

Analysis and Prediction of Brain Tumor Mortality Trends in China, 2000-2019: Postprint

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Abstract

Background: Worldwide, the health hazards of brain tumors to the population have received extensive attention, but there are still no relevant studies on the analysis and prediction of brain tumor mortality trends in China.

Objective: To analyze the mortality trend of brain and central nervous system cancers (abbreviated as brain tumors) in China from 2000 to 2019, and to predict the crude mortality rate of brain tumors in the next five years, providing reference for brain tumor prevention and control.

Methods: Mortality data for brain tumors in China from 2000-2019 were collected from the Global Health Data Exchange (GHDx) database. The Joinpoint regression model was applied to analyze mortality trends, and the intrinsic estimator (IE) method and Age-period-cohort (APC) model were used to estimate age, period, and birth cohort effects on mortality rates. Using R (version 4.1.3), a GM(1,1) model was established based on brain cancer mortality data from 2000-2019 for forecasting.

Results: From 2000 to 2019, the age-standardized mortality rates of brain tumors in Chinese males and females showed a decreasing trend. The APC model revealed that mortality risk for both sexes increased with age and period, while later birth cohorts had lower mortality risk than earlier cohorts. The model predicted that after 2019, the crude mortality rate of brain tumors in China will continue to rise, reaching 4.54 per 100,000 in 2024.

Conclusion: From 2000 to 2019, the age-standardized mortality rate of brain tumors in China overall showed a decreasing trend, while mortality risk increased with advancing age and over time, with earlier birth cohorts experiencing greater risk. Prediction results indicate that both incidence and mortality rates will continue to rise in the next five years, and the situation of brain tumor prevention and control in China remains severe. Prevention and control publicity efforts

for high-risk populations should be strengthened, healthy and proper lifestyles should be promoted, and the disease burden of brain tumors should be reduced.

Full Text

Analysis and Prediction of Brain Tumor Mortality Trends in China, 2000-2019

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Abstract

Background: While the health burden of brain tumors has garnered widespread global attention, research specifically analyzing and predicting mortality trends for brain tumors in China remains scarce.

Objective: To analyze the mortality trends of brain and central nervous system cancers (brain tumors) in China from 2000 to 2019 and predict crude mortality rates for the next five years, providing evidence for brain tumor prevention and control.

Methods: Brain tumor mortality data for China from 2000-2019 were extracted from the Global Health Data Exchange (GHDx) database. Joinpoint regression models were used to analyze mortality trends, while the intrinsic estimator (IE) method and Age-Period-Cohort (APC) model were employed to estimate age, period, and birth cohort effects. The GM(1,1) model was constructed using R (version 4.1.3) to predict future trends based on 2000-2019 brain cancer mortality data.

Results: From 2000 to 2019, age-standardized mortality rates (ASMR) for brain tumors in both Chinese men and women showed declining trends. The APC model revealed that mortality risk increased with age and calendar period for both sexes, while later birth cohorts exhibited lower mortality risk than earlier cohorts. Model predictions indicated that crude mortality will continue rising after 2019, reaching 4.54 per 100,000 in 2024.

Conclusion: Between 2000 and 2019, China's brain tumor ASMR generally declined, though mortality risk increased with advancing age and calendar time, with earlier-born cohorts facing greater risk. Predictions suggest both incidence and mortality will continue rising over the next five years, indicating that China's brain tumor prevention and control situation remains serious. Enhanced prevention efforts targeting high-risk populations, promotion of healthy lifestyles, and reduction of disease burden are urgently needed.

Keywords: Brain tumor; Mortality trend; Age-Period-Cohort model; Prediction

Introduction

According to China's National Cancer Center, brain tumors caused 16,351 deaths in 2016, ranking 10th in the national cancer mortality spectrum [1]. In 2020, China, India, and the United States had the highest numbers of brain tumor deaths worldwide [2]. Brain tumors invariably cause increased intracranial pressure and compression of brain tissue, resulting in painful symptoms and severe central nervous system damage [3]. They may also cause serious disabilities, including seizures, memory or language problems, and physical dysfunction [4]. Due to the special location of brain tumors, complex diagnostic methods, and China's progressively aging population, the disease burden of brain tumors is increasing annually [5,6], representing a major challenge in current chronic disease prevention and control. Therefore, conducting long-term epidemiological studies on brain tumors in China and appropriately predicting future changes can help identify etiological clues and provide timely, scientifically effective prevention and control measures.

This study extracted brain tumor mortality data for China from 2000-2019 in the GBD 2019 database, analyzed and evaluated mortality rates using Joinpoint regression and APC models, and predicted mortality trends for the next five years using the grey model GM(1,1) to provide evidence for brain tumor prevention, control, and burden reduction in China.

Methods

1.1 Data Sources Data were obtained from the GBD 2019 database (official website: <https://www.healthdata.org/>), which enables analysis of epidemiological characteristics (incidence, prevalence, mortality, etc.) for 328 diseases and injuries across 195 countries and territories [7], and assesses disease burden. The database also analyzes disease impact on patient survival through indicators such as tumor location, treatment access, and treatment quality [8]. This study extracted brain tumor mortality data for China from 2000-2019 [9], including crude mortality rates (CMR). Brain tumor cases were identified using

International Classification of Diseases (ICD) 10th revision codes C70–C72 for the brain and central nervous system.

1.2.1 Basic Indicators Brain tumor mortality data for China from 2000–2019 extracted from the GBD 2019 database were organized and stratified by sex and age to calculate age-standardized mortality rates (ASMR). The standard population structure used 2019 global population data provided by the database [10].

1.2.2 Joinpoint Regression Model Developed by the U.S. National Cancer Institute, this model uses a log-linear model based on Poisson distribution to fit cancer mortality rates, dividing trends into segments with connection points called “joinpoints.” The Monte Carlo permutation test determines joinpoint location, number, and P-values [11].

Model equation: (2-1)

In the equation: y represents brain tumor mortality, x represents observation year, β_0 is the constant term, β are regression coefficients for each segment ($i=1,2,3,\dots,k$), and τ represent joinpoints ($i=1,2,3,\dots,k$).

1.2.3 APC Model The APC model is a multivariate regression model based on Poisson distribution that represents mortality trends across three dimensions—age, period, and birth cohort—while controlling for interaction effects to quantitatively analyze risk factors [12,13]. However, because birth cohort equals period minus age, severe multicollinearity exists among the three variables, yielding infinite solutions without unique effect estimates. Since Poisson distribution requires parameter independence, this issue must be resolved. To avoid these limitations, this study applied the intrinsic estimator (IE) method, which solves the non-estimability problem while producing a unique solution without requiring restrictive assumptions, offering broad applicability [14,15].

Using Stata 15.0, this study applied the APC model to describe and estimate age, period, and cohort effects on brain tumor mortality. The APC model expression is: $\ln(R_{ijk})$ (2-2)

In the expression: $\ln(R_{ijk})$ represents the natural logarithm of brain tumor mortality; α is the intercept; β is the age effect for the i th age group; γ is the period effect for the j th period; δ is the cohort effect for the k th cohort.

1.2.4 GM(1,1) Model The GM(1,1) model is the core of grey prediction models, established using mathematical concepts such as grey derivatives and relational analysis, representing a substructure of econometric models [11]. Its advantage lies in not relying on large sample sizes or statistical methods to extract information patterns, but rather using accumulated generation to transform original data sequences and mine patterns from the accumulated sequence [16].

The GM(1,1) model is widely applied across social fields, particularly in situations with “small samples, poor information, and incomplete data mastery” [17].

Grey sequence GM(1,1) model construction and prediction steps:

- (1) Let the original data sequence be: $x^{(0)}$, (2-3)
- (2) Generate accumulated and moving average sequences:
Perform first-order accumulated generating operation (AGO) on the original data sequence to create an increasing sequence: $X^{(1)}$, and calculate the moving average sequence: $Z^{(1)}(k)$. ,...
- (3) Exponential pattern and smoothness testing:
When $t > 3$, if $\sigma(t) < 1.5$ the quasi-exponential pattern is satisfied; if $\sigma(t) < 0.5$ the quasi-smoothness condition is satisfied.
- (4) Establish GM(1,1) equation:
where a is the development coefficient, u is the grey action quantity, $k=0,1,2,3,\dots,n$
- (5) Generate predicted values $X^{(0)}$: This process is achieved through inverse accumulated generating operation.
- (6) Prediction accuracy testing:
GM(1,1) model prediction accuracy can be tested using the posterior variance ratio (C) and small error probability (p). (2-4) (2-5) (2-6) (2-7) (2-8) (2-9) (2-10)
Where: S_1 and S_2 are standard deviations of actual values and residuals respectively; \bar{r} is the mean residual. Model prediction accuracy criteria are:
Excellent: $p \geq 0.95$ and $C \leq 0.35$ Good : $p \geq 0.80$ and $C \leq 0.50$ Moderate : $p \geq 0.70$ and $C \leq 0.65$
Poor: $p < 0.70$ and $C > 0.65$ [14]
- (7) Precision testing:
GM(1,1) model precision can be tested using mean absolute percentage error (MAPE) and model precision δ . If $MAPE \leq 10\%$, the model meets precision requirements.

1.3 Statistical Methods Joinpoint Regression Program 4.7.0.0 software was used for regression analysis, fitting Joinpoint models to brain tumor ASMR for both sexes to calculate annual percent change (APC) and average annual percent change (AAPC), evaluating mortality trends from 2000-2019. The Joinpoint model identifies turning points in ASMR across years. $APC < 0$ indicates declining mortality over time; $APC > 0$ indicates increasing mortality; if no turning points exist, $APC = AAPC$, indicating a monotonic trend [18].

For the APC model using IE, age was grouped in 5-year intervals (20 age groups total). APC models require equal interval widths for period and age groups,

so 2000–2019 was divided into 4 periods of consecutive years; correspondingly, 1904–2018 birth cohorts were divided into 23 cohorts of consecutive 5-year intervals. The model evaluated mortality changes across age, period, and cohort groups, calculating effect coefficients where values <0 indicate decreased mortality and >0 indicate increased mortality, with higher values reflecting higher mortality. All tests were two-sided with $\alpha=0.05$.

The GM(1,1) model was constructed and predictions made using R (version 4.1.3). Test level $\alpha=0.05$.

Results

2.1 Trends in Crude and Age-Standardized Mortality Rates From 2000–2019, brain tumor CMR in China showed an upward trend. National CMR increased from 3.59 to 4.47 per 100,000; male CMR increased from 3.86 to 4.92 per 100,000; female CMR increased from 3.29 to 4.00 per 100,000. Overall, brain tumor ASMR in China showed a downward trend. National ASMR decreased from 4.10 to 3.63 per 100,000, an 11.46% decline from 2000–2019; male ASMR decreased from 4.58 to 4.20 per 100,000 (8.30% decline); female ASMR decreased from 3.66 to 3.11 per 100,000 (15.03% decline). See Figure 1.

Figure 1 [Figure 1: see original paper] Trends of CMR and ASMR of brain tumors in China from 2000 to 2019 across the country and between sexes

Joinpoint regression analysis revealed that overall, national and sex-specific brain tumor ASMR showed declining trends, with AAPC values of -0.68%, -0.47%, and -0.87% respectively, all statistically significant. This indicates that from 2000–2019, national brain tumor ASMR declined by an average of 0.68% annually, male ASMR by 0.47%, and female ASMR by 0.87%. National ASMR during 2014–2019 showed no statistically significant APC, indicating no change during this period, while male ASMR during 2000–2004 and 2015–2019 showed no significant changes. See Table 1.

Table 1 Trends of brain tumor ASMR in China from 2000 to 2019

Group	ASMR (/10 ⁵)	APC (95%CI)	AAPC (95%CI)
Overall	-1.02 ^a (-1.08–-0.96)	<0.001	-0.68 ^a (-0.76–-0.60)
Male	0.27 (-0.01–0.55)	-0.16 (-0.52–0.20)	-1.33 ^a (-2.24–-0.24)
Female	0.11 (-0.20–0.42)	-1.55 ^a (-1.73–-1.37)	<0.001
2015–2019	0.49 ^a (0.27–0.71)	<0.001	-

Note: a indicates $P<0.05$, statistically significant difference.

2.2.1 APC Model Analysis of Brain Tumor Mortality in Chinese Males Age effects showed that male brain tumor mortality risk initially de-

creased, then increased, then decreased again with age. The 20-<25 age group had the lowest risk (effect coefficient = -1.28), while the 90-<95 age group had the highest (effect coefficient = 1.25), representing a 197.66% increase from lowest to highest. Period effects showed gradually increasing mortality risk over time, with the lowest risk in 2000-2004 (effect coefficient = -0.09) and highest in 2015-2019 (effect coefficient = 0.08). Cohort effects showed a gradual decline, with coefficients decreasing from 0.62 in the 1904-1908 cohort to -1.28 in the 2014-2019 cohort. See Figure 2 [Figure 2: see original paper].

Figure 2 [Figure 2: see original paper] Age, period, cohort effect coefficient and 95%CI of Chinese male brain tumor mortality from 2000 to 2019

2.2.2 APC Model Analysis of Brain Tumor Mortality in Chinese Females Age effects showed increasing mortality risk with age, with the lowest risk in the 25-<30 age group (effect coefficient = -1.19) and highest in the 95+ age group (effect coefficient = 1.29), representing a 208.40% increase from lowest to highest. Period effects showed gradually increasing risk, with the lowest coefficient in 2000-2004 (-0.03) and highest in 2015-2019 (0.04). Cohort effects showed an initial increase followed by decline, rising from 0.36 in the 1904-1908 cohort to 0.57 in the 1929-1933 cohort, then gradually decreasing to -1.16 in the 2014-2019 cohort. See Figure 3 [Figure 3: see original paper].

Figure 3 [Figure 3: see original paper] Age, period, cohort effect coefficient and 95%CI of Chinese female brain tumor mortality from 2000 to 2019

2.3.1 GM(1,1) Model Feasibility Testing The original data sequence was accumulated and moving average sequences calculated for smoothness and exponential pattern testing. Results showed that when $k > 3$, $(k) < 0.5$ and $\sigma(k)$ (1,1.5), satisfying both smoothness and exponential pattern conditions. See Table 2 .

Table 2 Sequence and feasibility test of crude mortality rate ($/10^5$) of brain tumors in China from 2000 to 2019

Year (k)	Accumulated Sequence	Moving Average Sequence	Exponential Pattern Test (Ratio)	Smoothness Test (Smoothness Ratio)

2.3.2 Model Construction and Precision Testing Having passed feasibility testing, a grey sequence GM(1,1) model was constructed for $X^{(1)}(k)$ using R 4.1.3. Results showed: development coefficient $a = -0.0112$, grey action quantity $b = 3.4511$. The model equation is $Y(k) = 311.7483e^{\wedge}(0.0112(k-2000)) - 308.1618$. Comparing predicted versus actual mortality for 2000-2019, residual testing yielded MAPE = 1.68% and model precision = 98.32%; posterior variance ratio $C = 0.16$ and small error probability $p = 1.00$. Both accuracy indicators rated the model as “excellent,” suitable for 5-year trend prediction.

2.3.3 Model Prediction Results Model predictions show China's brain tumor crude mortality will continue rising over the next five years, reaching 4.34, 4.39, 4.44, 4.49, and 4.54 per 100,000 in 2020–2024 respectively. See Figure 4 [Figure 4: see original paper].

Figure 4 [Figure 4: see original paper] Model fitting and prediction results of brain tumor mortality in China from 2000 to 2024

Discussion

Worldwide cancer incidence and mortality are rising rapidly, driven primarily by population aging and growth, changing prevalence and distribution of major risk factors, and socioeconomic development [19]. As a major cancer type, brain tumor incidence has been increasing for decades [20]. Global detection rates of new brain tumor cases vary substantially [21], and epidemiological trends indicate brain tumor incidence will surge dramatically in coming decades, particularly in low- and middle-income countries [22]. GLOBOCAN 2020 estimated 308,102 new brain tumor cases globally (1.6% of all cancers, ranking 19th) and 251,329 deaths (2.5% of cancer deaths, ranking 13th) [19]. China's age-standardized mortality rate is 3.63 per 100,000 (male: 4.20; female: 3.11), exceeding global averages and indicating a severe burden.

Our results show China's brain tumor ASMR fluctuated but overall declined from 2000–2019. Notably, after reaching its lowest point, ASMR has recently trended upward, suggesting an increasing burden. Understanding these trends and making reasonable predictions is crucial for reducing disease burden and controlling brain tumor progression.

Mortality risk for both sexes showed a pattern of initial decline, then sustained increase, then final decline with age. Effect values were negative through the 50–<55 age group, becoming positive thereafter, indicating that risk increases with age after 55. This may relate to increased exposure to carcinogens like radiation, electromagnetic waves, microwaves, and N-nitroso compounds [23], as well as declining physiological function and population aging [5]. China's 2020 aging bulletin reported 264.02 million people aged 60+ (18.70% of population) and 190.64 million aged 65+ (13.50%) [24], indicating accelerated aging will further increase brain tumor burden.

Period effects analysis revealed that both male and female effects turned from negative to positive after 2010–2014, showing rising mortality across 2000–2019. This may relate to socioeconomic development, urbanization, industrialization, increased environmental carcinogens, greater exposure probability, and unhealthy lifestyles (overeating, staying up late, smoking, lack of exercise). Males have higher rates of unhealthy habits and occupational exposure than females [25], potentially explaining their higher burden.

Cohort effects for both sexes initially increased then continuously decreased.

Risk was positive through the 1964–1968 cohort, indicating later-born cohorts face lower risk, though peak effect cohorts differed by sex: males peaked in 1924–1928 (coefficient = 0.63), females in 1929–1933 (coefficient = 0.57). Post-peak declines may reflect: (1) Pre-1930s cohorts experiencing war, poor social conditions, scarce resources, and inadequate healthcare; (2) Improved economy and healthcare enabling early intervention and treatment (surgery, radiotherapy, traditional Chinese medicine) [26]; (3) Health education reducing unhealthy behaviors and improving health awareness [27].

The GM(1,1) model, rated as excellent in precision, predicts continuously rising crude mortality over the next five years, reaching 4.54 per 100,000 in 2024. This may relate to lack of simple early screening technology, nonspecific early symptoms easily misdiagnosed as migraines [28], and suboptimal post-surgical outcomes. As the world's largest developing country, China's rapid economic growth has introduced health challenges: widespread electronics use, air pollution, pesticide exposure, and other factors may correlate with brain tumor incidence and mortality [29–31].

This study utilized 20 years of GBD mortality data and applied the IE method to resolve APC multicollinearity, yielding more reliable results. Limitations include analyzing only mortality without incidence data to assess risk factors, and GBD's lack of urban-rural stratification for China. Future research with regional data would be more informative.

In conclusion, China's prominent population aging will likely worsen brain tumor burden. Prevention should focus on elderly populations, reduce occupational exposure, promote smoking cessation, limit alcohol, maintain healthy weight, and strengthen health education. Enhanced early diagnosis and treatment for those over 50 [32] and better therapeutic approaches are needed. Improved tumor registry data collection, particularly by pathological type, is essential for reducing China's brain tumor burden [6].

Author Contributions

DUAN Zhaohui conceived and designed the study and drafted the manuscript; DUAN Zhaohui and ZHANG Min collected and organized data and created figures; ZHANG Min, XU Jieru, and XIONG Wenjing revised the manuscript; CHEN Lei, ZHAO Xiangling, and ZHANG Yiyun performed quality control and final approval; all authors approved the final manuscript.

Conflict of Interest: The authors declare no conflict of interest.

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