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Epidemiology Analysis on the Association of Inhalable Particulate Matters with Cardiovascular Diseases in an Industrial City

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ABSTRACT

Linyi, a typical industrial city, has historically experienced severe air pollution. However, since the environmental protection inspection in 2014, there has been a significant improvement in air quality. The question remains as to whether this improvement has reduced the incidence of cardiovascular disease (CVD). This study examines the associations between inhalable particulate matter ($PM_{2.5}$ and PM_{10}) and CVD in Linyi from 2014 to 2019. A distributed lag non-linear model (DLNM) was used to analyze the exposure-response relationship between particulate matter and CVD. The results confirmed that exposure to $PM_{2.5}$ and PM_{10} significantly increases the risk of CVD. The highest relative risk (RR) was observed in severe $PM_{2.5}$ pollution ($PM_{2.5}$ = 217 μg m^{-3}, RR = 1.64, 95% CI: 1.12–2.41). Both females and individuals aged over 65 years showed increased susceptibility to air pollution, particularly at high PM concentrations. The highest RRs for females exposed to $PM_{2.5}$ and PM_{10} were 1.89% (95% CI: 1.20–2.97) and 1.45% (95% CI: 0.98–2.14), respectively. For the elderly population, the highest RRs associated with $PM_{2.5}$ and PM_{10} were 2.07% (95% CI: 1.22–3.50) and 1.58% (95% CI: 1.01–2.49), respectively. High temperatures significantly increased the impact of $PM_{2.5}$ and PM_{10} on CVD risks, especially when $PM_{2.5}$ concentrations were at intermediate levels (50^{th} percentile) during the warm season. This research suggests that despite improvements in air quality, the health risks associated with particulate matters for CVDs persist. It is recommended that local authorities develop long-term strategies for improving air quality, especially in high-risk areas. These findings provide a comprehensive health risk assessment and can serve as a scientific basis for air pollution mitigation and the protection of vulnerable populations.

Keywords: Particulate matter, Cardiovascular diseases, Outpatient visits, Distributed Lag Non-Linear Model

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1 INTRODUCTION

Cardiovascular diseases (CVDs) have consistently been the primary cause of mortality worldwide, as reported by the World Health Organization (WHO) (Vos *et al.*, 2020; Yang *et al.*, 2019). The Global Burden of Disease (GBD) studies have meticulously evaluated significant health risks and elevated mortality rates attributable to ambient air pollution. Notably, these studies have highlighted that particulate matter (PM) pollution has precipitated the most substantial augmentation in risk exposure factors, which has a profound impact on global public health (Murray *et al.*, 2020; Krittanawong *et al.*, 2023). Numerous epidemiological studies have demonstrated that exposure to $PM_{2.5}$ and PM_{10} can precipitate the progression of CVDs and instigate acute cardiac events

(Chang *et al.*, 2020). These include heart failure, myocardial ischemia and infarctions, strokes, arrhythmias, hypertension, and an elevated mortality rate (Lederer *et al.*, 2021). Both long-term and short-term exposure to particulate matter (PM) escalate the risk of CVDs (Meo and Suraya, 2015; Liang *et al.*, 2020). Specifically, long-term exposure to PM has been identified as a unique modifiable risk factor precipitating cardiovascular mortality (Kim *et al.*, 2017; Argacha *et al.*, 2018).

A global study on PM and cardiovascular disease (CVD) revealed that a 10 μg m^{-3} increase in the two-day moving average of $PM_{2.5}$ corresponded to a 0.55% rise (95% CI: 0.45%–0.66%) in daily cardiovascular mortality (Liu *et al.*, 2019a). A meta-analysis, focusing on short-term effects in China, synthesized the evidence and determined that each 10 μg m^{-3} increment in $PM_{2.5}$ was linked with a 0.68% (95% CI: 0.39%–0.97%) heightened risk of cardiovascular mortality (Zhao *et al.*, 2017). Evidence from both United States and Europe have shown that high PM levels are associated with an increased risk of CVD mortality (Pinault *et al.*, 2017; Vidale *et al.*, 2017). For example, studies in the United States suggest that ambient $PM_{2.5}$ and PM_{10} pose a higher risk for CVD (Feng and Yang, 2012). Beyond CVD mortality, substantial positive correlations between PM exposure and the frequency of CVD outpatient visits have been corroborated in various Chinese cities (Liang *et al.*, 2020), including Beijing (Chen, 2016), Shanghai (Xu *et al.*, 2017), Shijiazhuang (Tan *et al.*, 2019), and Linyi (Li *et al.*, 2020). Furthermore, the evidence from both epidemiological and experimental studies reinforces that PM adversely impacts human health via reactive oxygen species and inflammation. High concentrations of PM are conducive to thrombus formation due to an upsurge in coagulation factors and platelet activation (Cohen *et al.*, 2017; Robertson and Miller, 2018). Therefore, it is crucial to evaluate the health risks associated with PM exposure, considering its significant role as a risk factor for CVDs, particularly in areas severely affected by air pollution.

In China, a significant annual reduction in PM concentration has been observed since 2013, primarily attributed to the implementation of stringent preventive and control measures (Tang *et al.*, 2019; Xue *et al.*, 2019). The projected national population-weighted annual $PM_{2.5}$ concentration decreased from 61.8 μg m^{-3} (95% CI: 53.3–70.0) in 2013 to 42.0 μg m^{-3} (95% CI: 35.7–48.6) in 2017 (Zhang *et al.*, 2019). Concurrently, the Air Pollution Prevention and Control Action Plan led to substantial health benefits as air quality improved significantly. In 2017, deaths attributed to $PM_{2.5}$ pollution were reduced by 64,000 (6.8%) compared to 2013. Nevertheless, severe air pollution continued to be a prevalent issue during the winter months, with a 36.1% increase in premature fatalities linked to $PM_{2.5}$ between the years 2000 and 2017 (Yue *et al.*, 2020). Air pollution accounted for 1.0–1.6 million premature deaths annually in China (Fang *et al.*, 2013; Maji *et al.*, 2018b). The morbidity and mortality rates linked to $PM_{2.5}$ pollution depend on variables such as the level of exposure to pollution, its duration, and individual susceptibility. The correlation between disease incidence rate and pollutant concentration is nonlinear, exhibiting significant hysteresis (Liu *et al.*, 2019b; Mokoena *et al.*, 2019, 2020). Therefore, short-term improvements in air quality may not significantly mitigate long-term exposure risks associated with air pollutants. Even minimal levels of exposure to PM can potentially increase mortality risk (Liu *et al.*, 2019b; Yue *et al.*, 2020). Given the nonlinear correlation between ambient air pollution exposure and health impacts, it is imperative for public health practitioners to conduct health impact assessments of ambient air pollution. Prior research has examined the detrimental health effects of urban air pollution on exposed populations, revealing significant discrepancies in various cities in China (Chen *et al.*, 2017b; Feng *et al.*, 2019; Maji *et al.*, 2018a; Gu *et al.*, 2019; Mokoena *et al.*, 2019; Chang *et al.*, 2020). These disparities can be attributed to variations in economic levels, industrial structures, air pollutants and concentrations, geographical environments, meteorological conditions, as well as differences in ethnicity, gender, age composition, and individual susceptibility. Consequently, health risk posed by air pollutants in one city should not be directly extrapolated to assess the health risks in other cities (Maji *et al.*, 2018a). It is crucial to establish specific assessment standards for air pollution and impact on population health.

This study examines the temporal characteristics of CVDs in Linyi from 2014 to 2019. As a representative industrialized city, Linyi has experienced severe air pollution, presenting significant health risks to the inhabitants (Wu *et al.*, 2021). In 2015, the Ministry of Ecology and Environment of China conducted a comprehensive environmental audit to assess the air quality in Linyi. Following this inspection, Linyi implemented a series of stringent measures to reduce air pollution. In recent years, there has been a discernible improvement in air quality (Ye *et al.*, 2018; Yao *et*

al., 2019). This study aims to evaluate the health implications of particulate matter pollution in Linyi from 2014 to 2019, specifically focusing on its impact on the incidence of CVDs. To determine whether improved air quality has led to a decrease in CVD occurrences. Furthermore, to investigate if this effect varies across different age and gender groups. Finally, to elucidate the influence of temperature and particulate matter concentration, considering varying particle sizes, on the frequency of outpatient visits for CVDs.

2 STUDY AREA AND METHODS

2.1 Study Area

Linyi, situated in the southwestern of Shandong Province, China (34°22N–36°13N, 117°24E–119°11E), which has the highest population of 10.67 million in Shandong Province. However, due to rapid urbanization and a proliferation of small-to-medium enterprises, with large air pollution emissions (Bai *et al.*, 2021). The current ambient air quality in Linyi has not yet achieved the average annual concentration level 2 limits stipulated by the China ambient air quality standard (PM_{10}, 70 μg m^{-3}; $PM_{2.5}$, 35 μg m^{-3}) (GB3095-2012, China). The northern region is encompassed by elevated mountains, notably Mount Yi Meng, characterized by terrain exceeding 1,000 meters. In contrast, the central and southern regions are flat terrains. The prevailing winds in these areas are predominantly northerly and southerly respectively, potentially contributing to the elevated air pollutant concentrations observed in central Linyi (Fig. S1). Severe air pollution significantly impacts the health of residents. Cardiovascular diseases, cerebrovascular diseases, and malignant tumors were identified as the top three prevalent health conditions in Linyi, and the mortality rate of CVDs has been increasing annually (Linyi Center for Disease Control, 2016).

2.2 Data Collection and Process

Hourly concentration of air pollutants (PM_{10}, $PM_{2.5}$, SO_2, NO_2, CO, and O_3) from 2014 to 2019 were sourced from air quality monitoring stations in Linyi. These stations span the entire study area, comprising 8 national and provincial controlled stations as well as 118 country level stations located in suburban areas. This ensures a balanced distribution of monitoring locations. The daily average concentration was derived from 126 fixed monitoring stations. The quality of these monitoring data was assessed annually and supervised. In this study, the exposure concentration for $PM_{2.5}$ and PM_{10} were defined as the yearly and daily averages of 24-hour measurements taken by all monitors in Linyi over the study period.

Daily meteorological data, encompassing daily average temperature, relative humidity, wind speed, and air pressure, were sourced from the China Meteorological Data Service Center. Outpatient visit data of cardiovascular disease from January 1, 2014, to December 31, 2019, were amassed from Linyi People's Hospital—the sole grade A tertiary hospital in Linyi. Outpatient visits to the hospital accounted for 80% of the total outpatient population in Linyi City (Li *et al.*, 2020). The data extracted from the outpatient medical records encompassed patient demographics such as gender, age, residential address, disease diagnosis, department of treatment, date of treatment, and identification number. To ensure that all data were sourced exclusively from residents, patients with registered permanent residences outside Linyi were excluded. The International Statistical Classification of Diseases and Related Health Problems (ICD-10) (10th rev. Geneva) was utilized to evaluate the number of outpatient visits for cardiovascular disease (CVD) (ICD-10: I00–I99) across health endpoints. Daily CVD counts were subsequently categorized into two subgroups based on sex (male and female) and age (0–65 years and 66 years or older).

2.3 Time Series Analysis Based on the Distributed Lag Non-Linear Model (DLNM)

The DLNM is capable of concurrently modeling the non-linear relationship between multiple air pollutant exposures and the lag effect on disease (Chang *et al.*, 2020; Wang *et al.*, 2021). In this study, we employed a DLNM in conjunction with Poisson regression to evaluate the short-term impacts of $PM_{2.5}$ and PM_{10} on CVD outpatients. All other variables were incorporated into the model as confounding factors through a natural spline function, barring the association between

air quality parameters and daily outpatient counts of CVD. To regulate the long-term trend of time variables, a natural spline function was integrated. Additionally, to manage the "day of the week effect" on daily outpatient visits, week-specific variables were also included in the DLNM as dummy variables. The final model is detailed below.

$$\log[E(Y_i)] = \alpha + \beta basis.\ PM_{ij} + ns(time_i, df) + ns(temp_i, df) + ns(rhum_i, df) + ns(ws_i, df) + \lambda DOW_i \quad (1)$$

where Y_i is the number of daily outpatients of CVD on day i; α is the intercept; β is the coefficient of the matrix; *basis.* PM is a two-dimensional matrix of the air quality factors, which is calculated from the "cross basis" function in DLNM; $time_i$ is the new settled time series variable for controlling the long-term trend; *ns* represents a date variable with natural cubic spline to account for unmeasured time-varying confounders, long-term trends, and seasonality; *temp*, *rhum,* and *ws* are temperature, humidity, and maximum wind speed, respectively; *DOW* is the dummy variable of day *i* of the week; and *df* is the degree of freedom. By adjusting the degree of freedom with the Akaike information criterion (AIC), the degrees of freedom for meteorological factors and time variables were three and seven annually, respectively. The maximum lag days were set as 21 days, and the relative risk (RR) and 95% CI were the indices used for evaluating PM exposure effect.

To account for potential collinearity or interactions between variables, Spearman's rank correlation coefficient was employed to identify the most significant pollutants and meteorological factors. This was achieved through backward elimination, while other collinear or highly correlated environmental factors were excluded. Subsequently, these covariates were incorporated into the model for subsequent analysis. Fig. S2 presents the Spearman's rank correlation coefficient matrix of pollutants and meteorological factors. To prevent collinearity, when examining the exposure-response model of $PM_{2.5}$ and CVD, SO_2, NO_2, CO, and PM_{10} were excluded, preventing synchronization of ozone, air pressure, and temperature within the model. Similarly, high correlation factors were not considered in the analysis of the exposure-response model of PM_{10}.

To assess the potential effect modification, stratified analyses were performed for gender (male vs. female), age ($\leq$ 65 vs. $>$ 65 years), and PM levels (25^{th}, 50^{th}, 75^{th}, 95^{th}) (Shi *et al.*, 2020). Considering the possible risk of CVDs in populations due to particulate matter, which is affected by seasonal and temperature variations, the model was divided into two categories: warm season (April to September) and cold season (October to March of the following year). Furthermore, sensitivity analyses were conducted to verify the robustness of the results. The lag days were adjusted to 7 or 14 days to determine whether 21 lag days were enough to model its impact on CVD. The degrees of freedom for the meteorological variables were adjusted between 3 and 6, and for the time of the year ranged from 6 to 10. All analyses were conducted using the packages (DLNM and mgcv) of R statistical software (version 4.3.0).

3 RESULTS AND DISCUSSION

3.1 Descriptive Analysis of CVD Incidence and PM

Table 1 presents the demographic data of CVD in Linyi from 2014 to 2019. Over this period, a total of 228,676 outpatient visits were recorded, with 104 daily CVD outpatient visits specifically noted. The number of CVD outpatient visits in Linyi escalated from 22,082 (in 2014) to 64,310 (in 2019). Both the CVD outpatient visits and the prevalence rate demonstrated an upward trend annually, reaching a prevalence rate of 327 per 100,000 individuals. Notably, the outpatient visits for pulmonary heart disease, hypertension, chronic rheumatic heart disease, and ischemic heart disease accounted for 3079 cases (1.34%), 121,143 cases (53.01%), 14,548 cases (6.36%), and 89,698 cases (39.26%) respectively.

From a gender- and age-based perspective, the incidence of cardiovascular disease (CVD) was found to be higher among women and older adults. The daily average concentration of PM_{10}, $PM_{2.5}$, SO_2, NO_2, and O_3 from 2014 to 2019 were recorded as 129.0, 67.9, 29.9, 45.8, and 100.5 μg m^{-3} respectively. Over this period, there was an overall upward trend in outpatient visits for CVD. Additionally, the concentrations of $PM_{2.5}$ and PM_{10} showed a gradual decrease from 2014 to 2019 (Fig. 1). However, the annual concentrations of $PM_{2.5}$ and PM_{10} still exceeded the China ambient

Table 1. Summary statistics of demographic characteristics of daily CVD outpatient visits, air pollutants, and meteorology factors in Linyi, from 2014 to 2019.

Variables	Subgroup	Mean	Min	Max	Percentiles			
					25th	50th	75th	95th
CVD outpatient visits	Total	104	2	301	51	84	159	219
	Male	54	0	177	25	42	85	117
	Female	50	0	144	26	43	74	104
	0–65	72	1	219	36	59	106	148
	> 65	32	0	107	14	25	50	73
Air pollutants	PM_{10} (μg m^{-3})	129	5	561	72	112	165	274
	$PM_{2.5}$ (μg m^{-3})	68	3.2	350	33	54	87	167
	SO_2 (μg m^{-3})	30	3.1	204	12	21	38	84
	NO_2 (μg m^{-3})	46	8.6	140	30	42	58	86
	O_3 (μg m^{-3})	100	8.3	267	57	92	138	195
Meteorological factors	Temperature (°C)	18	−11	33	6	16	24	28
	Humidity (%)	65	14	100	53	66	78	90
	Air pressure (hPa)	1,007	974	1,033	998	1,006	1,013	1,023

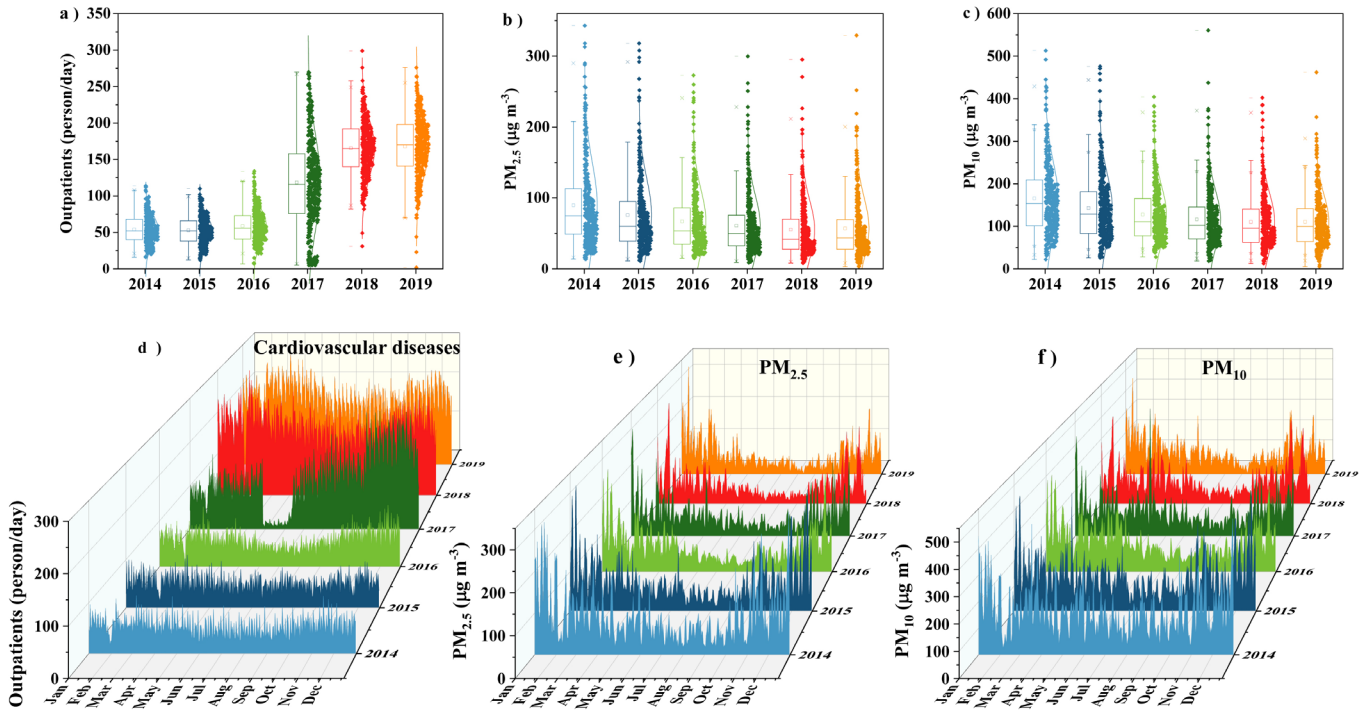


Fig. 1. The distribution of daily CVD outpatient visits and the annual average concentration of atmospheric PM (A, B, C) and time series (D, E, F) of Linyi from 2014 to 2019. The China ambient air quality standard average annual concentration level 2 limits (PM_{10}, 70 μg m^{-3}; $PM_{2.5}$, 35 μg m^{-3}) and the level 1 limits (PM_{10}, 40 μg m^{-3}; $PM_{2.5}$, 15 μg m^{-3}) refer to the standard of Chinese GB3095-2012.

air quality standard average annual concentration level 2 limits (PM_{10}, 70 μg m^{-3}; $PM_{2.5}$, 35 μg m^{-3}). Notably, the $PM_{2.5}$ concentration was approximately seven times greater than the WHO Air Quality Guideline (10 μg m^{-3}). In 2019, the population's exposure to $PM_{2.5}$ and PM_{10} concentrations decreased compared to that in 2014. Despite the significant downward trend in PM concentration ($p < 0.05$), there was an increase in the number of outpatient visits for CVD.

A significant increase of outpatient visits for cardiovascular diseases were observed periodically in winter. This aligns with the peak concentration of particulate matter. The combination of high PM concentrations and low temperatures during winter is conducive to the hypertension and other

heart diseases (Talbott *et al.*, 2014). Additionally, temperature fluctuations, such as a decrease in temperature, can lead to increased levels of biomarkers indicative of inflammation, coagulation, and vasoconstriction, thereby potentially exacerbating adverse cardiovascular outcomes (Cai *et al.*, 2016). Notably, the elderly population is at a higher risk for CVD, and individuals with CVD are particularly susceptible to air pollution during winter (Lelieveld *et al.*, 2020; Liang *et al.*, 2020).

Prior research has demonstrated that enhanced air quality and a decline in $PM_{2.5}$ concentration resulted in a 14% reduction, from 1.2 to 1.0 million, in premature deaths attributable to long-term exposure in China between 2013 and 2017 (Xue *et al.*, 2019). However, while the annual $PM_{2.5}$ levels have declined swiftly, the health advantages stemming from decreased long-term exposure remain constrained. In most Chinese cities, $PM_{2.5}$ concentrations persist at the segment where the exposure-response curve is less steep than at the lower concentration. Furthermore, due to the hysteresis effect between disease incidence and pollutant exposure, there is no significant decrease in the incidence of cardiovascular diseases (Yue *et al.*, 2020). For instance, Linyi has seen improvements in air quality, but it has yet to meet the second-level limit (PM_{10}, 70 μg m^{-3}; $PM_{2.5}$, 35 μg m^{-3}) and remains significantly above the first-level limit (PM_{10}, 40 μg m^{-3}; $PM_{2.5}$, 15 μg m^{-3}). Consequently, there is an urgent need to bolster measures for pollutant reduction and enhance air quality monitoring policies.

3.2 Risk Analysis of PM and CVD with DLNM

3.2.1 RR of CVD associated with ambient $PM_{2.5}$ and PM_{10}

Fig. 2 illustrates the relative risks (RRs) and 95% confidence intervals (CI) derived from the DLNM. The cumulative risk effects of $PM_{2.5}$ and PM_{10} on CVD outpatient visits demonstrated a significant variation with increasing PM concentration. The most significant cumulative effect of $PM_{2.5}$ on CVD was noted at a concentration of 217 μg m^{-3}, with the RR value of 1.64 (95% CI: 1.12–2.41). Specifically, both male and female exhibited positive correlations with CVD at high $PM_{2.5}$ concentrations. Such as, elevated relative risks were observed at a $PM_{2.5}$ concentration of 150 μg m^{-3} for females. To ascertain whether these associations varied based on age, the analysis was divided into two age categories: those aged 0–65 years and those aged > 65 years. The findings revealed that $PM_{2.5}$ had positively correlated with CVD in those aged 0–65 years and elderly individuals aged > 65 years at elevated PM concentration ($PM_{2.5}$ = 189 μg m^{-3}, RR = 1.68 (95% CI: 1.28–2.20); $PM_{2.5}$ = 148 μg m^{-3}, RR = 1.65 (95% CI: 1.05–2.60). For individuals aged over 66 years, elevated RRs were observed at $PM_{2.5}$ concentrations approximately at 150 μg m^{-3}. Conversely, for those aged between 0 and 65 years, the RRs demonstrated a consistent upward trajectory with escalating $PM_{2.5}$ concentrations. The study found a positive correlation between PM_{10} concentration and cardiovascular disease. The RRs demonstrated a consistent upward trend with increasing PM_{10} concentrations, a pattern that was observed across both gender and age subgroups.

Table S1 shows the cumulative RRs and 95% CI for associations between PM and CVD at lags of 0–21 days by sex and age. Overall, high RRs were observed at a high $PM_{2.5}$ concentration (95^{th}, 185 μg m^{-3}, RR = 1.58; 95% CI: 1.08–2.31). In the subgroup analysis by sex, the effect of PM exposure on CVD incidence was significantly higher in females (RR = 1.37; 95% CI: 1.09–1.73) than in males (RR = 1.35; 95% CI: 1.10–1.67) at a 25^{th} $PM_{2.5}$ concentration. At a high $PM_{2.5}$ concentration (95^{th}, 185 μg m^{-3}), a large cumulative RR was observed in females (RR = 1.89; 95% CI: 1.20–2.97). When modification effects were considered across different age groups, the estimates of the effect of $PM_{2.5}$ exposure on CVD were significant among individuals aged > 65 years. The estimated effects of $PM_{2.5}$ exposure on daily CVD outpatient visits in older individuals at low, medium, and high $PM_{2.5}$ concentrations were 1.40 (1.06–1.87), 1.01 (0.99–1.02), and 2.07 (1.22–3.50), respectively. A large cumulative RR was also observed in older individuals for PM_{10} (RR = 1.58; 95% CI: 1.01–2.49). The group comparison results showed that females and the elderly were more vulnerable to PM at high concentrations and had a greater risk of CVD than males and younger individuals.

The effect of PM on CVD may be sex-specific. In this study, we found a positive association between $PM_{2.5}$ and PM_{10} concentrations in females but not in males. Other epidemiological studies have also reported that the effects of air pollutants on CVD incidence were stronger in women (Chen *et al.*, 2017a). Miller *et al.* (2007) suggested that the greater effect of air pollution on respiratory health in women was due to social, behavioral, and biological differences. Sex-related characteristics affect the biological transport of environmental chemicals, while gender-related

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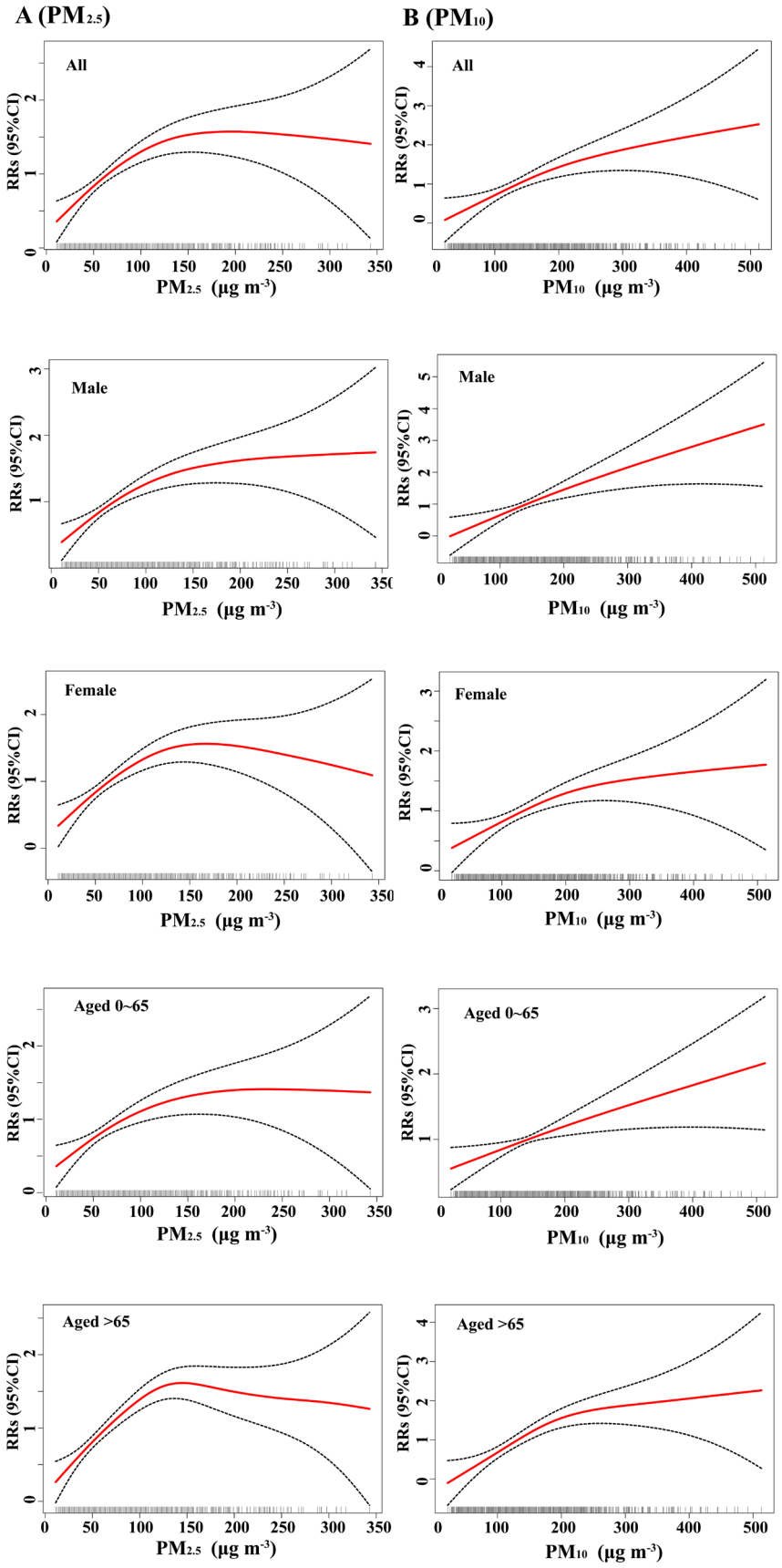


Fig. 2. Exposure-response curve for (A) $PM_{2.5}$ and (B) PM_{10} associated with CVD incidence (Natural spline, 3 degrees of freedom), Linyi, 2014–2019.

behaviors determine the distribution of air pollution exposure. Females are exposed to higher doses of indoor air pollutants than males and have greater deposition of particulate matter and higher absorption of air pollutants. Another possible reason for the sex-specific associations between air pollution and CVD is the different smoking habits in China and the large differences in smoking rates between men and women. The increased relative risk (RR) of CVD incidence associated with air pollution exposure may be reduced or even offset by heavy smoking among men. When the analysis was further stratified by age, a positive association between $PM_{2.5}$ and PM_{10} concentrations was observed in participants aged 65 years. Epidemiological studies have also shown that the effect of air pollution on CVD is more pronounced in older adults (Chen *et al.*, 2010). Consistent with previous reports, our results indicate that older adults are more vulnerable to acute effects of air pollution and thus at higher risk for CVD. The physiological changes associated with aging may increase susceptibility to air pollutants (Bell *et al.*, 2013). Respiratory or cardiovascular diseases can make individuals more susceptible to air pollutants; there is some overlap between older adults and patients with heart or lung disease (Kan *et al.*, 2008).

3.2.2 Lag association between CVD and levels of $PM_{2.5}$/PM_{10}

The three-dimensional graphs illustrating the lag dose–response relationship between PM and RRs of CVD revealed high RRs from the current day (lag 0) to a seven-day lag (lag 7) (Fig. S3). Consequently, an analysis was conducted on the lag associations and RR in CVD outpatient visits with varying $PM_{2.5}$ and PM_{10} concentrations in Linyi from 2014 to 2019 (Fig. 3). A positive correlation was observed between increased levels of $PM_{2.5}$ and PM_{10} and the risk of CVD in women and elderly individuals aged > 66. For females, the highest RR was noted at high $PM_{2.5}$ and PM_{10} concentrations (95^{th}) at a three-day lag, with RRs for $PM_{2.5}$ and PM_{10} being 1.0485 (95% CI: 1.01–1.09) and 1.05 (95% CI: 1.01–1.08), respectively. Stratified statistics showed that elderly individuals over the age of 65 had high RRs at a three-day lag for both $PM_{2.5}$ (RR = 1.06; 95% CI: 1.01–1.10) and PM_{10} (RR = 1.04; 95% CI: 1.00–1.08).

3.2.3 Effect of temperature on particulate matter and cardiovascular disease

To evaluate the impact of temperature on particulate matter's CVD risk, the year was bifurcated into warm (April–September) and cold seasons (October–March), with stratified analysis employed to integrate model statistics (Fig. 4 and Fig. 5). In the cold season, temperature significantly influenced cardiovascular disease risk (Abrignani *et al.*, 2022). Moreover, PM_{10} exhibited significant relative risks (RRs) at low-medium concentrations (25^{th}, 50^{th}) with a cumulative lag of 3–6 days (lag03–lag06). As PM_{10} concentration increased (95^{th}), there was a notable elevation in CVD RRs corresponding to an increase in lagged days. $PM_{2.5}$ was significant at high concentrations (95^{th}), with RRs escalating as lagged days increased. In the warm season, both $PM_{2.5}$ and PM_{10} concentrations, along with temperature, were significant relative risks for CVD. The cumulative lagged risk rose with an increase in lagged days, particularly for $PM_{2.5}$ in relation to CVD risk.

The findings indicated a correlation between temperature and particulate matter, with an increase in both variables heightening the risk of cardiovascular diseases (Fig. 6). The total number of outpatient visits for CVDs rose with $PM_{2.5}$ concentration during both cold and warm seasons. In the cool season, outpatient visits were notably higher at $PM_{2.5}$ concentrations exceeding 200 $\mu g\ m^{-3}$; the peak number of CVD visits occurred when temperatures ranged from 10°C to 15°C. Conversely, in the warm season, outpatient visits were significantly elevated at $PM_{2.5}$ concentrations above 100 $\mu g\ m^{-3}$. The highest incidence of CVD visits was noted at temperatures between 25°C and 30°C. Furthermore, the impact of $PM_{2.5}$ on total CVD visits was more pronounced in the warm than in the cold season. The study observed similar results for total cardiovascular disease visits in relation to both PM_{10} concentration and temperature. Notably, there was a significantly higher risk associated with PM_{10} concentrations exceeding 250 $\mu g\ m^{-3}$ during the cold season, as well as temperatures higher than 10°C. Conversely, in the warm season, outpatient visits were notably higher at a PM_{10} concentration of 200 $\mu g\ m^{-3}$ and a temperature range of 25–30°C. The impact of PM_{10} on total CVD visits was more pronounced in the cool season compared to the warm one. In summary, the interaction between temperature and particulate matter revealed that total CVD visits increased proportionally with particulate matter concentration. Furthermore, it was found that $PM_{2.5}$ had a more significant effect on CVD visits in the warm

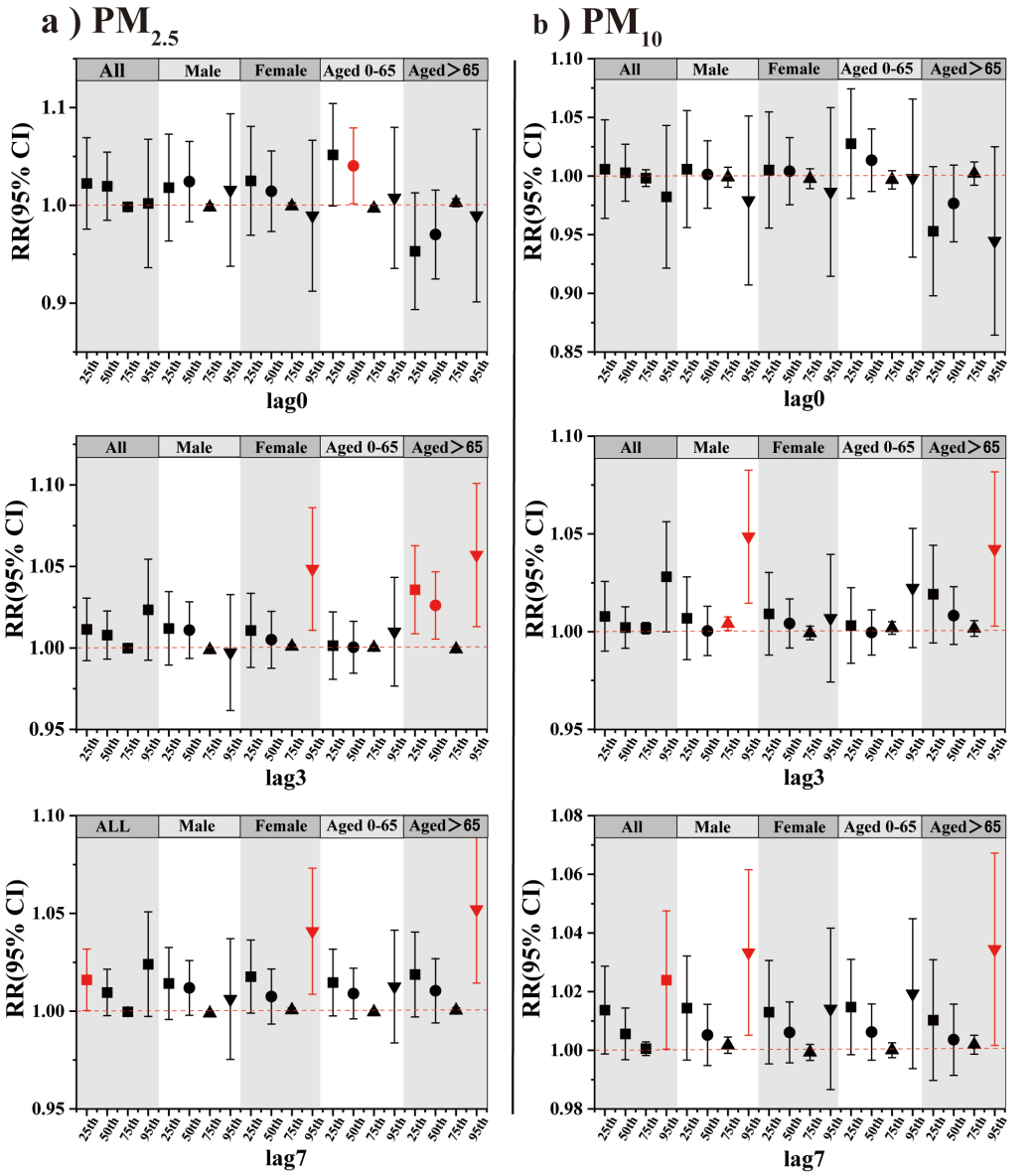


Fig. 3. The lag associations and RR in CVD outpatient visits with (A) $PM_{2.5}$ and (B) PM_{10} concentration, Linyi, 2014–2019.

season than in the cold one, while PM_{10} had a more substantial effect on CVD visits in the cold season than in the warm one.

Zhang *et al.* (2020a) conducted a study examining the moderating effect of temperature on the relationship between mortality and $PM_{2.5}$ exposure in 15 Chinese cities from 2014 to 2016. The findings revealed that high-temperature exposure significantly exacerbated the adverse impacts of $PM_{2.5}$ exposure on non-accidental deaths and cardiovascular events within these cities. Tian *et al.* (2018) investigated the modified effects of temperature of PM_{10} on daily non-accidental, cardiovascular, and respiratory mortality rates in Beijing from 2006 to 2009. The results indicated that the impacts of PM_{10} on non-accidental, cardiovascular, and respiratory deaths were more pronounced at higher temperature levels than at lower ones. Specifically, there was a 0.12% (95% CI: 0.02–0.23) increase in cardiovascular mortality for every 10 μg m^{-3} increase in PM_{10} when controlling for a temperature moving average lag of 14 days. Zhang *et al.* (2020b) indicated that high temperature significantly enhanced the effects of particulate matter (BC, $PM_{2.5}$, and $PM_{2.5\text{-}10}$) and mortality (non-accidental, respiratory, and cardiovascular mortality) in Beijing, China.

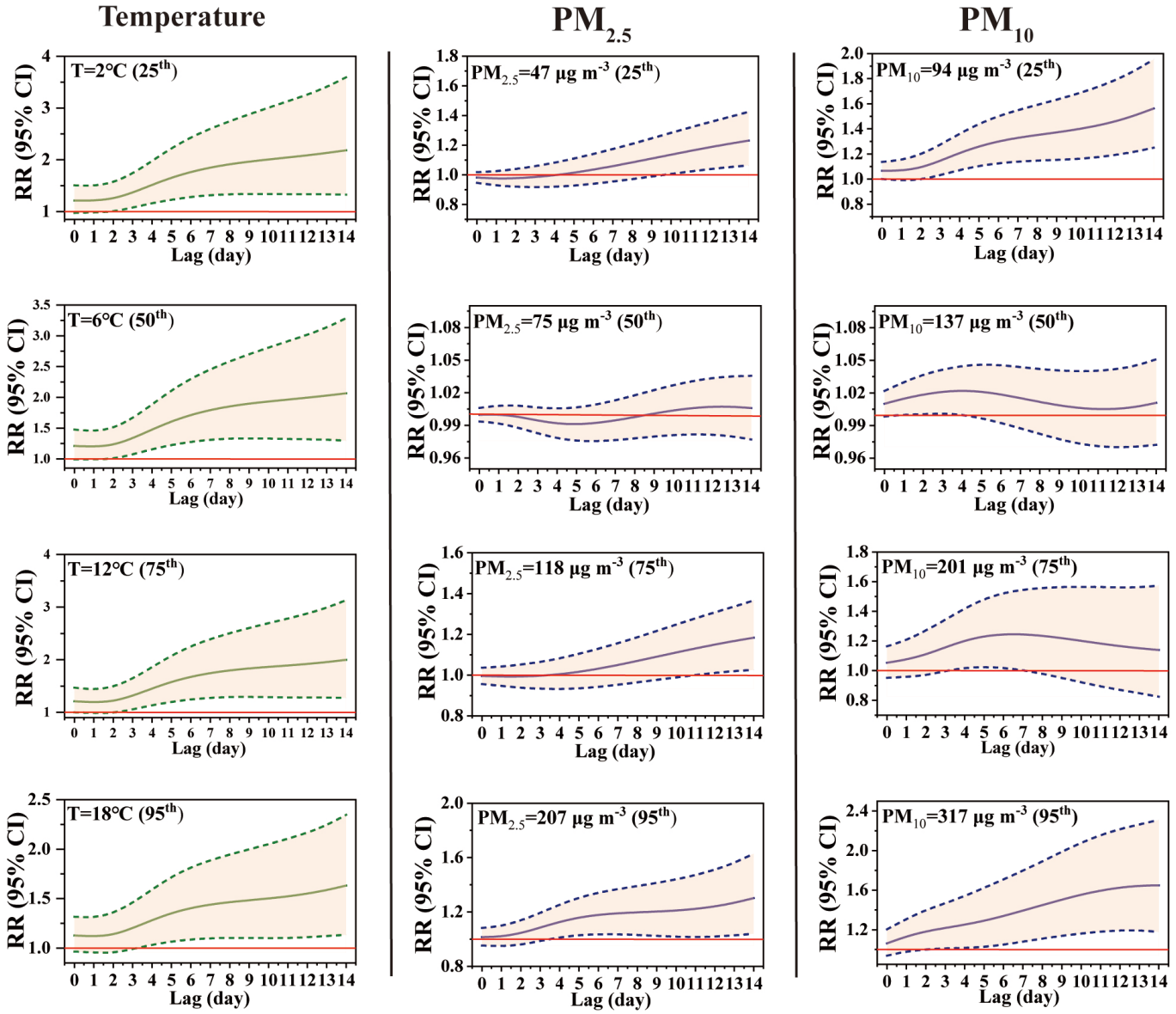


Fig. 4. Cumulative lagged effects and 95% CI of different $PM_{2.5}$ and PM_{10} concentration and temperature (25^{th}, 50^{th}, 75^{th}, and 95^{th}) on cardiovascular diseases in cold season.

3.3 Discussion

In this study, a significant association was observed between PM exposure and the CVD outpatient visits in Linyi from 2014 to 2019. The data indicated that both $PM_{2.5}$ and PM_{10} were positively correlated with the number of CVD outpatient visits, particularly among females and elderly individuals exposed to high PM concentrations. This positive relationship between ambient PM and CVD has been previously confirmed (Talbott *et al.*, 2014; Li *et al.*, 2020; Liang *et al.*, 2020). A previous study conducted in Linyi in 2015 reported that PM associations for circulatory disease morbidity, with the strongest effect observed for $PM_{2.5}$ and PM_{10}, increased outpatient visit numbers by 1.71% and 1.44%, respectively, at a lag of 0 days (Li *et al.*, 2020). The RRs associated with ambient PM ($PM_{2.5}$, 77 μg m^{-3}; PM_{10}, 145 μg m^{-3}) and daily outpatient visits for CVD in Linyi were comparable to those found in other Chinese cities such as Beijing ($PM_{2.5}$, 103.4 μg m^{-3}; PM_{10}, 111.5 μg m^{-3}) and Shanghai ($PM_{2.5}$, 56.3 μg m^{-3}; PM_{10}, 76.0 μg m^{-3}). These values were higher than those obtained in a global meta-analysis but lower than those found in Shijiazhuang (in severe air pollution with $PM_{2.5}$ more than 100 μg m^{-3} and PM_{10} more than 300 μg m^{-3}). A time-series study conducted in Ganzhou City, Jiangxi Province, found that for every 10 μg m^{-3} increase in

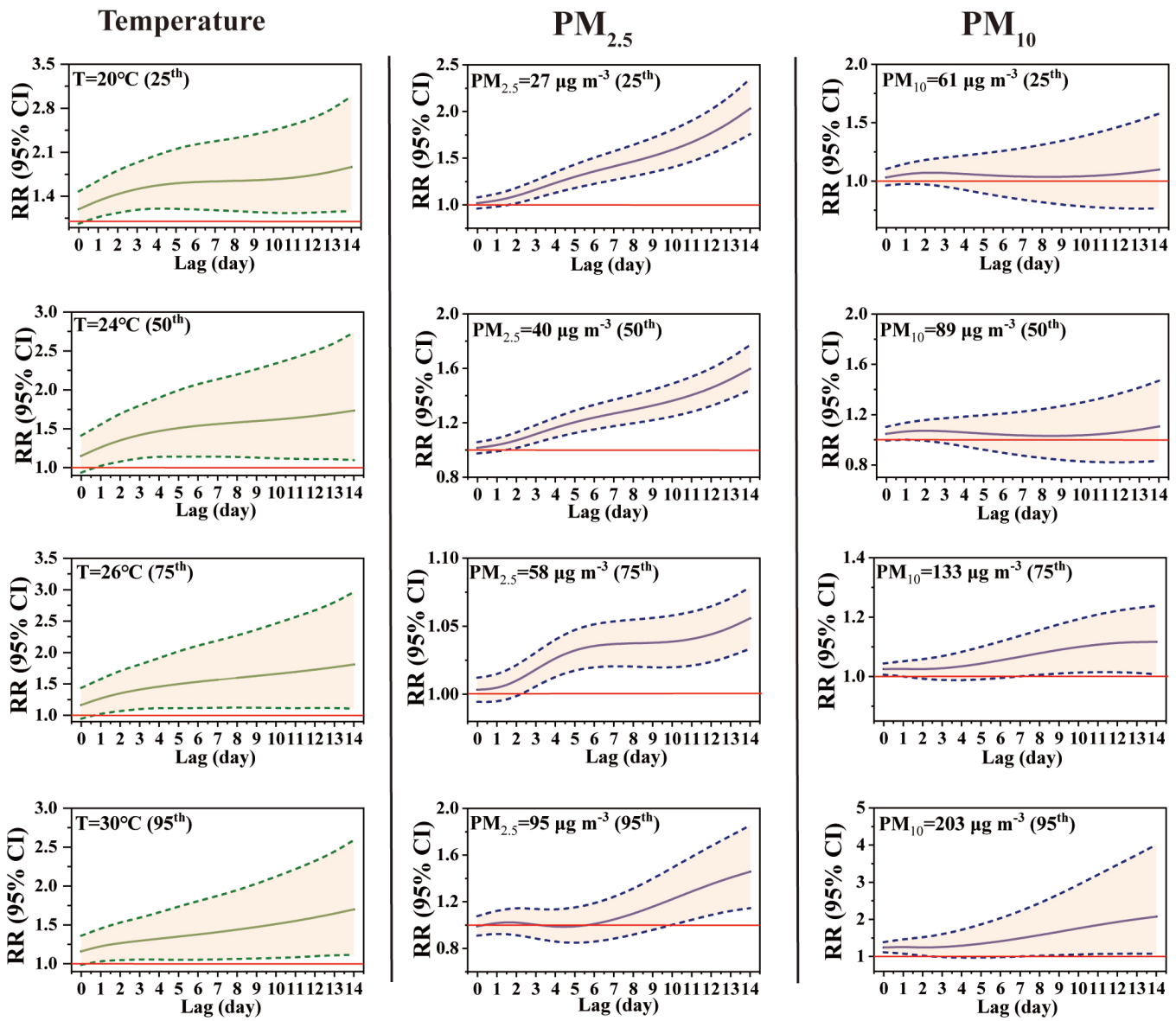


Fig. 5. Cumulative lagged effects and 95% CI of different $PM_{2.5}$ and PM_{10} concentration and temperature (25th, 50th, 75th, and 95th) on cardiovascular diseases in warm season.

$PM_{2.5}$ and PM_{10}, there was a 7.92% (95% CI: 5.48%–10.42%) and 4.46% (95% CI: 2.86%–5.65%) increase in hypertension hospitalizations, respectively (Li *et al.*, 2022). A study conducted in Yancheng found that $PM_{2.5}$ was associated with an increased risk of hospitalization for atrial fibrillation by 2.81% (95% CI: 1.44%–4.20%) and PM_{10} was associated with an increased risk of hospitalization for atrial fibrillation by 1.67% (95% CI: 0.77%–2.59%) for each 10 μg m^{-3} increase in pollutant concentration (Fang *et al.*, 2021) (Fig. 7).

Even in areas with low levels of air pollution, the excess risk (ER) of cardiovascular disease mortality was 1.50% (95% CI: 0.51–2.50%) and 2.09% (95% CI: 0.79–3.41%) when the concentration of $PM_{2.5}$ increased by 10 μg m^{-3} on lag05 days and lag0–2 days, respectively (Cai *et al.*, 2018). Studies conducted in Sydney, Australia, indicated that ambient $PM_{2.5}$ and PM_{10} posed higher risks for daily emergency department attendances in the elderly population (65+ years); the RRs for $PM_{2.5}$ and PM_{10} were 2.26% (95% CI: 1.56–2.96) and 1.72% (95% CI: 1.14–2.60), respectively, which were higher than those obtained in the current study ($PM_{2.5}$, 2.07%; 95% CI: 1.22–3.50; PM_{10}, 1.59%; 95% CI: 1.01–2.49) (Jalaludin *et al.*, 2006). A study in the United States also found that a 10 μg m^{-3} increase in $PM_{2.5}$ was associated with a 16% (95% CI: 9%–22%) increase in

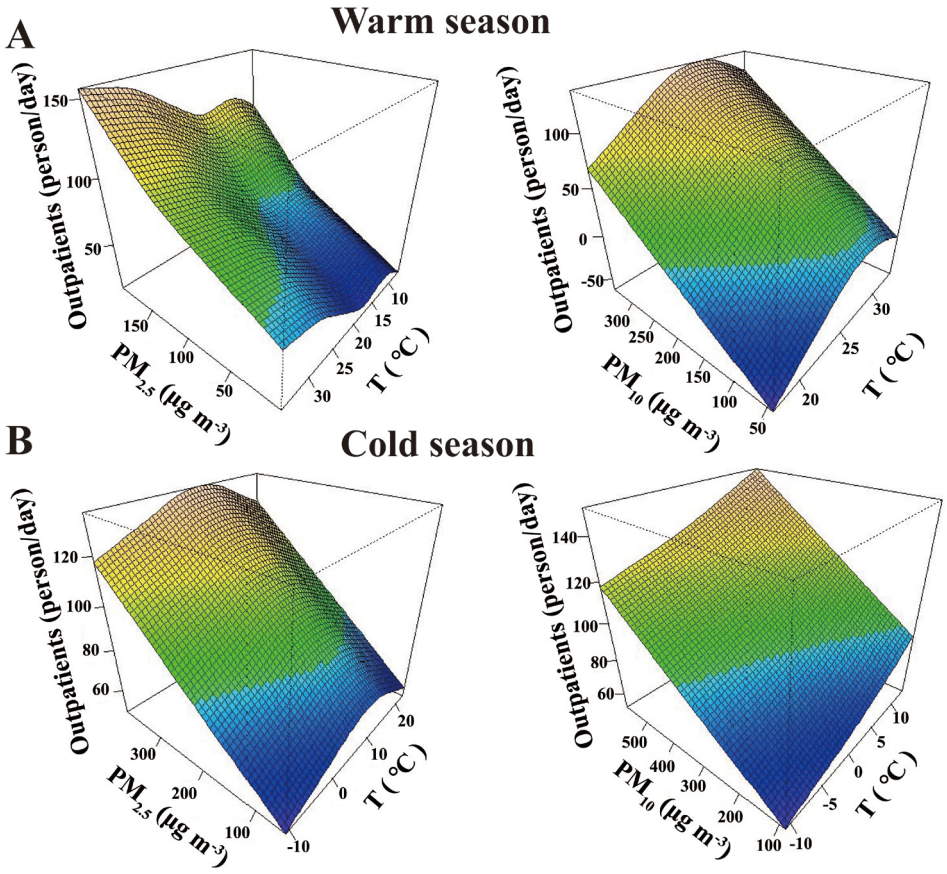


Fig. 6. The modifying effect of temperature on particulate matter and CVD risk, the whole year was divided into the (A, April–September) warm season and (B, October–March) cold season.

ischemic heart disease mortality and a 14% (95% CI: 2%–27%) increase in stroke mortality (Hayes *et al.*, 2020). A study conducted in Mexico found every 10 μg m^{-3} elevation in PM_{10} concentration increased the risk of emergency cardiovascular admissions of 2.8% (95% CI: 0.6–5.0%) at a lag of 0–5 days, and $PM_{2.5}$ was associated with an increased risk of emergency cardiovascular admissions at a lag of 0–6 days (RR: 3.7%; 95% CI: 0.1–7.6%) (Ugalde-Resano *et al.*, 2022).

In addition, the exposure-response curve of $PM_{2.5}$ and PM_{10} for CVD outpatient visits was nonlinear, with a sharp increase in CVD risk at high concentrations of PM. Although most studies have shown that there is a linear dose-response relationship between PM and CVD risk (Miller *et al.*, 2007; Liu *et al.*, 2019a; Liang *et al.*, 2020), some studies have reported nonlinear health effects of PM. Chen *et al.* (2017a) conducted a meta-analysis of 272 Chinese cities and found a nonlinear exposure-response relationship between $PM_{2.5}$ and mortality in Northeast and Northwest China. In general, the exposure-response curve of $PM_{2.5}$ and PM_{10} for CVD in populations should be close to the cumulative normal curve. However, due to differences in industrial structure, air pollutant concentration and components, economic level, and meteorological conditions, the exposure-response curve may be nonlinear in some cities. For example, although the curve for all of China is linear, it is nonlinear for northwest and northeast cities in China. Therefore, the nonlinearity observed in this study may be related to the higher annual concentration of PM in Linyi ($PM_{2.5}$, 77 μg m^{-3}) than in the national study in China ($PM_{2.5}$, 56 μg m^{-3}). This study was conducted in a highly polluted city with various air pollutants including coal combustion, industrial emissions, and traffic congestion. Although the concentration of PM has decreased, the CVD risk associated with $PM_{2.5}$ and PM_{10} still exists, which highlights the need for more stringent sustainable emission reduction policies. Further research on pollution relationships in highly polluted areas will help policymakers make decisions.

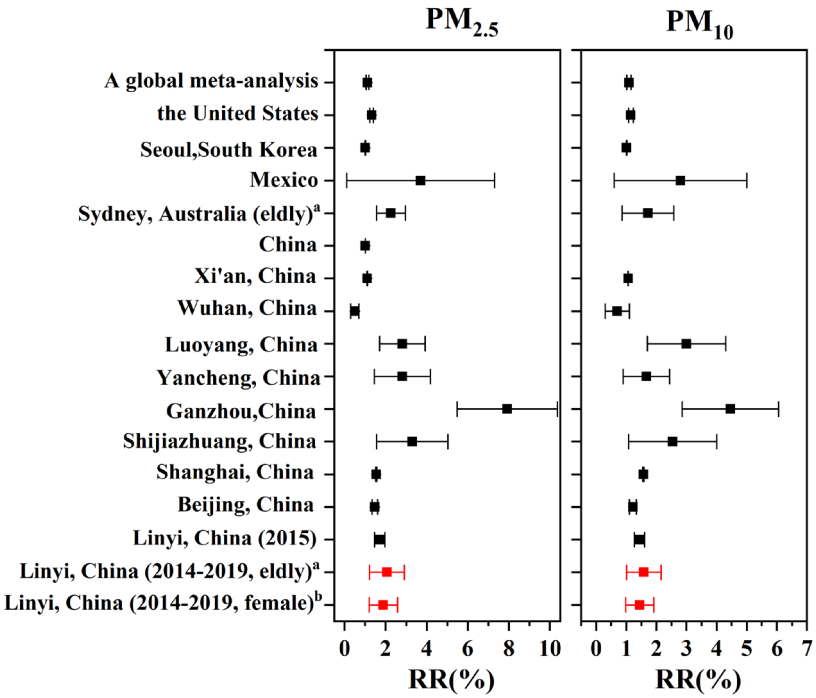


Fig. 7. Associations between ambient PM and daily outpatient visits for CVD. The RRs with CVD outpatient visits are the maximum cumulative RRs for females and elder adults. A global meta-analysis (Yang *et al.*, 2019); the United States (Feng and Yang, 2012); Seoul, South Korea (Hwang *et al.*, 2017); Mexico (Ugalde-Resano *et al.*, 2022); Sydney, Australia (Bin *et al.*, 2006); China (Ruan and Zeng, 2022); Xi'an, China (Wang *et al.*, 2022); Wuhan, China (Meng *et al.*, 2023); Luoyang, China (Guo *et al.*, 2021); Yancheng, China (Fang *et al.*, 2021); Ganzhou, China (Li *et al.*, 2022); Shijiazhuang, China (Tan *et al.*, 2019); Shanghai, China (Xu *et al.*, 2017); Beijing, China (Chen, 2016); Linyi (2015), China (Li *et al.*, 2020); Linyi (2014–2019), China (this study), a, the RR for elders (65+ years); b, the RR for females.

4 CONCLUSIONS

This study examined the exposure-response relationship between airborne particulate matter and cardiovascular diseases (CVDs) in an industrial city in northern China. A distributed lag nonlinear model was employed to elucidate the CVD risk associated with $PM_{2.5}$ and PM_{10}. The findings demonstrated a nonlinear association between particulate matters and CVD relative risks, with a significant correlation observed between high levels of $PM_{2.5}$ and PM_{10} concentrations and CVD. Stratified analyses revealed that females and the elderly were more vulnerable to exposure to PM, potentially due to physiological differences and population susceptibility. These findings suggest that air pollutants significantly influence the CVD in this industrial city. The cumulative lag effect of varying particulate matter concentration and temperature on CVD showed that the risk for CVD increased with elevated concentrations of $PM_{2.5}$ and PM_{10} during both warm and cold seasons, primarily presenting a significant risk at cumulative lags of 3–6 days (lag03–lag06). The total CVD outpatient visits increased with elevated temperature and particulate matter. $PM_{2.5}$ had a greater effect on CVD visits in the warm season than in the cold season. PM_{10} posed a higher risk on CVD visits in the cold season than in the warm season. Despite significant improvements in air quality, atmospheric particulate matter still poses a high risk of cardiovascular disease in the population. Therefore, sustained measures and policies to reduce atmospheric emissions are necessary. Numerous small to medium-sized industrial cities similar to Linyi exist in China. The results of this study provide crucial information that can inform the development of such policies in other industrialized cities. These results offering a scientific foundation for air pollution control and the protection of vulnerable populations' health.

ADDITIONAL INFORMATION AND DECLARATIONS

Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics Approval and Consent to Participate

This study has received approval by the Ethics Committee of the Linyi People's Hospital with an exemption from informed consent.

Availability of Data and Material

The raw/processed data required to reproduce these findings can be shared by requiring from the corresponding author.

Authors' Contributions

Min Wei: Conceptualization, Methodology, Writing-Original draft preparation; **Qun He, Meifui Feng:** Data curation, Visualization, Writing- Reviewing and Editing; **Xin Wu, Jing Yang:** Data curation, Software; **Hongmin Zhou:** Visualization, Investigation; **Houfeng Liu**: Data curation, Validation; **Xin Bo:** Supervision, Writing- Reviewing and Editing.

Supplementary Material

Supplementary material for this article can be found in the online version at https://doi.org/10.4209/aaqr.240132

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