



Lag effects of size-fractionated particulate matter pollution on outpatient visits for respiratory diseases in Lanzhou, China

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Abstract

Introduction. A large body of evidence suggests that an increase in atmospheric particulate matter (PM) concentrations will lead to an increase in morbidity due to adverse health conditions, such as respiratory diseases (RESD). Lanzhou is located in northwest China, central Gansu Province. Due to limited research and data, the impact of PM on human health have not been systematically acknowledged.

Objective. The aim of the study is to investigate the association between size-fractionated PM pollution and outpatients visits for RESD.

Materials and method. Data on outpatient visits for RESD, air pollutants and meteorological indices in Lanzhou were collected from 1 February 2014 – 31 December 2017, and the associations of three types of PM ($PM_{2.5}$, PM_{c} and PM_{10}) with outpatient visits for RESD were evaluated using generalized additive models (GAMs).

Results. Findings showed that $PM_{2.5}$ and PM_{c} had the most significant impact on outpatient visits for RESD at seven cumulative lag days. PM_{10} was not significantly associated with outpatient visits for RESD. In subgroup analysis, the impact of atmospheric PM on outpatient visits for RESD was significantly modified by gender and age; men, and children aged 0–5 years old, were more sensitive to $PM_{2.5}$ pollution.

Conclusions. Increased atmospheric PM concentration is associated with an increase in outpatient visits for RESD, and it has a lag effect. The increase in outpatient visits for RESD appears to be driven by increased $PM_{2.5}$ concentrations. The results obtained may provide reference values for formulating preventive strategies to protect the population from the adverse impact of PM pollution.

Key words

Particulate matter; Respiratory diseases; Daily outpatient visits; Generalized additive model

Abbreviations

GAM – Generalized Additive Model; **RESD** – Respiratory Diseases; **AIC** – Akaike's Information Criterion; **ER** – Excessive Risk; **PM** – Particulate Matter

INTRODUCTION

With the acceleration of industrialization and urbanization in recent years, energy consumption has dramatically increased with a subsequent increase in air pollution, which poses the most severe environmental health risk globally [1]. According to the *China Ecological Environment Status Bulletin 2016*, air quality index (AQI) greater than 100 was considered to exceed the standard; 254 out of 338 (75.1%) cities at or above the prefectural level in China did not meet the minimum standards for environmental air quality in 2016; the number of days with heavy pollution and above were dominated by particulate matter 2.5 ($PM_{2.5}$), and PM_{10} accounted for 80.3% and 20.4%, respectively, of the total. Atmospheric PM pollution is currently the leading cause of smog in China. Atmospheric PM includes total suspended particulates (TSP), inhalable particulates, fine particulates and ultrafine particulates. Among them, inhalable particulates (also

known as PM_{10}) are defined as particulates that can enter the respiratory tract and have an aerodynamic diameter of $\leq 10 \mu\text{m}$. Fine particulates, also known as $PM_{2.5}$, are small particles easily retained in the terminal bronchioles and alveoli, with an aerodynamic diameter of $\leq 2.5 \mu\text{m}$; some finer ones can enter the bloodstream through the alveoli [2–3]. PM_{c} is a PM with an aerodynamic diameter of 2.5–10 μm [4].

Over the last few years, there has been intense research interest in the adverse effects of environmental pollution on human health. Previous studies have demonstrated that short-term exposure to atmospheric PM is associated with increased morbidity, hospitalization and mortality due to respiratory diseases (RESD) [5–9]. Epidemiological studies conducted in China and elsewhere have mostly focused on all-cause mortality outcomes. However, unlike Western countries, outpatient visits far exceed hospital admissions in China, indicating an acute effect of PM pollution on population health [7]. Therefore, it appears that morbidity may be a more appropriate index for quantifying impact of PM pollution on health rather than mortality. Existing studies on the impact of atmospheric PM with different particle sizes on RESD in China have so far been conducted

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in Beijing, Nanjing, Dongguan, Guangzhou and Ningbo [4;7;10–12]. However, the components of atmospheric PM vary significantly from region to region, and its impact on health is also different [7]. In previous studies, outpatient data were rarely used to simultaneously evaluate the impact of three types of PM ($PM_{2.5}$, PM_C , and PM_{10}) on patients with RESD, with stratification by gender and age groups.

Lanzhou, the capital and largest city of central Gansu Province in northwest China, is an industrial city dominated by petrochemicals, metallurgy and machinery. It is surrounded by mountains, forming a bead-like river valley terrain with canyons and basins, and to the northeast of Lanzhou lies the Qinghai-Tibet Plateau. Due to its topographic conditions and geographic location, the atmosphere of Lanzhou remains in an ultra-stable state, which is not conducive to the diffusion and dilution of atmospheric pollutants. Furthermore, fossil fuel consumption has increased due to the acceleration of industrialization and urbanization and increased ownership of motor vehicles, thus raising the atmospheric $PM_{2.5}$ concentration. Also, the Tengger Desert, one of the three major dust sources in China, is only 200 kilometers from Lanzhou, and the Badain Jaran Desert is located 500 kilometers to the northwest of Lanzhou; natural dust fall is therefore severe and sand-dust weather frequently occurs in Lanzhou [13]. Studies have shown that surface soil accounts for 46.33% of PM_{10} in Lanzhou due to the dry weather [14], so atmospheric PM_{10} concentration in Lanzhou is increased by sand-dust weather. Between 2007–2017, the annual average PM_{10} concentration in Lanzhou exceeded the second-level standard of environmental air quality in China ($70 \mu\text{g}/\text{m}^3$). The $PM_{2.5}$ concentration remained at $60\text{--}70 \mu\text{g}/\text{m}^3$, which also exceeded the national second-level standard by 1.5 times. Given the increasing air pollution and concerns with adverse health effects, there has been an increasing number of research studies on atmospheric particulate pollutants in Lanzhou, focusing on TSP, dust fall and floating dust. There are limited studies on pollution characteristics, chemical composition and sources of PM_{10} and $PM_{2.5}$ [15–16]. To our knowledge, no study has yet evaluated the impact of $PM_{2.5}$, PM_C and PM_{10} on RESD in Lanzhou.

OBJECTIVES

The aim of the study was to investigate the association between size-fractionated PM pollution and outpatients visits for RESD, with the objective of clarifying the adverse effects of RESD due to PM pollution in Lanzhou, which may help in formulating preventive strategies.

MATERIALS AND METHOD

Study area. Lanzhou is the capital of Gansu Province, located in northwestern China and central Gansu Province ($102^{\circ}24'\text{--}104^{\circ}33'\text{E}$, $35^{\circ}23'\text{--}37^{\circ}42'\text{N}$). It has a typical temperate semi-arid continental monsoon climate. The annual average temperature is 10.3°C , the summer is warm and short and the winter is cold and long. During the summer, precipitation is small and concentrated; it is dry and windy and the day-night temperature difference is substantial. The city covers a total area of 13,100 square kilometers and the total population of the municipal district is about three million.

Data sources. Data on daily outpatient visits for RESD in Lanzhou from 1 February 2014 – 31 December 2017 were obtained from three local Grade A Class 3 hospitals. These included the home address, gender, age, date of outpatient visit, disease diagnosis and visit ID of patients. Non-local patients were excluded based on their home addresses. Disease diagnoses were coded according to the 10th edition of the International Classification of Diseases (ICD-10) codes (J00–J99). The disease of concern primarily included upper respiratory tract infection (URTI; ICD-10: J00–J06 and J30–J39), lower respiratory tract infection (LRTI; ICD-10: J20–J22 and J40–J47), and asthma (ICD-10: J45–J46). Asthma accounted for 3.24% of all outcomes, upper respiratory tract infections for 69.51%, lower respiratory tract infections for 20.59% and others for 6.67%.

Data on atmospheric pollutants were obtained from the national urban air quality real-time publishing platform (<http://106.37.208.233:20035/>), and daily monitoring data of Lanzhou were selected, including $PM_{2.5}$, PM_{10} , sulfur dioxide (SO_2), and nitrogen dioxide (NO_2). The daily average concentration of pollutants was the arithmetic mean of the data from the four State-controlled monitoring points in Lanzhou. Both data integrity and consistency complied with the requirements of the national ambient air quality monitoring specifications, without abnormally high or low values and missing values, but with higher accuracy. The location distribution of hospitals and environmental monitoring points in Lanzhou are shown in Figure 1. The meteorological data came from Gansu Meteorological Bureau, which included average temperature and relative humidity.

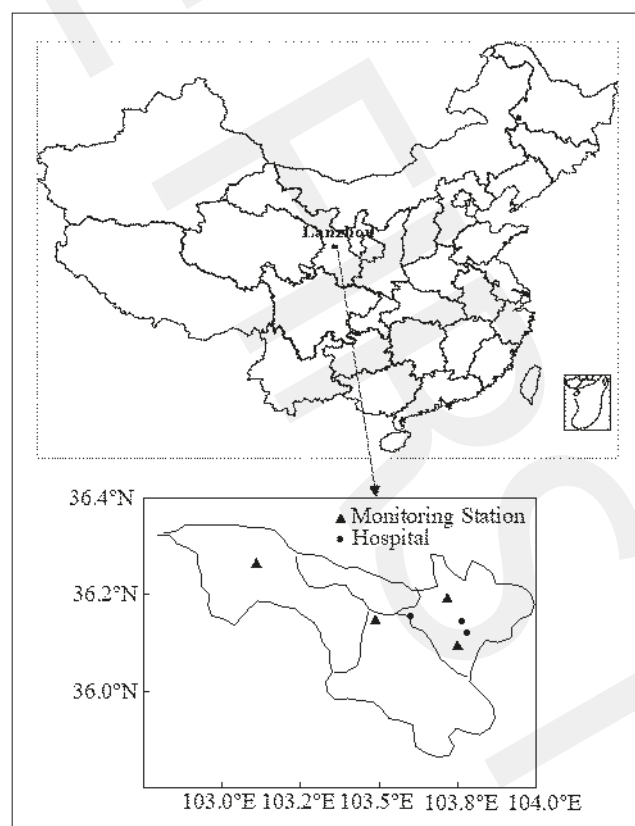


Figure 1. Location of Lanzhou in China and air pollution monitor and hospital

Statistical analysis. Since the proportion of daily outpatient visits for RESD in the total population was small and approximately conforms to the Poisson distribution, the short-term impact of atmospheric PM on daily outpatient visits for RESD was analyzed using a semi-parametric generalized additive model (SGAM) based on Poisson regression. The basic model formula is as follows:

$$\text{Log}[E(Y_t)] = \alpha + \beta Z_t + ns(\text{time}, df) + ns(\text{Temp}_t, df) + ns(\text{RH}_t, df) + \text{DOW} + \text{Holiday}$$

In the formula, Y_t represents the outpatient visits on the t day; $E(Y)$ represents the expected outpatient visits on the t day; α is the intercept; Z_t indicates the pollutant concentration on the t day; β is the regression coefficient; ns indicates the natural cubic spline; time is the time variable; Temp_t indicates the average temperature on the t day; RH_t represents the average relative humidity on the t day; DOW indicates the day-of-the-week effect; Holiday indicates the holiday effect; both DOW and Holiday were used as dummy variables.

The degree of freedom of each variable in the model was determined according to the Akaike Information Criterion (AIC). More specifically, seven was selected as the degree of freedom of time variable to eliminate secular trends and seasonality. To control for the interference of confounding factors in the model [17], the natural cubic spline with a

degree of freedom of three was selected, thus controlling the influence of temperature and humidity [18–19]. The PM pollution effect was quantitatively evaluated through the increase in the value of the relative risk of outpatient visits for every $10 \mu\text{g}/\text{m}^3$ increase in pollutant concentration [18;20–21]. The results were expressed as excess risk (ER), which was estimated using: $ER = (e^{10 \times \beta} - 1) \times 100\%$.

Previously, it has been confirmed that the impact of air pollutants on the respiratory system has a lag effect, and the lag effect alone may reduce the association between air pollutants and disease [7;22]. Therefore, single lag effects (lag 1, lag 2, lag 3, lag 4, lag 5, lag 6, and lag 7d) and cumulative lag effects (lag01, lag02, lag03, lag04, lag05, lag06, and lag07d) of $\text{PM}_{2.5}$, PM_C , and PM_{10} on outpatient visits for RESD were analyzed in this study. For the single lag effect, lag x ($x=1, 2, 3, \dots, 7$) represents lag associated with the mass concentration of PM in the previous x days; for the cumulative lag effect, lag $0x$ ($x=1, 2, 3, \dots, 7$) represents lag associated with the average mass concentration of PM on the current day and the previous x days.

The outpatient medical records were stratified based on gender (male, female), age (0–5, 6–14, 15–59, ≥ 60 -years-old), and season. The impact of $\text{PM}_{2.5}$, PM_C , and PM_{10} on daily outpatient visits in these different subgroups and their seasonal differences were then explored.

As shown in Table S1, the two-pollutant and multi-

Table S1. Percentage increase in RESD daily outpatients for a $10 \mu\text{g}/\text{m}^3$ increase in daily PM pollutants on lag07 day in sensitivity analyses

Model*	Total	Male	Female	0–5 years	6–14 years	15–59 years	≥ 60 years
$\text{PM}_{2.5}$							
df for temporal trends							
df=5/year	1.441(0.977,1.906)	1.401(0.926,1.878)	1.487(1.012,1.965)	2.571(1.973,3.171)	0.664(-.111,1.446)	-0.021(-.535,0.497)	0.793(0.170,1.420)
df=6/year	1.322(0.867,1.779)	1.278(0.812,1.746)	1.373(0.905,1.842)	2.38(1.797,2.966)	0.532(-.242,1.312)	-0.056(-.571,0.462)	0.706(0.088,1.329)
df=8/year	1.434(0.802,1.869)	1.109(0.261,1.460)	1.463(0.322,1.907)	2.243(1.734,2.754)	0.562(-.327,0.958)	-0.029(-.555,0.501)	0.728(0.095,1.365)
df for temperature							
df=4	1.351(0.888,1.816)	1.317(0.843,1.794)	1.391(0.917,1.867)	2.464(1.868,3.064)	0.507(-0.27,1.29)	-0.077(-.592,0.442)	0.766(0.140,1.395)
df=5	1.325(0.861,1.792)	1.298(0.822,1.776)	1.358(0.882,1.835)	2.427(1.829,3.028)	0.557(-.222,1.341)	-0.097(-.615,0.424)	0.687(0.060,1.318)
df=6	1.290(0.826,1.756)	1.261(0.785,1.740)	1.324(0.848,1.802)	2.387(1.789,2.989)	0.497(-.284,1.284)	-0.121(-0.64,0.400)	0.648(0.022,1.279)
PM_C							
df for temporal trends							
df=5/year	0.465(0.231,0.699)	0.446(0.206,0.687)	0.487(0.248,0.726)	0.757(0.451,1.064)	0.37(-0.028,0.771)	0.046(-0.207,0.3)	0.222(-0.077,0.523)
df=6/year	0.425(0.195,0.655)	0.405(0.169,0.642)	0.447(0.213,0.683)	0.701(0.402,1.023)	0.328(-0.071,0.728)	0.032(-0.221,0.287)	0.189(-0.109,0.488)
df=8/year	0.421(-0.098,0.641)	0.412(-0.116,0.641)	0.432(-0.191,0.735)	0.676(0.338,1.092)	0.329(-0.079,0.74)	0.034(-0.224,0.292)	0.190(-0.134,0.474)
df for temperature							
df=4	0.472(0.242,0.704)	0.453(0.216,0.691)	0.495(0.260,0.731)	0.761(0.459,1.063)	0.379(-0.016,0.775)	0.057(-0.195,0.31)	0.229(-0.071,0.529)
df=5	0.474(0.244,0.705)	0.456(0.219,0.694)	0.494(0.260,0.730)	0.756(0.461,1.069)	0.4(0.006,0.796)	0.056(-0.197,0.309)	0.210(-0.089,0.51)
df=6	0.493(0.263,0.724)	0.478(0.241,0.715)	0.511(0.277,0.747)	0.791(0.491,1.092)	0.431(0.036,0.828)	0.057(-0.196,0.311)	0.235(-0.063,0.535)
PM_{10}							
df for temporal trends							
df=5/year	0.478(0.302,0.654)	0.462(0.281,0.643)	0.496(0.317,0.676)	0.816(0.589,1.045)	0.310(0.007,0.615)	0.024(-0.169,0.218)	0.238(0.01,0.467)
df=6/year	0.438(0.265,0.611)	0.421(0.243,0.599)	0.458(0.281,0.635)	0.757(0.534,0.98)	0.265(-0.038,0.570)	0.021(-0.183,0.205)	0.207(-0.02,0.435)
df=8/year	0.429(0.012,0.647)	0.470(0.0204,0.604)	0.490(0.201,0.660)	0.764(0.534,0.965)	0.294(-0.019,0.509)	0.019(-0.182,0.215)	0.200(-0.033,0.434)
df for temperature							
df=4	0.468(0.293,0.642)	0.452(0.273,0.632)	0.486(0.308,0.664)	0.800(0.574,1.025)	0.291(-0.011,0.594)	0.023(-0.17,0.216)	0.237(0.009,0.466)
df=5	0.465(0.29,0.639)	0.451(0.271,0.631)	0.481(0.303,0.659)	0.794(0.568,1.019)	0.311(0.01,0.613)	0.02(-0.174,0.213)	0.216(-0.013,0.445)
df=6	0.470(0.296,0.644)	0.457(0.278,0.637)	0.485(0.307,0.663)	0.804(0.579,1.029)	0.319(0.017,0.622)	0.017(-0.176,0.211)	0.225(-0.003,0.454)

* Results obtained from single-pollutant models for lag07 day; Abbreviations: df, degree of freedom

pollutant models were established by introducing other coexisting pollutants, and the degree of freedom of the time variable ($df=6-10$) was altered for sensitivity analysis. All statistical analyses were conducted using R software (version 3.4.4) with 'mgcv' package and $P<0.05$ was considered to be statistically significant.

RESULTS

Descriptive data on daily outpatient visits for RESD, the daily average concentration of air pollutants and meteorological data, are shown in Table 1. A total of 633 people had an outpatient visit for RESD, on average, every day in the three hospitals in Lanzhou from 1 February 2014 – 31 December 2017. These included 342 males and 291 females (1.18:1) and 300 were aged 0–5 years, 93 aged 6–14 years, 188 aged 15–59 years and 52 aged ≥ 60 years. The daily average concentration of $PM_{2.5}$, PM_C , PM_{10} , NO_2 and SO_2 was $52.81 \mu\text{g}/\text{m}^3$, $69.91 \mu\text{g}/\text{m}^3$, $122.65 \mu\text{g}/\text{m}^3$, $45.88 \mu\text{g}/\text{m}^3$ and $21.91 \mu\text{g}/\text{m}^3$, respectively. According to the annual concentration limits specified in *Ambient Air Quality Standard* (GB3095–2012), the second-level annual average concentration threshold of $PM_{2.5}$, PM_{10} and NO_2 were $35 \mu\text{g}/\text{m}^3$, $70 \mu\text{g}/\text{m}^3$ and $40 \mu\text{g}/\text{m}^3$, respectively; the concentration of $PM_{2.5}$, PM_{10} and NO_2 exceeded the national second-level standard. In contrast, the annual average concentration of SO_2 did not exceed the national second-level standard ($60 \mu\text{g}/\text{m}^3$) during the study period. The annual average temperature and annual average relative humidity were 11.66°C and 50.94% , respectively.

As shown in Figure 2, the concentrations of $PM_{2.5}$, PM_C and PM_{10} in Lanzhou in 2014–2017 displayed an evident seasonal trend, with a decline in summer and an increase in winter.

Table 1. Descriptive statistics on RESD outpatient visits, air pollutant levels and meteorological variables in Lanzhou during 2014–2017

Variable	$\bar{x}\pm\text{SD}$	Min	Percentile			Max
			P ₂₅	P ₅₀	P ₇₅	
RESD outpatient visits						
Total	633.00 \pm 243.82	1.00	476.00	598.50	736.00	2130.00
Male	342.43 \pm 128.84	1.00	259.00	323.00	396.00	1103.00
Female	290.56 \pm 116.80	1.00	216.00	276.00	339.00	1027.00
0-5 years	299.92 \pm 121.19	1.00	224.00	276.50	342.00	1041.00
6-14 years	93.37 \pm 49.89	1.00	63.00	81.00	107.00	422.00
15-59 years	188.09 \pm 88.93	1.00	118.00	187.00	238.00	556.00
≥ 60 years	51.62 \pm 30.90	1.00	25.00	51.00	69.00	189.00
Meteorological factors						
Mean temperature($^\circ\text{C}$)	11.66 \pm 9.68	-12.30	3.40	13.07	19.90	30.40
Relative humidity (%)	50.94 \pm 15.14	18.00	39.43	50.66	62.00	96.09
Air pollutants						
$PM_{2.5}$ ($\mu\text{g}/\text{m}^3$)	52.81 \pm 26.94	12.73	35.24	45.14	62.40	269.43
PM_C ($\mu\text{g}/\text{m}^3$)	69.91 \pm 61.91	2.27	41.31	58.68	84.21	1251.40
PM_{10} ($\mu\text{g}/\text{m}^3$)	122.65 \pm 78.83	18.98	80.50	107.63	144.76	1484.54
SO_2 ($\mu\text{g}/\text{m}^3$)	21.91 \pm 14.18	3.54	10.82	17.94	29.68	81.87
NO_2 ($\mu\text{g}/\text{m}^3$)	45.88 \pm 15.85	7.80	36.36	45.30	52.76	146.60

Note: \bar{x} , SD, Min, Max, P₂₅, P₇₅ represented the mean, standard deviation, minimum, maximum, the 25th percentile, and the 75th percentile of variables, respectively.

Table 2. Spearman correlation coefficients between daily air pollutants and weather conditions in Lanzhou, 2014–2017

Pollutants	$PM_{2.5}$	PM_C	PM_{10}	SO_2	NO_2	Temperature
PM_C	0.51*					
PM_{10}	0.81*	0.72*				
SO_2	0.64*	0.37*	0.56*			
NO_2	0.41*	0.35*	0.42*	0.38*		
Temperature	-0.46*	-0.14*	-0.33*	-0.62*	-0.20*	
Humidity	-0.14*	-0.47*	-0.34*	-0.19*	-0.14*	-0.08*

* $P<0.01$

The change in the trend of outpatient visits for RESD was consistent for $PM_{2.5}$; outpatient visits were lower in summer and peaked in the winter.

The estimated Spearman correlation coefficients between air pollutants and meteorological factors are listed in Table 2. There were significant positive correlations among $PM_{2.5}$, PM_C , PM_{10} , NO_2 and SO_2 ($p<0.05$). $PM_{2.5}$, PM_C , PM_{10} , NO_2 and SO_2 were negatively correlated with daily average temperature and average relative humidity ($p<0.05$). Atmospheric pollutants had strong correlations with meteorological factors.

After accounting for confounding factors, GAM analysis was conducted to assess the impact of the daily average concentration of $PM_{2.5}$, PM_C and PM_{10} on daily outpatient visits for RESD in subgroups on the same day and different lag days. It was observed that: the single lag effect of $PM_{2.5}$ on the entire population was not statistically significant at lag5, and statistically significant on other lag days (lag0-lag4, lag6–7). The cumulative lag effect of $PM_{2.5}$ was statistically significant throughout the cumulative lag period (lag01-lag07).

The single lag effect of PM_C on the entire population was only statistically significant at lag7, and its cumulative lag effect was not statistically significant throughout the cumulative lag period (lag01-lag07).

Moreover, the single lag effect of PM_{10} on the entire population was not statistically significant throughout the lag period (lag0-lag7), with no evidence of statistical significance detected in its cumulative lag effect throughout the cumulative lag phase (lag01-lag07).

Subgroup analyses were conducted according to age and gender. The impact of $PM_{2.5}$, PM_C and PM_{10} on outpatient visits in each subgroup are shown in Tables 3–5. In the analysis by gender, the single lag effect of $PM_{2.5}$ on men was not statistically significant at lag5, and its harmful effect was most remarkable at lag7, in which case outpatient visits increased by 0.793 (95% CI: 0.349, 1.239) for every $10 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ concentrations. Its single lag effect on women was not statistically significant at 4 and 5 lag days (lag4-lag5), and the maximum ER (0.832) was found at lag7 (95% CI: 0.395, 1.272). The cumulative lag effect of $PM_{2.5}$ on men and women were both statistically significant throughout the cumulative lag phase, and outpatient visits of men were higher than those of women for every $10 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ concentration.

Furthermore, the single lag effect of PM_C between men and women was statistically significant only at lag7, and its cumulative lag effects on men and women were not statistically significant throughout the cumulative lag phase. The single and cumulative lag effects of PM_{10} on men and women were not statistically significant throughout the lag phase.

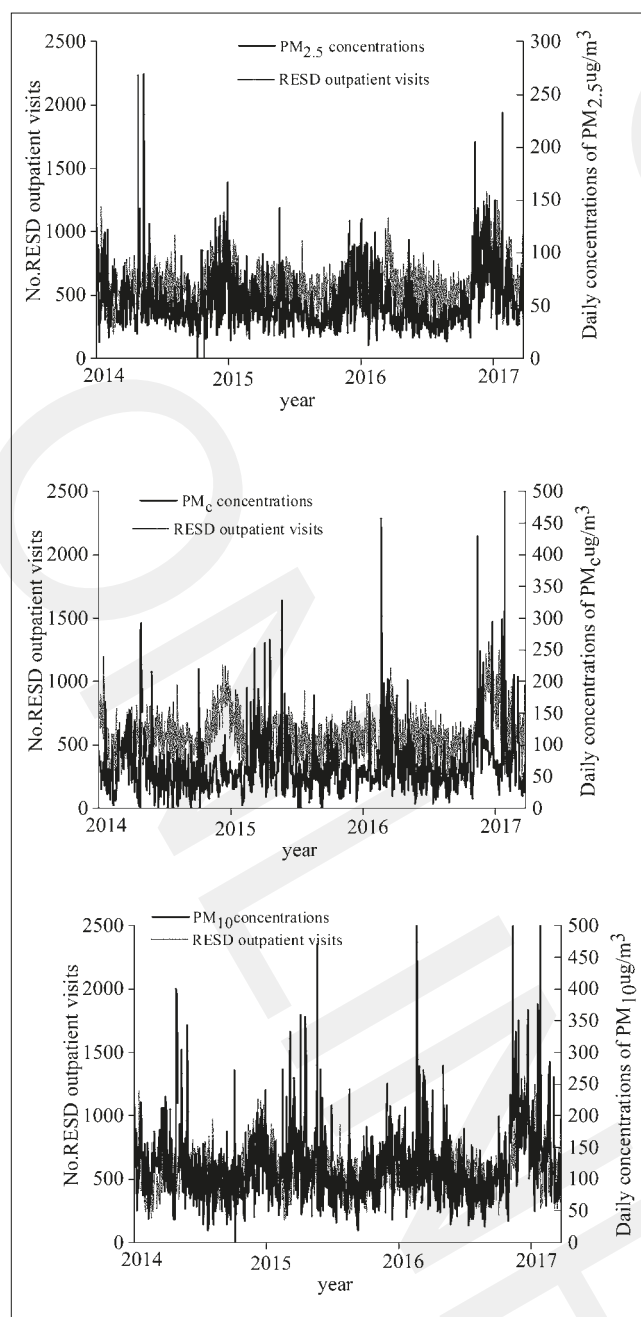


Figure 2. Concentrations of $PM_{2.5}$, PM_c and PM_{10} from 2014 to 2017 in Lanzhou in different season

In the subgroup analysis by age, the single and cumulative lag effects of $PM_{2.5}$ on children aged 0–5 years were statistically significant throughout the lag phase, with no statistical significance in people aged 6–14 and 15–59. Among people aged ≥ 60 years, the single lag effect was statistically significant at 1–3 lag days (lag1–lag3), whereas the cumulative lag effect was statistically significant at 2–4 cumulative lag days (lag02–lag04) and seven cumulative lag days (lag07). Overall, the risk of outpatient visits by children aged 0–5 years was higher than that of other age subgroups for every $10 \mu\text{g}/\text{m}^3$ increase in $PM_{2.5}$ concentration.

Furthermore, the single lag effect of PM_c on children aged 0–5 years was statistically significant at 6–7 lag days (lag6–lag7). In contrast, this effect on people aged 6–14,

15–59 and ≥ 60 -years-old was not statistically significant. The cumulative lag effect of PM_c was not statistically significant in all age subgroups.

Also, the single lag effect of PM_{10} in each age subgroup was not statistically significant; its cumulative lag effect on children aged 0–5 years was statistically significant only at seven cumulative lag days (lag07), with no evidence of statistical significance observed throughout the cumulative lag phase in other age subgroups.

Based on the findings of lag effects of the single-pollutant model, population-wide daily outpatient visits for RESD at seven cumulative lag days (lag07) with the most significant impact were selected to fit the multi-pollutant model. As Table 6 shows, after controlling for gaseous pollutants SO_2 and NO_2 separately or simultaneously in the multi-pollutant model, ER of $PM_{2.5}$, PM_c and PM_{10} on outpatient visits for RESD had smaller changes than that in the single-pollutant model, and the direction remained unchanged, indicating that the fit of the single-pollutant model was better and the results were relatively stable.

The exposure-response curves between concentrations of $PM_{2.5}$, PM_c and PM_{10} and outpatient visits of children for RESD at seven cumulative lag days (lag07) are shown in Figure 3. The exposure-response relationship of each of the three types of PM was non-linear under different pollution concentrations when other pollutants were not adjusted for. When the $PM_{2.5}$ concentration was $10\text{--}55 \mu\text{g}/\text{m}^3$, the curve was relatively steep, while the curve flattened out beyond this concentration. The exposure-response curves of PM_c and PM_{10} were an inverted U-shaped, and the relative risk initially increased and then declined with an increase in the concentration of each PM.

DISCUSSION

In the current study, SGAM was used to evaluate the association of size-fractionated PM pollution with outpatient visits for RESD involving 905,188 cases in Lanzhou, China. Findings showed significant associations of increased $PM_{2.5}$ concentrations with increased daily outpatient visits for RESD, with modest associations for larger particles.

Previous studies showing that increased $PM_{2.5}$ concentrations could significantly increase outpatient visits for RESD [4;7;9;21] are consistent with the current findings, which generally showed that the adverse impact caused by $PM_{2.5}$ is higher than that of PM_c and PM_{10} , findings which are also supported by previous studies [21;23–25]. For example, Chen et al. [25] reported that $PM_{2.5}$ was significantly associated with an increased risk of emergency hospital visits. However, contrasting findings from a case-crossover study conducted in Toronto, Canada, showed that PM_c was more strongly associated with asthma than $PM_{2.5}$ and PM_{10} in a time-series analysis [26].

It is still unclear which size of PM has a substantial impact on RESD, irrespective of the current study findings, which showed that $PM_{2.5}$ appeared to be the main driver for the increase in outpatient visits for RESD. Some underlying pathological mechanisms are postulated for the obtained findings. Given that $PM_{2.5}$ has a smaller size, larger active surface area, and higher capacity for absorbing toxic air pollutants per mass unit [27], this PM can quickly gain access via inhalation into the respiratory tract and deposited in lung

Table 3. Percentage changes (95% CI) of RESD daily outpatients associated with a 10 $\mu\text{g}/\text{m}^3$ increase of $\text{PM}_{2.5}$ concentrations by gender and age using the single-pollutant model

Lag days	Total			Male (501131 cases)			Female (424625 cases)			0-5 years (438734 cases)			6-14 years (137514 cases)			15-59 years (274225 cases)			≥ 60 years (75283 cases)		
	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	
lag0	0.702	(0.283,1.122)	0.767	(0.333,1.202)	0.625	(0.197,1.056)	1.229	(0.738,1.723)	0.194	(-0.571,0.964)	0.064	(-0.445,0.576)	0.162	(-0.453,0.781)							
lag1	0.683	(0.260,1.107)	0.687	(0.249,1.126)	0.678	(0.246,1.113)	1.126	(0.63,1.624)	0.067	(-0.694,0.834)	0.084	(-0.434,0.604)	0.785	(0.161,1.413)							
lag2	0.601	(0.169,1.035)	0.571	(0.125,1.02)	0.637	(0.194,1.082)	1.050	(0.549,1.553)	-0.153	(-0.918,0.617)	-0.002	(-0.542,0.541)	0.752	(0.087,1.421)							
lag3	0.603	(0.192,1.016)	0.614	(0.189,1.041)	0.593	(0.172,1.015)	1.015	(0.532,1.500)	-0.067	(-0.81,0.681)	0.146	(-0.358,0.653)	0.627	(0.022,1.237)							
lag4	0.428	(0.026,0.831)	0.517	(0.102,0.934)	0.324	(-0.087,0.737)	1.094	(0.617,1.573)	0.123	(-0.608,0.86)	-0.392	(-0.875,0.093)	-0.205	(-0.787,0.38)							
lag5	0.338	(-0.067,0.745)	0.386	(-0.034,0.808)	0.282	(-0.132,0.698)	1.096	(0.616,1.578)	-0.029	(-0.769,0.716)	-0.607	(-1.094,-0.118)	-0.192	(-0.777,0.396)							
lag6	0.494	(0.078,0.911)	0.548	(0.117,0.98)	0.430	(0.005,0.857)	1.129	(0.637,1.622)	0.008	(-0.751,0.774)	-0.364	(-0.868,0.142)	0.201	(-0.402,0.808)							
lag7	0.811	(0.383,1.241)	0.793	(0.349,1.239)	0.832	(0.395,1.272)	1.434	(0.93,1.942)	0.191	(-0.586,0.975)	-0.078	(-0.599,0.446)	0.644	(0.017,1.274)							
lag01	0.946	(0.452,1.443)	0.996	(0.485,1.51)	0.888	(0.382,1.396)	1.932	(1.274,2.594)	0.174	(-0.715,1.071)	0.106	(-0.495,0.711)	0.65	(-0.075,1.38)							
lag02	1.117	(0.554,1.682)	1.139	(0.557,1.725)	1.091	(0.515,1.67)	2.264	(1.539,2.993)	0.002	(-0.999,1.012)	0.091	(-0.598,0.784)	0.941	(0.105,1.784)							
lag03	1.314	(0.695,1.938)	1.336	(0.695,1.981)	1.291	(0.656,1.93)	2.667	(1.879,3.462)	-0.091	(-1.189,1.02)	0.164	(-0.596,0.93)	1.204	(0.287,2.13)							
lag04	1.455	(0.782,2.132)	1.515	(0.819,2.216)	1.386	(0.697,2.08)	3.083	(2.229,3.944)	-0.077	(-1.27,1.13)	-0.017	(-0.84,0.812)	1.088	(0.094,2.092)							
lag05	1.552	(0.824,2.284)	1.627	(0.874,2.386)	1.466	(0.721,2.216)	3.471	(2.559,4.392)	-0.174	(-1.464,1.132)	-0.299	(-1.183,0.592)	0.995	(-0.075,2.076)							
lag06	1.698	(0.922,2.48)	1.794	(0.991,2.604)	1.587	(0.793,2.387)	4.018	(3.044,5.002)	-0.257	(-1.636,1.141)	-0.443	(-1.38,0.503)	1.063	(-0.071,2.21)							
lag07	1.990	(1.162,2.824)	2.074	(1.216,2.938)	1.894	(1.047,2.747)	1.932	(1.274,2.594)	-0.251	(-1.721,1.241)	-0.478	(-1.473,0.528)	1.303	(0.097,2.524)							

Table 4. Percentage changes (95% CI) of RESD daily outpatients associated with a 10 ug/m³ increase of PMc concentrations by gender and age using the single-pollutant model

Lag days	Total			Male (501131 cases)			Female (424625 cases)			0-5 years (438734 cases)			6-14 years (137514 cases)			15-59 years (274225 cases)			≥60 years (75283 cases)		
	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	
lag0	0.093	(-0.033,0.219)	0.103	(-0.027,0.234)	0.081	(-0.047,0.21)	0.123	(-0.029,0.275)	-0.072	(-0.305,0.162)	0.131	(-0.049,0.31)	0.133	(-0.074,0.341)							
lag1	0.011	(-0.120,0.142)	0.013	(-0.137,0.136)	0.024	(-0.109,0.158)	0.039	(-0.119,0.196)	-0.152	(-0.391,0.087)	-0.032	(-0.224,0.161)	0.04	(-0.184,0.264)							
lag2	0.034	(-0.104,0.172)	0.011	(-0.132,0.154)	0.062	(-0.079,0.203)	0.059	(-0.103,0.222)	-0.154	(-0.4,0.092)	0.068	(-0.144,0.28)	0.004	(-0.262,0.272)							
lag3	0.11	(-0.028,0.247)	0.100	(-0.042,0.242)	0.122	(-0.018,0.262)	0.127	(-0.036,0.29)	0.022	(-0.226,0.27)	0.147	(-0.066,0.361)	0.099	(-0.162,0.36)							
lag4	-0.027	(-0.162,0.108)	-0.012	(-0.152,0.128)	-0.044	(-0.182,0.093)	0.104	(-0.06,0.269)	0.098	(-0.143,0.339)	-0.315	(-0.517,-0.112)	-0.322	(-0.557,-0.087)							
lag5	-0.048	(-0.188,0.092)	-0.038	(-0.183,0.107)	-0.06	(-0.203,0.083)	0.096	(-0.072,0.264)	0.081	(-0.156,0.266)	-0.294	(-0.504,-0.084)	-0.285	(-0.528,-0.041)							
lag6	0.113	(-0.053,0.28)	0.120	(-0.053,0.293)	0.106	(-0.064,0.275)	0.201	(0.001,0.402)	0.007	(-0.305,0.319)	0.057	(-0.198,0.313)	0.137	(-0.162,0.436)							
lag7	0.210	(0.044,0.376)	0.203	(0.03,0.376)	0.218	(0.049,0.387)	0.337	(0.138,0.536)	0.107	(-0.203,0.418)	0.022	(-0.235,0.28)	0.154	(-0.149,0.458)							
lag01	-0.023	(-0.209,0.164)	-0.03	(-0.223,0.164)	-0.014	(-0.203,0.176)	-0.069	(-0.295,0.158)	-0.245	(-0.58,0.09)	0.074	(-0.145,0.293)	0.126	(-0.13,0.381)							
lag02	-0.041	(-0.256,0.174)	-0.064	(-0.286,0.16)	-0.014	(-0.233,0.206)	-0.1	(-0.357,0.158)	-0.318	(-0.697,0.062)	0.103	(-0.155,0.361)	0.125	(-0.183,0.434)							
lag03	-0.004	(-0.245,0.237)	-0.033	(-0.283,0.217)	0.032	(-0.214,0.278)	-0.082	(-0.369,0.206)	-0.276	(-0.698,0.149)	0.171	(-0.121,0.463)	0.174	(-0.175,0.523)							
lag04	-0.06	(-0.326,0.206)	-0.085	(-0.361,0.191)	-0.03	(-0.301,0.242)	-0.097	(-0.416,0.223)	-0.214	(-0.681,0.256)	-0.007	(-0.327,0.314)	-0.024	(-0.403,0.356)							
lag05	-0.124	(-0.414,0.167)	-0.144	(-0.445,0.158)	-0.098	(-0.394,0.199)	-0.122	(-0.472,0.229)	-0.215	(-0.727,0.3)	-0.152	(-0.499,0.196)	-0.170	(-0.578,0.239)							
lag06	-0.108	(-0.427,0.213)	-0.131	(-0.463,0.202)	-0.079	(-0.405,0.249)	-0.114	(-0.5,0.273)	-0.217	(-0.784,0.353)	-0.141	(-0.522,0.241)	-0.133	(-0.58,0.316)							
lag07	-0.064	(-0.412,0.286)	-0.09	(-0.452,0.272)	-0.031	(-0.387,0.325)	-0.05	(-0.47,0.372)	-0.188	(-0.807,0.435)	-0.145	(-0.56,0.271)	-0.094	(-0.581,0.395)							

Table 5. Percentage changes (95% CI) of RESD daily outpatients associated with a 10 $\mu\text{g}/\text{m}^3$ increase of PM_{10} concentrations by gender and age using the single-pollutant model

Lag days	Total			Male (501131 cases)			Female (424625 cases)			0-5years (438734 cases)			6-14 years (137514 cases)			15-59 years (274225 cases)			≥ 60 years (75283 cases)		
	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	ER	95% CI	
lag0	0.045	(-0.111,0.200)	0.052	(-0.109,0.213)	0.037	(-0.122,0.196)	0.008	(-0.183,0.200)	-0.133	(-0.42,0.156)	0.093	(-0.055,0.242)	0.105	(-0.067,0.278)							
lag1	-0.081	(-0.245,0.083)	-0.100	(-0.271,0.071)	-0.059	(-0.226,0.107)	-0.113	(-0.312,0.087)	-0.237	(-0.533,0.06)	-0.014	(-0.17,0.142)	0.093	(-0.087,0.273)							
lag2	-0.041	(-0.214,0.133)	-0.072	(-0.252,0.108)	-0.003	(-0.18,0.174)	-0.076	(-0.282,0.130)	-0.207	(-0.512,0.098)	0.044	(-0.127,0.215)	0.078	(-0.132,0.289)							
lag3	0.071	(-0.104,0.246)	0.054	(-0.128,0.235)	0.092	(-0.087,0.27)	0.024	(-0.186,0.234)	0.051	(-0.258,0.361)	0.107	(-0.061,0.276)	0.131	(-0.072,0.334)							
lag4	-0.118	(-0.29,0.054)	-0.11	(-0.289,0.068)	-0.126	(-0.301,0.049)	-0.040	(-0.253,0.174)	0.129	(-0.168,0.428)	-0.244	(-0.405,-0.083)	-0.230	(-0.417,-0.043)							
lag5	-0.139	(-0.317,0.04)	-0.131	(-0.317,0.054)	-0.146	(-0.328,0.036)	-0.060	(-0.279,0.160)	0.007	(-0.312,0.327)	-0.258	(-0.426,-0.09)	-0.204	(-0.398,-0.01)							
lag6	0.063	(-0.157,0.283)	0.059	(-0.170,0.288)	0.067	(-0.157,0.291)	0.028	(-0.241,0.297)	0.017	(-0.393,0.429)	-0.024	(-0.220,0.173)	0.111	(-0.118,0.341)							
lag7	0.154	(-0.065,0.374)	0.147	(-0.081,0.375)	0.163	(-0.06,0.386)	0.202	(-0.063,0.468)	0.144	(-0.262,0.552)	0.002	(-0.195,0.2)	0.180	(-0.052,0.412)							
lag01	0.07	(-0.078,0.219)	0.07	(-0.084,0.225)	0.071	(-0.081,0.223)	0.107	(-0.071,0.286)	-0.147	(-0.417,0.123)	0.057	(-0.121,0.235)	0.138	(-0.069,0.346)							
lag02	0.076	(-0.095,0.246)	0.063	(-0.114,0.240)	0.091	(-0.083,0.265)	0.117	(-0.085,0.320)	-0.209	(-0.513,0.096)	0.074	(-0.133,0.282)	0.164	(-0.082,0.411)							
lag03	0.119	(-0.07,0.309)	0.103	(-0.094,0.300)	0.140	(-0.054,0.334)	0.163	(-0.061,0.387)	-0.188	(-0.525,0.15)	0.123	(-0.110,0.357)	0.221	(-0.055,0.498)							
lag04	0.1	(-0.108,0.309)	0.091	(-0.125,0.307)	0.113	(-0.100,0.326)	0.199	(-0.048,0.447)	-0.146	(-0.516,0.226)	-0.007	(-0.262,0.248)	0.085	(-0.215,0.386)							
lag05	0.073	(-0.155,0.301)	0.068	(-0.168,0.304)	0.080	(-0.152,0.313)	0.231	(-0.039,0.502)	-0.156	(-0.562,0.252)	-0.126	(-0.402,0.15)	-0.017	(-0.341,0.309)							
lag06	0.107	(-0.142,0.356)	0.102	(-0.156,0.361)	0.113	(-0.141,0.368)	0.294	(-0.002,0.591)	-0.167	(-0.614,0.282)	-0.135	(-0.437,0.167)	0.021	(-0.333,0.375)							
lag07	0.171	(-0.099,0.442)	0.164	(-0.117,0.445)	0.181	(-0.095,0.458)	0.404	(0.083,0.726)	-0.151	(-0.638,0.338)	-0.142	(-0.469,0.185)	0.074	(-0.308,0.458)							

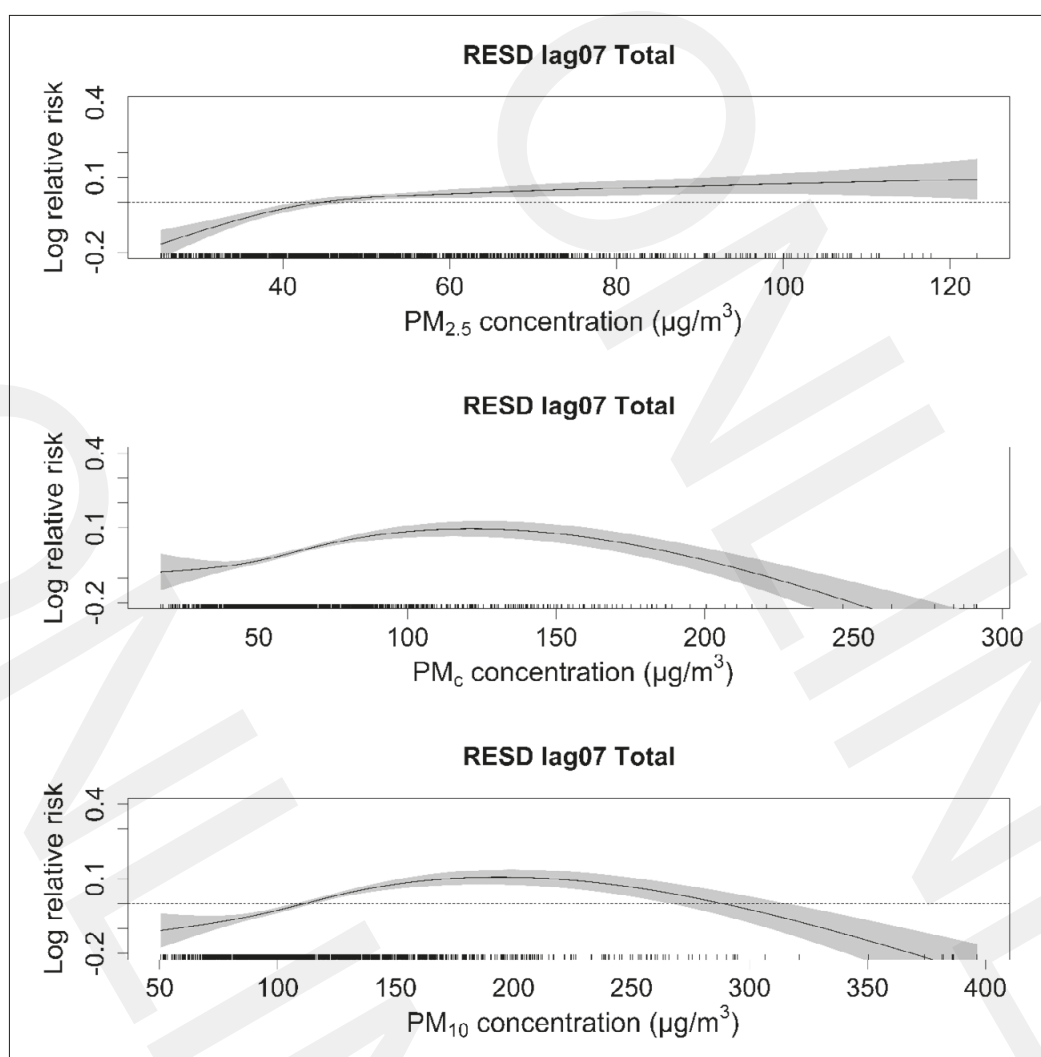


Figure 3. Curve of exposure-reaction relationship between concentration of PM_{2.5}, PM_c & PM₁₀ and outpatient visits for respiratory disease at lag07

Table 6. Association with a 10 µg/m³ increase in air pollutants for RESD daily outpatients using single, two and three pollutant models during 2014–2017

Pollutants and Model ^a	ER	95%CI
PM_{2.5}		
Single pollutant model	1.990	(1.162,2.824)
+NO ₂	1.717	(0.862,2.579)
+SO ₂	1.503	(0.484,2.532)
+ NO ₂ +SO ₂	1.520	(0.502,2.549)
PM_c		
Single pollutant model	-0.064	(-0.412,0.286)
+NO ₂	-0.041	(-0.490,0.208)
+SO ₂	-0.062	(-0.511,0.188)
+ NO ₂ +SO ₂	-0.085	(-0.535,0.165)
PM₁₀		
Single pollutant model	0.171	(-0.099,0.442)
+NO ₂	0.155	(-0.188,0.36)
+SO ₂	0.145	(-0.277,0.289)
+ NO ₂ +SO ₂	0.160	(-0.29,0.275)

Note: The effects of multiday lag (lag07 for PM_{2.5}, PM_c and PM₁₀) were used for RESD daily outpatients

alveoli [28]. Small fractions are more likely to be deposited in deep pulmonary sections and get into close contact with epithelial cells and macrophages [29], leading to increased airway reactivity, and subsequently promoting oxidative stress and increased inflammation [30]. Larger particles, such as PM_c and PM₁₀ can be deposited in the upper airways through sedimentation or impaction in the lower airways [28]. This may explain the more significant adverse impact of PM_{2.5} on human health than PM_c and PM₁₀.

In the presented study it was found that the ER of PM_{2.5} was statistically significant throughout the whole lag period and consistently elevated with increased lag days, showing the sustained effects of PM on RESD. The ER peaked at lag 07, lag 05 and lag 07 for PM_{2.5}, PM_c and PM₁₀, respectively, though the ER for PM_c and PM₁₀ was not statistically significant. This finding was consistent with that of a study conducted in Denver, USA, by Kim et al. [31]. The authors reported that the impact was more considerable at longer lag periods for total RESD in the five-county Denver metropolitan area. In contrast, some previous studies showed that PM usually showed acute effects on RESD. Yao et al. [21] reported that the peak adverse effect on RESD occurred on lag01 for both PM_{2.5} and PM₁₀; Qiu et al. [27] found a significant association between asthma hospitalization and PM_c; Jiang et al. [32]

showed PM_C generated the maximum impact on respiratory outpatients at lag05.

The heterogeneous findings among these studies may be attributed to the following reasons. First, the compositions of PM pollution vary across different regions [28]. The essential components of $PM_{2.5}$ were carbonaceous aerosol, water-soluble ion and a low quantity of polycyclic aromatic hydrocarbons (PAHs) in Lanzhou [33]; PAHs could damage the respiratory system due to their toxicity and carcinogenicity. Second, there were differences in data collection periods, population distribution, medical resource capacity and prevention measures across the studies; hence the impact of PM pollution on health outcomes may be different.

Stratified analysis demonstrated gender differences in the associations of PM pollution with RESD. More substantial effects were observed of $PM_{2.5}$ and PM_C , but weaker effects of PM_{10} on RESD in males than females. Though the ERs of PM_C and PM_{10} were not statistically significant, the findings were consistent with previous epidemiological studies on air pollution [22;34]. Nevertheless, studies conducted in Beijing and Nanjing reported results that were contrary to the findings obtained in the current study. Xu et al. [35] demonstrated that females were at higher risk of RESD after $PM_{2.5}$ exposure in Beijing; Wang et al. [7] reported that the impact of short-term PM exposure was not significantly different between males and females in Nanjing. The difference in findings among males and females may be attributed to the following reasons. Lifestyle individual habits of males and females suggest that males tend to have more outdoor activities, which is associated with increased frequency of smoking and alcohol consumption, with subsequent exposure to PM pollution [34]. Circulating sex hormones may also be a factor for the discordant findings among males and females [36].

The presented results suggest that children aged 0–5 and the elderly aged ≥ 60 years are more susceptible to the adverse respiratory effects of PM, compared to those aged 6–14 and 15–59 years; furthermore, $PM_{2.5}$ was the most essential PM triggering RESD in children aged 0–5 and the elderly aged ≥ 60 years. These findings were consistent with those reported in previous studies [21;35;37–38]; however, the results reported by Wang et al. [39] showed that younger age groups were more vulnerable to the effects of air pollution than the elderly, which were inconsistent with the findings in the presented study. The differences may be attributed to the physiological structure and immune status in these groups. The immune system is weaker in children aged 0–5 and elderly aged ≥ 60 years, compared to other age groups; hence, they are more susceptible to the adverse health effects of air pollution.

To the best knowledge of the authors, this is the first study to evaluate the associations of size-fractionated particle matter pollution with outpatient visits for RESD in Lanzhou. The findings provide some reference data for local public health authorities to assist in planning and implementing more efficacious preventative strategies for particulate matter pollution. The analyses were comprehensive, and were controlled for the confounding effects of air pollution variables such as SO_2 and NO_2 .

Some limitations deserve acknowledgment. First, air pollution data collected from air monitoring stations was used to represent the individual exposures; hence, there may be some deviations. Second, it was not possible to control some potential factors, for example, personal

habits, living circumstances and chronic diseases like diabetes and hypertension, which could bias the results.

CONCLUSIONS

The results obtained showed significant associations of increased $PM_{2.5}$ concentrations with increased daily outpatient visits for RESD with lag effects. There were modest associations for larger particles. In subgroup analysis, the impact of atmospheric PM on outpatient visits for RESD was significantly modified by gender and age; men, and children aged 0–5 years were more sensitive to $PM_{2.5}$ pollution. Ther study findings are potentially crucial for formulating preventive strategies to protect the population from the adverse impact of PM pollution. Relevant public health departments should put in place measures to reduce pollution emissions, such as reducing fossil fuel combustion, limiting the number of vehicles on the road, and promoting the use of public transport travel, etc.

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