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# Acute effects of fine particulate matter (PM<sub>2.5</sub>) on hospital admissions for cardiovascular diseases in Lanzhou, China: a time-series study

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## Abstract

**Background:** Up until now, evidence pertaining to the short-term effects of fine particulate matter (PM<sub>2.5</sub>) in cardiovascular diseases (CVD) is scarce in China. In this study, we aim to estimate the association between short-term exposure to PM<sub>2.5</sub> and hospitalizations for total and cause-specific CVD in Lanzhou of China.

**Methods:** Daily counts of cardiovascular admissions were obtained from three large general hospitals in Lanzhou, China between 2014 and 2019. Air quality and meteorological data were obtained from the monitoring stations nearest to the admitting hospitals. We utilized Quasi-Poisson time-series regressions with distributed lag nonlinear models (DLNM) to assess the association between PM<sub>2.5</sub> and CVD admitted in the three general hospitals. A stratified analysis was also conducted for age, sex, and disease subcategories.

**Results:** PM<sub>2.5</sub> was positively correlated with daily admissions for total or other cause-specific CVD under different lag patterns. For every 10 µg/m<sup>3</sup> increase in the PM<sub>2.5</sub> concentration, the relative risk of daily admissions for total CVD, ischemic heart disease (IHD), heart rhythm disturbances (HRD), heart failure (HF), and cerebrovascular disease (CD) was: 1.011 [95% confidence interval (CI), 1.001–1.020] in lag01; 1.020 (95% CI 1.004–1.036) in lag07; 1.013 (95% CI 1.001–1.026) in lag7; 1.018 (95% CI 1.005–1.038) in lag1; and 1.007 (95% CI 1.001–1.018) in lag1. Both low and high temperatures increased the risk of cardiovascular hospitalization. No differences were found after stratification by gender and age. We found an almost linear relationship between the exposure to PM<sub>2.5</sub> and cause-specific CVD admissions with no threshold effect. Males as well as the elderly, aged ≥ 65 years, were more vulnerable to PM<sub>2.5</sub> exposure.

**Conclusions:** Our results have demonstrated that PM<sub>2.5</sub> has adverse impacts on cardiovascular hospitalizations in Lanzhou, especially on IHD.

**Keywords:** Air pollution, Fine particulate matter, Cardiovascular diseases, Hospital admission

## Introduction

Cardiovascular disease (CVD) is the leading causes of death in China [1]. Health Statistics Yearbook in China, 2019, reported that the mortality associated with cardiovascular disease in China remained the highest since 2018, higher than tumors and other diseases.

Cardiovascular disease accounted for 46.66% and 43.81% of causes of death in rural and urban areas, respectively, in 2018. Two out of every five deaths were due to cardiovascular disease [2]. At present, the prevalence of CVD in China is still rising. According to the data from the China Cardiovascular Report 2020, it is estimated that there are 330 million CVD patients in the country, of which 245 million cases associated with hypertension, 13 million cases of stroke, and at least 11 million cases of coronary heart disease [3]. Cardiovascular disease is forcing an increasing burden on the economic system and

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society general. Aside from conventional risk factors such as high blood pressure, high cholesterol, diabetes, obesity, tobacco use, alcohol consumption, physical inactivity and unhealthy diets, air pollution may be crucial factors causing the occurrence and development of CVD [3]. In recent years, a large body of epidemiological and clinical research have indicated that exposure to air pollution, especially fine particulate matter [particles with a aerodynamic diameter of  $\leq 2.5 \mu\text{m}$  ( $\text{PM}_{2.5}$ )], is associated with an increase in CVD morbidity [4–12]. For example, the findings of a study conducted by Kloog et al. showed a  $10 \mu\text{g}/\text{m}^3$  increase of  $\text{PM}_{2.5}$  was associated with an increase in daily cardiovascular disease morbidity of 3.12% (95% CI 0.30–4.29%) [4]. A time-series analysis demonstrated that short-term exposure to ambient concentrations of  $\text{PM}_{2.5}$  increases CVD morbidity ( $\text{ER} = 0.51\%$ ; 95% CI 0.12–0.90) per  $10 \mu\text{g}/\text{m}^3$  by Stafoggia et al. [5]. In a study using a population from New York, USA, an increase of  $10 \mu\text{g}/\text{m}^3$  in  $\text{PM}_{2.5}$  was associated with a 2.143% increase in hospital admissions related to cardiovascular disease [6]. A  $10 \mu\text{g}/\text{m}^3$  elevation in  $\text{PM}_{2.5}$  concentrations was associated with a 0.87% (95% CI 0.05–1.70%) rise in CVD admissions in Wuhan, China [7]. In Beijing, the estimated risk increment for CVD admissions was 0.84% (95% CI 0.60–1.07%) for a  $10 \mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$ , respectively [8]. A cross-sectional study of 5 urban districts in Chengdu, China, also showed a correlation between PM and CVD. For each  $10 \mu\text{g}/\text{m}^3$  elevation in  $\text{PM}_{2.5}$ , the ERs for CVD hospitalization increased by 0.55 [9]. A multicity study in China suggests that short-term exposure to  $\text{PM}_{2.5}$  is associated with increased CVD hospitalization [10]. In addition, hospitalizations of CVD was significantly associated with short-term exposure to high particulate matter pollution in Yichang [11]. However, particulate matter pollution are not the only environmental risk factors associated with CVD morbidity [13]. Several other studies have proven that outdoor temperature serves as another major ambient risk factor affecting cardiovascular events [14–17]. For instance, studies conducted in Shanghai, Hefei, China and Sabzevar city, Iran identified that both low and high temperatures are associated with an increased CVD risk [14–16]. Other studies conducted in Beijing, China, reported an increased CVD risk during extremely high temperatures [17]. Therefore, both particulate matter pollution and extreme temperatures increase the risk of CVD. It is important to also consider how CVD hospital admissions are affected by these ambient exposures, as CVD also accounts for almost one half of all mortalities. However, there are limited studies on the interaction between temperature and pollutants on various CVD outcomes. For example, Li et al. reported on the interaction between temperature and pollutants for CVD, but not for respiratory disease [18]. In another

study, conducted by Lokys et al. no interaction was found for either CVD disease [19]. In addition, studies that simultaneously evaluate CVD morbidity in association with temperature and pollutants, for various diseases, are limited.

As located in the semi-arid city, the temperature of Lanzhou is also unique when it is compared to the other cities in China. This is because Lanzhou has four distinct seasons and the climate varies relatively significantly with the seasons. Given the lack of evidence on the association between air pollution, temperature, and CVD morbidity in Lanzhou, we chose, in this study, to assess the impact of short-term exposure to  $\text{PM}_{2.5}$  and temperature on the hospitalizations of cause-specific CVD, including heart disease (IHD), heart rhythm disturbances (HRD), heart failure (HF), and cerebrovascular disease (CD), in Lanzhou, China.

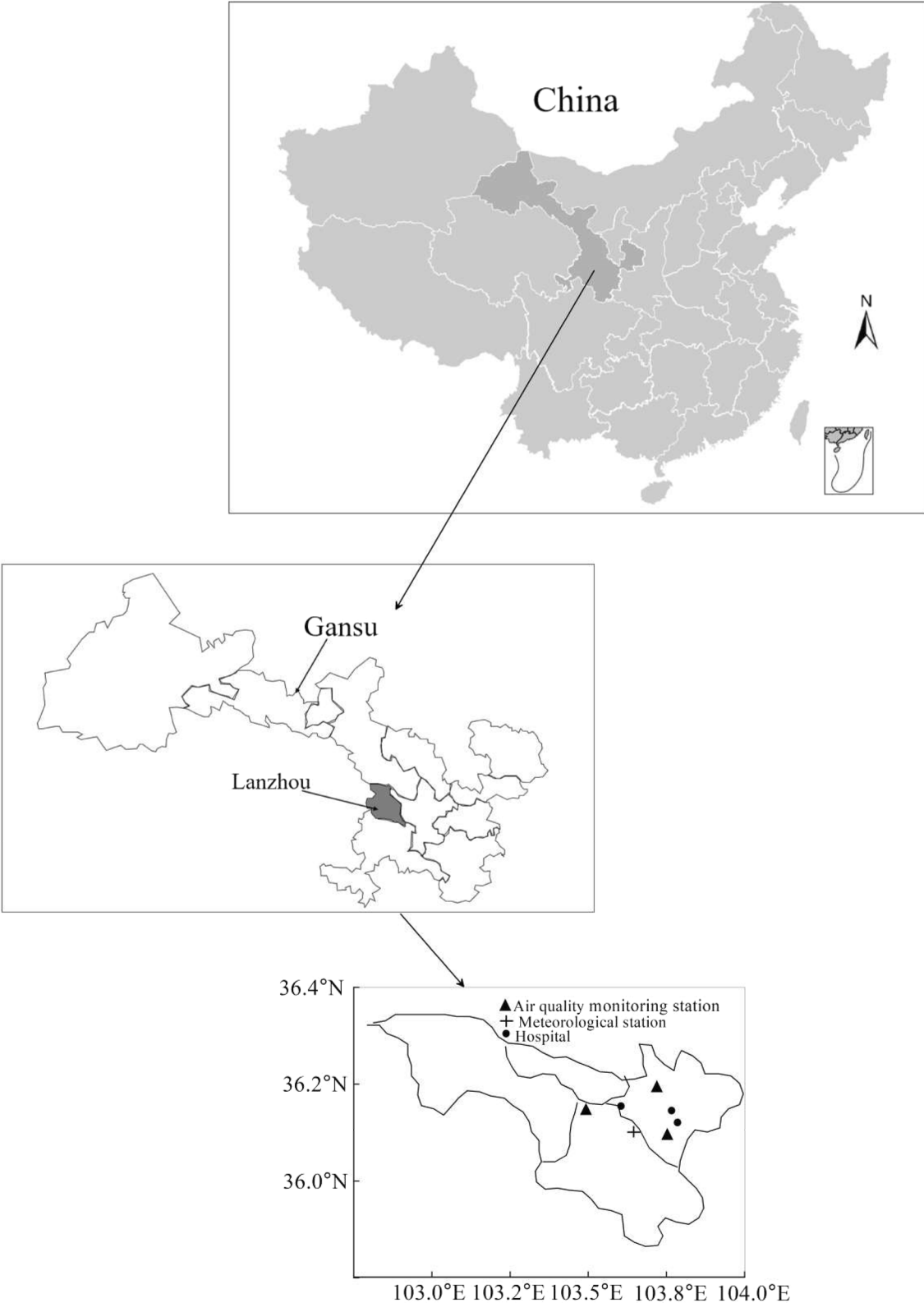
## Materials and methods

### Study area

Lanzhou City (N 35° 23′–37° 42′, E102° 24′–104° 33′, Fig. 1), located in the west of China, is the largest city consisting of the largest population in the Gansu Province; by the end of 2019, the total registered population of the entire city was 3.79 million. This city has a typical temperate semi-arid climate and is surrounded by mountains. The local industries are mainly petrochemical, metallurgy or machinery related.

### Data collection

According to the hospital admissions and geographical locations of large general hospitals in Lanzhou, three large general hospitals with complete electronic medical record systems were selected as data sources. The city territory is geographical orientated on the slopes of the mountains and descends from the southern side to the northern side with a 40 km urban line stretching along the river from the west to the east (see Additional file 1: Fig. S1). Residential areas are mainly distributed in strips from east to west, and these three hospitals are located in the central district with access to convenient transportation, which are surrounded by high-density population regions in Lanzhou. All densely populated areas, in addition to the selected three hospitals are located within a 15 km radius of them. These three hospitals are the largest hospitals in Lanzhou, with 2500, 3500, 2100 inpatient beds, and 8420, 11,860, 8530 inpatients reported in 2019, respectively. We selected these three hospitals for this study mainly due to their reputable levels of medical care, sophisticated medical departments, and their proven capabilities to diagnose and treat patients with CVD. It was estimated that these three hospitals serve roughly 75 percent of all patients in Lanzhou [20], which



**Fig. 1** Locations of air pollutant monitoring stations, the meteorological station, and the three hospitals in Lanzhou, China

is a preferable choice for local patients in Lanzhou with CVD. Daily counts of hospital admission on CVD were collected from these three hospitals between 1 January 2014 and 12 December 2019. Our collected research data included the patient's date of admission, principal diagnosis, age and gender. All subjects with CVD were diagnosed by specialist physicians according to the International Classification of Diseases, 10th revision (ICD-10: I00–I99). Patients were selected according to their primary diagnosis ICD-10 codes in the electronic medical record. Then we calculated the daily count of CVD admission (ICD-10 code: I00–I99). In addition, we also extracted Cause-specific CVD hospitalizations, including IHD (ICD-10 code: I20–I25), heart rhythm disturbances (HRD, ICD-10 code: I44–I49), Heart failure (HF, ICD-10 code: I50), and cerebrovascular events (CD, ICD-10 code: I60–I69), the most common cardiovascular disease diagnosed in Lanzhou [20]. To avoid exposure misclassification, patients from locations other than Lanzhou were excluded. We excluded from the study those with two or more hospitalization records found in the hospital information system (HIS).

Daily (24 h) average concentrations of air pollutants, including particulate matter ( $PM_{2.5}$ ,  $PM_{10}$ , unit:  $\mu g/m^3$ ), sulfur dioxide ( $SO_2$ :  $\mu g/m^3$ ), nitrogen dioxide ( $NO_2$ :  $\mu g/m^3$ ), carbon monoxide ( $CO$ :  $mg/m^3$ ), and the maximum daily 8 h moving average concentration of ozone ( $O_3$ 8h:  $\mu g/m^3$ ) were acquired from Lanzhou Environmental Monitoring Centre, which were gathered consecutively in 3 designated monitoring stations covering urban districts of Lanzhou. According to construction norms for air quality monitoring stations, these 3 monitoring stations are located far from sources of pollution, urban transportation, and buildings, hence, the data obtained from these stations are representative of the overall levels of air pollution in the city. In the Chinese air quality online monitoring system,  $PM_{2.5}$  and  $PM_{10}$  were monitored by using a continuous automatic  $\beta$ -ray monitoring system.  $SO_2$  and  $O_3$  were monitored using ultraviolet fluorescence,  $NO_2$  by chemiluminescence and  $CO$  by infrared absorption. All measurements were made in line with China's National Air Quality Control standards (GB3095-2012). Since Lanzhou is a long but "narrow" city that is situated along a river valley approximately 40 km long from east to west and 3–8 km wide from north to south, the urban area is small (see Additional file 1: Fig. S1). Therefore, the three hospitals and the three monitoring stations are within 5–15 km of one another, and the average data of the three monitoring stations can better reflect the actual air pollution exposure in Lanzhou City. However, we were not able to geocode the locations of the monitoring stations or the residential addresses pertaining to the patients using Baidu Map API. Because

the home address history of the individuals who came to get medical treatment were not recorded, detailed, and standardized by the operators from the three hospitals, the home addresses of participants information could not be converted into the corresponding latitude and longitude coordinates obtained from the Baidu Map website (<http://api.map.baidu.com/lbsapi/>) and managed by ArcGIS10.0 (Redlands, CA, USA). Therefore, it was not possible to use spatial interpolation or pollution data from the nearest air quality monitoring station to reflect the exposure level of the hospital population. After consulting the relevant literature [8, 21, 22], the values from the above three urban stations were averaged to calculate one daily concentration value for  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ , and  $NO_2$ , and the corresponding air pollutant concentration values were set as the average pollutant exposure levels of urban residents according to the recommended methods.

There is one weather monitoring station located in the urban area of Lanzhou, and most of the air quality monitoring stations in Lanzhou are located within a 19 km radius of the meteorological station. The data, including daily average temperature ( $^{\circ}C$ ) and relative humidity (%) were obtained from this monitoring station in the urban area of Lanzhou (N 103° 53, E36° 03). For evaluating city-wide temperature effects on morbidity, a time-series model, based on one monitoring station temperature, is equal to spatiotemporal model that utilizes spatial temperatures [23]. Monitoring of meteorological data was conducted in accordance with the mandatory quality assurance/quality control (QA/QC) procedures set by the Chinese meteorological administration, ensuring the high standard of meteorological monitoring data. No air pollutant data or meteorological information were realized missing during the study period.

### Statistical analyses

Daily hospital admissions of CVD are relatively small in number and the case data on CVD often appear over-dispersed, in addition to approximately following Poisson distribution. For this reason, we estimated the short-term association between air pollutants and temperature on CVD daily morbidity by conducting a quasi-Poisson regression analysis using a distributed lag nonlinear model (DLNM). Table 2 shows the correlations between weather conditions and air pollutants. Spearman correlation analysis indicated a strong correlation among air pollutants. To avoid a multicollinearity problem, only those factors with a correlation of  $|r| < 0.8$  were incorporated into the model. We ran a single-pollutant model, including only one contaminant in each model. The relationship between air pollutants and CVD daily morbidity was as follows:

$$\begin{aligned}\text{Log}[E(Y_t)] = & \alpha + \beta X_{t,l} + \text{ns}(\text{Tem}_t, \text{df}) \\ & + \text{ns}(\text{rh}_t, \text{df}) + \text{ns}(\text{Time}_t, \text{df}) \\ & + \text{ns}(\text{Season}, \text{df}) + \text{factor}(\text{Dow}_t) \quad (1) \\ & + \text{factor}(\text{Holiday}_t),\end{aligned}$$

where  $Y_t$  represents the count of hospital visits for CVD or other disease on day  $t$ ;  $E(Y_t)$  represents the expected number of daily hospital visits for CVD or other disease on day  $t$ ;  $\alpha$  represents the constant term;  $X_{t,l}$  represents the cross-basis matrix obtained by applying the DLNM to the concentration of  $\text{PM}_{2.5}$ ; and  $l$  represents lag day (we used natural cubic spline for the nonlinear effect and a polynomial function for the lagged effect);  $\text{ns}()$  indicates the smoother of the nature cubic spline;  $\text{Tem}_t$  represents daily average on day  $t$ ; and  $\text{rh}_t$  represents the daily average relative humidity.  $\text{Time}_t$  refers to the calendar time. *Season* refers to the day/days of year variable, which controls the seasonal trends.  $\text{DOW}_t$  and  $\text{Holiday}_t$  refer to the dummy viable of the day of the week and public holiday.  $\text{ns}(\text{Tem}_t, \text{df})$ ,  $\text{ns}(\text{rh}_t, \text{df})$  and  $\text{ns}(\text{Time}_t, \text{df})$  are natural cubic spline functions to control potential nonlinear confounding effects of the underlying temporal trends of temperature, relative humidity and time, each with 3, 3 and 5 degrees of freedom. According to the minimum Akaike information criterion for the quasi-Poisson model (Q-AIC), the optimal degrees of freedom (df) were set as 3 for both temperature and humidity and 5 for per year time trend.  $\text{Ns}(\text{Season}, \text{df})$  is used to adjust and control seasonal trends. The seasonal degree of freedom was set as  $\text{df}=4/\text{year}$  [24], and the four seasons, spring (March, April, May), summer (June, July, August), autumn (September, October, November), and winter (December, January, February) were included in the model.

A similar approach was adopted to assess the association between temperature and the CVD hospitalization, and the model formula was defined as:

$$\begin{aligned}\text{Log}[E(Y_t)] = & \alpha + \beta \text{TEM}_{t,l} + \text{ns}(\text{Time}_t, \text{df}) \\ & + \text{ns}(\text{rh}_t, \text{df}) + \text{ns}(\text{PM}_{10t}, \text{df}) \\ & + \text{ns}(\text{SO}_{2t}, \text{df}) + \text{ns}(\text{NO}_{2t}, \text{df}) \quad (2) \\ & + \text{ns}(\text{Season}, \text{df}) + \text{factor}(\text{Dow}_t) \\ & + \text{factor}(\text{Holiday}_t),\end{aligned}$$

where  $t$  represents day of observation;  $E(Y_t)$  represents the expected number of hospital admissions for CVD or other disease on day  $t$ ;  $\alpha$  represents the intercept;  $\text{TEM}_{t,l}$  represents the matrix obtained by applying the DLNM to temperature;  $\beta$  represents the vectors of coefficients for  $\text{TEM}_{t,l}$ ;  $l$  represents the lag days and a natural cubic spline (knots at equally spaced percentiles by default). 5 degrees of freedom (df) were used for the exposure–response relationship and natural cubic splines (knots at

equally spaced values in the log scale of lags by default), and 4 degrees of freedom for the lag–response relationship.  $\text{ns}()$  represents the natural cubic spline in DLNM. To account for the nonlinear variables (i.e., time trend and relative humidity),  $\text{Time}_t$  represent the long-term temporal trend and the seasonal trend. Df represents the degree of freedom.  $\text{Rh}_t$  represents the relative humidity of day  $t$ .  $\text{PM}_{10t}$  represents particulate matter less than  $10 \mu\text{m}$  in aerodynamic diameter day  $t$ .  $\text{SO}_{2t}$  represents sulfur dioxide day  $t$ .  $\text{NO}_{2t}$  represents sulfur dioxide day  $t$ . The meaning of *Season*,  $\text{Dow}_t$  and  $\text{holiday}_t$  are the same as the aforementioned description in the preceding formula. The selection of degree of freedom was based on minimizing Akaike Information Criterion for quasi-Poisson (Q-AIC).  $\text{Ns}$  represents a smoothed function of  $\text{Time}_t$  (df=5),  $\text{rh}_t$  (df=3),  $\text{PM}_{10t}$  (df=3),  $\text{SO}_{2t}$  (df=3),  $\text{NO}_{2t}$  (df=3) and *Season* (df=4).

Considering that there may be a delayed effect of air pollutants, therefore, the single-day lag effect (lag 0 to 7 days) and the cumulative lag effect (lag 01 to 07 days) were analyzed. The greatest effects of both single-day lag and cumulative lag for each pollutant were used in further analysis. The cumulative lag days were defined as the mean of the current day and several prior days (1–7 days, lag01 to lag07). We also explored the effect of daily temperatures on total and cause-specific CVD hospitalizations by choosing 7 days as the maximum lag periods [16].

In this study, the zero value of the daily  $\text{PM}_{2.5}$  was used as a reference, and relative risk (RR) and 95% CI was also used to represent the specific lag and cumulative risk of CVD hospitalization for every  $10 \mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  concentration. For mean daily temperature, the 5th percentile for cold and the 95th percentile for heat were compared with the median temperature and relative risk (RR). The 95% confidence interval (95% CI) were also calculated.

In order to identify the susceptible populations, we also performed subgroup analysis by gender (male and female) and age (<65 years and  $\geq 65$  years). We further conducted a Z-test to verify the statistical significance of the stratified analysis differences by using the formula below [25, 26]:

$$(\beta_1 - \beta_2) / \sqrt{\text{SE}_1^2 + \text{SE}_2^2},$$

where  $\beta_1$  and  $\beta_2$  represent the estimates for the two categories, and  $\text{SE}_1$  and  $\text{SE}_2$  represent their respective standard errors.

Residual plots and Shapiro–Wilk normality test of residuals were used to assess the appropriateness of models [27]. In an attempt to minimize autocorrelation, plots of partial autocorrelation function (PACF) were



examined to evaluate whether the parameter selections in the model were appropriate.

For assessing the stability of result, several sensitivity analyses are performed. Firstly, we changed df in the smooth function: long-term trend (df: 6–10). Secondly, two-pollutant models were constructed to investigate the confounding or compound effects of other pollutants, with the exception of PM<sub>2.5</sub> and PM<sub>10</sub>. This was because the high Spearman's correlation coefficients existed between PM<sub>2.5</sub> and PM<sub>10</sub> (Spearman rank correlations of 0.86; Table 2). Thirdly, stratified analyses based on three air quality monitors were performed to examine the stability of the model by using average concentrations on their model by using single (reference site) or multiple sites. We also plotted the exposure–response curves for the associations of hospital admissions for total CVD or other disease with PM<sub>2.5</sub> at different exposure concentrations. The exposure–response curve is presented by using cubic spline functions with 4 degrees of freedom, in line with previous studies [28].

All statistical analyses were conducted with R software (version 3.6.3) using “dlnm” and “mgcv” packages.

## Results

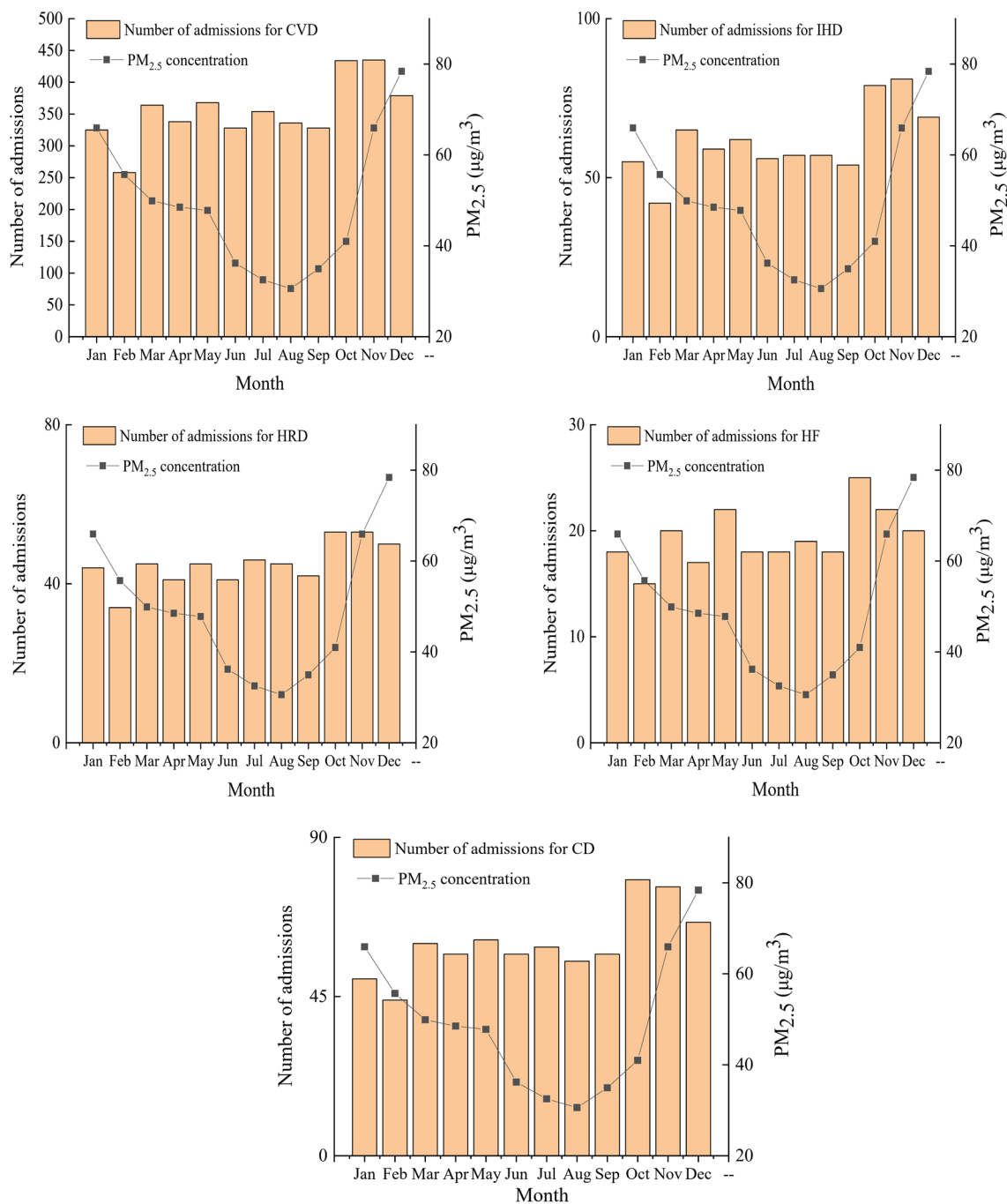
Table 1 shows the descriptive analysis of daily counts of CVD patients, as well as air pollution and meteorological variables. A total of 254,898 patients were admitted to hospitals because of CVD (daily mean, 116 cases). The daily mean counts for cause-specific cardiovascular diseases were 21 cases (IHD), 16 cases (HRD), 5 cases (HF) and 20 cases (CD) (Table 1). Of these admissions, 59.5% were males, and 54.3% were over 65 years of age. The daily mean concentrations of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub>8h and CO were 48.92, 114.84, 21.12, 47.34, 88.24 µg/m<sup>3</sup> and 1.24 mg/m<sup>3</sup>, respectively. The average daily temperature and humidity were 11.34 °C and 51.03%, respectively.

Figure 2 shows PM<sub>2.5</sub> concentrations that suggest higher values during the period from November to the following January compared with other months between 2014 and 2019. According to the season, the daily hospital admissions for cardiovascular diseases were similar to trends observed of PM<sub>2.5</sub>, which increase in November and the following 2 months.

The correlations between various air pollutants, temperature and the relative humidity are shown in

**Table 1** Descriptive statistics of daily count of hospital admissions for CVD, air pollutants, and weather conditions in Lanzhou, China, from Jan 1, 2014 to Dec 31, 2019

	$\bar{X} \pm S$	Minimum	Percentile			Maximum
			$P_{25}$	$P_{50}$	$P_{75}$	
CVD patients (I00–I99)						
Total	116 ± 111	1	39	84	150	676
Male	69 ± 67	1	23	48	87	398
Female	47 ± 45	1	17	34	62	304
< 65	53 ± 50	1	17	35	65	332
≥ 65	63 ± 57	1	22	46	85	366
IHD (I20–I25)	21 ± 19	1	7	14	28	126
HRD (I47–I48)	16 ± 14	1	4	10	22	111
HF (I50)	5 ± 4	1	2	3	7	27
CD (I60–I69)	20 ± 14	1	10	18	26	100
Air pollutants						
PM <sub>2.5</sub> (μg/m <sup>3</sup> )	48.92 ± 26.92	9.00	31.34	42.57	59.13	278.00
PM <sub>10</sub> (μg/m <sup>3</sup> )	114.84 ± 82.94	16.00	71.00	99.52	136.30	1484.54
SO <sub>2</sub> (μg/m <sup>3</sup> )	21.12 ± 13.83	3.54	10.35	17.00	28.23	81.87
NO <sub>2</sub> (μg/m <sup>3</sup> )	47.34 ± 17.28	7.80	36.08	45.91	54.61	146.60
O <sub>3</sub> 8h (μg/m <sup>3</sup> )	88.24 ± 38.77	8.00	58.00	82.00	114.00	222.00
CO (mg/m <sup>3</sup> )	1.24 ± 0.71	0.20	0.76	1.00	1.52	4.65
Meteorological factors						
Mean temperature (°C)	11.34 ± 9.83	− 12.30	2.40	12.70	19.90	30.40
Relative humidity (%)	51.03 ± 15.08	11.71	39.50	51.17	62.00	96.09



**Fig. 2** Monthly distributions of  $PM_{2.5}$ , and numbers for total and cause-specific cardiovascular diseases in Lanzhou, 2014–2019

Table 2.  $PM_{2.5}$  was positively correlated with  $PM_{10}$  ( $r=0.86$ ). Temperature was negatively correlated with  $PM_{2.5}$  ( $r=-0.45$ ),  $PM_{10}$  ( $r=-0.32$ ),  $SO_2$  ( $r=-0.57$ ),  $NO_2$  ( $r=-0.22$ ), and CO ( $r=-0.48$ ). In contrast, temperature revealed a significant positive correlation with ozone ( $r=0.64$ ). In addition, the relative humidity

was negatively correlated with all air pollutants except for CO.

Table 3 shows the RR and 95% CI of total, and cause-specific, cardiovascular hospital admissions in single-pollutant models. Significantly positive associations were found between  $PM_{2.5}$  and all CVD counts at

**Table 2** The coefficient of Spearman rank correlation between daily air pollutants and weather conditions in Lanzhou, 2014–2019

	PM <sub>2.5</sub>	PM <sub>10</sub>	SO <sub>2</sub>	NO <sub>2</sub>	O <sub>3</sub> 8h	CO	Temperature	Relative humidity
PM <sub>2.5</sub>	1.000	0.86*	0.67*	0.47*	−0.32*	0.72*	−0.45*	−0.08*
PM <sub>10</sub>		1.000	0.60*	0.46*	−0.14*	0.58*	−0.32*	−0.32*
SO <sub>2</sub>			1.000	0.51*	−0.38*	0.81*	−0.57*	−0.19*
NO <sub>2</sub>				1.000	0.05*	0.58*	−0.22*	−0.11*
O <sub>3</sub> 8h					1.000	−0.38*	0.64*	−0.23*
CO						1.000	−0.48*	0.01
Temperature							1.000	0.026
Relative humidity								1.000

\*  $P < 0.05$ **Table 3** Relative risk (95% CI) of daily hospital admissions for total and cause-specific CVD associated with a 10  $\mu\text{g}/\text{m}^3$  increase in PM<sub>2.5</sub> with different lag days in Lanzhou during 2014–2019

Lag days	Total		IHD		HRD		HF		CD	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
lag0	1.003	(0.994,1.013)	1.004	(0.992,1.015)	1.000	(0.987,1.013)	1.003	(0.990,1.016)	1.000	(0.990,1.010)
lag1	1.007	(0.998,1.017)	1.013	(1.001,1.025)	1.004	(0.990,1.017)	1.018	(1.005,1.038)	1.007	(1.001,1.018)
lag2	0.993	(0.983,1.003)	0.990	(0.978,1.002)	0.998	(0.984,1.011)	0.991	(0.977,1.004)	0.992	(0.982,1.002)
lag3	1.006	(0.997,1.016)	1.011	(1.000,1.023)	1.001	(0.988,1.014)	1.008	(0.995,1.022)	1.006	(0.996,1.016)
lag4	0.997	(0.987,1.006)	0.995	(0.984,1.007)	1.001	(0.988,1.014)	0.994	(0.981,1.007)	1.001	(0.992,1.011)
lag5	1.002	(0.992,1.012)	1.005	(0.993,1.017)	1.008	(0.995,1.021)	0.999	(0.985,1.013)	0.997	(0.987,1.007)
lag6	0.999	(0.989,1.010)	0.993	(0.980,1.005)	0.991	(0.977,1.005)	0.998	(0.984,1.012)	0.998	(0.988,1.009)
lag7	1.005	(0.996,1.015)	1.009	(0.998,1.021)	1.013	(1.001,1.026)	1.009	(0.996,1.022)	1.000	(0.991,1.010)
lag01	1.011	(1.001,1.020)	1.017	(1.005,1.028)	1.004	(0.990,1.017)	1.011	(0.998,1.025)	1.006	(0.997,1.017)
lag02	1.003	(0.993,1.014)	1.006	(0.994,1.019)	1.001	(0.987,1.016)	1.002	(0.987,1.017)	0.999	(0.988,1.010)
lag03	1.010	(0.998,1.021)	1.018	(1.004,1.032)	1.002	(0.986,1.018)	1.010	(0.994,1.026)	1.005	(0.993,1.017)
lag04	1.006	(0.994,1.018)	1.013	(0.999,1.028)	1.003	(0.986,1.019)	1.004	(0.987,1.021)	1.006	(0.994,1.019)
lag05	1.008	(0.995,1.021)	1.019	(1.003,1.034)	1.010	(0.993,1.028)	1.003	(0.985,1.020)	1.003	(0.990,1.016)
lag06	1.007	(0.994,1.020)	1.010	(0.995,1.027)	1.001	(0.983,1.019)	1.001	(0.983,1.019)	1.001	(0.988,1.015)
lag07	1.012	(0.999,1.025)	1.020	(1.004,1.036)	1.012	(0.997,1.032)	1.010	(0.992,1.028)	1.002	(0.988,1.015)

lag01 (RR: 1.011, 95% CI 1.001–1.020). The association between PM<sub>2.5</sub> and cause-specific cardiovascular hospital admissions differed from one another. For IHD, there were significant associations on lag1, lag3, lag01, lag03, lag05 and lag 07. Moreover, the most significant effect on IHD was found at lag07 (RR: 1.020, 95% CI 1.004–1.036). For the other 3 circulatory system diseases, the significantly positive correlations were found in HRD, HF, CD at lag7, lag1, and lag1, with a 10  $\mu\text{g}/\text{m}^3$  increase in ambient PM<sub>2.5</sub>. The positive results are shown in Table 3 for HRD (RR: 1.013, 95% CI 1.001–1.026), HF (RR: 1.018, 95% CI 1.005–1.038), and CD (RR: 1.007, 95% CI 1.001, 1.018). Among the four major cardiovascular diseases, IHD had the largest RR of morbidity.

Stratified and sensitivity analyses were performed on the basis of reaching the largest estimated effect in the

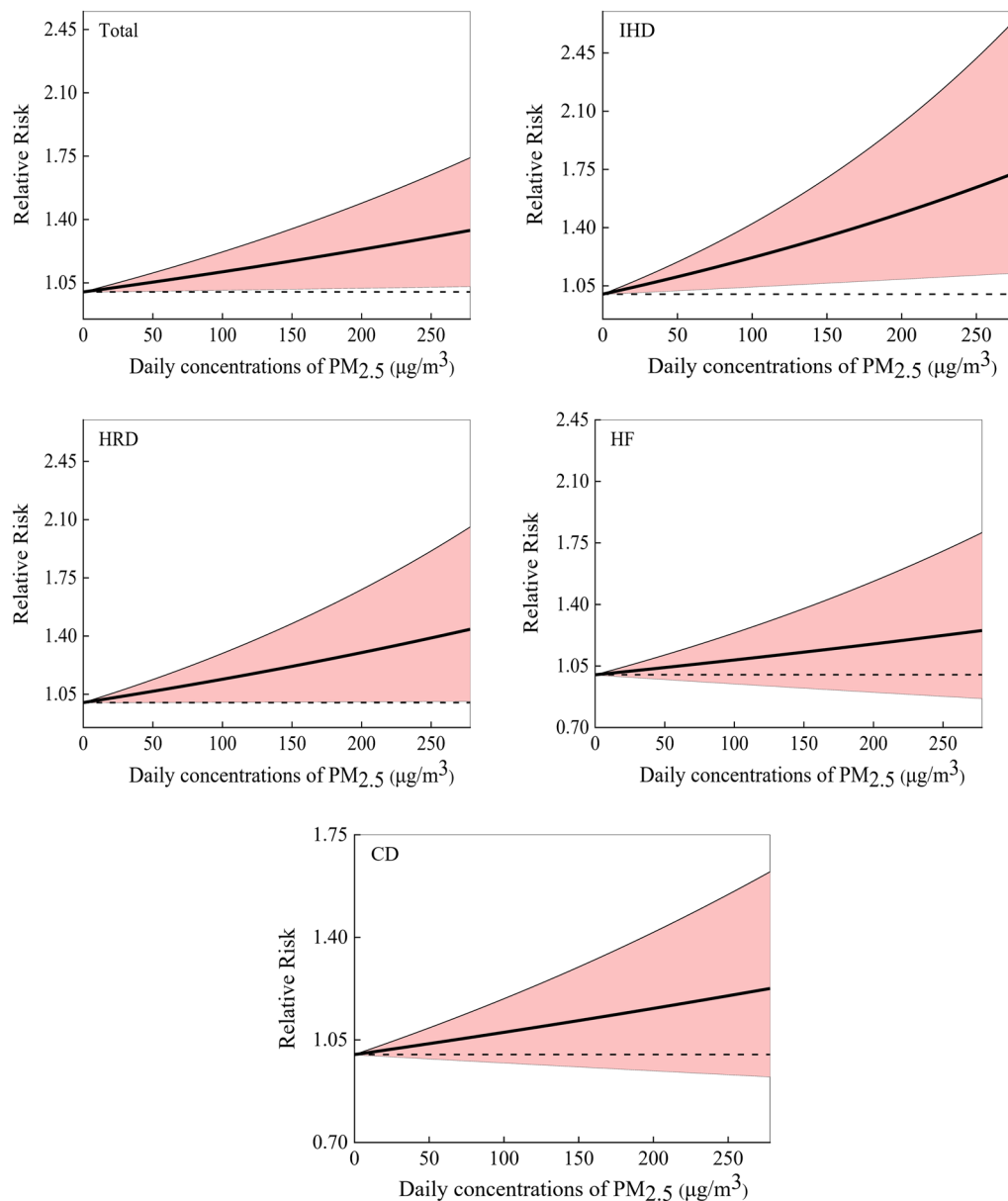
single-pollutant model. The associations between PM<sub>2.5</sub> and hospital admissions for total and cause-specific CVD that were stratified by gender and age are demonstrated in Table 4. Although the difference between gender and age groups were not significant, we observed that the RR of total and cause-specific CVD that was associated with exposure to PM<sub>2.5</sub> was consistently higher in males compared with females, and consistently higher among older patients (age  $\geq 65$ ) compared with patients aged less than 65 years.

The exposure–response curves for PM<sub>2.5</sub> with hospitalizations for total and cause-specific CVD are displayed in Fig. 3. An approximate linear relationship was observed overall and in each of the subgroups of CVD patients. We found no discernible threshold concentration between PM<sub>2.5</sub> and CVD. Generally, when compared with other



**Table 4** Relative risks of (95% CI) of daily hospital admissions for total and cause-specific CVD per 10  $\mu\text{g}/\text{m}^3$  increase in the concentration of  $\text{PM}_{2.5}$  for sex, age

Category	Groups	CVD (lag01)	IHD (lag07)	HRD (lag7)	HF (lag1)	CD (lag1)
Sex	Males	1.016 (1.006,1.027)	1.028 (1.008,1.048)	1.020 (1.005,1.034)	1.013 (0.997,1.029)	1.009 (0.997,1.022)
	Females	1.007 (0.997,1.017)	1.018 (1.002,1.035)	1.015 (0.999,1.043)	1.009 (0.992,1.027)	1.007 (0.996,1.018)
	<i>p</i> -value	0.190	0.300	0.178	0.378	0.388
Age	< 65	1.005 (0.994,1.015)	1.012 (0.995,1.029)	1.010 (0.994,1.026)	1.005 (0.990,1.021)	1.001 (0.989,1.012)
	$\geq 65$	1.015 (1.005,1.025)	1.015 (1.001,1.032)	1.014 (1.001,1.029)	1.016 (0.996,1.035)	1.017 (1.005,1.029)
	<i>p</i> -value	0.399	0.386	0.373	0.274	0.067

**Fig. 3** Exposure–response curves for the association between  $\text{PM}_{2.5}$  and total CVD (lag01), IHD (lag07), HRD (lag7), HF (lag1), and CD (lag1) hospitalizations

**Table 5** Relative risk (RR) and 95% confidence intervals (CI) for total and cause-specific CVD associated with daily mean temperatures (at P5, P95) in comparison with medium at different lag days

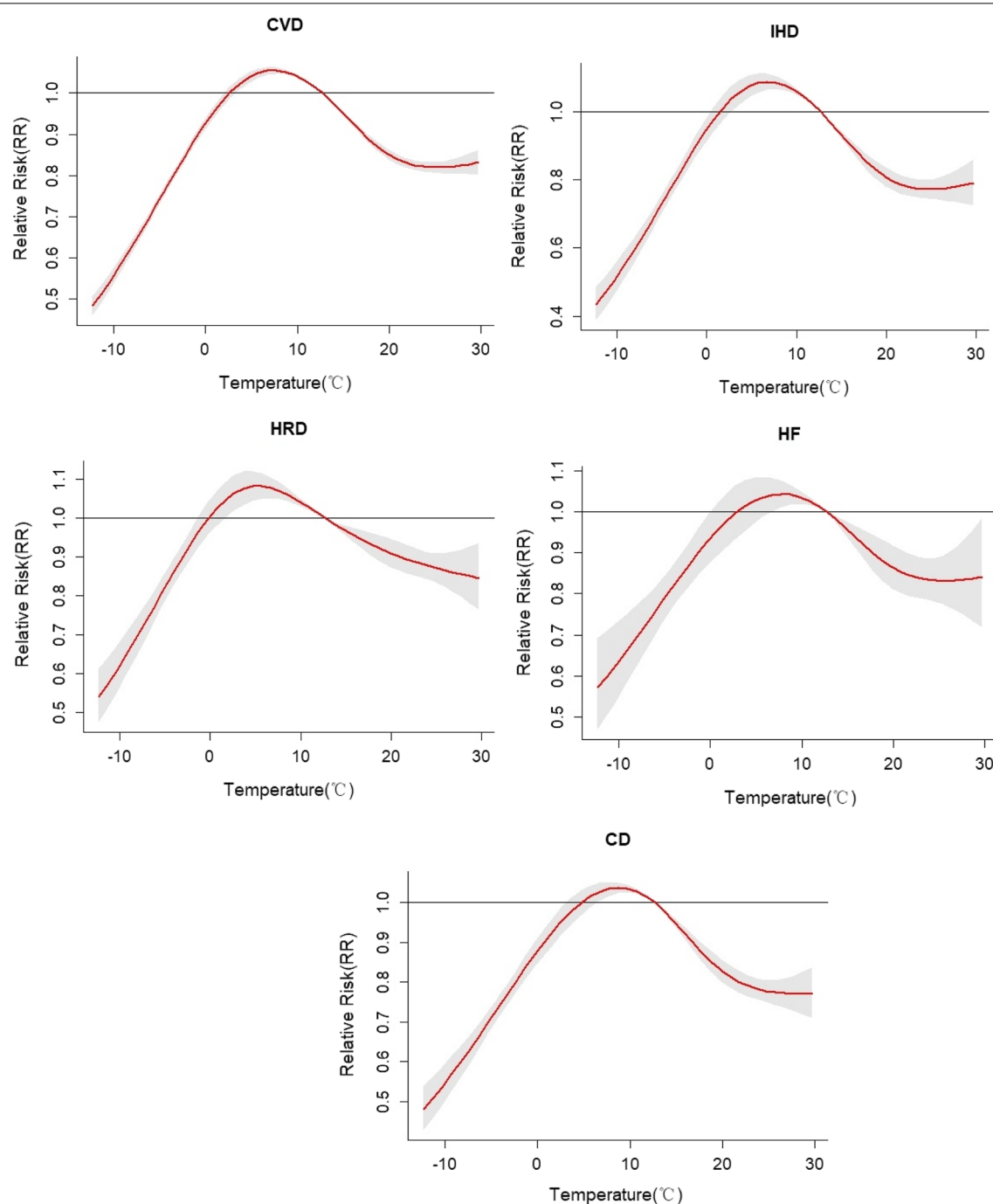
Variables	lag	RR (95%CI)				
		Total	IHD	HRD	HF	CD
P5	lag0	1.055 (1.039,1.070)	1.075 (1.037,1.113)	1.020 (0.978,1.064)	1.047 (0.981,1.118)	1.079 (1.040,1.118)
	lag1	1.029 (1.018,1.040)	1.043 (1.017,1.070)	1.009 (0.979,1.040)	1.026 (0.979,1.075)	1.044 (1.018,1.072)
	lag2	1.005 (0.998,1.011)	1.012 (0.997,1.028)	0.998 (0.979,1.016)	1.005 (0.977,1.035)	1.011 (0.995,1.027)
	lag3	0.981 (0.978,0.983)	0.983 (0.976,0.989)	0.987 (0.979,0.994)	0.985 (0.973,0.997)	0.979 (0.972,0.986)
	lag4	0.957 (0.955,0.960)	0.954 (0.947,0.960)	0.976 (0.968,0.983)	0.965 (0.954,0.977)	0.948 (0.941,0.954)
	lag5	0.934 (0.928,0.941)	0.925 (0.911,0.940)	0.965 (0.947,0.983)	0.946 (0.919,0.973)	0.918 (0.903,0.932)
	lag6	0.912 (0.902,0.922)	0.898 (0.876,0.921)	0.954 (0.925,0.984)	0.926 (0.884,0.971)	0.888 (0.866,0.912)
	lag7	0.890 (0.877,0.904)	0.872 (0.841,0.903)	0.944 (0.904,0.984)	0.908 (0.851,0.969)	0.860 (0.830,0.892)
	lag01	1.085 (1.058,1.114)	1.121 (1.055,1.191)	1.029 (0.957,1.106)	1.074 (0.961,1.202)	1.126 (1.059,1.199)
	lag02	1.091 (1.056,1.126)	1.135 (1.051,1.225)	1.026 (0.937,1.124)	1.066 (0.976,1.164)	1.139 (1.053,1.231)
	lag03	1.069 (1.033,1.107)	1.115 (1.027,1.210)	1.013 (0.918,1.117)	0.993 (0.938,1.052)	1.115 (1.025,1.212)
	lag04	1.024 (0.990,1.058)	1.063 (0.983,1.150)	0.988 (0.900,1.085)	1.044 (0.964,1.129)	1.056 (0.975,1.144)
	lag05	0.957 (0.930,0.983)	0.984 (0.921,1.051)	0.953 (0.881,1.030)	1.080 (0.939,1.243)	0.969 (0.907,1.036)
	lag06	0.872 (0.855,0.890)	0.884 (0.844,0.926)	0.909 (0.861,0.961)	1.082 (0.969,1.209)	0.861 (0.821,0.903)
	lag07	0.777 (0.765,0.788)	0.770 (0.744,0.798)	0.858 (0.824,0.894)	0.983 (0.914,1.056)	0.741 (0.715,0.767)
P95	lag0	1.032 (1.021,1.043)	1.033 (1.006,1.060)	1.048 (1.017,1.080)	1.029 (0.983,1.077)	1.000 (0.974,1.027)
	lag1	1.016 (1.008,1.024)	1.014 (0.995,1.033)	1.029 (1.007,1.052)	1.014 (0.981,1.048)	0.991 (0.972,1.010)
	lag2	0.999 (0.994,1.004)	0.995 (0.984,1.007)	1.010 (0.996,1.024)	0.999 (0.978,1.020)	0.982 (0.970,0.994)
	lag3	0.983 (0.981,0.986)	0.977 (0.971,0.983)	0.992 (0.985,0.999)	0.984 (0.974,0.995)	0.973 (0.967,0.979)
	lag4	0.968 (0.965,0.970)	0.959 (0.954,0.965)	0.973 (0.966,0.980)	0.970 (0.959,0.981)	0.964 (0.958,0.970)
	lag5	0.952 (0.947,0.957)	0.942 (0.930,0.953)	0.956 (0.942,0.969)	0.956 (0.935,0.976)	0.955 (0.944,0.967)
	lag6	0.937 (0.929,0.944)	0.925 (0.907,0.943)	0.938 (0.918,0.959)	0.942 (0.910,0.974)	0.947 (0.929,0.965)
	lag7	0.922 (0.912,0.932)	0.908 (0.884,0.932)	0.921 (0.893,0.949)	0.928 (0.886,0.972)	0.938 (0.914,0.963)
	lag01	1.048 (1.029,1.068)	1.047 (1.001,1.096)	1.079 (1.024,1.136)	1.030 (0.954,1.113)	0.991 (0.947,1.037)
	lag02	1.048 (1.024,1.072)	1.043 (0.985,1.104)	1.089 (1.020,1.163)	0.895 (0.841,0.952)	0.973 (0.919,1.030)
	lag03	1.030 (1.004,1.057)	1.019 (0.958,1.084)	1.080 (1.006,1.160)	0.896 (0.831,0.966)	0.947 (0.890,1.007)
	lag04	0.997 (0.973,1.022)	0.978 (0.921,1.038)	1.052 (0.981,1.127)	0.816 (0.767,0.869)	0.913 (0.859,0.969)
	lag05	0.949 (0.929,0.970)	0.921 (0.874,0.970)	1.005 (0.946,1.068)	0.990 (0.926,1.057)	0.872 (0.827,0.919)
	lag06	0.889 (0.873,0.905)	0.852 (0.816,0.888)	0.943 (0.897,0.991)	0.863 (0.812,0.918)	0.826 (0.791,0.862)
	lag07	0.819 (0.806,0.833)	0.773 (0.743,0.804)	0.868 (0.829,0.909)	0.831 (0.774,0.892)	0.775 (0.745,0.805)

disease, IHD seemed to be more susceptible to higher doses of PM<sub>2.5</sub>.

Table 5 shows the adverse effects of cold and hot temperatures on overall and cause-specific CVD admissions at different lags. For cold effect, we calculated the effects by comparing the 5th percentile of mean temperature ( $-4.1^{\circ}\text{C}$ ) with the 50th percentile of mean temperature ( $12.7^{\circ}\text{C}$ ) along the lags. Generally, there was a significantly increased risk of CVD admissions in the overall CVD, IHD, CD, while the cold effect was found to be non-significant for HRD and HF. For the effect of heat, we calculated its effects by comparing the 95th percentile of mean temperature ( $25.4^{\circ}\text{C}$ ) with the 50th percentile of mean temperature ( $12.7^{\circ}\text{C}$ ) along the lags. For the short lags (lag 0 and Lag1), the

high temperatures were significantly associated with increased risk of CVD admission overall, especially in IHD and HRD; whereas, for long lags (lag07), both cold and high temperatures had significant protective effect on overall and cause-specific CVD admissions.

Figure 4 presents the overall cumulative temperature–CVD association curves over 7 days for total patients and subgroups by CVD. We observed an inverse U-shaped relationship between mean temperature amongst all and cause-specific CVD morbidity, with one peak during  $5\text{--}11^{\circ}\text{C}$ . In addition, the relationship between CVD morbidity and ambient temperature was found to be significant when the ambient temperature was between 5 and  $11^{\circ}\text{C}$ . However, the significant



**Fig. 4** Association between temperature change between temperature (lag 07) and total and cause-specific cardiovascular diseases in Lanzhou, 2014–2019

protective effect was found when the temperature exceeded the given range.

The results of model checking are provided in the Additional file 1: Fig. S2, 3). Analyses stratified by three air quality sites showed a similar temporal variability feature,

and the associations of  $PM_{2.5}$  had no distinct difference across the three sites studied (Additional file 1: Fig. S2). Additionally, The PACF of residuals of the model (1) was smaller than 0.1 for all the lags, which meant there were no discernible patterns and no autocorrelation in the

residuals, showing that the core model was set up adequately to remove the potential confounding in the daily variations of CVD admissions (Additional file 1: Fig. S3).

The associations between total cause-specific CVD hospital admissions and  $PM_{2.5}$  in two-pollutant models are shown in Additional file 1: Table S1. Given that there is a strong correlation between particulate matters, we did not include  $PM_{10}$  in two-pollutant models. The associations of  $PM_{2.5}$  remained robust after controlling all other air pollutants. In addition, the estimated effects of  $PM_{2.5}$  on CVD hospital admissions did not change substantially after varying the df values for temporal trends (Additional file 1: Table S2).

## Discussion

In this study, we have provided new insight into the epidemiological associations between  $PM_{2.5}$  and hospital admissions for total and cause-specific CVD, and the results varied with specific circulatory system diseases. Short-term exposure to  $PM_{2.5}$  was found to be significantly correlated with an increased risk of hospitalizations for CVD, IHD, HRD, HF, and CD, whereas the  $PM_{2.5}$ -related increase of admissions is largest for IHD. We also observed that the male and elderly (aged  $\geq 65$  years) populations were more vulnerable to  $PM_{2.5}$  exposure than other gender and age groups. In addition, these associations were almost linear without any discernible threshold, below which the associations were not statistically significant.

This study observed significant associations between short-term exposure to  $PM_{2.5}$  and hospital admissions for CVD; the highest effect was observed at lag 01 (RR = 1.011, 95% CI 1.001–1.020), which was consistent with several previous. For example, a multicity study in China suggested that the associations between ambient  $PM_{2.5}$  (per 10  $\mu\text{g}/\text{m}^3$  increase) and hospital admissions for CVD was: relative risk (RR) 1.003, 95% CI 1.002–1.004 [10]. Another study done in the state of New York, USA, found that exposure to  $PM_{2.5}$  was linked to the increase of hospital admissions for cardiovascular and cerebrovascular diseases, with RRs 1.009 (95% CI 1.004–1.012) [6]. Domestic research results from Wuhan, Beijing and Yichang also showed that each 10  $\mu\text{g}/\text{m}^3$  increase in  $PM_{2.5}$  increased the risk of hospital admissions for cardiovascular disease, with RR 1.009 (95% CI 1.001–1.017), RR 1.003 (95% CI 1.002–1.005), and RR 1.011 (95% CI 1.004–1.018), respectively [7, 8, 11]. On the other hand, another study reported no significant association between CVD hospitalization and increased  $PM_{2.5}$  concentrations [9]. Therefore, study results differ most likely due to the level of local pollutants, composition of particulate matter, and meteorological factors [29, 30].

In the present study, we found a short-term association between  $PM_{2.5}$  and subcategories of cardiovascular admissions, including IHD, HRD, HF, and CD. Per 10  $\mu\text{g}/\text{m}^3$  increase in  $PM_{2.5}$ , RR of IHD, HRD, HF, and CD were reported to be 1.020 (95% CI 1.004–1.036), 1.013 (95% CI 1.001–1.026), 1.018 (95% CI 1.005–1.038), and 1.007 (95% CI 1.001, 1.018), respectively. Similar to a study by Tian et al. a 10  $\mu\text{g}/\text{m}^3$  increase in  $PM_{2.5}$  increased the risk of IHD, HRD, and HF admissions, with RR 1.003 (95% CI 1.002–1.004), RR 1.003 (95% CI 1.001–1.005), and RR 1.003 (95% CI 1.000–1.05), respectively [10]. Other studies in the state of New York US have also showed that  $PM_{2.5}$  was associated with hospital admissions for IHD, HF, but not with HRD or CD [6]. Furthermore, Zhu et al. in Chengdu, China, confirmed no significant associations for short-term  $PM_{2.5}$  exposure with HRD, HF, and CD risk in the general adult population, but reported that stronger associations were found among IHD patients [9]. The differences between our results and previous findings may be due to different study designs, different regional factors, various weather conditions, major sources of pollutants as well as differing study population.

In gender-specific analyses, males were more susceptible to be affected by  $PM_{2.5}$ . Gender was not a significant modifier in our study since no significant difference was observed between them, which was in line with several previous studies [10]. Inconsistent with the above research results, Amsalu et al. found that  $PM_{2.5}$  was associated with hospital admissions for cardiovascular disease in females [8]. Nevertheless, domestic and foreign research results on gender-specific effects of  $PM_{2.5}$  were inconsistent [7, 9–11]. The gender difference was difficult to explain because the smoking rate in males was much higher than that in females in Lanzhou residents, possibly making males more sensitive to fine particulate matters. Conversely, females in China are known to spend more time in the kitchen compared with males using bio-fuels, exposing themselves to biomass burning. The effect of indoor vs outdoor separation would likely be significant. Moreover, females may be more vulnerable to  $PM_{2.5}$  pollution because of the increasing deposition of particulate in the lung and higher airway reactivity [31]. Further studies are still needed to evaluate whether gender is an effect modifier with regard to the association between ambient  $PM_{2.5}$  and cardiovascular events. Regarding age, a stronger effect was observed among those aged  $\geq 65$  years than those aged  $< 65$  years, although the age difference was not statistically significant, which was consistent with several previous studies [8, 10, 11]. This could be explained by the fact that the elderly has weaker immune systems and may suffer from a variety of other chronic diseases.

The shape of the exposure–response curve plays a role in the public health policy and proper prevention. In the present study, we observed an approximately linear relationship of PM<sub>2.5</sub> with hospitalizations for total CVD and the four specific cardiovascular disease with no noticeable threshold. This was in accordance with other findings in previous studies [8]. However, a multicity study in that investigated 184 cities in China showed that the exposure–response relationship between PM<sub>2.5</sub> and CVD morbidity could be nonlinear [10]. In addition, curves for IHD, related to PM<sub>2.5</sub>, were steeper at higher levels of exposure compared with lower levels; it might suggest that high concentrations of PM<sub>2.5</sub> are often accompanied by air pollution warnings where the public would be encouraged to avoid or reduce outdoor activity, or take protective measures such as using face masks to reduce exposure.

This study has several limitations: first, the concentration data of the three environmental monitoring stations reflect the real exposure level of the population; however, because of living conditions and personal habits, the real exposure level of individuals may differ. Secondly, the potential miscoding or diagnosis of CVD events should be considered when interpreting; it is not likely to be a problem in this study because all data obtained from different hospitals underwent stringent quality checks and we performed coding verification before they were included in the larger data pool. Third, we could not obtain data on CVD mortality, this limited our comprehensive analysis of PM<sub>2.5</sub>. Fourth, during the data collection stage, information on socioeconomic status was not collected for privacy protection, such as barriers to seeking treatment.

## Conclusions

Our findings show that, in Lanzhou, short-term exposure to PM<sub>2.5</sub> significantly increased the risk of hospitalizations for total CVD, especially for IHD. Male and elderly populations were found to be relatively more sensitive.

## Abbreviations

CVD: Cardiovascular diseases; CD: Cerebrovascular disease; DLNM: Distributed Lag Nonlinear Model; GAM: Generalized Additive Model; Q-AIC: Quasi-Poisson Akaike information criteria; RR: Relative risk; IHD: Ischemic heart disease; HRD: Heart rhythm disturbances; HF: Heart failure.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12302-022-00634-y>.

**Additional file 1: Figure S1.** Location of Lanzhou city in China (Cheng et al., 2020). **Figure S2.** RR (95% CIs) of total and cause-specific CVD with an increase of 10 µg/m<sup>3</sup> in PM<sub>2.5</sub> concentrations according to

single-pollutant model based on different sites. **Figure S3.** Residual scatter plot and partial autocorrelation function (PACF) plot of the single-pollutant model. **Table S1.** Relative risk (95% CI) in hospital admissions for total and cause-specific CVD with a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentrations when using single, two-pollutant models. **Table S2.** Relative risk (95% CI) in hospital admissions for total and cause-specific CVD with a 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentrations in sensitivity analyses.

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## Author contributions

TW, XX and MB contributed to the conception or design of the work. XY, AC, and YP contributed to the acquisition, analysis, or interpretation of data for the work. TW drafted the manuscript. TW and ZZ critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy. All authors read and approved the final manuscript.

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## Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to confidentiality agreements, however they are available upon request from the corresponding author if required.

## Declarations

### Ethics approval and consent to participate

The present study is considered exempt from institutional review board approval since the data used were collected for administrative purpose without any personal identifiers.

### Consent to Publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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