Prolonged Life Expectancy for Those Dying of Stroke by Achieving the Daily PM$_{2.5}$ Targets

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This time-series study collects data on stroke-related mortality, years of life lost (YLL), air pollution, and meteorological conditions in 96 Chinese cities from 2013 to 2016 and proposes a three-stage strategy to generate the national and regional estimations of avoidable YLL, gains in life expectancy and stroke-related population attributable fraction by postulating that the daily fine particulate matter (PM$_{2.5}$) has been kept under certain standards. A total of 1,318,911 stroke deaths are analyzed. Each 10 $\mu$g m$^{-3}$ increment in PM$_{2.5}$ at lag03 is associated with a city-mean increase of 0.31 (95% CI: 0.19, 0.44) years of life lost from stroke. A number of literatures have demonstrated associations between ambient fine particulate matter pollution (PM$_{2.5}$) with premature mortality from stroke.$^{[5]}$ Our previous studies also suggested that each 10 $\mu$g m$^{-3}$ increase in the moving average (lag0) PM$_{2.5}$ was associated with an increase of 3.07% in the stroke mortality and that a reduction in pollution levels during the Asian Games was related to a decreased risk of stroke mortality.$^{[6]}$ In addition, findings from the USA also suggested a 1.78% increase in stroke death for each 10 $\mu$g m$^{-3}$ greater increment of 2-day averaged PM$_{2.5}$.$^{[7]}$

1. Introduction

Stroke leads to both high mortality and disability in the world.$^{[1,2]}$ The Global Burden of Diseases, Injuries, and Risk Factors Study 2017 (GBD 2017) indicated that stroke caused more than six million life lost worldwide (11.02% of all deaths), which corresponded to 113 million years of life lost (6.89% of the total loss).$^{[3]}$ In China, an estimated 106 people per 100,000 population died from stroke in 2017.$^{[4]}$

A number of literatures have demonstrated associations between ambient fine particulate matter pollution (PM$_{2.5}$) with premature mortality from stroke.$^{[5]}$ Our previous studies also suggested that each 10 $\mu$g m$^{-3}$ increase in the moving average (lag0) PM$_{2.5}$ was associated with an increase of 3.07% in the stroke mortality and that a reduction in pollution levels during the Asian Games was related to a decreased risk of stroke mortality.$^{[6]}$ In addition, findings from the USA also suggested a 1.78% increase in stroke death for each 10 $\mu$g m$^{-3}$ greater increment of 2-day averaged PM$_{2.5}$.$^{[7]}$

A few studies used years of life lost (YLL) or excess risk as indicators to examine the disease burden due to air pollution.$^{[8,9]}$ For example, Yang et al. reported that a 10 $\mu$g m$^{-3}$ increase in 2-day average PM$_{10}$ concentration was associated with 0.9 YLL in Guangzhou, China.$^{[10]}$ One study from another Chinese city also reported that PM$_{10}$ exposure was associated with increases in both stroke mortality and stroke-related years of life lost.$^{[11]}$ However, no previous report has addressed the relation between daily PM$_{2.5}$ exposure and YLL due to stroke.

Considering the widely reported association between PM pollution and increased premature stroke mortality, we hypothesized that daily PM$_{2.5}$ exposure was also associated with increased years of life lost and could therefore lead to shorter life expectancy among those stroke patients. In other words, reducing PM$_{2.5}$ to a certain level could mean prolonged life expectancy for stroke survivors.

This research aimed to estimate the possible attainments in stroke-related life expectancy by reaching different standards for daily PM$_{2.5}$ level, which included the Chinese National Ambient Air Quality Standard (NAAQS), as well as the AQG and three Interim Targets (ITs) set by WHO, in 96 Chinese cities during the years of 2013 to 2016.

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DOI: 10.1002/gch2.202000048
## 2. Methods

### 2.1. Data Collection

This time-series study was based on a nationwide dataset containing the daily data on stroke mortality, concentration of pollutants, climatic conditions in 96 Chinese cities (Table S1, Supporting Information) from 2013 to 2016. We chose these cities based on the criteria: 1) data on the daily stroke mortality counts, air pollution, and meteorological factors of each city were available and reliably collected during the study period; 2) there were no adjustments to the cities’ administrative area during the study period; and 3) the daily stroke mortality counts in these cities did not have large fluctuations during the study period.

We classified the study cities into seven regions according to previous experience,[12] which was based on the cities’ geographical location, custom, culture, and climate (Figure 1): northeast \((n = 13)\), north \((n = 8)\), northeast \((n = 14)\), central \((n = 15)\), east \((n = 29)\), southwest \((n = 9)\) and South \((n = 8)\).

The stroke mortality data were extracted from the Cause of Death Reporting System (CDRS), which was managed by the Chinese Center for Disease Control and Prevention (China CDC). The stroke mortality data quality was ensured by multiple administrative levels in the China CDC network. The mortality data have been used to evaluate disease burden and the health impact of air pollution.[13,14] The International Classification Disease, tenth revision (ICD-10, 160–164) were classified as stroke, which was further divided into hemorrhagic stroke (ICD-10 code: 160-161) and ischemic stroke (ICD-10 code: 163).

Additionally, we obtained the Chinese national life table (2013-2016) from the WHO’s website (http://apps.who.int/gho/data/node.main.687?lang=en). We matched age and sex of each death to the Chinese national life table, then calculated their corresponding YLL, following the model established in a previous study, the R codes for calculating the YLL were provided in the Supplemental material.[15] We then summed the overall YLLs for all stroke daily deaths in a city, and this value represented the daily YLLs from stroke of the cities. The flow chart of data sources and the statistical analysis was summarized in Figure 2.

### 2.2. Air Pollutants and Meteorological Factors

The real-time concentrations of PM<sub>2.5</sub>, sulfur dioxide \((SO_2)\), nitrogen dioxide \((NO_2)\), and ozone \((O_3)\) were measured by state-controlled monitoring stations,[16] which were available from the air quality sharing platform of China (http://106.37.208.233:20035). We then averaged the daily PM<sub>2.5</sub>, SO<sub>2</sub>, NO<sub>2</sub> and 8-h maximum O<sub>3</sub> concentrations for each city.

Furthermore, the daily relative humidity (%) and temperature (°C) data were downloaded from the open website of China’s meteorological data sharing platform (http://data.cma.cn).

### 2.3. Statistical Analysis

#### 2.3.1. Descriptive Analyses

The daily mean concentrations of air pollution, meteorological factors, stroke mortality, and YLL were summarized using a descriptive analysis. The Spearman rank correlation was employed to examine the correlations between pollutants and meteorological factors.

![Figure 1. Location of the 96 cities across seven regions of mainland China. The cities are indicated by dark blue dots (•).](image-url)
2.3.2. Step One: City-Specific Associations between PM$_{2.5}$ and Stroke-Related Mortality and YLL

The associations of daily PM$_{2.5}$ with stroke-related outcomes were examined through a three-stage strategy at both the national and regional levels, and similar approach has been recently introduced in our previous studies on all-cause mortality.[12,17] The city-specific relation between PM$_{2.5}$ level and stroke-related death count were first analyzed using a generalized additive model (GAM) with a quasi-Poisson link. The association between stroke-related YLL and PM$_{2.5}$ was examined by a GAM with Gaussian link. In this stage, daily mortality count or YLL from stroke in each city were the dependent variables with daily mean PM$_{2.5}$ concentration as the independent variable. Both day of the week (DOW) and public holidays (PH) were adjusted in the analyses. Temperature, relative humidity, long-term and seasonal trends were controlled by the penalized smoothing splines function.[18] The supplemental Table S2, Supporting Information display a list of covariates and degrees of freedom (df) of the smoothers being used in the models, which were selected based on previously similar studies.[19] A df of six per year for temporal trends, a df of six for temperature, and a df of three for relative humidity were used to adjusted for the potential nonlinear relationships. The formula can be specified as:

$$YLL = \alpha + \beta_1 \text{PM}_{2.5} + \beta_2 \text{DOW} + \beta_3 \text{PH} + s(t, df = 6/\text{year}) + s(\text{TM}, df = 6) + s(\text{RH}, df = 3)$$

(1)

In this formula, YLL means the years of life lost from stroke mortality, PM$_{2.5}$ is the concentration of fine particulate matter, TM is air temperature, and RH is relative humidity.

We evaluated the lagged effects of daily PM$_{2.5}$ on stroke-related mortality and YLL for the current day (lag0), 1 day (lag1), 2 days (lag2), 3 days (lag3) before, and moving averages for the current day and the previous 1, 2, and 3 days (lag01, lag02, lag03). We also performed these analyses for two main types of strokes: ischemic and hemorrhagic strokes.

2.3.3. Step Two: Calculate the City-Specific Avoidable YLLs

At the second stage, based on the established model, we evaluated the city-specific avoidable YLLs from stroke by postulating that the daily PM$_{2.5}$ level had been kept under a series of air pollution standards, such as the NAAQS and AQG. Then, we calculated the possible attainments in stroke-related life expectancy by averaging the avoidable YLLs on the city-specific stroke mortality; this calculation process can be expressed by the following formula:

$$\text{Potential benefits to life expectancy} = \frac{\text{Avoidable stroke-related YLLs}}{\text{Stroke mortality count}}$$

(2)

In this formula, the avoidable stroke-related YLLs was the estimated years of life lost related to stroke that can be avoided if daily PM$_{2.5}$ level was kept under different standards in each city. The stroke mortality count refers to the overall death number due to stroke of the corresponding city. The reference standards being used for PM$_{2.5}$ level in our study included the AQG (25 µg m$^{-3}$) and IT-1 (75 µg m$^{-3}$, also the currently used NAAQS), IT-2 (50 µg m$^{-3}$), and IT-3 (37.5 µg m$^{-3}$).

In order to show the proportion of stroke-related YLL caused by a higher-than-standard level of PM$_{2.5}$ exposure, we computed the city-specific population attributable fraction (PAF) by the formula as below:

$$\text{PAF} = \frac{\text{Avoidable stroke-related YLLs}}{\text{Stroke-related YLLs}}$$

(3)

Where PAF was the population attributable fraction; avoidable stroke-related YLLs was the estimated years of life lost from stroke that can be saved if the daily PM$_{2.5}$ level was kept under different standards in the study city; and stroke-related YLL is the total YLL for stroke-related deaths of the corresponding city.
2.3.4. Step Three: Calculating the Overall Potential Life Expectancy Benefits and PAF

At the third stage, we separately pooled the values of different cities to generate the regional and national estimates of stroke-YLL association, stroke-related avoidable YLL, potential life expectancy benefits and the population attributable fraction by conducting random-effect meta-analyses.[20,21]

2.3.5. Sensitivity Analyses

To verify the robustness of the results, a number of sensitivity analyses were conducted. First, we tested two-pollutant models by simultaneously including PM$_{2.5}$ and one other pollutant (e.g., SO$_2$, NO$_2$ or O$_3$) in the model analyses. We also employed the mixed-effects generalized additive models to estimate the national and regional associations, with the city variable being used as a random-effect term. Furthermore, the city-specific coefficients for the associations of daily PM$_{2.5}$ with stroke-related mortality count and YLL were statistically weighted to represent five million Chinese population to conduct the population-weighted meta-analyses. Finally, we used a meta-regression method to check whether the differential associations across the cities might be attributable to the following city characteristics: 1) annual mean PM$_{2.5}$, CO, O$_3$, NO$_2$ and SO$_2$ levels; 2) geographical features and annual meteorological conditions such as elevation, temperature, precipitation, relative humidity, and air pressure; 3) socio-demographic characteristics such as education, poverty, population density, gross domestic product (GDP) and per capita GDP.

The data analyses were conducted with the “mgcv” and “metafor” packages in R software (version 3.6.2).[21,22] Two-sided tests with $p$-values less than 0.05 were considered statistically significant for the analyses. And the sample R codes for our main analyses were illustrated in the supplemental material.

2.4. Data Availability

The Chinese national life table (2013–2016) are publicly available at the WHO’s website (http://apps.who.int/gho/data/node.main.687?lang=en). The stroke mortality data were extracted from the CDRS that was managed by the China CDC. The real-time concentrations of air pollutants were available from the air quality sharing platform of China (http://106.37.208.233:20035), and the meteorological data were downloaded from the open website of China’s meteorological data sharing platform (http://data.cma.cn).

3. Results

3.1. Descriptive Results

A total of 131891 stroke deaths were collected. Among them, 744 682 were males, and 574 229 were females. They included 567 787 deaths due to ischemic strokes, 668 343 deaths due to hemorrhagic strokes, and 82 781 undetermined strokes.

The number of cities, pollution levels, meteorological factors, daily mean mortality count, and YLL from stroke in different regions are displayed in Table 1. The daily PM$_{2.5}$, SO$_2$, NO$_2$ and O$_3$ levels were 46.92 to 87.24, 26.13 to 59.53, 28.02 to 45.21, and 71.19 to 96.20, respectively. The daily mean temperature ranged from 8.57 to 22.01 °C, while the daily mean relative humidity ranged from 52.11% to 78.28%. In addition, the daily mortality counts from stroke (ischemic and hemorrhagic stroke) ranged from 7.25 (3.61 and 4.83) to 15.06 (7.86 and 9.10), and the corresponding daily mean YLLs ranged from 977.72 (3706 and 69.69) to 218.20 (93.89 and 126.13).

Low to moderate correlations were observed between the pollutants and meteorological factors (Table S3, Supporting Information). For example, PM$_{2.5}$ was shown to have relatively low and positive relation with O$_3$ and SO$_2$ (coefficients: 0.36 and 0.29, respectively) and was shown to have a moderate positive correlation with NO$_2$ with a coefficient of 0.49. PM$_{2.5}$ also had very low negative correlations with relative humidity and air temperature, and the coefficients were −0.01 and −0.15, respectively.

3.2. The Relation between PM$_{2.5}$ Level and Stroke-Related YLL

The regional and lag-specific relation between daily mean PM$_{2.5}$ level and stroke-related mortality and YLL varied in single-pollutant models (Figure 3). We observed that the daily PM$_{2.5}$ concentrations were positively associated with stroke-related excess risk of mortality in all the study regions, and the daily PM$_{2.5}$ concentrations were also positively associated with YLL from stroke in the seven regions and the national level, with the lag$_{03}$ models being the strongest lag association. Each 10 µg m$^{-3}$ increment in the daily PM$_{2.5}$ levels at lag$_{03}$ was related to an excess mortality risk of 0.22 (95% CI: 0.12, 0.31) and an increase of 0.31 (95% CI: 0.19, 0.44) years of life lost from stroke at the national level (Table S4, Supporting Information), though the associations varied by region according to the region-specific analyses. For example, the South region had the highest association between daily PM$_{2.5}$ level and stroke-related mortality count, with each 10 µg m$^{-3}$ increment in the daily PM$_{2.5}$ levels at lag$_{01}$ was related to an excess mortality risk of 0.66 (95% CI: 0.38, 0.95). The Northwest region, on the other hand, had the lowest excess risk of 0.06 (95% CI: −0.16, 0.29) and was not statistically significant. The Southwest region had the highest correlation between PM$_{2.5}$ and stroke-related YLL with the coefficient of 1.28 (95% CI: 0.14, 2.43), and the Central area had the lowest correlation (β = 0.16, 95% CI: −0.07, 0.39). A series of model diagnostic graphs such as residual plots (Figure S1, Supporting Information), plots of partial autocorrelation function (PACF, Figure S2, Supporting Information), and Q–Q plots (Figure S3, Supporting Information) for six provincial capital cities were provided as the online supplemental figures. These results suggested that the goodness of fit of the models were acceptable.

The sensitivity analyses showed consistent associations of PM$_{2.5}$ with daily mortality count and YLL from stroke (Table S4, Supporting Information). For example, each 10 µg m$^{-3}$ increment in the daily PM$_{2.5}$ level may cause excess risks of 0.19 (95% CI: 0.10, 0.29), 0.14 (95% CI: 0.06, 0.22), or 0.20 (95% CI: 0.11, 0.30) in mortality from stroke at the national level when
Abbreviations: PM$_{2.5}$ = particulate matter with an aerodynamic diameter less than or equal to 2.5 $\mu$m; SO$_2$ = sulfur dioxide; NO$_2$ = nitrogen dioxide; O$_3$ = ozone; YLL = years of life lost.

Table 1. Characteristics of the study cities by regions, 2013–2016.

| Variable | Northwest | North | Northeast | Central | East | Southwest | South | National |
|----------|-----------|-------|-----------|---------|------|-----------|-------|----------|
| Number of cities | 13 | 8 | 14 | 15 | 29 | 9 | 8 | 96 |
| Daily mean concentration of air pollutants [µg m$^{-3}$] | | | | | | | | |
| PM$_{2.5}$ | 54.12 | 87.24 | 58.20 | 76.12 | 72.66 | 46.92 | 49.90 | 66.08 |
| SO$_2$ | 34.26 | 59.53 | 41.35 | 33.00 | 42.68 | 27.20 | 26.13 | 38.80 |
| NO$_2$ | 29.96 | 45.21 | 35.37 | 35.81 | 38.56 | 28.02 | 30.47 | 35.68 |
| O$_3$ | 80.93 | 96.20 | 86.35 | 81.20 | 89.56 | 71.19 | 87.24 | 85.60 |
| Daily mean meteorological factors | | | | | | | | |
| Temperature [°C] | 11.53 | 12.36 | 8.57 | 17.33 | 15.92 | 17.14 | 22.01 | 14.88 |
| Relative humidity [%] | 52.11 | 55.36 | 61.58 | 73.33 | 71.30 | 66.70 | 78.28 | 66.72 |

Table 2 shows the avoidable YLL and PAF. Stricter air pollution standards could generally result in reductions of stroke-related years of life lost, and we estimated that a relatively low city-mean of 10.89 (95% CI: 2.44, 19.33) years of life lost from stroke may be saved by achieving the current daily standard (75 µg m$^{-3}$), which could increase to 914.11 YLL (95% CI: 539.28, 1288.94) by attaining the WHO’s AQG (25 µg m$^{-3}$). Moreover, different effect estimates were found in the seven regions. For example, the Southwest region had the largest, significant city-mean avoidable stroke-related YLL of 3422.37 (95% CI: −1202.10, 8046.85) that could be attained by achieving the WHO’s AQG, while the Northwest region only yield 411.57 YLL avoided (95% CI: −164.68, 98783) under the same standard. Figure 4 displays the potential gains in life expectancy under different standards in both the regional and national level. Specifically, we found that about 0.001 (95% CI: 0.0001, 0.0014) and 0.11 (95% CI: 0.08, 0.15) years might be saved for each stroke-related death by achieving China’s NAAQS (75 µg m$^{-3}$) and the WHO’s AQG (25 µg m$^{-3}$), respectively. Additionally, the largest and smallest significant values of 0.18 (95% CI: 0.04, 0.32) and 0.07 (95% CI: −0.003, 0.14) was estimated in the Southwest and the Northeast regions, respectively, when adopting AQG as the recommended target.

Using NAAQS and AQG as references, we estimated that about 0.01% (95% CI: 0.006%, 0.01%) and 0.91% (95% CI: 0.62%, 1.19%) of the total years of life lost from stroke, respectively, might be explained by the daily excess PM$_{2.5}$ exposures (Table 2). Moreover, the estimates were also found to be heterogeneous among different regions, with the largest significant PAF being found in the South and Southwest region [1.46% (0.85%, 2.08%) and 1.46% (0.36%, 2.55%)] and the smallest being found in the Northeast region [0.47% (−0.01%, 0.95%)].

The stratified analyses for ischemic and hemorrhagic stroke suggested that the benefits in life expectancy of reducing daily PM$_{2.5}$ level were more pronounced for ischemic than hemorrhagic stroke (Tables S7 and S8, Supporting Information). To be specific, we found that an increase of 0.13 (95% CI: 0.08, 0.18) years of life expectancy might be obtained by attaining the AQG (25 µg m$^{-3}$), with a PAF of 1.21% (95% CI: 0.73%, 1.70%) for the total YLLs due to ischemic stroke, while for hemorrhagic...
stroke, the corresponding benefit in life expectancy was 0.07 (95% CI: 0.02, 0.12) years and a 0.50% (95% CI: 0.18%, 0.82%) PAF for YLL.

Our meta-regression analysis suggested that the correlation between daily PM$_{2.5}$ level and stroke-related life expectancy was relatively higher in cities with higher GDP, lower annual O$_3$ levels, and higher annual mean temperature (Table S9, Supporting Information). Each IQR (218.20 billion, CNY) increase in average GDP was associated with a 0.18 (0.06, 0.30) increment in the regression coefficient, each IQR (20.45 µg m$^{-3}$) increment in annual mean levels of O$_3$ was related to 0.26 (0.01, 0.51) decrease in the regression coefficient, and each IQR (6.15 °C) increment in annual mean temperature was related to 0.39 (0.01, 0.77) increase in the regression coefficient. However, no significant effect was found for other city-level factors, such as GDP per capita, population density, or elevation.

4. Discussion

To our knowledge, this study is among the first efforts to examine the effects of daily air pollution on life expectancy due to stroke mortality. Based on a large dataset covering 96 cities across the seven geographic regions of China, our study suggested that daily PM$_{2.5}$ exposure was associated with stroke-related years of life lost, especially for ischemic stroke. Moreover, our results suggested that by attaining stricter ambient air pollution standards, a person can have a longer life expectancy.

The observed correlation between daily PM$_{2.5}$ level and stroke-related life expectancy was supported by the widely-reported associations between daily PM$_{2.5}$ exposure and premature mortality from stroke. For example, one of our former studies revealed that each 10 µg m$^{-3}$ increase in 4-day moving average PM$_{2.5}$ was associated with a 0.06% (95% CI: 0.01%, 0.11%) increase in stroke mortality risk.
Table 2. The avoidable stroke-related years of life lost, potential gains in life expectancy and PAF for those dying of stroke by enhancing PM$_{2.5}$ level to Chinese and WHO’s guidelines in the study cities during 2013–2016.

| Region       | Avoidable YLL (95% CI) | Benefits in life expectancy (95% CI) | PAF [%] 95% CI |
|--------------|------------------------|-------------------------------------|----------------|
|              | China’s standard (IT-1) | WHO’s AQG                           | China’s standard (IT-1) | WHO’s AQG |
| Northwest    | 17.07 (–7.29, 41.44)    | 411.57 (–164.68, 987.83)             | 0.01 (–0.01, 0.04)     | 0.16 (0.03, 0.29) |
| North        | 295.76 (–135.75, 727.27) | 1009.35 (–410.39, 2429.10)          | 0.02 (–0.01, 0.05)     | 0.09 (–0.02, 0.19) |
| Northeast    | 157.58 (–49.10, 364.26) | 896.82 (–273.18, 2066.82)           | 0.02 (0.01, 0.03)      | 0.07 (–0.003, 0.14) |
| Central      | 46.61 (–90.13, 183.35)  | 607.45 (–315.24, 1530.13)           | 0.01 (–0.01, 0.03)     | 0.08 (–0.01, 0.18) |
| East         | 5.79 (–11.13, 22.72)    | 1085.18 (148.42, 2021.94)           | 0.02 (0.005, 0.03)     | 0.10 (0.03, 0.17) |
| Southwest    | 3.23 (–1.27, 7.74)      | 3422.37 (–1202.10, 8046.85)         | 0.0004 (–0.0002, 0.001) | 0.18 (0.04, 0.32) |
| South        | 113.33 (5.18, 221.48)   | 2042.97 (1041.70, 3044.23)          | 0.04 (0.01, 0.07)      | 0.17 (0.10, 0.25) |
| National     | 10.89 (2.44, 19.33)     | 914.11 (133.28, 1288.94)            | 0.001 (0.0001, 0.0014) | 0.11 (0.08, 0.15) |

Moving average of lag 0 to lag 3 (lag03) for daily PM$_{2.5}$ level was used; the reference PM$_{2.5}$ standards were the IT-1 or Chinese NAAQS (75 µg m$^{-3}$) and WHO’s AQG (25 µg m$^{-3}$); abbreviations: PM$_{2.5}$ = particulate matter with an aerodynamic diameter less than or equal to 2.5 µm; YLL = years of life lost; PAF = population attributable fraction; IT = interim targets; NAAQS = National Ambient Air Quality Standards; AQG = Ambient Air Quality Guidelines.

Our findings of the possible attainments in life expectancy by achieving daily PM$_{2.5}$ guidelines are in agreement with several other studies. For example, one US study found that an increase of 2.8 µg m$^{-3}$ in annual average PM$_{2.5}$ concentrations was associated with life expectancy losses of 0.15 years in females and 0.13 years in males. Results from another study showed that an increase of 2 µg m$^{-3}$ in the annual PM$_{2.5}$ concentration led to a loss of 0.64 years of life in certain areas of Spain. Moreover, there is evidence that reducing PM$_{2.5}$ concentrations would substantially increase life expectancy; specifically, one study found that, in the Medicare population, that 23.5% of people would die before the age of 76 years if they were exposed to an annual average PM$_{2.5}$ concentration of 12 µg m$^{-3}$ and that that percentage would decline to 20.1% for a lower annual average PM$_{2.5}$ level of 7.5 µg m$^{-3}$.

The linkage between exposure to PM$_{2.5}$ and life expectancy is biologically plausible. The direct effects of PM$_{2.5}$ on lung receptors and the cardiovascular system may lead to acute cardiovascular responses and contribute to cardiovascular dysfunction. Another potential mechanism may be the abnormal activation of the hemostatic system. Moreover, lung and systemic inflammation, oxidative stress, and the formation of

Figure 4. Life gains by achieving different recommend levels for PM$_{2.5}$ control. Moving average of lag 0 to lag 3 (lag03) for daily PM$_{2.5}$ level was used. Abbreviations: PM$_{2.5}$ = particulate matter with an aerodynamic diameter less than or equal to 2.5 µm; IT = Interim Targets; AQG = WHO’s Ambient Air Quality Guidelines.

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atherosclerotic plaque resulting from PM$_{2.5}$ inhalation may also lead to increased mortality and morbidity from cardiovascular and cerebrovascular diseases.$^{[29,31,32]}$ Additionally, evidence from an intervention study showed a significant improvement on the microvascular function in the elderly after a reduction of particulate matter levels via an indoor air filtration system.$^{[33]}$ Since 2013, the toughest-ever clean air policy was implemented in China, which has introduced remarkable improvements in air quality, and significant declines in PM$_{2.5}$ levels have been achieved nationwide.$^{[34]}$ Our study provides substantial evidence for the fact that stricter PM$_{2.5}$ standards may lead to longer stroke-related life expectancy. A relatively larger benefit in life expectancy was observed when adopting AQG (25 µg m$^{-3}$) as the recommended level, compared to the benefits gained by adopting NAAQS (75 µg m$^{-3}$). The model suggested that a lower air quality limit like the WHO’s AQG would result in more benefits in life expectancy. The results of this study indicated that 0.11 years of life per stroke survivor would be prolonged in China by attaining the WHO’s air quality guideline on daily concentration of PM$_{2.5}$, while the benefits in stroke-related life expectancy by attainment of the current China’s PM$_{2.5}$ NAAQS (75 µg m$^{-3}$) only yield an extremely low value of 0.001 years, which suggested that this standard may be no longer enough in reducing the risk of death from stroke. This also concurs with previous studies which showed that the short-term PM$_{2.5}$ effects were smaller than the long-term effects.$^{[35]}$ This finding can be partially explained by the cumulative effects of long-term exposures.$^{[36]}$ Nevertheless, study on the short-term effects of PM$_{2.5}$ may also help us to understand if even a short-term exposure to higher levels of PM$_{2.5}$ have adverse impacts on life expectancy.

In our stratified analyses, we observed more pronounced inverse associations between PM$_{2.5}$ and YLL from ischemic than from hemorrhagic stroke. These results were consistent with earlier studies that differentiated the impacts of air pollution on ischemic and hemorrhagic stroke. For example, one study concluded that an interquartile range increase in PM$_{2.5}$ may result in a 1.0% increase in ischemic stroke admissions at lag 3 days in 26 Chinese cities, but no significant association was observed for hemorrhagic stroke.$^{[37]}$ In another study, the odds ratios of hospital admission due to ischemic and hemorrhagic strokes were 2.071 and 1.941, respectively, per interquartile range increase in the same-day PM$_{2.5}$ concentrations.$^{[38]}$ One recent long-term study also found that, for each 10 µg m$^{-3}$ increase in PM$_{2.5}$ concentration, the incident ischemic stroke increased by 20%, which was higher than the increment of 12% found for hemorrhagic stroke.$^{[39]}$ Moreover, these findings were further supported by a study which demonstrated that the relative risk was 1.010 for ischemic stroke for each 10 µg m$^{-3}$ increase in PM$_{2.5}$ and 1.004 for hemorrhagic stroke.$^{[40]}$

Our sensitivity analyses suggested that the estimated associations were robust. Specifically, results in the two-pollutant models which further adjusted for several pollutants, including SO$_2$, NO$_2$, and O$_3$, were in accord with those results in the main models, suggesting that these air pollutants were not confounders in the associations between PM$_{2.5}$ and stroke-related YLL. However, results from the two-pollutant analyses generally showed the smallest correlations between PM$_{2.5}$ and stroke-related YLL when we included NO$_2$. The reason for this is not clear, but it may because PM$_{2.5}$ and NO$_2$ had a moderate positive correlation ($r = 0.49$). Another possible explanation for this might be due to the similar emission sources for these two air pollutants.$^{[41,42]}$

The heterogeneous extents in the correlation between daily PM$_{2.5}$ and stroke-related YLL among the seven regions is consistent with previous reports,$^{[43]}$ and the Southwest, South, Northwest and East regions displayed relatively more reliable associations between PM$_{2.5}$ and stroke-related YLL. However, although the North, Northeast and Central regions also displayed a positive association, they were statistically insignificant. Such heterogeneity might be explained in part by the different chemical constituents of PM$_{2.5}$ in these regions.$^{[44]}$ For example, it is reasonable that the PM$_{2.5}$ in the Southwest is more hazardous than that in other regions because much of the particle matter is related to biomass combustion in these two regions, which has been proven to be more toxic than other sources, according to previous reports.$^{[45]}$ Recent findings reported by Want et al. (2019) showed that the elemental carbon and some metallic constituents of PM$_{2.5}$ may lead to ischemic stroke.$^{[46]}$ Our meta-regression analysis found that the observed PM$_{2.5}$–YLL association was relatively higher in cities with lower annual O$_3$ levels, which might be because people from high polluted environment usually have more awareness of better protective measures.$^{[47]}$ Additionally, the areas with higher annual temperature also tended to have higher PM$_{2.5}$–YLL associations, which indicates that this association may be influenced by meteorological factors.

Although based on a large dataset, this study was subject to a few limitations. First, we cannot make a causal conclusion for the relationship between PM$_{2.5}$ and reduced life expectancy due to the time-series design, which lacked the measurements at the individual level, such as the personal exposure and smoking status which was an established risk factor for stroke.$^{[48]}$ In addition, exposure misclassification was likely due to the usage of city-averaged PM$_{2.5}$ concentrations as a surrogate of exposure. However, in such a large epidemiologic study, it is difficult to directly measure individual exposures, and city-averaged PM$_{2.5}$ levels have been widely adopted in previous studies.$^{[46,47]}$ Another potential problem of this study was that our findings may be somewhat limited by the representativeness of some geographical regions which included relatively fewer cities, especially the North and South regions. Moreover, the collinearity between PM$_{2.5}$ and other air pollutants may also be a weakness, but the robustness of our findings was further confirmed in the two-pollutant models. Despite these limitations, this research certainly adds to our understanding of the benefits of PM$_{2.5}$ control.

5. Conclusion

This nationwide study suggests that daily PM$_{2.5}$ exposure is associated with YLL due to stroke, and that life expectancy can be longer by reducing daily PM$_{2.5}$ concentrations, especially for ischemic stroke. Our results provide further evidence for the fact that the current PM$_{2.5}$ standard may not be enough in protecting population’s mortality risk from stroke, and future prospective studies on this topic will need to be undertaken.
6. Experimental Section
The study was approved by the Ethical Review Committee of the School of Public Health, Sun Yat-Sen University ([2019] No.149). As all of the analyses were based on aggregated data, this study did not require individual consent. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed in reporting the study.

Supporting Information
Supporting Information is available from the Wiley Online Library or from the author.

Acknowledgements
Z.R. and J.Q. contributed equally to this work. This work is supported by the National Key R&D Program of China (2016YFC0206501) and the National Natural Science Foundation of China (81972993).

Conflict of Interest
The authors declare no conflict of interest.

Keywords
air quality standards, fine particulate matter, life expectancy, multi-city studies, stroke

Received: July 1, 2020
Published online: October 13, 2020

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