Original Article

Changes on Stroke Burden Attributable to Ambient Fine Particulate Matter in China*

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Abstract

Objective In recent decades, China has implemented a series of policies to address air pollution. We aimed to assess the health effects of these policies on stroke burden attributable to ambient fine particulate matter ($PM_{2.5}$).

Methods *Joinpoint* regression was applied to explore the temporal tendency of stroke burden based on data from the Global Burden of Disease 2019 study.

Results The age-standardized rates of disability-adjusted life year (DALY) for stroke attributable to ambient $PM_{2.5}$ in China, increased dramatically during 1990−2012, subsequently decreased at an annual percentage change (APC) of −1.98 (95% confidence interval [*CI*]: −2.26, −1.71) during 2012−2019. For ischemic stroke (IS), the age-standardized DALY rates doubled from 1990 to 2014, and decreased at an APC of −0.83 (95% *CI*: −1.33, −0.33) during 2014−2019. Intracerebral hemorrhage (ICH) showed a substantial increase in age-standardized DALY rates from 1990 to 2003, followed by declining trends, with APCs of −1.46 (95% *CI*: −2.74, −0.16) during 2003−2007 and −3.33 (95% *CI*: −3.61, −3.06) during 2011−2019, respectively. Conversely, the age-standardized DALY rates for subarachnoid hemorrhage (SAH) generally declined during 1990−2019.

Conclusion Our results clarified the dynamic changes of the ambient $PM_{2.5}$-attributable stroke burden in China during 1990−2019, highlighting the health effects of air quality improvement policies.

Key words: Ambient fine particulate matter; Stroke; Disease burden; Temporal trend; Policy

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INTRODUCTION

Stroke is the third leading cause of disability-adjusted life years (DALYs), and is a major public health issue worldwide[1]. According to the Global Burden of Disease 2019 (GBD 2019) study , the incident cases, deaths and DALYs of stroke have increased sharply in the past three decades, reaching 12.2 million, 6.55 million and 143 million in 2019, respectively[2]. The burden of stroke is more pronounced in developing countries such as China[3]. A remarkable increase of stroke burden occurred in China during 1990-2019. It is estimated that 3.94 million new stroke cases, 13 million patients, 2.19 million deaths, and 45.9 million DALYs occurred in China in 2019[4-6].

Ambient fine particulate matter with an aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$) has been proved to be one of the leading environmental risk factors for population health in many countries[7-9], and it has presented a stronger effect on stroke compared to others pollutants, such as PM_{10} and NO_2[10,11]. As the largest developing country, China has experienced severe air pollution in recent decades[12]. Previous studies in China have showed that a 10 μg/m^3 increment in $PM_{2.5}$ can lead to a 0.34% increase in hospital admission of ischemic stroke for short-term exposure[13], and a 13% higher risk of incident stroke for long-term exposure[14]. Air pollution has caused widespread concern in China, and a series of governance policies have been implemented in recent years[15]. Subsequently, the national $PM_{2.5}$ concentration in China has gradually decreased since 2011[16]. Improvements in air quality can lead to significant public health benefits. Understanding the temporal patterns of the $PM_{2.5}$-attributable stroke burden is essential for developing tailored strategies for stroke prevention[17]. Thus, previous studies explored the trends in stroke burden attributable to $PM_{2.5}$ using the GBD 2019 study[18,19]. However, they simply focused on the general increasing trends since 1990, without a comprehensive analysis of the change patterns in different periods, especially the trends after the implementation of policies on air quality improvement in recent decades. Moreover, $PM_{2.5}$ has different effects on stroke subtypes[14]. Therefore, the dynamic trends in the burden of stroke and its subtypes attributable to ambient $PM_{2.5}$ in China, remain unclear. There is an urgent need to further evaluate the temporal trends for stroke and its subtypes.

Based on the GBD 2019 study, we aimed to comprehensively elaborate on the changing patterns in the disease burden of stroke and its subtypes attributable to ambient $PM_{2.5}$ at different stages across the past three decades in China.

MATERIALS AND METHODS

Data Sources

We obtained age-standardized rates, percents and numbers of DALY, death, year lived with disability (YLD), and year of life lost (YLL) for stroke and its subtypes attributable to ambient $PM_{2.5}$ in China during 1990-2019 from the GBD 2019 study. Age-standardized rates were computed using the 2019 Global Standard Population (Supplementary Table S1, available in www.besjournal.com)[20]. DALY indicates health loss from both non-fatal and fatal outcomes, and is calculated as the sum of YLL and YLD[4]. YLL is the loss of life due to premature death, and is computed as the number of stroke deaths multiplied by the standard remaining life expectancy at the time of death[4]. YLD is the loss of a healthy life caused by disability, and is calculated using stroke prevalence multiplied by the corresponding disability weights, representing the extent of health loss related to a particular health outcome[4]. These metrics can help policymakers better understand the disease burden caused by $PM_{2.5}$, improve air quality, and further contribute to stroke prevention and control. The prevalence estimates of stroke in China were based on systematic reviews of current Chinese researches, using a Bayesian meta-regression tool[4,21]. Stroke deaths in the GBD 2019 study were estimated using the Cause of Death Ensemble modelling method based on data mainly from surveillance systems, surveys, and the Center for Disease Control and Prevention in China[4,21].

Definition of Stroke

In the GBD 2019 study, stroke was identified as a rapidly progressing clinical sign of disturbance of cerebral function lasting more than 24 h or resulting in death according to the World Health Organization clinical criteria[21]. Stroke was classified as ischemic stroke (IS), intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH). IS was defined as an episode of neurological dysfunction triggered by focal cerebral, spinal, or retinal infarction; ICH was diagnosed as a non-traumatic hemorrhagic stroke with focal accumulation of blood in the brain; SAH was identified as a non-traumatic stroke caused by bleeding into the subarachnoid space in the brain. The International Classification of Diseases codes for stroke and its subtypes are listed in Supplementary Table S2 (available in www.besjournal.com)[4].

Estimates of Stroke Burden Attributable to Ambient $PM_{2.5}$

The exposure levels of ambient $PM_{2.5}$ in the GBD 2019 study were estimated by an improved rigorous modelling approach called the Data Integration Model for Air Quality, using multiple data sources, including satellite observations of aerosols in the atmosphere, $PM_{2.5}$ ground measurements, population data and chemical transport model simulations[7]. Notably, the GBD 2019 study made important changes to revise the relationship between $PM_{2.5}$ and stroke, including recruiting recent Chinese studies on $PM_{2.5}$, and using flexible splines to fit the risk data[7]. The ambient $PM_{2.5}$-attributable disease burden of stroke and its subtypes was evaluated by comparing the distribution of exposure to ambient $PM_{2.5}$ with exposure-risk estimates at each exposure level[21].

Statistical Analysis

Joinpoint regression was used to analyze the changing patterns of the burden of ambient $PM_{2.5}$-attributable stroke and its subtypes during 1990–2019. Grid search algorithm was selected to identify the optimal number and position of joinpoints, which were then verified using the Bayesian Information Criterion test. The maximum number of joinpoints in the *Joinpoint* regression model was set to five. The annual percentage change (APC) of each slope segment and the average annual percentage change (AAPC) from 1990 to 2019 showed the average degree of change in stroke burden over a specific period, and their 95% confidence intervals (*CI*) were calculated based on the t-distribution[22]. To compare the stroke burden in China with that globally, a z-test was applied[23]. All statistical tests were 2-sided and P < 0.05 was considered as statistically significant. Additionally, we calculated the contributions of YLLs and YLDs to DALYs for stroke attributable to $PM_{2.5}$ in China during 1990-2019. We further described the sex- and age-specific changing patterns of $PM_{2.5}$-attributable stroke burden.

The GBD Data Tool repository (http://ghdx.healthdata.org/gbd-results-tool) was used to obtain the available stroke burden data, and all analyses were performed using *Joinpoint* software, version 4.9.0.1, National Cancer Institute.

RESULTS

Age-Standardized Rates of DALY

The global ambient $PM_{2.5}$-attributable age-standardized DALY rates for stroke have fluctuated slightly over the past three decades, with values of 348.06, 146.16, 174.82 and 27.08 per 100,000 in 2019 for stroke, IS, ICH and SAH, respectively (Supplementary Figure S1, available in www.besjournal.com). Notably, China had much higher rates than the global level for most years (Supplementary Tables S3-S6, available in www.besjournal.com). As shown in Figure 1A and Table 1, the age-standardized DALY rates per 100,000 for stroke in China increased dramatically from 490.54 in 1990 to 727.08 in 2012, thereafter it decreased consistently with an APC of −1.98 (95% *CI*: −2.26, −1.71) during 2012−2019. It is worth noting that a brief decline was observed during 2004−2007, showing an APC of −1.31 (95% *CI*: −3.37, 0.79). Distinct trends were observed for different stroke subtypes. The age-standardized DALY rates per 100,000 for IS climbed from 141.06 to 303.55 during 1990−2014, then persistently decreased with an APC of −0.83 (95% *CI*: −1.33, −0.33) during 2014−2019, demonstrating a noticeable decline in most age groups among people aged 45 years or above (Figure 2A). For ICH, the DALY rates per 100,000 increased substantially from 273.64 in 1990 to 426.36 in 2003, and presented downward trends subsequently, with APCs of −1.46 (95% *CI*: −2.74, −0.16) during 2003−2007 and −3.33 (95% *CI*: −3.61, −3.06) during 2011−2019, respectively. We observed significant decreases of DALY rates for ICH during 2003−2019 among population aged ≥40 years (Figure 2B). In contrast, the DALY rates for SAH showed a general downward trend over the past three decades, with an AAPC of −2.64 (95% *CI*: −2.92, −2.37). Among the stroke subtypes, ICH had the highest $PM_{2.5}$-attributable age-standardized DALY rates, followed by IS. However, the gaps between ICH and IS have attenuated in recent decades. The trends in age-standardized DALY rates for stroke and its subtypes related to ambient $PM_{2.5}$ in males were similar to those in females, while males had much higher rates than females (Figure 1B and Supplementary Table S7, available in www.besjournal.com).

Age-Standardized Percents of DALY Attributable to Ambient $PM_{2.5}$

As shown in Supplementary Figure S2 and

Supplementary Table S8 (available in www.besjournal.com), the age-standardized percents of stroke burden attributable to ambient $PM_{2.5}$ increased with an AAPC of 2.86 (95%*CI*: 2.69, 3.03) during 1990–2019 in China, with a significant decline occurring after 2014. This phenomenon was also observed for ICH, IS and SAH. We found similar declining trends in both males and females, with males showing a greater decline than females.

Numbers of DALY

The numbers of DALY for stroke attributable to ambient $PM_{2.5}$ in China presented an upward trend over the past three decades, which increased consistently from 4.18 million in 1990 to 12.85 million in 2019, with an AAPC of 3.94 (95% *CI*: 3.61, 4.26) (Figure 1C and Table 1). The similar upward trend occurred in DALYs for IS, with an AAPC of 5.79 (95% *CI*: 5.50, 6.08). For ICH, the DALYs increased rapidly from 2.38 million in 1990 to 6.48 million in 2011, and then presented an obvious downward trend during 2011–2019, with an APC of −0.48 (95% *CI*: −0.76, −0.19). For SAH, DALYs fluctuated at a relatively low level over the entire period. Among the stroke subtypes, ICH dominated more than half of the stroke DALYs attributable to $PM_{2.5}$ in China each year from 1990 to 2019. By contrast, contribution of IS on stroke DALYs rose dramatically from 26.89% to 44.66% during 1990–2019, while contribution of SAH declined from 16.16% to 5.49%. We found that males and females shared similar trends in DALYs for stroke and its subtypes, whereas males had much higher DALYs than females (Figure 1D and Supplementary Table S9, available in www.besjournal.com).

Age-Standardized Rates of YLL and YLD

Considering that the DALY comprises YLL and

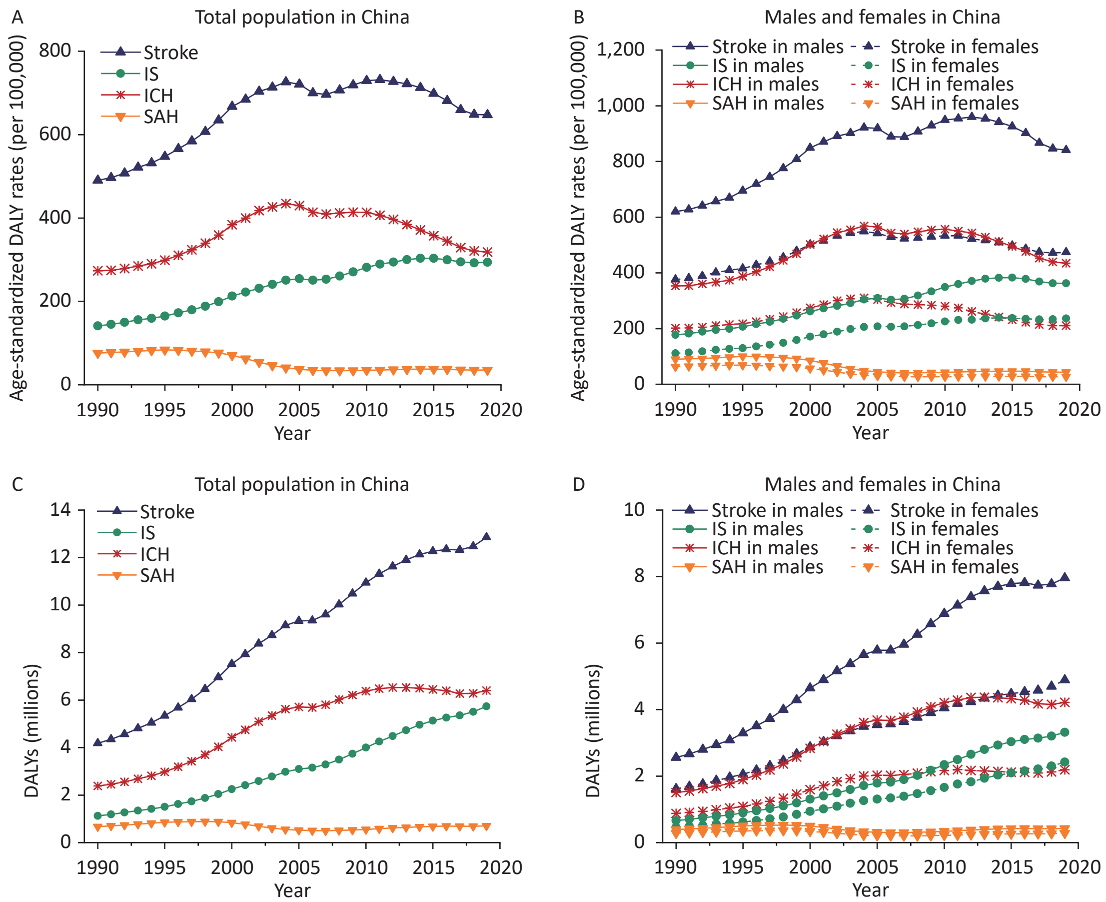

Figure 1. Age-standardized Rates and Numbers of DALY for Stroke Attributable to $PM_{2.5}$ in China from 1990 to 2019. (A) Age-standardized DALY rates in total population; (B) Age-standardized DALY rates in males and females, respectively; (C) Numbers of DALY in total population; (D) Numbers of DALY in males and females, respectively. DALY, disability-adjusted life year; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

YLD, we further elaborated on their trends, separately (Figure 3). The age-standardized YLL rates for stroke and its subtypes attributable to ambient $PM_{2.5}$ in China were much higher than those in YLD. Age-standardized YLL rates showed similar trends to DALY regardless of stroke subtype and sex. In comparison, the age-standardized YLD rates for stroke and its subtypes showed upward trends, especially for IS, which sharply increased from 22.34 to 68.92 per 10,000 during 1990-2019. The age-standardized rates of YLD for IS ranked first across the past 30 years, which was even 5-fold and 14-fold higher than those for ICH and SAH in 2019, respectively. Additionally, we found that the age-standardized YLD rates for stroke and its subtypes were higher in females than males except for ICH,

Table 1. The Trends in age-standardized rates and numbers of DALY for stroke attributable to Ambient $PM_{2.5}$ in China during 1990−2019 using Join-Point regression.

Variables	Age-standardized DALY Rates				Numbers of DALY		
	Segments	Period	APC (95% *CI*)	*P* value	Period	APC (95% *CI*)	*P* value
Stroke	1	1990−1995	2.18 (1.70, 2.66)	<0.001	1990−1995	5.00 (4.52, 5.47)	<0.001
	2	1995−2001	3.99 (3.50, 4.48)	<0.001	1995−2001	7.03 (6.54, 7.51)	<0.001
	3	2001−2004	1.88 (−0.25, 4.05)	0.079	2001−2004	4.67 (2.57, 6.81)	<0.001
	4	2004−2007	−1.31 (−3.37, 0.79)	0.199	2004−2007	1.69 (−0.35, 3.77)	0.097
	5	2007−2012	1.08 (0.41, 1.76)	0.004	2007−2012	4.15 (3.48, 4.81)	<0.001
	6	2012−2019	−1.98 (−2.26, −1.71)	<0.001	2012−2019	1.12 (0.85, 1.39)	<0.001
	AAPC (95%*CI*)	1990−2019	0.94 (0.61, 1.27)	<0.001	1990−2019	3.94 (3.61, 4.26)	<0.001
IS	1	1990−1995	3.15 (2.63, 3.67)	<0.001	1990−1997	6.34 (6.09, 6.59)	<0.001
	2	1995−2004	4.92 (4.66, 5.18)	<0.001	1997−2000	9.30 (7.42, 11.22)	<0.001
	3	2004−2007	−0.16 (−2.39, 2.12)	0.881	2000−2004	7.36 (6.43, 8.30)	<0.001
	4	2007−2011	3.55 (2.39, 4.73)	<0.001	2004−2007	3.31 (1.53, 5.12)	0.001
	5	2011−2014	1.58 (−0.69, 3.90)	0.158	2007−2013	6.49 (6.08, 6.91)	<0.001
	6	2014−2019	−0.83 (−1.33, −0.33)	0.004	2013−2019	2.96 (2.66, 3.27)	<0.001
	AAPC (95%*CI*)	1990−2019	2.54 (2.17, 2.91)	<0.001	1990−2019	5.79 (5.50, 6.08)	<0.001
ICH	1	1990−1995	1.77 (1.18, 2.37)	<0.001	1990−1995	4.49 (3.88, 5.10)	<0.001
	2	1995−2003	4.99 (4.62, 5.36)	<0.001	1995−2001	8.38 (7.75, 9.02)	<0.001
	3	2003−2007	−1.46 (−2.74, −0.16)	0.030	2001−2004	5.77 (3.03, 8.58)	<0.001
	4	2007−2011	−0.13 (−1.43, 1.18)	0.832	2004−2007	1.04 (−1.58, 3.72)	0.410
	5	2011−2019	−3.33 (−3.61, −3.06)	<0.001	2007−2011	3.04 (1.70, 4.40)	<0.001
	6	—	—	—	2011−2019	−0.48 (−0.76, −0.19)	0.003
	AAPC (95%*CI*)	1990-2019	0.49 (0.21, 0.77)	0.001	1990-2019	3.45 (3.02, 3.88)	<0.001
SAH	1	1990-1996	1.77 (1.42, 2.11)	<0.001	1990-1996	4.63 (4.27, 4.99)	<0.001
	2	1996-2000	−3.82 (−4.77, −2.86)	<0.001	1996-2000	−0.81 (−1.81, 0.21)	0.109
	3	2000-2004	−13.68 (−14.54, −12.82)	<0.001	2000-2004	−10.77 (−11.67, −9.86)	<0.001
	4	2004-2007	−6.24 (−8.09, −4.36)	<0.001	2004-2007	−3.34 (−5.29, −1.36)	0.003
	5	2007-2014	1.88 (1.54, 2.22)	<0.001	2007-2014	4.56 (4.20, 4.92)	<0.001
	6	2014-2019	−1.49 (−1.92, −1.05)	<0.001	2014-2019	0.89 (0.43, 1.35)	0.001
	AAPC (95%*CI*)	1990-2019	−2.64 (−2.92, −2.37)	<0.001	1990-2019	0.13 (−0.16, 0.42)	0.379

Note. DALY, disability-adjusted life year; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; APC, annual percent change; AAPC, average annual percent change; *CI*, confidence interval.

with the greatest difference observed for IS.

Numbers of YLL and YLD

We further evaluated the trends in the numbers of YLL and YLD (Figure 4). The DALYs of stroke arose mostly from the YLLs every year over the entire period. Therefore, the YLLs showed trends similar to those of the DALYs. The YLDs for stroke increased dramatically from 1990 to 2019, particularly for IS, which climbed from 0.20 million to 1.38 million. Moreover, we observed that females had noticeably higher YLDs for IS than males. As for the contribution of YLL to DALY, we noticed that the proportion obviously decreased from 81.89% in 2004 to 76.01% in 2019 for IS, and from 96.09% in 1990 to 86.12% in 2019 for SAH (Supplementary Figure S3, available in www.besjournal.com).

Age Standardized Rates and Numbers of Mortality

We also estimated trends in the age-standardized rates and numbers of mortality for stroke and its subtypes attributable to ambient $PM_{2.5}$. We found that the mortality of stroke and its subtypes shared similar trends with DALY (Supplementary Figure S4, Supplementary Table S10 and Supplementary Table S11, available in www.besjournal.com).

DISCUSSION

Based on the GBD 2019 study, we found that China has much higher age-standardized DALY rates for stroke than the global level. A declining trend has been observed for age-standardized DALY rates of stroke in recent years, although there was a general upward trend in China from 1990 to 2019. However, we did not find a downward trend in the numbers of DALY. Among the stroke subtypes, the age-standardized DALY rates for ICH ranked first and then decreased from 2003, thereafter the numbers of DALY declined from 2011. Although the age-standardized DALY rates for IS have decreased since 2014, the downward trend in the ratio of YLL to DALY started as early as 2004. Conversely, the SAH burden showed a successive downward trend over the past three decades. We found that YLLs contributed most of the DALYs for stroke and subtypes attributable to $PM_{2.5}$ throughout the study period. In addition, males had higher DALYs and YLLs for $PM_{2.5}$-attributable stroke and its subtypes than females. However, females had higher YLDs for stroke, IS and SAH than males did.

The age-standardized rates, percents and numbers of DALY for stroke attributable to $PM_{2.5}$ in China all increased dramatically during 1990-2004, which could be explained by the increasing emission of ambient particulate matter due to rapid economic growth and growing energy consumption over the past decades[12,24]. Since the early 2000s, China has been actively addressing air pollution and its adverse health effects, implementing policies aimed at improving air quality and reducing the disease burden. A slight decrease in the $PM_{2.5}$-attributable age-standardized rates of DALY for stroke existed

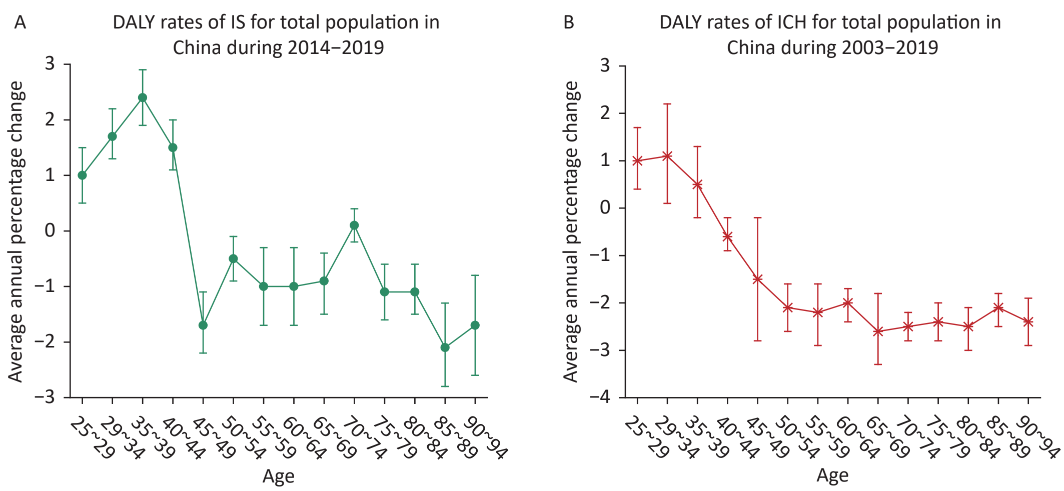

Figure 2. Average Annual Percentage Change of DALY Rates for Stroke Attributable to $PM_{2.5}$ in China. (A) Average annual percentage change of DALY rates for IS during 2014-2019; (B) Average annual percentage change of DALY rates for ICH during 2003-2019. DALY, disability-adjusted life year; IS, ischemic stroke; ICH, intracerebral hemorrhage.

during 2004-2007, especially for ICH during 2003-2007, which may be related to stricter emission standards of particulate matter for power plants in 2003 and the subsequent implementation of energy-conservation and emission-reduction policies[15]. In addition, stringent emission controls on regional air quality in preparation for the 2008 Beijing Olympic Games could partially contribute to the slight decrease in stroke burden[25]. Although no apparent decrease in $PM_{2.5}$ occurred during this period, these policies might have led to changes in the chemical composition and sources of ambient $PM_{2.5}$, especially the decrease in fossil fuels and industrial sources, and further influenced its pathogenic and lethal effects on stroke[16,26,27]. The influence of these policies was not strong enough to reduce the DALY rates for IS in the early stages, but it evidently decreased the proportion of YLL to DALY, implying a weakened lethal effect of $PM_{2.5}$. Since 2011, China has paid more attention to $PM_{2.5}$, promulgated brand-new national ambient air quality standard, issued new air quality assessment indicators, optimized the national air monitoring system, promoted the enforcement of the first National Action Plan on Air Pollution Prevention and Control, and developed the air pollution and health effects monitoring system[15,28-30]. Consequently, population-weighted mean geophysical $PM_{2.5}$ concentrations in China have shown an apparent downward trend since 2011[16]. This was consistent with the markedly declining trends in the age-standardized rates and percents of DALY for stroke attributable to $PM_{2.5}$ after 2012 and 2014, respectively. It also reduced the numbers of DALY for ICH considerably at the same time, which indicates the effectiveness of the policies for improving air quality in public health.

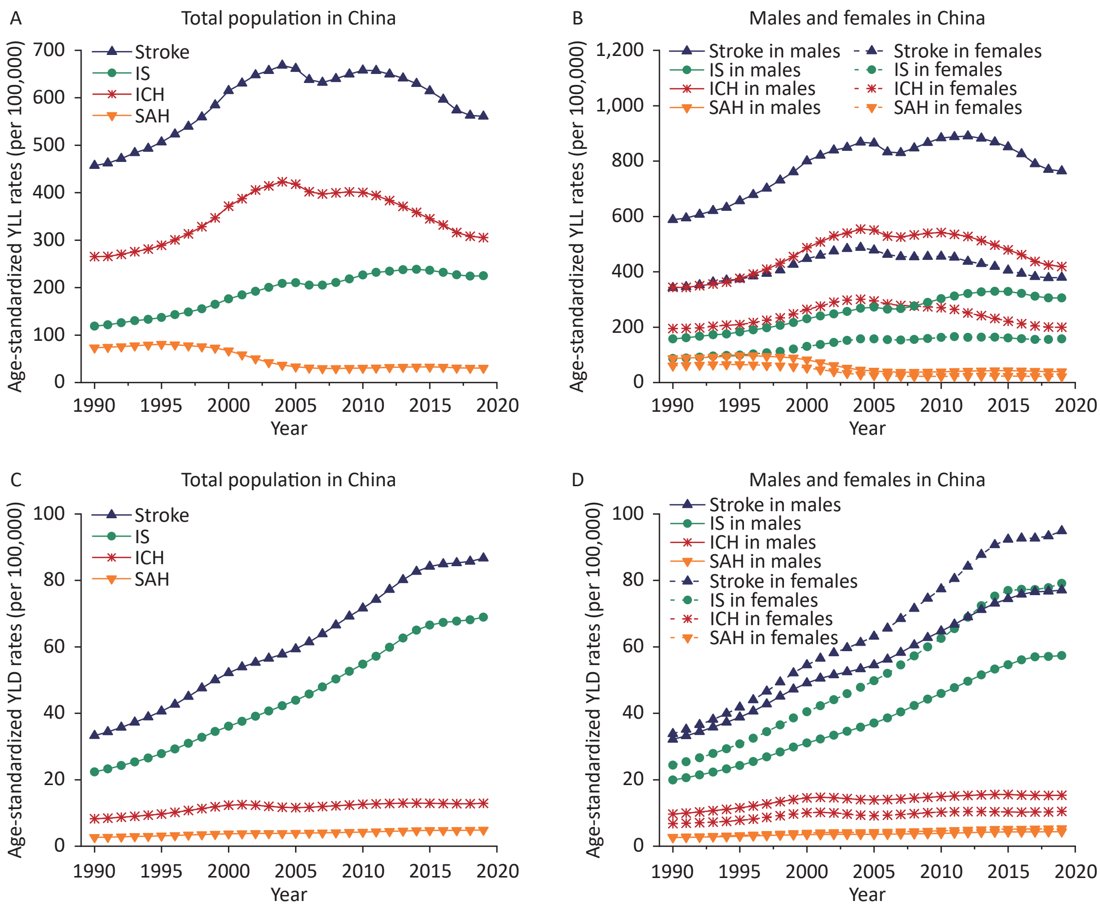

Figure 3. Age-standardized Rates of YLL and YLD for Stroke Attributable to $PM_{2.5}$ in China from 1990 to 2019. (A) Age-standardized YLL rates in total population; (B) Age-standardized YLL rates in males and females, respectively; (C) Age-standardized YLD rates in total population; (D) Age-standardized YLD rates in males and females, respectively. YLL, year of life lost; YLD, year lived with disability; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

Additionally, in recent years, policies focusing on desulfurization and denitrification have greatly contributed to reducing the precursors of $PM_{2.5}$, playing an important role in the decline of stroke burden[31,32]. In summary, our study suggests that remarkable public health benefits can be obtained through policies that control air pollution.

This study identified different changing patterns in the burden of stroke subtypes attributable to ambient $PM_{2.5}$. The declining trend in $PM_{2.5}$-related age-standardized DALY rates for ICH occurred earlier and more substantially than that for IS. This suggests that the reduction in $PM_{2.5}$, with the implementation of the policies, could yield more health benefits for ICH. This may be explained by the fact that $PM_{2.5}$ is more relevant to ICH than IS[33]. Additionally, it may be related to the fact that $PM_{2.5}$ could trigger an increase of blood pressure which has twice the effect on ICH compared to IS, and the fatality rate of ICH is triple that of IS in China[34-37]. In contrast, the SAH burden attributed to ambient $PM_{2.5}$ remained at a lower level and showed a general downtrend during 1990-2019. This may be more attributable to the substantial improvement in diagnosis and treatment, but less so for $PM_{2.5}$. For example, more non-fatal non-aneurysmal SAH cases have been identified due to improvements in imaging technology, whereas case fatality has decreased because of advances in surgical and medical management[38].

Our study also showed sex differences in the stroke burden attributable to ambient $PM_{2.5}$. The $PM_{2.5}$-related stroke burden was much higher in males than females, particularly the fatal stroke burden (YLL). This phenomenon may be explained by the higher probability of ambient $PM_{2.5}$ exposure in

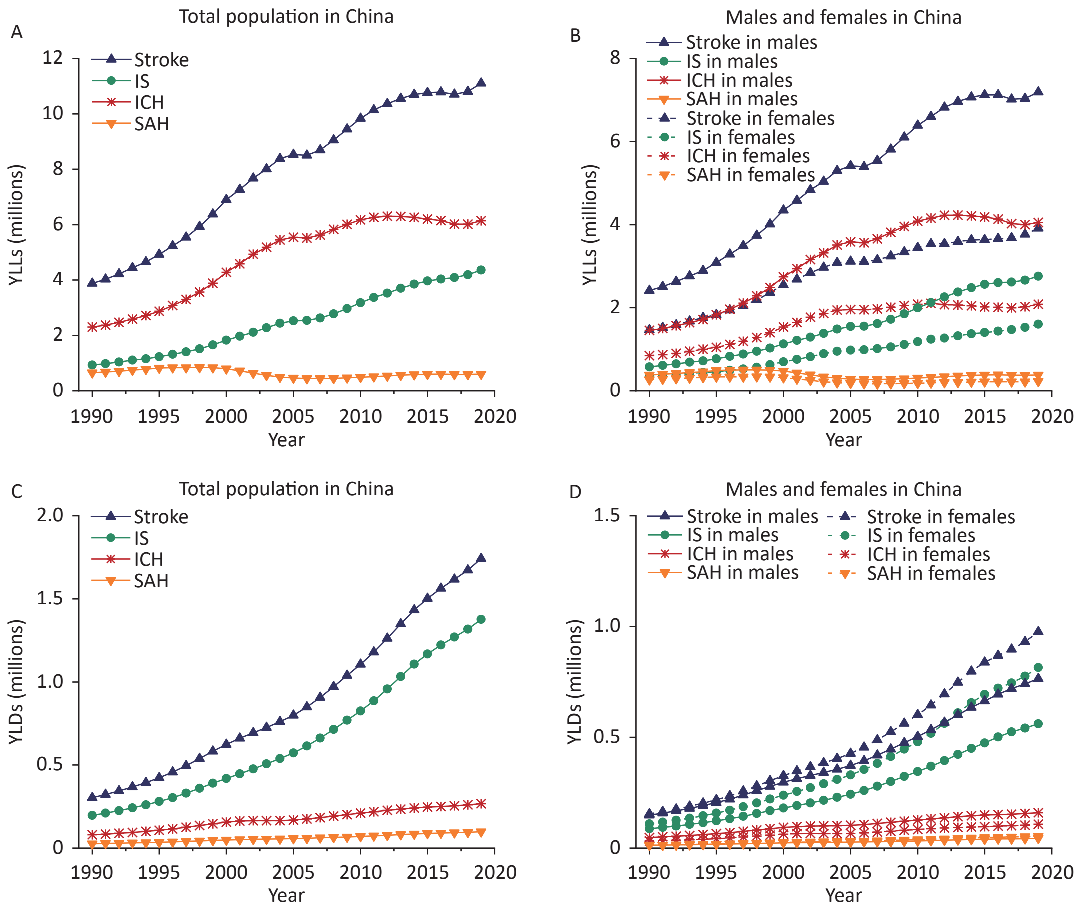

Figure 4. Numbers of YLL and YLD for Stroke Attributable to $PM_{2.5}$ in China from 1990 to 2019. (A) Numbers of YLL in total population; (B) Numbers of YLL in males and females, respectively; (C) Numbers of YLD in total population; (D) Numbers of YLD in males and females, respectively. YLL, year of life lost; YLD, year lived with disability; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

males due to a higher proportion of outdoor work[39,40], and the higher prevalence of risk factors for stroke in males, including hypertension, diabetes, tobacco use, and alcohol consumption[41-44]. In addition, it may be related to the different pathophysiological functions of cerebral circulation between males and females related to sex hormones[45]. Therefore, strategies for reducing $PM_{2.5}$-related stroke burden should be given more attention to males, and provide more protection in high $PM_{2.5}$-pollution settings. However, it is worth noting that females had higher levels of YLD for stroke than males, particularly for IS, implying females have a greater non-fatal stroke burden. This may be explained by the protective effect of estrogen, which makes females less likely to die from stroke[45].

This study has some limitations. First, the stroke burden attributed to ambient $PM_{2.5}$ in the GBD 2019 study is not directly observed data, but estimated data generated through mathematical conversion. Therefore, caution should be exercised when interpreting these results. Second, our study is a population-based analysis of trends in stroke burden, which may be inapplicable at the individual level due to potential ecological fallacy and regression dilution bias[46,47]. Third, the stroke burden at the provincial level in China was not analyzed, because of the lack of relevant data in the GBD 2019 study. Forth, toxic chemicals bounded to $PM_{2.5}$, like heavy metals and organic matters, can accumulate in blood and organs, leading to inflammation and further increasing the risk of stroke[48,49]. Moreover, other determinants, such as ambient temperature, relative humidity, and other pollutants (SO_2, NO_2, CO, O_3 and PM_{10}), also affect stroke[11,50]. They could confound the association between $PM_{2.5}$ and stroke, which requires further research in the future.

CONCLUSIONS

Our results illustrate different changing patterns of disease burden for stroke subtypes attributable to ambient $PM_{2.5}$ in China from 1990 to 2019, reflecting the health effects of the policies on improving air quality. Moreover, our results suggest that effective policies should be implemented persistently, and more attention should be paid to males.

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All authors contributed to the interpretation of results and critically revised the draft. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

CONFLICT OF INTEREST

The authors have no competing interests to declare that are relevant to the content of this article.

AUTHOR CONTRIBUTION

WANG Jing Yu: Methodology, Formal analysis, Visualization, Writing-original draft, Writing- review & editing. WANG Yan: Methodology, Software, Writing-original draft, Writing- review & editing. LIANG Xiao Hua: Methodology, Software, Writing-original draft, Writing- review & editing. HUANG Ke Yong: Writing- review & editing. LIU Fang Chao: Funding acquisition, Writing- review & editing. CHEN Shu Feng: Funding acquisition, Writing- review & editing. LU Xiang Feng: Funding acquisition, Writing-review & editing. LI Jian Xin: Conceptualization, Funding acquisition, Writing- review & editing.

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Supplementary Table S1. 2019 GBD world population age standard

Age group (yeas)	Percent of population (%)
< 1	2.03
1 to 4	7.91
5 to 9	9.57
10 to 14	8.99
15 to 19	8.32
20 to 24	7.87
25 to 29	7.63
30 to 34	7.33
35 to 39	6.81
40 to 44	6.14
45 to 49	5.51
50 to 54	4.92
55 to 59	4.35
60 to 64	3.68
65 to 69	2.99
70 to 74	2.27
75 to 79	1.61
80 to 84	1.11
85 to 89	0.62
90 to 94	0.26
95 plus	0.08

Note. In GBD 2019, the age standardized rates were calculated with a global age structure called the GBD world population age standard, which had been updated in 2019. The standard was developed based on the non-weighted mean of the age-specific proportional distributions for national locations with populations greater than 5 million in 2019.

Supplementary Table S2. ICD codes for stroke categories

Stroke Category	ICD-9 Codes	ICD-10 Codes
Ischemic Stroke	433-435.9, 437.0-437.1, 437.5-437.8	G45-G46.8, I63-I63.9, I65-I66.9, I67.2-I67.3, I67.5-I67.6, I69.3
Intracerebral Hemorrhage	430.1, 430.3-432.9, 437.2	I61-I62.9, I67.0-I67.1, I68.1-I68.2, I69.0-I69.2
Subarachnoid Hemorrhage	430.2	I60

Note. ICD, International Classification of Diseases.

Supplementary Table S3. The global and Chinese age-standardized rates for stroke during 1990−2019

Year	Age-standardized DALY rate for stroke (95% *CI*)		*P*-value
	Global	China	
1990	319.34 (219.46, 433.52)	490.54 (231.12, 832.24)	0.293
1991	319.70 (220.57, 429.91)	496.64 (242.61, 816.42)	0.256
1992	323.03 (224.97, 428.21)	507.67 (254.89, 815.97)	0.225
1993	330.08 (231.51, 437.22)	521.41 (266.31, 824.00)	0.207
1994	334.68 (235.39, 442.02)	532.17 (283.45, 840.87)	0.193
1995	335.99 (238.71, 442.40)	547.48 (294.24, 838.56)	0.154
1996	337.33 (238.81, 436.70)	566.04 (315.03, 849.87)	0.116
1997	340.25 (244.15, 440.26)	584.45 (337.86, 855.05)	0.084
1998	343.63 (249.49, 440.95)	607.10 (362.37, 873.20)	0.058
1999	350.66 (259.30, 448.59)	634.62 (398.11, 902.02)	0.039
2000	357.21 (261.28, 451.72)	667.22 (420.74, 925.66)	0.024
2001	359.92 (266.75, 452.11)	684.72 (445.93, 932.95)	0.015
2002	363.71 (268.51, 454.27)	703.40 (463.93, 940.04)	0.009
2003	364.33 (271.87, 455.74)	713.74 (488.38, 944.41)	0.005
2004	362.62 (268.66, 448.21)	726.17 (498.61, 937.17)	0.003
2005	361.52 (269.28, 445.26)	720.96 (498.16, 933.87)	0.003
2006	355.44 (268.82, 431.59)	699.78 (506.75, 871.31)	<0.001
2007	355.40 (272.48, 429.80)	696.28 (510.25, 861.19)	<0.001
2008	359.71 (279.55, 432.60)	706.65 (538.57, 857.47)	<0.001
2009	361.66 (284.53, 430.63)	718.94 (550.96, 866.33)	<0.001
2010	364.26 (288.42, 434.02)	729.51 (559.72, 866.96)	<0.001
2011	364.23 (289.53, 434.60)	731.53 (577.11, 873.19)	<0.001
2012	364.48 (292.78, 429.67)	727.08 (579.63, 859.85)	<0.001
2013	363.73 (289.29, 428.62)	721.62 (573.14, 852.03)	<0.001
2014	361.68 (292.64, 423.64)	712.49 (577.01, 840.95)	<0.001
2015	359.45 (287.64, 416.52)	698.51 (561.12, 821.39)	<0.001
2016	352.87 (284.60, 413.35)	681.39 (550.14, 799.00)	<0.001
2017	345.24 (278.75, 404.15)	659.52 (531.04, 777.30)	<0.001
2018	344.23 (280.67, 401.24)	648.46 (518.63, 768.28)	<0.001
2019	348.06 (283.29, 404.35)	647.63 (525.39, 772.78)	<0.001

Note. DALY, disability-adjusted life year; *CI*, confidence interval; *P*-value: *z* test.

Supplementary Table S4. The global and Chinese age-standardized rates for IS during 1990−2019.

Year	Age-standardized DALY rate for IS (95% *CI*)		*P*-value
	Global	China	
1990	130.81 (93.18, 169.76)	141.06 (67.56, 238.25)	0.830
1991	130.46 (93.63, 167.76)	144.85 (71.38, 236.53)	0.755
1992	131.35 (95.59, 168.61)	150.06 (77.38, 241.97)	0.684
1993	134.60 (98.62, 172.10)	155.81 (80.70, 247.05)	0.648
1994	135.95 (99.86, 174.25)	159.58 (86.07, 249.25)	0.606
1995	135.15 (99.11, 172.77)	164.92 (89.06, 252.42)	0.515
1996	134.06 (99.18, 169.53)	172.47 (96.79, 256.18)	0.387
1997	133.63 (99.50, 167.89)	179.56 (103.79, 259.74)	0.290
1998	133.55 (99.59, 166.50)	188.20 (113.32, 270.07)	0.209
1999	135.46 (102.41, 168.85)	199.18 (126.47, 282.61)	0.141
2000	137.33 (104.40, 170.61)	212.59 (136.21, 294.21)	0.085
2001	138.49 (105.46, 170.95)	222.27 (146.72, 300.86)	0.049
2002	139.91 (107.86, 170.86)	231.20 (154.77, 310.75)	0.033
2003	140.89 (108.34, 172.44)	241.06 (166.64, 317.02)	0.016
2004	140.51 (108.68, 171.43)	250.83 (175.67, 321.93)	0.007
2005	140.86 (109.24, 170.88)	254.25 (178.73, 325.10)	0.005
2006	138.69 (109.39, 166.64)	251.04 (183.50, 312.89)	0.002
2007	138.86 (110.21, 167.10)	253.23 (187.52, 312.23)	0.001
2008	140.99 (113.02, 168.01)	260.86 (200.17, 315.97)	<0.001
2009	142.41 (115.10, 168.67)	270.80 (211.75, 324.26)	<0.001
2010	144.42 (117.19, 170.28)	281.51 (218.68, 334.98)	<0.001
2011	145.13 (117.15, 171.40)	289.36 (228.68, 344.84)	<0.001
2012	145.96 (118.90, 171.63)	294.30 (237.01, 347.05)	<0.001
2013	146.92 (119.21, 172.39)	300.29 (239.87, 354.34)	<0.001
2014	147.34 (120.71, 172.35)	303.55 (246.17, 356.72)	<0.001
2015	147.48 (121.36, 172.16)	303.22 (245.37, 357.34)	<0.001
2016	145.49 (118.54, 170.53)	299.56 (242.11, 352.04)	<0.001
2017	143.49 (117.64, 167.04)	294.61 (238.83, 346.71)	<0.001
2018	144.00 (117.55, 168.91)	292.40 (234.36, 345.35)	<0.001
2019	146.16 (119.78, 171.23)	294.05 (239.00, 352.73)	<0.001

Note. DALY, disability-adjusted life year; IS, ischemic stroke; *CI*, confidence interval; *P*-value: *z* test.

Supplementary Table S5. The global and Chinese age-standardized rates for ICH during 1990−2019

Year	Age-standardized DALY rate for ICH (95% *CI*)		*P*-value
	Global	China	
1990	152.22 (98.85, 215.36)	273.64 (128.05, 466.76)	0.184
1991	152.66 (99.61, 214.12)	274.42 (131.87, 457.77)	0.167
1992	154.80 (102.86, 213.47)	279.04 (138.00, 455.76)	0.148
1993	158.05 (105.33, 216.99)	284.88 (143.97, 459.21)	0.137
1994	160.91 (108.52, 220.23)	290.39 (151.43, 460.47)	0.122
1995	162.70 (110.23, 220.15)	298.80 (158.70, 461.82)	0.098
1996	165.39 (112.20, 224.08)	310.76 (171.89, 467.64)	0.072
1997	169.10 (117.42, 226.73)	323.93 (186.47, 477.62)	0.051
1998	172.85 (120.44, 228.46)	339.59 (202.00, 496.04)	0.039
1999	178.31 (126.20, 235.96)	359.04 (224.12, 510.30)	0.021
2000	184.13 (130.46, 242.06)	383.78 (241.32, 538.82)	0.014
2001	187.63 (132.76, 242.40)	399.91 (258.43, 545.74)	0.007
2002	191.98 (136.48, 246.55)	417.95 (273.52, 566.03)	0.005
2003	193.58 (138.97, 247.37)	426.36 (286.40, 565.95)	0.002
2004	193.83 (139.74, 242.68)	434.72 (297.12, 566.20)	0.001
2005	193.21 (139.72, 243.27)	429.50 (293.38, 557.42)	0.001
2006	189.87 (141.01, 235.07)	413.83 (301.25, 521.18)	<0.001
2007	189.83 (142.51, 233.70)	409.24 (299.85, 507.05)	<0.001
2008	191.88 (147.21, 233.63)	412.02 (311.44, 502.13)	<0.001
2009	192.39 (147.41, 232.53)	413.99 (313.77, 500.19)	<0.001
2010	192.74 (149.62, 232.46)	413.28 (315.71, 493.65)	<0.001
2011	191.76 (149.46, 231.12)	406.73 (319.03, 486.22)	<0.001
2012	191.00 (151.98, 227.96)	396.40 (311.94, 471.62)	<0.001
2013	189.03 (148.80, 225.51)	384.29 (303.07, 456.72)	<0.001
2014	186.43 (148.17, 219.49)	371.38 (298.00, 441.92)	<0.001
2015	184.05 (145.45, 215.37)	357.81 (285.70, 421.04)	<0.001
2016	179.85 (142.58, 213.49)	344.72 (277.55, 408.95)	<0.001
2017	174.81 (138.17, 206.50)	329.10 (261.82, 391.35)	<0.001
2018	173.41 (140.41, 205.04)	320.93 (253.91, 381.95)	<0.001
2019	174.82 (140.07, 206.00)	318.40 (255.96, 382.95)	<0.001

Note. DALY, disability-adjusted life year; ICH, intracerebral hemorrhage; *CI*, confidence interval; *P*-value: *z* test.

Supplementary Table S6. The global and Chinese age-standardized rates for SAH during 1990−2019

Year	Age-standardized DALY rate for SAH (95% *CI*)		*P*-value
	Global	China	
1990	36.32 (22.06, 54.88)	75.85 (31.51, 135.05)	0.154
1991	36.58 (22.17, 55.36)	77.37 (32.95, 133.25)	0.130
1992	36.87 (22.41, 53.42)	78.57 (34.79, 130.93)	0.106
1993	37.43 (23.18, 53.89)	80.72 (37.77, 135.48)	0.097
1994	37.83 (23.60, 54.65)	82.19 (38.37, 135.47)	0.088
1995	38.14 (24.05, 54.56)	83.75 (39.21, 133.79)	0.072
1996	37.89 (24.02, 53.39)	82.81 (40.62, 129.65)	0.060
1997	37.53 (24.57, 51.99)	80.96 (41.61, 124.67)	0.052
1998	37.23 (24.69, 50.59)	79.31 (41.35, 120.37)	0.047
1999	36.88 (25.11, 50.00)	76.39 (42.06, 114.17)	0.042
2000	35.75 (24.61, 48.10)	70.85 (39.84, 104.02)	0.044
2001	33.80 (23.57, 44.79)	62.54 (37.35, 89.32)	0.045
2002	31.83 (22.28, 42.14)	54.26 (34.37, 75.79)	0.056
2003	29.85 (21.20, 39.77)	46.32 (30.05, 63.30)	0.090
2004	28.29 (20.42, 37.24)	40.62 (26.86, 54.25)	0.133
2005	27.44 (19.93, 35.94)	37.21 (24.92, 49.59)	0.193
2006	26.88 (19.55, 35.25)	34.91 (24.23, 45.00)	0.227
2007	26.71 (19.60, 34.86)	33.81 (24.07, 42.77)	0.249
2008	26.84 (19.90, 34.74)	33.77 (25.06, 42.12)	0.230
2009	26.86 (20.23, 34.43)	34.15 (25.67, 42.54)	0.195
2010	27.09 (20.58, 34.52)	34.72 (26.31, 43.17)	0.172
2011	27.34 (20.94, 34.50)	35.45 (27.14, 43.74)	0.138
2012	27.52 (21.32, 34.61)	36.38 (27.95, 44.47)	0.101
2013	27.77 (21.40, 34.75)	37.04 (28.23, 45.03)	0.090
2014	27.90 (21.58, 34.66)	37.56 (29.09, 45.59)	0.072
2015	27.92 (21.72, 34.46)	37.48 (28.25, 45.07)	0.076
2016	27.54 (21.53, 34.10)	37.11 (27.95, 45.29)	0.080
2017	26.94 (21.31, 32.89)	35.81 (27.16, 44.01)	0.089
2018	26.82 (21.20, 32.78)	35.13 (26.25, 43.82)	0.122
2019	27.08 (21.35, 32.74)	35.18 (26.18, 44.60)	0.143

Note. DALY, disability-adjusted life year; SAH, subarachnoid hemorrhage; *CI*, confidence interval; *P*-value: *z* test.

Supplementary Table S7. The trends in age-standardized rates of DALY for stroke attributable to ambient $PM_{2.5}$ for males and females in China during 1990−2019 using Join-Point regression

Variables	Segments	Males			Females		
		Period	APC (95% *CI*)	*P* value	Period	APC (95% *CI*)	*P* value
Stroke	1	1990−1994	1.93 (1.21, 2.66)	<0.001	1990−1996	2.22 (1.80, 2.64)	<0.001
	2	1994−2001	3.92 (3.53, 4.32)	<0.001	1996−2003	3.76 (3.33, 4.18)	<0.001
	3	2001−2004	1.80 (−0.46, 4.12)	0.110	2003−2007	−1.31 (−2.50, −0.11)	0.034
	4	2004−2007	−1.16 (−3.35, 1.09)	0.283	2007−2011	0.40 (−0.81, 1.62)	0.494
	5	2007−2012	1.85 (1.13, 2.58)	<0.001	2011−2019	−1.65 (−1.91, −1.39)	<0.001
	6	2012−2019	−2.16 (−2.45, −1.86)	<0.001	—	—	—
	AAPC (95%*CI*)	1990−2019	1.05 (0.70, 1.40)	<0.001	1990−2019	0.76 (0.50, 1.02)	<0.001
IS	1	1990−1995	3.12 (2.60, 3.64)	<0.001	1990−1997	3.49 (3.16, 3.81)	<0.001
	2	1995−2004	4.51 (4.25, 4.77)	<0.001	1997−2001	6.45 (5.20, 7.72)	<0.001
	3	2004−2007	−0.12 (−2.36, 2.18)	0.914	2001−2004	4.52 (2.08, 7.02)	0.001
	4	2007−2011	4.31 (3.13, 5.50)	<0.001	2004−2007	0.40 (−1.95, 2.79)	0.723
	5	2011−2014	2.12 (−0.17, 4.46)	0.067	2007−2013	2.25 (1.71, 2.79)	<0.001
	6	2014−2019	−1.33 (−1.83, −0.83)	<0.001	2013−2019	−0.31 (−0.71, 0.09)	0.113
	AAPC (95%*CI*)	1990−2019	2.48 (2.12, 2.85)	<0.001	1990−2019	2.62 (2.23, 3.00)	<0.001
ICH	1	1990−1995	1.79 (1.23, 2.36)	<0.001	1990−1996	1.88 (1.47, 2.30)	<0.001
	2	1995−2001	5.43 (4.85, 6.02)	<0.001	1996−2003	4.95 (4.52, 5.37)	<0.001
	3	2001−2004	2.85 (0.33, 5.43)	0.029	2003−2011	−1.66 (−1.97, −1.34)	<0.001
	4	2004−2007	−1.79 (−4.20, 0.67)	0.139	2011−2017	−4.02 (−4.53, −3.50)	<0.001
	5	2007−2011	0.91 (−0.33, 2.17)	0.138	2017−2019	−0.91 (−3.27, 1.50)	0.43
	6	2011−2019	−3.25 (−3.51, −2.99)	<0.001	—	—	—
	AAPC (95%*CI*)	1990−2019	0.72 (0.32, 1.12)	<0.001	1990−2019	0.18 (−0.05, 0.42)	0.133
SAH	1	1990−1996	2.16 (1.79, 2.52)	<0.001	1990−1995	1.89 (1.39, 2.39)	<0.001
	2	1996−2000	−3.58 (−4.60, −2.56)	<0.001	1995−2000	−3.46 (−4.13, −2.79)	<0.001
	3	2000−2004	−13.85 (−14.76, −12.93)	<0.001	2000−2004	−13.64 (−14.58, −12.68)	<0.001
	4	2004−2007	−6.03 (−8.00, −4.02)	<0.001	2004−2007	−6.46 (−8.49, −4.38)	<0.001
	5	2007−2014	2.43 (2.07, 2.80)	<0.001	2007−2014	1.06 (0.68, 1.43)	<0.001
	6	2014−2019	−1.79 (−2.25, −1.32)	<0.001	2014−2019	−1.10 (−1.59, −0.62)	<0.001
	AAPC (95%*CI*)	1990−2019	−2.46 (−2.75, −2.17)	<0.001	1990−2019	−2.89 (−3.18, −2.60)	<0.001

Note. DALY, disability-adjusted life year; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; APC, annual percent change; AAPC, average annual percent change; *CI*, confidence interval.

Supplementary Table S8. The trends in age-standardized percents of DALY attributable to ambient $PM_{2.5}$-related stroke in China during 1990−2019 using Join-Point regression.

Variables	Segments	Total population			Males			Females		
		Period	APC (95% *CI*)	*P* value	Period	APC (95% *CI*)	*P* value	Period	APC (95% *CI*)	*P* value
Stroke	1	1990−1995	3.78 (3.50, 4.06)	<0.001	1990−1995	3.39 (3.15, 3.62)	<0.001	1990−1995	4.13 (3.83, 4.43)	<0.001
	2	1995−1999	4.89 (4.27, 5.52)	<0.001	1995−1999	4.52 (3.98, 5.05)	<0.001	1995−1999	5.34 (4.66, 6.02)	<0.001
	3	1999−2014	3.09 (3.03, 3.15)	<0.001	1999−2014	2.73 (2.68, 2.78)	<0.001	1999−2014	3.43 (3.37, 3.49)	<0.001
	4	2014−2017	−0.82 (−1.99, 0.37)	<0.001	2014−2017	−0.83 (−1.83, 0.19)	0.104	2014−2017	−0.73 (−2.01, 0.56)	0.246
	5	2017−2019	0.50 (−0.69, 1.70)	<0.001	2017−2019	0.33 (−0.69, 1.35)	0.509	2017−2019	1.01 (−0.29, 2.32)	0.120
	6	—	—	—	—	—	—	—	—	—
	AAPC (95%*CI*)	1990−2019	2.86 (2.69, 3.03)	<0.001	1990−2019	2.54 (2.40, 2.69)	<0.001	1990−2019	3.20 (3.02, 3.39)	<0.001
IS	1	1990−1995	3.58 (3.45, 3.7)	<0.001	1990−1995	3.25 (3.10, 3.39)	<0.001	1990−1995	3.93 (3.77, 4.09)	<0.001
	2	1995−1999	4.59 (4.31, 4.88)	<0.001	1995-2000	4.02 (3.81, 4.23)	<0.001	1995−1999	5.08 (4.71, 5.45)	<0.001
	3	1999−2009	3.05 (3.00, 3.11)	<0.001	2000−2014	2.50 (2.47, 2.53)	<0.001	1999−2009	3.49 (3.42, 3.55)	<0.001
	4	2009−2014	2.74 (2.56, 2.91)	<0.001	2014−2017	−0.95 (−1.58, −0.32)	0.006	2009−2014	2.97 (2.74, 3.20)	<0.001
	5	2014−2017	−0.79 (−1.33, −0.24)	0.008	2017−2019	0.26 (−0.37, 0.90)	0.396	2014−2017	−0.60 (−1.30, 0.10)	0.085
	6	2017−2019	0.37 (−0.18, 0.93)	0.165	—	—	—	2017−2019	0.78 (0.07, 1.49)	0.033
	AAPC (95%*CI*)	1990−2019	2.71 (2.63, 2.79)	<0.001	1990−2019	2.37 (2.28, 2.46)	<0.001	1990−2019	3.07 (2.97, 3.18)	<0.001
ICH	1	1990−1993	3.53 (2.85, 4.22)	<0.001	1990−1994	3.41 (3.03, 3.79)	<0.001	1990−1993	3.90 (3.09, 4.71)	<0.001
	2	1993−2000	4.62 (4.39, 4.86)	<0.001	1994−2000	4.30 (4.03, 4.57)	<0.001	1993−2000	5.00 (4.73, 5.28)	<0.001
	3	2000−2005	2.55 (2.12, 2.98)	<0.001	2000−2005	2.27 (1.89, 2.64)	<0.001	2000−2005	2.88 (2.38, 3.39)	<0.001
	4	2005−2009	3.75 (3.06, 4.43)	<0.001	2005−2009	3.33 (2.73, 3.93)	<0.001	2005−2009	4.10 (3.29, 4.92)	<0.001
	5	2009−2014	2.97 (2.54, 3.40)	<0.001	2009−2014	2.68 (2.30, 3.06)	<0.001	2009−2014	3.15 (2.64, 3.66)	<0.001
	6	2014−2019	−0.12 (−0.41, 0.18)	0.404	2014−2019	−0.20 (−0.46, 0.06)	0.125	2014−2019	0.17 (−0.18, 0.52)	0.319
	AAPC (95%*CI*)	1990−2019	2.92 (2.76, 3.08)	<0.001	1990−2019	2.63 (2.49, 2.77)	<0.001	1990−2019	3.23 (3.05, 3.42)	<0.001
SAH	1	1990−1994	3.67 (3.45, 3.88)	<0.001	1990−1994	3.28 (3.06, 3.50)	<0.001	1990−1995	4.10 (3.90, 4.31)	<0.001
	2	1994−2000	4.56 (4.41, 4.72)	<0.001	1994−2000	4.01 (3.85, 4.17)	<0.001	1995−1999	5.23 (4.77, 5.70)	<0.001
	3	2000−2010	3.89 (3.82, 3.95)	<0.001	2000−2010	3.43 (3.37, 3.50)	<0.001	1999−2010	4.35 (4.28, 4.42)	<0.001
	4	2010−2014	2.93 (2.59, 3.27)	<0.001	2010−2014	2.71 (2.36, 3.06)	<0.001	2010−2014	3.13 (2.68, 3.58)	<0.001
	5	2014−2017	−0.19 (−0.84, 0.47)	0.550	2014−2017	−0.28 (−0.96, 0.40)	0.389	2014−2017	0.01 (−0.87, 0.89)	0.985
	6	2017−2019	0.98 (0.31, 1.65)	0.007	2017−2019	0.72 (0.04, 1.41)	0.040	2017−2019	1.49 (0.61, 2.39)	0.003
	AAPC (95%*CI*)	1990−2019	3.23 (3.13, 3.33)	<0.001	1990−2019	2.85 (2.75, 2.95)	<0.001	1990−2019	3.60 (3.47, 3.74)	<0.001

Note. Percent, the age-standardized proportion of stroke burden attributable to ambient $PM_{2.5}$ within the total stroke burden; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; APC, annual percent change; AAPC, average annual percent change; *CI*, confidence interval.

Supplementary Table S9. The trends in numbers of DALY for stroke attributable to ambient $PM_{2.5}$ for males and females in China during 1990−2019 using Join-Point regression

Variables	Males				Females		
	Segments	Period	APC (95% *CI*)	*P* value	Period	APC (95% *CI*)	*P* value
Stroke	1	1990–1994	4.73 (3.99, 5.48)	<0.001	1990–1996	5.04 (4.63, 5.45)	<0.001
	2	1994–2001	6.94 (6.53, 7.34)	<0.001	1996–2001	7.19 (6.41, 7.97)	<0.001
	3	2001–2004	4.76 (2.44, 7.13)	0.001	2001–2004	4.57 (2.18, 7.01)	0.001
	4	2004–2007	1.83 (−0.42, 4.14)	0.104	2004–2007	1.30 (−1.01, 3.67)	0.248
	5	2007–2012	4.72 (3.98, 5.46)	<0.001	2007–2011	3.55 (2.36, 4.75)	<0.001
	6	2012–2019	0.78 (0.48, 1.08)	<0.001	2011–2019	1.77 (1.52, 2.03)	<0.001
	AAPC (95%*CI*)	1990–2019	3.98 (3.63, 4.34)	<0.001	1990–2019	3.85 (3.46, 4.23)	<0.001
IS	1	1990–1995	6.06 (5.54, 6.59)	<0.001	1990–1997	6.33 (6.03, 6.64)	<0.001
	2	1995–2004	7.66 (7.40, 7.92)	<0.001	1997–2000	10.08 (7.75, 12.46)	<0.001
	3	2004–2007	2.88 (0.61, 5.20)	0.016	2000–2004	7.79 (6.64, 8.95)	<0.001
	4	2007–2011	7.38 (6.18, 8.58)	<0.001	2004–2007	3.27 (1.09, 5.51)	0.006
	5	2011–2014	5.61 (3.28, 7.99)	<0.001	2007–2013	5.72 (5.22, 6.23)	<0.001
	6	2014–2019	2.27 (1.76, 2.78)	<0.001	2013–2019	3.52 (3.14, 3.89)	<0.001
	AAPC (95%*CI*)	1990–2019	5.69 (5.32, 6.06)	<0.001	1990–2019	5.88 (5.52, 6.24)	<0.001
ICH	1	1990–1995	4.60 (3.84, 5.36)	<0.001	1990–1995	4.42 (3.85, 5.00)	<0.001
	2	1995–2002	8.58 (7.99, 9.18)	<0.001	1995–2003	7.75 (7.40, 8.11)	<0.001
	3	2002–2012	2.90 (2.59, 3.20)	<0.001	2003–2011	1.36 (1.02, 1.69)	<0.001
	4	2012–2019	−0.84 (−1.27, −0.41)	0.001	2011–2017	−0.72 (−1.27, −0.18)	0.013
	5	—	—	—	2017–2019	2.20 (−0.29, 4.74)	0.080
	6	—	—	—	—	—	—
	AAPC (95%*CI*)	1990–2019	3.61 (3.38, 3.84)	<0.001	1990–2019	3.23 (2.98, 3.48)	<0.001
SAH	1	1990–1996	4.97 (4.59, 5.34)	<0.001	1990–1995	4.78 (4.27, 5.30)	<0.001
	2	1996–2000	−0.68 (−1.72, 0.37)	0.186	1995–2000	−0.27 (−0.96, 0.43)	0.425
	3	2000–2004	−10.78 (−11.71, −9.83)	<0.001	2000–2004	−10.95 (−11.93, −9.96)	<0.001
	4	2004–2007	−3.18 (−5.19, −1.12)	0.006	2004–2007	−3.52 (−5.63, −1.36)	0.004
	5	2007–2014	5.07 (4.70, 5.44)	<0.001	2007–2014	3.77 (3.38, 4.16)	<0.001
	6	2014–2019	0.44 (−0.03, 0.92)	0.064	2014–2019	1.60 (1.10, 2.10)	<0.001
	AAPC (95%*CI*)	1990–2019	0.27 (−0.03, 0.57)	0.075	1990–2019	−0.04 (−0.35, 0.26)	0.778

Note. DALY, disability-adjusted life year; IS ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; APC, annual percent change; AAPC, average annual percent change; *CI*, confidence interval.

Supplementary Table S10. The trends in age-standardized mortality of stroke attributable to ambient $PM_{2.5}$ in China during 1990−2019 using Join-Point regression

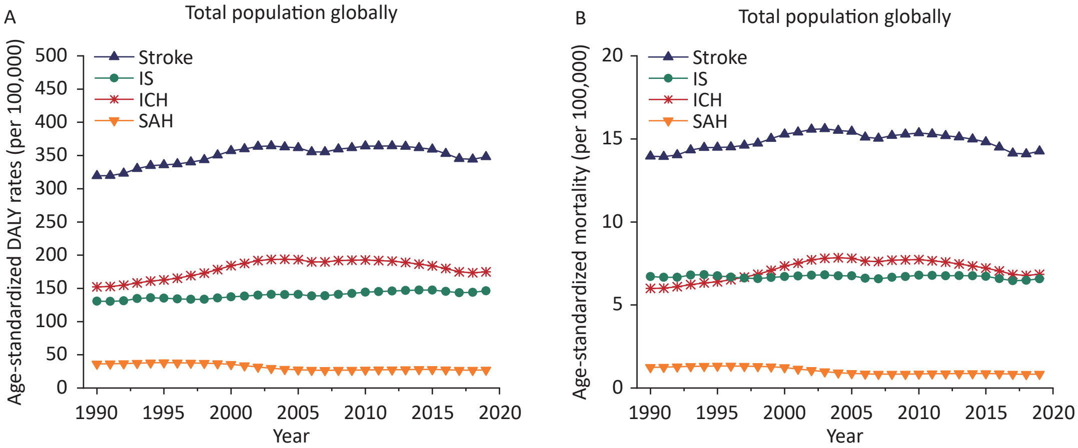
Variables	Segments	Total population			Males			Females		
		Period	APC (95% *CI*)	*P* value	Period	APC (95% *CI*)	*P* value	Period	APC (95% *CI*)	*P* value
Stroke	1	1990–1996	2.59 (2.17, 3.01)	<0.001	1990–1994	2.23 (1.38, 3.07)	<0.001	1990–1996	2.20 (1.82, 2.59)	<0.001
	2	1996–2001	4.48 (3.68, 5.28)	<0.001	1994–2001	4.11 (3.65, 4.57)	<0.001	1996–2003	4.20 (3.81, 4.60)	<0.001
	3	2001–2004	2.18 (−0.26, 4.67)	0.076	2001–2004	2.07 (−0.57, 4.77)	0.114	2003–2007	−1.35 (−2.44, −0.24)	0.021
	4	2004–2007	−1.66 (−4.01, 0.74)	0.158	2004–2007	−1.16 (−3.71, 1.46)	0.353	2007–2011	0.48 (−0.63, 1.61)	0.366
	5	2007–2011	1.65 (0.44, 2.89)	0.012	2007–2012	2.04 (1.20, 2.89)	<0.001	2011–2017	−2.80 (−3.28, −2.32)	<0.001
	6	2011–2019	−2.31 (−2.57, −2.06)	<0.001	2012–2019	−2.73 (−3.07, −2.39)	<0.001	2017–2019	−0.53 (−2.72, 1.71)	0.618
	AAPC (95%*CI*)	1990–2019	0.92 (0.53, 1.31)	<0.001	1990–2019	1.05 (0.65, 1.46)	<0.001	1990–2019	0.70 (0.42, 0.98)	<0.001
IS	1	1990–1995	3.32 (2.66, 3.98)	<0.001	1990–1994	3.07 (2.18, 3.96)	<0.001	1990–1997	3.50 (3.12, 3.89)	<0.001
	2	1995–2004	5.27 (4.94, 5.60)	<0.001	1994–2004	4.71 (4.45, 4.97)	<0.001	1997–2001	7.11 (5.63, 8.61)	<0.001
	3	2004–2007	−0.52 (−3.33, 2.38)	0.703	2004–2007	0.02 (−2.67, 2.78)	0.989	2001–2004	4.75 (1.88, 7.71)	0.003
	4	2007–2011	3.78 (2.30, 5.27)	<0.001	2007–2011	4.83 (3.41, 6.26)	<0.001	2004–2007	−0.49 (−3.22, 2.32)	0.708
	5	2011–2014	0.65 (−2.20, 3.57)	0.636	2011–2014	1.84 (−0.90, 4.65)	0.172	2007–2011	2.72 (1.30, 4.16)	0.001
	6	2014–2019	−1.45 (−2.08, −0.82)	<0.001	2014–2019	−2.15 (−2.75, −1.56)	<0.001	2011–2019	−0.85 (−1.15, −0.55)	<0.001
	AAPC (95%*CI*)	1990–2019	2.46 (2.00, 2.92)	<0.001	1990–2019	2.50 (2.06, 2.94)	<0.001	1990–2019	2.37 (1.90, 2.84)	<0.001
ICH	1	1990–1995	1.96 (1.09, 2.84)	<0.001	1990–1995	2.03 (1.39, 2.67)	<0.001	1990–1996	1.89 (1.41, 2.36)	<0.001
	2	1995–2003	5.16 (4.63, 5.70)	<0.001	1995–2001	5.55 (4.90, 6.22)	<0.001	1996–2003	5.46 (4.97, 5.95)	<0.001
	3	2003–2011	−0.87 (−1.38, −0.36)	0.002	2001–2004	3.08 (0.24, 6.00)	0.035	2003–2011	−1.41 (−1.78, −1.05)	<0.001
	4	2011–2019	−3.70 (−4.10, −3.30)	<0.001	2004–2007	−1.98 (−4.68, 0.80)	0.146	2011–2017	−4.51 (−5.10, −3.92)	<0.001
	5	—	—	—	2007–2011	0.80 (−0.60, 2.21)	0.241	2017–2019	−0.88 (−3.59, 1.91)	0.510
	6	—	—	—	2011–2019	−3.85 (−4.14, −3.55)	<0.001	—	—	—
	AAPC (95%*CI*)	1990–2019	0.44 (0.18, 0.70)	0.001	1990–2019	0.60 (0.16, 1.05)	0.008	1990–2019	0.26 (−0.01, 0.53)	0.059
SAH	1	1990–1996	1.94 (1.53, 2.35)	<0.001	1990–1996	2.47 (2.02, 2.91)	<0.001	1990–1995	1.97 (1.39, 2.55)	<0.001
	2	1996–2000	−4.47 (−5.59, −3.33)	<0.001	1996–2000	−4.05 (−5.28, −2.81)	<0.001	1995–2000	−4.23 (−5.00, −3.45)	<0.001
	3	2000–2004	−15.59 (−16.58, −14.59)	<0.001	2000–2004	−15.49 (−16.57, −14.39)	<0.001	2000–2004	−15.89 (−16.95, −14.81)	<0.001
	4	2004–2007	−7.79 (−9.94, −5.59)	<0.001	2004–2007	−6.93 (−9.30, −4.51)	<0.001	2004–2007	−8.49 (−10.79, −6.13)	<0.001
	5	2007–2014	1.74 (1.33, 2.15)	<0.001	2007–2015	1.84 (1.49, 2.19)	<0.001	2007–2014	1.10 (0.67, 1.54)	<0.001
	6	2014–2019	−2.01 (−2.53, −1.49)	<0.001	2015–2019	−3.33 (−4.12, −2.54)	<0.001	2014–2019	−1.65 (−2.20, −1.08)	<0.001
	AAPC (95%*CI*)	1990–2019	−3.29 (−3.61, −2.96)	<0.001	1990–2019	−3.05 (−3.40, −2.69)	<0.001	1990–2019	−3.67 (−4.00, −3.33)	<0.001

Note. IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; APC, annual percent change; AAPC, average annual percent change; *CI*, confidence interval.

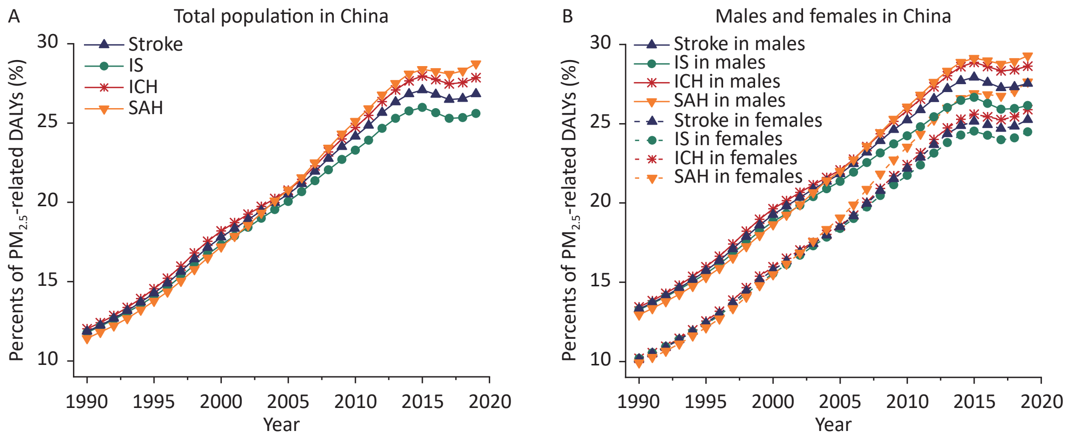
Supplementary Table S11. The trends in numbers of death for stroke attributable to ambient $PM_{2.5}$ in China during 1990−2019 using Join-Point regression

Variables	Segments	Total population			Males			Females		
		Period	APC (95% *CI*)	*P* value	Period	APC (95% *CI*)	*P* value	Period	APC (95% *CI*)	*P* value
Stroke	0	1990−1996	5.46 (5.04, 5.88)	<0.001	1990-1994	5.10 (4.25, 5.96)	<0.001	1990−1996	5.01 (4.64, 5.38)	<0.001
	1	1996−2001	7.81 (7.01, 8.61)	<0.001	1994−2001	7.42 (6.95, 7.88)	<0.001	1996−2003	7.57 (7.19, 7.95)	<0.001
	2	2001−2004	5.52 (3.07, 8.03)	<0.001	2001−2004	5.49 (2.81, 8.24)	0.001	2003−2007	1.84 (0.78, 2.90)	0.002
	3	2004−2007	1.45 (−0.91, 3.86)	0.209	2004−2007	1.79 (−0.79, 4.44)	0.160	2007−2011	3.90 (2.83, 4.99)	<0.001
	4	2007−2011	5.01 (3.78, 6.25)	<0.001	2007−2012	5.06 (4.21, 5.92)	<0.001	2011−2017	1.14 (0.67, 1.61)	<0.001
	5	2011−2019	1.39 (1.13, 1.65)	<0.001	2012−2019	0.97 (0.62, 1.31)	<0.001	2017−2019	3.58 (1.45, 5.77)	0.003
	AAPC (95%*CI*)	1990−2019	4.24 (3.85, 4.64)	<0.001	1990−2019	4.32 (3.91, 4.74)	<0.001	1990−2019	4.11 (3.84, 4.38)	<0.001
IS	0	1990−1996	6.51 (6.04, 6.98)	<0.001	1990−1995	6.41 (5.81, 7.02)	<0.001	1990−1997	6.40 (6.01, 6.79)	<0.001
	1	1996−2004	8.98 (8.60, 9.36)	<0.001	1995−2004	8.37 (8.08, 8.67)	<0.001	1997−2001	10.92 (9.43, 12.45)	<0.001
	2	2004−2007	2.59 (−0.05, 5.30)	0.054	2004−2007	2.81 (0.25, 5.44)	0.034	2001−2004	8.49 (5.57, 11.48)	<0.001
	3	2007−2011	7.38 (5.99, 8.79)	<0.001	2007−2010	8.55 (5.84, 11.33)	<0.001	2004−2007	2.75 (−0.01, 5.59)	0.051
	4	2011−2014	4.68 (1.99, 7.45)	0.002	2010−2014	5.93 (4.60, 7.28)	<0.001	2007−2011	6.32 (4.89, 7.78)	<0.001
	5	2014−2019	2.69 (2.09, 3.29)	<0.001	2014−2019	2.18 (1.60, 2.76)	<0.001	2011−2019	3.41 (3.10, 3.71)	<0.001
	AAPC (95%*CI*)	1990−2019	6.03 (5.59, 6.47)	<0.001	1990−2019	6.04 (5.62, 6.47)	<0.001	1990−2019	5.99 (5.52, 6.47)	<0.001
ICH	0	1990−1995	4.77 (3.90, 5.64)	<0.001	1990−1995	4.93 (4.28, 5.58)	<0.001	1990−1996	4.76 (4.27, 5.25)	<0.001
	1	1995−2003	8.53 (8.00, 9.07)	<0.001	1995−2001	9.00 (8.33, 9.68)	<0.001	1996−2003	8.86 (8.35, 9.36)	<0.001
	2	2003−2011	2.45 (1.94, 2.96)	<0.001	2001−2004	6.56 (3.65, 9.55)	<0.001	2003−2011	1.88 (1.51, 2.26)	<0.001
	3	2011−2019	−0.14 (−0.55, 0.26)	0.471	2004−2007	1.14 (−1.62, 3.98)	0.392	2011−2017	−0.66 (−1.27, −0.05)	0.036
	4	—	—	—	2007−2011	3.96 (2.53, 5.40)	<0.001	2017−2019	2.95 (0.16, 5.83)	0.040
	5	—	—	—	2011−2019	−0.38 (−0.68, −0.08)	0.017	—	—	—
	AAPC (95%*CI*)	1990−2019	3.76 (3.50, 4.02)	<0.001	1990−2019	3.89 (3.44, 4.35)	<0.001	1990−2019	3.65 (3.38, 3.93)	<0.001
SAH	0	1990−1996	4.84 (4.42, 5.26)	<0.001	1990−1996	5.46 (5.03, 5.89)	<0.001	1990−1995	4.76 (4.16, 5.38)	<0.001
	1	1996−2000	−1.30 (−2.47, −0.13)	0.033	1996−2000	−0.87 (−2.06, 0.33)	0.141	1995−2000	−1.08 (−1.89, −0.26)	0.014
	2	2000−2004	−12.52 (−13.55, −11.47)	<0.001	2000−2004	−12.36 (−13.41, −11.29)	<0.001	2000−2004	−12.96 (−14.09, −11.82)	<0.001
	3	2004−2007	−4.62 (−6.86, −2.33)	0.001	2004−2007	−4.08 (−6.37, −1.74)	0.002	2004−2007	−5.34 (−7.77, −2.84)	0.001
	4	2007−2014	5.06 (4.64, 5.48)	<0.001	2007−2014	5.46 (5.03, 5.89)	<0.001	2007−2014	4.44 (3.98, 4.90)	<0.001
	5	2014−2019	1.24 (0.71, 1.78)	<0.001	2014−2019	0.81 (0.26, 1.35)	0.007	2014−2019	1.93 (1.34, 2.53)	<0.001
	AAPC (95%*CI*)	1990−2019	−0.13 (−0.47, 0.21)	0.442	1990−2019	0.15 (−0.19, 0.50)	0.386	1990−2019	−0.49 (−0.84, −0.13)	0.007

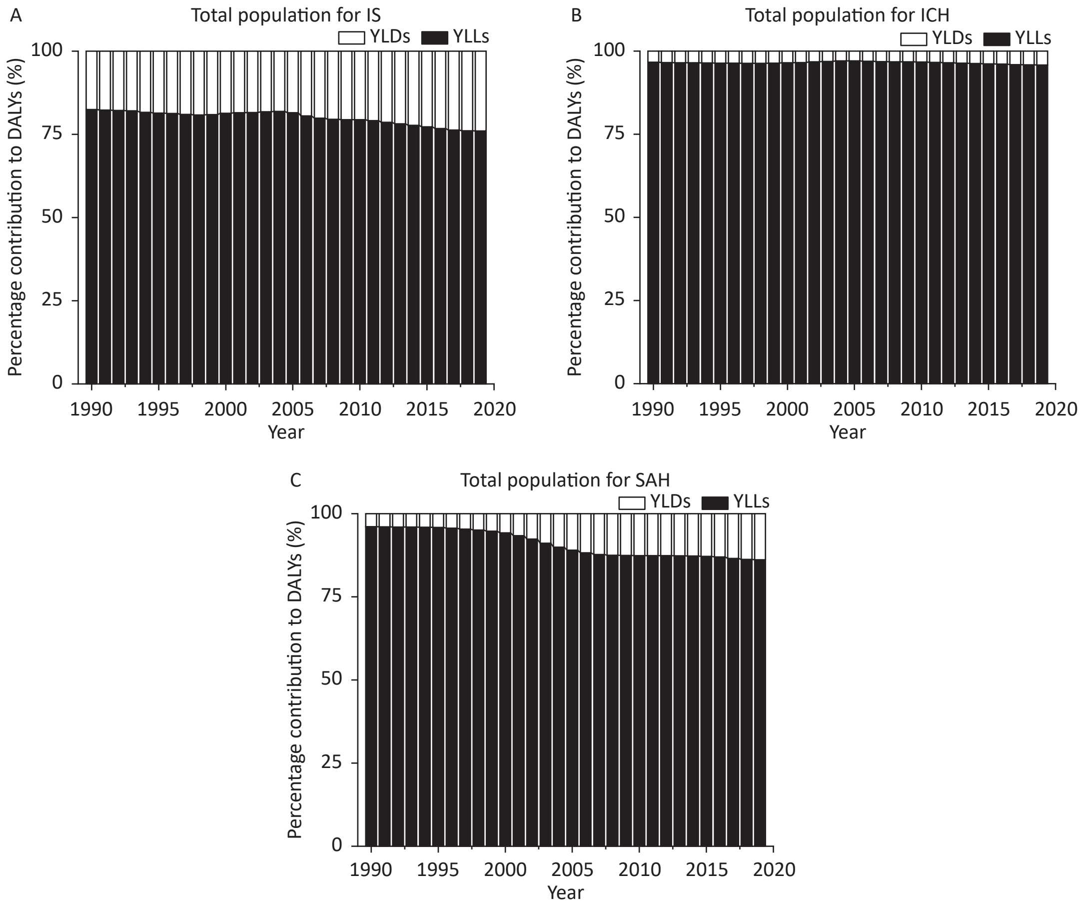
Note. IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; APC, annual percent change; AAPC, average annual percent change; *CI*, confidence interval.



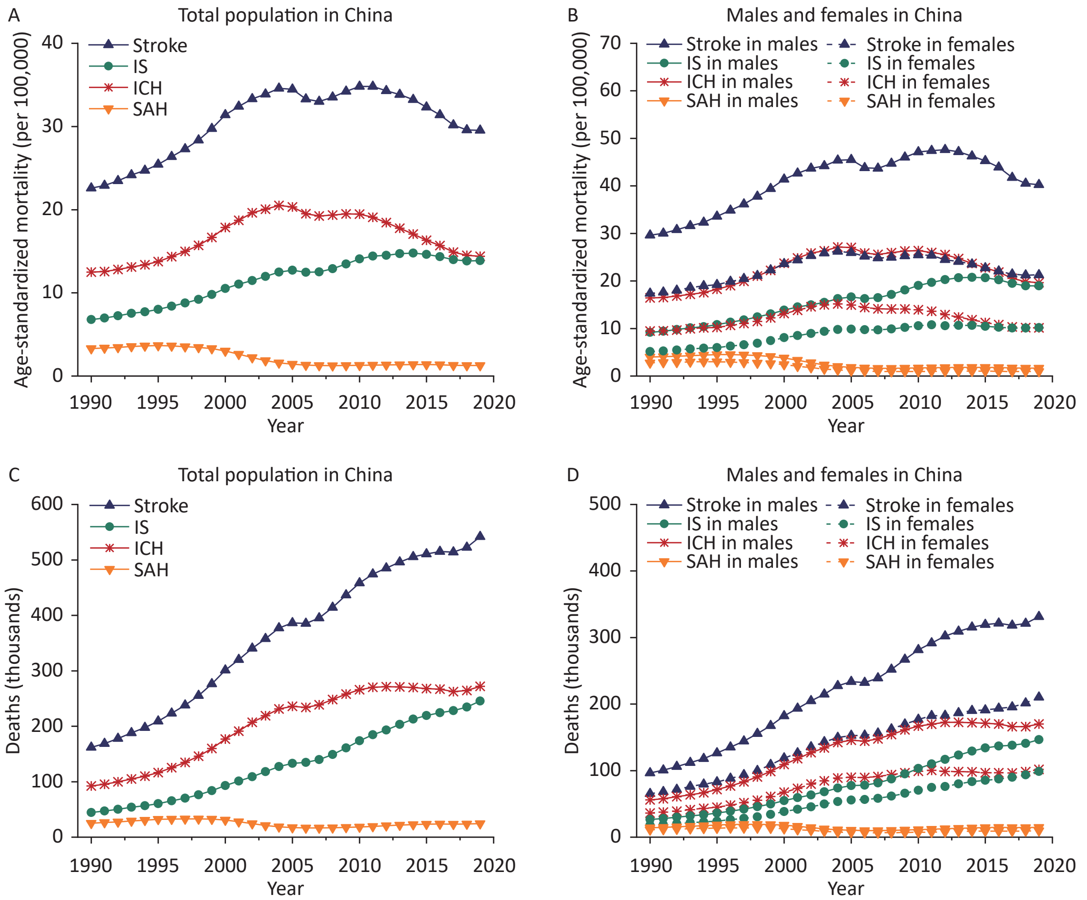
Supplementary Figure S1. Age-standardized Rates of DALY and Mortality for Stroke Attributable to $PM_{2.5}$ From 1990 to 2019 Globally. (A) Age-standardized DALY rates in total population; (B) Age-standardized mortality in total population. DALY, disability-adjusted life year; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.



Supplementary Figure S2. Age-standardized Percents of DALY Attributable to Ambient $PM_{2.5}$-related Stroke in China From 1990 to 2019 Globally. Age-standardized percents of DALY in total population; (B) Age-standardized percents of DALY in males and females, respectively. Percent, the age-standardized proportion of stroke burden attributable to ambient $PM_{2.5}$ within the total stroke burden; DALY, disability-adjusted life year; IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.



Supplementary Figure S3. Contribution of YLL and YLD to DALY for Stroke Attributable to Ambient $PM_{2.5}$ in China During 1990-2019. Contribution of YLL and YLD for IS; Contribution of YLL and YLD for ICH; (C) Contribution of YLL and YLD for SAH.. YLL, year of life lost; YLD, year lived with disability; DALY, disability-adjusted life year; ICH, intracerebral hemorrhage; IS, ischemic stroke.



Supplementary Figure S4. Age-standardized Rates and Numbers of Death for Stroke Attributable to $PM_{2.5}$ in China From 1990 to 2019. (A) Age-standardized mortality in total population; Age-standardized mortality in males and females, respectively; Numbers of death in total population; (D) Numbers of death in males and females, respectively. IS, ischemic stroke; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.