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Short-Term Exposure to Ambient Air Pollution and Hospital Admissions for Sequelae of Stroke in Chinese Older Adults

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Key Points:

- Short-term exposure to ambient carbon monoxide (CO) was significantly associated with an increased odds of hospital admissions for sequelae of stroke
- Ambient CO exposure may contribute to considerable excess hospital admissions for sequelae of stroke
- Our findings provide useful clues for the public to help prevent hospital admissions for sequelae of stroke by considering the effect of CO exposure

Supporting Information:

Supporting Information may be found in the online version of this article.

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Abstract Extensive evidence suggests that ambient air pollution contributes to a higher risk of hospital admissions for cerebrovascular diseases; however, its association with admissions for sequelae of stroke remains unclear. A time-stratified case-crossover study was conducted among 31,810 older adults who were admitted to hospital for sequelae of stroke in Guangzhou, China during 2016–2019. For each subject, daily residential exposure to fine particulate matter ($PM_{2.5}$), inhalable particulate matter (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) was extracted from a validated grid data set. Conditional logistic regression models were used for exposure-response analyses. In single-pollutant models, each interquartile range (IQR) increase of lag 04-day exposure to CO (IQR: 0.25 mg/m^3) and lag 3-day exposure to O_3 (69.6 μg/m^3) was significantly associated with a 4.53% (95% confidence interval: 1.67%, 7.47%) and 5.63% (1.92%, 9.48%) increase in odds of hospital admissions for sequelae of stroke, respectively. These associations did not significantly vary across age or sex. With further adjustment for each of the other pollutants in 2-pollutant models, the association for CO did not change significantly, while the association for O_3 disappeared. We estimated that 7.72% of the hospital admissions were attributable to CO exposures. No significant or consistent association was observed for exposure to $PM_{2.5}$, PM_{10}, SO_2, or NO_2. In conclusion, short-term exposure to ambient CO, even at levels below the WHO air quality guideline, was significantly associated with an increased odds of hospital admissions for sequelae of stroke, which may lead to considerable excess hospital admissions.

Plain Language Summary Stroke continues to be the global leading cause of death and adult disability. Despite obvious improvements in the treatment of stroke, about one-third of stroke survivors experience significantly physical and neuropsychological sequelae. Sequelae of stroke is always disabling and prolonged, which may impose substantially direct and indirect economic burden for individuals, family, and the society. Thus, identifying risk factors for sequelae of stroke is critical to prevent hospital admissions and reduce its burden of disease. As an ongoing public health concern worldwide, ambient air pollution has been linked to a variety of cerebrovascular diseases; however, the adverse effects of ambient air pollution on sequelae of stroke are yet to be evaluated. In this study, we used a case-crossover design to investigate the effects of ambient air pollution on hospital admissions for sequelae of stroke. We found that short-term exposure to ambient carbon monoxide (CO) was significantly associated with an increased odds of hospital admissions for sequelae of stroke and posed considerable excess hospital admissions even at CO levels lower than the WHO air quality guideline. Our findings provide new evidence that reducing ambient CO exposures may be an effective approach to prevent hospital admissions for sequelae of stroke.

1. Introduction

As a major cerebrovascular disease, stroke has become one of the leading causes of death and acquired disability in adults globally (GBD 2019 Stroke Collaborators, 2021). Notably, with improved treatments of stroke during recent years, the acute stroke mortality has decreased and the proportion of survivors with sequelae has dramatically increased (Béjot et al., 2016). Each year, about 15 million people suffer a stroke worldwide, and 5 million

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of them are left significantly physical (e.g., motor and sensory deficits, aphasia) and/or neuropsychological (e.g., cognitive disorder, apathy, depression, and anxiety) sequelae (Chohan et al., 2019; Ferro et al., 2016; Harrison et al., 2013). Because sequelae of stroke has imposed enormous direct (e.g., medical and non-medical care) and indirect (e.g., productivity losses) economic burden on individuals and the society (Rochmah et al., 2021), it has emerged as a public health priority to improve the health management and prognosis for sequelae of stroke.

Ambient air pollution remains a critical public health issue globally. Extensive evidence has demonstrated that short-term exposure to ambient air pollution can trigger cerebrovascular diseases, especially stroke (Niu et al., 2021; Requia et al., 2018). Previous studies have linked short-term exposure to several air pollutants including fine particulate matter ($PM_{2.5}$), inhalable particulate matter (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) to a higher risk of stroke morbidity and mortality (Niu et al., 2021). However, for patients with sequelae who survived from stroke, the potential effects of ambient air pollution exposures are yet to be evaluated, which is necessary and important given the substantial individual and social burden introduced by sequelae of stroke.

Therefore, we conducted a case-crossover study to quantitatively evaluate the association between short-term exposure to six criteria ambient air pollutants and hospital admissions for sequelae of stroke in Chinese older adults, and estimate the corresponding excess hospital admissions in Guangzhou, China during 2016–2019.

2. Methods

2.1. Study Population

Hospital admission data for sequelae of stroke from 2016 to 2019 were obtained from the Guangzhou Health Technology Identification and Human Resources Assessment Center. This data set included all hospitals (up to 372 in 2019) equipped with inpatient care services in Guangzhou, China. A total of 31,833 adults aged ≥60 years who were from Guangdong province and were for the first time admitted to hospital for sequelae of stroke in Guangzhou were identified during the study period. After excluding subjects without detailed information on residential address ($n = 23$), we finally included 31,810 subjects in our study. For each subject, demographic data including sex, date of birth, race, residential address, and date of admission were collected. With an exemption from informed consent, the Ethical Committee of School of Public Health, Sun Yat-sen University approved this study.

2.2. Outcome

Hospital admissions for sequelae of stroke were identified using the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes with I69.0-I69.4, including sequelae of hemorrhagic stroke (ICD-10 codes: I69.0-I69.2), sequelae of ischemic stroke (ICD-10 code: I69.3), and sequelae of stroke unspecified hemorrhagic or ischemic (ICD-10 code: I69.4).

2.3. Study Design

A time-stratified case-crossover design was employed in this study (Carracedo-Martínez et al., 2010; Y. Liu et al., 2019, 2021). In this design, each subject served as his or her own reference. For each subject, the date of admission was defined as the case day, while days with the same year, month, and day of week as the case day were defined as the corresponding control days. During 2016–2019, we matched 108,135 control days for 31,810 case days. The case-crossover design has been demonstrated to adequately control potential confounding effects of stable individual-specific covariates (Carracedo-Martínez et al., 2010).

2.4. Exposure Assessment

We collected daily $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3 concentrations during 2016–2019 in Guangdong province from a full-coverage, high-quality, and ground-level air pollutant data set for China (ChinaHighAirPollutants [CHAP]) with a spatial resolution of 10 × 10 km (Wei, Li, Li, et al., 2022; Wei, Li, Lyapustin, et al., 2021; Wei, Li, Wang, et al., 2022; Wei, Li, Xue, et al., 2021; Wei, Liu, et al., 2022; Wei et al., 2020). Generated based on our proposed artificial intelligence models combining with big data (including ground measurements, satellite remote sensing products, and atmospheric reanalysis), the CHAP data set has relatively high cross-validation coefficients of determination (R^2) ranging from 0.80 to 0.91 for the six ambient air pollutants. From the CHAP data set, we extracted daily 24-hr average $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO, and maximum 8-hr average O_3 concentrations at each subject's geocoded residential address. As proposed in previous studies, the association between O_3 exposure and hospital admissions was assessed in warm season (from 1 May to 31 October) (Di et al., 2017). We used different lag structures (single-day lags: from lag 0-day to lag 4-day and multi-day lags: from lag 01-day to lag 04-day) to assess the lag effects of air pollution exposure on hospital admissions.

2.5. Covariates

Using data from the National Meteorological Information Center in China, we obtained daily grid weather data with a spatial resolution of 0.0625° × 0.0625° in Guangdong province from 2016 to 2019 (J. Liu et al., 2020). For each subject, daily 24-hr average temperature (°C) and relative humidity (%) based on his or her geocoded residential address were retrieved during the case day and corresponding control days (Zhou et al., 2020). Public holiday information was obtained for each day during the study period. Because individual-specific covariates (e.g., sex, age at admission, and race) remained constant in comparing the case days and corresponding control days, we did not include them as potential confounding factors in the analysis (Janes et al., 2005).

2.6. Statistical Analysis

Conditional logistic regression models were performed to quantitatively assess the exposure-response associations of the six ambient air pollutants with hospital admissions for sequelae of stroke. Exposure to each air pollutant was included as the main effect in a seperate model. To control potential confounders, we adjusted for daily temperature and relative humidity as natural cubic splines with 6 and 3 degrees of freedom (*df*), respectively. A binary variable for public holiday (yes, no) was also included in the model. We estimated the percent change in odds and its 95% confidence interval (CI) for admissions per interquartile range (IQR) increase of exposure to each of the six air pollutants. In addition, a natural cubic spline ($df = 3$) of each air pollutant was included in the model and likelihood ratio tests were used to evaluate the nonlinearity of associations.

We calculated excess hospital admissions using excess fraction of admissions and number of excess admissions to quantify the hospital admission burden of sequelae of stroke attributable to air pollution according to the established associations with the following formula:

$$\text{Excess fraction} = \frac{\sum_{i=1}^{N} 1 - \frac{1}{e^{\beta \times (C_i - C_0)}}}{N} \times 100\%$$

where β is the point estimate in the conditional logistic regression model; N is the count of subjects; C_i is the concentration of each air pollutant on case days with pollutant concentration levels above C_0; C_0 is the minimum exposure level for each air pollutant (Cohen et al., 2017; Xu et al., 2022). The corresponding number of excess admissions was calculated as $\text{excess fraction} \times N$.

Stratified analyses by age (≤75 years, >75 years) and sex (male, female) were conducted to explore their potential effect modifications. For each stratification, we fitted conditional logistic regression models and quantified the corresponding exposure-response association for each air pollutant. The difference of associations across each stratification variable was examined using 2-sample z tests (Altman & Bland, 2003).

We performed sensitivity analyses to test the robustness of our results. First, for each air pollutant (e.g., PM_{10}), we added each of the other pollutants (e.g., CO) in the same model to fit a 2-pollutant model (e.g., PM_{10} + CO), and tested their difference using the likelihood ratio test. Second, we restricted the analysis to subjects who lived within the Guangzhou city. Third, we adjusted for both two weather conditions as natural cubic splines ($df = 3$) in all models. Finally, we restricted the analysis to subjects who were admitted to hospital for sequelae of ischemic stroke only. We did not restrict our analysis to subjects who were admitted for sequelae of hemorrhagic stroke due to its small sample size. We performed all analyses with R version 4.1.2 (R Core Team, 2021), and considered a 2-sided P value < 0.05 as statistically significant.

Table 1
Characteristic of Study Subjects in Guangdong Province, China, 2016–2019

Characteristic	Sequelae of stroke	Sequelae of ischemic stroke	Sequelae of hemorrhagic stroke
Case days, *n*	31,810 (100)	27,750 (87.2)	3,871 (12.2)
Control days, *n*	108,135	94,321	13,160
Age, years, mean ± SD	76.0 (9.1)	76.5 (9.1)	72.8 (8.9)
≤75	14,606 (45.9)	12,149 (43.8)	2,366 (61.1)
>75	17,204 (54.1)	15,601 (56.2)	1,505 (38.9)
Sex, *n* (%)			
Male	17,128 (53.8)	14,790 (53.3)	2,227 (57.5)
Female	14,682 (46.2)	12,960 (46.7)	1,644 (42.5)
Race, *n* (%)			
Han	31,699 (99.7)	27,652 (99.6)	3,858 (99.7)
Other	111 (0.3)	98 (0.4)	13 (0.3)
Season at admission, *n* (%)			
Warm (May–October)	15,857 (49.8)	13,923 (50.2)	1,852 (47.8)
Cool (November–April)	15,953 (50.2)	13,827 (49.8)	2,019 (52.2)

3. Results

During 2016–2019, we included 31,810 admissions for sequelae of stroke, including 27,750 for sequelae of ischemic stroke, 3,871 for sequelae of hemorrhagic stroke, and 189 for sequelae of stroke unspecified as hemorrhagic or ischemic. The average age at admission was 76.0 years (standard deviation [SD]: 9.1 years). Among these cases, 92.0% (29,250 cases) lived in Guangzhou, most of whom were Han race, 54.1% were aged >75 years, 53.8% were male, and 87.2% were admitted for sequelae of ischemic stroke (Table 1, Figure 1).

The mean concentration of ambient $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3 on case days was 34.6, 56.4, 10.9, 46.9, 0.89, and 108.5 μg/m^3, respectively. The mean temperature and relative humidity on case days were 23.4°C and 76.2%, respectively (Table 2). Table S1 in Supporting Information S1 shows the correlations among six air pollutants and two weather conditions on case days and control days. The exposures to air pollutants were significantly and positively correlated (all $P < 0.05$).

In single-pollutant models, short-term exposure to CO (lag 0-day, lag 2-day, lag 3-day, lag 01-day, lag 02-day, lag 03-day, and lag 04-day) and O_3 (lag 3-day) was significantly associated with an increased odds of hospital admissions for sequelae of stroke ($P < 0.05$; Figure 2). Each IQR increase of lag 04-day exposure to CO (IQR: 0.25 mg/m^3) and lag 3-day exposure to O_3 (69.6 μg/m^3) was significantly associated with a 4.53% (95% CI: 1.67%, 7.47%) and 5.63% (1.92%, 9.48%) increased odds of hospital admissions, respectively. There was no evidence of nonlinearity for these observed associations (all *P* for nonlinearity >0.05; Figure 3). No significant association for $PM_{2.5}$, PM_{10}, SO_2, or NO_2 was observed in single-pollutant models. In 2-pollutant models, the association for CO exposure remained consistent, but the association for O_3 exposure became insignificant with adjustment for other pollutants (Table S2 in Supporting Information S1). The associations for $PM_{2.5}$, PM_{10}, SO_2, and NO_2 were consistently insignificant with further adjustment for each of other pollutants, except that the association for SO_2 became significant after adjusting for $PM_{2.5}$ (*P* for difference >0.05). Overall, an estimated 7.72% (95% CI: 2.97%, 12.20%) of hospital admissions for sequelae of stroke were attributable to ambient CO exposure, corresponding to 2,456 (945, 3,882) hospital admissions.

In stratified analysis, no effect modification was observed across by age or sex (*P* for difference >0.05; Table 3). Restricting the analysis to subjects living within Guangzhou, adjusting for two weather conditions as natural cubic splines with *df* of 3, and only including subjects who were admitted for sequelae of ischemic stroke yielded similar results (Figures S1–S3 in Supporting Information S1).

4. Discussion

In this study of 31,810 older adults in Guangzhou, China during 2016–2019, short-term exposure to ambient CO was significantly associated with an increased odds of hospital admissions for sequelae of stroke. Each IQR increase of lag 04-day exposure to CO was significantly associated with a 4.53% increase in odds of hospital admissions, and the association did not vary across age or sex. In addition, we estimated that up to 7.72% of the hospital admissions were attributable to CO exposures.

The acute adverse effects of ambient air pollution on risk of hospital admissions for physical and neuropsychological sequelae of stroke have not been investigated. Nevertheless, as two common causes of hospitalization among patients with sequelae of stroke, stroke and neuropsychological impairments have been linked to air pollution exposures in previous investigations. Niu et al. (2021) conducted a meta-analysis on 23 million subjects and concluded that acute exposure to CO was significantly associated with a higher risk of hospital admissions for stroke, whereas no significant association was observed for stroke mortality or incidence (Niu et al., 2021). In addition, epidemiological studies have demonstrated that short-term exposure to ambient CO was significantly associated with a greater risk of hospital admissions for cognitive and mental disorders (e.g.,

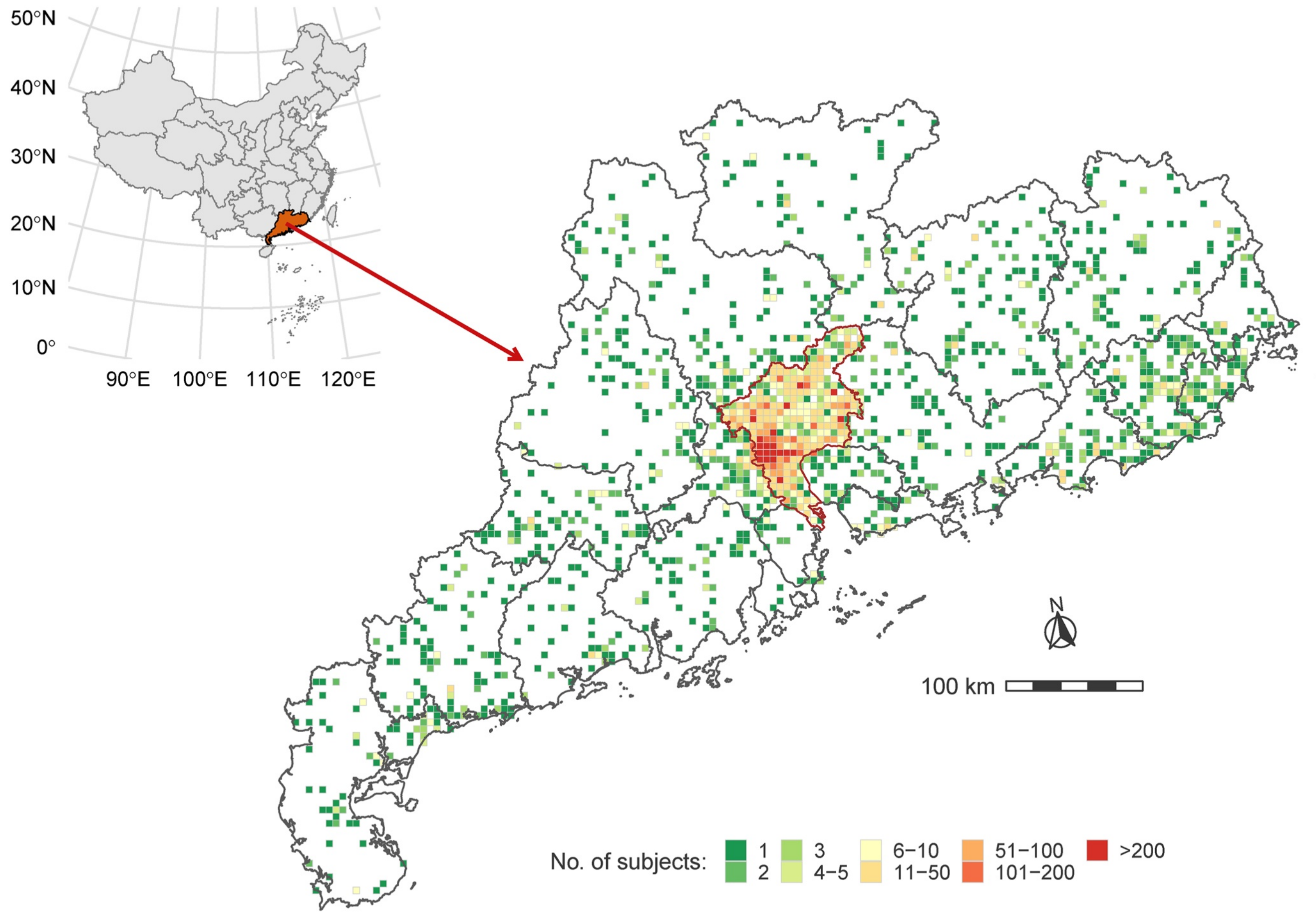

Figure 1. Spatial distribution of the study subjects' residential addresses in Guangdong province, China, 2016–2019. The grids (spatial resolution: 5 × 5 km) with different colors represent the number of subjects. The area with red boundaries represents Guangzhou city.

dementia, Alzheimer's disease, depression) (Bagheri & Rashedi, 2020; C. Chen et al., 2018; Kim et al., 2021; Peters et al., 2019). Despite post-stroke people admitted to hospital for stroke or neuropsychological diseases are not necessarily comparable with those for sequelae of stroke, our study provided similar evidence on the acute adverse effects of CO exposures on hospital admissions for sequelae of stroke. Furthermore, we did not identify

Table 2
Distribution of Ambient Air Pollutants and Weather Conditions on Case Days

	Mean (SD)	Min	P_{25}	P_{50}	P_{75}	IQR	Max
Air pollutant							
$PM_{2.5}$, μg/m^3	34.6 (19.2)	4.4	21.2	30.1	43.2	22.0	211.6
PM_{10}, μg/m^3	56.4 (27.9)	9.1	37.2	49.6	68.5	31.3	284.9
SO_2, μg/m^3	10.9 (4.0)	2.5	7.9	10.1	13.0	5.1	44.0
NO_2, μg/m^3	46.9 (21.3)	2.3	32.4	43.4	56.0	23.7	231.4
CO, mg/m^3	0.89 (0.22)	0.33	0.74	0.85	0.99	0.25	2.45
O_3, μg/m^3	108.5 (50.3)	4.0	71.3	101.9	141.0	69.6	289.6
Weather condition							
Temperature, °C	23.4 (6.1)	3.2	19.0	24.6	28.5	9.5	34.3
Relative humidity, %	76.2 (13.7)	21.0	68.4	78.9	86.7	18.4	98.0

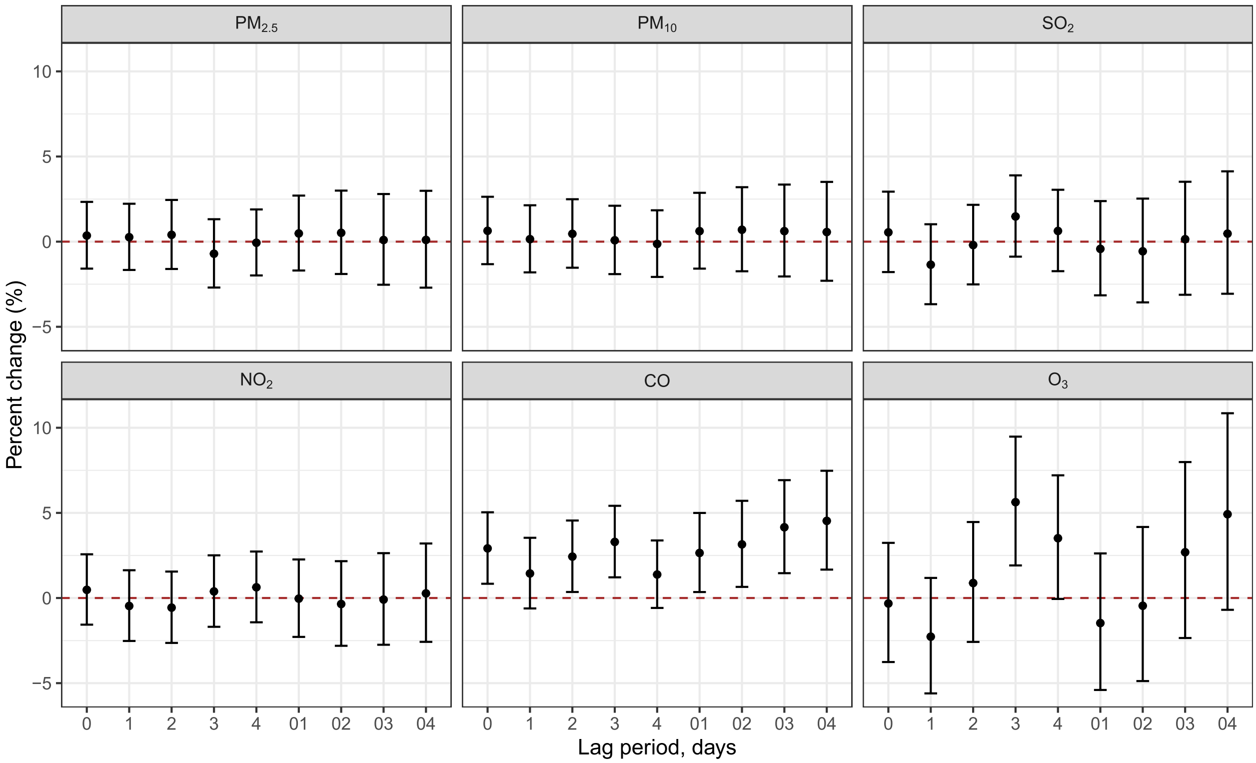

Figure 2. Estimated percent change (95% CI) in odds of hospital admissions for sequelae of stroke associated with each IQR increase of short-term exposure to ambient air pollutants. CI, confidence interval; CO, carbon monoxide; IQR, interquartile range; NO_2, nitrogen dioxide; O_3, ozone; $PM_{2.5}$, fine particulate matter; PM_{10}, inhalable particulate matter; and SO_2, sulfur dioxide.

significant or consistent association for $PM_{2.5}$, PM_{10}, SO_2, NO_2, or O_3. More studies are warranted to evaluate possible effects of these pollutants on patients with sequelae of stroke and confirm our results.

This study is the first to explore potential adverse effects of short-term exposure to air pollutants on hospital admissions for sequelae of stroke. Our findings provide novel evidence that short-term CO exposure was significantly associated with a greater risk of sequelae of stroke admissions, suggesting that CO exposure may exacerbate sequelae of stroke and trigger hospital admissions. It should be noted that this association was identified with exposure levels (up to 2.45 mg/m^3) well below the 2021 WHO air quality guideline value (4 mg/m^3). In addition, the excess admissions due to CO exposure were substantial. These findings indicate that ambient CO exposure may have considerable adverse acute effects on older adults with sequelae of stroke, and the current WHO air quality guideline and air quality standard in China for ambient CO (4 mg/m^3) may need to be further evaluated. As a traffic-related air pollutant, ambient CO is mainly formed by incomplete combustion of fossil fuels from vehicles and has become a major environmental problem especially in large cities (K. Chen et al., 2021). Given its ubiquity in the air and substantial disease burden, our results highlight that policymakers may need to take effective interventions by reducing individual CO exposures to prevent hospital admissions for sequelae of stroke, which can yield important public health benefits.

Although little was known about the exact pathophysiological mechanisms of acute adverse effects of CO exposures on physical and neuropsychological sequelae of stroke, several hypotheses have been proposed in previous investigations. For physical sequelae of stroke particularly for cerebrovascular impairments, results of both observational and controlled exposure studies suggest that the increased risks of cerebrovascular events after acute exposure to ambient CO, even at a low concentration, may be partially explained by oxidative injuries (Koehler & Traystman, 2002; Parkinson et al., 2002). After being inhaled into the respiratory system, ambient CO can directly enter circulation system, bind to hemoglobin, sequentially reduce delivery of oxygen, and cause significant oxidative stress on both the local and systemic levels (Prockop & Chichkova, 2007). This may induce several pathophysiological changes, including cerebrovascular endothelial dysfunction, plasma viscosity increasing, and trigger thromboembolism, which can accelerate the progress of cerebrovascular events (Gawlikowski

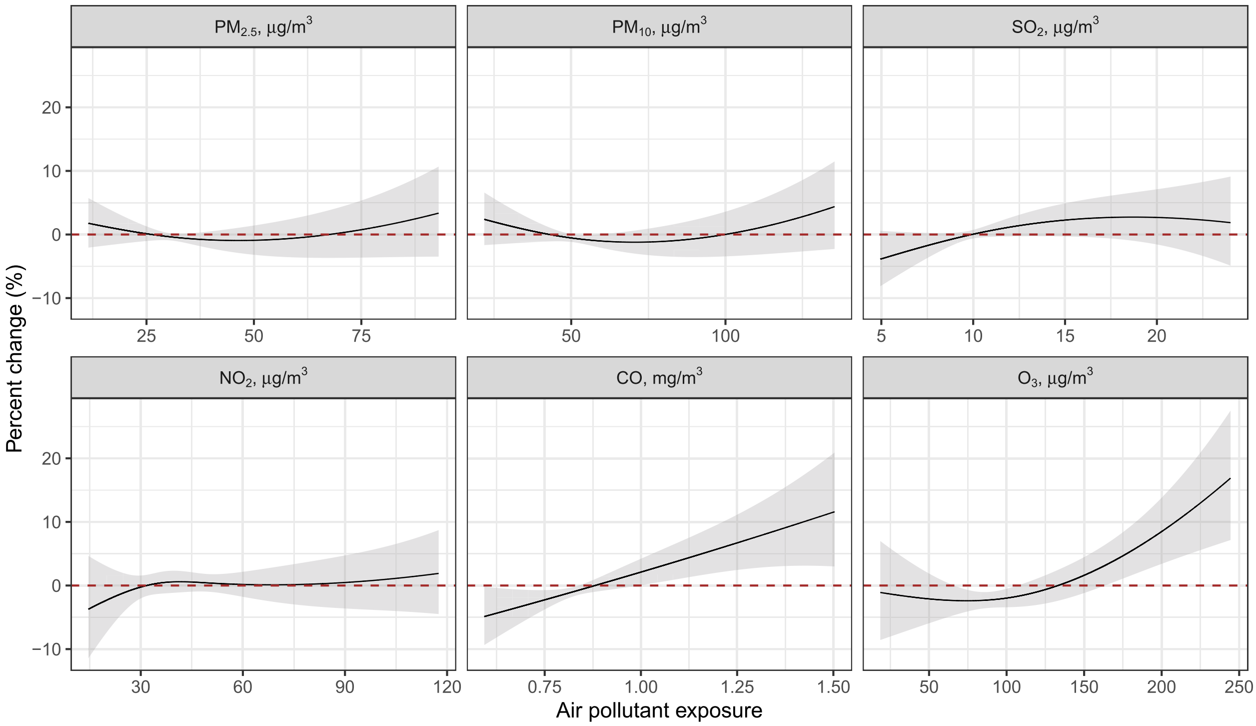

Figure 3. Exposure-response curves for the association of short-term exposure to ambient air pollutants with hospital admissions for sequelae of stroke. The black solid lines represent percent changes in odds of hospital admissions and the shaded regions represent the corresponding 95% confidence intervals. Abbreviations as in Figure 2.

et al., 2013; Koehler & Traystman, 2002). Additionally, for neuropsychological disorders, animal studies have provided evidence that oxidative stress and mitochondrial impairments induced by CO can impair cognitive and behavioral functions (Salvi et al., 2020). Nonetheless, further investigations are encouraged to clarify the detailed biological mechanisms.

Our study has several strengths. First, benefiting from a relatively large sample size and wide range of air pollution exposure concentrations, we were able to detect potential acute effects of air pollution on hospital admissions for sequelae of stroke with a sufficient statistical power and representative estimates. Second, each subject served as his or her own reference in the case-crossover design, which allowed us to account for long-term trends, time-varying covariates (e.g., socioeconomic status, chronic diseases, and genetics) that did not change between case and control days, and time-varying meteorological conditions in the analysis. Third, owing to the application of case-crossover design, we evaluated each subject's exposures in the individual-level from a spatially refined

Table 3
Association of Short-Term Exposure to Ambient Air Pollution With Hospital Admissions for Sequelae of Stroke, Stratified by Age and Sex

	Percent change in odds of hospital admissions, % (95% CI)			
Air pollutant	Age, ≤75 years	Age, >75 years	Sex, male	Sex, female
$PM_{2.5}$	−1.83 (−5.26, 1.73)	2.46 (−0.89, 5.93)	−0.25 (−3.48, 3.1)	1.41 (−2.18, 5.12)
PM_{10}	−1.25 (−4.76, 2.39)	2.31 (−1.07, 5.80)	−0.13 (−3.41, 3.25)	1.65 (−1.98, 5.42)
SO_2	0.25 (−3.16, 3.79)	2.56 (−0.70, 5.92)	0.93 (−2.25, 4.22)	2.19 (−1.29, 5.79)
NO_2	−0.35 (−3.51, 2.91)	1.47 (−1.17, 4.18)	−1.41 (−4.20, 1.46)	2.87 (−0.11, 5.93)
CO	4.49 (0.29, 8.87)	4.79 (0.93, 8.81)	3.29 (−0.55, 7.28)	5.88 (1.66, 10.28)
O_3[a]	5.17 (−0.21, 10.83)	6.05 (0.96, 11.39)	2.13 (−2.79, 7.30)	9.73 (4.16, 15.59)

[a]Restricted to warm season (May–October).

grid data set (CHAP). In addition to including all targeted subjects who lived in Guangdong province, our analysis performed more accurate individual-level exposure assessments in comparison with most previous studies that typically used city-level exposure as a proxy for individual-level exposure.

There are also some limitations in our study. First, we extracted pollution data from a predicted data set to assess individual-level pollutant exposures rather than directly measured subjects' actual personal exposure. The relatively coarse spatial resolution (10 km) of the CHAP data set and failure to account for personal time-activity patterns could lead to exposure misclassifications, which were likely to be non-differential and therefore biased the estimates toward the null (Guo et al., 2013). This may in part explain why we did not observe any significant associations for exposure to other traffic-related air pollutants (e.g., NO_2), which can be of high spatial variability in a city scale and be insufficiently captured in our exposure assessment (Alexeeff et al., 2018; Allen et al., 2009). Second, despite we applied the case-crossover design to control essential time-invariant individual-level or time-variant confounders in the analysis, there was still possibly residual or unobserved bias in our study. Third, the relatively high collinearity among different air pollutants made it difficult for us to distinguish the independent adverse effects of a specific air pollutant on hospital admissions for sequelae of stroke. Finally, because we conducted this study in the capital city in Guangdong province and only included subjects 60 years or older, it should be cautious when generalizing our findings to other populations.

5. Conclusions

This study provides consistent evidence that short-term exposure to ambient CO, even at levels below the WHO air quality guideline, was significantly associated with an increased odds of hospital admissions for sequelae of stroke, which may lead to considerable excess hospital admissions. These results add new evidence to the adverse effects of CO on cerebrovascular diseases and highlight a potential approach to prevent hospital admissions for sequelae of stroke by reducing ambient CO exposures.

Conflict of Interest

The authors declare no conflicts of interest relevant to this study.

Data Availability Statement

Air pollution data sets for this research are available at: $PM_{2.5}$, https://doi.org/10.5281/zenodo.3539349; PM_{10}, https://doi.org/10.5281/zenodo.3752465; SO_2, https://doi.org/10.5281/zenodo.4641538; NO_2, https://doi.org/10.5281/zenodo.4641542; CO, https://doi.org/10.5281/zenodo.4641530; and O_3, https://doi.org/10.5281/zenodo.4400042. The meteorological data can be accessed at http://data.cma.cn, which is administrated by the China National Meteorological Information Center, but users need to register at this website for free before they can access the data. The clinical hospital admission data are not accessible to the public due to data policies of the Guangzhou Health Technology Identification & Human Resources Assessment Center in China. All analyses in this study are made with software R version 4.1.2 (R Core Team, 2021), licenses and other information can be found at https://www.R-project.org.

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