

# Air Pollution and Childhood Asthma Hospitalizations in Chengdu, China: A Time-Series Study

Zijin Chen, Lei Zhang, Tao Ai, Yinghong Fan, Yanru Liu, Li Wang, Cheng Xie

Division of Pediatric Pulmonology, Chengdu Women's and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology of China, Chengdu, Sichuan, People's Republic of China

Correspondence: Lei Zhang, Email 534167313@qq.com

**Purpose:** Research on the relationship between air pollutants and hospitalization for asthma in children in developing countries remains inadequate. This study aimed to assess the short-term effects of air pollutants, including sulfur dioxide (SO<sub>2</sub>), nitrogen dioxide (NO<sub>2</sub>), carbon monoxide (CO), ozone (O<sub>3</sub>), particulate matter ≤ 2.5 μm (PM<sub>2.5</sub>), and particulate matter ≤ 10 μm (PM<sub>10</sub>), on children hospitalized for asthma in Chengdu, China, from 2017–2022.

**Patients and Methods:** During the study period, 5592 children were hospitalized for asthma. A generalized additive model was used to control for seasonality, long-term trends, weather, day of the week, and holidays. The analysis was further stratified by age, sex, and season to estimate the associations.

**Results:** PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and CO were significantly associated with an increased risk of hospitalization due to asthma. A 10 μg/m<sup>3</sup> increase in PM<sub>2.5</sub>, PM<sub>10</sub>, and CO at lag04 corresponded to an increase of 2.07%, 1.56%, and 0.33% in daily hospital admissions for asthma, respectively. A 10 μg/m<sup>3</sup> increase in SO<sub>2</sub> and NO<sub>2</sub> at lag05 corresponded to an increase of 45.69% and 8.16% in daily hospital admissions for asthma, respectively. Further analysis by age found that PM<sub>10</sub> and PM<sub>2.5</sub> had a greater impact on children aged 5–6 years old while NO<sub>2</sub> and CO mainly affected children under 7 years old. Analysis by sex found that pollutants had a greater impact on hospital admissions in girls. Seasonal analysis revealed that pollutants had a more significant effect on admission during the winter.

**Conclusion:** Our results suggest that increased concentrations of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and CO in Chengdu lead to hospitalization for asthma in children and that a lag effect was observed, especially with SO<sub>2</sub>. These findings highlight the need for stricter air quality controls to reduce childhood asthma hospitalizations.

## Plain Language Summary:

- Exposure to air pollutants increases the risk of hospitalization for children with asthma.
- The effect of each studied air pollutant varies according to the age and sex of the child.
- The effect of air pollutants on children with asthma was stronger in the winter.
- Air quality control standards are needed to reduce hospitalizations for asthma in children.

**Keywords:** pediatric asthma, air pollutants, stratified analysis, in-patient

## Introduction

Asthma is a heterogeneous disease with different clinical phenotypes, mainly characterized by chronic airway inflammation,<sup>1</sup> and is the most common chronic inflammatory disease of the respiratory tract in children.<sup>2</sup> It involves reversible expiratory airflow restriction and is often accompanied by recurrent wheezing, shortness of breath, chest tightness, and cough.<sup>3</sup> Without thorough treatment, asthma can continue into adulthood, with severe cases posing life-threatening risks, significantly affecting children's physical and mental health. Asthma is the leading cause of emergency

hospitalization in children under 5 years of age, with its prevalence increasing over the past 20 years.<sup>4,5</sup> According to the International Study of Asthma and Allergies in Childhood (ISAAC), the global prevalence of asthma symptoms in children increased from 11.1% to 11.6% between phase one and phase three of the study.<sup>2</sup> A doctor confirmed asthma in 6.3% of children across 44 research centers in 16 countries.<sup>1</sup> The prevalence of asthma in children aged 0–14 years in China has also increased from 0.91% in 1990 to 3.02% in 2010.<sup>6</sup>

The pathogenesis of asthma is complex and results from interactions between genetic and environmental factors.<sup>3</sup> With the rapid development of the industrial revolution, the impact of air pollution on asthma has received increasing attention from researchers. Epidemiological and clinical trial studies have found that exposure to air pollutants is not only a significant risk factor for asthma attacks but may also be associated with new-onset asthma.<sup>7–12</sup> An increasing number of studies have linked exposure to air pollutants and acute asthma attacks; however, most of these studies were conducted in developed countries, and the subjects and results were not consistent.<sup>13–17</sup> For example, a New York study revealed no association between pollutants and emergency asthma among children living in neighborhoods with higher asthma prevalence.<sup>13</sup> However, a study showed that increases in ozone and sulfur dioxide(SO<sub>2</sub>) concentrations were associated with increased asthma morbidity in children in Indianapolis.<sup>17</sup> Many Asian countries, especially China and India, have significantly higher levels of air pollutants than developed countries did.<sup>18,19</sup> Moreover, meteorological conditions and other factors in these developing countries differ from those in developed countries. In China, where people's lifestyles are different from those in developed countries, a heavy reliance on coal consumption persists, which accounts for 64% of domestic energy consumption, significantly exceeding the world average. Air pollution in China is worsening due to industrial and traffic emissions and natural phenomena (eg, dust, smog).<sup>20</sup>

Chengdu is located in southwestern China in the western Sichuan Basin. The elevation difference in the Sichuan Basin region is 5000 m, with significant terrain variations among mountainous, hilly, and plain areas. This region is relatively closed, and the winter wind is weak, making it difficult for air to spread. As a major city in western China, it has a concentration of industrial populations, contributing to heavy air pollution and frequent hazy weather conditions. Chengdu was ranked as the 15th most polluted city in China in 2014 based on its particulate matter  $\leq 2.5 \mu\text{m}$  (PM<sub>2.5</sub>) levels (Greenpeace East Asia, 2014). In addition, we noticed that the prevalence of asthma in children in Chengdu was increasing,<sup>21</sup> and thus we hypothesized whether a correlation exists between air pollution and admission to hospital for acute asthma attacks in children in Chengdu. In southwest China, studies on the relationship between air pollution and acute asthma attacks in children remain lacking. In China, the treatment of acute asthma attacks is usually unscheduled and less affected by factors, such as regular clinical appointments and personal health insurance, making it a good indicator for epidemiological studies.

The purpose of this study was to investigate the effect of air pollutants on hospital admissions for acute asthma attacks in children using a time-series analysis to understand the relationship between air pollution and asthma in Chengdu. This study can guide government personnel in formulating relevant health interventions to reduce the adverse effects of air pollution on children with asthma.

## Material and Methods

### Study Setting

Chengdu is located in southwest China and is the capital city of Sichuan. Our study location is the metropolitan area of Chengdu, covering an area of 3639.81 km<sup>2</sup>, including 14 urban districts namely Jinjiang, Chenghua, Jinniu, Qingyang, Wuhou, Gaoxin, Longquanyi, Shuangliu, Pidu, Xindu, Wenjiang, Tianfu, Qingbaijiang, and Xinjin. Daily admission cases of childhood asthma were obtained from one of the largest pediatric specialist hospitals in the region, which has four wards. This national tertiary Grade A women and children's medical and health institution integrates medical care, health care, scientific research, and teaching with specialized facilities. We systematically retrieved daily asthma admissions of children aged 0–18 years from hospital electronic medical records from January 1, 2017 to December 31, 2022 (2191 days), including admission date, age, sex and International Classification of Diseases (ICD-10). The diagnostic criteria of asthma are based on the recommendations for diagnosis and management of bronchial

asthma in children (2020).<sup>22</sup> The diagnosis of asthma in children under 6 years of age remains a challenging clinical problem, suggesting that the main clinical features of asthma in young children include: frequency of wheezing attacks; exercise-related wheezing and coughing; non-specific cough at night or at a fixed time; symptoms persist up to 3 years of age; anti-asthma treatment is effective, repeated after withdrawal. Risk factors such as family history of allergy, personal history of allergic disease and early allergen sensitization were also considered. Asthma was coded according to the ICD-10: asthma (J45) and status asthmaticus (J46).

## Pollutant and Weather Data

Daily (24 h) air pollution concentration data were collected by the China National Environmental Monitoring Center from January 2017 to December 2022, including sulfur dioxide (SO<sub>2</sub>), ozone (O<sub>3</sub>), carbon monoxide (CO), nitrogen dioxide (NO<sub>2</sub>), particulate matter ≤ 10 μm (PM<sub>10</sub>), and PM<sub>2.5</sub>, from seven monitoring stations. Mean levels of SO<sub>2</sub>, CO, NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> were the average of 24 h values; O<sub>3</sub> was calculated from the mean of 8 h maximum concentration. Additionally, daily weather data, including daily relative humidity (%) and average temperature (°C), were obtained from the Chengdu Meteorological Monitoring Bureau. No data were missing. The average of daily mean levels of air pollutants, from all seven stations (Sanwayao, Shahepu, Junpingjie, Dashixilu, Liangjiaxiang, Jinquanhe, Shilidian) represented the daily exposure of children to asthma during the study period.

## Statistical Methods

A time-series regression analysis was used to investigate the short-term relationship between daily hospitalizations for asthma and exposure to air pollutants (SO<sub>2</sub>, O<sub>3</sub>, CO, NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>).<sup>23</sup> Because the number of daily hospitalizations for asthma is a low-probability event that roughly follows a Poisson distribution, we utilized a generalized additive model (GAM) to model the time-series data and control for the effects of seasonality, long-term trends, weather, workdays, and holidays.<sup>24</sup>

The model is as follows:

$$Y_t \sim \text{Poisson}(\mu_t)$$

$$\text{Log}(\mu_t) = \beta X_t + s(t, \text{dft}) + s(Z_t, \text{dft}) + \text{Holiday} + \text{DOW} + \alpha$$

Where  $t$  represents the day of observation;  $Y_t$  represents the number of hospitalizations due to asthma on day  $t$ ;  $\mu_t$  represents the expected number of hospitalizations on day  $t$ ;  $X_t$  represents the concentration of atmospheric pollutants on day  $t$  (including SO<sub>2</sub>, O<sub>3</sub>, CO, NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>);  $\beta$  is the regression coefficient;  $s$  represents natural smooth splined function;  $Z_t$  represents the meteorological factor of day  $t$  (including average temperature, relative humidity);  $\text{dft}$  is the degree of freedom of a non-parametric smoothing function;  $\text{Holiday}$  is a binary variable for national holidays in China;  $\text{DOW}$  is a day of the week (value ranges from 1 to 7 on Sunday to Saturday);  $\alpha$  is intercept. For adjustment of the delayed and non-linear confounding effects of temperature and humidity, we adjusted the degrees of freedom (DOF) several times in the model, and combined with previous studies, applied the distributed lag non-linear models with three degrees of freedom in the natural smooth splined function.<sup>24,25</sup> According to the Partial Autocorrelation Function (PACF), the DOF of the model's summary non-parametric smoothing function was determined to be 6 years to control seasonal, long-term trends in the time-series dataset.

We used a single-day lag (from lag0 to lag5) and a multi-day cumulative lag (from lag01 to lag05) to estimate the lag effect of air pollutants. Single-day lag is expressed as lag0, lag1... lag5, where lag0 represents the day of exposure; The cumulative lag is expressed as lag01, lag02... lag05, where lag01 represents the cumulative effect on the day of exposure and 1 day of lag. Our choice of lag days was based on the fact that asthma's response to environmental factors is acute and does not extend for a long time. After establishing the basic model, air pollutants were sequentially introduced into single models to explore their correlation with asthma hospitalization. Moreover, to investigate possible effect modification by season (spring: March through May; summer: June through August; autumn: September through November; winter: December through February), sex, and age (0–4 years old; 5–6 years old; 7–18 years old) group, we performed separate analysis stratified by these potential modifiers.

For sensitivity analysis, the cumulative lag day with the most significant exposure effect was selected in the single pollutant model as the research object, while controlling for other confounding factors. The robustness of the model was tested by establishing a two-pollutant model to see if the effects of pollutants remain have statistical significance.

SPSS 22.0 was used for descriptive analysis of weather data and air pollutant concentration. The indicators included mean, standard deviation, minimum, maximum, and percentile (P5, P25, P50, P75, P95), and Spearman rank correlation method was used for the correlation analysis. Using the software package “dlnm” in R software, a generalized additive Poisson regression model was used for time-series analysis. The results were expressed as the rate of daily increase in asthma hospitalization (excess risk, ER) and 95% confidence interval (CI) per 10  $\mu\text{g}/\text{m}^3$  increase in air pollutant concentration.

## Results

**Table 1** summarizes the primary statistical data of the study participants. In our study area, from 2017 to 2022, the total number of hospitalizations for asthma was 5592, with an average daily admission of 2.55. Most patients (67.06%) were boys. Children aged 0–4, 5–6, and 7–18 years accounted for 81.56%, 9.91%, 8.53% of cases, respectively. A total of 1384 (24.75%) patients hospitalized in spring (March–May), 1303 (23.30%) patients hospitalized in summer (June–August), 1689 (30.20%) patients hospitalized in autumn (September–November), and 1216 (21.75%) patients hospitalized in winter (December–February), were recorded.

**Table 2** summarizes the descriptive statistical data for the air pollutants and meteorological conditions. During the study period, the average daily concentrations of  $\text{SO}_2$ ,  $\text{NO}_2$ ,  $\text{O}_3$ ,  $\text{PM}_{2.5}$ , and  $\text{PM}_{10}$  were 7.35, 39.29, 96.52, 46.05, and 71.99  $\mu\text{g}/\text{m}^3$ , respectively. The average daily CO concentration was 0.83  $\text{mg}/\text{m}^3$ . The daily relative humidity and average temperature were 80.44% and 16.88°C, respectively.

**Figure 1** shows raw time-series plots for each air pollution variable.  $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{O}_3$ , CO, and  $\text{NO}_2$  showed a certain degree of seasonal fluctuation, whereas  $\text{SO}_2$  exhibited a declining trend over the six years.

**Table 1** Summary Statistics of Children Hospitalized for Asthma by Sex, Age, and Season, 2017–2022

Characteristics	Number of Patients	Percentage %
Sex		
Boys	3750	67.06
Girls	1842	32.94
Age (years)		
0–4	4561	81.56
5–6	554	9.91
7–18	477	8.53
Season		
Spring	1384	24.75
Summer	1303	23.30
Autumn	1689	30.20
Winter	1216	21.75
Total	5592	100.00

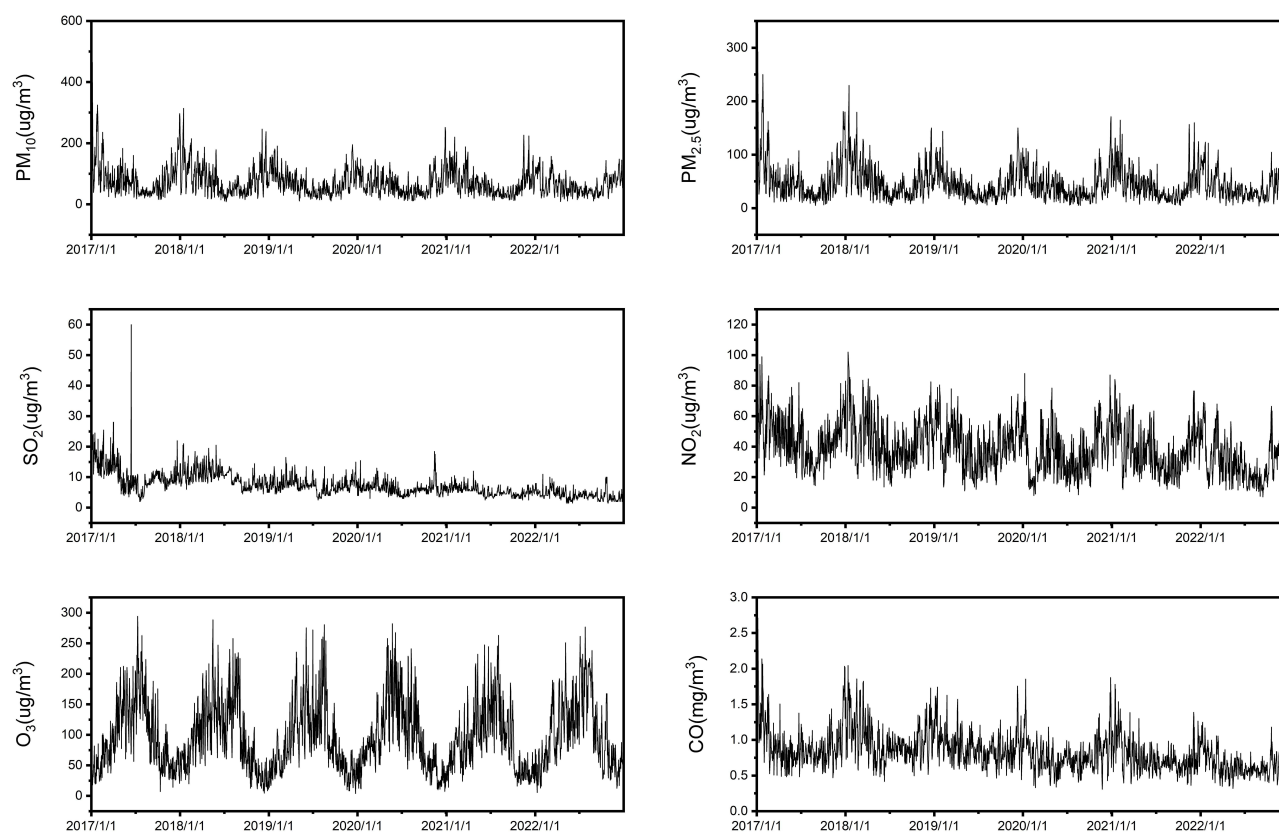
**Notes:** Spring: March–May; Summer: June–August; Autumn: September–November; Winter: December–February.

**Table 2** Summary Statistics for Air Pollutants Concentrations and Weather Conditions in Chengdu, 2017–2022

	Mean	SD	Percentiles					Max	Min	Days Exceeded WHO AQG
			5	25	50	75	95			
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	46.05	31.94	12.500	24.00	38.00	60.00	106.20	292.50	4.00	1477 (67.41)
PM <sub>10</sub> (µg/m <sup>3</sup> )	71.99	45.70	22.500	39.50	60.50	94.00	155.50	465.00	8.50	1992 (90.92)
CO (mg/m <sup>3</sup> )	0.83	0.27	0.49	0.65	0.79	0.96	1.35	2.71	0.31	0 (0)
SO <sub>2</sub> (µg/m <sup>3</sup> )	7.35	3.86	3.00	5.00	6.50	9.00	14.50	60.00	1.50	1 (0.04)
NO <sub>2</sub> (µg/m <sup>3</sup> )	39.29	16.18	16.50	27.00	37.50	50.00	67.50	114.50	7.00	1735 (79.19)
O <sub>3</sub> (µg/m <sup>3</sup> )	96.52	56.80	23.00	52.00	84.00	135.00	208.40	294.00	4.00	887 (40.48)
Temperature (°C)	16.88	7.41	5.31	9.98	16.99	23.34	27.49	32.36	0.75	
Humidity (%)	80.44	9.00	65.25	74.25	80.86	87.25	94.13	99.00	39.88	

**Abbreviations:** WHO, World Health Organization; AQG, air quality guidelines; PM, particulate matter; CO, carbon monoxide; SO<sub>2</sub>, sulfur dioxide; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; SD, standard deviation.

Table 3 shows the relationship between the air pollutant levels and meteorological conditions. PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>2</sub> were positively correlated, with PM<sub>10</sub> and PM<sub>2.5</sub> having the closest correlation ( $R = 0.959$ ,  $P < 0.01$ ). O<sub>3</sub> had no obvious correlation with SO<sub>2</sub>, and was negatively correlated with the other three pollutants, which were positively correlated. Temperature was negatively correlated with all pollutants except O<sub>3</sub>, and humidity was negatively correlated with all pollutants except CO.

**Figure 1** Time-series plots of air pollutant variables in Chengdu, 2017–2022.

**Abbreviations:** PM, particulate matter; CO, carbon monoxide; SO<sub>2</sub>, sulfur dioxide; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone.

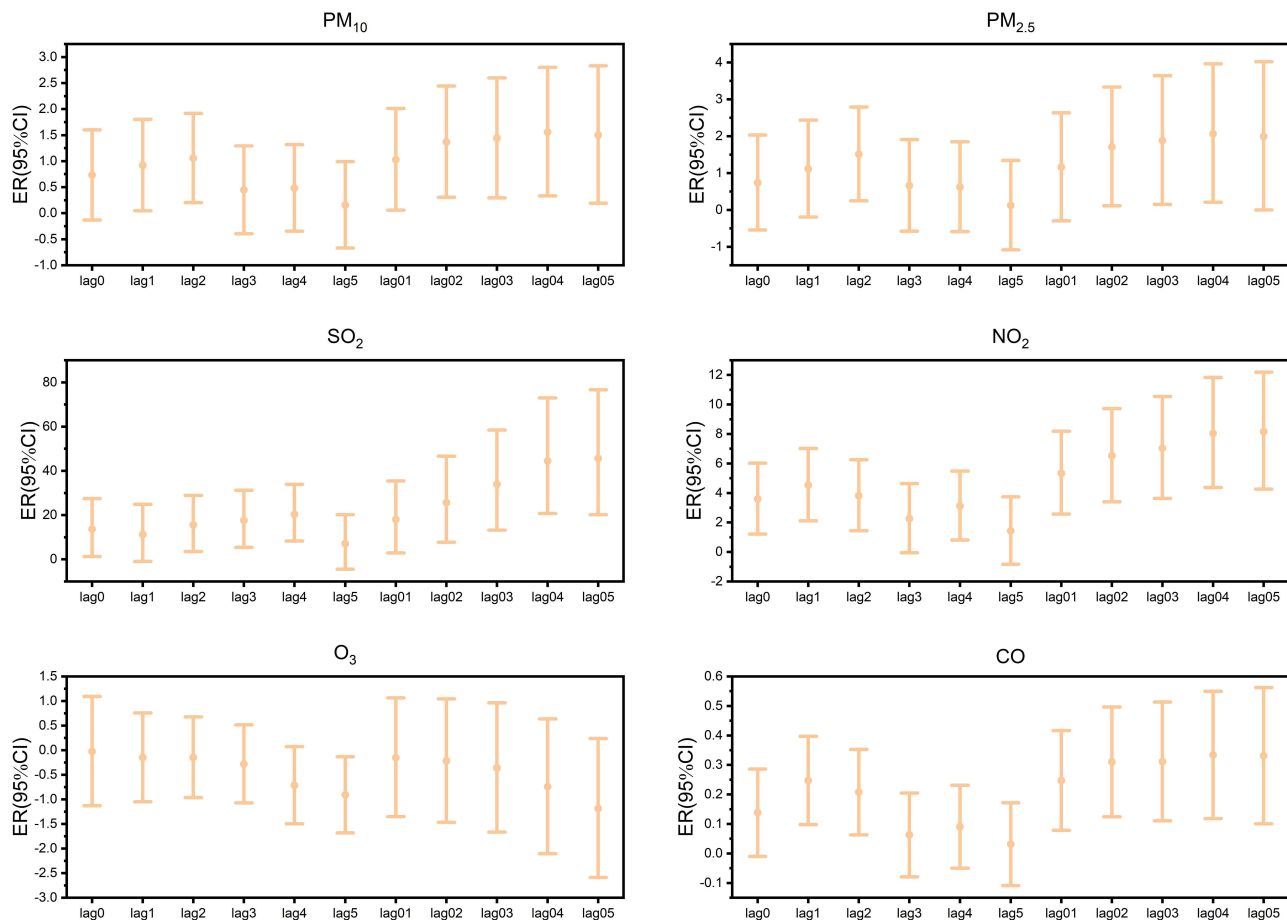
**Table 3** Pearson’s Correlation Matrix Between Air Pollutant Concentrations and Weather Conditions in Chengdu, 2017–2022

	PM <sub>2.5</sub>	PM <sub>10</sub>	CO	SO <sub>2</sub>	O <sub>3</sub>	NO <sub>2</sub>	Temperature	Humidity
PM <sub>2.5</sub>	1.000	<b>0.959**</b>	<b>0.664**</b>	<b>0.424**</b>	<b>-0.219**</b>	<b>0.729**</b>	<b>-0.460**</b>	<b>-0.142**</b>
PM <sub>10</sub>		1.000	<b>0.616**</b>	<b>0.454**</b>	<b>-0.189**</b>	<b>0.772**</b>	<b>-0.442**</b>	<b>-0.235**</b>
CO			1.000	<b>0.559**</b>	<b>-0.160**</b>	<b>0.665**</b>	<b>-0.267**</b>	<b>0.066**</b>
SO <sub>2</sub>				1.000	0.004	<b>0.555**</b>	<b>-0.161**</b>	<b>-0.186**</b>
O <sub>3</sub>					1.000	<b>-0.205**</b>	<b>0.778**</b>	<b>-0.440**</b>
NO <sub>2</sub>						1.000	<b>-0.365**</b>	<b>-0.180**</b>
Temperature							1.000	<b>-0.050*</b>
Humidity								1.000

Notes: \*P < 0.05; \*\*P < 0.01; bold: significant p-values.

Abbreviations: PM, particulate matter; CO, carbon monoxide; SO<sub>2</sub>, sulfur dioxide; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone.

Figure 2 shows the results from the single-lag day models (lag0–lag5) and multi-day cumulative lag models (lag01–lag05) for the percentage increase in hospitalization per 10 µg/m<sup>3</sup> increase in pollution. The single-day lag effect of PM<sub>2.5</sub> was significant only at lag2 [RR = 1.002 (95% CI: 1.000–1.003)], with the risk of asthma admission increasing by 1.51% (95% CI: 0.25–2.79%) per 10 µg/m<sup>3</sup> increase. The cumulative lag effect of PM<sub>2.5</sub> was significant at lag02–lag05, with the largest effect observed at lag04, where a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> increased the risk of



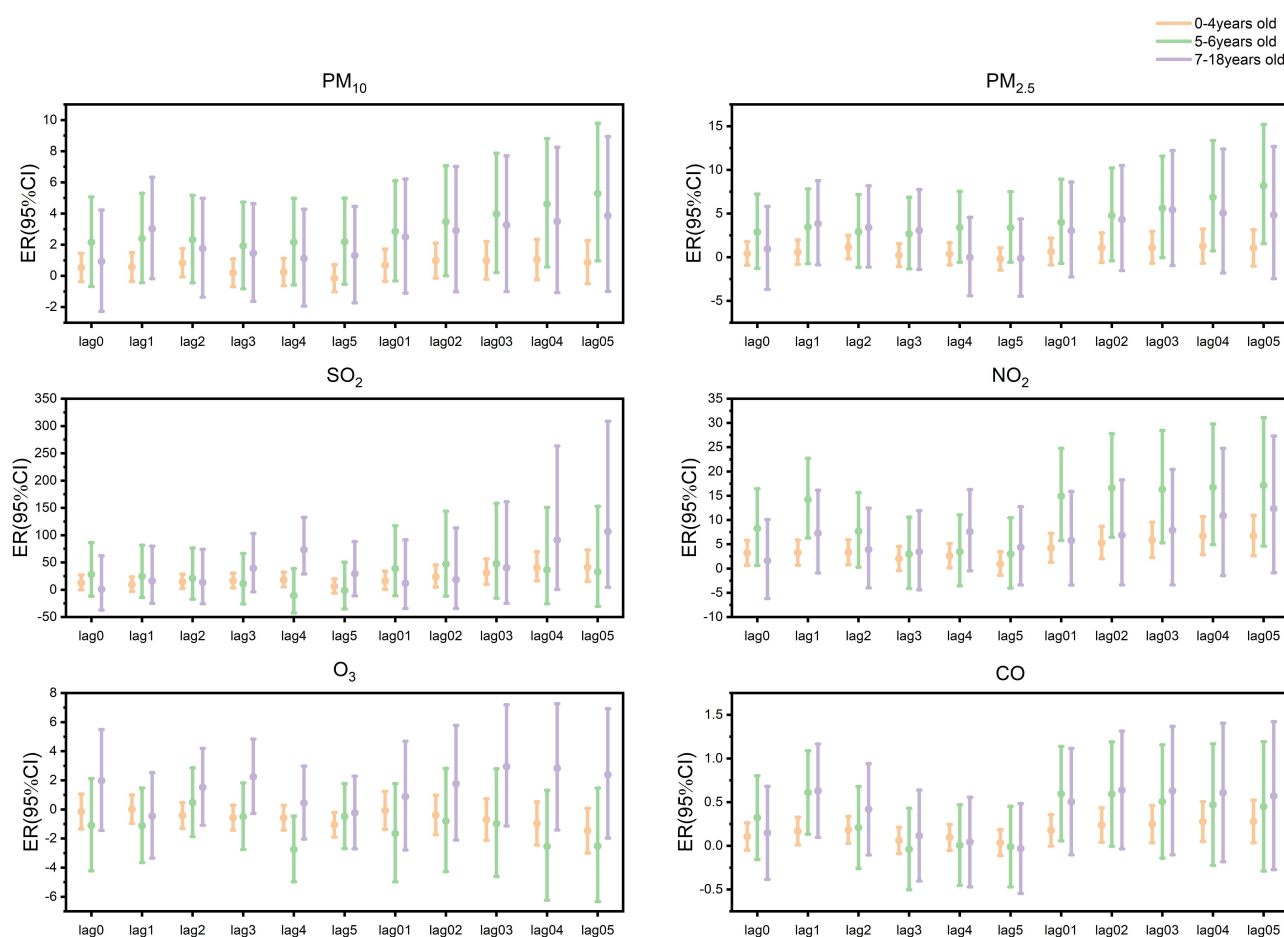
**Figure 2** In single-lag models (lag 0, 1, 2, 3, 4, and 5) and cumulative lag models (lag 01, 02, 03, 04, and 05), a 10 µg/m<sup>3</sup> increase in air pollutants corresponds to a percentage increase in daily asthma hospitalizations (with 95% CI).

Abbreviations: PM, particulate matter; CO, carbon monoxide; SO<sub>2</sub>, sulfur dioxide; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; ER, excess risk.



asthma admission by 2.07% (95% CI: 0.21–3.96%). The single-day lag effect of PM<sub>10</sub> was significant at lag1 and lag2, and the cumulative lag effect of PM<sub>10</sub> was significant at lag01–lag05, with the largest effect observed at lag04. For every 10 µg/m<sup>3</sup> increase in PM<sub>10</sub>, the risk of asthma admissions increased by 1.56% (95% CI: 0.33–2.80%). The single-day lag effect of SO<sub>2</sub> was the largest at lag 4 (*RR* = 1.019 [95% CI: 1.008–1.030]), and its cumulative lag effects were all significant, showing a gradually increasing trend. The cumulative lag effects of NO<sub>2</sub> were similar to those of SO<sub>2</sub>. A 10µg/m<sup>3</sup> increase in SO<sub>2</sub> and NO<sub>2</sub> at lag05 was associated with 45.69% (95% CI: 20.17–76.62%) and 8.16% (95% CI: 4.26–12.20%) increments in daily admission for asthma, respectively. The single-day lag effects of CO were significant at lag1 and lag2, with the largest effect at lag1 (*RR* = 1.280 [95% CI: 1.103–1.486]). The cumulative lag effect was significant, and the most prominent effect was observed at lag04. For every 10 µg/m<sup>3</sup> increase in CO, the risk of asthma hospitalization increased by 0.33% (95% CI: 0.12–0.55%). The single-day lag effect of O<sub>3</sub> was negative and significant only at lag5 (*RR* = 0.999 [95% CI: 0.998–1.000]). A 10 µg/m<sup>3</sup> increase in O<sub>3</sub> reduced the risk of asthma admission by 0.91% (95% CI: 1.68–0.13%), with the cumulative effect not being significant.

Figure 3 shows the effects of six air pollutants on acute asthma attacks in children of different ages. The effect of PM<sub>2.5</sub> on asthma admissions in children aged 5–6 years was similar to that in the total study population. The cumulative lag effect was significant at lag04–lag05, and the largest effect was observed at lag05. The risk of hospitalization for asthma was increased by 8.18% (95% CI: 1.57–15.21%). However, the effects on admission rates for children aged 0–4 years and 7–18 years were not statistically significant. The effect of PM<sub>10</sub> on asthma in different age groups was similar

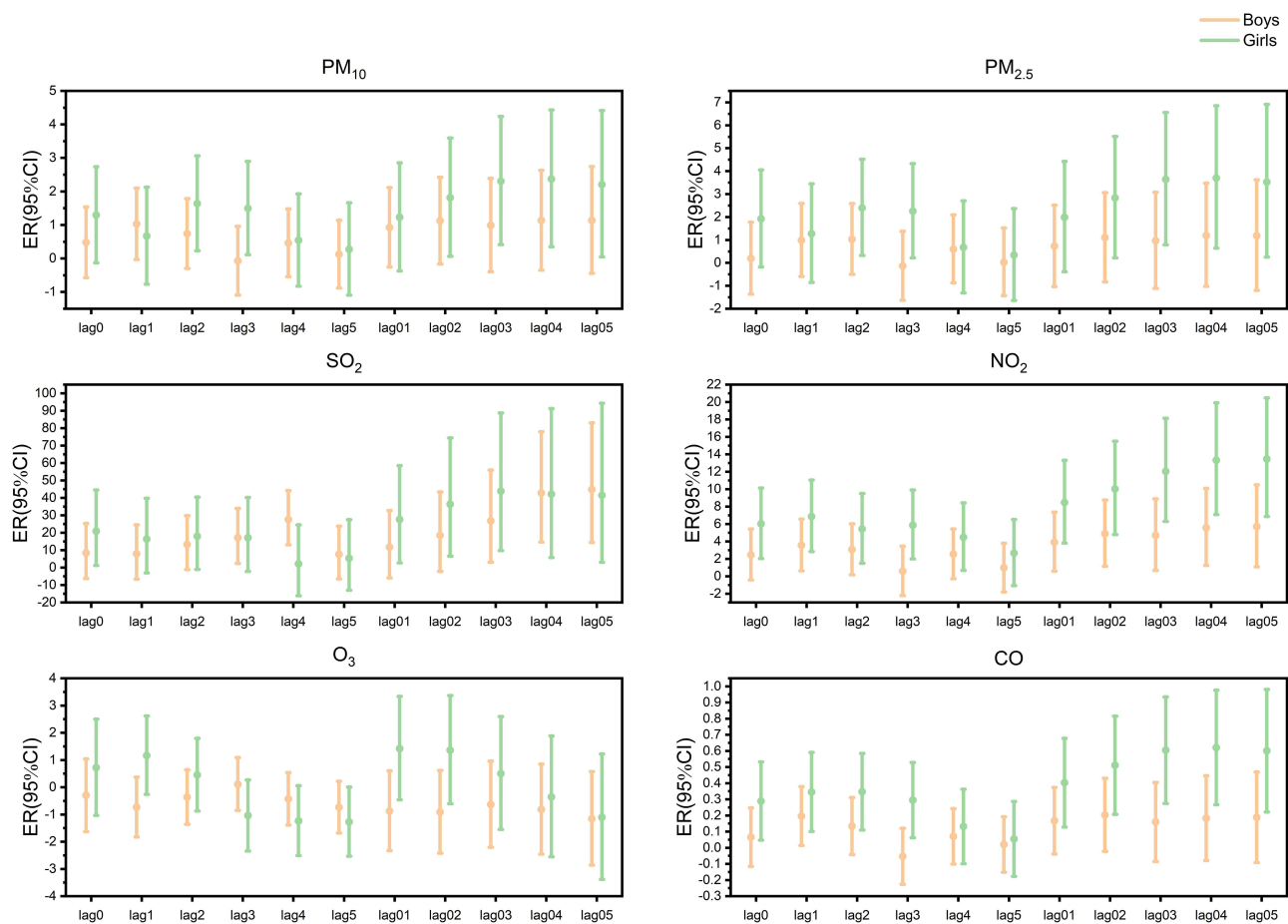


**Figure 3** In single-lag models (lag 0, 1, 2, 3, 4, and 5) and cumulative lag models (lag 01, 02, 03, 04, and 05) stratified by age group, a 10 µg/m<sup>3</sup> increase in air pollutants corresponds to a percentage increase in daily asthma hospitalizations (with 95% CI).

**Abbreviations:** PM, particulate matter; CO, carbon monoxide; SO<sub>2</sub>, sulfur dioxide; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; ER, excess risk.

to that of  $PM_{2.5}$ , and the cumulative lag effect in children aged 5–6 years old reached a maximum at lag05, with the risk of asthma admission increasing by 5.29% (95% CI: 0.98–9.79%). The effects of  $SO_2$  on asthma admissions in children aged 0–4 years was similar to that in the total study population. The single-day lag effect reached a maximum at lag4, with the risk of hospitalization increasing by 17.94% (95% CI: 5.34–32.05%) per  $10\mu\text{g}/\text{m}^3$  increase in  $SO_2$ . The cumulative lag effect was significant in lag01–lag05 and reached a maximum at lag05, with the risk of hospitalization increasing by 41.10% (95% CI: 15.10–72.97%) per  $10\mu\text{g}/\text{m}^3$  increase in  $SO_2$ . The single-day lag effect of  $SO_2$  on admission for asthma in children aged 7–18 years was significant only at lag4, while the cumulative lag effect was significant at lag04 and lag05; however, the effect on admission rates for children aged 5–6 years was not statistically significant. The effect of  $NO_2$  on admission for asthma in children aged 0–4 years and 5–6 years was similar to that in the total study population, with cumulative lag effect reaching its maximum at lag05 for both age groups, while the effect on admission for asthma in children aged 7–18 years was not statistically significant. The effect of CO on asthma admissions in children aged 0–4 years was similar to that in the total study population, with significant cumulative lag effect at lag02–lag05 and the greatest effect at lag05.

Figure 4 shows the effect of the six air pollutants on asthma admissions in children of different sexes. The impact of  $PM_{2.5}$  on asthma admissions in girls was similar to that in the total study population. The single-day lag effect was significant at lag2 and lag3, and the cumulative lag effect was significant at lag02–lag05, with the largest effect observed at lag03. The risk of asthma admission increased by 3.64% (95% CI: 0.79–6.56%). However, there was no statistically significant impact on hospital admissions in boys. The effects of  $PM_{10}$  were similar to those of  $PM_{2.5}$ , with the largest cumulative lag effect at lag04, where the risk of asthma admission increased by 2.37% (95% CI: 0.35–4.43%). The



**Figure 4** In single-lag models (lag 0, 1, 2, 3, 4, and 5) and cumulative lag models (lag 01, 02, 03, 04, and 05) stratified by sex group, a  $10\mu\text{g}/\text{m}^3$  increase in air pollutants corresponds to a percentage increase in daily asthma hospitalizations (with 95% CI).

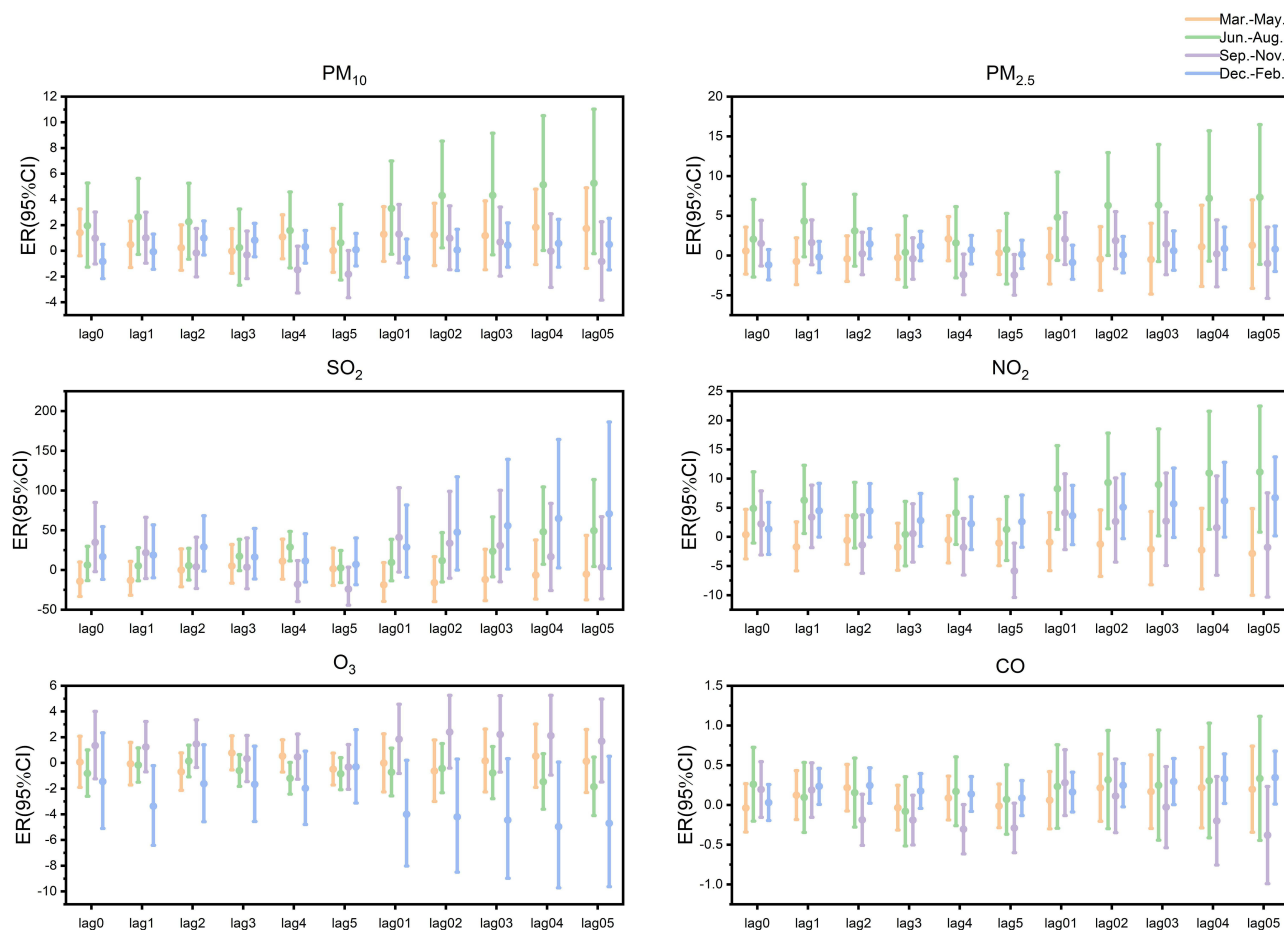
**Abbreviations:** PM, particulate matter; CO, carbon monoxide;  $SO_2$ , sulfur dioxide;  $NO_2$ , nitrogen dioxide;  $O_3$ , ozone; ER, excess risk.



impact of SO<sub>2</sub> exposure in boys was similar to that in the total study population; however, the single-day effect on hospital admission in girls was significant only at lag0. The impact of NO<sub>2</sub> on asthma admissions in children of different sexes was similar to that observed in the total study population, with the single-day lag effect reaching a maximum at lag1. The cumulative lag effect reached its maximum at lag 05, with the risk of admission for asthma increasing by 13.46% (95% CI: 6.86–20.48%) in girls and by 5.70% (95% CI: 1.09–10.51%) in boys. The impact of CO on girls was similar to that on the total study population. However, the single-day lag effect on hospital admission for boys with asthma was significant only at lag1.

Figure 5 shows the effects of the seasonality on asthma admissions in children. CO, SO<sub>2</sub>, and NO<sub>2</sub> had significant effects on the admission of children with asthma in the winter but had no significant relationship with the concentration of pollutants in other season. However, the effects of PM<sub>10</sub> and PM<sub>2.5</sub> on admission were not significantly modified by season.

In the two-pollutant model, two atmospheric pollutants (SO<sub>2</sub>, CO, O<sub>3</sub>, NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>) were included to study their impact on the percentage change in daily hospitalization for children with asthma. Since PM<sub>2.5</sub> and PM<sub>10</sub> were highly correlated ( $R = 0.959$ ), they were not included in the same model to avoid multicollinearity affecting the model stability. O<sub>3</sub> had no statistically significant effect on the hospitalization of children with asthma over the entire cumulative lag interval, and no separate two-pollutant model was established. As shown in Table 4, when PM<sub>2.5</sub> was included in the SO<sub>2</sub>, NO<sub>2</sub>, CO, and O<sub>3</sub> models, only O<sub>3</sub> was statistically significant. When PM<sub>10</sub> was included in the SO<sub>2</sub>, NO<sub>2</sub>, CO, and O<sub>3</sub> models, the statistical significance was lost after NO<sub>2</sub> was included, whereas the other two pollution models remained significant, with O<sub>3</sub> having the greatest effect. SO<sub>2</sub> showed statistical significance after including NO<sub>2</sub>, CO, O<sub>3</sub>, PM<sub>10</sub>,



**Figure 5** In single-lag models (lag 0, 1, 2, 3, 4, and 5) and cumulative lag models (lag 01, 02, 03, 04, and 05) stratified by season group, a 10  $\mu\text{g}/\text{m}^3$  increase in air pollutants corresponds to a percentage increase in daily asthma hospitalizations (with 95% CI).

**Abbreviations:** PM, particulate matter; CO, carbon monoxide; SO<sub>2</sub>, sulfur dioxide; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; ER, excess risk.

**Table 4** In a Two-Pollutant Model, a 10 $\mu\text{g}/\text{m}^3$  Increase in Pollutant Concentrations Corresponds to a Percentage Increase in Asthma Hospitalizations (Mean and 95% CI)

Pollutants		RR	Estimate
PM <sub>2.5</sub>	NULL	1.002(1.0002–1.004)*(lag04)	2.067 (0.208–3.960)*
	+SO <sub>2</sub>	1.002(0.999–1.004)	1.836 (–0.034–3.742)
	+NO <sub>2</sub>	1.002(0.999–1.003)	1.553 (–0.334–3.475)
	+CO	1.002(0.999–1.004)	1.664 (–0.268–3.632)
	+O <sub>3</sub>	1.002(1.000–1.004)*	2.072 (0.211–3.968)*
PM <sub>10</sub>	NULL	1.002(1.000–1.003)*(lag04)	1.558 (0.332–2.800)*
	+SO <sub>2</sub>	1.001(1.000–1.003)*	1.403 (0.167–2.656)*
	+NO <sub>2</sub>	1.001(0.999–1.002)	1.174 (–0.083–2.446)
	+CO	1.001(1.000–1.003)*	1.326 (0.059–2.609)*
	+O <sub>3</sub>	1.002(1.000–1.003)*	1.562 (0.333–2.805)*
SO <sub>2</sub>	NULL	1.039(1.019–1.059)*(lag05)	45.689 (20.172–76.623)*
	+PM <sub>10</sub>	1.035(1.016–1.055)*	42.879 (17.430–73.843)*
	+NO <sub>2</sub>	1.033(1.014–1.052)*	39.972 (15.078–70.252)*
	+CO	1.036(1.017–1.055)*	43.408 (18.150–74.066)*
	+O <sub>3</sub>	1.038(1.019–1.057)*	46.170 (20.487–77.326)*
	+PM <sub>2.5</sub>	1.037(1.018–1.056)*	44.525 (18.772–75.864)*
NO <sub>2</sub>	NULL	1.008(1.004–1.012)*(lag05)	8.157 (4.264–12.196)*
	+PM <sub>10</sub>	1.008(1.004–1.012)*	8.289 (3.973–12.784)*
	+SO <sub>2</sub>	1.007(1.004–1.011)*	7.585 (3.626–11.695)*
	+CO	1.008(1.004–1.011)*	7.769 (3.665–12.036)*
	+O <sub>3</sub>	1.008(1.004–1.012)*	8.283 (4.360–12.354)*
	+PM <sub>2.5</sub>	1.009(1.004–1.013)*	8.631 (4.538–13.367)*
CO	NULL	1.0003(1.0001–1.0005)*(lag04)	0.334 (0.118–0.550)*
	+PM <sub>10</sub>	1.0003(1.0001–1.0005)*	0.300 (0.074–0.527)*
	+SO <sub>2</sub>	1.0003(1.0001–1.0005)*	0.208 (0.090–0.525)*
	+NO <sub>2</sub>	1.0003(1.0001–1.0005)*	0.278 (0.059–0.498)*
	+O <sub>3</sub>	1.0003(1.0001–1.0005)*	0.334 (0.118–0.551)*
	+PM <sub>2.5</sub>	1.0003(1.0001–1.0006)*	0.324 (0.095–0.553)*

**Notes:** \*P < 0.05; Null: pollution effect corresponding to single pollution model.

**Abbreviations:** CI, confidence interval; PM, particulate matter; CO, carbon monoxide; SO<sub>2</sub>, sulfur dioxide; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; RR, relative risk.

and PM<sub>2.5</sub>, with O<sub>3</sub> having the greatest effect. NO<sub>2</sub> remained statistically significant after including SO<sub>2</sub>, CO, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>, with the inclusion of PM<sub>2.5</sub> having the greatest effect. CO was statistically significant when NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> models were included, with O<sub>3</sub> having the greatest effect.

## Discussion

Our study showed that environmental levels of SO<sub>2</sub>, NO<sub>2</sub>, CO, PM<sub>10</sub>, and PM<sub>2.5</sub> were associated with hospitalization in children with asthma, with SO<sub>2</sub> having the strongest association. A stratified analysis by sex showed that CO, PM<sub>10</sub>, and PM<sub>2.5</sub> had greater impacts on asthma admissions in girls, and SO<sub>2</sub> had a greater impact on asthma admissions in boys. A stratified analysis by age showed that PM<sub>2.5</sub> and PM<sub>10</sub> had greater impacts on asthma admissions in children aged 5–6 years old; SO<sub>2</sub> mainly affected children aged 0–4 years and 7–18 years, whereas NO<sub>2</sub> and CO mainly affected children aged under 7 years old. Stratified analysis by season showed that SO<sub>2</sub>, NO<sub>2</sub>, and CO significantly influenced asthma admission during the winter.

Many previous studies have shown a relationship between air pollutants and asthma. Nonetheless, most of these studies have focused on developed countries in Europe and the United States or on adults.<sup>25–28</sup> However, due to factors such as longer outdoor stays, more active outdoor activities, higher respiratory rates, limited metabolic capacity owing to incomplete lung development, and more air pollutants inhaled and retained per unit weight, children are often more vulnerable to the adverse effects of air pollution than adults.<sup>29</sup> Recently, an increasing number of Chinese researchers have focused on the harmful effects of atmospheric pollution on children's respiratory health.<sup>20,30</sup>

This is the first study in Chengdu on the relationship between air pollutants and asthma admissions in children. Our findings may provide a reference for improving environmental air quality, thereby preventing asthma attacks, and reducing the burden of asthma.

In the Air Quality Guideline (AQG) recommended by the World Health Organization in 2021, the AQG values of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, CO and O<sub>3</sub> were 15µg/m<sup>3</sup>, 45µg/m<sup>3</sup>, 40µg/m<sup>3</sup>, 25µg/m<sup>3</sup>, 4 mg/m<sup>3</sup> and 100 µg/m, respectively.<sup>3,31</sup> Except for CO, all other pollutant concentrations exceeded the AQG values, particularly PM<sub>10</sub>, which exceeded 90.92% of the days during the study period. For children aged < 5 years, airway hyper-responsiveness and asthma symptoms are more common in boys than in girls, with a ratio of approximately 2:1. High sensitivity to asthma in males persists until adolescence, making them vulnerable to ambient air pollution.<sup>32</sup> Children aged 0–4 years accounted for 81.56% of the study participants, and most (67.06%) were boys. Other scholars have found similar research results.<sup>33–37</sup>

Particulate matter (PM) originates from a wide range of sources and consists of a mixture of liquid and solid particles suspended in air. It is the main carrier of pollutants released by human activity. PM<sub>10</sub> and PM<sub>2.5</sub> refer to particles with a diameter < 10 µm and < 2.5 µm, respectively.<sup>20</sup> The respiratory system is the direct target organ of PM<sub>2.5</sub> and PM<sub>10</sub>, and the mechanism of PM-induced asthma attacks may be related to oxidative stress, immune inflammation damage, and airway hyperresponsiveness.<sup>12</sup> Our study found that levels of PM<sub>2.5</sub> and PM<sub>10</sub> were significantly related to hospitalization for asthma in children, with a more significant cumulative lag effect, which is consistent with other studies conducted in Turkey, Denmark, and China.<sup>35–40</sup> A study in Hong Kong on the impact of air pollution on asthma hospital admission rates found that PM<sub>2.5</sub> concentration led to the greatest increase in the risk of asthma admission at lag04 (2.4%) and PM<sub>10</sub> at lag05 (2.3%) in the 0–14 year age group.<sup>14</sup> This was consistent with our findings that PM<sub>2.5</sub> had the greatest increase in asthma admission risk at lag04 and PM<sub>10</sub> at lag05. A Greek study of factors influencing acute hospitalizations for asthma in children aged 0–14 years found that for every 10 µg/m<sup>3</sup> increase in PM<sub>10</sub>, the number of children hospitalized for asthma increased by 2.54% (95% CI: 0.06–5.08%),<sup>33</sup> which is consistent with our study findings. However, a study in New York found no association between pollutants and urban asthma among children with higher asthma prevalence.<sup>13</sup> This may be related to the differences in age structure, sex ratio, lifestyle, behavioral activities, and air pollutant concentration of different populations. A clear explanation for this difference in the impact of PM<sub>10</sub> and PM<sub>2.5</sub> on asthma-related hospitalizations remains elusive.

The main sources of SO<sub>2</sub> in China are emissions during energy production and industrial processes, and their toxic effects on patients with asthma are biologically reasonable. Studies have found that SO<sub>2</sub> is associated with the onset and exacerbation of asthma caused by increased airway inflammation, eosinophilia, bronchospasm, and airway obstruction. The higher the concentration of SO<sub>2</sub>, the more severe the airway contraction.<sup>12</sup> Our study found a significant correlation between SO<sub>2</sub> exposure and hospitalization for childhood asthma, consistent with the conclusions of other studies<sup>33,35,37,38</sup> and meta-analyses.<sup>41,42</sup> Our study also found that SO<sub>2</sub> had the greatest impact on hospital admissions for asthma, which

is consistent with the research findings in Taiwan.<sup>37</sup> However, a study in Hong Kong found no significant association between increased SO<sub>2</sub> concentrations and the risk of hospitalization for asthma in children aged 0–14 years.<sup>14</sup> In China, burning coal fuel for home heating also produces SO<sub>2</sub>. We speculate that the source and distribution concentration of SO<sub>2</sub> may be inconsistent in different countries or in different regions of the same country, and the different economic conditions and behavioral activities of the study population may also lead to different research results.

NO<sub>2</sub> is formed mainly by the O<sub>3</sub> reaction with the NO emitted during the burning of fossil fuels.<sup>12</sup> Although many epidemiological studies have shown that NO<sub>2</sub> exposure is significantly associated with an increase in asthma incidence,<sup>35,37–39</sup> relatively few toxicological studies exist. Some studies have shown that the toxic effect of NO<sub>2</sub> might be related to the lipid peroxidation of cell membranes caused by O<sub>3</sub> and the production of various free radicals, which altogether damage the structure and function of the asthmatic airway and enhance the airway response of asthmatic individuals to inhaled allergens.<sup>43</sup> A study in Hong Kong found that elevated NO<sub>2</sub> concentrations led to the greatest increase (3.9%) in the risk of asthma hospitalization in the 0–14 year age group at lag04 day,<sup>14</sup> which is similar to our findings.

Unfortunately, it remains uncertain whether a direct relationship exists between CO and asthma, and some studies on the relationship between CO and asthma have been conducted only in adults and outpatient visits. A study in Chongqing found that short-term exposure to CO might lead to hospitalization for childhood asthma.<sup>35</sup> A meta-analysis showed that the lag exposure was 1 d for CO,<sup>44</sup> which was consistent with our finding that the single-day lag effect of CO was the greatest at lag1.

O<sub>3</sub> is a strong oxidant that can cause respiratory symptoms by inducing increased airway reactivity, airway damage, inflammation, and systemic oxidative stress.<sup>45</sup> O<sub>3</sub> contributes to more severe asthma symptoms and an increase in hospital admissions.<sup>46</sup> Currently, research on the impact of O<sub>3</sub> exposure on asthma remains inconsistent. A study conducted in Seoul, South Korea, showed that an increase in O<sub>3</sub> levels (IQR) could lead to a 5% increase in daily hospital admissions for children with asthma.<sup>47</sup> A study in Hefei, China, found that O<sub>3</sub> concentration was positively associated with hospitalization rates in children with asthma.<sup>36</sup> A study in Hong Kong found that an increase in O<sub>3</sub> concentration increased asthma hospitalization risk by 3.9% in children in the 0–14 age group.<sup>14</sup> However, this study did not find a clear correlation between O<sub>3</sub> and asthma admissions in children, which is consistent with the results of a study in Chongqing.<sup>35</sup> This may be related to factors, such as the different sources of pollutants, population characteristics, and regional climate change in different countries. For example, according to the descriptive results of Hefei,<sup>36</sup> the O<sub>3</sub> concentration in Hefei was higher than that in Chengdu, which may have led to a stronger correlation. In summary, the relationship between O<sub>3</sub> levels and hospitalization due to asthma in children requires further investigation.

Subgroup analyses by age showed that PM<sub>2.5</sub> and PM<sub>10</sub> had greater impacts on asthma admissions in children aged 5–6 years old; however, the effects on admission rates for children aged 0–4 years and 7–18 years were not statistically significant, which is consistent with the findings of a study in Lisbon that found no significant correlation with environmental variables in children aged 0–4 years.<sup>15</sup> A study in Mexico found that an increase in PM<sub>10</sub> and PM<sub>2.5</sub> significantly reduced the relative risk of asthma admissions in children under 5 years old, suggesting no relationship between PM and asthma attacks in this group of young children.<sup>16</sup> A study in Shanghai found that the impact of PM<sub>2.5</sub> on children aged 5–14 years was higher than on children aged 0–4 years ( $P < 0.05$ ).<sup>34</sup> These findings align with our results, possibly because school-aged children engage in more outdoor activities and have prolonged exposure to pollutants. In contrast, preschoolers might be well protected by their parents and may have less exposure to air pollutants. Our study also found that SO<sub>2</sub>, NO<sub>2</sub>, and CO had a larger impact on asthma admissions in children under 5 years of age, possibly due to the frequent exposure of children under 5 years of age to indoor air pollutants produced by burning coal-fired fuel at home and exposure to second-hand smoke. However, a study in Turkey found that an increase in PM<sub>2.5</sub> and PM<sub>10</sub> levels was more closely related to asthma hospitalization in children under 5 years old.<sup>38</sup> This close relation might be due to the varying levels of air pollution and age distribution of populations in different regions.

To date, it has not been confirmed whether sex influences the relationship between asthma admissions and air pollutants. Most studies have concluded that boys are more affected by outdoor air pollution than girls did,<sup>33,37,39,44</sup>

which is inconsistent with our findings. Whether sex affects the relationship between asthma-related hospitalization and air pollutants remains to be confirmed.

We found that PM<sub>2.5</sub> had a significant effect in the single-pollutant model; however, after SO<sub>2</sub>, NO<sub>2</sub>, CO, and O<sub>3</sub> were included, only O<sub>3</sub> remains statistically significant. This indicated that PM<sub>2.5</sub> might be affected by other air pollutants in the single-pollutant model, consistent with the findings of the Hefei study.<sup>36</sup>

This study has some limitations. First, the study was conducted in one city, and the data were obtained from one hospital, limiting the generalizability of our results. Second, the use of the average value of pollutants from fixed monitoring stations cannot reflect children's actual exposure. Pollutant concentrations in different locations within a city can vary greatly depending on traffic intensity, wind direction, speed, and building topography. Third, our study did not include individual factors, such as indoor pollution exposure, smoking, and activity patterns. Finally, although Chengdu is rich in flora and pollen, we did not have pollen data to be used in our models and did not consider the impact of the COVID-19 pandemic and winter flu outbreaks.

## Conclusion

Our study found that air pollutants, including SO<sub>2</sub>, NO<sub>2</sub>, CO, PM<sub>2.5</sub>, and PM<sub>10</sub>, were associated with the risk of hospitalization for childhood asthma, with SO<sub>2</sub> showing the strongest association. We believe that reducing air pollution in Chengdu could prevent hospitalization with asthma as the primary diagnosis. Air pollution indicators can serve as predictive factors for asthma, providing epidemiological evidence for developing prevention strategies to reduce childhood asthma hospitalization risks. Further studies are planned to explore the long-term effects of air pollution on childhood asthma, consider indoor pollution and other individual factors, and include diverse geographical locations for broader applicability.

## Abbreviations

AQG, air quality guidelines; CI, confidence interval; CO, carbon monoxide; DOF, degree of freedom; DOW, day of the week; ER, excess risk; PACF, Partial Autocorrelation Function; GAM, generalized additive model; IQR, interquartile range; ISAAC, International Study of Asthma and Allergies in Childhood; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; PM, particulate matter; R, correlation coefficient; RR, relative risk; SO<sub>2</sub>, sulfur dioxide; WHO, World Health Organization.

## Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Chengdu Women's and Children's Central Hospital [approval B2021(5)]. The study was conducted according to the Declaration of Helsinki. Informed consent was obtained from all the parents or guardians of minors. All research activities were conducted in accordance with hospital's guidelines and requirements.

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## Disclosure

The author(s) report no conflicts of interest.

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