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Short-term exposure to ambient air pollution and hospital admissions for angina among older adults in South China

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HIGHLIGHTS

- Short-term exposure to ambient NO_2 was associated with an increased odds of angina admissions in older adults.
- The association for NO_2 was stronger in cool season.
- Reducing traffic-related air pollution may be helpful in preventing angina admissions.

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ABSTRACT

Ambient air pollution has been linked to an increased risk of various acute cardiovascular outcomes; however, its effects on hospital admissions for angina are yet to be evaluated. We conducted a time-stratified case-crossover study with conditional logistic regression models among 46,687 adults 60 years or older who were admitted to hospital for angina in Guangzhou, China during 2016–2019 to investigate the association of exposure to ambient particulate matter with an aerodynamic diameter ≤2.5 μm ($PM_{2.5}$), particulate matter with an aerodynamic diameter ≤10 μm (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) with hospital admissions for angina. Daily residential air pollutant exposures were extracted from a grid dataset. Each 10 $\mu g/m^3$ increase of lag 0-day exposure to PM_{10}, SO_2, NO_2, CO, and O_3 was significantly associated with a 0.80% (95% confidential interval: 0.32%, 1.28%), 4.04% (0.34%, 7.89%), 2.47% (1.81%, 3.12%), 0.13% (0.07%, 0.19%), and −0.38% (−0.74%, −0.01%) increase in odds of admission, respectively. The association for NO_2 exposure remained stable, while the associations for PM_{10}, SO_2, CO, and O_3 became insignificant with adjustment for other air pollutants. The association for NO_2 exposure was stronger in cool season. We estimated that up to 9.12% of angina admissions were attributable to NO_2 exposure. Our findings suggest that ambient NO_2 may trigger hospital admissions for angina in Chinese older adults, which highlights the importance to prevent angina by reducing individual NO_2 exposures.

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1. Introduction

Ambient air pollution is still a major global public health issue. The Global Burden of Disease (GBD) Study 2019 reported that exposure to air pollution causes 6.7 million deaths and 213.3 million disability adjusted life-years (DALYs) globally (GBD 2019 Risk Factors Collaborators., 2020); in China, ambient air pollution was the third risk factor affecting DALYs (Ma et al., 2022). Extensive epidemiological evidence has linked air pollution to an increased risk of various acute cardiovascular diseases, including angina (Abed Al Ahad et al., 2020; Biggeri et al., 2004; Lin et al., 2003). It has been demonstrated that patients with angina are more likely to suffer from certain comorbidities including hypertension, diabetes, peripheral vascular disease, and heart failure, which can cause more complex conditions and poor prognosis (Kloner and Chaitman, 2017). In the US, approximately 10 million people had angina and there were over 500,000 cases diagnosed annually (Gillen and Goyal, 2022), while the prevalence of chronic stable angina was 9.6% (about 130 million people) in China, which had posed a considerable burden on health care and medical expenses (Zhao et al., 2019). In angina cases, about half were older adults aged 65 and above, who often had poor basic physique and other diseases, which made the condition more complicated and the prognosis worse (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators., 2018). With the increase of the elderly population, the form of social aging is becoming more and more serious, and the burden of older adults admission for angina cannot be ignored. Given considerable disease burden of air pollution and worse prognosis of angina, the potential effects of air pollution exposure on angina have attracted more and more attentions worldwide.

To date, only a few studies have assessed the associations of short-term exposure to ambient particulate matter with an aerodynamic diameter $\leq$2.5 μm ($PM_{2.5}$), particulate matter with an aerodynamic diameter $\leq$10 μm (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) with angina hospital admissions, and the results are mixed (Hosseinpoor et al., 2005; Kuźma et al., 2020a, 2020b; Lu et al., 2019; Von Klot et al., 2005). While some of these studies found positive associations between $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and/or O_3 exposures and hospital admissions for angina, the other studies did not identify significant association. In addition, previous studies reported that people 65 years or older accounted for about half of all cases of angina, which were more likely to develop frailty (Kloner and Chaitman, 2017; Oliveros et al., 2020; Waheed et al., 2019); however, it remains less clear if and how air pollution exposure affects angina among older adults.

As the disease burden of air pollution was large, the prognosis of angina was poor, and the number of older adults was relatively large, the impact of air pollution exposure on angina in older adults needs to be studied. A comprehensive and systematic assessment of the association between air pollutants and the risk of hospital admission for angina in older adults, as well as an assessment of the risk of air pollution health hazards, will provide scientific basis and clues for relevant departments to formulate air pollution control strategies and improve the management of angina patients. In this population-based case-crossover study, our objective was to explore the association of short-term exposure to ambient air pollution with angina hospital admissions among Chinese older adults in Guangzhou during 2016–2019, and to estimate the corresponding excess hospital admissions. Our hypothesis is that certain air pollutants contribute to an increased risk of angina hospitalization in older adults.

2. Methods

2.1. Study population

From the Guangzhou Health Technology Identification and Human Resources Assessment Center, we identified 46,687 patients who were admitted for angina and were aged $\geq$60 years in Guangzhou, China from 2016 to 2019. The hospital admission data covered individual clinical hospitalization information from all hospitals that equipped with inpatient services in Guangzhou, China. As the capital city of Guangdong province, Guangzhou is located at South China and had a population of 15.31 million in 2019. We collected individual data on race, sex, cause of hospitalization, residential address, date of birth, and date of admission. This study was approved by the Ethics Committee of School of Public Health, Sun Yat-sen University with a waiver of informed consent.

2.2. Outcomes

The angina hospital admissions was the study outcome. We used the International Statistical Classification of Disease and Related Health Problems, 10th Revision (ICD-10) code of I20 to identify hospital admissions for angina.

2.3. Study design

As in extensive studies investigating transient effects of air pollution on a large number of health outcomes, we used a time-stratified case-crossover design to evaluate the association of short-term exposure to ambient air pollutants with hospital admissions for angina (Xu et al., 2022c, 2023). This design is featured that each subject used himself or herself as a control, which compares exposures at different periods within the same time stratum (e.g., a month) and can therefore naturally control potential confounders including individual factors (age, gender, ethnicity), seasonality, day of the week, and long-term time trend effects (Bateson and Schwartz, 1999; Peng et al., 2005). For each admission, we defined the date of admission as the case day, while days with the same year, month, and day of week within the same stratum as the case day were chosen as the control days (Xu et al., 2022a). For example, if a subject was admitted to hospital for angina on September 9, 2019 (Monday), we defined the case day as September 9, 2019 and defined the control days as all other Mondays in September 2019 (i.e., September 2, 16, 23 and 30). According to this method, a case day was matched for 3 or 4 control days.

2.4. Exposure assessment

A grid data on 24-h average $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and daily maximum 8-h average O_3 concentrations with a spatial resolution of 10 km × 10 km in Guangzhou during 2016–2019 were obtained from the ChinaHighAirPollutants (CHAP) dataset (https://weijing-rs.github.io/product.html) (Wei et al., 2020, 2021a,b, 2022a,b, 2023), which has been validated in previous studies. The coefficient of determination (R^2) of $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3 was 0.91, 0.86, 0.84, 0.84, 0.80, and 0.87, respectively; the root mean square error was 12.67 μg/m^3, 24.34 μg/m^3, 10.07 μg/m^3, 7.99 μg/m^3, 0.29 mg/m^3, and 17.1 μg/m^3, respectively. We assessed daily exposures during 0–6 days before admission by extracting pollutant concentrations from each subject's residential address. To determine the time of lag effect, multiple single-day lag (lag 0–6 day) and moving average lag (lag 01–06 day) exposures were considered in the preliminary analysis.

2.5. Covariates

We used data from the China Meteorological Administration Land Data Assimilation System (CLDAS version 2.0) to obtain daily meteorological grid data in Guangzhou, China during 2016–2019, including 24-h average temperature (°C) and relative humidity (%) (Han et al., 2020; J. Liu et al., 2019; Tie et al., 2022). For each admission, daily exposure to temperature and relative humidity was assessed by patient's geocoded residential address on case and control days. In this study, we selected the cases themselves as the control and limited the time within one month, without considering the personal-level covariates (e.g., race, age, sex, genetic, and lifestyle), since these factors would hardly change in the short term and would not lead to bias (Carracedo-Martínez et al., 2010).

2.6. Statistical analysis

Spearman's correlation coefficient was used to determine whether and how the six ambient air pollutants and the two meteorologic factors were correlated. We used conditional logistic regression models to quantitatively assess the association of short-term exposure to ambient air pollution with angina admissions. In the main model, air pollutants were included as a continuous variable, temperature was included as a cubic spline function with 6 degrees of freedom (*df*), and relative humidity was included into the model as a cubic spline function with 3 *df*. We quantified the associations by percent change ($[odds\ ratio - 1] \times 100$) in odds and its 95% confidence interval (CI) per 10 μg/m^3 increase of pollutant exposure. We further calculated Akaike information criterion (AIC) values to evaluate the goodness-of-model fits for different lag day. The model with the minimum AIC value represented the best fit, and the corresponding lag day was considered as optimum. In addition, air pollution was incorporated into the model as a natural cubic spine function of 3 *df* and an exposure-response curve was plotted. In order to confirm whether the association was nonlinear, the likelihood ratio test was performed. As proposed in previous studies, analysis on O_3 was restricted in warm season (Di et al., 2017; Y. Liu et al., 2019).

To estimate the burden of angina admissions attributable to exposure to ambient air pollution, we assessed the excess hospital admissions (EHA) for each air pollutant, as shown in Equation (1):

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

In this equation, β is the air pollutant's point estimate of the conditional logistic regression model; C_i is air pollutant exposure on the case day for each subject; C_0 is the referent air pollutant concentrations, including the minimum air pollutant exposure level and the air pollutant concentrations of the World Health Organization (WHO) and China's air quality guidelines (Xu et al., 2022b); N is the total number of angina admissions. The number of excess admissions for angina attributable to exposure to air pollution was estimated with EHA × N.

Stratified analyses by sex, age, and season were performed to explore potential vulnerable populations. Warm season was from May to October, while cool season was from November to April. A 2-sample *z* test was used to examine the differences of associations across stratification variables, as shown in Equation (2) (Altman and Bland, 2003):

$$z = \frac{\beta_1 - \beta_2}{\sqrt{SE_1^2 + SE_2^2}} \quad (2)$$

In this equation, β_1 and β_2 are stratification-specific regression coefficients of the conditional logistic regression models; SE_1 and SE_2 are the standard errors of β_1 and β_2, respectively.

To assess the robustness of our results, we used several sensitivity analyses, including: 1) incorporating each of the other pollutants into the single-pollutant model to build the 2-pollutant models (Liu et al., 2021; Zhou et al., 2022); 2) adjusting for temperature using a *df* of 3; 3) taking holidays as covariates. We performed all statistical analyses in R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria), and considered bilateral p value less than 0.05 to be statistically significant.

3. Results

During 2016–2019, a total of 46,687 angina subjects with 62,562 case days and 212,530 control days were identified. Among these admissions, the mean age was 73.5 years, 53.5% were male, 99.3% were Han race, 55.9% were admitted before 75 years old, and 50.5% were admitted in warm season (Table 1). Mean values of ambient $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3 exposures were 33.6 μg/m^3, 55.6 μg/m^3, 10.6 μg/m^3, 45.1 μg/m^3, 0.88 mg/m^3, and 108.9 μg/m^3, respectively (Table 2). Exposure to air pollutants on the date of admission was positively correlated, while the correlation between O_3 exposure and CO exposure was negative (all $p < 0.01$, Table 3).

We observed that short-term exposure to ambient PM_{10} (lag 0 and 01 day), SO_2 (lag 0, 02, 03, and 04 day), NO_2 (lag 0, 1, 2, 3, 01, 02, 03, and 04 day), and CO (lag 0, 1, 01, 02, and 03 day) was significantly associated with an increased odds of angina admissions, while exposure to O_3 (lag 0, 1, 2, 01, 02, and 03 day) was significantly associated with a decreased odds of angina admissions (Fig. S1). Each 10 μg/m^3 increase of exposure to PM_{10}, SO_2, NO_2, CO, and O_3 at lag 0 day was associated with a 0.80% (95% CI: 0.32%, 1.28%), 4.04% (0.34%, 7.89%), 2.47% (1.81%, 3.12%), 0.13% (0.07%, 0.19%), and −0.38% (−0.74%, −0.01%) increase in odds of angina admissions, respectively (Fig. S1; Table 4). According to the exposure-response curves, the associations for SO_2, NO_2, and O_3 exposures were linear (all $p > 0.05$; Fig. 1), while the associations for $PM_{2.5}$, PM_{10}, and CO exposures were nonlinear (all $p < 0.001$; Fig. 1). The association between NO_2 exposure and angina admissions was stable. The associations for PM_{10}, SO_2, CO, and O_3 exposures decreased or became significantly negative when adjusted for other certain air pollutants in 2-pollutant models (Table 4). No significant association was observed between $PM_{2.5}$ exposure and angina admissions ($p > 0.05$). Whether temperature and relative humidity were included in the single-pollutant model as cubic spline functions with 3 *df*, or holidays were included as covariates in the single-pollutant model, the association between NO_2 exposure and angina admissions remained robust. Each 10 μg/m^3 increase of exposure to NO_2 at lag 0 day was associated with a 2.28% (1.64%, 2.93%) and 1.02% (0.37%, 1.68%) increase in odds of angina admissions, respectively.

The stratified analyses showed that the positive associations of exposure to SO_2, NO_2, and CO with angina admissions were stronger in people admitted during cool season than in those admitted during warm season, while the negative association between exposure to O_3 and angina admissions was found in men but not in women (all p for difference <0.05; Table 5).

A total of 9.12% (95% CI: 6.83%, 11.33%) of hospital admissions for angina, corresponding to 5,694 (4,268, 7,076) admissions, was attributable to exposure to NO_2. In addition, we estimated that 4.84% (95% CI: 3.62%, 6.03%) and 0.31% (0.23%, 0.38%) of angina admissions can be reduced if the NO_2 exposure level was lowed to the WHO (25 μg/m^3) and China's (80 μg/m^3) air quality guideline values, respectively.

Table 1
Characteristics of the study population in Guangzhou, China during 2016–2019.

Characteristic	Value
No. of angina patients	46,687
No. of case days	62,562
No. of control days	212,530
Sex	
Male	33,470 (53.5%)
Female	29,092 (46.5%)
Age, years, mean (SD)	73.5 (8.7)
<75	34,974 (55.9%)
≥75	27,588 (44.1%)
Race	
Han	62,119 (99.3%)
Other	203 (0.3%)
Unknown	240 (0.4%)
Season at hospital admissions	
Cool (November to April)	30,976 (49.5%)
Warm (May to October)	31,586 (50.5%)

Abbreviations: SD, standard deviation.

Table 2
Distributions of exposure to ambient air pollutants and meteorological conditions on the date of angina admissions in Guangzhou, China during 2016–2019.

Parameter	Mean (SD)	Min	P_{25}	Median	P_{75}	Max
Air pollutant						
$PM_{2.5}$, μg/m^3	33.6 (18.6)	4.3	20.7	29.5	41.9	226.1
PM_{10}, μg/m^3	55.6 (27.4)	6.4	36.6	48.9	68.1	295.4
SO_2, μg/m^3	10.6 (3.9)	2.4	7.8	9.9	12.5	47.3
NO_2, μg/m^3	45.1 (21.8)	5.3	30.1	41.3	54.6	247.2
CO, mg/m^3	0.88 (0.21)	0.26	0.74	0.84	0.97	2.89
O_3[a], μg/m^3	108.9 (49.5)	3.3	72.9	101.4	139.3	309.3
Meteorological condition						
Temperature, °C	23.5 (5.8)	2.2	19.5	24.5	28.3	34.4
Relative humidity, %	76.6 (13.6)	21.0	69.3	79.8	87.0	98.5

Abbreviations: SD, standard deviation; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone.
[a] Restricted in warm season (May to October).

4. Discussion

In this population-based case-crossover study, we found that short-term exposure to NO_2 was consistently associated with angina admissions among older adults in Guangzhou, China from 2016 to 2019. Per 10 μg/m^3 increase of exposure to NO_2 (lag 0 day) was significantly associated with a 2.47% increase in odds of angina admissions, which was more pronounced during cool season. Exposure to NO_2 was responsible for up to 9.12% of the angina admissions, while 4.84% and 0.31% of the admissions can be avoided by reducing NO_2 levels to the WHO and China's air quality guideline values, respectively.

So far, four studies have evaluated the association of short-term exposure to NO_2 with angina admissions, and the results were inconsistent (Hosseinpoor et al., 2005; Kuźma et al., 2020a, 2020b; Von Klot et al., 2005). The European multicenter cohort study of 3,541 angina patients who were survivors of a first myocardial infarction from 1992 to 2000 reported that per 8 μg/m^3 increase of exposure to NO_2 at lag 0 day was significantly associated with a 3.2% increase in risk of angina admissions (Von Klot et al., 2005); likewise, a significant association was also identified in the case-crossover study in Poland (percent change in odds: 14.0% per 10 μg/m^3) (Kuźma et al., 2020a). These effect estimates were much higher than our estimates (percent change in odds: 2.47% per 10 μg/m^3). In contrast, the other two time-series studies in Iran (Hosseinpoor et al., 2005) and Poland (Kuźma et al., 2020b) reported null association between NO_2 and angina admissions. Overall, the heterogeneity of study design, exposure assessment, characteristic of study population may be possible reasons for the differences in effect estimates.

Over the past few decades, the global environmental NO_2 level has remained stable or even increased slightly because of the continuous motor vehicle increments (Chen et al., 2018). Traffic vehicles were one of the main ways to produce NO_2, which has caused serious environmental air pollution especially in developed cities. Guangzhou, a core city of Pearl River Delta (PRD, one of the major economic centers in China) in South China, is now suffering from similar air pollution problems as other fast-growing cities in the country (Gu et al., 2017). Guangzhou had a high level of NO_2, with about 60% of people experienced NO_2 concentration above the China air quality standard (Wei et al., 2022b; Huang et al., 2022; He et al., 2019). In the present study, we observed a consistent association of short-term exposure to NO_2 with an increased odds of angina admissions, which posed up to 9.12% of the angina admissions. Given that hospitalization of angina in older adults imposes a significant disease burden, it is of important public health significance to reduce NO_2 emissions and exposures. In addition, our study estimated that up to 4.84% of the angina admissions would be reduced when the NO_2 level is lowed to the WHO air quality guidelines, which suggests that the current air quality standards (especially NO_2) may still contribute to an increased risk of hospital admissions for angina.

In our study, we found that O_3 exposure was associated with a slightly decreased odds of angina admissions although this association was unstable with further adjustment for other air pollutants. While the European study reported significant associations between lag 0 day exposure to O_3 and an increased risk of angina admissions (Von Klot et al., 2005), the Iran study failed to observe any significant association (Hosseinpoor et al., 2005), which was inconsistent with neither of our results. It should be noted that the population of the European study was people survived from acute myocardial infarction, which may be more susceptible when exposed to air pollution. In addition, our findings were partly supported by evidence from the UK and Korea observed that exposure to O_3 was negatively associated with cardiovascular disease morbidity and mortality (Carey et al., 2013; Son et al., 2013). Nonetheless, more literatures are still warranted to confirm our results and illustrate the underlying mechanisms.

The underlying biological mechanism of the effects of ambient air pollution on angina has not been fully elucidated and may include oxidative stress and systemic inflammatory response. Some researchers have proposed that inhaled air pollutants can seriously cause local and systemic inflammation (Van Eeden and Hogg, 2002) and damage vascular endothelial cells (Münzel et al., 2018) which may further lead

Table 3
Spearman's correlation coefficients of exposure to ambient air pollutants and meteorological conditions on the case days and control days, 2016–2019.

	PM_{10}	SO_2	NO_2	CO	O_3	Temperature	Relative humidity
On case days (n = 62,562)							
$PM_{2.5}$	0.96	0.66	0.62	0.56	0.29	−0.32	−0.46
PM_{10}	–	0.68	0.65	0.50	0.36	−0.25	−0.50
SO_2	–	–	0.37	0.27	0.32	−0.08	−0.50
NO_2	–	–	–	0.53	0.04	−0.26	−0.20
CO	–	–	–	–	−0.15	−0.46	−0.06
O_3	–	–	–	–	–	0.43	−0.47
Temperature	–	–	–	–	–	–	0.22
On control days (n = 212,530)							
$PM_{2.5}$	0.95	0.65	0.61	0.56	0.60	−0.31	−0.47
PM_{10}	–	0.68	0.64	0.50	0.64	−0.24	−0.51
SO_2	–	–	0.36	0.27	0.36	−0.06	−0.51
NO_2	–	–	–	0.53	0.20	−0.25	−0.21
CO	–	–	–	–	0.17	−0.46	−0.07
O_3	–	–	–	–	–	0.38	0.59
Temperature	–	–	–	–	–	–	0.22

Abbreviations: $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone.

Table 4
Percent change in odds of angina admissions associated with each 10 μg/m^3 increase of lag 0 day exposure to ambient air pollution in single- and 2-pollutant models.

Model	Percent change in odds (95% CI)	p for difference[a]
$PM_{2.5}$	0.47 (−0.22, 1.15)	
+ SO_2	−0.01 (−0.91, 0.90)	0.32
+ NO_2	−2.87 (−3.82, −1.91)	<0.001
+ CO	−0.80 (−1.67, 0.07)	<0.001
+ O_3	1.15 (0.41, 1.90)	<0.001
PM_{10}	0.80 (0.32, 1.28)	
+ SO_2	0.87 (0.21, 1.54)	0.75
+ NO_2	−1.61 (−2.36, −0.85)	<0.001
+ CO	0.18 (−0.43, 0.80)	<0.001
+ O_3	1.34 (0.82, 1.86)	<0.001
SO_2	4.04 (0.34, 7.89)	
+ $PM_{2.5}$	5.25 (0.32, 10.42)	<0.001
+ PM_{10}	0.01 (−4.85, 5.12)	<0.001
+ NO_2	−6.82 (−11.06, −2.37)	<0.001
+ CO	1.20 (−2.86, 5.43)	<0.001
+ O_3	6.19 (2.27, 10.27)	<0.001
NO_2	2.47 (1.81, 3.12)	
+ $PM_{2.5}$	4.37 (3.42, 5.34)	<0.001
+ PM_{10}	3.80 (2.71, 4.89)	<0.001
+ SO_2	3.31 (2.47, 4.15)	0.01
+ CO	2.48 (1.67, 3.30)	<0.001
+ O_3	3.05 (2.37, 3.74)	<0.001
CO	0.13 (0.07, 0.19)	
+ $PM_{2.5}$	0.18 (0.10, 0.25)	<0.001
+ PM_{10}	0.10 (0.02, 0.18)	<0.001
+ SO_2	0.13 (0.07, 0.20)	0.68
+ NO_2	−0.01 (−0.09, 0.06)	<0.001
+ O_3	0.16 (0.10, 0.22)	<0.001
O_3[b]	−0.38 (-0.74, −0.01)	
+ $PM_{2.5}$	−0.57 (−1.02, −0.12)	<0.001
+ PM_{10}	−0.66 (−1.10, −0.21)	<0.001
+ SO_2	−0.16 (−0.55, 0.24)	0.054
+ NO_2	−0.51 (−0.91, −0.11)	0.08
+ CO	−0.31 (−0.70, 0.09)	0.29

Abbreviations: CI, confidence interval; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone.
[a] p value was estimated by the likelihood ratio test.
[b] Restricted in warm season (May to October).

to atherosclerosis and thrombosis (Robertson and Miller, 2018; Suwa et al., 2002). This series of reactions has been proposed to adversely impact the cardiac autonomic system regulation, coronary endothelial vasoconstriction, and blood viscosity, and finally result in plaque rupture, ischemia events, and arrhythmia especially in patients with coronary heart disease including angina. (Becker et al., 2002, 2005; Brook et al., 2010; Mustafic et al., 2012; Parnia et al., 2014). It was demonstrated that NO_2 was biologically associated with angina admissions in older adults. NO_2 is considered a proxy for traffic-related pollutants and often accompanied by traffic noise, leading to stress responses and sleep disturbances, which are also associated with poor cardiovascular health outcomes (Cai et al., 2018). Our findings of a significant association of exposure to NO_2 with angina admissions in older adults provide epidemiological evidence on related research directions and are conducive to promote relevant intervention measurements, which is of great significance to public health. In addition, our study showed that ambient NO_2, SO_2, and CO exposures might pose more considerable adverse effects on angina admissions of older adults during cold season. Exposure to ambient cold temperatures increased vascular resistance and blood pressure, which led to an increase in oxygen demand (Argilés et al., 1998; Hayward et al., 1976), raising the risk of angina attacks. Nonetheless, the stronger association between ambient air pollution and hospital admissions for angina of older adults during cold season needs to be further investigated.

Our study has several strengths. First, our study population was from a base population of 15.31 million over a 4-year period, and the hospital admission data covered all individual clinical data from all hospitals in Guangzhou city during the study period. Our large sample size allowed us to provide more representative effect estimates. Second, owing to the time-stratified case-crossover design, we were able to control the effects of seasonality, day of the week, long-term time trends, and certain personal-level confounders (such as age, sex, and race) in all analyses, and achieved more accurate individual-level exposure assessments. Third, we investigated the associations for six criteria air pollutants to provide more comprehensive evidence of exposure-response associations and conducted sensitivity analysis to confirm that our results were robust.

Some limitations should be discussed. First, due to absence of data for the individual activity pattern of the older adults and indoor air pollution, exposure misclassification can be introduced. However, it has been proposed that the misclassification was nondifferential and may bias our results to be insignificant (Whitcomb and Naimi, 2020). Second, because there were mixed correlations among exposure to air pollutants, it was difficult to fully distinguish the independent effect on angina admissions for each air pollutant. Finally, this study is based on the admissions of angia among older adults from a single capital city in Guangdong province, China. Cautions are needed when extrapolating our findings to other populations or regions.

5. Conclusions

In conclusion, short-term exposure to ambient NO_2 was significantly associated with an increased odds of angina admissions, which posed considerable excess hospital admissions among older adults. Our study highlights that reducing traffic-related air pollution exposure may be an efficient measurement in preventing angina admissions. Future researches are needed to confirm our results in other regions or populations, and to explore the underlying biological mechanisms.

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CRediT authorship contribution statement

Luxi Xu: Formal analysis, and, Investigation, Writing – original draft, preparation, Writing – review & editing. **Ruijun Xu:** Formal analysis, and, Investigation, Writing – original draft, preparation, Writing – review & editing. **Yunshao Ye:** Formal analysis, and, Investigation, Data curation. **Rui Wang:** Writing – review & editing. **Jing Wei:** Data curation. **Chunxiang Shi:** Data curation. **Qiaoxuan Lin:** Formal analysis, and, Investigation, Data curation. **Ziquan Lv:** Writing – review & editing. **Suli Huang:** Writing – review & editing. **Qi Tian:** Conceptualization, Writing – review & editing, Project administration, Funding acquisition, Supervision. **Yuewei Liu:** Conceptualization, Writing – review & editing, Project administration, Funding acquisition, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The air pollution data were available at https://weijing-rs.github.io/product.html. The meteorological condition data and clinical data are not publicly available.

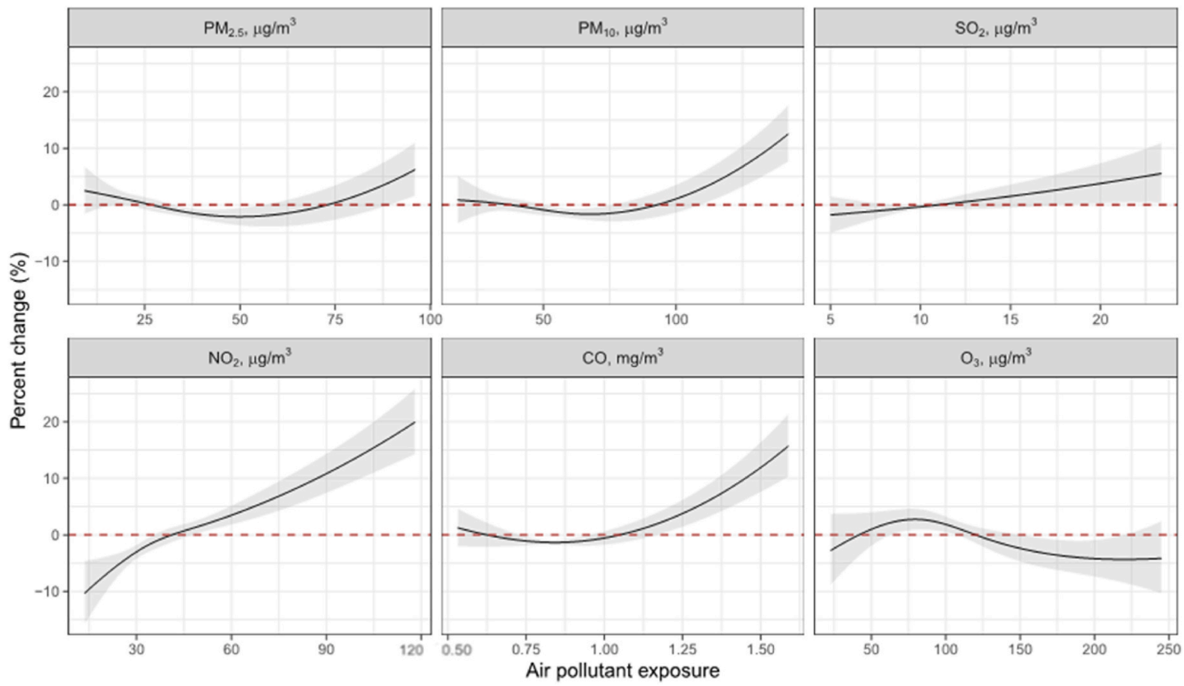

Fig. 1. Exposure-response curve of association between lag 0 day exposure to ambient air pollution and hospital admissions for angina.
Abbreviations: $PM_{2.5}$, particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone.

Table 5
Percent change in odds of hospital admissions for angina associated with each 10 μg/m^3 increase of lag 0 day exposure to ambient air pollution, stratified by age, sex, and season.

Stratification	Percent change in odds (95% CI)					
	$PM_{2.5}$	PM_{10}	SO_2	NO_2	CO	O_3[a]
Age						
<75	0.14 (−0.81, 1.10)	0.73 (0.06, 1.39)	2.64 (−2.36, 7.89)	2.77 (1.86, 3.70)	0.13 (0.04, 0.21)	−0.10 (−0.60, 0.39)
≥75	0.75 (−0.23, 1.74)	0.84 (0.15, 1.53)	5.31 (−0.11, 11.03)	2.05 (1.12, 2.99)	0.14 (0.05, 0.22)	−0.70 (-1.22, −0.17)
p for difference[b]	0.38	0.83	0.49	0.28	0.88	0.11
Sex						
Male	0.05 (−0.90, 1.00)	0.40 (−0.26, 1.07)	2.04 (−2.93, 7.26)	2.41 (1.49, 3.33)	0.18 (0.10, 0.27)	−0.74 (−1.24, −0.24)
Female	0.89 (−0.09, 1.89)	1.19 (0.51, 1.88)	6.25 (0.78, 12.02)	2.50 (1.57, 3.44)	0.08 (−0.01, 0.16)	0.02 (−0.49, 0.55)
p for difference[b]	0.23	0.11	0.28	0.89	0.08	0.04
Season						
Cool	0.81 (0.01, 1.62)	1.13 (0.56, 1.69)	13.46 (8.36, 18.79)	3.29 (2.53, 4.04)	0.21 (0.14, 0.28)	–
Warm	0.20 (−1.15, 1.57)	0.44 (−0.50, 1.39)	−8.64 (−14.11, −2.82)	0.73 (−0.65, 2.13)	−0.08 (−0.20, 0.04)	−0.38 (−0.74, −0.01)
p for difference[b]	0.45	0.22	<0.001	0.002	<0.001	–

Abbreviations: CI, confidence interval; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone.
[a] Restricted in warm season (May to October).
[b] p value was estimated by the 2-sample *z* test.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atmosenv.2023.120198.

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