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**Key Points:**

- Short-term exposure to air pollutants is significantly associated with increased hospitalization for cardiovascular disease (CVD)
- Our findings indicate lag effects of air pollution on CVD admissions
- The effects of different lag days of air pollutants on CVD admissions vary by season, gender and age

**Supporting Information:**

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

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# Association Between Air Pollution and Cardiovascular Disease Hospitalizations in Lanzhou City, 2013–2020: A Time Series Analysis

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**Abstract** Extensive evidence has shown that air pollution increases the risk of cardiovascular disease (CVD) admissions. We aimed to explore the short-term effect of air pollution on CVD admissions in Lanzhou residents and their lag effects. Meteorological data, air pollution data, and a total of 309,561 daily hospitalizations for CVD among urban residents in Lanzhou were collected from 2013 to 2020. Distributed lag non-linear model was used to analyze the relationship between air pollutants and CVD admissions, stratified by gender, age, and season. $PM_{2.5}$, $NO_2$, and CO have the strongest harmful effects at lag03, while $SO_2$ at lag3. The relative risks of CVD admissions were 1.0013(95% CI: 1.0003, 1.0023), 1.0032(95% CI: 1.0008, 1.0056), and 1.0040(95% CI: 1.0024, 1.0057) when $PM_{2.5}$, $SO_2$, and $NO_2$ concentrations were increased by 10 μg/m³, respectively. Each 1 mg/m$^3$ increase in CO concentration was associated with a relative risk of cardiovascular hospitalization of risk was 1.0909(95% CI: 1.0367, 1.1479). We observed a relative risk of 0.9981(95% CI: 0.9972, 0.9991) for each 10 μg/m³ increase in $O_3$ for CVD admissions at lag06. We found a significant lag effects of air pollutants on CVD admissions. $NO_2$ and CO pose a greater risk of hospitalization for women, while $PM_{2.5}$ and $SO_2$ have a greater impact on men. $PM_{2.5}$, $NO_2$, and CO have a greater impact on CVD admissions in individuals aged <65 years, whereas $SO_2$ affects those aged ≥65 years. Our research indicates a possible short-term impact of air pollution on CVD. Local public health and environmental policies should take these preliminary findings into account.

**Plain Language Summary** Extensive evidence indicates that air pollution increases the risk of cardiovascular disease (CVD) admissions. We explored the effect of air pollution on the number of CVD admissions among Lanzhou residents and its lag effects. Meteorological data, air pollution data, and a total of 309,561 daily hospital admissions for CVD among urban residents in Lanzhou were collected from 2013 to 2020. Distributed lag non-linear model was used to analyze the relationship between air pollutants and CVD admissions, stratified by gender, age, and season. We found a significant lag effects of air pollutants on CVD admissions. $NO_2$ and CO caused a greater risk of admissions in women, while the opposite was true for $PM_{2.5}$ and $SO_2$. $PM_{2.5}$, $NO_2$ and CO had a greater effect on people under 65 years of age, while the opposite was true for $SO_2$. Our findings suggest that air pollution has a short-term effect on CVD. These findings have important implications for local public and environmental policies and strategies.

## 1. Introduction

As the world's climate and air quality deteriorate, public health authorities are gravely concerned about the health damage caused by exposure to air pollution (Heroux et al., 2015). A landmark resolution on air quality and health was accepted by the World Health Assembly in 2015, acknowledging air pollution as a risk factor for non-communicable diseases. Almost all of the world's population breathes air that exceeds the air quality guideline limit set by the World Health Organization (Perez Velasco & Jarosinska, 2022). Both long-term and short-term air pollution can cause a significant burden of disease, including an increased risk of hospitalization for CVD (Cohen et al., 2017; He et al., 2022). According to a study published in Journal of the American College of Cardiology, numerous studies have shown that air pollution and the development of CVD are generally correlated (Rajagopalan et al., 2018). About one-third of all deaths worldwide in 2019 had the CVD as the primary cause, accounting for 8.9 million deaths in female and 9.6 million deaths in men. The highest number of CVD deaths occurred in China (Newman et al., 2020). China, which has the world's biggest population, is struggling with a serious problem with ambient air pollution (Luo et al., 2017). Furthermore, exposure to ambient air pollution

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not only has a negative impact on public health but also has a negative financial impact (Jaafar et al., 2018; Zha et al., 2022). The exploration of the magnitude and extent of air pollution and its relationship to CVD provides better evidence for understanding the actual impact of air pollution on CVD. It also helps to focus the attention of relevant authorities on air pollution as a little-known but important determinant of CVD (Fuller et al., 2018). It is necessary to study the effects of air pollution on these CVD in order to prevent them in a targeted manner in China.

Lanzhou is one of the first cities in China to receive modern industrial civilization, and is also an important comprehensive transportation hub and the core node city of the Silk Road Economic Belt. During the past period, Lanzhou was one of the most polluted cities in China, but in recent years it has seen a significant reduction in air pollution and was mentioned in the 2015 Paris Climate Change Conference as having good air pollution control (Su et al., 2019). This transformation enables us to conduct more rigorous research on whether short-term exposure to environmental air pollutants in Lanzhou continues to have deleterious impacts on human health.

In this study, we collected daily air pollutants, daily mean temperatures, and daily hospitalization data for CVD of residents from 1 January 2013 to 31 December 2020 in Lanzhou city. We used distributed lag non-linear models (DLNM) to analyze the short-term effects of air pollutants on the number of urban residents hospitalized with CVD and their lag effects, and also stratified the hospitalized patients by gender, age, and season to provide a scientific basis for taking appropriate measures against climate change.

## 2. Materials and Methods

### 2.1. Study Area

Lanzhou, with a permanent population of approximately 4.4 million, is the capital of Gansu Province and located at the geometric center of China's land area map (longitude 102°36′ ~ 104°35′ east and latitude 35°34′ ~ 37°00′ north). According to the relevant data from the Government Statistical Bureau, the male population accounts for 51.38% of the total population, while the population aged ≥65 years accounts for 11.70%. It is an industrial city primarily focused on petrochemical and machinery industries, with major sources of pollution including vehicular emissions and industrial discharge. Lanzhou sits at an altitude of about 1,520 m, deep in the northwest inland, and has a temperate continental climate. It is a typical river valley basin with an average annual temperature of 10.3°C and an average annual precipitation of 327 mm. Lanzhou experiences strong sunshine, low precipitation, high evaporation, low wind speed, and a high incidence of temperature inversion, resulting in frequent temperature inversion events.

### 2.2. Material Sources

#### 2.2.1. Hospital Data

Based on a comprehensive consideration of factors such as service quality, medical expertise, and location of hospitals within the urban area of Lanzhou, this study selected seven Grade III general hospitals, which are widely regarded as the best comprehensive hospitals in Lanzhou and have authoritative status in the diagnosis and treatment of CVD. These hospitals cover the main urban areas of Lanzhou. Admission and discharge data of local residents in Lanzhou city diagnosed with cardiovascular system diseases from 1 January 2013 to 31 December 2020 were collected, including information on gender, age, home address, date of hospitalization, date of discharge, and hospital diagnosis. The collected data covers patients of all ages and distinguishes them into two groups: ≥65 years old and <65 years old (Cheng et al., 2019; Ma, Zhao, et al., 2017). Data of hospitalized patients was screened according to the International Classification of Diseases, Tenth Revision, and all cases coded I00 to I99 (CVD) were included in this study. The inpatient medical record data used in the study was directly obtained from the hospital information center. The inpatient data was logically corrected to exclude data with missing and duplicate information such as gender, age, date of visit, and International Classification of Diseases (ICD) code in the visit data. Patients were screened according to their residential address, and those whose residential address was not in Lanzhou were excluded to ensure that all included patients were local residents of Lanzhou. Over 85% of urban residents diagnosed with CVD in Lanzhou would choose these hospitals for diagnosis and treatment, suggesting that the hospitalization data collected in this study is a representative sample of the common CVD in Lanzhou (Ma, Zhang, et al., 2017).

### 2.2.2. Air Pollution Data and Meteorological Data

Air pollution monitoring data for Lanzhou City from 1 January 2013 to 31 December 2020 were collected from the National Real-Time Urban Air Quality Release Platform, including daily monitoring data for $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, $O_3$, and CO. The $O_3$ is the 8-hr daily maximum average and all other air pollutants are 24-hr averages. The air pollutant information comes from three state-controlled monitoring stations in Lanzhou city, namely the Provincial Construction Workers' Hospital, the Railway Design Institute, and the Biological Products Research Institute. This study monitored the air quality in Lanzhou city at three national-level air quality monitoring stations according to the standards (GB3095-2012) and (HJ633-2012), and the results were released in real-time by the China Environmental Monitoring Station. The measured indicators include the 1-hr and 24-hr average concentrations of $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, $O_3$ and CO, as well as the daily maximum 8-hr sliding average concentration of $O_3$. The missing value percentages for $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, $O_3$, and CO are 0.75%, 0.62%, 0.72%, 0.58%, 0.62%, and 0.82%, respectively. For missing values of pollutant concentrations, adjacent day averages were used to predict the missing data. The maximum correlation coefficients between air pollutants $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, $O_3$, and CO at the three monitoring stations are 0.844, 0.883, 0.732, 0.803, 0.808, and 0.877, respectively, indicating significant correlations (Phosri et al., 2019; Sofwan et al., 2021). It indicates that daily average concentrations can represent the exposure level, and this is consistent with previous studies (Motesaddi Zarandi et al., 2022; Zhang et al., 2017). To prevent pollution sources from exerting dominant influence on monitoring data, these national-level air quality monitoring stations are located far away from the main roads, industrial sources, and pollutants, ensuring that the monitoring results can reflect the overall air pollution level in Lanzhou. The reliability and accuracy of the data are guaranteed. The meteorological monitoring data utilized in this study was sourced from government meteorological departments and included information on temperature and average humidity. The data was collected from a robust and dependable monitoring system, and subjected to rigorous quality control and verification procedures by professional meteorological monitoring personnel, thereby ensuring the completeness and accuracy of the data set.

## 2.3. Statistical Analysis

Descriptive analyses of meteorological indicators, atmospheric pollutant concentrations, and CVD admissions were performed for the study period. The indicators analyzed were means, standard deviations, minimum, maximum, and quartiles ($P_{25}$, $P_{50}$, $P_{75}$). In this study, air pollutants were used as the main exposure variable, while meteorological factors such as temperature and relative humidity were proposed to be included in the model as confounding factors. But multicollinearity may exist among the factors, and Spearman correlation analysis was first performed for each pollutant to reduce the effect of multicollinearity on the results. Considering that the effect of air pollutants on disease presents a nonlinear effect with some persistence and lag, a distributed lag nonlinear model was used to analyze the relationship between air pollutants and daily hospitalizations for CVD, and since daily hospitalizations for CVD are small probability events whose distribution approximates a Poisson distribution, to avoid the problem of overdispersion, quasi-Poisson was used as the connecting function, and each pollutant was modeled separately. The effects of the day of week (DOW) and Holiday were controlled by using a categorical variable. Therefore, we combined the generalized additive model (GAM) with a quasi-Poisson distribution to construct DLNM to estimate the relationship between exposure to pollutants and CVD admissions. The model is constructed as follows:

$$\begin{aligned}\mathrm{Log}(\mu t) = \alpha + \beta Xt, l + ns(\mathrm{Temp}, df = 3) + ns(\mathrm{RHt}, df = 3)\\ + ns(\mathrm{time}, df = 7) + \mathrm{DOW} + \mathrm{Holiday}\end{aligned}$$

$\alpha$ represents the intercept; $Xt,l$ is the air pollutant cross-base matrix; $\beta$ is the matrix coefficient; $t$ represents inpatient days, and $l$ is the number of lag days; *ns* represents the natural smoothing spline function; DOW represents the indicator variable for the "day of the week effect"; Holiday is the day of the holiday effect. This study employed the Quasi Akaike Information Criterion (Q-AIC) to assess model fitting and integrated prior literature to determine the optimal model with the most suitable degrees of freedom. A natural spline function with degrees of freedom set to 3 was used to control for temperature and relative humidity. Using ns fitted time functions, the choice of degrees of freedom is more critical, combining previous studies to choose $df = 7$, controlling for long-term trends and seasonality. In our study, we choose the degrees of freedom based on the minimum value of Q-AIC, and a smaller value of Q-AIC indicates a better model.

We first used a single-pollutant model to explore the short-term effects of each air pollutant concentration on CVD admissions. We identified the lag day with the largest estimated effect in the single-pollutant model to conduct the following subgroup analysis. Effects were observed for different lag days, including single-day lags (lag0–lag7) and cumulative lags (lag01–lag07). To explore the different effects of air pollutants on CVD in different seasons of the year, we divided it into the warm season (April to September) and cool season (October to December, January to March) for seasonal analysis. In addition, we also examined the effects of air pollutants on age (<65, ≥65) and gender (female and male).

All results were presented as relative risk (RR) of cardiovascular admissions and their 95% Confidence Interval (95% CI). RR was calculated for each 10 μg/$m^3$ increase in air pollutant ($PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and $O_3$) concentration and each 1 mg/$m^3$ increase in CO. The R4.2.2 statistical software was applied for all statistical analysis and the "dlnm" package was to fit the regression model.

### 2.4. Sensitivity Analysis

In order to test the reliability and stability of the results, two methods were used in this study for sensitivity analysis. The lag day with the largest RR value for each pollutant was selected and fitted using a two-pollutant model, and the results were compared between the single and two-pollutant models to verify the reliability and stability of the model. Using different time variables with degrees of freedom (6–10), the change in RR values was observed. If the RR values do not change significantly, it means that the model has some stability and the results are credible.

## 3. Results

The geographical location of Lanzhou city and the distribution of air monitoring stations are shown in Figure 1. Table 1 summarizes the basic statistics of CVD admissions, air pollutants and meteorological factors in Lanzhou

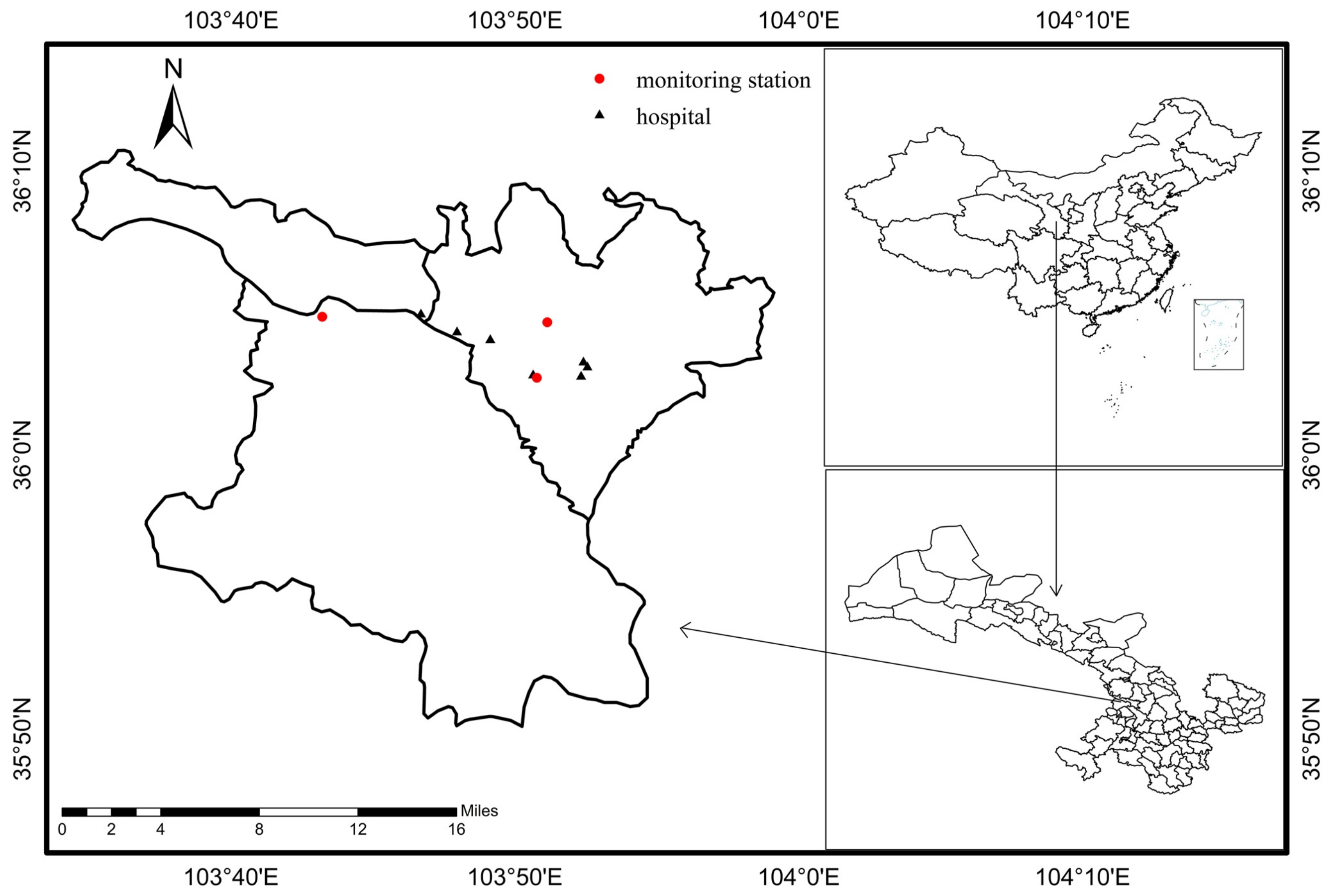


**Figure 1.** Geographic location of air monitoring stations and hospitals in Lanzhou.

from 2013 to 2020. During the study period, there were a total of 309,561 admissions due to CVD, among which 182,713(59.02%) were males. Additionally, 173,168(55.94%) were <65 years old. For atmospheric pollutants, the concentrations of $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, $O_3$, and CO were 114.65 μg/m³, 49.74 μg/m³, 21.64 μg/m³, 45.89 μg/m³, 83.76 μg/m³, and 1.16 mg/m³, respectively (2013–2020). The average daily temperature was 11.13°C and the average relative humidity was 51.19%.

Figure 2 and Figure S2 in Supporting Information S1 demonstrate the relative risks of CVD hospitalization with a lag of 0–7 days after exposure to air pollution, using both three-dimensional and contour plots. The contour plot allows for a clear visualization of the RR values across the entire range. Figure 3 presents a time series plot showing the daily variation in air pollutant concentrations and CVD admissions over the study period. CVD admissions fluctuated seasonally, with slightly more CVD admissions occurring during the cold season (October to March of the following year) than during the warm season (April to September), and CVD admissions increasing each year over the research period. The daily concentrations of $PM_{10}$, CO, $SO_2$, and $PM_{2.5}$ generally show a decreasing trend year by year, and $NO_2$ and $O_3$ show an increasing trend year by year. However, they all have cyclical fluctuation characteristics. The seasonal patterns of $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and CO are low concentrations in warm season and high concentrations in cold season, and the opposite for $O_3$.

We describe the correlations between meteorological factors and air pollutants. The correlation coefficient ($r = 0.850$) indicates that $PM_{2.5}$ and $PM_{10}$ exhibit the strongest correlation among the variables studied. Both CO and $O_3$ have a negative association with other air pollutants. The results of the correlation analysis between other air pollutants are similarly listed (Table S2 in Supporting Information S1).

Figure 4 shows the RR of CVD admissions for each 10 $\mu g/m^3$ increase in air pollutant ($PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and $O_3$) concentrations and each 1 $mg/m^3$ increase in CO in the single pollutant model. All five air pollutants other than ozone contributed to the increase in CVD admissions. Table S4 in Supporting Information S1 shows the specific values of RR and 95% confidence intervals for air pollutants with different lag days. The relative risks of CVD admission were 1.0013(95% CI: 1.0003, 1.0023), 1.0032(95% CI: 1.0008, 1.0056), and 1.0040(95% CI: 1.0024, 1.0057) when $PM_{2.5}$, $SO_2$, and $NO_2$ concentrations were increased by 10 $\mu g/m^3$, respectively. Each 1 $mg/m^3$ increase in CO concentration was associated with a RR of cardiovascular hospitalization was 1.0909(95% CI: 1.0367, 1.1479). $O_3$ was associated with a RR of 0.9981(95% CI: 0.9972, 0.9991) at lag06 and reached a maximum of 1.0004(95% CI: 0.9998, 1.0011) at lag4, after which the RR of each air pollutant gradually decreased. However, $PM_{10}$ was not found to be significantly associated with CVD admissions at any lag day. CO had the greatest effect on CVD admissions among the six pollutants. Considering the cumulative lag effects, Figure 5 shows the RR of cumulative lag day of CVD admissions for each 10 $\mu g/m^3$ increase in air pollutant ($PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and $O_3$) concentration and each 1 $mg/m^3$ increase in CO. The largest effects of air pollution-related CVD hospitalization were observed for $NO_2$, CO, and $PM_{2.5}$ at lag03, respectively, while $SO_2$ at lag3. However, no significant associations for CVD admissions were found for $PM_{10}$ and $SO_2$ at any cumulative lag day. It was observed that the RR of CVD admissions varied by age and gender group for each air pollutant concentration increase. Figure 6 illustrates the RR (95% CI) of CVD admissions due to air pollution in different seasons, including single and cumulative lags for all days.

Figure 7 depicts the exposure-response curves for the effect of each pollutant on the number of CVD admissions. It can be seen that the trend of exposure-response relationship between the effects of $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, $O_3$ and CO on CVD admissions and air pollution is approximately linear. The values of RR increased with increasing pollutant concentrations.

The stratified analysis also showed that the effect between air pollutants and CVD admissions differed between the cold and warm seasons (Figure S1 in Supporting Information S1). A significant association between air pollutants and CVD admissions in the whole population was observed only for CO and $NO_2$ in the cold period, while in the warm season, a greater effect of $PM_{10}$ and $PM_{2.5}$ was observed for females compared to males. In the cold season, the effects of $SO_2$ and CO were greater in males and in the ≥65 years group. $NO_2$ has a higher effect on males than females in the cold season.

After determining the highest RR for each pollutant in the single-pollutant model, we added additional pollutants to constructed the two-pollutant model (Table S1 in Supporting Information S1). Only the two-pollutant model

**Table 1**
*Descriptive Statistics for Air Pollutants, Meteorological Factors and Cardiovascular Disease Admissions in Lanzhou, China, 2013–2020*

| | Mean (SD) | Min | $P_{25}$ | Median | $P_{75}$ | Max | Cases |
|---|---|---|---|---|---|---|---|
| Air pollutant concentration | | | | | | | |
| $PM_{10}$ μg/m³ | 114.65(83.11) | 16.00 | 70.00 | 98.78 | 136.21 | 1484.54 | – |
| $PM_{2.5}$ μg/m³ | 49.74(29.27) | 9.00 | 31.00 | 42.77 | 60.80 | 278.00 | – |
| $SO_2$ μg/m³ | 21.64(14.47) | 3.54 | 10.86 | 17.57 | 28.60 | 115.51 | – |
| $NO_2$ μg/m³ | 45.89(17.95) | 6.32 | 34.00 | 44.56 | 54.63 | 146.60 | – |
| $O_3$ μg/m³ | 83.76(43.56) | 8.00 | 53.00 | 76.00 | 107.00 | 462.00 | – |
| CO mg/m³ | 1.16(0.69) | 0.05 | 0.70 | 0.96 | 1.41 | 4.65 | – |
| Meteorological measurement data | | | | | | | |
| Temperature (°C) | 11.13(9.88) | −12.30 | 2.23 | 12.60 | 19.78 | 30.40 | – |
| RH (%) | 51.19(15.28) | 11.71 | 40.00 | 51.85 | 62.00 | 96.09 | – |
| Hospital admissions | | | | | | | |
| Total | 106(70) | 0 | 42 | 100 | 145 | 419 | 309,561(100%) |
| Female | 43(29) | 0 | 17 | 42 | 61 | 179 | 126,848(40.98%) |
| Male | 62(41) | 0 | 26 | 59 | 86 | 254 | 182,713(59.02%) |
| Age <65 years | 59(40) | 0 | 21 | 44 | 64 | 228 | 173,168(55.94%) |
| Age ≥65 years | 47(30) | 0 | 11 | 18 | 29 | 212 | 136,393(44.06%) |
| Cold | 105(72) | 0 | 42 | 101 | 151 | 419 | 153,408(49.56%) |
| Warm | 107(65) | 0 | 45 | 102 | 143 | 397 | 156,153(50.44%) |

constructed with CO had lower effects on CVD admissions than the single-pollutant model, while all other two-pollutant models had higher effects on CVD admissions.

Sensitivity analysis showed that the effect was robust when the degrees of freedom were changed. We adjusted the *df* from 6 to 10, and even after using different degrees of freedom (Table S3 in Supporting Information S1), the RR of $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, CO, and $O_3$ remained relatively stable, indicating that the model we construct is relatively robust.

## 4. Discussion

In this study, the short-term association between exposure to air pollutants ($PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, CO, and $O_3$) and CVD admissions in Lanzhou City from 2013 to 2020 was investigated using a time-series model. The results showed that short-term exposure to $PM_{2.5}$, $SO_2$, $NO_2$, and CO was positively associated with increased risk of CVD admissions, and that there was a significant lag effects of air pollutants on CVD admissions.

From 2013 to 2020, the atmospheric pollutant concentrations in Lanzhou remained relatively stable. Specifically, the annual average concentrations of $PM_{2.5}$ and $PM_{10}$ exceeded the first-tier National Ambient Air Quality Standard (NAAQS) but remained below the second-tier standard. On the other hand, the concentrations of $SO_2$, $NO_2$, $O_3$, and CO were all below the first-tier NAAQS. The pollutant levels demonstrate relative stability throughout the year, but they reach their highest point during the winter season. In the northern regions of China, the burning of coal is a significant method of heating during the winter months. Furthermore, due to the substantial rise in motor vehicle ownership in recent years, motor vehicle emissions have emerged as one of the primary contributors to ambient air pollution in Lanzhou. Additionally, the lower temperatures during winter hinder the dispersion of pollutants in the atmosphere, resulting in their accumulation and culminating in a peak during this season.

In our study, we found that $PM_{2.5}$ had a short-term effect and influenced cardiovascular admissions. Our study is in line with similar research findings. A study conducted in Poland, which involved 31 cities, also confirmed the correlation between hospitalization and concentrations of particulate matter (Adamkiewicz et al., 2022). Another study in Italy showed relative increases in total cardiovascular admissions of 0.55% and 0.97% for each

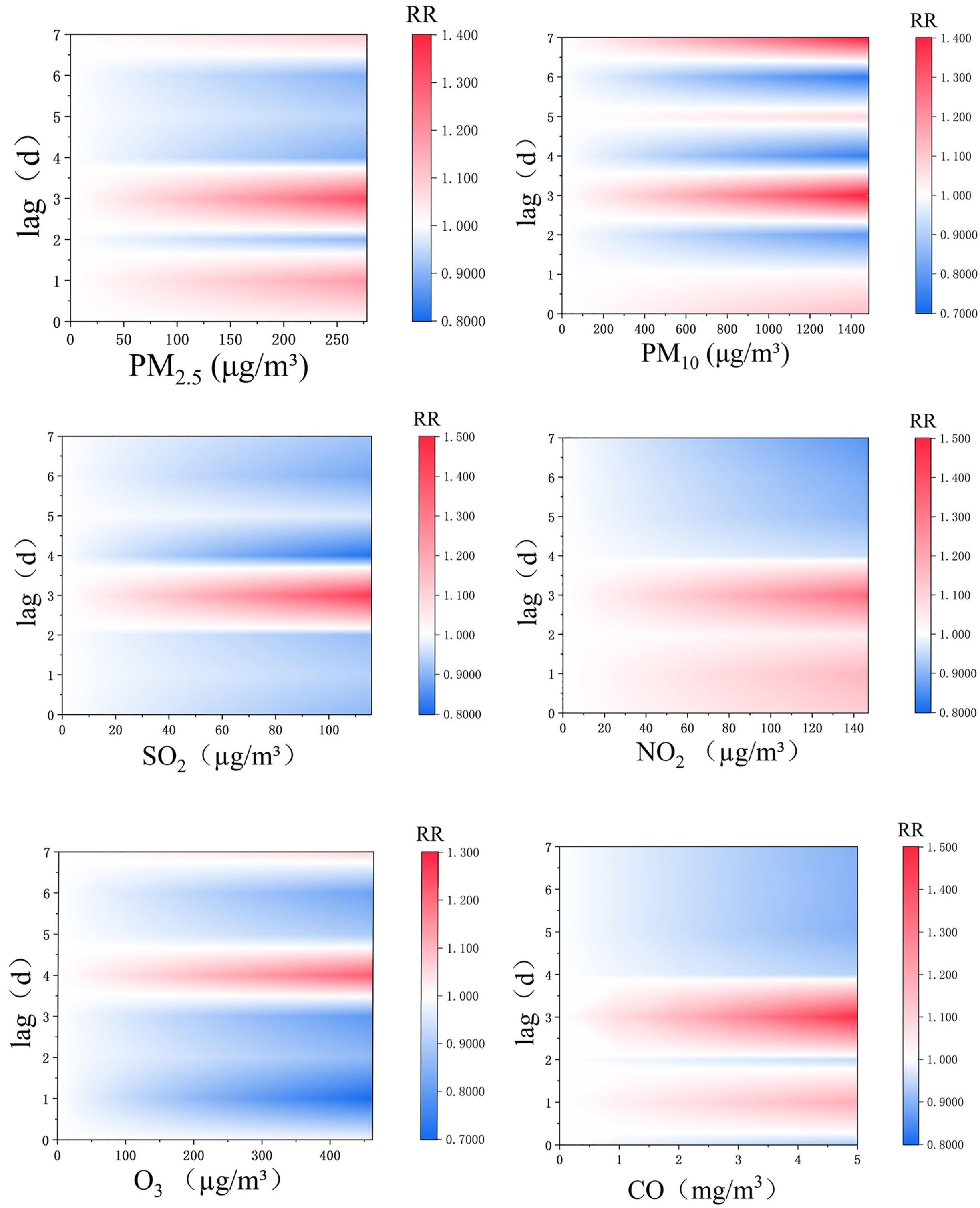


**Figure 2.** Contour plot of the relationship between air pollution and cardiovascular disease admissions.

10 μg/m³ change in $PM_{10}$ and $PM_{2.5}$, respectively (Stafoggia et al., 2022). In a comprehensive study carried out in China, it was evidenced that every 10 μg/m³ rise in $PM_{2.5}$ was correlated with a 0.26% surge (95% CI: 0.17%, 0.35%) in same-day hospitalizations for CVD (Tian et al., 2019). Stratified analysis indicates that males and adults are at a higher risk and more susceptible to the influence of $PM_{2.5}$. The differential social roles and

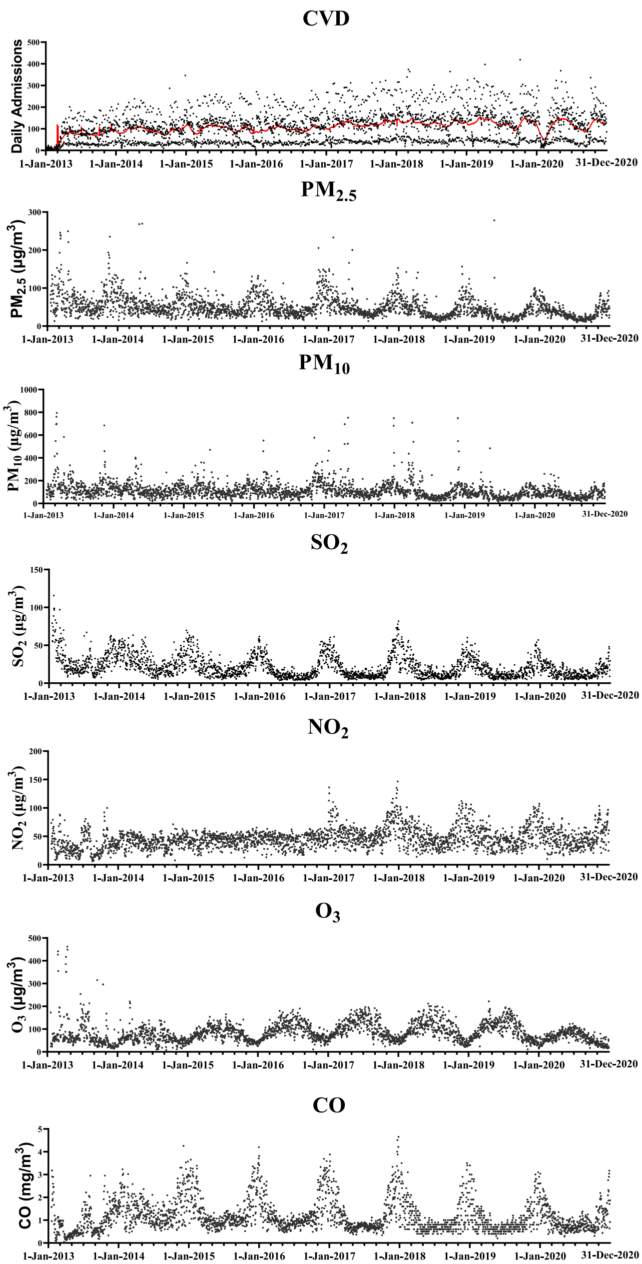


**Figure 3.** Time series of air pollutants and cardiovascular disease admissions in Lanzhou, China.

occupations of males may also contribute to their exposure to air pollution, while young individuals may engage more in outdoor activities, making them more susceptible to air pollution sources. Based on our observations, it has been found that women are more susceptible to the impact of $PM_{2.5}$ during warmer seasons. The harmful effect of $PM_{10}$ on the total hospitalization of CVD during the entire lag period is not significant. The newest reviews also summarized the latest information on CVD after particulate matter exposure, emphasizing the harmful effects of particulate matter inhalation on CVD. Those researches already found sufficient strength of evidence for both short-term exposure to PM and increased risk of CVD mortality and hospitalization rate (Combes & Franchineau, 2019; de Bont et al., 2022; Liu et al., 2013; Orellano et al., 2020).

Abundant research indicates that particulate matter may contribute to an increase in hospitalization rates for cardiovascular diseases. The impact of particulate matter on the cardiovascular system is mediated through various mechanisms, including inflammation, oxidative stress, vascular dysfunction, and disturbances in the central and autonomic nervous systems (Combes & Franchineau, 2019; Rajagopalan et al., 2018; Rao et al., 2018; Ying et al., 2014). These mechanisms may lead to the development and progression of cardiovascular diseases such as atherosclerosis, hypertension, and myocardial infarction. In rodent animal models, prolonged exposure to high concentrations of $PM_{2.5}$ has been shown to induce pathological changes and impaired function in the heart (Li et al., 2015; Su et al., 2020). Notably, even with the many studies on particulate matter and CVD, there is insufficient quantitative evidence to definitively give a precise concentration threshold for particulate matter. Our study provides new and compelling evidence for the link between air pollution and CVD.

Harmful effects of $SO_2$ were observed in both the general population and subgroups. Males and those aged ≥65 had a higher risk. Similar research have discovered a direct association between $SO_2$ levels and both overall and cause-specific CVD admission rates (Amsalu et al., 2019). A similar study conducted in Hefei showed that males and elderly individuals are more susceptible to the effects of $SO_2$ (Zhang et al., 2017). The study conducted in Panzhihua City found a significant correlation between $SO_2$ and increased hospitalization risk for CVD, with a stronger correlation during the cold season than the warm season (Li et al., 2022). Harmful effects of $NO_2$ were observed in both the general population and subgroups. Moreover, females had a higher risk. A study in Kuala Lumpur (Sofwan et al., 2021) and a study in England and Wales (Milojevic et al., 2014) both showed a significant effect of $NO_2$ on increasing CVD admissions. The research conducted in Beijing, Shanghai, and Hefei consistently demonstrates a notable connection between the rise in $NO_2$ concentration and hospital admissions related to CVD (Chen et al., 2018; Ma, Zhao, et al., 2017; Zhang et al., 2017). $SO_2$ mainly originates from the combustion and refining processes of sulfur-containing fuels, whereas $NO_2$ is not only derived from the usage of fossil fuels but also from the increasing emissions of vehicular exhaust (Halim et al., 2020; Jion et al., 2023). During the cold season, increased heating and traffic activities, coupled with stable atmospheric conditions, lead to an increase in pollutants such as $SO_2$ and $NO_2$. Elderly individuals exhibit relatively fragile physiological and immune systems, rendering them more susceptible to environmental pollutants. The mechanisms by which the two gaseous pollutants $SO_2$ and $NO_2$ contribute to CVD can also be explained through several biological pathways, including oxidative stress, the autonomic nervous system, and inflammation (Chuang et al., 2007; Routledge et al., 2006).

We found a significant lag effect of CO on CVD admission. A significant effect was observed in male and elderly. The CO in the environment is primarily generated from incomplete combustion of fossil fuels and biofuels.

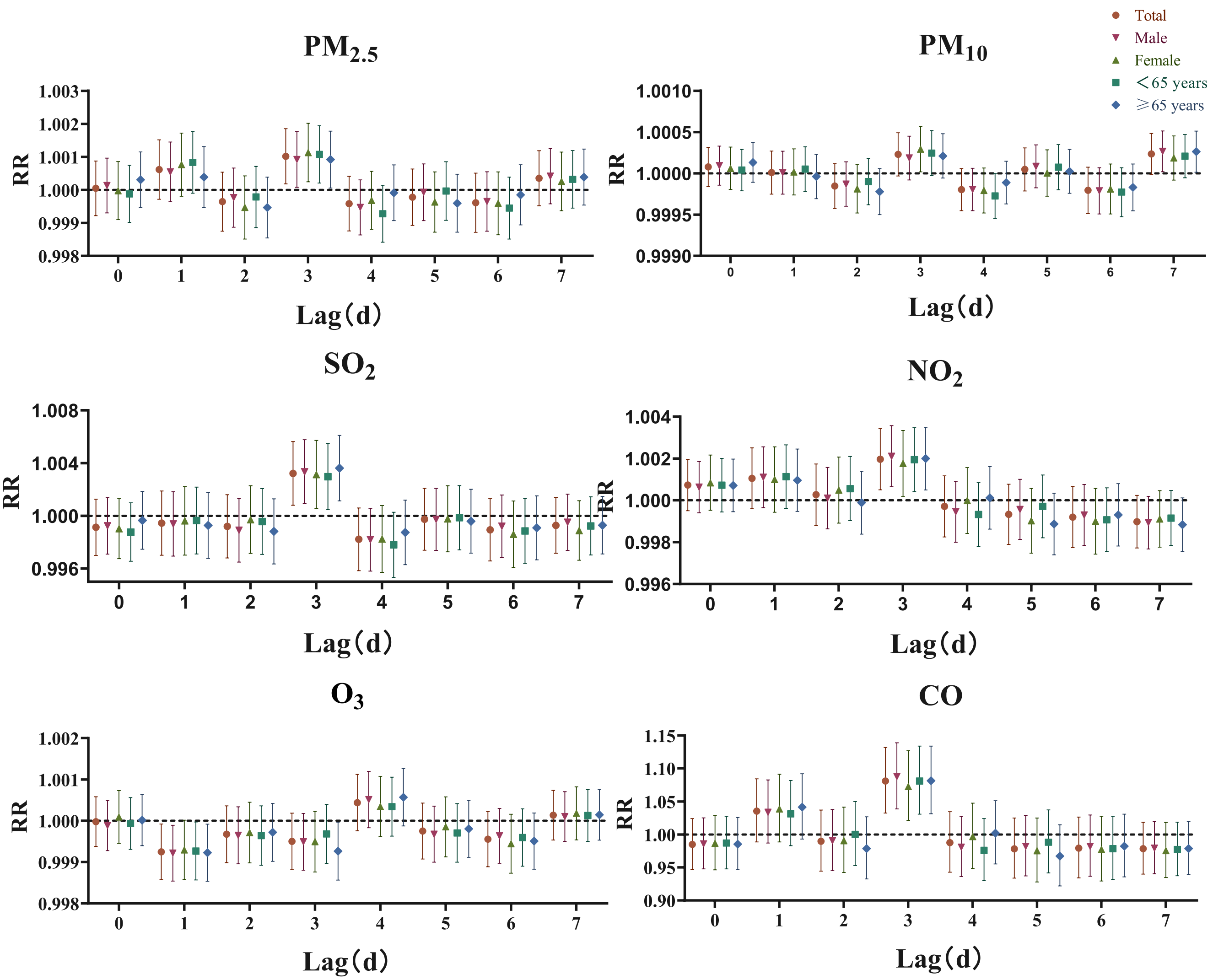


**Figure 4.** Relative risk of single-day lag of cardiovascular disease admissions for each 10 μg/m$^3$ increase in air pollutant ($PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and $O_3$) concentration and each 1 mg/m$^3$ increase in CO.

Similarly, a previous study in Lanzhou showed that each 1 mg/m$^3$ increase in CO concentration was associated with an 11% (95% CI: 3%–20%) increase in the total number of CVD hospitalizations (Cheng et al., 2019). Another study offered definitive evidence establishing that exposure to carbon monoxide below China's current ambient air quality requirements still significantly influences the rate of CVD hospitalizations (Cheng et al., 2019). Male individuals and the elderly are also likely to be more vulnerable to the effects of CO due to physiological differences and higher exposure to environments with elevated CO pollution. As evident from other research findings, there is no discernible threshold between CO and CVD. Thus, in our study, despite the annual average concentration of CO remaining significantly below the current air quality standard in China, we still observed a significant association between short-term exposure to CO and hospitalization for CVD (Liu et al., 2018).

Our research findings also indicate a negative association between $O_3$ exposure and hospitalization due to CVD. Similar studies conducted in London and Singapore have also discovered a negative correlation between $O_3$ exposure and CVD hospitalization rates (Chit-Ming Wong et al., 2002; Ho et al., 2022). Certain clinical applications have indicated that $O_3$ therapy may be especially efficacious for treating CVD (Bocci & Di Paolo, 2009). The review article elucidates the mechanism of action of $O_3$, where short and controlled oxidative stress leads to the generation of reactive oxygen species and lipid peroxidation, while triggering beneficial adaptive responses through the Nrf2 pathway (Re, 2022). However, there is also epidemiological and toxicological evidence suggesting that $O_3$ may have adverse effects on the cardiovascular system (Nuvolone et al., 2018; Phosri et al., 2019).

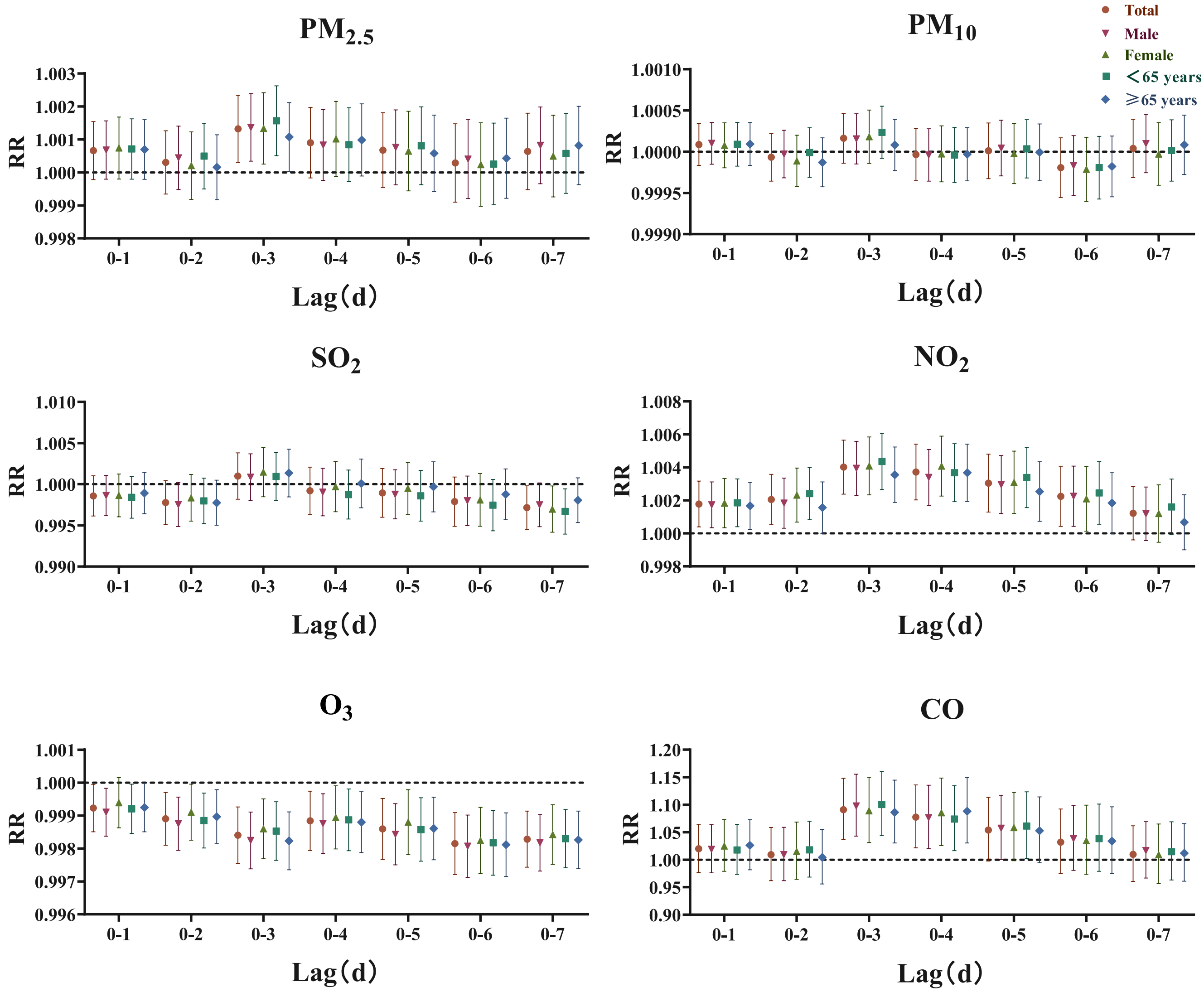


**Figure 5.** Relative risk of cumulative-day lag of cardiovascular disease admissions for each 10 μg/m$^3$ increase in air pollutant ($PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and $O_3$) concentration and each 1 mg/m$^3$ increase in CO.

In a multi-city survey conducted in China, a significant correlation was observed between short-term exposure to ozone and higher CVD mortality rates (Yin et al., 2017). Short-term exposure to $O_3$ in the environment can increase the levels of ACE and ET-1 in human serum, decrease their DNA methylation, and alter lipid metabolism, which may be one of the reasons for ozone's impact on the cardiovascular system (Xia et al., 2018). Empirical studies conducted on animals have provided evidence of the cardiovascular effects of $O_3$ exposure, which include increased heart rate and diastolic pressure, vascular oxidative stress and inflammation (Chuang et al., 2009; Perepu et al., 2010). $O_3$ is a very paradoxical air pollutant. Existing research and clinical applications suggest that the inhalation of $O_3$ is primarily harmful to the entire organism. However, calibrated, low-dose $O_3$ therapy that is appropriately matched to the robust antioxidant capacity of blood can elicit beneficial biochemical mechanisms and reactivate the antioxidant system (Bocci et al., 2009). Determining the effects of environmental $O_3$ exposure on cardiovascular hospitalization remains a significant challenge. The understanding of how $O_3$ affects cardiovascular health is relatively limited, and there is currently no consensus, necessitating further research.

Limitations should be noted when interpreting our results. In this study, our methodology relied on utilizing the mean values of air pollutant concentration measurements obtained from stationary monitoring sites as a proxy for individual exposure, and as such, we did not have access to data on individual-level exposure (Zhang et al., 2017).

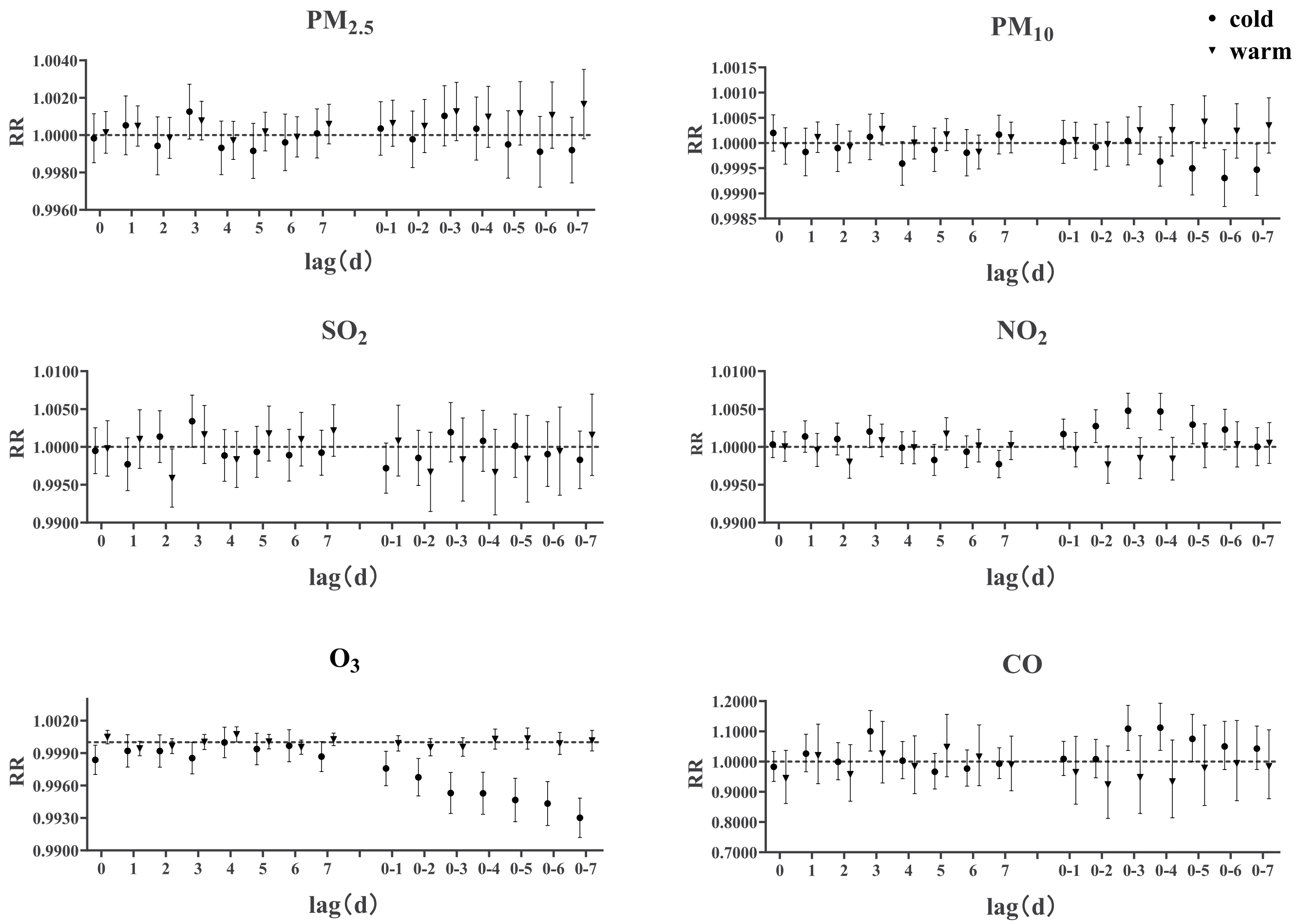


**Figure 6.** The relative risk (95% CI) of cardiovascular disease admissions due to air pollution by season.

A study conducted in Beijing found that using environmental pollution concentration as a proxy for personal exposure may be inaccurate, as the correlation between particulate matter and systemic inflammation weakened when using environmental data (Fan et al., 2020). The absence of individual-level data, including measures of socioeconomic status, occupation, marital status, educational attainment, and smoking behavior, as well as the inability to control for other potential confounding factors that may influence cardiovascular hospitalization, limits the ability to accurately assess the health risks associated with air pollution (Ma, Zhao, et al., 2017). We acknowledge that this study suffers from ecological study biases. Over 85% of Lanzhou residents in our study sought medical services at the hospitals included in the research. While the sample is relatively representative, there is a presence of selection bias, particularly highlighting the Berkson's bias (Wang et al., 2018). As an observational study, this research on the epidemiology of the population in Lanzhou city is typically insufficient to establish causal relationships and can only provide correlations at the group level. Further research is needed to strengthen the investigation of the biological mechanisms underlying the adverse cardiovascular effects of exposure to environmental air pollution. The study did not consider indoor environmental conditions, and the actual concentrations of pollutants indoors and outdoors may differ. This could lead to potential misinterpretations of the research results (Rodopoulou et al., 2015).

## 5. Conclusion

The increase in concentrations of $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and CO is associated with cardiovascular hospitalizations among residents of Lanzhou City, and there are lag effects. When selecting the concentration corresponding to the maximum RR value and lag day as the air pollutant exposure level for CVD hospitalization patients, the effects of the six pollutants on the risk of CVD hospitalization do not have a threshold value. As

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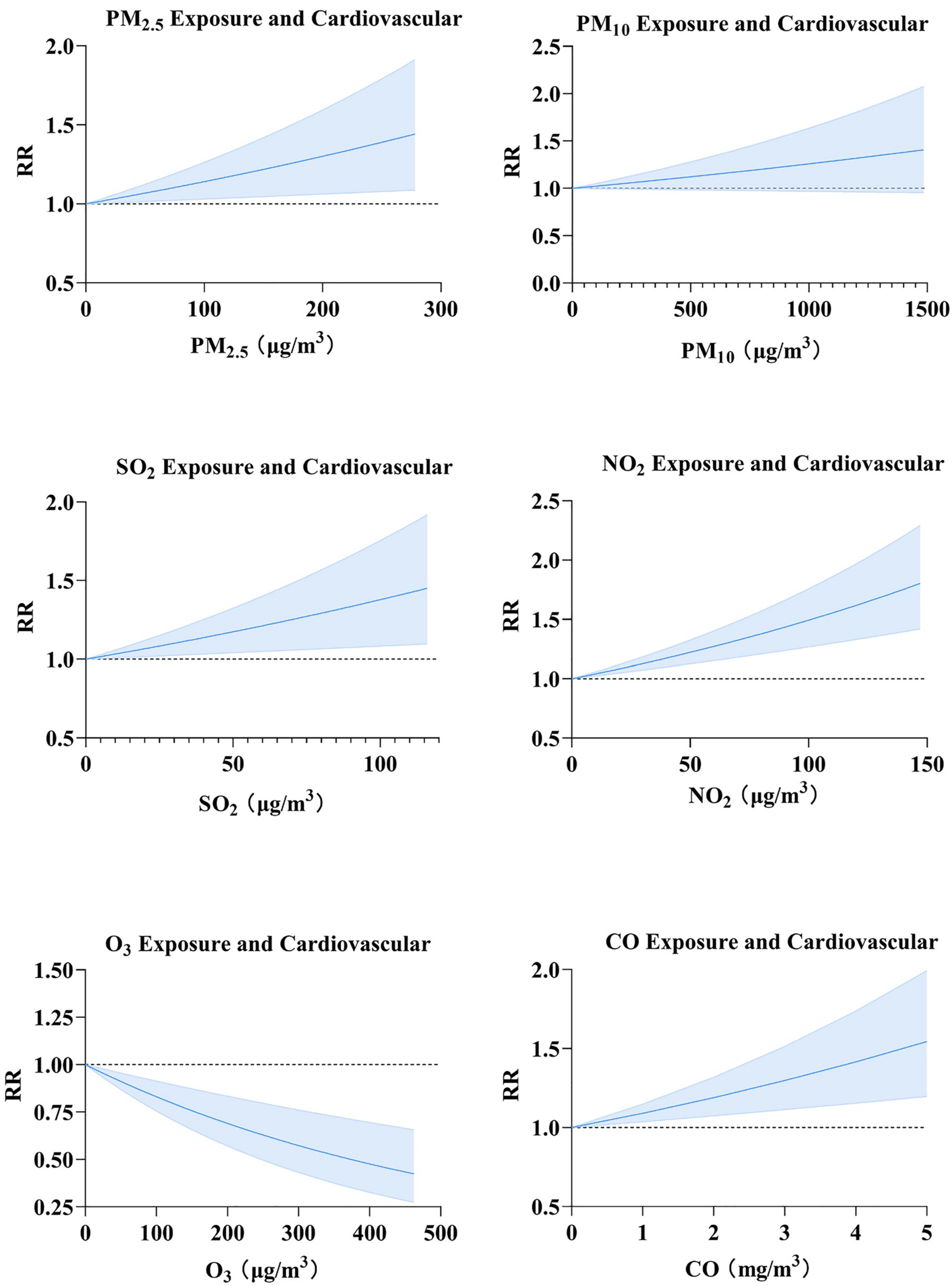


**Figure 7.** Exposure response relationships between six air pollutants and cardiovascular disease admissions.

the concentrations of $PM_{2.5}$, $PM_{10}$, $SO_2$, $NO_2$, and CO increase, the corresponding RR values increase, while $O_3$ shows the opposite trend. The effects of $NO_2$ and CO on females are greater than on males, while the effects of $PM_{2.5}$ and $SO_2$ are the opposite. $PM_{2.5}$, $NO_2$, and CO have the greatest impact on CVD hospitalization in the age group under 65, while $SO_2$ is more likely to affect the age group of 65 and above. The relationship between air pollutants in Lanzhou City and the total number of CVD hospitalizations exhibits a certain seasonal pattern, with the strongest harmful effects often observed during the cold season. Studies have shown that air pollution is closely associated with health problems such as CVD, even at low concentrations of air pollutants. Therefore, further epidemiological research and experimental exploration of biological mechanisms are needed to better understand the impacts of air pollution. Meanwhile, preventive measures should be actively taken to reduce daily air pollution and thus decrease the health risks to humans, including reducing emissions from transportation and industry and promoting the use of clean energy sources.

## Conflict of Interest

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

## Data Availability Statement

Data supporting this research are available in Health Commission of Lanzhou City, with information concerning required licensing and agreements. Other researchers must obtain permission from the relevant authorities to use this data. Due to data policies of the National Health Commission of the People's Republic of China and relevant departments of Lanzhou city, clinical admission data is not open to the public. The air pollution data required for this study can be accessed through the China Air Quality Online Monitoring and Analysis Platform (2023). Translation available via browser plug-in. Presently, the platform provides unfettered and cost-free access to data from a total of 367 cities. To retrieve the data, kindly navigate to the website, select "Lanzhou," and choose data from various time periods. Meteorological data can be accessed at National Meteorological Information Centre of China (2023). Translation available via browser plug-in. Researchers need to register for free on this website before they can access the required data. Clinical hospital admission data are not available to the public. R statistical software and associated packages are openly available for download on GitHub and comprehensive R archive network (CRAN) (Antonio Gasparrini, 2021; Team, 2022).

## Abbreviations

| | |
|---|---|
| CVD | cardiovascular diseases |
| DLNM | distributed lag non-linear models |
| RR | relative risk |
| Q-AIC | Quasi Akaike Information Criterion |
| CI | confidence intervals |
| WHO | World Health Organization |
| PM | particulate matter |
| $PM_{2.5}$ | fine particulate matter |
| $PM_{10}$ | inhalable particles |
| $SO_2$ | sulfur dioxide |
| $NO_2$ | nitrogen dioxide |
| CO | carbon monoxide |
| $O_3$ | Ozone |
| Nrf2 | Nuclear factor erythroid 2-related factor 2 |
| ACE | angiotensin-converting enzyme |
| EF-1 | elongation factor 1 |

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