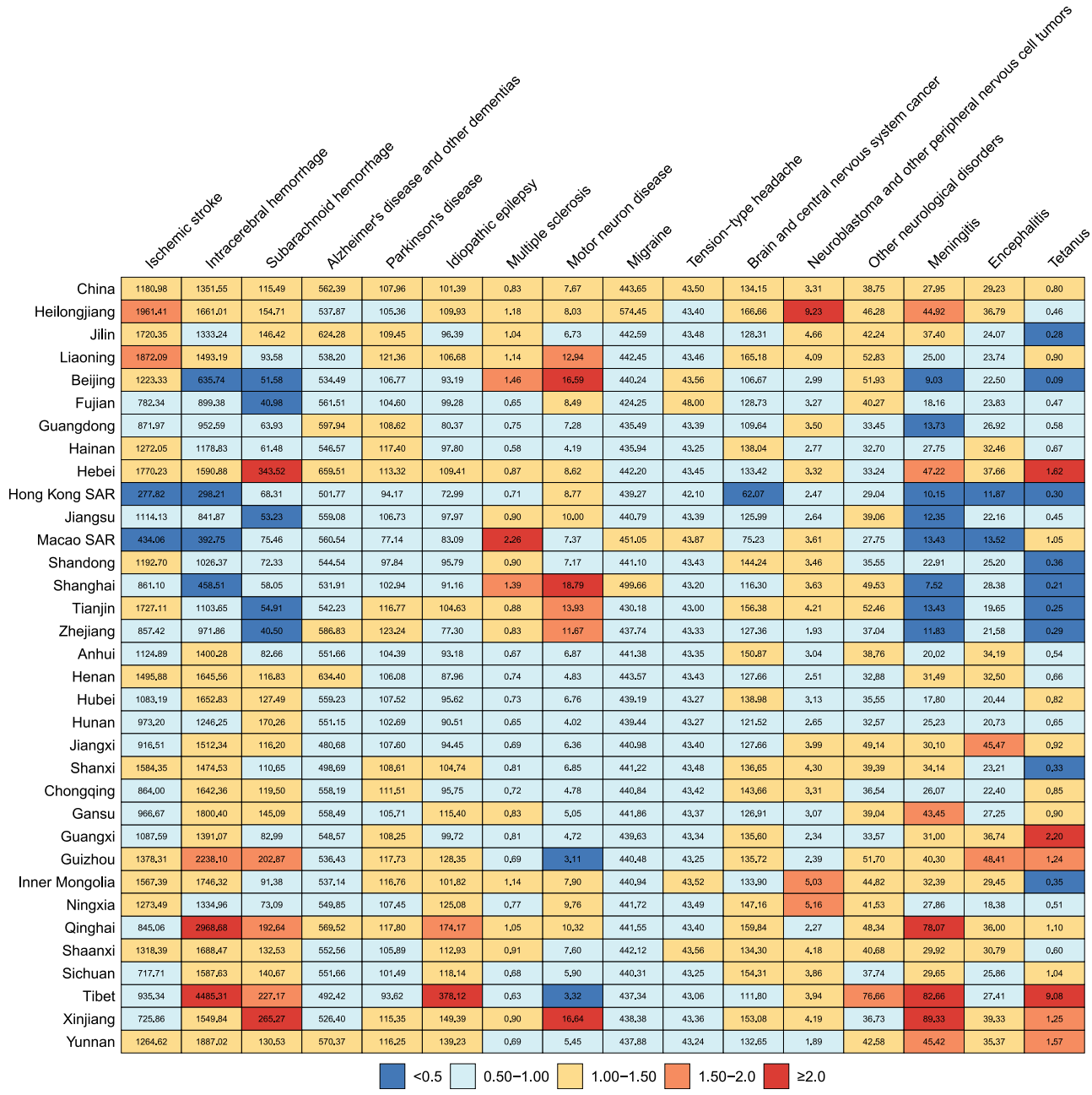

Figure 5. The age-standardized DALY rates (per 100,000) of neurological disorders in China and its provinces in 2021

Provinces are grouped by regions in China (northeastern, eastern, central, and western regions) and alphabetically ordered. Colored key represents the ratio of the provincial DALY rate to the national average DALY rate for each neurological disorder. DALY, disability-adjusted life year; SAR, special administrative region.

During the study period, non-communicable neurological disorders not only accounted for the vast majority of neurological burden but also exhibited noticeable increases in prevalence and DALYs, with population aging emerging as a major driver. The knowledge about vulnerable populations and regions in China could inform policies and targeted strategies to address neurological disorders.

Existing studies consistently showed that stroke, including ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage, was the leading contributor to neurological health loss in most GBD regions.[2,3,7] Notably, we found that stroke accounted for 68% of total neurological DALYs in China, much higher than the global level (42.2%),[2] and the proportions reported in the EU28 (35%)[6] and India (37.9%).[4] Firstly, the substantial stroke burden in China may be partly due to the rising stroke prevalence, driven by population aging and improved survival rates.[9,18] Although the morbidity and mortality of hemorrhagic stroke have significantly declined, ischemic stroke, the

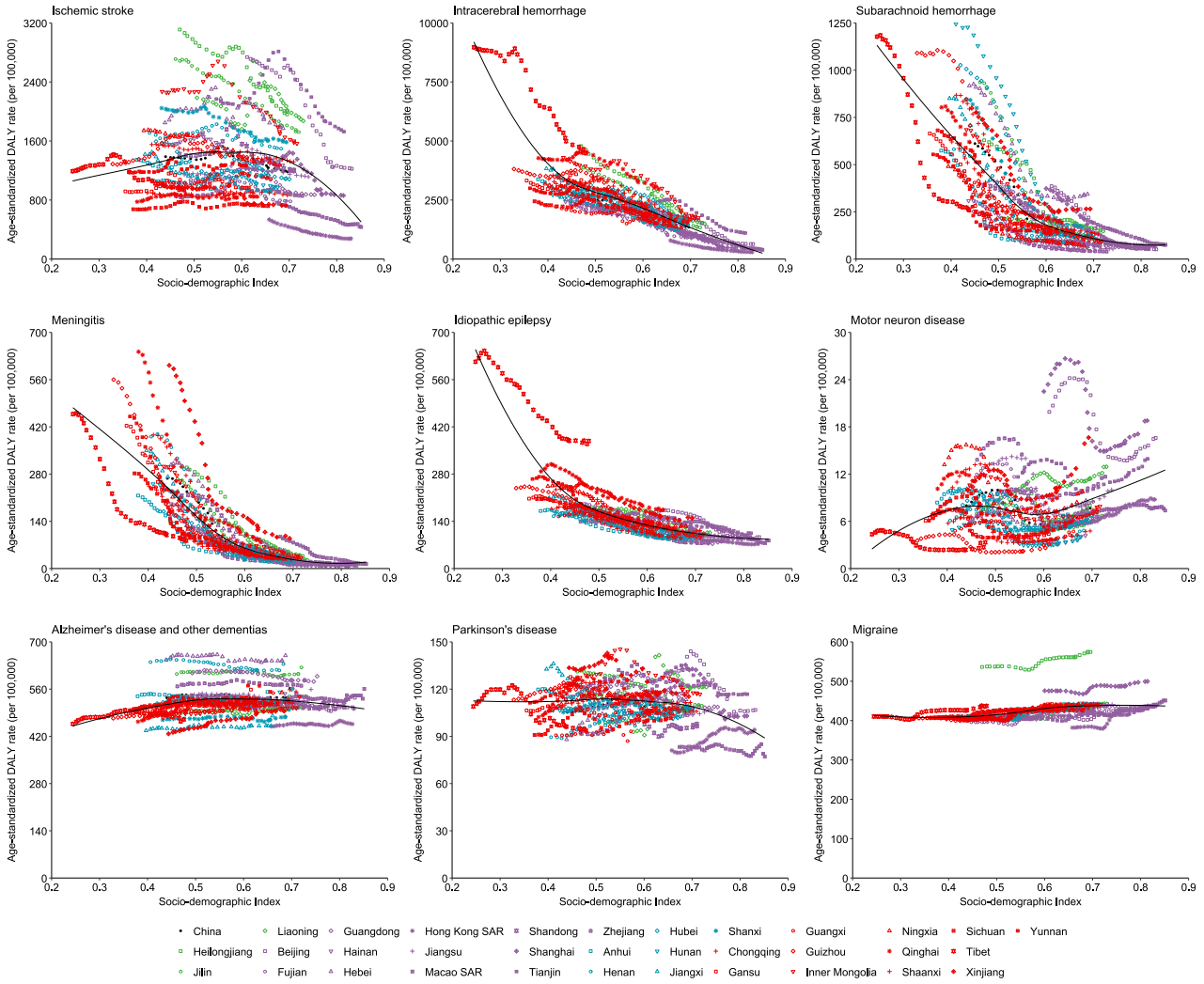

Figure 6. Age-standardized DALY rates for individual neurological disorders in China and its provinces by SDI, 1990–2021

The black line indicates the expected relationship between SDI and age-standardized DALY rates for each neurological disorder based on values from all provinces over the entire period from 1990 to 2021. DALYs, disability-adjusted life years; SDI, socio-demographic index.

predominant subtype, continues to exhibit an increasing incidence in China.[9] Secondly, stroke mortality in China remains relatively high. Despite significant advancements in acute hospital-based stroke care and improvements in hospital stroke outcomes over the past decades,[19,20] China still faces challenges such as salient prehospital delays, insufficient primary and secondary prevention, and unmet rehabilitation needs.[21,22] Meanwhile, the large provincial variation in stroke burden across China was associated with socioeconomic development and suggested that other attributable risk factors, such as metabolic comorbidities, air pollution, and unhealthy behaviors, also contribute to the stroke burden.[9] For example, hypertension, as the leading risk factor of stroke, demonstrated low treatment (34.6%) and control (12.0%) rates in China, particularly in rural areas.[23] This highlights the need for enhanced interventions on modifiable risk factors to reduce premature deaths, supporting Healthy China 2030 and Sustainable Development Goal 3.4.[24]

The neurological burden in China, which predominantly affected the elderly, bore a close resemblance to that in the aging societies of Europe.[6] Population aging, as the primary driver, fueled the increasing burden of chronic neurodegenerative diseases, particularly AD and other dementias, and PD. However, the minimal changes in DALYs of these conditions with increasing SDI suggested that factors other than sociodemographic development were responsible for the rising burden. Accumulating evidence has identified multiple risk factors associated with increased dementia prevalence and adverse health outcomes, including parental history, unhealthy lifestyles, smoking, and various vascular and metabolic factors.[7,10] Environmental factors relevant to pesticides and industrialization may contribute to the increase in the prevalence of PD, with a shortage of high-quality evidence.[25,26] Going along with the WHO's advocacy for healthy aging,[27] China has implemented a wide range of policy initiatives on health literacy education,

improving geriatric medical services and facilitating long-term care to promote health and care for older people,[14] while inadequate awareness, discrimination, and stigma against dementia and movement disorders may pose barriers to help seeking in health facilities.[28,29] Considering the irreversible disease progression, investigating modifiable risk factors is vital for disease prevention, and research on genetic variation and early pathogenic mechanisms is essential to enable early diagnosis and intervention.[30]

Notably, the burden of idiopathic epilepsy has shown a steady decline with improvements in SDI over time, particularly in western provinces of China. The demographic change in China, with a declining fertility rate and rising life expectancy, partly contributed to the decrease in epilepsy burden.[31,32] Importantly, a substantial reduction in premature mortality primarily accounted for the reduced burden of epilepsy. As epilepsy is a highly treatable condition, efforts for better accessibility to treatment are instrumental for epilepsy control. In the early 21st century, the WHO's Global Campaign Against Epilepsy project in China indicated that optimal management at a primary health level could effectively reduce the treatment gap of epilepsy, which greatly promoted epilepsy intervention in rural areas.[33] And yet, major issues remain in terms of threats to the health of children and adolescents, stigmatization and discrimination, inadequate and inappropriate treatment, and uneven distribution of professional resources, necessitating strengthening national disease surveillance, scaling up effective interventions, and enhancing international collaboration to address unmet needs for epilepsy care.[34,35]

Actions are also needed for rare neurological diseases such as MS and MND, given their substantial, increasing burden in China. Advances in understanding rare conditions enabled better diagnosis and increasing epidemiological evidence.[36,37] However, the growing burden and geographic disparity indicated inadequate disease management, which may be influenced by sociodemographic development. Ever since Healthy China 2030 emphasized health priority and the health of all people,[38] multiple measures have been adopted to promote standardized diagnosis and treatment for rare diseases, including establishing the China Alliance for Rare Diseases and issuing the First and Second List of Rare Diseases, thus speeding up the entry of overseas new drugs urgently needed in clinical settings, which are greatly benefiting families with rare diseases.[39]

As the most prevalent neurological condition, primary headaches affected people across a broad age spectrum, and migraine was the major cause of disability in China. However, the finding that there was little change in headache burden over time, with minimal variation among provinces, might partly reflect the suboptimal management of these conditions. A nationwide population-based survey in China,[40] supported by Lifting The Burden: The Global Campaign against Headache, reported that only 46.6% of individuals had consulted physicians for their headaches, and more than half of headaches were underdiagnosed or misdiagnosed. Incorrect treatment was ubiquitous in East Asia, with high usage of over-the-counter medication and low usage of prescription medication.[41] Accordingly, policy action is necessary to increase public awareness and professional education for optimized headache care, like implementing a hierarchical headache care system[42] and promoting the continuing medical education program Headache Schools.[43]

Geographical variation across China remains larger in the burden attributable to neurological disorders, with notable differences between well-developed eastern and less-developed western regions. Economic development and healthcare reforms have narrowed health inequalities through advanced medical services and increased insurance coverage,[44,45] possibly contributing to the universal decline of burdens from several neurological conditions across the country. Nevertheless, there are unmet needs and gaps for neurologists and subspecialized neurological services to get appropriate diagnosis and treatment. As the Neurology Atlas from the WHO reported,[46] the median number of neurologists was 1.09 per 100,000 people in upper-middle-income countries (including China), with only 19% of the countries having neurologists in rural areas. Therefore, several specific strategies targeted at prevention and treatment could be implemented to reduce regional disparities, which include enhancing primary healthcare guidance for standardized treatment and strengthening neurology specialties and training by telemedicine to improve medical accessibility.[47]

This study presented the extensive affected population and the huge burden caused by neurological disorders in China, elucidating the priorities for reducing the neurological burden. Although several conditions have featured declines in morbidity and mortality, the large increases in burden from age-related neurological disorders are posing enormous challenges to the healthcare system. The heterogeneous distribution of neurological burden in China could inform policymakers and healthcare professionals in developing targeted strategies. For instance, enhancing public awareness of modifiable risk factors could promote healthier lifestyles, thereby reducing the burden of preventable neurological diseases. Strengthening identification and medication guidance for common chronic diseases in primary care would facilitate long-term management of treatable neurological conditions. Furthermore, developing neurology specialties and enhancing training programs could improve access to neurological services.

Limitations of the study

Several limitations should be noted in this study. First, although great efforts were dedicated to the collection of all available data to estimate disease burden in the GBD study, the quality and quantity of the existing data on neurological disorders, as well as the methodological heterogeneity in the data sources, might affect the accuracy of the estimation. A major strength of the GBD study is the robust modeling to enforce consistency among epidemiological parameters and to estimate comparable prevalence, deaths, and DALYs, as discussed in previous studies.[48,49] Second, the geographic variation could be biased because of the extensive input data sources with variations in diagnostic criteria and measurement methods. Although the GBD study used Bayesian statistical models to correct this bias for generating optimal estimates,[7] some results with wide uncertainty bounds should be treated with caution. For instance, the rising trends in the burden of rare neurological disorders might be associated with medical advancement and under-ascertainment in less-developed regions. Third, some neurological diseases

are likely to have comorbidities correlated with the variation of age, sex, or location, while comorbidity adjustment in the GBD study assumes independent distributions of comorbid conditions, which may affect the estimation of disability burden.[7] Given that the aggregation could not be done at the draw level, the non-fatal burden might be overestimated with wide uncertainty. Future research needs to take the variable correlation between GBD causes and comorbidities into consideration. Fourth, we were unable to further explore additional factors that may influence the burden of neurological disorders, such as risk factors, medical advancements, and other social changes. Except for stroke, only a small proportion of the neurological burden was attributable to the given risk factors in GBD. These determinants, including environmental, behavioral, and metabolic factors, have been described in the global analysis of neurological burden.[7] Further research is needed to investigate detailed and specific determinants for individual neurological conditions. Finally, several widely recognized neurological diseases were classified under the category of other neurological disorders in the GBD study, such as neuromyelitis optica and myasthenia gravis.[12] Through international collaboration, future GBD iterations could improve the granularity of the analysis to include a broader range of neurological disorders and provide more precise estimates and detailed insights into the global neurological burden.

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Junwei Hao (haojunwei@vip.163.com).

Materials availability

This study did not generate new unique reagents.

Data and code availability

- This study follows the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).
- The data of GBD 2021 used in this study can be accessed from the Global Health Data Exchange GBD 2021 website (ghdx.healthdata.org and https://ghdx.healthdata.org/gbd-2021).
- This paper does not report original code.
- Additional information that may not be publicly available will be shared by request from any qualified investigator.

CONSORTIA

The members of GBD 2021 China Neurological Disorders Collaborators are Chen Zhang, Xuan Yang, Dongshan Wan, Qingfeng Ma, Peng Yin, Ahmed Abu-Zaid, Isaac Yeboah Addo, Saryia Adra, Williams Agyemang-Duah, Danish Ahmad, Ayman Ahmed, Syed Anees Ahmed, Mohammed Ahmed Akkaif, Abdelazeem M. Algammal, Abid Ali, Mohammed Usman Ali, Waad Ali, Sheikh Mohammad Alif, Najim Z. Alshahrani, Mohammad Al-Wardat, Sohrab Amiri, Abhishek Anil, Anayochukwu Edward Anyasodor, Thomas Astell-Burt, Alok Atreya, Shahkaar Aziz, Ahmed Y. Azzam, Giridhara Rathnaiah Babu, Saeed Bahramian, Ruhai Bai, Abdulaziz T. Bako, Senthilkumar Balakrishnan, Azadeh Bashiri, Hameed Akande Bashiru, Mohammad-Mahdi Bastan, Akshaya Srikanth Bhagavathula, Sonu Bhaskar, Priyadarshini Bhattacharjee, Fan Cao, Ester Cerin, Vijay Kumar Chattu, Hui Chen, Bryan Chong, Hongyuan Chu, Sheng-Chia Chung, Rosa A.S. Couto, Samuel Demissie Darcho, Kuldeep Dhama, Amol S. Dhane, Ojas Prakashbhai Doshi, Robert Kokou Dowou, Chadi Eltaha, Alireza Feizkhah, Ginenus Fekadu, Xiaoqi Feng, Nuno Ferreira, Getahun Fetensa, Takeshi Fukumoto, Balasankar Ganesan, Xiang Gao, Miglas Welay Gebregergis, Mesfin Gebrehiwot, Mahaveer Golechha, Shi-Yang Guan, Cui Guo, Md Saquib Hasnain, Simon I. Hay, Yuta Hiraike, Nguyen Quoc Hoan, Sorin Hostiuc, Chengxi Hu, Junjie Huang, Farideh Iravanpour, Md. Rabiul Islam, Sheikh Mohammed Shariful Islam, Assefa N. Iyasu, Louis Jacob, Ammar Abdulrahman Jairoun, Mihajlo Jakovljevic, Reza Jalilzadeh Yengejeh, Zixiang Ji, Yusheng Jia, Jost B. Jonas, Kehinde Kazeem Kanmodi, Ibraheem M. Karaye, Faham Khamesipour, Mohammad Jobair Khan, Majid Khosravi, Min Seo Kim, Adnan Kisa, Sezer Kisa, Mukhtar Kulimbet, Munjae Lee, Wei-Chen Lee, Wei Li, Xiaopan Li, Jialing Lin, Xiaofeng Liu, Xuefeng Liu, José Francisco López-Gil, Jay B. Lusk, Zheng Feei Ma, Roy Rillera Marzo, Yasith Mathangasinghe, Steven M. McPhail, Tesfahun Mekene Meto, Hadush Negash Meles, Jama Mohamed, Nouh Saad Mohamed, Sumaira Mubarik, Yanjinlkham Munkhsaikhan, Christopher J.L. Murray, Ghulam Mustafa, Ayoub Nafei, Ganesh R. Naik, Gurudatta Naik, Van Thanh Nguyen, Fred Nugen, Bogdan Oancea, Sylvester Reuben Okeke, Osaretin Christabel Okonji, Andrew T. Olagunju, Sok King Ong, Mahesh P.A., Jagadish Rao Padubidri, Songhomitra Panda-Jonas, Shrikant Pawar, Prince Peprah, Michael R. Phillips, Maarten J. Postma, Reza Pourbabaki, Jalandhar Pradhan, Jagadeesh Puvvula, Gangzhen Qian, Vafa Rahimi-Movaghar, Mosiur Rahman, Masoud Rahmati, Shakthi Kumaran Ramasamy, Sheena Ramazanu, Elrashdy M. Redwan, Jefferson Antonio Buendia Rodriguez, Nitai Roy, Cameron John Sabet, Pragyan Monalisa Sahoo, Mohamed A. Saleh, Yoseph Leonardo Samodra, Abdallah M. Samy, Aswini Saravanan, Chinmoy Sarkar, Gargi Sachin Sarode, Sachin C. Sarode, Maheswar Satpathy, Monika Sawhney, Siddharthan Selvaraj, Sunder Sham, Muhammad Aaqib Shamim, Nigussie Tadesse Sharew, Mahabalesh Shetty, Premalatha K. Shetty, Aminu Shittu, Seyed Afshin Shorofi, Jasvinder A Singh, Puneetpal Singh, Surjit Singh, Muhammad Suleman, Jing Sun, Zhong Sun, Chandan Kumar Swain, Lukasz Szarpak, Sree Sudha T.Y., Seyyed Mohammad Tabatabaei, Jabeen Taiba, Haosu Tang, Manoj Tanwar, Masayuki Teramoto, Ramna Thakur, Jansje Henny Vera Ticoalu, Jasmine T .Tran, Thang Huu Tran, Atta Ullah, Saeed Ullah, Jibrin Sammani Usman, Asokan Govindaraj Vaithinathan, Fang Wang, Shu Wang, Yanzhong Wang, Muhammad Waqas, Abdul Waris, Nuwan Darshana Wickramasinghe, Chenkai Wu, Hong Xiao, Hanzhang Xu, Xiaoyue Xu, Pengpeng Ye, Xinglin Yi, Dehui Yin, Dong Keon Yon, Iman Zare, Mohammed G.M. Zeariya, Haijun Zhang, Liqun Zhang, Yunquan Zhang, Zhi-Jiang Zhang, Zhiqiang Zhang, Hanqing Zhao, Yang Zhao, Zhongyi Zhao, Claire Chenwen Zhong, Shang Cheng Zhou, Bin Zhu, Magdalena Zielińska, Sa'ed H. Zyoud, Maigeng Zhou, and Junwei Hao.

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AUTHOR CONTRIBUTIONS

J.H., M.Z., and C.Z. designed the overall experiments, and J.H. and M.Z. had unrestricted access to all data. C.Z., X.Y., D.W., Q.M., and P.Y. performed the experiments. C.Z., X.Y., D.W., J.H., and M.Z. performed statistical analyses and reviewed the article. C.Z. prepared the first draft of the manuscript and edited it. Please see the supplemental information for more detailed information about individual author contributions to the research. All authors read and approved the final article and take responsibility for its content.

DECLARATION OF INTERESTS

The authors declare no competing interests.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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SUPPLEMENTAL INFORMATION

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Software and algorithms		
R 4.4.0	R	http://www.r-project.org/
2021 Global Burden of Disease Study	IHME	https://www.healthdata.org/; https://vizhub.healthdata.org/gbd-results/

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

This study did not generate experimental model or enroll subjects.

METHOD DETAILS

Overview

GBD 2021 produced comparable estimates of the burden for 371 diseases and injuries in 204 countries and territories from 1990 to 2021, and detailed information was reported in the GBD capstones.[48,49] The methodology for the estimation of neurological conditions has been extensively described in the GBD publication on the global burden of disorders affecting the nervous system from GBD 2021.[7] The present study was designed to conduct a comprehensive analysis of the overall burden of neurological disorders at the national and provincial levels of China for the entire population between 1990 and 2021. The 31 provinces, autonomous regions, and municipalities, and two special administrative regions (Hong Kong and Macao) in mainland China are termed provinces in this study, and categorized into four economic regions (Western, Central, Northeastern, and Eastern regions, with development levels from low to high) based on the classification by the National Bureau of Statistics of China.[50]

We included 16 neurological disorders in which neurologists play a predominant role in diagnosis, treatment, and care in China, including non-communicable neurological disorders [ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, Alzheimer's disease (AD) and other dementias, Parkinson's disease (PD), idiopathic epilepsy, multiple sclerosis (MS), motor neuron disease (MND), migraine, tension-type headache (TTH), brain and central nervous system (CNS) cancer, neuroblastoma and other peripheral nervous cell tumors, and a residual category for other neurological disorders], and communicable neurological disorders (meningitis, encephalitis, and tetanus). The neurological burden was quantified by the measures of prevalence, deaths, disability-adjusted life-years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs) for all these neurological disorders.

Data sources

All estimates in this study were extracted from the GHDx query tool (https://vizhub.healthdata.org/gbd-results/), and the data processing and estimation followed the general analytic framework used by GBD 2021. GBD 2021 synthesizes a great number of input sources to estimate disease burden, including national surveys, vital registration, censuses, clinical informatics, administrative data, and scientific literature.[48,49] The data sources have been archived in the Global Health Data Exchange website, which is currently the largest depository of health data globally (https://ghdx.healthdata.org/gbd-2021). For this study, mortality data for estimates of death due to neurological disorders were mainly obtained from the surveillance systems (the Disease Surveillance Point system and the Maternal and Child Surveillance System), the Chinese Center for Disease Control and Prevention cause-of-death reporting system, vital registration systems, cancer registries, and scientific publications. Data on non-fatal estimates of neurological disorders were primarily derived from surveillance systems, national surveys, cancer registries, and published literature. The full list of the data input resources for each neurological disorder can be downloaded from the Data Input Sources Tool of the GHDx.

Case definition

Cause	Definition
Ischemic stroke	Neurological dysfunction caused by focal cerebral, spinal, or retinal infarction. Stroke cases are considered acute from the day of incidence of a first-ever stroke through day 28 following the event. Stroke cases are considered chronic beginning 28 days following the occurrence of an event, and include all recurrent stroke events.

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Cause	Definition
Intracerebral hemorrhage	A focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma. Stroke cases are considered acute from the day of incidence of a first-ever stroke through day 28 following the event. Stroke cases are considered chronic beginning 28 days following the occurrence of an event; including all recurrent stroke events.
Subarachnoid hemorrhage	Bleeding into the subarachnoid space (the space between the arachnoid membrane and the pia mater of the brain or spinal cord). Stroke cases are considered acute from the day of incidence of a first-ever stroke through day 28 following the event. Stroke cases are considered chronic beginning 28 days following the occurrence of an event, and include all recurrent stroke events.
Alzheimer's disease and other dementias	A progressive, degenerative, and chronic neurological disorder typified by memory impairment and other neurological dysfunctions. Defined based on DSM III, IV or V, or ICD case criteria, including cognitive deficits that must include memory impairment, functional impairment, and gradual onset and continued decline.
Parkinson's disease	A chronic, degenerative, and progressive neurological condition typified by loss of motor mobility and control, most notably causing tremors. Requires the presence of two of the four primary symptoms and is consistent with the Gelb criteria: (1) tremors/trembling, (2) bradykinesia, (3) stiffness of limbs and torso, and (4) posture instability.
Idiopathic epilepsy	A condition characterized by recurrent (two or more) epileptic seizures, unprovoked by any immediate identified cause. Active epilepsy is at least one epileptic seizure in the past five years, regardless of antiepileptic drug treatment. Diagnosis criteria based on "Guidelines for Epidemiological Studies on Epilepsy" (commissioned by the International League Against Epilepsy).
Multiple sclerosis	A chronic, degenerative, and progressive condition typified by damage to the myelin sheaths around neurons. Accepted diagnostic criteria include McDonald's, Poser, Schumacher, and McAllen), or diagnosis via a clinical neurological exam.
Motor neuron disease	A set of chronic, degenerative, and progressive neurological conditions typified by the destruction of motor neurons and the subsequent deterioration of voluntary muscle activity. The most common type is amyotrophic lateral sclerosis (ALS). Gold-standard diagnosis uses the El Escorial Criteria with clinical examination, as well as imaging and electrophysiology.
Migraine	A disabling primary headache disorder, typically characterized by recurrent moderate or severe unilateral pulsatile headaches, either without aura or with aura (transient neurological symptoms). Diagnosis based on International Classification of Headaches (ICD-3) criteria of 5+ attacks that (1) last 4–72 hours, (2) cause nausea and/or vomiting or photophobia and phonophobia, (3) have at least two of the following – unilateral location, pulsating quality, moderate or severe pain, aggravation by or causing avoidance of routine physical activity; (4) not due to other diagnoses. Definite migraines meet all of the above criteria and probably meet all but one of the above criteria.
Tension-type headache	Characterized by a dull, non-pulsatile, diffuse, band- or vice-like pain of mild to moderate intensity in the head or neck. Diagnosed based on ICD-3 criteria of 10+ attacks that (1) last 30 minutes to 7 days, (2) no nausea or vomiting and no more than one of photophobia or phonophobia, (3) have at least two of the following – bilateral location, pressing or tightening quality, mild or moderate pain, not aggravated by routine physical activity, (4) not due to other diagnoses. Definite migraines meet all of the above criteria, and probably meet all but one of the above criteria.
Brain and central nervous system cancer	Malignant neoplasm of the brain or central nervous system. This category encompasses pediatric and adult cases, which include primary malignancies but not metastases.
Neuroblastoma and other peripheral nervous cell tumors	Malignant neoplasm of the peripheral nervous system. This category encompasses pediatric and adult cases, which include primary malignancies but not metastases.
Other neurological disorders	A residual category which groups together neurological conditions that are not directly estimated in the GBD, for example, muscular dystrophy, Huntington's disease, and myasthenia gravis.
Meningitis	A disease caused by inflammation of the meninges, the protective membrane surrounding the brain and spinal cord, that is typically caused by an infection in the cerebrospinal fluid. Symptoms include headache, fever, stiff neck, and sometimes seizure. Gold-standard diagnosis in inpatient hospital clinical data or literature via antigen test, blood test, cerebrospinal fluid test, or latex agglutination test.

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Cause	Definition
Encephalitis	A disease caused by acute inflammation of the brain, which can cause flu-like symptoms such as headaches, fever, drowsiness, fatigue, and at times, seizures, hallucinations, or stroke. Reference definition is based on ICD-10 criteria from inpatient data.
Tetanus	A life-threatening disease caused by infection with the toxin-producing bacterium Clostridium tetani and acquired via contamination of wounds. Tetanus is typically characterized by generalized, painful muscular spasms, with complications including mechanical respiratory failure, autonomic dysfunction, and death. Neonatal tetanus is often caused by contamination of the umbilical stump; initial symptoms include failure to feed and excessive crying, progressing to the typical clinical presentation of tetanus.

ICD-10 and ICD-9 codes

Cause	ICD10	ICD9
Ischemic stroke	G45, G46, I63, I65, I66, I67.2-I67.6, I67.5-I67.6, I69.3	433, 434, 435, 437
Intracerebral hemorrhage	I61, 162, I68.1-I68.2, I69.1-I69.2	431, 432, 437.2
Subarachnoid hemorrhage	I60, I62.0, I67.0-I67.1, I69.0	430
Alzheimer's disease and other dementias	F00, F01, F02, F03, G30, G31	290, 291.2, 291.8, 294, 331
Parkinson's disease	F02.3, G20-G20.9	332-332.0
Idiopathic epilepsy	G40, G41	345
Multiple sclerosis	G35	340
Motor neuron disease	G12	335
Migraine	G43-G43.919	346-346.93
Tension-type headache	G44.2-G44.229, G44.4-G44.41	307.81, 339.1-339.12, 339.3
Brain and central nervous system cancer	C70-C72	191
Neuroblastoma and other peripheral nervous cell tumors	C47	
Other neurological disorders	F02.2, G10, G11, G12, G12.0, G12.1, G13, G23, G24, G25, G26, G26.0, G36, G37, G61, G70, G71, G72, G73, G90, G95, M33	330, 331.8, 331.9, 333, 334, 335.3 336, 337, 341, 349, 349.2, 349.3, 349.8, 353.8, 353.9, 356, 357.0, 357.1, 357.3, 357.4, 357.7, 358, 359, 728.88, 775.2
Meningitis	A39, A87, D86.81, G00-G03.0	036, 047-049.9, 320.0-320.3, 320.5-320.9, 321-322.9
Encephalitis	A83-A86.4, B94.1, F07.1, G04-G05.8, G21.3	062, 063, 064, 139.0, 323
Tetanus	A33-A35.0, Z23.5	037-037.9, 771.3, V03.7

Fatal estimates

The single underlying cause of death was classified and determined for every death using the ICD-9 and ICD-10. The Cause of Death Ensemble modeling (CODEm) was applied to estimate deaths due to 14 fatal neurological disorders, which is a highly systematized tool that applies different models to the same data and selects an ensemble of models that best reflects all available and accessible input data, producing estimates of death for all locations across the time series.[49] YLLs were calculated for each disease by multiplying the death count by the standard life expectancy at the age of death.

Non-fatal estimates

Prevalence of nonfatal outcomes for neurological disorders was estimated by using the DisMod-MR 2.1 modeling tool. The DisMod-MR 2.1, a Bayesian meta-regression tool, is a standard GBD modeling method for estimating non-fatal health outcomes, which identifies and evaluates all available data on incidence, prevalence, remission, and mortality to generate consistent and comparable estimates of nonfatal burden by age, sex, year, and geographic location. The total number of prevalent cases for all neurological disorders was calculated by multiplying the number of people in the population by the aggregated prevalence rate through a comorbidity correction. The aggregated prevalence rate was calculated as follows: $Prevalence_{total}=1-[(1-prevalence_{disease1}) * (1-prevalence_{disease2}) * (1-prevalence_{disease3}) * \ldots (1-prevalence_{disease16})]$.[7] YLDs were calculated by multiplying the number of prevalent cases for each disease sequela by the disability weight. DALYs, representing the combined fatal and non-fatal health loss of

each condition, were calculated as the sum of YLLs and YLDs. For migraine and TTH not recognized as causes of death, DALYs were estimated only as YLDs.

Decomposition analysis

Decomposition analysis was conducted to quantify the potential drivers leading to changes in the absolute number of DALYs for each cause, according to the methods developed by Das Gupta.[51,52] We divided the changes from 1990 to 2021 into three explanatory components: population growth, population aging, and age-specific DALY rates, and estimated their respective contributions. For each neurological disorder, we adopted a counterfactual approach to calculate two different sets of the numbers of DALYs. In the first scenario, the population size was set to the 2021 values, while the age structure and age-specific DALY rates were held constant at their 1990 values. In the second scenario, both the population size and age structure were adjusted to the 2021 values, but the age-specific DALY rates remained at 1990 values. Consequently, changes in DALYs due to population growth were calculated by the difference between the number of DALYs in the first scenario and the actual number of DALYs in 1990. Changes in DALYs due to population aging were defined as the difference between the first and the second scenario. Changes in DALYs attributed to shifts in age-specific DALY rates were calculated by the difference between the actual numbers of DALYs in 2021 and those in the second scenario.

Socio-demographic index

Socio-demographic Index (SDI) is a composite indicator of lag-distributed income per person, average educational attainment among population older than 15 years, and the total fertility rate in females younger than 25 years, which comprehensively indicates social and demographic development status of countries or regions.[48] The SDI values range from 0 to 1, with higher values representing better socioeconomic development status. The SDI for China in 2021 was 0.70 and ranged from 0.48 to 0.88 at the province level.

QUANTIFICATION AND STATISTICAL ANALYSIS

All measures in this study were presented in terms of absolute numbers (in thousands), and age-standardized rates per 100,000 population (with 95% uncertainty intervals [UIs]), and were stratified by neurological disorder category, age, sex, and province from 1990 to 2021. The age-standardized rates were calculated using the GBD standard population.[48] For age-specific measures, the population of all ages was divided into 20 age groups from age under 5 years to age 95 years and older at 5-year intervals. For changes over time, percentage change between 1990 and 2021 was calculated as (2021 estimates - 1990 estimates) /1990 estimates * 100, with statistical significance determined by a 95% UIs excluding zero. The 95% UIs were calculated based on creating 500 runs from the posterior distribution of the model for each estimate of interest, with the 12.5th and 487.5th ordered values.[7] The expected relationships between age-standardized DALY rates and SDI across all provinces over the entire study period were estimated for individual neurological disorders using locally weighted regression. All data analysis and graphics were performed by using R version 4.4.0.