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RESEARCH ARTICLE

# Ambient air pollution and cerebrovascular disease mortality: an ecological time-series study based on 7-year death records in central China

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## Abstract

Most studies of short-term exposure to ambient air pollution and cerebrovascular diseases focused on specific stroke-related outcomes, and results were inconsistent due to data unavailability and limited sample size. It is unclear yet how ambient air pollution contributes to the total cardiovascular mortality in central China. Daily deaths from cerebrovascular diseases were obtained from the Disease Surveillance Point System (DSPs) of Wuhan Center for Disease Control and Prevention during the period from 2013 to 2019. Air pollution data were obtained from Wuhan Ecology and Environment Institute from 10 national air quality monitoring stations, including average daily $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and $O_3$. Average daily temperature and relative humidity were obtained from Wuhan Meteorological Bureau. We performed a Poisson regression in generalized additive models (GAM) to examine the association between ambient air pollution and cerebrovascular disease mortality. We observed a total of 84,811 deaths from cerebrovascular diseases from 1 January 2013 to 31 December 2019 in Wuhan. Short-term exposure to $PM_{2.5}$, $PM_{10}$, $SO_2$, and $NO_2$ was positively associated with daily deaths from cerebrovascular diseases, and no significant association was found for $O_3$. The largest effect on cerebrovascular disease mortality was found at lag0 for $PM_{2.5}$ (ERR: 0.927, 95% CI: 0.749–1.105 per 10 μg/m3) and lag1 for $PM_{10}$ (ERR: 0.627, 95% CI: 0.493–0.761 per 10 $\mu g/m^3$), $SO_2$ (ERR: 2.518, 95% CI: 1.914, 3.122 per 10 $\mu g/m^3$), and $NO_2$ (ERR: 1.090, 95% CI: 0.822–1.358 per 10 $\mu g/m^3$). The trends across lags were statistically significant. The stratified analysis demonstrated that females were more susceptible to $SO_2$ and $NO_2$, while elder individuals aged above 65 years old, compared with younger people, suffered more from air pollution, especially from $SO_2$. Short-term exposure to $PM_{2.5}$, $PM_{10}$, $SO_2$, and $NO_2$ were significantly associated with a higher risk of cerebrovascular disease mortality, and elder females seemed to suffer more from air pollution. Further research is required to reveal the underlying mechanisms.

**Keywords** Cerebrovascular diseases · Mortality · Air pollution · Times-series · Generalized additive model

## Introduction

Cerebrovascular disease, including a range of conditions that affect the flow of blood through the brain, is highly prevalent in older people and remaining a leading cause of death throughout the world (Truelsen et al. 2000; Feigin et al. 2017). Scientific evidence has shown that air pollution and cerebrovascular diseases are positively related, which could be mediated through direct and indirect effects of exposure to air pollutants on vascular tone, endothelial function, thrombosis, and myocardial ischemia (Brook et al. 2002; Lucking et al. 2008; Lundbäck et al. 2009; Mills et al. 2011). According to the GBD (Global Burden of Disease) report, 12.8% of DALYs for stroke in China were attributable to air pollution in 2017 (Yin et al. 2020). Globally, air pollution was

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the sixth cause of stroke death from 1990 to 2017 and accounted for 28.1% of DALYs for stroke from environmental factors exposure (air pollution, Pb) (Avan et al. 2019).

A few studies have explored associations between air pollution and cerebrovascular-related outcomes. A meta-analysis with a total of 6.2 million events across 28 countries from 94 studies reported that stroke hospitalization or stroke mortality was positively associated with a short-term increase in concentrations of $PM_{2.5}$ (RR: 1.011, 95% CI: 1.011–1.012 per 10 μg/m$^3$), $PM_{10}$ (RR: 1.003, 95% CI: 1.002–1.004 per 10 μg/m$^3$), $SO_2$ (RR: 1.019, 95% CI: 1.011–1.027 per 10 ppb), $NO_2$ (RR: 1.014, 95% CI: 1.009–1.019 per 10 ppb), and $O_3$ (RR: 1.011, 95% CI: 1.011–1.012 per 10 μg/m$^3$) (Shah et al. 2015). More recently, a time-series study in Mexico City showed an increase of 10 μg/m$^3$ in $PM_{2.5}$ was associated with increased cerebrovascular mortality by 3.43% (95% CI: 0.10–6.28) for lag days 0 to 1, and stronger effects were identified among people over 65 years old (Gutiérrez-Avila et al. 2017). However, results were inconsistent in countries of low-level exposure. Two prospective studies in Sweden and Spain showed no significant associations between long-term exposure to particulate matters and incident stroke events (Ljungman et al. 2019; Vivanco-Hidalgo et al. 2019). In a US study conducted in 2019, short-term exposure to $NO_2$ (OR: 1.24, 95% CI: 1.01–1.52 per interquartile) was found to increase the risk of hemorrhagic stroke, whereas no substantial association was observed for $PM_{2.5}$, $PM_{10}$, $NO_2$, and $SO_2$ with a risk of total stroke in post-menopausal women (Sun et al. 2019).

As the largest and most populous city in central China, health effects of air pollution in Wuhan are worth studying. However, most previous studies focused on specific stroke-related health outcomes, and it is not clear yet how air pollution affects the total cerebrovascular disease mortality in Wuhan. Besides, data in previous studies were mostly collected from hospitals (Xiang et al. 2013; Wang et al. 2019; Qi et al. 2020), which may lead to a lack of representativeness and selection bias. In this study, we obtained integral and accurate Wuhan death records directly from the Disease Surveillance Point System (DSPs) and employed generalized additive models (GAM) to explore the association between short-term exposure to air pollution and cerebrovascular disease mortality in Wuhan, China during 2013–2019. This study may have important implications for the risk assessment and prevention of cerebrovascular disease and provide certain epidemiological evidence for policy-makers to curb ambient air pollution in Wuhan.

## Materials and methods

### Data collection

Cerebrovascular disease mortality data were collected from Disease Surveillance Point System (DSPs) of Wuhan Center for Disease Control and Prevention from 1 January 2013 to 31 December 2019. All death cases are from local residents registered in Wuhan Hukou System. We obtained individual death registration records for cerebrovascular diseases (International Classification of Diseases, 10th revision—ICD10: I60-I69) including death date, age group, gender, and death reason. And then we created a dataset including the daily counts of deaths from cerebrovascular disease chronologically for this period.

Air pollution data were obtained from 10 national air quality monitoring stations in Wuhan operated by the Wuhan Ecology and Environment Bureau. The average concentration of air pollutants measured in these monitoring stations was used as a proxy for daily exposure to air pollution in Wuhan. We included five air pollutants in our analysis, including average daily $PM_{2.5}$ (mass of particles with aerodynamic diameter < 2.5 μm), $PM_{10}$ (mass of particles with aerodynamic diameter < 10 μm), $SO_2$ (sulfur dioxide), $NO_2$ (nitrogen dioxide), and $O_3$ (ground-level ozone) from 1 January 2013 to 31 December 2019. Meteorological data, including average daily temperature and relative humidity, were obtained from Wuhan Meteorological Administration.

The study was approved by the ethics committee of the Wuhan Centers for Disease Control and Prevention. Since the data was analyzed at an aggregate level with no individual information involved, informed consent from the participants was waived for this study.

### Statistical analysis

A time-series study design was used to evaluate the association between air pollution and cerebrovascular disease mortality. We first created a time-series dataset including the daily deaths from cerebrovascular disease, day of the week (DOW), the concentration of air pollutants, average daily temperature, and humidity for the period from 1 January 2013 to 31 December 2019 before statistical analysis. Daily deaths from cerebrovascular disease, air pollutants, and meteorological factors were described as mean, standard deviation (SD), and quartiles. Spearman correlation was conducted to explore the relationship between pollutant concentrations and meteorological factors.

A generalized additive regression model (GAM), based on Poisson distribution, was used in performing a time series on daily counts of deaths from cerebrovascular disease and air pollution. The model is as follows:

$$\lg E(\mathrm{Yt}) = \alpha + \beta \mathrm{Zt} + \mathrm{DOW} + \mathrm{ns}(\mathrm{time}, \mathrm{df}) + \mathrm{ns}(\mathrm{temperature}, \mathrm{df}) + \mathrm{ns}(\mathrm{humidity}, \mathrm{df})$$

where $E(\mathrm{Yt})$ is the estimated daily counts of deaths from cerebrovascular diseases at day $t$; $\alpha$ is the intercept of the model;

Zt represents the concentration of each air pollutant on day *t*, μg/m$^3$; $\beta$ is the log of relative risk in daily deaths from cerebrovascular disease based on an increase of 10 μg/m$^3$ in air pollutant concentrations; DOW was included as an indicator variable to adjust the weekends. ns is the natural cubic smoothing function for the nonlinear variables such as temperature, humidity, and calendar time, which was applied to control multi-annual and seasonal trends, as well as the meteorological factors; Degrees of freedom (df) was selected by referring to previous literature; In the final model, we defined 7 df per year for time trends, 6 and 3 df per year for temperature and relative humidity respectively (Peng et al. 2006; Zanobetti and Schwartz 2009; Chen et al. 2010).

$PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and $O_3$ were incorporated into the model separately to evaluate the relationship between daily deaths from cerebrovascular disease and each air pollutant. Due to the potential delayed effects of air pollution on cerebrovascular diseases (Shang et al. 2013), we constructed both single-day lag models including lag0–lag5 and multi-day lag models from lag 0–1 to lag 0–5 to explore the adverse effect of air pollutants on developing cerebrovascular diseases at different lag days in this study. We also performed multi-pollutant models to explore the possible confounding effects from the presence of co-pollutants. Furthermore, we tested for potential effect modification by performing additional analysis stratified by gender (males, females) and age group (< 65, ≥ 65).

The effect of each air pollutant on the risk of cerebrovascular disease mortality was reported as excess relative risk (ERR) with 95% confidence intervals (CI). All data sorting and statistical analysis were performed using Excel 2019 and R (version 3.3.3) packages "mgcv" and "nlme". Results with a 2-sided and $p$ value < 0.05 were statistically significant.

## Results

A total of 84,811 cerebrovascular disease deaths were collected from 1 January 2013 to 31 December 2019 in Wuhan. Among all subjects, 53.3% were males, and 83% were 65 years or older (Table 1). During the 7-year period of our study, mean ± SD exposure to air pollution was 64.05 ± 46.29 μg/m$^3$, 95.86 ± 56.09 μg/m$^3$, 15.73 ± 14.37 μg/m$^3$, 54.51 ± 30.49 μg/m$^3$, and 87.21 ± 48.99 μg/m$^3$ for $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and $O_3$, respectively. Daily mean temperature was 17.18 ± 9.26 °C and relative humidity was 79.07 ± 10.33% (Table 2). According to Pearson's correlation analysis, most air pollutants were highly correlated with each other except $O_3$ and moderately or poorly correlated with temperature and relative humidity (Table 3).

Table 4 shows the results of the single-pollutant model for exposure to air pollution at different lag days, expressed as ERRs with 10 μg/m$^3$ increments in five air pollutants. When adjusting for average daily temperature, relative humidity, and weekend, as expected, we observed a positive association between $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and cerebrovascular disease mortality. For single-day effects, the largest positive percent changes of daily deaths from cerebrovascular disease with a 10 μg/m$^3$ increment in pollutant concentration were found at lag0 for $PM_{2.5}$ (ERR: 0.927%, 95% CI: 0.749–1.105) and at lag1 for $PM_{10}$ (ERR: 0.627%, 95% CI: 0.493–0.761), $SO_2$ (ERR: 2.518%, 95% CI: 1.914–3.122), and $NO_2$ (ERR: 1.090%, 95% CI: 0.822–1.358), respectively. The effect values gradually reduced with the lag days increasing. In terms of multi-day lags, the strongest effects of $PM_{2.5}$, $PM_{10}$, $SO_2$, and $NO_2$ on cerebrovascular mortality were 0.995% (95% CI: 0.774, 1.216) at lag 0–3 days, 0.792% (95% CI: 0.629, 0.954), 2.961% (95% CI: 2.239, 3.683), and 1.151% (95% CI: 0.844, 1.459) at lag 0–2 days, respectively. The effect values in multi-day lags were larger than those single-day lags. Besides, the effects of $SO_2$ on cerebrovascular mortality at all lags were the greatest while the associations were similar among $PM_{2.5}$, $PM_{10}$, $SO_2$, and $NO_2$. The evidence of an association between exposure to $O_3$ and mortality due to cerebrovascular diseases was uncertain. (Table 3)

Results of stratified analysis by gender and age group are shown in Fig. 1. Generally, the effects of air pollutants on cerebrovascular disease mortality are similar between different genders, but the effect of $SO_2$ and $NO_2$ is significantly greater in females than males among most lag days. Consistent with the single pollutant model, $SO_2$ has the maximum impact on both males and females among all pollutants. The effect was significantly greater among elders over 65 years old. In contrast, the effect of $PM_{2.5}$ on young people was similar to or slightly higher than that on the elders. It is

**Table 1** Description of characteristics of all subjects collected during 2013–2019

| Characteristics | | 2013 (%) | 2014 (%) | 2015 (%) | 2016 (%) | 2017 (%) | 2018 (%) | 2019 (%) |
|---|---|---|---|---|---|---|---|---|
| Gender | Male | 6691 (53.2%) | 6138 (52.5%) | 6628 (53.4%) | 6701 (53.6%) | 6484 (54.4%) | 6509 (53.7%) | 6095 (52.6%) |
| | Female | 5888 (46.8%) | 5555 (47.5%) | 5792 (46.6%) | 5791 (46.4%) | 5436 (45.6%) | 5619 (46.3%) | 5484 (47.36%) |
| Age group | < 65 | 2243 (17.8%) | 2105 (18.0%) | 2112 (17.0%) | 2034 (16.3%) | 2108 (17.7%) | 1993 (16.4%) | 1775 (15.3%) |
| | ≥ 65 | 10336 (82.2%) | 9588 (82.0%) | 10308 (83.0%) | 10458 (83.7%) | 9812 (82.3%) | 10135 (83.5%) | 9804 (84.7%) |
| Total | | 12579 | 11693 | 12420 | 12492 | 11920 | 12128 | 11579 |

**Table 2** Description of air pollution and meteorological factors in Wuhan from 2013 to 2019

| Variables | Mean | SD | Min | 25th | 50th | 75th | Max |
|---|---|---|---|---|---|---|---|
| $PM_{2.5}$ (μg/m$^3$) | 64.05 | 46.29 | 5.20 | 32.33 | 51.70 | 80.80 | 369.80 |
| $PM_{10}$ (μg/m$^3$) | 95.86 | 56.09 | 7.60 | 55.00 | 85.70 | 122.98 | 531.60 |
| $SO_2$ (μg/m$^3$) | 15.73 | 14.37 | 2.30 | 6.80 | 11.00 | 18.18 | 107.20 |
| $NO_2$ (μg/m$^3$) | 54.51 | 30.49 | 5.80 | 33.53 | 46.80 | 66.20 | 223.40 |
| $O_3$ (μg/m$^3$) | 87.21 | 48.99 | 5.30 | 47.80 | 79.10 | 120.48 | 261.50 |
| Temperature (°C) | 17.18 | 9.26 | − 3.80 | 33.90 | 9.10 | 18.10 | 25.00 |
| Relative humidity (%) | 79.07 | 10.33 | 41.00 | 72.00 | 80.00 | 87.00 | 100.00 |

*SD*, standard deviation

noted that among all pollutants, $SO_2$ has the greatest effect on the elderly, and no significant effect was found of $O_3$ on cerebrovascular disease mortality of both two gender groups.

Figure 2 illustrates the Exposure-Response (E-R) relationship between the concentration of air pollutants at lag0 and the relative risks of daily deaths. Generally, the curves of five pollutants presented positive trends, which indicated that the higher concentration of air pollutants might cause a mortality increase. The E-R curve of $PM_{2.5}$ was S-shaped, first rose sharply towards the peak concentration at about 50 μg/m$^3$, and then slowly increased. The E-R curves of $PM_{10}$ and $O_3$ grew steadily at low concentrations and then became flat for the concentrations ≥ 100 μg/m$^3$. The almost linear E-R curves of $SO_2$ and $NO_2$ showed a steady trend of continuous growth, indicating that the risk of cerebrovascular mortality ascended steadily as the pollutant concentration increases

## Discussion

In our study, based on integral and accurate death records directly from the Disease Surveillance Point System (DSPs) from 2013 to 2017, we have explored the association between cerebrovascular disease mortality and short-term exposure to multiple air pollutants in Wuhan, China. We concluded that after adjusting for temperature, relative humidity, and weekend effect, ambient air pollution was positively associated with the daily deaths from cerebrovascular diseases. We found a stronger association for $SO_2$ and no significant association for $O_3$. In single-pollutant models, the largest effect was found at lag0 for $PM_{2.5}$ and lag1 for $PM_{10}$, $SO_2$, $NO_2$. The effect values gradually reduced with the lag days increasing, and the trends across lags were statistically significant. Stratified analysis demonstrated that females were more vulnerable to $SO_2$ and $NO_2$, and compared with younger people, elders over 65 years old suffered more from air pollution, especially from $SO_2$. This study may have important implications for the risk assessment and prevention of cerebrovascular diseases and provides certain epidemiological evidence for policy-makers to curb ambient air pollution in Wuhan, China.

Our results suggest that short-term exposure to $PM_{2.5}$, $PM_{10}$, $SO_2$, and $NO_2$ was positively associated with an increased risk of cerebrovascular disease mortality, which is consistent with many previous studies (Zhang et al. 2017; Leepe et al. 2019; Wu et al. 2019). In our single-pollutant models, the adverse effects of $PM_{2.5}$ on cerebrovascular disease mortality reached peaks at lag0 and $PM_{10}$, $SO_2$, and $NO_2$ at lag1 in single-day lags. Likewise, these time-lag effects of air pollution on cerebrovascular-related outcomes have also been discussed before, and we found that the effect was greater at short-term lag days, mostly at lag 0 and lag 1 in some Asia studies. A similar study conducted in Taipei showed that $PM_{2.5}$ and $PM_{10}$ lagged 3 days; $O_3$ lagged 0 days were significantly associated with increased emergency admissions for cerebrovascular diseases by 2.1% (95% CI: 1.005–1.037), 3% (95% CI: 1.011–1.037), and 3.1% (95% CI:

**Table 3** Spearman correlation between $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, $O_3$, temperature, and relative humidity

| Meteorological factors and pollutants | $PM_{2.5}$ | $PM_{10}$ | $SO_2$ | $NO_2$ | $O_3$ | Temperature | Relative humidity |
|---|---|---|---|---|---|---|---|
| $PM_{2.5}$ | 1 | | | | | | |
| $PM_{10}$ | 0.839** | 1 | | | | | |
| $SO_2$ | 0.695** | 0.733** | 1 | | | | |
| $NO_2$ | 0.539** | 0.632** | 0.622** | 1 | | | |
| $O_3$ | − 0.168** | 0.103** | − 0.066** | − 0.151** | 1 | | |
| Temperature | − 0.537** | − 0.277** | − 0.359** | − 0.175** | 0.526** | 1 | |
| Relative humidity | − 0.057** | − 0.335** | − 0.353** | − 0.195** | − 0.364** | − 0.126** | 1 |

**Correlation is significant at the 0.01 level (2-tailed).

**Table 4** Estimated excess relative risks (ERRs) and 95% CIs of daily deaths from cerebrovascular diseases for a 10 μg/m$^3$ increase of pollutant concentration at different lags

| Lag days | $PM_{2.5}$ | $PM_{10}$ | $SO_2$ | $NO_2$ | $O_3$ |
|---|---|---|---|---|---|
| lag0 | 0.927 (0.749, 1.105) | 0.625 (0.484, 0.765) | 2.033 (1.398, 2.668) | 0.673 (0.401, 0.945) | 0.039 (− 0.167, 0.245) |
| lag1 | 0.714 (0.539, 0.889) | 0.627 (0.493, 0.761) | 2.518 (1.914, 3.122) | 1.090 (0.822, 1.358) | 0.190 (− 0.005, 0.386) |
| lag2 | 0.485 (0.308, 0.661) | 0.421 (0.288, 0.554) | 1.870 (1.269, 2.47) | 0.865 (0.598, 1.131) | 0.054 (− 0.131, 0.239) |
| lag3 | 0.408 (0.229, 0.586) | 0.245 (0.112, 0.378) | 1.112 (0.507, 1.717) | 0.287 (0.022, 0.553) | − 0.055 (− 0.235, 0.126) |
| lag4 | 0.225 (0.044, 0.405) | 0.100 (− 0.033, 0.234) | 0.491 (− 0.114, 1.097) | − 0.010 (− 0.275, 0.255) | − 0.235 (− 0.414, − 0.055) |
| lag5 | 0.251 (0.070, 0.432) | 0.055 (− 0.079, 0.188) | 0.353 (− 0.257, 0.962) | 0.121 (− 0.144, 0.385) | − 0.107 (− 0.286, 0.072) |
| lag01 | 0.988 (0.795, 1.182) | 0.766 (0.614, 0.918) | 2.768 (2.085, 3.451) | 1.031 (0.74, 1.322) | 0.152 (− 0.077, 0.38) |
| lag02 | 0.991 (0.783, 1.199) | 0.792 (0.629, 0.954) | 2.961 (2.239, 3.683) | 1.151 (0.844, 1.459) | 0.140 (− 0.098, 0.379) |
| lag03 | 0.995 (0.774, 1.216) | 0.764 (0.592, 0.935) | 2.850 (2.097, 3.604) | 1.048 (0.727, 1.37) | 0.086 (− 0.159, 0.331) |
| lag04 | 0.965 (0.732, 1.199) | 0.714 (0.533, 0.894) | 2.588 (1.808, 3.367) | 0.899 (0.565, 1.233) | − 0.018 (− 0.269, 0.234) |
| lag05 | 0.961 (0.717, 1.206) | 0.665 (0.477, 0.854) | 2.392 (1.589, 3.196) | 0.833 (0.488, 1.177) | − 0.052 (− 0.309, 0.205) |

1.010–1.056), respectively (Chan et al. 2006); a time-series study conducted in Thailand found that $PM_{10}$ and $NO_2$ have largest effects on total cardiovascular admissions at lag1 with an increase of 0.73% (95% CI: 0.15–1.32), 1.28 (95% CI: 0.65–1.91) while $SO_2$ at lag0 (Phosri et al. 2019). A multicity study of short-term effects of air pollution on mortality conducted in Asia also showed that the average lag 0–1 days usually generated the highest excess risk of cardiovascular mortality in most cities concluded in this study (Wong et al. 2008). This finding is crucial to take timely measures to effectively prevent air pollution and protect the population's health.

This study also showed that $SO_2$ was the major air pollutant affecting the cerebrovascular mortality among all the five pollutants included in this study and no significant association was found for $O_3$. The results of some previous studies are consistent

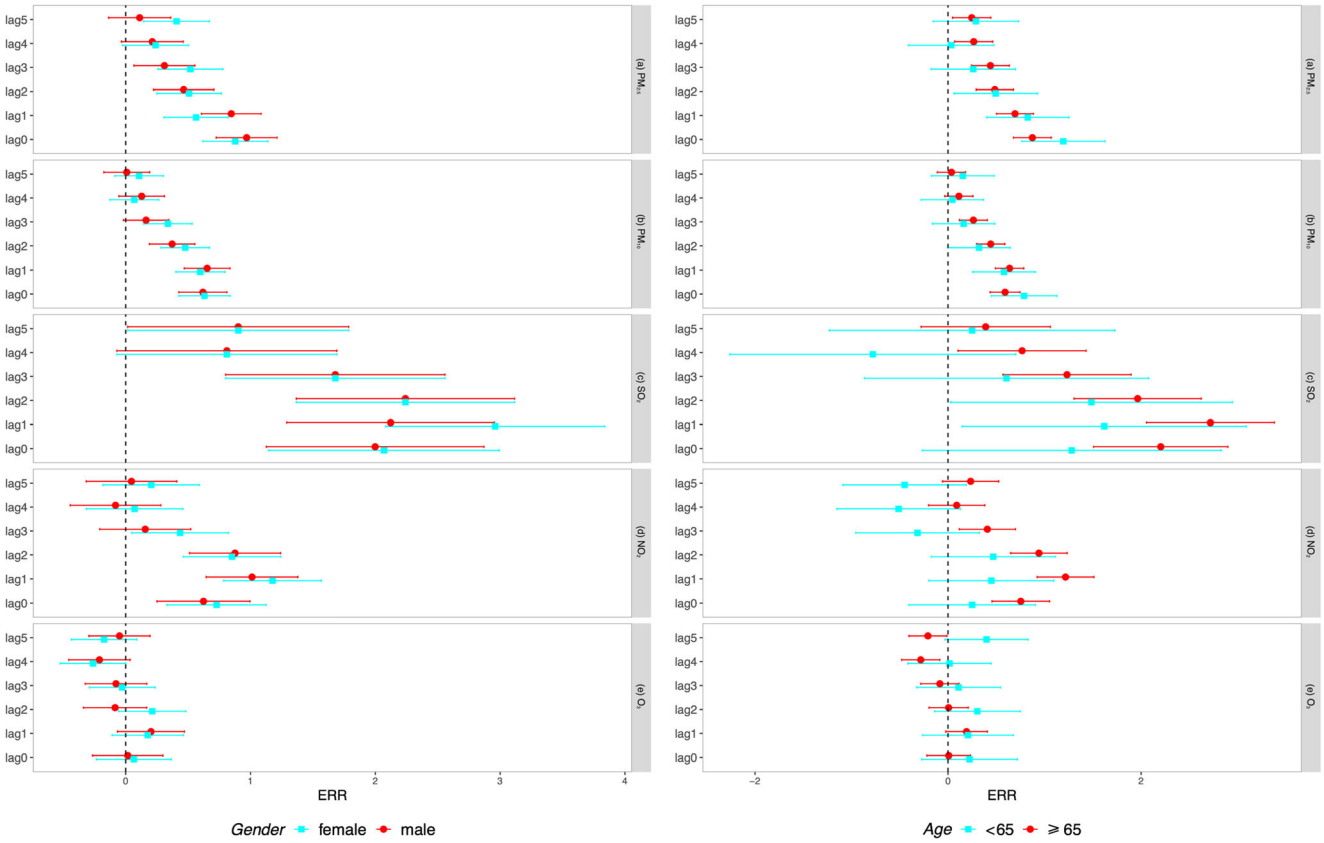


**Fig. 1** ERRs and 95% CIs for daily deaths from cerebrovascular diseases with a 10-mg/m$^3$ increase in air pollutants by gender and age in single-pollutant models

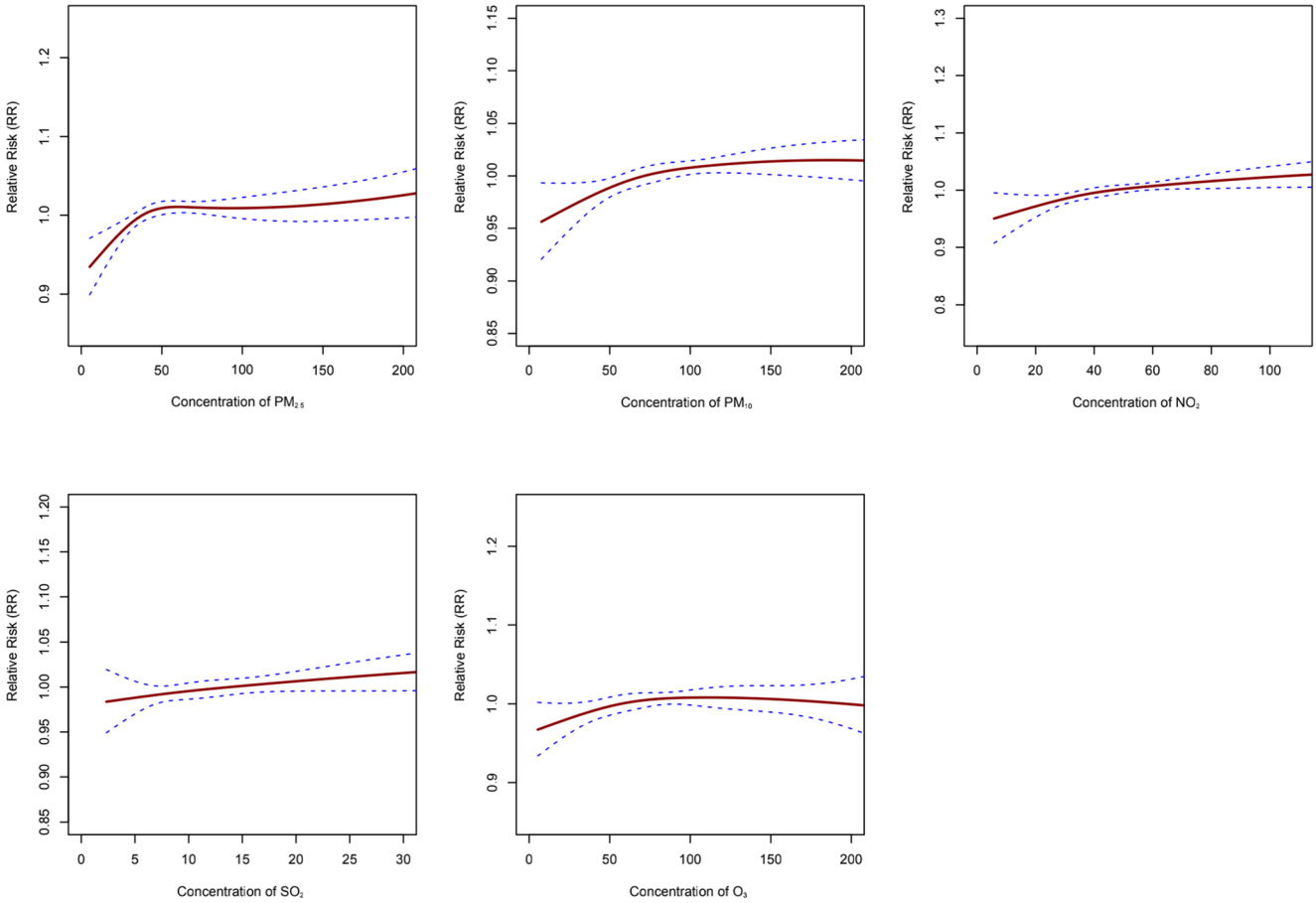


**Fig. 2** The exposure-response relationship curves of air pollutants with daily deaths from cerebrovascular diseases

with our findings (Ren et al. 2017; Zhang et al. 2017; Nhung et al. 2020). A nationwide time-series analysis conducted in China observed that an increment of 1.37% (95% CI: 1.05–1.70) in daily hospital admissions for ischemic stroke was significantly associated with per 10-μg/m3 increase in $SO_2$ (mean $SO_2$ concentration was 27.9 μg/m$^3$) (Tian et al. 2018), which is slightly lower than the estimates of 2.52% in our study. According to a previous meta-analysis, the risks of cardiovascular disease mortality were reduced at higher $PM_{2.5}$ concentrations (Vodonos et al. 2018), and it is uncertain whether a similar pattern of effect also exists in $SO_2$ which needs further research.

Stratified analysis showed that elder females seemed to suffer more risk of cerebrovascular disease mortality from ambient air pollution. Consistent with previous studies (Shah et al. 2015; Hystad et al. 2020), we found higher vulnerability to air pollution among elderly individuals, especially to $SO_2$. Although the mechanism still remains unclear, according to early research results, older age was the main contributor to cerebrovascular diseases (Kelly-Hayes et al. 2003). Also, the larger risk estimates in elder populations might be associated with differences in the distribution of our research subjects with a majority of older people aged above 65 years old. We also concluded that females were more vulnerable to ambient exposure to $SO_2$ and $NO_2$. A latest prospective cohort study across 21 high-income, middle-income, and low-income countries have reported similar results of gender difference in ambient air pollution on cardiovascular disease mortality (Hystad et al. 2020). However, an ecological time-series study in northern Thailand showed that $PM_{10}$ exposure was positivity associated with cerebrovascular disease visits with an incidence rate ratio of 1.025% (95% CI: 1.004–1.046) while the relationship for females was insignificant (Mueller et al. 2020). The reasons for our gender-specific findings are unclear and need further investigation. We suggest that more research should focus on the physiological characteristics of different genders to further explain and examine this difference. Given the difference in the population susceptibility to $SO_2$, effective public health prevention policies can be made to reduce the burden of cerebrovascular diseases.

Explanation of the trend of E-R relationships is important for public health development, especially for those sensitive populations that could be protected by limiting ambient air pollutants below threshold levels (Song et al. 2019). In this study, the typical S-shaped curve for $PM_{2.5}$ tends to hit a plateau at high concentrations. This may be a consequence of the "harvesting effect" that susceptible populations might have already developed symptoms and visited clinics before air pollutant

concentration reached a reasonably high level (Chen et al. 2017). That might also explain the linear E-R curve of $PM_{10}$ and $O_3$, where the daily deaths for cerebrovascular diseases grew significantly slower or even dropped at high concentrations. Specially, we observed a threshold relationship between $O_3$ and cerebrovascular mortality whose curve remained flat and then rose rapidly after the concentration was above 100 μg/m$^3$, which is quite close to the threshold limits for $O_3$ according to WHO Air Quality Guidelines (AQG-global update 2005).

Several studies have explored city-level difference in the relationships between air pollution and cardiovascular-related outcomes in China. According to a national time series analysis (Yin et al. 2017), we found that the $PM_{10}$ concentration (54.3 μg/m$^3$) in Wuhan ranked 10th among 38 major cities in China**,** and the maximum likelihood estimates (percentage) (lag = 0) in Wuhan of 10 μg/m$^3$ on total mortality for deaths due to cardiorespiratory diseases were slightly higher than the pooled results. Although the mechanical explanation of adverse effects of air pollution on cerebrovascular mortality remains unclear, several pathways including oxidative stress, systemic inflammation, thrombosis, and vascular endothelial dysfunction have been stated (Huang et al. 2017; Dong et al. 2018; Tian et al. 2018; Yang et al. 2020). Vascular function injury might be central to mechanisms for air pollution-related stroke, which could lead to raised blood pressure and plasma viscosity (Münzel et al. 2018; Chen et al. 2019). It has been shown that exposure to ambient air pollution was associated with increased thrombosis and vascular endothelial dysfunction by provoking oxidative stress and releasing systemic inflammatory cytokines (Rich et al. 2012). Besides, evidence also suggested that exposure to air pollution can lead to dysfunction of the autonomic system, which has been found as the major pathway that could result in air pollution-related adverse cerebrovascular outcomes (Wu et al. 2010).

Our study has several limitations. First, as an inherent limitation of ecological studies, we used the average concentration of air pollutants measured in ten air monitoring stations in Wuhan as a proxy to represent the individual exposure, which may cause misclassification of exposure and ignores the spatial impact of air pollution on cerebrovascular mortality (Winzar 2015). Second, due to data unavailability, we cannot adjust other personal-level risk factors related to cerebrovascular diseases like tobacco use, physical activity, and diet habits (Stafoggia et al. 2014). Third, the detailed information about age was not accessible**,** so the pooled estimation may bias the effects of air pollutants on specific age groups. Future studies could split the population into more multiple age subgroups to further explore the effect modification of age on the relationship between air pollution and cerebrovascular mortality. Fourth, we cannot rule out the nonrelevant death records due to poor physical condition or other reasons than air pollution. Fifth, meteorological exposure assessment may not be comprehensive enough due to data unavailability. More studies are needed to warrant the reliability and generalization of our study.

## Conclusions

In our study, based on 7-year death records in Wuhan, we found that exposure to $PM_{2.5}$, $PM_{10}$, $SO_2$, and $NO_2$ was positively associated with a higher risk of adverse cerebrovascular events, especially for elder females. Our findings could provide epidemiological evidence for risk assessment of air pollution on cerebrovascular mortality, which may have important implications for policy-makers to curb and prevent ambient air pollution in Wuhan, China.

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**Availability of data and materials** The data on air pollution and meteorological factors can be obtained from the National Air Pollution Monitoring System (http://www.cnemc.cn) and the China Meteorological Data Sharing Service System (https://data.cma.cn). The data on cerebrovascular disease mortality are available from the corresponding author upon reasonable request.

## Compliance with ethical standards

**Competing interests** The authors declare that they have no conflict of interest.

**Ethics approval and consent to participate** The study was approved by the ethics committee of the Wuhan Centers for Disease Control and Prevention. Since the data was analyzed at an aggregate level with no individual information involved, informed consent from the participants was waived for this study.

**Consent for publication** Not applicable

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