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RESEARCH ARTICLE

Study on the association between ambient air pollution and daily cardiovascular death in Hefei, China

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Abstract

Cardiovascular disease has always been the most serious public health problem in China. Although many studies have found that the risk of death caused by cardiovascular disease is related to air pollutants, the existing results are still inconsistent. The aim of this study was to investigate the effects of air pollutants on the risk of daily cardiovascular deaths in Hefei, China. Daily data on cardiovascular deaths, daily air pollutants, and meteorological factors from 2007 to 2016 were collected in this study. A time-series study design using a distributed lag nonlinear model was employed to evaluate the association between air pollutants and cardiovascular deaths. First, a single air pollutant model was established based on the minimum value of Akaike information criterion (AIC), and the single day lag effects and multi-day lag effects were discussed separately. Then, two-pollutant models were fitted. Subgroup analyses were conducted by gender (male and female), age (< 65 age and ≥ 65 age), and disease type (ischemic heart disease and cerebral vascular disease). There were 34,500 cases of cardiovascular deaths during the period 2007–2016, and the average concentrations of air pollutants (PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, O_3) were 106.11, 20.34, 30.49, 72.59, 958.7, and 67.88 μg/m^3, respectively. An increase of interquartile range (IQR) in PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 were associated with an increase of 4.34% (95%CI 1.54~7.23%) at lag 0–6, 5.79% (95%CI 2.43~9.27%) at lag 0–5, 4.47% (95%CI 1.64~7.37%) at lag 0–5, 3.14% (95%CI 0.03~6.36%) at lag 0–4, 3.11% (95%CI 0.21~6.10%) at lag 0–3, and 8.17% (95%CI 1.89~14.84%) at lag 0–5 in cardiovascular deaths, respectively. Females, older group (≥ 65 years) and deaths from cerebral vascular disease were more vulnerable to air pollution than males, younger individuals (< 65 years) and deaths from ischemic heart disease. Our results suggest that air pollution increased the risk of cardiovascular deaths in Hefei. These findings can provide evidence for effective air quality interventions in Hefei.

Keywords Cardiovascular disease · Air pollution · Distribution lag nonlinear model · Sensitive population

Jixiang Xu and Wenfeng Geng contributed equally to this work.

Highlights
- The risk of CVD deaths increased with the rising in air pollutant concentrations.
- Females were more vulnerable to air pollution exposure as compared to males which were similar to comparison of ages ≥ 65 and < 65 ages.
- The ER of cerebral vascular disease was significantly correlated with the concentration of PM_{10}, SO_2, and NO_2, where as ischemic heart disease was only determined by O_3.

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Introduction

Cardiovascular disease (CVD) is the leading cause of death in the world (Venkatesan 2016). As estimated by the World Health Organization (WHO), 17.7 million people died of CVD in 2015, accounting for 45% of the world's nonaccidental deaths, and 82% of these CVD deaths occurred in low and middle-income countries (Butler 2011). With the development of economy and the aggravation of population aging, CVD has posed the greatest health burden to the healthcare system of China. In addition, the prevalence and mortality of CVD will continue to rise in the next 10 years (Chen et al. 2017).

CVD is a multi-factorial disorder induced by interaction of heredity, circumstance, and behavior. Smoking and air pollution are the major risk factors of CVD (Gakidou et al. 2017). With the rapid development of industrialization and urbanization, the air quality of China has deteriorated seriously over the past few years. In 2016, air pollution was the fourth-highest risk factor of global burden of disease, leading to approximately 1.58 million deaths and 32.28 million DALYs (Gakidou et al. 2017). The decrease of air pollutant concentration and the improvement in personal protection can prevent CVD effectively, thereby reducing the health and economic burden of CVD.

Previous studies have suggested that air pollution is more associated with lung and respiratory diseases, such as pneumonia (Jiang et al. 2018; Nhung et al. 2017) and asthma (Guo et al. 2018). However, growing number of studies have shown that there is a link between short-term exposure to air pollution and CVD in China (Dehbi et al. 2017; Feng et al. 2019; Liu et al. 2019; Wu et al. 2019; Ye et al. 2016). Dehbi et al. (2017) used a cohort analysis of two large follow-up years in the UK and found that CVD deaths increased with increasing PM_{10}, $PM_{2.5}$, and SO_2. Liu et al. (2019) assessed the association between air pollutants and CVD mortality in Shenyang, China, from 2013 to 2016, and observed that the increments in $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3 were associated with an increase of CVD mortality. Wu et al. (2019) examined the effects of atmospheric particulate matter on CVD deaths due to different causes in Lanzhou, during 2014–2015, and found that elevated concentrations of $PM_{2.5}$, PMC, and PM_{10} had different effects on CVD deaths due to different causes. Ye et al. (2016) reported that for every 10 μg/m^3 increase in $PM_{2.5}$ and PM_{10}, coronary heart disease increased by 0.74% and 0.23% in Shanghai. Feng et al. (2019) explored the relationship between PM_{10} and CVD emergency department admissions in Beijing between January 2013 and December 2013 and found that for a 10 μg/m^3 increment of PM_{10}, the total CVD emergency department admissions increased by 0.29%.

These different studies have demonstrated that air pollutants have a detrimental effect on the occurrence or exacerbation of CVD, but most prior studies were conducted in large cities. The effect of air pollutants on health varied across different regions (Chen et al. 2013; Dong et al. 2013). Hefei is a city with frequent haze events occurring, and its air quality exceeds the national secondary concentration limit every year (Zhang et al. 2017a). Therefore, it is essential to conduct study on the effects of air pollution on residents' health in Hefei.

This time-series analysis aimed to estimate the association of short-term exposure to air pollution and deaths due to CVD in Hefei during 2007–2016. Stratified analyses by age, gender, and disease type were conducted to identify the vulnerable subgroups.

Materials and methods

Study Area

Hefei (30° 57′–32° 32′ north, 116° 41′–117° 58′) is the capital of Anhui province, and it has a subtropical monsoon humid climate with obvious monsoons. Hefei has a total area of 11,445 km^2. By the end of 2016, the population of Hefei is 7.87 million, of which 2.59 million are registered residents. Hefei has 4 districts, 4 counties, and 1 county-level city. The cardiovascular death population included in this study was only the registered population in Hefei urban area (Yaohai, Luyang, Shushan, and Baohe districts). The cardiovascular death data of the surrounding suburbs such as Changfeng County, Feidong County, and Feixi County were not obtained, and the air quality monitoring stations in Hefei City were located in the urban area. The level of air pollutants in the suburbs was quite different from that in the urban area, so it was not included in the study.

Air pollution and meteorology data

The daily data on air pollutants, including PM_{10}, NO_2, $PM_{2.5}$, CO, SO_2, and O_3, were provided by the Hefei Environmental Monitoring Center. Daily air pollutant values were calculated by averaging the 24-h values. The data were originally collected from 10 air quality monitoring stations. The daily meteorological factors of Hefei from 2007to 2016 were obtained from the China Meteorological Data Network (http://data.cma.gov.cn/).

Cardiovascular death data collection

We obtained the 2007–2016 resident death data from the Hefei Municipal Center for Disease Control and extracted the CVD deaths data using the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). Specifically, data on cardiovascular disease (I00–I99), ischemic heart disease (I20–I25), and cerebral vascular disease (I60–I69) were extracted. In order to identify the subgroups vulnerable to air pollutants, we conducted stratified analyses by gender (male and female), age (< 65 years old and ≥ 65 years old), and disease type (ischemic heart disease and cerebral vascular disease) (Zhu et al. 2017).

Statistical analysis

Daily CVD deaths, air pollutants, and meteorological factors were described as mean standard deviation (SD) and quartiles. Spearman rank correlation analysis was conducted to estimate the relationships between air pollutants and meteorological factors. A time-series analysis approach in DLNM was applied to estimate the association between ambient air pollution and CVD deaths. Studies have shown that daily CVD deaths are consistent with the Poisson distribution, and the number of daily deaths may be excessively discrete (Lu et al. 2015; Maji et al. 2017). Therefore, the quasi-Poisson distribution was adopted in the DLNM model in our study (Lu et al. 2015; Yang et al. 2016a; Zhu et al. 2017).

We use cubic spline functions to control the confounding effects of long-term trends, seasons, day of the week, and public holiday, and meteorological factors (average temperature, average pressure, relative humidity, wind speed, and precipitation) were sequentially included in the model; the Akaike information criterion (AIC) (Gasparrini et al. 2010) was used to measure the goodness of fit of the model, and the minimum AIC value is expressed as the preferred model. Finally, the model of the average temperature and relative humidity is introduced. The basic model of this study is as follows:

$$Y_t \sim Poisson(\mu_t)$$
$$Log(\mu_t) = \alpha + ns(Time_t, df) + DOW_t + \text{Holiday}_t + ns(Temp_t, df) + ns(RH_t, df) \quad (1)$$

where t is the time observed (days); Y_t is the dependent variable, number of CVD deaths at t day; μ_t is the expected mean of Y_t; α is the constant of model; ns is the natural cubic spline function; Time_t is the time variable, day t, used to control the long-term trend and seasonality of time; df is the degree of freedom; DOW_t is the day of the week effect; Temp_t is the average temperature on day t; and RH_t is the average relative humidity of the day t. According to previous research experience, the mean temperature and relative humidity degrees were both set to 4 (Li et al. 2015), the maximum lag days of average temperature and relative humidity were 27 (Guo et al. 2011) days and the current day (Luo et al. 2018), respectively, the degree of freedom of the time variable in the model is selected as 7 df/year (Yang et al. 2016b). A single-contaminant model was established to assess the impact of single air pollutants on CVD deaths in residents. The single pollutant model is shown as follows:

$$Y_t \sim \text{Poisson}(\mu_t)$$
$$\text{Log}(\mu_t) = \alpha + COVS + \lambda X_t, l1 \quad (2)$$

where $X_{t,l1}$ represents pollutant concentrations at day t (PM_{10}, $PM_{2.5}$, NO_2, SO_2, CO, and O_3), λ is the coefficient of the matrix, and $l1$ is the maximum number of days of lag in air pollutants. COVs denotes all the confounders in the core model (1). We examined the associations with different lag structures from the current day (lag 0) up to 7 days before (lag 7). We also estimated the cumulative effect of air pollution with distributed lag models (defined as lag 0–1, lag 0–2,…, lag 0–7). According to the Akaike information criterion (AIC) (Li et al. 2015), the df for air pollutants lag days was specified to be 5.

Based on the single pollutant model, a multiple-pollutant model was constructed to assess the stability of each air pollutant's impact on CVD deaths. Optimal lag day for each contaminant in the single-contaminant model were fixed, then we added additional air pollutants for adjustment. Considering the collinearity between air pollutants, PM_{10} and $PM_{2.5}$ do not appear in the model simultaneously (see Supplementary material 1). We used nonparametric tests to compare whether the effect of air pollution on CVD deaths were significantly different by gender (male and female), age (< 65 years and ≥ 65 years), and different types of CVD (ischemic heart disease and cerebral vascular disease), and the effects of air pollutant concentration on CVD deaths in subgroups were analyzed. Sensitivity analysis were conducted by varying dfs for time (6,8,9), temperature and relative humidity (3,5,6) to examine the robustness of the results in our study.

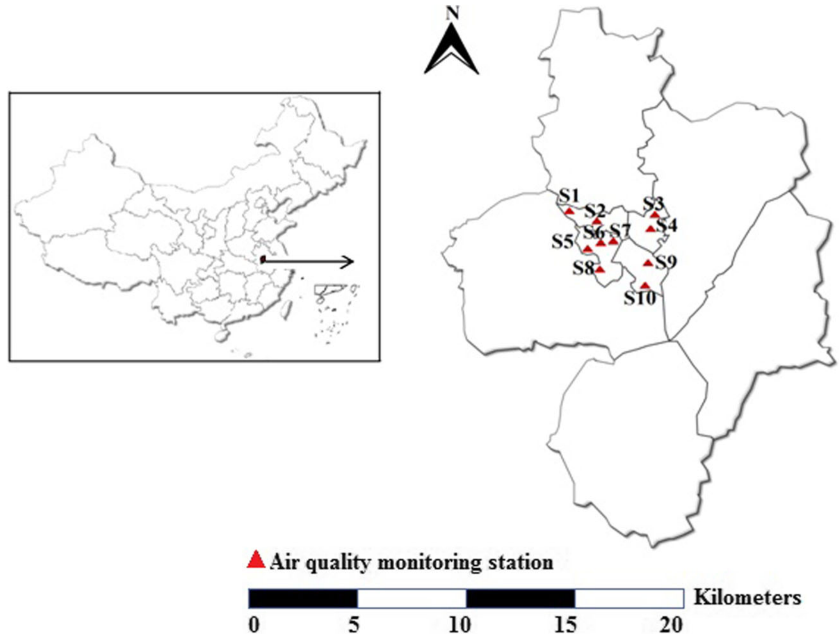
Time-series analysis was performed using the "dlnm" and "splines" software packages in R3.3.3. The results were expressed as excess risk (ER) and 95% CI, where ER = (RR − 1) × 100% (Zhang et al. 2017b), that mean with per interquartile range (IQR) increase in air pollutant. The results were shown by the excess relative risk [(relative risk − 1) × 100%] with their 95% confidence intervals (95%CI) associated with per interquartile range (IQR) increase in air pollutant (Lu et al. 2015; Tao et al. 2014), percentage change in risk of CVD deaths, P value < 0.05 was considered to be statistically significant.

Results

Description of data

The geographical location of Hefei and the distribution of air monitoring stations are shown in Fig. 1. Table 1 summarizes the basic statistics of CVD deaths, air pollutants, and meteorological factor in Hefei from 2007 to 2016. During the study period, a total of 34,500 deaths caused by CVD were involved, of which 18,774 (54.41%) and 15,726 (45.59%) were male and female; 5222 (14.92%) and 29,278 (84.86%) were <

Fig. 1 Geographic location and distribution of air monitoring sites in Hefei city



65 age and ≥ 65 age. There were 10,837 (31.41%) deaths caused by ischemic heart disease and 14,382 (41.69%) deaths caused by cerebral vascular disease. For air pollutants, the daily average concentrations of PM_{10}, SO_2, and NO_2 were 106.11, 20.34, and 30.49 μg/m^3 (2007–2016); the average daily concentrations of $PM_{2.5}$, CO, and O_3 were 72.59, 958.7, and 67.88 μg/m^3 (2013–2016). The IQR of PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 were 64.4, 14.3, 15.8, 46.2, 400, and 50.1 μg/m^3, respectively. The average daily temperature is 16.73 °C, and the average relative humidity is 74.43%.

Time-series analysis

The time-series plot showed the daily mutations of air pollutant concentrations and CVD deaths during the study period (Fig. 2). CVD deaths showed seasonal changes during the study, CVD deaths in winter (In December of that year to February of the next year) is significantly higher than in summer (June–August), and CVD deaths is increasing year by year. The PM_{10}, SO_2, and $PM_{2.5}$ daily concentration generally have been declining year by year, and NO_2, CO, and O_3

Table 1 Descriptive statistics for cardiovascular disease death, air pollutants, and meteorological factors in Hefei, China, 2007–2016

Factors	Mean ± SD	Min	P_{25}	Median	P_{75}	Max	IQR
Total death counts	9.44 ± 4.11	0	6	9	12	27	6
Male	5.14 ± 2.70	0	3	5	7	18	4
Female	4.30 ± 2.45	0	2	4	6	18	4
< 65	1.43 ± 1.26	0	0	1	2	8	2
≥ 65	8.01 ± 3.75	0	5	8	10	25	5
Ischemic diseases	2.97 ± 2.13	0	1	3	4	15	3
Cerebral vascular disease	3.59 ± 2.64	0	3	5	7	20	4
Air pollutants (μg/m^3)							
PM_{10}	106.11 ± 54.28	6	68.8	99	133.2	545	64.4
SO_2	20.34 ± 12.64	1	11.7	18	26	111.6	14.3
NO_2	30.49 ± 13.63	8	21	27.6	36.8	133.5	15.8
$PM_{2.5}$	72.59 ± 46.15	4.6	42.8	62	89	373	46.2
CO	958.7 ± 380.7	227	700	900	1100	4034	400
O_3	67.88 ± 38.57	11.5	38	57	88.1	212.1	50.1
Meteorological factors							
Temperature (°C)	16.73 ± 9.46	-5.9	8.4	18.1	24.8	34.4	16.4
Relative humidity (%)	74.43 ± 14.31	21	65	76	85	100	20

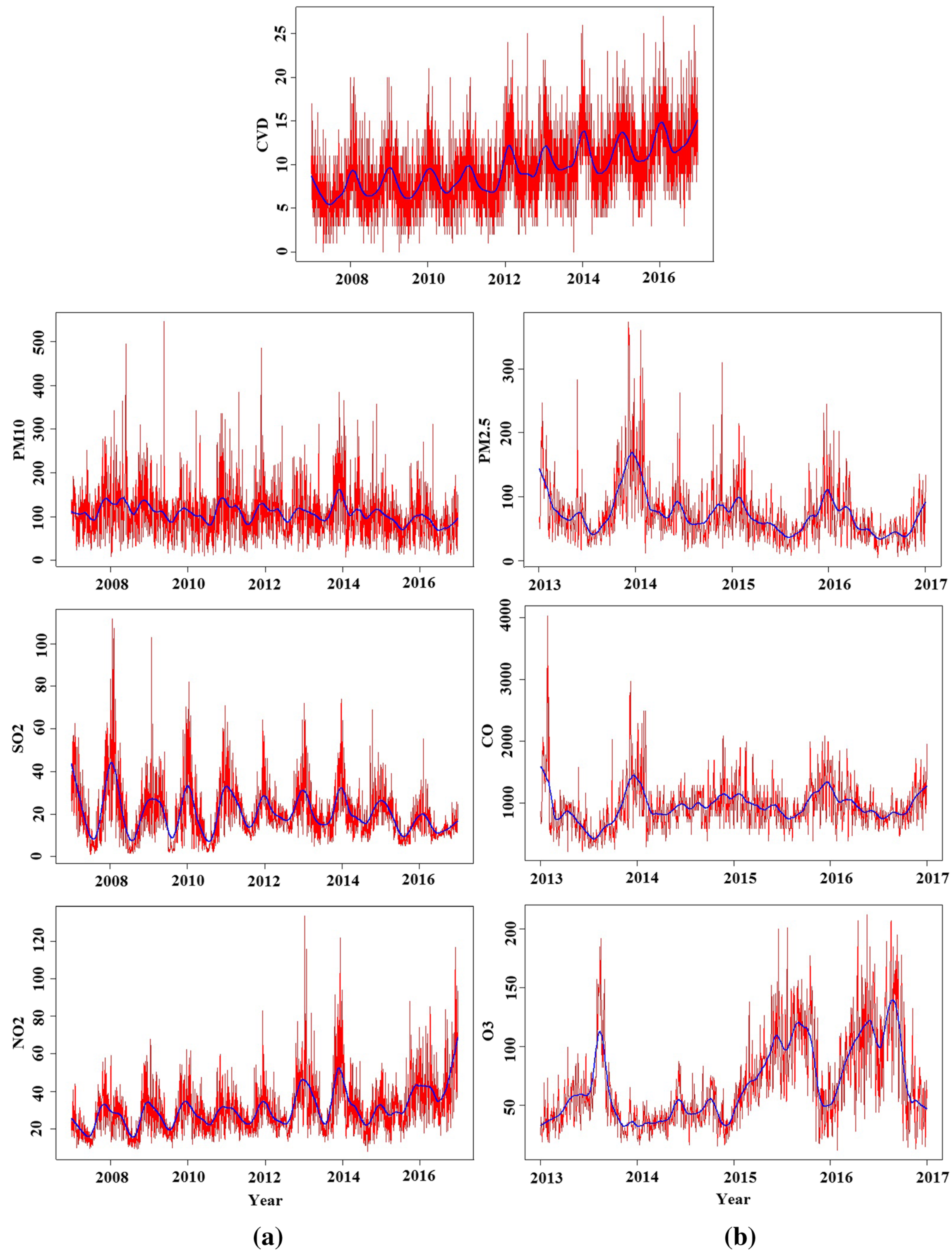


Fig. 2 Time series of air pollutants and CVD death in Hefei, China

showed an upward trend year by year. But all of them had similar characteristics of periodic fluctuation, the seasonal pattern of PM_{10}, SO_2, $PM_{2.5}$, NO_2, CO, and O_3 showed low concentration in summer and autumn and high concentration in winter and spring.

Spearman's correlation analysis and exposure-response relationships

Table 2 describes the correlation between meteorological factors and air pollutants. There was a high correlation between

Table 2 Spearman correlation between air pollutions and meteorological factors in Hefei, China, 2007–2016

Factors[a]	PM_{10}	$PM_{2.5}$[a]	SO_2	NO_2	CO[a]	O_3[a]	Temperature	Relative humidity
PM_{10}	1.000							
$PM_{2.5}$	0.804*	1.000						
SO_2	0.592*	0.641*	1.000					
NO_2	0.486*	0.484*	0.515*	1.000				
CO	0.547*	0.674*	0.427*	0.577*	1.000			
O_3	− 0.050	− 0.267*	− 0.302*	− 0.050	− 0.133*	1.000		
Temperature	− 0.125*	− 0.380*	− 0.577*	− 0.375*	− 0.308*	0.492*	1.000	
Relative humidity	− 0.386*	− 0.135*	− 0.421*	− 0.234*	0.030	− 0.241*	0.129*	1.000

* $P < 0.05$ Note: Italicized item * means $P<0.05$

[a] Correlation between $PM_{2.5}$, CO, O_3, and other variables as the result of data analysis for 2013–2016

$PM_{2.5}$ and PM_{10} ($r = 0.804$), and PM_{10} was moderately correlated with other air pollutants and weather factors. There is a positive correlation ($P < 0.05$) between PM_{10} and $PM_{2.5}$, SO_2, NO_2, and CO, while it is negatively correlated with O_3, temperature, and relative humidity ($P < 0.05$); $PM_{2.5}$ is positively correlated with NO_2, SO_2, and CO, negatively correlated with O_3, temperature, and relative humidity ($P < 0.05$); NO_2, SO_2, and CO related analysis result is in accord with the result of $PM_{2.5}$ and PM_{10} analysis (see Table 2). It is recommend that full consideration shall be given to the confounding effect of meteorological factor in the research on the influences of air pollutions on the deaths caused by CVD, and multi-pollutant model shall be employed to control the influences of other pollutants.

Figure 3 illustrates the exposure-response relationships between six air pollutants at the current day and the relative risk of CVD deaths. We can also find that the curves associated with PM_{10}, SO_2, NO_2, $PM_{2.5}$, and CO presented similar linear trends, which indicated that the higher concentration of air pollutants might cause a significant increase in CVD deaths, and O_3 curve tended to be not associated with CVD deaths.

Analysis of the DLNM

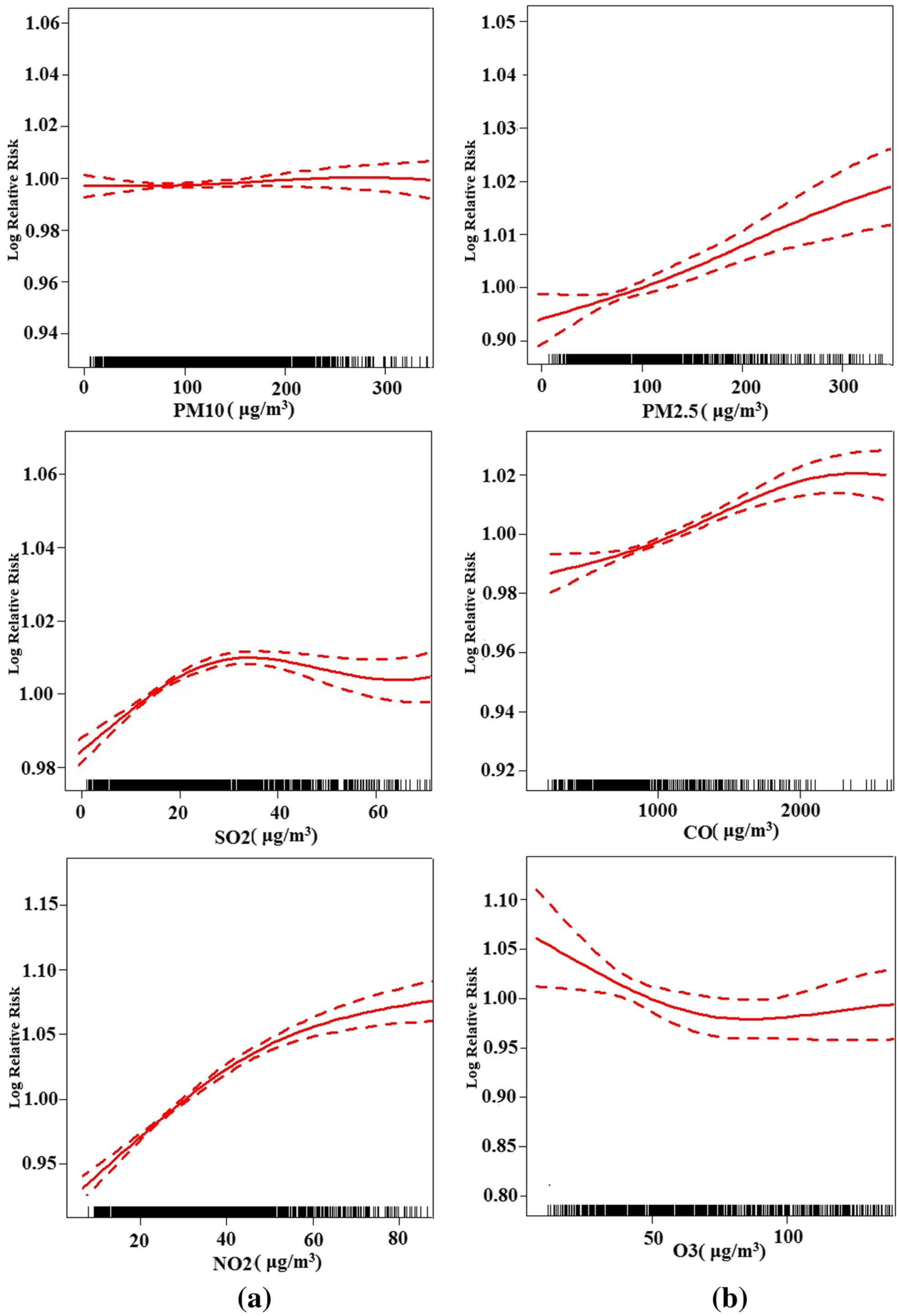
Single pollutant model analysis

Three-dimensional plot of relative risks (RRs) of CVD deaths along air pollutions and lag 0~lag 7 days are shown in Fig. 4. The distributed lag surface reveals that CVD deaths risk increased with an increase in PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3. We presented the associations of PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 with CVD deaths over different lag days in Table 3. For the single-day lag effects, the greatest impact on the risk of CVD deaths with per IQR increment in PM_{10} were found at lag 0 with 1.64% (95%CI 0.46~2.83%), SO_2 at lag 2 with 1.45% (95%CI 0.72~2.18%), NO_2 at lag 1 with 1.04% (95%CI 0.27~1.55%), $PM_{2.5}$ at lag 1 with 0.84% (95%CI 0.04~1.65%), CO at lag 0 with 1.66% (95%CI 0.04~3.31%), and O_3 at lag 2 with 1.83% (95%CI 0.51~3.18%). In terms of multi-day lag effects, the strongest effects of PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 on CVD deaths were 4.34% (95%CI 1.54~7.23%) at lag 0–6, 5.79% (95%CI 2.43~9.27%) at lag 0–5, 4.47% (95%CI 1.64~7.37%) at lag 0–5, 3.14% (95%CI 0.03~6.36%) at lag 0–4, 3.11% (95%CI 0.21~6.10%) at lag 0–3, and 8.17% (95%CI 1.89~14.84%) at lag 0–5, respectively.

Subgroup analysis

It was found that air pollutants have significant effects on CVD deaths in male and female ($Z = 13.539$, $P = 0.000$), < 64 ages and ≥ 65 ages ($Z = 70.201$, $P = 0.000$), ischemic heart disease, and cerebral vascular disease ($Z = 19.278$, $P = 0.000$). The percent change of overall CVD deaths with per IQR increment in single pollutants by gender and age are shown in Fig. 5 and Supplementary Tables S1–S2. PM_{10}, SO_2, and NO_2 both increased the risk of CVD deaths in male and female. The strongest effects of PM_{10}, SO_2, and NO_2 on male CVD deaths were 4.76% (95%CI 0.49~7.20%) at lag 0–7, 5.69% (95%CI 1.23~10.34%) at lag 0–5, and 3.46% (95%CI 0.00~7.04%) at lag 0–4; the strongest effects of PM_{10}, SO_2, and NO_2 on female CVD deaths were 5.37% (95%CI 1.60~9.27%) at lag 0–5, 5.97% (95%CI 1.11~11.06%) at lag 0–5, and 5.65% (95%CI 1.55~9.92%) at lag 0–5. However, $PM_{2.5}$, CO, and O_3 have been found to exhibit sex selective effect; this study did not find significant statistical significance between $PM_{2.5}$, CO, and O_3 and CVD deaths in male, but female was just the opposite; the strongest effects of $PM_{2.5}$, CO, and O_3 on female CVD deaths were 5.06% (95%CI 0.03~10.34%) at lag 0–5, 5.63% (95%CI 1.30~10.14%) at lag 0–3, and 15.40% (95%CI 5.67~26.03%) at lag 0–5, which means females suffered more from the adverse effects of air pollutants. For age subgroups, pollutants also exhibit age-selective effects, and only SO_2, NO_2, and $PM_{2.5}$ increased the risk of CVD deaths on age < 65 years group; the strongest effects of SO_2, NO_2, and $PM_{2.5}$ on age < 65 years group CVD deaths

Fig. 3 Exposure response relationships between six air pollutants and CVD deaths. The *x*-axis represented the concentration of air pollutants (μg/m^3) at the current day, the *y*-axis indicated log relative risk of CVD deaths. The imaginary lines were the 95%CI. All models were adjusted for time, temperature, relative humidity, weekend, and holiday



were 8.62% (95%CI 0.18~17.78%) at lag 0–5, 5.94% (95%CI 0.13~12.08%) at lag 0–2, and 15.18% (95%CI 2.31~29.66%) at lag 0–7. The strongest effects of PM_{10}, SO_2, NO_2, CO, and O_3 on age ≥ 65 years group CVD deaths were 4.45% (95%CI 1.00~8.01%) at lag 0–7, 5.97% (95%CI 1.11~11.06%) at lag 0–5, 4.32% (95%CI 1.31~7.42%) at lag 0–5, 5.09% (95%CI 0.25~10.17%) at lag 0–3, and 8.06 (95%CI 1.38~15.19%) at lag 0–5; elderly groups (aged 65+) suffered more from the adverse effects of air pollutants. Grouped according to different types of CVD such as ischemic heart disease and cerebral vascular disease, it was found that there was only statistical significance between O_3 and ischemic heart disease; the strongest effects were 13.08% (95%CI 1.97~25.39%) at lag 0–5. Cerebral

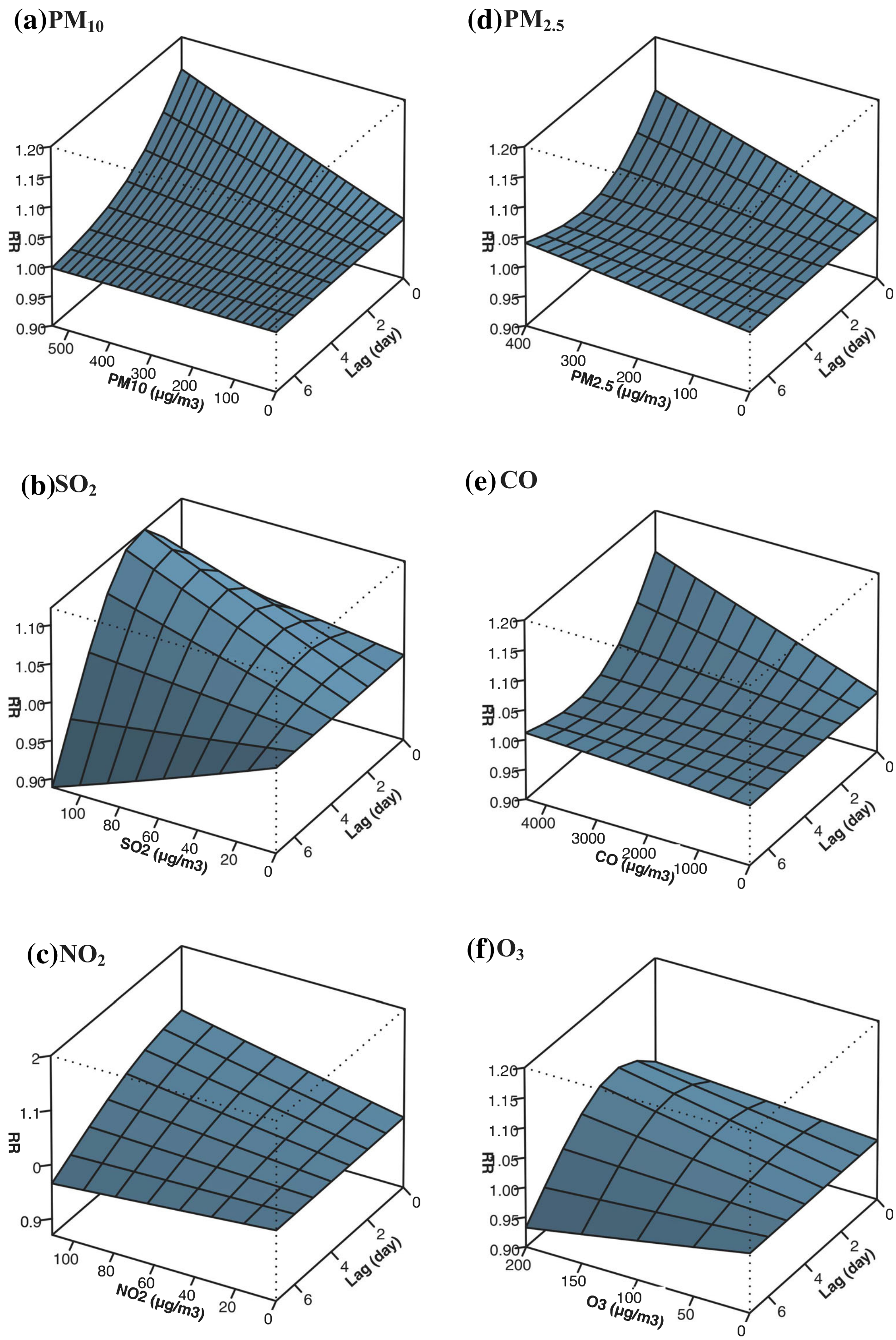


Fig. 4 The 3D graph for the association of air pollutions and CVD deaths

vascular disease was mainly affected by PM_{10}, SO_2, and NO_2; the strongest effects of PM_{10}, SO_2, and NO_2 on cerebral vascular disease were 6.25% (95%CI 1.31~11.43%) at lag 0–7, 5.68% (95%CI 0.55%~11.07%) at lag 0–5, and 6.34% (95%CI 1.93~10.95%) at lag 0–5 (Table 4).

Multi-pollutant model analysis

After determining the optimal lag for each pollutant in a single pollutant model, we added additional contaminants to adjustment. The percent increase and 95%CI for CVD deaths associated with per IQR increment of air pollutants in multi-

Table 3 The excess risk for cardiovascular mortality associated with an interquartile range increase in the concentration of air pollutions in Hefei, China, 2007–2016

Lag days	PM_{10}		SO_2		NO_2		$PM_{2.5}$[a]		CO[a]		O_3[a]	
	ER	*95%CI*	*ER*	*95%CI*	*ER*	*95%CI*	*ER*	95%CI	*ER*	*95%CI*	*ER*	*95%CI*
Lag 0	*1.64**	*0.46~2.83*	0.48	− 1.04~2.02	1.13	-0.24~2.51	1.32	− 0.18~2.85	*1.66**	*0.04~3.31*	1.17	− 1.75~4.18
Lag 1	*1.14**	*0.53~1.75*	*1.11**	*0.30~1.92*	*1.04**	*0.35~1.74*	*0.84**	*0.04~1.65*	*0.95**	*0.12~1.80*	*1.63**	*0.09~3.20*
Lag 2	*0.72**	*0.17~1.28*	*1.45**	*0.72~2.18*	*0.91**	*0.27~1.55*	0.48	−0.25~1.20	0.40	− 0.36~1.16	*1.83**	*0.51~3.18*
Lag 3	0.43	− 0.20~1.06	*1.38**	*0.55~2.21*	0.71	− 0.03~1.45	0.27	− 0.54~1.09	0.07	− 0.80~0.94	*1.66**	*0.17~3.17*
Lag 4	0.23	− 0.35~0.81	*0.96**	*0.21~1.72*	0.45	− 0.21~1.12	0.20	− 0.55~0.95	− 0.08	− 0.87~0.72	1.17	− 0.18~2.54
Lag 5	0.10	− 0.39~0.59	0.29	− 0.35~0.93	0.16	− 0.39~0.71	0.23	− 0.41~0.87	− 0.10	− 0.77~0.58	0.45	− 0.67~1.57
Lag 6	0.02	− 0.60~0.65	− 0.55	− 1.34~0.25	− 0.17	− 0.88~0.55	0.32	− 0.50~1.14	− 0.02	− 0.88~0.85	− 0.42	− 1.84~1.02
Lag 7	− 0.03	− 1.03~0.97	− 1.46	− 2.71~−0.19	− 0.50	− 1.66~0.67	0.45	− 0.85~1.76	0.11	− 1.27~1.50	− 1.36	− 3.64~0.98
Lag 0–1	*2.80**	*1.06~4.56*	1.59	− 0.65~3.88	*2.18**	*0.19~4.21*	2.18	-0.05~4.46	*2.63**	*0.25~5.07*	2.83	− 1.51~7.35
Lag 0–2	*3.54**	*1.59~5.53*	*3.06**	*0.52~5.68*	*3.11**	*0.90~5.36*	*2.66**	*0.13~5.26*	*3.04**	*0.38~5.77*	4.71	− 0.20~9.87
Lag 0–3	*3.98**	*1.85~6.16*	*4.48**	*1.68~7.36*	*3.84**	*1.46~6.27*	*2.94**	*0.15~5.81*	*3.11**	*0.21~6.10*	*6.45**	*1.10~12.07*
Lag 0–4	*4.22**	*1.86~6.63*	*5.49**	*2.38~8.68*	*4.31**	*1.69~6.98*	*3.14**	*0.03~6.36*	3.02	− 0.20~6.36	*7.69**	*1.85~13.87*
Lag 0–5	*4.32**	*1.74~6.97*	*5.79**	*2.43~9.27*	*4.47**	*1.64~7.37*	3.38	− 0.06~6.93	2.93	− 0.63~6.61	*8.17**	*1.89~14.84*
Lag 0–6	*4.34**	*1.54~7.23*	*5.21**	*1.64~8.91*	*4.29**	*1.28~7.40*	3.71	−0.05~7.61	2.91	− 0.98~6.95	**7.72***	*1.07~14.80*
Lag 0–7	*4.31**	*1.10~7.62*	3.68	-0.27~7.78	*3.77**	*0.36~7.30*	4.17	− 0.15~8.68	3.02	− 1.46~7.69	6.26	− 1.11~14.17

Note: Italicized item * means $P<0.05$

$^{*}P < 0.05$

[a] $PM_{2.5}$, CO, and O_3 were data for 2013–2016

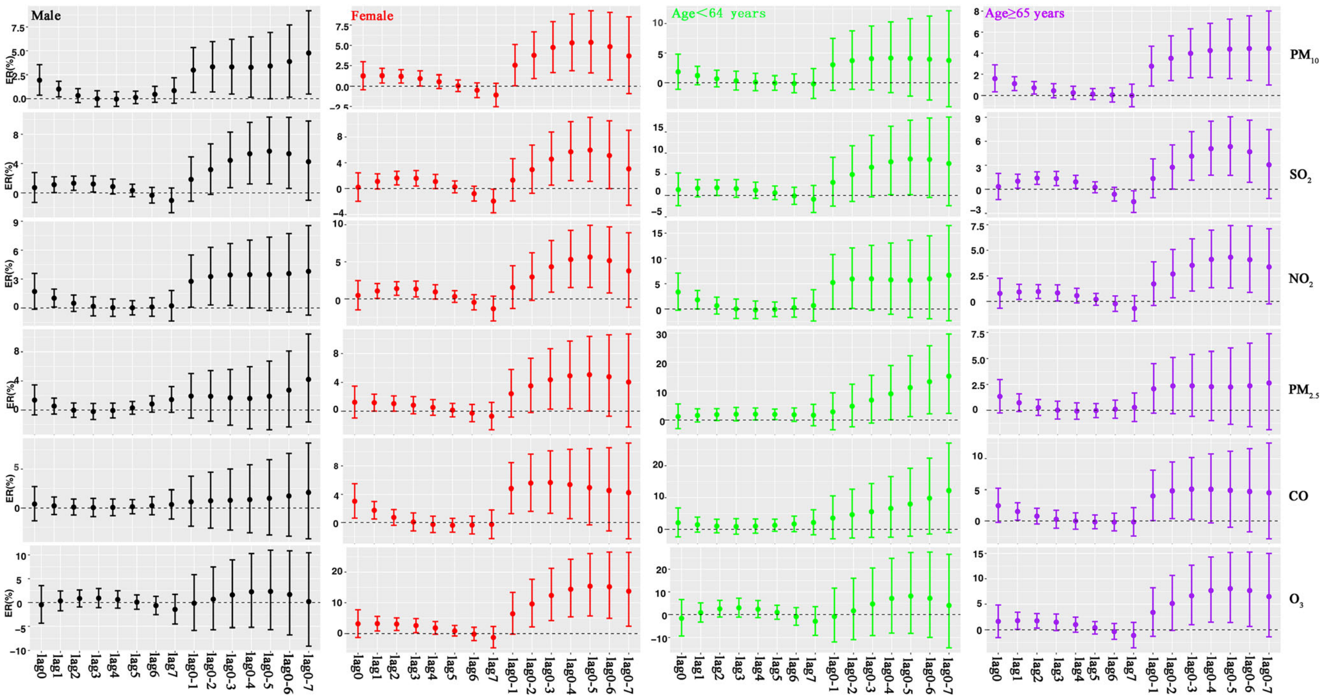


Fig. 5 The percent change and 95%CI for deaths due to CVD associated with per IQR increase in air pollutants concentrations by gender and age in single-pollutant models in Hefei, China

pollutant models are presented in Table 5. The results of the air pollutants in the two pollutants were lower than those of the single pollutant model, and only the effects of SO_2 and O_3 on CVD deaths were more stable ($P < 0.05$). The fitting results of other pollutants PM_{10}, NO_2, $PM_{2.5}$, and CO in the multi-pollutant model were not statistically significant ($P > 0.05$).

Sensitivity analysis

In the range of (6,8,9), the change of *df*/year has no significant effect on the connection of air pollution with CVD deaths (Supplementary Fig. S1). In addition, we obtained similar results when modifying *df* (3,5,6) for the mean temperature and relative humidity (Supplementary Figs. S2–S3).

Discussion

In this study, the DLNM was utilized to analyze the relationship between air pollutants and CVD from 2007 to 2016 in Hefei. The results showed that PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 had significant adverse effects on overall CVD and its subtypes, including ischemic heart disease and cerebral vascular disease. Subgroup analysis showed that females were more sensitive to the effects of PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 than males, and regarding gender, residents aged ≥ 65 years were more susceptible to the effects of PM_{10}, CO, and O_3 than residents < 65 years old, but < 65 years old were more susceptible to the effects of SO_2, NO_2, and $PM_{2.5}$ than aged ≥ 65 years. Our results may be relevant for the prevention and treatment of CVD and provide constructive advice for controlling air pollution in Hefei, China.

The exceeded days of PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 (based on the first-class concentration limit of China's "Environmental Air Quality Standards" (GB3095-2012)) were 87.72%, 3.18%, 0.68%, 84.87%, 0.07%, and 2.33%, respectively. PM_{10}, $PM_{2.5}$, and SO_2 were the major pollutants in Hefei. Hefei Air Quality ranks 48th out of 74 cities, and the average concentration of PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 was ranked 38th, 38th, 32th, 71th, 37th, and 36th, respectively. Studies have shown that particulate matter (PM_{10}, $PM_{2.5}$) mainly comes from various industrial production, construction, and road dust. SO_2 is mainly derived from the combustion of coal oil and the exhaust of motor vehicles. Therefore, it was of great meaning and emergency to predict the risk of CVD caused by air pollution in Hefei. We concluded that with per IQR increase in PM_{10}, CVD deaths were significantly increased by 1.64% (95%CI 0.46~2.83%) at lag 0 in single-day lags and 4.34% (95%CI 1.54~7.23%) at lag 0–6 in multi-day lags. Our results are similar to previous studies, Zahra Soleimani et al. (2019). Exploring the relationship between air pollution and hospitalization rates for CVD, they observed a 1.08% increase in CVD hospitalization for every 10 μg/m^3 increase in PM_{10}. Zhang et al. (2017b) concluded that with per 10 μg/m^3 increases in PM_{10}, CVD mortality was significantly increased by 1.012% (1.011–1.013) at lag 1 day. However, we found no

Table 4 The excess risk for different causes of cardiovascular deaths associated with an interquartile range increase in air pollutions in Hefei, 2007–2016

Lag days	PM_{10}		SO_2		NO_2		$PM_{2.5}$		CO		O_3	
	ER	95%CI	ER	95%CI	ER	95%CI	ER	95%CI	ER	95%CI	ER	95%CI
Ischemic diseases												
Lag 0	− 1.43	− 3.48~0.66	− 0.40	− 3.11~2.39	− 0.77	− 3.09~1.60	− 0.45	− 3.02~2.18	− 0.3	− 3.04~2.52	− 2.57	− 7.40~2.51
Lag 1	− 0.10	− 1.18~1.00	0.46	− 0.99~1.93	0.10	− 1.09~1.30	0.21	− 1.18~1.62	0.02	− 1.42~1.48	1.28	− 1.38~4.00
Lag 2	0.82	− 0.16~1.80	0.98	− 0.33~2.29	0.71	− 0.38~1.81	0.66	− 0.59~1.93	0.29	− 1.02~1.60	*3.92**	*1.59~6.30*
Lag 3	1.09	− 0.03~2.22	0.99	− 0.49~2.49	0.94	− 0.33~2.23	0.81	− 0.60~2.23	0.48	− 1.01~1.99	*4.63**	*1.99~7.34*
Lag 4	0.83	− 0.20~1.87	0.60	− 0.76~1.97	0.85	− 0.30~2.02	0.69	− 0.59~2.00	0.61	− 0.76~2.00	*3.72**	*1.34~6.16*
Lag 5	0.17	− 0.70~1.05	− 0.11	− 1.24~1.05	0.52	− 0.42~1.48	0.39	− 0.72~1.51	0.69	− 0.47~1.87	1.62	− 0.32~3.59
Lag 6	− 0.75	− 1.86~0.38	− 1.01	− 2.43~0.44	0.04	− 1.18~1.27	− 0.05	− 1.46~1.38	0.75	− 0.74~2.25	− 1.22	− 3.65~1.27
Lag 7	− 1.78	− 3.53~0.00	− 2.00	− 4.24~0.30	− 0.53	− 2.52~1.51	− 0.54	− 2.75~1.71	0.78	− 1.58~3.21	− 4.35	− 8.16~− 0.38
Lag 0–1	− 1.53	− 4.51~1.54	0.06	− 3.92~4.20	− 0.68	− 4.01~2.78	− 0.25	− 4.02~3.68	− 0.28	− 4.26~3.87	− 1.33	− 8.44~6.33
Lag 0–2	− 0.73	− 4.08~2.74	1.04	− 3.45~5.73	0.03	− 3.65~3.86	0.41	− 3.88~4.91	0.00	− 4.45~4.67	2.54	− 5.66~11.45
Lag 0–3	0.35	− 3.31~4.16	2.04	− 2.86~7.18	0.97	− 3.00~5.11	1.22	− 3.53~6.22	0.48	− 4.39~5.60	7.29	− 1.87~17.30
Lag 0–4	1.18	− 2.88~5.42	2.65	− 2.74~8.33	1.83	− 2.54~6.41	1.93	− 3.39~7.53	1.09	− 4.34~6.84	*11.28**	*1.04~22.55*
Lag 0–5	1.36	− 3.09~6.00	2.54	− 3.27~8.70	2.37	− 2.38~7.34	2.32	− 3.53~8.52	1.80	− 4.22~8.19	*13.08**	*1.97~25.39*
Lag 0–6	0.60	− 4.18~5.62	1.51	− 4.63~8.03	2.40	− 2.65~7.72	2.27	− 4.09~9.05	2.56	− 4.06~9.63	*11.70**	*0.06~24.68*
Lag 0–7	− 1.19	− 6.57~4.49	− 0.52	− 7.27~6.72	1.86	− 3.85~7.92	1.72	− 5.49~9.47	3.36	− 4.28~11.61	6.84	− 5.64~20.96
Cerebral vascular diseases												
Lag 0	*3.00**	*1.2~4.83*	− 0.28	− 2.6~2.09	2.04	− 0.08~4.20	1.99	− 0.42~4.45	2.16	− 0.43~4.81	3.83	− 0.98~8.88
Lag 1	*1.78**	*0.85~2.72*	0.78	− 0.46~2.03	*1.61**	*0.54~2.69*	0.88	− 0.40~2.18	1.20	− 0.13~2.55	2.01	− 0.48~4.56
Lag 2	*0.83**	*0.00~1.68*	*1.47**	*0.35~2.60*	*1.20**	*0.22~2.19*	0.13	− 1.02~1.29	0.45	− 0.76~1.67	0.72	− 1.39~2.88
Lag 3	0.26	− 0.69~1.22	*1.62**	*0.34~2.91*	0.81	− 0.32~1.96	− 0.13	− 1.42~1.18	− 0.02	− 1.40~1.38	0.17	− 2.21~2.61
Lag 4	− 0.01	− 0.88~0.87	*1.31**	*0.15~2.49*	0.44	− 0.59~1.49	0.03	− 1.15~1.23	− 0.25	− 1.51~1.03	0.22	− 1.95~2.44
Lag 5	− 0.05	− 0.79~0.70	0.67	− 0.31~1.66	0.09	− 0.76~0.94	0.50	− 0.52~1.53	− 0.31	− 1.38~0.76	0.73	− 1.08~2.57
Lag 6	0.06	− 0.89~1.02	− 0.20	− 1.42~1.05	− 0.26	− 1.35~0.85	1.18	− 0.12~2.50	− 0.26	− 1.62~1.13	1.53	− 0.80~3.93
Lag 7	0.25	− 1.27~1.79	− 1.16	− 3.10~0.81	− 0.60	− 2.39~1.22	1.97	− 0.10~4.09	− 0.14	− 2.33~2.09	2.50	− 1.32~6.48
Lag 0–1	*4.83**	*2.17~7.57*	0.49	− 2.91~4.02	*3.68**	*0.59~6.87*	2.89	− 0.67~6.58	3.38	− 0.41~7.32	5.92	− 1.21~13.57
Lag 0–2	*5.71**	*2.70~8.80*	1.97	− 1.89~5.99	*4.93**	*1.49~8.47*	3.02	− 1.01~7.21	3.85	− 0.39~8.27	6.69	− 1.29~15.30
Lag 0–3	*5.98**	*2.71~9.36*	3.62	− 0.63~8.06	*5.78**	*2.07~9.62*	2.89	− 1.53~7.51	3.83	− 0.78~8.66	6.87	− 1.66~16.14
Lag 0–4	*5.97**	*2.35~9.73*	*4.98**	*0.26~9.92*	*6.25**	*2.17~10.49*	2.93	− 2.00~8.09	3.57	− 1.54~8.95	7.10	− 2.13~17.21
Lag 0–5	*5.92**	*1.95~10.04*	*5.68**	*0.55~11.07*	*6.34**	*1.93~10.95*	3.44	− 2.00~9.19	3.25	− 2.37~9.19	7.88	− 2.07~18.84
Lag 0–6	*5.99**	*1.67~10.48*	*5.47**	*0.02~11.23*	*6.07**	*1.37~10.99*	4.67	− 1.34~11.04	2.98	− 3.14~9.50	9.54	− 1.18~21.42
Lag 0–7	*6.25**	*1.31~11.43*	4.25	− 1.8~10.67	5.43	0.13~11.02	6.73	− 0.24~14.2	2.84	− 4.19~10.38	12.28	− 0.03~26.11

Note: Italicized item * means $P<0.05$

*$P < 0.05$

Table 5 Multi-pollutant model analysis results of the effects of air pollutants on cardiovascular deaths in Hefei

Model	Single-day lag maximum effect		Multi-day lag cumulative maximum effect	
	ER	95%CI	ER	95%CI
PM_{10}[a]				
Single pollutant model	*1.64**	*0.46~2.83*	*4.31**	*1.10~7.62*
$+SO_2$	1.61	− 0.46~2.74	3.87	− 0.08~8.01
$+NO_2$	1.38	− 0.04~2.81	3.37	− 0.58~7.47
SO_2[a]				
Single pollutant model	*1.45**	*0.72~2.18*	*5.79**	*2.43~9.27*
$+PM_{10}$	*1.27**	*0.38~2.17*	3.74	− 0.27~7.92
$+NO_2$	*1.22**	*0.35~2.10*	4.10	0.16~8.19
NO_2[a]				
Single pollutant model	*0.91**	*0.27~1.55*	*4.47**	*1.64~7.38*
$+PM_{10}$	0.56	− 0.25~1.37	2.31	− 1.23~5.97
$+SO_2$	0.33	− 0.43~1.09	2.57	− 0.74~5.99
$PM_{2.5}$[b]				
Single pollutant model	*0.84**	*0.04~1.65*	*3.14**	*0.03~6.36*
$+SO_2$	0.22	− 0.68~1.13	0.67	− 2.78~4.25
$+NO_2$	0.05	− 0.89~0.99	0.31	− 3.30~4.05
+CO	0.32	− 0.97~1.62	2.12	− 2.91~7.40
$+O_3$	0.59	− 0.26~1.44	2.01	− 1.30~5.44
CO[b]				
Single pollutant model	*1.66**	*0.04~3.31*	*3.11**	*0.21~6.10*
$+PM_{10}$	0.51	− 1.75~2.82	− 0.7	− 4.54~3.28
$+SO_2$	1.22	− 0.58~3.05	1.2	− 1.95~4.45
$+NO_2$	0.23	− 1.75~2.26	− 0.53	− 4.06~3.13
$+PM_{2.5}$	1.48	− 0.97~3.99	1.77	− 2.85~6.60
$+O_3$	1.4	− 0.24~3.07	2.22	− 0.79~5.32
O_3[b]				
Single pollutant model	*1.83**	*0.51~3.17*	*8.17**	*1.89~14.84*
$+PM_{10}$	1.16	− 0.27~2.62	4.2	− 2.46~11.32
$+SO_2$	1.23	− 0.14~2.63	5.28	− 1.12~12.09
$+NO_2$	1.17	− 0.23~2.59	4.33	− 2.24~11.34
$+PM_{2.5}$	*1.63**	*0.24~3.04*	6.61	− 0.04~13.71
+CO	*1.65**	*0.28~3.03*	*6.99**	*0.48~13.92*

Note: Italicized item * means $P<0.05$

[a] PM_{10}, SO_2, and NO_2 during 2007–2016. PM_{10}, SO_2, and NO_2 obtained the maximum single-day lag effect value in lag 0, lag 2, and lag 1; the maximum multi-day lag cumulative effect value was obtained in lag 0–6, lag 0–5, and lag 0–5

[b] $PM_{2.5}$, CO, and O_3 during 2013–2016. $PM_{2.5}$, CO, and O_3 obtained the maximum single-day lag effect value in lag 1, lag 0, and lag 2; the maximum multi-day lag cumulative effect value was obtained in lag 0–4, lag 0–3, and lag 0–5

statistical association between PM_{10} CVD deaths in a study in Wuhan. The inconsistent results may be due to the concentration of PM_{10} in different regions and demographic differences.

For SO_2, we concluded that with per IQR increase in SO_2, CVD deaths and cerebral vascular disease were significantly increased by 1.45% (95%CI 0.72~2.18%) at lag 2 and 1.61% (95%CI 0.54~2.69%) at lag 1 in single day, and the effects in multi-day lags were greater than single-day lags, which were consistent with most previous studies. In Beijing, the relative risks (95%CI) of per 10 mg/m^3 increased to SO_2 were 1.008 (0.999–1.018) on cardiovascular emergency room admissions (Ma et al. 2017). Dong et al. studied the effects of air pollution on CVD morbidity in three cities in Northeast China, and it was found that for every 20 μg/m^3 increase in SO_2 concentration, CVD rate increased by 1.14% (Dong et al. 2013). The acute effects of SO_2 on population death in the atmosphere of six cities in China, we can find that the effect of SO_2 on CVD death is different, but they all have an obvious correlation (Zeng et al. 2015).

This study found that the concentrations of NO_2 and O_3 were increasing year by year, and O_3 had the greatest adverse effect on CVD deaths; we concluded that with per IQR increase in O_3, CVD was significantly increased by 1.83% (95%CI 0.51~3.18%) at lag 3 in single-day lags and 8.17% (95%CI 1.89~14.84%) at lag 0–5 in multi-day lags. Different from other studies (Huang et al. 2018; Yang et al. 2018), of the six air pollutants in this study, only O_3 has an effect on ischemic heart disease. We found that with per IQR increase in NO_2 at lag 0–5 days, it could lead to a 1.04% (95%CI 0.27~1.55%) and 1.61% (95%CI 0.54~2.69%) increment in CVD deaths and cerebral vascular disease. Our finding was also consistent with other previous studies (Huang et al. 2018; Yang et al. 2018). NO_2 and O_3 can inhibit the activity of enzymes, affect the metabolism of lipoproteins, induce systemic inflammatory reactions, and cause CVD diseases (Faridi et al. 2018). Our study showed that SO_2+ NO_2 and O_3+CO still have significant effects on CVD deaths in the two-pollutant models; this suggests that SO_2, NO_2, O_3, and CO were powerful predictors of CVD deaths in Hefei, China. In other multi-pollution models, we did not find that the combined effect of pollutants has an effect on CVD deaths, probably due to the strong correlation between pollutants, affecting their death effects on CVD.

Consistent with previous studies (Garcia et al. 2016; Zhu et al. 2017), females were more susceptible to the effects of PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 than males. Although this relationship is not evident, some biological and abiotic factors can explain this phenomenon (Bennett et al. 1996; Eaker et al. 1993); first, in anatomy, females have smaller respiratory tract diameters, so females have higher airway responses and particulate deposition effects than males. For the age subgroup, the study showed that residents ≥ 65 years old were more sensitive to PM_{10}, CO, and O_3 than residents < 65 years old; the results of SO_2, NO_2, and $PM_{2.5}$ were exactly the opposite. This may be explained by differences in exposure to air pollutants among residents of different ages, and it is more common in older people with chronic diseases (Roth et al. 2017).

In this study, there are several advantages: first, this study had a longer time span than similar studies in the past (generally 2–5 years), the time span of this study reached 10 years, can reveal the long-term exposure effects of air pollutants, and compared to previous studies, the types of air pollutants in our study are more comprehensive, and it is a good response to the effects of air pollutants on CVD deaths, so the results were more reliable and accurate. Second, this study used a distributed-lag nonlinear model to quantitatively analyze the effects of air pollutants on CVD in residents, and the model is more active than the generalized additive model. Third, the study compared different genders, ages, and the effects of air pollutants on different types of CVD deaths in the same population; sensitive populations were identified, and more favorable targeted preventive and control measures were proposed. Fourth, as we mentioned above, Hefei is the representative area for the combined pollution of coal smoke and motor vehicle exhaust in the central cities. This study will help us better understand the impact of air pollution on CVD deaths in a coal smoke and motor vehicle exhaust polluted region. Of course, this study also has some shortcomings. First, as with other similar studies, air pollutant concentration data and meteorological data are obtained from fixed detection sites, which could not represent total exposure to population, underestimate the health effects of air pollution. Second, due to the lack of data on indoor air pollutants, indoor air pollution is not considered in this study, which may also affect population exposure levels and overestimate the link between ambient air pollutants and death. Finally, this study only involves Hefei; the results of the study should be cautious when extrapolated. However, from the point of view of big data analysis, although there are some shortcomings, the research results still have some persuasion.

Conclusions

In summary, we evaluated the effects of ambient air pollutants on CVD deaths during 2007–2016 in Hefei. Through the DLNM of time-series analysis, we observed positive associations between PM_{10}, SO_2, NO_2, $PM_{2.5}$, CO, and O_3 concentration at different lag days and CVD deaths. NO_2 and SO_2 were the largest two risk pollutants of CVD deaths in Hefei. Females and elderly for CVD were more vulnerable to air pollution. In consequence, some effective measures should be taken to strengthen the management of the ambient air pollutants, and to enhance the protection of the high-risk population from air pollutants.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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