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Different sized particles associated with all-cause and cause-specific emergency ambulance calls: A multicity time-series analysis in China

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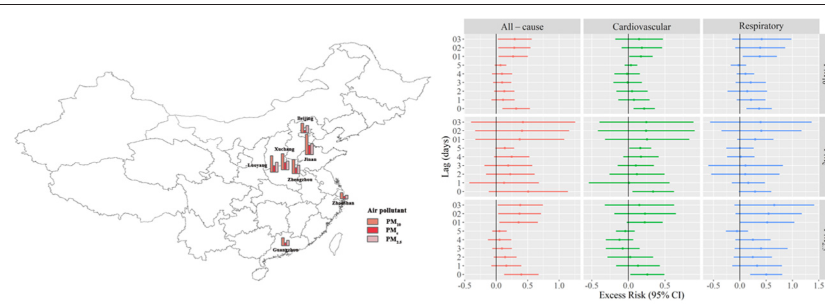
HIGHLIGHTS

- Both $PM_{2.5}$ and PM_{10} are significantly associated with emergency ambulance calls (EACs).
- $PM_{2.5}$ has the largest effect on EACs.
- This is the first multicity study examining the acute effects of different PM metrics on EACs in China.

GRAPHICAL ABSTRACT



Significant associations existed for both $PM_{2.5}$ and PM_{10} with emergency ambulance calls in 7 Chinese cities

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ABSTRACT

Background: Compared with mortality and hospital admission, emergency ambulance calls (EACs) could be a more accurate outcome indicator to reflect the health effects of short-term air pollution exposure. However, such studies have been scarce, especially on a multicity scale in China.

Methods: We estimated the associations of different diameter particles [i.e., inhalable particulate matter (PM_{10}), coarse particulate matter (PM_c), and fine particulate matter ($PM_{2.5}$)] with EACs for all-cause, cardiovascular, and respiratory diseases in seven Chinese cities. We collected data on EACs and air pollution from 2014 to 2019. We used generalized additive models and random-effects meta-analysis to examine the city-specific and overall associations. Stratified analyses were conducted to examine the effect modifications of gender, age, and season.

Results: Significant associations of PM_{10} and $PM_{2.5}$ with EACs were observed, while the PM_c associations were positive but not statistically significant in most analyses. Specifically, each 10 μg/m^3 increase in 2-day moving average concentration of PM_{10} was associated with a 0.25% [95% confidence interval (CI): 0.04%, 0.47%] increase in all-cause EACs, 0.13% (95% CI: −0.01%, 0.26%) in cardiovascular EACs, and 0.35% (95% CI: 0.04%, 0.66%) in respiratory EACs. The corresponding increases in daily EACs for $PM_{2.5}$ were 0.30% (95% CI, 0.03%, 0.57%), 0.13% (95% CI, −0.07%, 0.33%), and 0.46% (95% CI, 0.01%, 0.92%). Season of the year also modifies the association between particulate matter pollution and EACs.

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Conclusions: Short-term exposure to PM_{10} and $PM_{2.5}$ were positively associated with daily all-cause and respiratory-related EACs. The associations were stronger during warm season than cold season. Our findings suggest that the most harmful fraction of particulate matter pollution is $PM_{2.5}$, which has important implications for current air quality guidelines and regulations in China.

1. Introduction

In the past decade, multiple studies have observed that particulate matter (PM) pollution with an aerodynamic diameter smaller than 10 μm (PM_{10}) and 2.5 μm ($PM_{2.5}$), and coarse particles (particles between 10 and 2.5 μm in the diameter, PM_c) had negative health impacts, with no evidence for a threshold (Bennett et al., 2019; Chen et al., 2020; Qi et al., 2020; Yu et al., 2020). It is widely believed that the adverse effects of PM pollution were dependent on their particle size, with smaller particles demonstrating greater toxic impact than larger particles (Lin et al., 2016b; Pan et al., 2018; Tian et al., 2020). However, some studies reported that PM_c might have larger health effects than $PM_{2.5}$ (Qiu et al., 2014; Wang et al., 2018b), and the evidence on the effects of different particle sizes on human health has been relatively sparse, controversial, and in need of further investigations (Chen et al., 2015; Liu et al., 2013).

It is well documented that short-term exposure to PM pollution increases the incidence of adverse health outcomes, especially in cardiovascular and respiratory systems (Mentz et al., 2019; Torres et al., 2019; Yang et al., 2020; Zhang et al., 2020). The World Health Organization (WHO) stated that PM pollution is closely associated with increased mortality and morbidity (WHO, 2018). Previous studies have mainly focused on mortality, morbidity, and hospital admissions (Atkinson et al., 2014; Gu et al., 2020; Tian et al., 2019; Zhao et al., 2017). However, emergency ambulance calls (EACs) may be more sensitive to the acute health effects, and thus may be more apposite to reflect the acute effects of short-term exposure to PM pollution (Ai et al., 2019). For example, one study in Japan found that EACs might provide a more adequate endpoint for observing the acute health effects of $PM_{2.5}$ (Michikawa et al., 2015b). However, limited studies have examined EACs as their outcome, and the findings have been inconsistent. For instance, one study reported that PM_c was associated with an increase in cardiovascular-related EACs (OR = 1.05, 95% CI: 1.03, 1.07) (Xia et al., 2017); however, one case-crossover study did not observe significant associations between short-term exposure to PM_c and EACs from all-cause, cardiovascular, and respiratory diseases in Japan (Michikawa et al., 2015b). Furthermore, most of the studies estimated the associations in one single city or only a few cities, especially in China (Ai et al., 2019; Liu et al., 2017b; Yang et al., 2014). For instance, Ai's study found $PM_{2.5}$ and PM_{10} were associated with EACs in Luoyang (Ai et al., 2019). Liu's study showed that exposure to $PM_{2.5}$ was associated with EACs especially for respiratory and cardiovascular diseases in Chengdu (Liu et al., 2017b). Another study in Guangzhou demonstrated that short-term exposure to PM_{10} was associated with increased EACs due to heart failure (Yang et al., 2014).

We thus conducted this study intending to assess the overall effects of short-term exposure to PM pollution with different particle sizes (PM_{10}, PM_c, and $PM_{2.5}$) on EACs by using multicity data in China.

2. Methods

2.1. Study locations

We collected daily EACs data from seven representative medium and large cities in China (Fig. S1), including one in the north (Beijing), five in the central (Luoyang, Zhengzhou, Xuchang, Jinan, and Zhoushan), and one in the south (Guangzhou). These included four developed municipality/provincial capital cities (Guangzhou, Beijing, Zhengzhou, and Jinan), one coastal city (Zhoushan), and two less developed cities (Luoyang and Xuchang). The study periods were 2016–2018 for Beijing (Two district were used to represent Beijing due to the availability of EACs data); 2014–2018 for Guangzhou; 2014–2017 for Jinan; 2014–2018 for Zhoushan; 2015–2019 for Zhengzhou; 2017–2019 for Xuchang; and 2014–2016 for Luoyang. Guangzhou, Zhengzhou, Xuchang, Luoyang, Jinan, Zhoushan, and Beijing had 14.5, 9.9, 5.0, 6.8, 7.3, 1.2, and 2.5 million residents, respectively.

2.2. Daily EACs data

The daily counts of EACs due to respiratory, cardiovascular, and all-cause diseases were obtained from the local emergency centers in each city. EAC records were completed by trained medical personnel after each emergency call. The records include basic demographic information. Disease diagnoses were made based on clinical symptoms of the patients, medical interviews, and physical examinations in standardized processes where rigorous quality assurance was adopted. These diagnoses were made by clinical physicians (Wang et al., 2020). Thus, it was estimated that the misclassification rate was comparatively low. We excluded EAC recodes due to pregnancy, traffic accidents, drowning, electric shock, and suicide events.

2.3. Air pollutant and meteorological data

Daily pollution data were obtained from the environmental monitoring system of each city. We collected the daily mean concentrations of $PM_{2.5}$, PM_{10}, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone (O_3). PM_c concentrations were the difference between PM_{10} concentrations and $PM_{2.5}$ concentrations (Wang et al., 2018b). The city-specific daily concentrations were obtained from the mean of daily concentrations from every station within a city. The percentage of days with missing data was 0.7% for $PM_{2.5}$, 0.7% for PM_c, 0.7% for PM_{10}, 0.7% for SO_2, 0.8% for NO_2, and 0.7% for O_3. The missing data were imputed using a linear interpolation approach (the “na.approx” function in “zoo” package in R).

Daily mean temperature and relative humidity were acquired from the National Weather Data Sharing System (http://data.cma.cn/).

2.4. Statistical analyses

A two-stage analytic protocol was applied to examine city-specific and overall effects of different sized particles on all-cause, cardiovascular-related, and respiratory-related EACs. We first fit generalized additive models (GAM) for each city to estimate the associations between daily exposure of PM pollution and EACs. We further conducted a meta-analysis to pool the estimates of each city to derive overall effects.

In the city-specific models, we controlled for the following variables: long-term trends, seasonal patterns, day of the week (DOW), temperature, relative humidity, and public holidays. Following the analysis strategy used in previous studies (Liu et al., 2019), we applied a df of 6 per year for temporal trends, moving average temperature of the current day and previous three days ($Temp_{03}$). To control for potential nonlinear effects, the same day's relative humidity (RH) was included using a natural cubic spline with 3 df. We also included dummy variables for the day of the week (DOW) and public holiday (PH). The base model is defined as below:

$$\log[\mathrm{E}(Y_t)] = \alpha + \mathrm{s}(\mathrm{t}, \mathrm{df} = 6/year) + \mathrm{s}(Temp_{03}, \mathrm{df} = 6) + \beta_1 * DOW + \mathrm{s}(\mathrm{RH}, \mathrm{df} = 3) + \beta_2 * PH$$

where $E(Y_t)$ is the expected daily number of EAC on day t, α means the intercept, s() represents a smoothing function, t is the adjustment for long-term and seasonal trends, and β is the coefficient of the regression, $Temp_{03}$ is the moving average for the previous 4 days' temperature, DOW is an indicator for the day of the week, RH presents the humidity on the current day, PH represents a binary variable for the public holiday.

We pooled the estimates of the city-specific associations across the 7 cities in the second stage using random-effects meta-analysis. We then reported the overall estimates and 95% CI as the percentage change in EACs per 10 $\mu g/m^3$ increase in PM pollution. To assess for heterogeneity across the cities, we used the Cochran Q chi-square statistic and the I-squared statistic (Higgins and Thompson, 2002).

To consider the potential collinearity caused by inclusion of two highly correlated variables in the same model, we examined the correlation between independent variables, if the correlation was higher than 0.80, they did not include in the same two-pollutant models.

We constructed different lag structure models to determine the lagged effects. In the single-lag day models, we begin with the same day (lag_0) up to five days lag (lag_5). We also considered multi-lag days [moving average of current day and previous 1, 2, and 3 days (lag_{01}, lag_{02}, and lag_{03})]. The effects of single-lag days and multi-lag days were finally reported for each PM metric.

2.5. Sensitivity analyses

We assessed the robustness of the main models by sensitivity analyses. We changed the df for the calendar time (6–8 df per year) and meteorological variables (3–5 df) in models. We also performed two-pollutant model analyses. The models were considered steady if there were no substantial changes after df-changed or adjustment.

2.6. Stratified analyses

To evaluate the potential effect modifiers of the association between short-term exposure of particulate matter and EACs, we applied stratified analyses by gender (male and female), age group (<65 years and ≥65 years), and season (warm and cold). The warm season was defined as April to September, and the cold season was October to March. And the statistical significance of the difference between strata was calculated by the equation below:

$$Q_1 - Q_2 \pm 1.96\sqrt{(SE_1)^2 + (SE_2)^2}$$

where Q represents the estimated coefficient in each stratum, and SE is the corresponding standard error (Lin et al., 2016a, 2016b).

2.7. Estimating attributable burden to PM pollution

To estimate the burden of EACs attributable to PM pollution, we applied attributable number (AN) and attributable fractions (AF) as metrics. The guideline values set by the Chinese National Ambient Air Quality Standards (Lin et al., 2016a) and the WHO's Air Quality Guidelines (WHO, 2018) were used as the reference concentrations. PM_c was not directly regulated by the ambient air pollution standards/guidelines. According to our previous study (Wang et al., 2018a), the reference concentrations for PM_c were acquired by subtracting the standard concentrations of $PM_{2.5}$ from PM_{10}. In particular, the WHO's guideline (25 $\mu g/m^3$) and China's standard (75 $\mu g/m^3$) were used as the reference concentration for PM_c in our analyses. The methods to calculate AN and AF have been described elsewhere (Aik et al., 2020; Wu et al., 2020).

R software (version 3.6.1) was used and the "mgcv" and "metafor" packages were applied for this study. All statistical tests were two-sided and $P < 0.05$ was used to represent statistical significance. The effects of PM pollution are presented as excess risk (ER), which is defined as [relative risk (RR) − 1] ∗ 100%.

3. Results

Our study recorded a total of 1,626,017 EACs from all-cause, including 230,537 EACs from cardiovascular diseases, and 96,483 EACs from respiratory diseases. The daily average numbers of EAC due to all-cause, cardiovascular, and respiratory diseases ranged from 38 to 390, from 5 to 59, and from 1 to 26, respectively, across the 7 cities (Table 1). The mean concentrations of PM_{10}, PM_c, and $PM_{2.5}$ in the 7 cities ranged from 45.19 $\mu g/m^3$ to 150.24 $\mu g/m^3$, from 17.85 $\mu g/m^3$ to 69.31 $\mu g/m^3$, from 26.59 $\mu g/m^3$ to 80.94 $\mu g/m^3$, respectively. The daily mean temperature ranged from 12.89 to 22.31 °C, and relative humidity values ranged from 55.96% to 79.74%. In brief, PM_{10} was strongly correlated with $PM_{2.5}$ ($r = 0.85$); PM_c and $PM_{2.5}$ were low to moderately related, with a mean Spearman correlation coefficient of 0.30 (Table S1). Generally, the correlation of PM_{10} and $PM_{2.5}$ with gaseous pollutants was low to high (the coefficients ranging from −0.14 to 0.63). PM_c was moderately or weakly correlated with gaseous air pollutants (the coefficients ranging from −0.06 to 0.34).

$PM_{2.5}$ and PM_{10} were significantly associated with EACs due to all-cause and respiratory diseases in single pollutant models at lag_{01}, while all associations between PM_c and EACs were not significant (Table 2). In two-pollutant models, the associations of PM_{10} and $PM_{2.5}$ concentrations with EACs slightly decreased at lag_{01} after we adjusted for SO_2 and NO_2. The associations between $PM_{2.5}$ and PM_{10} and all-cause EACs remained significant after adjustment for O_3 and SO_2. Notably, the ER of EACs for all-cause associated with per 10 $\mu g/m^3$ increase was 0.30% (95% CI: 0.03%, 0.58%) in PM_{10}, and 0.35% (95% CI: 0.01%, 0.70%) in $PM_{2.5}$ after adjusting O_3. Similarly, when we controlled for SO_2, we estimated an increase of 0.12% (95% CI: 0.02%, 0.25%) in PM_{10}, and 0.18% (95% CI: 0.01%, 0.35%) in $PM_{2.5}$. The estimates were invariant when the df of "calendar time" (6–8), and "$Temp_{03}$" (3–5) were altered (shown in Table S2).

Fig. 1 represents the city-specific and overall effects associated with each 10 $\mu g/m^3$ increase of different sized particles at lag_{01}. Significant associations existed for both $PM_{2.5}$ and PM_{10} with all-cause EACs in most of the cities in our study, while the effects on cardiovascular- and respiratory-related EACs were only significant in a few cities. However, we only observed statistically significant associations of PM_c with EACs in Guangzhou. The overall effects showed that PM_{10} and $PM_{2.5}$ were significantly associated with EACs from all-cause and respiratory diseases. For instance, we estimated an increase of 0.30% (95% CI: 0.03%, 0.57%) in all-cause EACs, 0.13% (95% CI: −0.07%, 0.33%) in cardiovascular-related EACs, and 0.46% (95% CI: 0.01%, 0.92%) in respiratory-related EACs for each 10 $\mu g/m^3$ increment in $PM_{2.5}$ at lag_{01}.

We found evidence of spatial heterogeneity in the associations between PM concentration and daily EACs across the cities (Table S3). For example, the association between PM pollution and all-cause EACs was significantly heterogeneous with an I^2 of 86.53% for PM_{10}, 91.22% for PM_c, and 83.76% for $PM_{2.5}$. In general, the two measures, Q-test and I^2, produced consistent estimates on the heterogeneity attributed to the between-cities variability.

Similar patterns of lagged effects on all-cause and cause-specific EACs were observed for different sized particles (Fig. 2). Almost all associations decreased from lag 0-day to 5-day in single day lagged associations. In single lag day pattern, we observed positive associations of PM_{10} and $PM_{2.5}$ with daily EACs, however, we do not find significant associations between EACs and PM_c at lag_0. In moving averaged lags, the effects increased gradually from lag_{01} to lag_{03} and the largest effects

Table 1
Description of observation days, daily emergency ambulance calls count, characteristics of cases, air pollution, and meteorological factors in the seven cities.

	Guangzhou	Zhengzhou	Xuchang	Luoyang	Jinan	Zhoushan	Beijing
Observation days	1501	992	1034	1082	1461	1826	1065
Population *10,000	1449.84	988.07	495.63	682.30	732.12	116.80	251.9
Characteristics of EACs cases							
All-cause EACs, Mean ± SD	390 ± 39	372 ± 49	65 ± 11	102 ± 14	247 ± 44	51 ± 12	38 ± 7
Cardiovascular-related EACs, Mean ± SD	38 ± 8	34 ± 7	6 ± 3	25 ± 6	59 ± 14	5 ± 3	10 ± 3
Respiratory-related EACs, Mean ± SD	26 ± 7	22 ± 7	1 ± 1	4 ± 2	17 ± 7	2 ± 2	3 ± 2
Age, mean ± SD	54.8 ± 24.0	44.0 ± 23.6	48.2 ± 21.8	50.0 ± 20.0	54.2 ± 23.6	50.5 ± 23.8	58.6 ± 22.2
Male, %	56.07	59.31	55.04	59.92	54.59	66.97	57.94
Air pollution, μg/m^3							
PM_{10}, mean ± SD	58.36 ± 27.86	119.71 ± 68.67	104.60 ± 64.62	120.70 ± 74.16	150.24 ± 75.63	45.19 ± 26.48	70.88 ± 55.16
PM_c, mean ± SD	21.03 ± 9.89	54.33 ± 37.94	42.62 ± 38.74	46.86 ± 43.24	69.31 ± 45.66	18.61 ± 12.16	17.85 ± 28.82
$PM_{2.5}$, mean ± SD	37.33 ± 20.36	65.38 ± 52.30	61.99 ± 50.66	73.84 ± 54.78	80.94 ± 50.77	26.59 ± 18.20	53.05 ± 49.04
SO_2, mean ± SD	12.43 ± 4.86	15.23 ± 9.50	16.66 ± 11.47	46.35 ± 36.83	46.14 ± 38.81	8.95 ± 6.64	5.67 ± 4.94
NO_2, mean ± SD	46.48 ± 19.28	47.45 ± 18.39	37.96 ± 16.29	44.45 ± 17.43	52.10 ± 22.57	19.64 ± 11.00	25.51 ± 17.10
O_3, mean ± SD	46.81 ± 25.91	70.10 ± 38.20	68.93 ± 34.56	59.59 ± 34.63	70.08 ± 43.05	75.00 ± 26.61	99.26 ± 61.40
Weather							
Temperature (°C), Mean ± SD	22.31 ± 6.14	17.25 ± 10.35	15.72 ± 9.98	15.35 ± 9.36	15.42 ± 10.13	17.38 ± 8.01	12.89 ± 11.54
Humidity (%), mean ± SD	79.74 ± 10.17	57.56 ± 18.97	69.80 ± 16.34	67.93 ± 18.55	55.96 ± 19.21	78.92 ± 12.85	56.16 ± 20.43

Abbreviation: SD, standard deviation; EACs, emergency ambulance calls.

were found at a 4-day moving average (lag_{03}), while most of them were not statistically significant.

The estimated effects varied by age, gender, and season (Table 3), but only the difference in the effects on all-cause and cardiovascular EACs is statistically significant between warm and cold seasons. Specifically, the associations between a 10 μg/m^3 increase at lag_{01} in PM pollution and all-cause and cardiovascular-related EACs appeared to be higher among males. The opposite pattern was observed in respiratory-related EACs. We estimated an increase of 0.21% (95% CI: 0.02%, 0.44%) in all-cause EACs, 0.15% (95% CI: −0.02%, 0.32%) in cardiovascular-related EACs, and 0.32% (95% CI: −0.03%, 0.68%) in respiratory-related EACs for each 10 μg/m^3 increase of PM_{10} among males, compared with 0.13% (95% CI: −0.05%, 0.31%), 0.10% (95% CI: −0.13%, 0.34%), and 0.46% (95% CI: 0.20%, 0.73%) among females. The effect estimates of PM pollution were higher among the elderly than the younger population in all-cause EACs, but the estimates reversed in cardiovascular- and respiratory-related EACs. The associations were slightly stronger in the warm season than in the cold season, except for the effects in all-cause and respiratory-related EACs for PM_c.

Table 4 shows AN and AF of EACs due to PM pollution across seven cities in different scenarios. For instance, based on the China's standard, we estimated that 0.27% (95% CI: 0.04%, 0.51%), 0.28% (95% CI: −0.09%, 0.66%), and 0.39% (95% CI: 0.03%, 0.76%) of all-cause EACs were attributable to PM_{10}, PM_c, and $PM_{2.5}$, respectively. These estimates corresponded to 4387 (95% CI: 665, 8223), 4520 (95% CI: −1429, 10,780), and 6389 (95% CI: 557, 12,397) all-cause EAC cases among seven cities. We observed different disease burdens among different particle size fractions of PM pollution, with the largest AF and AM caused by $PM_{2.5}$ in China.

4. Discussion

Numerous studies in the literature have reported associations between acute exposure to air pollutants with health effects (Liang et al., 2020; Liu et al., 2021), while only a few have directly focused on EACs as an appropriate outcome indicator. We included multicity data on air pollution and EACs across seven cities to assess the associations between EACs and particulate matter with different aerodynamic

Table 2
Excess risk and 95% confidence interval for each 10 μg/m^3 increment in different PM metrics at lag_{01} across the seven cities.

Pollutants	Models	Excess risk (95% confidence interval)		
		All-cause	Cardiovascular	Respiratory
PM_{10}	Single pollutant model	0.25 (0.04, 0.47)	0.13 (−0.01, 0.26)	0.35 (0.04, 0.66)
	Two-pollutant models			
	Control for O_3	0.30 (0.03, 0.58)	0.18 (−0.02, 0.38)	0.39 (−0.01, 0.80)
	Control for SO_2	0.12(0.02, 0.25)	0.05 (−0.06, 0.17)	0.30 (0.01, 0.60)
	Control for NO_2	0.06 (−0.05, 0.16)	0.01 (−0.11, 0.12)	0.25 (0.00, 0.50)
PM_c	Single pollutant model	0.48 (−0.16, 1.12)	0.25 (−0.28, 0.79)	0.26 (−0.06, 0.57)
	Two-pollutant models			
	Control for O_3	0.58 (−0.18, 1.34)	0.32 (−0.35, 0.99)	0.34 (−0.04, 0.72)
	Control for SO_2	0.27 (−0.02, 0.56)	0.12 (−0.19, 0.43)	0.22 (−0.1, 0.55)
	Control for NO_2	0.14 (−0.03, 0.32)	0.08 (−0.22, 0.39)	0.17 (−0.15, 0.50)
$PM_{2.5}$	Single pollutant model	0.30 (0.03, 0.57)	0.13 (−0.07, 0.33)	0.46 (0.01, 0.92)
	Two-pollutant models			
	Control for O_3	0.35 (0.01, 0.70)	0.17 (−0.06, 0.41)	0.52 (−0.05, 1.09)
	Control for SO_2	0.18 (0.01, 0.35)	0.03 (−0.14, 0.20)	0.44 (−0.10, 0.97)
	Control for NO_2	0.01 (−0.15, 0.18)	−0.07 (−0.26, 0.12)	0.31 (−0.01, 0.64)

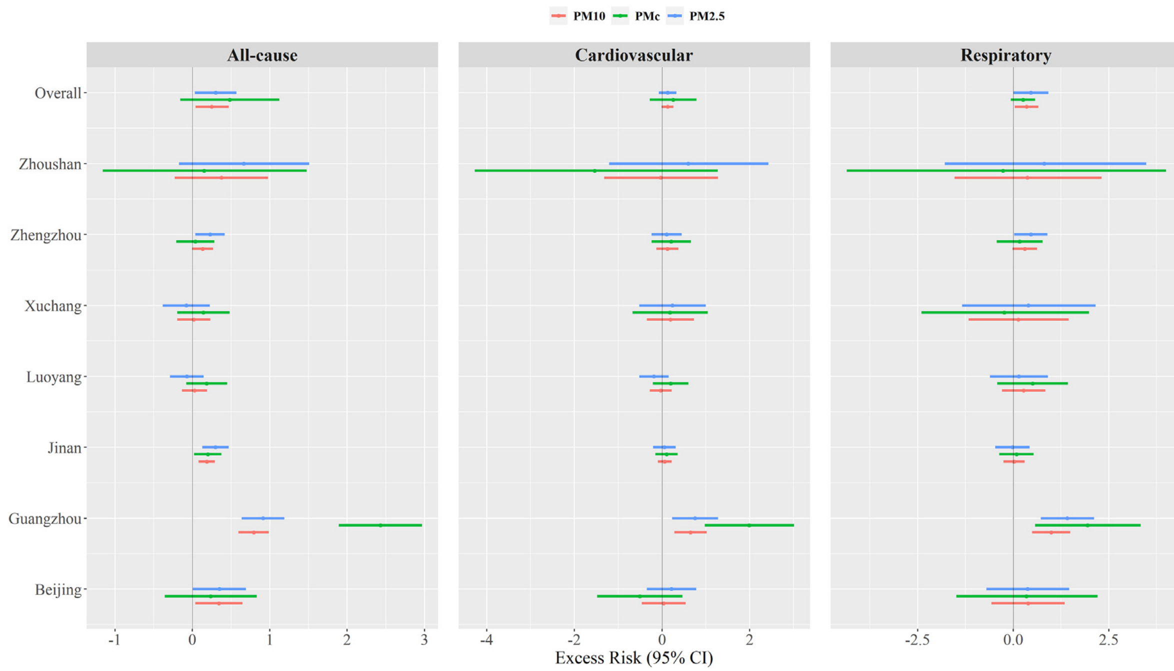

Fig. 1. City-specific and overall excess risk (and 95% confidence interval) of emergency ambulance calls for each 10 μg/m^3 increment in particulate matter concentrations at lag_{01}.

diameters in China. To our knowledge, this study is the first multicity analysis to examine those associations in China.

4.1. City-specific health effects of particulate air pollution

We identified stronger associations of PM exposures with EACs in municipality/provincial capital cities than in other cities. A possible explanation is that people in municipality/provincial capital cities tend to spend longer periods of time outdoors (Guo et al., 2010). In addition, the PM-EACs associations exhibited geographic heterogeneity. We found significant evidence of spatial heterogeneity in associations between PM and daily EACs across cities. As shown in Fig. 1, the estimates in some cities (Zhoushan, Xuchang, and Luoyang) were positive but not statistically significant. Several factors could contribute to this variability, including the different of PM compositions and gas mixtures, which vary according to the transportation and industrial activities in

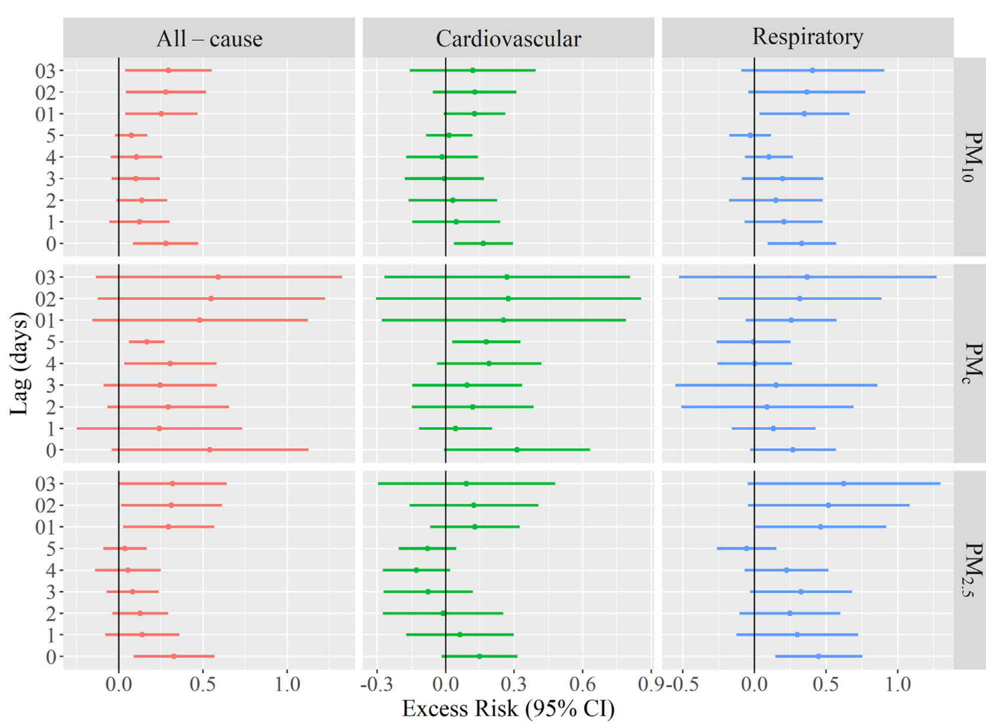

Fig. 2. Excess risk (and 95% confidence interval) of emergency ambulance calls due to all-cause, cardiovascular, and respiratory disease for each 10 μg/m^3 increment in particulate matter pollution with different lag days.

Table 3
Excess risks and 95% confidence interval of emergency ambulance calls for each 10 μg/m^3 increment in PM_{10}, PM_c, and $PM_{2.5}$ at lag_{01}, stratified by gender, age, and season.

Pollutants	Stratum	All-cause	Cardiovascular	Respiratory
PM_{10}	Gender			
	Male	0.21 (0.02, 0.44)	0.15 (−0.02, 0.32)	0.32 (−0.03, 0.68)
	Female	0.13 (−0.05, 0.31)	0.10 (−0.13, 0.34)	0.46 (0.20, 0.73)
	Age			
	<65	0.19 (−0.09, 0.47)	0.09 (−0.06, 0.24)	0.29 (0.02, 0.56)
	≥65	0.15 (−0.05, 0.35)	0.16 (−0.03, 0.36)	0.50 (0.04, 0.96)
	Season			
	Warm	0.27 (0.11, 0.43)	**0.35 (0.14, 0.57)**	0.34 (−0.04, 0.71)
	Cold	0.19 (−0.06, 0.44)	**0.05 (−0.09, 0.18)**	0.30 (0.01, 0.59)
PM_c	Gender			
	Male	0.36 (−0.17, 0.89)	0.18 (−0.10, 0.46)	0.06 (−0.37, 0.48)
	Female	0.29 (−0.08, 0.66)	0.06 (−0.18, 0.31)	0.53 (0.07, 0.98)
	Age			
	<65	0.55 (−0.26, 1.37)	0.32 (−0.37, 1.01)	0.34 (−0.13, 0.82)
	≥65	−0.02 (−0.08, 0.66)	0.14 (−0.13, 0.41)	0.27 (−0.22, 0.77)
	Season			
	Warm	0.18 (−0.11, 0.47)	0.32 (−0.02, 0.67)	0.42 (−0.14, 0.99)
	Cold	0.50 (−0.05, 1.06)	0.14 (−0.08, 0.36)	0.62 (−0.14, 1.38)
$PM_{2.5}$	Gender			
	Male	0.26 (−0.09, 0.61)	0.23 (−0.10, 0.56)	0.56 (−0.02, 1.14)
	Female	0.08 (−0.19, 0.36)	0.12 (−0.11, 0.36)	0.62 (0.23, 1.00)
	Age			
	<65	0.25 (−0.03, 0.53)	0.10 (−0.12, 0.33)	0.21 (−0.42, 0.83)
	≥65	0.16 (−0.19, 0.51)	0.24 (−0.06, 0.55)	0.75 (0.15, 1.35)
	Season			
	Warm	**0.70 (0.42, 0.97)**	**0.77 (0.28, 1.27)**	0.75 (−0.13, 1.64)
	Cold	**0.20 (−0.14, 0.54)**	**−0.01 (−0.19, 0.17)**	0.32 (−0.09, 0.73)

The bold type represents the statistically significant differences ($p < 0.05$).
The warm season: April to September and the cold season: October to March.

each city; and the differences in susceptibility to pollutant concentrations, which vary according to the genetic makeup and environmental factors in a particular location (Liu et al., 2017a).

The observed significant associations are similar to those found in previous studies (Michikawa et al., 2015a; Phung et al., 2018). For example, Michikawa's study indicated that $PM_{2.5}$ was associated with EACs in general (OR = 1.008, 95% CI: 1.002, 1.014) and respiratory-related EACs (OR = 1.027, 95% CI: 1.007, 1.048) at lag_{01}, and no significant association was observed for EACs due to cardiovascular diseases (Michikawa et al., 2015a). Another multicity study in Japan also found that $PM_{2.5}$ was significant associated with EACs due to all-cause and respiratory disease; however, no significant effect existed for cardiovascular-related EACs (Phung et al., 2018). Several mechanisms have been used to explain the associations. PM pollution exposure might cause lung and systemic inflammatory cell infiltration, increased lung and cardiac oxidative stress (Yue et al., 2019), reduced oxygen saturation (DeMeo et al., 2004), blood pressure changes (Yang et al., 2018), and decreases in heart rate variability (Jia et al., 2018).

4.2. Sensitivity analysis with two-pollutant models

In our study, after adjusting for O_3, the associations for PM_{10} and $PM_{2.5}$ remained positive and significant in all-cause EACs, while they became nonsignificant in cause-specific EACs. It is notable that the PM_{10}-EACs and $PM_{2.5}$-EACs associations slightly decreased after adjusting for $SO_2$and magnitude decreased after controlling for NO_2; and all associations become nonsignificant except in $PM_{10} + SO_2$ models for all-cause and respiratory-related EACs, and $PM_{2.5} + SO_2$ models for all-cause EACs. It was hard to examine the potential independent effects of each air pollution due to their close correlations. Our findings may be explained as a reflection of closer correlations of PM pollution with NO_2 caused by similar sources and seasonal patterns (Liu et al., 2019).

4.3. Overall effects of particulate matter exposure across seven cities

The overall estimates of associations between PM pollution and EACs with per 10 μg/m^3 increase were smaller compared to results

Table 4
The attributable numbers and fractions and 95% confidence interval of emergency ambulance calls due to exceeding PM_{10}, PM_c, and $PM_{2.5}$ at lag_{01} using WHO and China air quality standard.

Pollutants	Disease	Attributable fraction (%)		Attributable number	
		China's standard	WHO guideline	China's standard	WHO guideline
PM_{10}	All-cause	0.27 (0.04, 0.51)	1.18 (0.18, 2.21)	4387 (665, 8223)	19,165 (2905, 35,907)
	Cardiovascular	0.17 (−0.01, 0.36)	0.43 (−0.03, 0.90)	393 (−29, 823)	985 (−73, 2064)
	Respiratory	0.30 (0.03, 0.59)	1.62 (0.16, 3.14)	293 (29, 569)	1563 (155, 3034)
PM_c	All-cause	0.28 (−0.09, 0.66)	0.89 (−0.28, 2.13)	4520 (−1429, 10,780)	14,578 (−4612, 34,600)
	Cardiovascular	0.19 (−0.21, 0.61)	0.38 (−0.41, 1.21)	443 (−480, 1405)	877 (−954, 2779)
	Respiratory	0.16 (−0.04, 0.35)	0.48 (−0.11, 1.09)	151 (−36, 342)	462 (−110, 1047)
$PM_{2.5}$	All-cause	0.39 (0.03, 0.76)	0.87 (0.08, 1.69)	6389 (557, 12,397)	14,187 (1239, 27,481)
	Cardiovascular	0.21 (−0.11, 0.53)	0.30 (−0.16, 0.77)	478 (−254, 1227)	695 (−370, 1781)
	Respiratory	0.59 (0.01, 1.19)	1.31 (0.02, 2.66)	565 (9, 1151)	1262 (19, 2562)

The reference of PM_{10}, PM_c, and $PM_{2.5}$ concentration was based on the World Health Organization's Ambient Air Quality guidelines (50 μg/m^3, 25 μg/m^3, and 25 μg/m^3) and China's standard (150 μg/m^3, 75 μg/m^3, and 75 μg/m^3).

from other countries. A Japanese study reported a 0.64% increase for all-cause EACs and a 1.88% increase for respiratory-related EACs in eight cities (Phung et al., 2018). Another multicity study in Australia found that cardiovascular-related EACs increased with each 10 μg/m^3 increment of PM_{10} and $PM_{2.5}$ by 1.7% and 6.1%, respectively (Neuberger et al., 2013). The slightly weaker effects may be attributable to differences in particles components, lifestyles, and environmental exposures in China (Bell et al., 2013). Moreover, previous studies (Lee et al., 2015; Liu et al., 2019) have found that the observed dose-response curves seemed to flatten at high concentrations. China has relatively higher concentrations of air pollutants compared with the developed countries, and this may be the reason for our lower estimates.

We found that both PM_{10} and $PM_{2.5}$ were significantly associated with increasing EACs, while we did not find significant associations between PM_c and EACs, which suggested that particles with smaller size fraction are more harmful to human health. Probable reasons for this are as follows. Compared with PM_c, $PM_{2.5}$ has a larger surface area per unit mass, which allows them to carry a higher amount of toxic substances, including transition metals and oxidant gaseous pollutants. These substances would cause lung inflammation, vascular remodeling, atherosclerosis, and fibrosis (Lin et al., 2016b). Another reason is that the particle size of PM_c is larger than $PM_{2.5}$, which makes PM_c unable to penetrate, deposit and cause inflammation in the alveolus like $PM_{2.5}$ (Lippmann and Chen, 2009).

4.4. Subgroup analysis by age, sex, and season

Although not reaching statistical significance, we observed a higher risk of EACs for all-cause and cardiovascular diseases among males compared with females (except females had a slightly higher risk of respiratory-related EACs). This discrepancy might be attributed to differences in the biological and behavioral factors between females and males, such as physiological responses to the pollutants and differential time-activity patterns. Furthermore, we investigated a larger effect of PM_{10} and $PM_{2.5}$ on all-cause EACs among older people than younger ones. However, the opposite relationship was observed on cause-specific EACs.

Consistent with recent studies (Ai et al., 2019; Wang et al., 2020), the observed associations between PM and EACs were stronger during the warm season, and the difference of $PM_{2.5}$ on EACs for all-cause and cardiovascular diseases were significant between season-stratified subgroups. Such a difference could partly be explained as follows. High temperatures can increase the metabolic rates of humans, thus increasing the speed of the cycle of PM pollution in the body (Carder et al., 2008); marginally more people were exposed to pollution outdoors in the warm season compared to the cold season (Li et al., 2017).

3.5. Estimating attributable burden to particulate matter pollution

Another important finding was the attributable burden of EACs due to PM pollution. Our study indicated a moderate number of all-cause and cause-specific EACs could be avoided by attaining China's air quality standard, and substantial EACs could have been avoided if the WHO guidelines were adopted. The findings reported here shed light on the strict and effective air quality standards are warranted to shield the health of the local residents. Besides, we found different attributable burdens among different particle size fractions of PM pollution, with the largest AN and AF caused by $PM_{2.5}$ according to China's air quality standard. The insights gained from this study may optimize the policy considerations in environmental protection and public health interventions.

4.5. Strengths and limitations

There are several strengths of our study. First, we used EACs as a health indicator, which may better reflect the short-term effects of air pollution. Second, this is the first multicity study examining the acute effects of PM exposure on EACs in China. Furthermore, this study assessed the effects of particulate matter with different aerodynamic diameters on EACs.

At the same time, our study has several limitations. First, we used fixed-site environmental measurements to reflect personal exposure, which could lead to exposure misclassification. Second, the onsite diagnoses conducted by emergency physicians might not be completely accurate and absolutely consistent in various hospitals. However, considering that our study only analyzed cardiovascular and respiratory diseases, which are both common, the misclassification bias should be minimal. Third, some potential confounders, including built environment and behavioral patterns, were not controlled in the data analyses due to the unavailability of relevant individual data. Fourth, although our study was able to find PM-EACs associations in seven cities of China, these do not necessarily represent the overall situation for China. Therefore, further large-scale studies are necessary to confirm our findings. Fifth, there are a lot of outpatients and emergency room visits in the clinic and hospitals in Chinese cities every day, which could reduce the related EACs there. Careful attention should be paid to interpret the results and further research is needed. Finally, only two districts were used to represent Beijing in our analysis, which may lead to biased results. More studies with a larger sample size are needed to provide a more representative statistical analysis.

4. Conclusions

Both PM_{10} and $PM_{2.5}$ were associated with all-cause, respiratory-related, and cardiovascular-related EACs. Associations of EACs with both PM_{10} and $PM_{2.5}$ were stronger in the warm season. To reduce the demand for emergency ambulance services, further policies development for controlling air pollution are warranted in China.

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CRediT authorship contribution statement

Xiaojie Wang: Formal analysis, Writing - original draft, Writing - review & editing. **Meifang Leng**: Formal analysis, Writing - original draft, Writing - review & editing. **Yixuan Liu**: Investigation, Visualization, Writing - review & editing. **Zhengmin (Min) Qian**: Writing - review & editing. **Junguo Zhang**: Writing - review & editing. **Ziyi Li**: Writing - review & editing. **Liwen Sun**: Acquisition of data, Writing -review & editing. **Lijie Qin**: Acquisition of data, Writing -review & editing. **Chongjian Wang:** Acquisition of data, Writing -review & editing. **Steven W. Howard**: Writing - review & editing. **Michael G. Vaughn**: Writing - review & editing. **Yue Yan:** Acquisition of data, Writing -review & editing. **Hualiang Lin**: Conceptualization, Formal analysis, Writing - original draft, Writing -review & editing.

Declaration of competing interest

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.

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