Postprint: Analysis of Temporal Trends and Incidence Prediction for Intracerebral Hemorrhage Disease Burden in China and Worldwide, 1990-2021

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Abstract

Background Intracerebral hemorrhage (ICH) is one of the leading causes of death and disability worldwide, and analyzing its disease burden is of great significance for formulating prevention and control strategies. Objective To analyze the evolution of disease burden and risk factors of ICH in China and globally from 1990 to 2021, and to predict trends from 2022 to 2035, providing evidence for precise prevention and control. Methods Based on the Global Burden of Disease (GBD) 2021 database, we analyzed indicators such as incidence rate, mortality rate, and disability-adjusted life years (DALY) of ICH in China and globally. The Joinpoint regression model was used to calculate the average annual percentage change (AAPC) to assess trend changes, and the Bayesian age-period-cohort (BAPC) model was employed to predict the burden of incidence, mortality, and DALY from 2022 to 2035. Based on the GBD comparative risk assessment framework, we evaluated the attributable effects of risk factors such as high systolic blood pressure, smoking, and air pollution on DALY. Results In 2021, the number of ICH incident cases globally and in China were 3,444,338 and 1,173,288, respectively, representing increases of 46.1% and 51.6% compared to 1990. From 1990 to 2021, the global age-standardized incidence rate showed a decreasing trend (AAPC=-0.589%, P<0.001), with a more significant decline in China (AAPC=-1.507%, P<0.001). In 2021, the number of ICH deaths globally and in China were 3,308,367 and 1,322,893, respectively, representing increases of 41.3% and 44.9% compared to 1990; the global age-standardized mortality rate decreased at AAPC=-0.731% (P<0.001), while China reached AAPC=-2.265% (P<0.001). In 2021, China' s age-standardized DALY rate for ICH decreased significantly compared to 1990 (AAPC=-47.371%, P<0.001), and the global age-standardized DALY rate also declined (AAPC=-19.309%, P<0.001).

High systolic blood pressure, smoking, and ambient particulate matter pollution were the main risk factors. Gender and age distribution showed that the disease burden was higher in males than females both globally and in China, and was mainly concentrated in the elderly population aged 65 years and above. Predictive analysis indicated that the global ICH disease burden would show a decreasing trend from 2022 to 2035. Conclusion China has achieved positive results in controlling the disease burden of intracerebral hemorrhage, but continued attention to the prevention and control of males, elderly populations, and major risk factors is still needed. In the future, by strengthening public health policies, improving the efficiency of medical resource utilization, and promoting healthy lifestyles, it is expected that the disease burden of ICH can be further reduced and the quality of life of patients improved.

Full Text

Trend and Prediction Analysis of the Changing Disease Burden of Intracranial Hemorrhage in China and Worldwide from 1990 to 2021

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Abstract

Background Intracranial hemorrhage (ICH) is a leading cause of death and disability globally, and analyzing its disease burden is crucial for developing effective prevention strategies.

Objective To analyze the evolution of the ICH disease burden and its risk factors in China and globally from 1990 to 2021, and to predict the disease burden trend from 2022 to 2035, providing a scientific basis for precise prevention and control measures.

Methods Based on the Global Burden of Disease (GBD) 2021 database, we analyzed ICH incidence, mortality, and disability-adjusted life years (DALY) in China and globally. Joinpoint regression was used to calculate the average annual percentage change (AAPC) in disease burden trends, and a Bayesian

age-period-cohort (BAPC) model was applied to predict ICH incidence, mortality, and DALY burden from 2022 to 2035. The comparative risk assessment framework of GBD was used to evaluate the attributable effects of risk factors such as high systolic blood pressure, smoking, and air pollution on the disease burden.

Results In 2021, the number of ICH cases globally and in China was 3,444,338 and 1,173,288, respectively, representing increases of 46.1% and 51.6% compared to 1990. From 1990 to 2021, the global age-standardized incidence rate showed a downward trend (AAPC=-0.589%, P<0.001), with a more significant decline in China (AAPC=-1.507%, P<0.001). In 2021, the number of ICH deaths globally and in China was 3,308,367 and 1,322,893, respectively, representing increases of 41.3% and 44.9% compared to 1990. The global age-standardized mortality rate decreased (AAPC=-0.731%, P<0.001), with a more substantial decrease in China (AAPC=-2.265%, P<0.001). China's age-standardized DALY rate for ICH in 2021 showed a significant decline compared to 1990 (AAPC=-47.371%, P<0.001), while the global age-standardized DALY rate also decreased (AAPC=-19.309%, P<0.001). High systolic blood pressure, smoking, and environmental particulate pollution were the main risk factors. The disease burden was higher in males than in females across all age groups, with the highest burden in those aged 65 and older. Predictive analysis indicates a declining trend in the global ICH disease burden from 2022 to 2035.

Conclusion China has made positive progress in controlling the ICH disease burden but still needs to focus on prevention and control measures for males, the elderly, and major risk factors. In the future, strengthening public health policies, improving medical resource efficiency, and promoting healthy lifestyles could further reduce the ICH disease burden and enhance patients' quality of life.

Keywords Intracranial hemorrhage; Public health strategy; Global burden of disease; Risk factors; Predictive analysis

Introduction

Stroke has consistently ranked as a leading cause of death and disability worldwide [**?**]. Intracranial hemorrhage (ICH) is the second most common type of cerebrovascular disease after ischemic stroke [**?**]. Characterized by bleeding within the brain parenchyma, ICH is a common neurosurgical emergency with high incidence, disability, and mortality rates [**?**]. Over the past several decades, the incidence of ICH has shown a continuous upward trend both globally and in China [**?**]. In Western countries, ICH accounts for approximately 15% of all strokes and represents 10%–30% of all stroke hospitalizations [**?**]. The situation is more severe in China due to its large population, with ICH comprising about 18.0%–47.6% of all strokes in the country. The 30-day mortality rate reaches 35%–52%, and only about 20% of patients regain self-care ability within

six months [**?**]. Although ICH has a lower incidence than ischemic stroke, its higher mortality and morbidity risk places an increasing burden on healthcare systems and economies, making it a major public health concern [**?**].

In recent years, significant progress has been made in the diagnosis and treatment of ICH. Despite advances in public health services for blood pressure management, the incidence of ICH remains severe due to socioeconomic development, lifestyle changes, shifts in population risk factors, and demographic aging. Evidence from North America and Europe indicates that population aging and rising prevalence of important risk factors such as obesity, diabetes, and hypertension suggest that the burden of ICH may increase in the coming years [**?**].

Currently, research on ICH both domestically and internationally has focused primarily on clinical treatment and management, with relatively limited attention to the disease burden caused by ICH—an area that urgently needs greater focus. Existing studies often concentrate on individual risk factors, specific regions, and particular populations, resulting in a narrow research perspective that lacks breadth and systematicity. Domestic research on ICH epidemiological trends and disease burden is notably insufficient, particularly lacking systematic studies on long-term evolution patterns and longitudinal risk factor analysis. This limits the ability of current literature to fully reveal the characteristics of China' s ICH disease burden and constrains the development of scientific prevention and control strategies. This study utilizes the latest Global Burden of Disease Study database (GBD) to examine the spatiotemporal dynamics of ICH disease burden in China and globally from 1990–2021. Through statistical modeling, we systematically evaluate the evolution trends of disease burden indicators and major risk factors, and combine predictive models to forecast changes in ICH disease burden over the next 15 years (2022–2035), providing a basis for precise prevention and control.

Methods

1.1 Data Sources

The GBD 2021 study integrated multi-source heterogeneous data, including population surveys, census registrations, vital statistics systems, and other health-related data sources. Through standardized modeling methods, it quantified health loss from 371 diseases across 204 countries and regions. This assessment covers core indicators such as incidence and mortality, constructing a systematic disease burden evaluation framework [**?**].

1.2 Research Methods

This study calculated multiple indicators reflecting disease burden, including incidence rate, mortality rate, disability-adjusted life years (DALY), years lived with disability (YLD), and years of life lost (YLL). The general calculation

methods for these indicators have been described in previous reports [**?**]. Incidence rate represents disease frequency, defined as the number of new ICH cases per 100,000 population. Mortality rate refers to the actual number of deaths related to ICH. DALY is calculated by summing YLL and YLD [**?**], measuring both the reduction in life expectancy and disability caused by disease. The YLL calculation formula is: YLL = N × L, where N represents the number of deaths and L represents life expectancy at the time of death (in years). The YLD calculation formula is: YLD = I × DW × L, where I represents the number of cases, DW represents disability weight, and L represents the average duration of the case until remission or death [**?**]. Age-standardized rates for all indicators were standardized using the 2021 global population [**?**].

Additionally, this study systematically analyzed the impact of risk factors including high systolic blood pressure, smoking, ambient particulate matter pollution, and indoor air pollution from household solid fuel use on ICH disease burden, based on the GBD study' s comparative risk assessment framework [**?**].

1.3 Statistical Methods

This study used Joinpoint regression (https://surveillance.cancer.gov/joinpoint/) to calculate the average annual percentage change (AAPC). The Joinpoint regression model describes continuous changes in overall trend slopes through shift analysis and divides long-term trend lines into several statistically significant trend segments through model fitting. In this model, AAPC > 0 indicates an increasing trend, while AAPC < 0 indicates a decreasing trend. A trend is considered statistically significant only when its 95% confidence interval (CI) does not contain zero (i.e., the upper and lower bounds have the same sign); otherwise, the trend is considered stable. Simultaneously, we employed a Bayesian age-period-cohort (BAPC) model to construct a multidimensional prediction system [**?**], using the R package BAPC to forecast ICH incidence and mortality burden in China and globally from 2022–2035. For more intuitive data presentation, we used the ggplot2 package for data visualization.

Results

2.1 Epidemiological Analysis of ICH in China and Worldwide, 1990-2021

2.1.1 Trends in ICH Incidence Burden The number of ICH cases in China increased significantly from 774,011 in 1990 to 1,173,288 in 2021, representing a 51.6% increase. During the same period, global cases rose from 2,358,349 to 3,444,338, a 46.1% increase. China' s crude incidence rate increased from 65.792 to 82.466 per 100,000 person-years, showing a significant upward trend (AAPC = 0.593%, 95% CI = 0.526%-0.660%, P < 0.001). In contrast, the age-standardized incidence rate decreased from 108.931 to 61.153 per 100,000 person-years, with an average annual decline of -1.507% (95% CI = -1.568% to -1.446%, P < 0.001). Gender disparities continued to widen, with male crude

incidence rates consistently higher than female rates in both China and globally (male/female ratio: 1.13 in 1990, 1.31 in 2021). At the global level, the crude incidence rate remained stable (AAPC = 0.001%, 95% CI = -0.023%-0.026%, P > 0.05), while the age-standardized incidence rate declined significantly (AAPC = -0.589%, 95% CI = -0.612% to -0.565%, P < 0.001). Gender distribution showed that the global male age-standardized incidence rate was 45% higher than that of females (male/female ratio = 1.45 in 2021), see and [Figure 1: see original paper]A.

2.1.2 Trends in ICH Mortality Burden The number of ICH deaths in China increased from 913,023 in 1990 to 1,322,893 in 2021, a 44.9% increase. Global deaths rose from 2,341,558 to 3,308,367 during the same period, a 41.3% increase. China' s crude mortality rate increased from 77.608 to 92.982 per 100,000 person-years, showing a significant upward trend (AAPC = 0.506%, 95% CI = 0.425%-0.587%, P < 0.001). Global crude mortality rate decreased slightly (AAPC = -0.062%, 95% CI = -0.078% to -0.046%, P < 0.001). After age standardization, both China (AAPC = -2.265%, 95% CI = -2.377% to -2.154%, P < 0.001) and the world (AAPC = -0.731%, 95% CI = -0.752% to -0.710%, P < 0.001) showed overall declining trends in standardized mortality rates, with China' s decline being particularly pronounced. However, China' s age-standardized mortality rate remained significantly higher than the global average in both 1990 and 2021, see .

The line chart of standardized mortality rates shows that male ICH standardized mortality rates in both China and globally remained higher than female rates throughout 1990–2021. China' s standardized mortality rate fluctuated more significantly than the global rate, particularly among males. From 1990–2005, China' s male, female, and overall population ICH standardized mortality rates were all higher than global averages. Since 2005, the gap between China' s rates and global levels has narrowed substantially, see [Figure 1: see original paper]B.

2.2 Trends in ICH Disease Burden (YLD, YLL, and DALY) in China and Worldwide, 1990 and 2021

Overall, China' s age-standardized YLD rate, YLL rate, and DALY rate for the entire population were higher than global levels from 1990–2021. However, over time, China' s age-standardized DALY rate declined at a rate of -47.371% (95% CI = -49.142% to -45.601%, P < 0.001), significantly greater than the global decline (AAPC = -19.309%, 95% CI = -19.713% to -18.904%, P < 0.001). The difference in YLL rate decline was even more pronounced (China: AAPC = -46.804%, P < 0.001; Global: AAPC = -18.788%, P < 0.001). Although the YLD rate decline was modest, China (AAPC = -0.534%, P < 0.001) still outperformed the global average (AAPC = -0.294%, P < 0.001). The male-to-female DALY rate ratio in China increased from 1.33 in 1990 to 1.85 in 2021, indicating a worsening DALY burden among males. For YLD rates, the male-to-female ratio in China rose from 0.98 to 1.22, showing a more significant decline in female

YLD rates. For YLL rates, the male-to-female ratio in China increased from 1.34 to 1.88, meaning female YLL rates declined relatively faster. Globally, the male-to-female DALY rate ratio increased from 1.31 to 1.51, reflecting widening gaps between males and females worldwide. The YLD rate gender ratio rose from 1.05 to 1.20, indicating faster declines in female YLD rates globally. The male-to-female YLL rate ratio increased from 1.31 to 1.53, showing that global female YLL rates also declined faster than male rates, see [Figure 2: see original paper] and .

2.3 Age Distribution of ICH Disease Burden in China and Worldwide, 1990-2021

In terms of prevalence, incidence, mortality, and DALY rates in both China and globally increased significantly with age, particularly among the elderly. Incidence, mortality, and DALY rates in older populations were substantially higher than in younger and middle-aged groups, with even faster growth rates in those aged 75 and above. In 2021, the incidence rate among Chinese individuals over 75 was 1.73 times the global average; mortality was 1.68 times the global average; and DALY rate was 0.932 times the global average. By gender, males in both China and globally had higher incidence and mortality rates than females across all age groups. Specifically, Chinese males aged 65+ had higher incidence and mortality rates than females, while global males aged 60+ had higher rates than females. However, among the elderly—particularly females over 65 in China and over 75 globally—the increase in DALY rates was faster than in males, see [Figure 3: see original paper].

2.4 Risk Factors for ICH in China and Worldwide, 1990 and 2021

From 1999-2021, the main risk factors for ICH globally and in China were high systolic blood pressure, followed by smoking and ambient particulate matter pollution. These factors had the greatest impact on ICH DALYs across different years. The decline in age-standardized DALY rate attributable to high systolic blood pressure in China from 1990-2021 was greater than the global decline, with China' s reduction at 42.4% versus 32.2% globally. Smoking-related health risks in China decreased to some extent from 1990-2021, particularly after 2005 when the trend became more pronounced, though overall levels remained higher than the global average. Compared to the global situation, ambient particulate matter pollution and indoor air pollution from household solid fuel use posed a more significant burden in China, but the magnitude of decline was also more substantial than globally, see [Figure 4: see original paper].

2.5 Prediction of ICH Prevalence and Disease Burden in China and Worldwide, 2022-2035

BAPC model predictions show that ICH incidence rates in both China and globally are expected to decline overall from 2022-2035. In China, male incidence is projected to decrease from 75.59 per 100,000 person-years in 2022 to 62.86 per

100,000 person-years, while female incidence is expected to decline from 48.38 to 35.21 per 100,000 person-years. Globally, male incidence is projected to decrease from 48.90 to 42.97 per 100,000 person-years, and female incidence from 33.31 to 28.45 per 100,000 person-years. The decline in incidence among the Chinese population is expected to be more significant than the global average.

For mortality, both China and the world are expected to maintain an overall declining trend from 2022–2035, with China' s decline projected to be more pronounced. Mortality among Chinese males is expected to decrease from 95.88 to 74.41 per 100,000 person-years, while Chinese female mortality is projected to decline from 49.38 to 31.61 per 100,000 person-years. Globally, male mortality is expected to decrease from 47.46 to 39.70 per 100,000 person-years, and female mortality from 31.63 to 24.09 per 100,000 person-years.

Regarding DALY burden, both China and the world show declining trends, with China being particularly notable. Chinese male DALY rates are projected to decrease from 1,882.94 to 1,519.50 per 100,000 person-years, while female DALY rates are expected to decline from 961.02 to 632.48 per 100,000 person-years. Globally, male DALY rates are projected to decrease from 1,135.47 to 954.85 per 100,000 person-years, and female rates from 732.49 to 558.77 per 100,000 person-years. Overall, the declines in mortality, incidence, and DALY rates among Chinese males are expected to exceed those among females, while global gender differences are relatively smaller. Mortality, incidence, and DALY rates among males in both China and globally are projected to remain higher than those among females from 2022–2035, see [Figure 5: see original paper].

Discussion

3.1 China Faces Severe Challenges in ICH Prevention and Control, with Particularly Heavy Burden Among Males and the Elderly

Our findings show that China' s age-standardized ICH incidence, mortality, and DALY rates declined overall from 1990–2021, mirroring global trends. However, the magnitude of decline in China' s three indicators was more significant than the global average, though rates remained higher than global levels during the same period. This demonstrates that China has made remarkable progress in controlling ICH incidence, mortality, and DALY rates, but a gap still exists compared to global averages. China' s standardized DALY rate showed the largest decline, indicating significant achievements in reducing the disease burden caused by ICH, though further strengthening in disability management is still needed. In recent years, acupuncture as a traditional Chinese medicine therapy has received increasing attention for its role in ICH rehabilitation. Several studies have shown that acupuncture plays an important role in various aspects of ICH recovery, including motor function improvement, pain management, rehabilitation process promotion, and quality of life enhancement [**?**]. Therefore, government and relevant departments can effectively promote the application and development of acupuncture in ICH rehabilitation, thereby improving treat-

ment outcomes and quality of life for patients and advancing the development of traditional Chinese medicine.

From a gender perspective, both in China and globally, standardized incidence, mortality, and DALY rates were higher among males than females, with gender disparities widening over time and showing an increasing trend. The expanding gender gap may indicate that men face greater disparities than women in terms of exposure to health risk factors, access to health protection measures, and utilization of health services. Therefore, further research and policy interventions are needed to strengthen attention to male populations, reduce gender health disparities, and promote gender equality and health equity.

Across different age groups, statistics from both China and globally show that the elderly bear higher disease incidence, mortality risk, and heavier DALY burden, particularly in those aged 75 and above—consistent with previous research identifying the elderly as the high-incidence population for ICH [**?**]. This phenomenon indicates that the elderly are more susceptible to ICH due to factors such as physiological degeneration, accumulation of chronic diseases, and possible limitations in access to medical resources [**?**]. Additionally, the cerebrovascular systems of elderly populations may develop increased vulnerability with age, raising ICH risk. Compared globally, the differences in incidence, mortality, and DALY rates among China' s elderly population were particularly prominent from 1990–2021, likely reflecting intensified population aging and increased health problems among the elderly in China [**?**].

China entered an aging society in 2000 and has gradually become the country with the largest elderly population in the world [**?**]. This increasing disparity suggests a need for greater attention to the health of elderly populations and a shift in prevention and control focus toward this group. Future measures should include: (1) strengthening chronic disease management for the elderly, such as hypertension and diabetes, which are important risk factors for cerebrovascular diseases including ICH; (2) improving health education for the elderly to enhance awareness of healthy lifestyles, such as proper diet and appropriate exercise; (3) improving healthcare services for the elderly to ensure timely access to necessary medical care; and (4) strengthening the social security system for the elderly to reduce their economic burden.

3.2 High Systolic Blood Pressure and Smoking Are the Primary Risk Factors for ICH

In 1990 and 2021, high systolic blood pressure and smoking were the main risk factors for DALY rates in both China and globally. This finding aligns with existing research [**?**]. In 2019, stroke disability-adjusted life years attributable to high systolic blood pressure in China exceeded 25 million [**?**]. Evidence indicates that controlling hypertension is associated with significant reductions in ICH events and mortality [**?**]. In recent years, the prevalence of hypertension in China has continued to rise. However, patient awareness of their hypertension

status, treatment rates, and blood pressure control effectiveness remain relatively low [**?**]. Therefore, improving primary care systems, increasing insurance coverage, widely adopting evidence-based hypertension guidelines, and establishing health examination and screening centers nationwide will help reduce high systolic blood pressure and consequently decrease the associated disease burden [**?**]. Notably, the declining trend in DALY rates for hypertension-related ICH in China after 2005 may be attributed to multiple synergistic policies, including the National Essential Public Health Services Program (which launched standardized hypertension management in 2009), improved universal health insurance coverage increasing treatment accessibility, and advocacy for healthy lifestyles (such as salt reduction initiatives) [**?**]. Future efforts should further compress the disease burden attributable to hypertension by strengthening primary care capacity, expanding screening coverage, and implementing evidence-based stepped blood pressure-lowering strategies.

Among other top risk factors, air pollution (including ambient particulate matter pollution and household air pollution from solid fuel use) and smoking have consistently ranked high in both China and globally. Air pollution has remained an important risk factor worldwide, with its attributable DALY rate staying at high levels from 1990–2021. In China, this factor also showed high impact, particularly in rural households where solid fuel cooking is widespread [**?**]. Incomplete combustion of solid fuels produces compounds such as carbon monoxide, sulfur dioxide, and PM2.5 (fine particulate matter with diameter $ $2.5 m) [**?**]. Previous studies have confirmed that exposure to solid fuel use adversely affects health, increasing risks of hypertension, cardiovascular disease hospitalization, and stroke [**?**]. As China promotes clean energy and improves household environments, the impact of air pollution has decreased.

Secondly, smoking significantly affects ICH through multiple physiological mechanisms and risk factors. Heavy smokers face higher risks of intracerebral hemorrhage and subarachnoid hemorrhage, and smoking is also associated with poorer prognosis and higher mortality [**?**].

Among dietary factors, low fruit and vegetable intake and high sodium intake are major contributors to ICH disease burden. Sodium intake levels in China are notably higher than the global average. Previous studies have shown that high-sodium diets and insufficient intake of green foods like fruits and vegetables significantly affect ICH, potentially increasing not only its incidence but also impacting recovery [**?**]. Therefore, China needs to promote healthy dietary guidelines through education and policy, raise public awareness of healthy eating, encourage improved dietary structure, foster healthy lifestyles, control salt intake, implement smoking cessation and alcohol restriction, and adopt effective environmental pollution prevention measures to establish a comprehensive ICH prevention and control system covering the entire society.

3.3 Projected Declines in Age-Standardized Incidence, Mortality, and DALY Rates in China from 2022–2035

According to our predictions, both China and the world will see declines in age-standardized incidence, mortality, and DALY rates from 2022–2035, with China' s indicators showing more significant reductions. These achievements are attributable to government commitment, continuous improvement of the public health system, and increased public health awareness. Initiatives such as the Healthy China Action Plan aim to raise public health awareness and improve lifestyles and dietary habits, thereby reducing risk factors for chronic diseases [**?**]. Additionally, implementing stricter environmental protection regulations [**?**], improving indoor and outdoor air quality, and enhancing ICH-related awareness, treatment, and control rates through community health services and public health programs have helped reduce the disease burden from ICH among Chinese residents. When developing and implementing future policies, past experiences can be drawn upon to further strengthen and refine preventive measures for the continuous and effective management of China' s ICH disease burden.

3.4 Study Limitations

Although the GBD 2021 database provides comprehensive data support, the data collection process may have biases, and the completeness and accuracy of data from some regions are suboptimal, affecting result reliability. Disease burden indicator calculations rely on model assumptions and parameter estimates, which entail uncertainties even after rigorous validation. This study focused on major risk factors such as high systolic blood pressure and smoking and did not cover all potential risk factors, which may lead to underestimation or overestimation of some factors' impacts. While the results can provide general guidance for ICH prevention and control in China and globally, disease burden and risk factors vary across different regions and populations, requiring further detailed research to develop targeted strategies.

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Author Contributions

LIN Derong conceptualized the study, designed the research protocol, retrieved data from the GBD 2021 database, performed data collation and statistical analysis, and wrote the manuscript. LI Yue retrieved GBD 2021 database information, collated data, and prepared all figures and tables. ZHANG Xiaowen, YE Xiaolin, and RUAN Bo retrieved the GBD 2021 database, extracted data, and performed summarization, collation, and secondary verification. XUE Aiguo conducted quality control and review of the manuscript, revised the final version, and takes responsibility for the paper.

Conflict of Interest

The authors declare no conflict of interest.

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Note: Figure translations are in progress. See original paper for figures.