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Short-term PM_1 and $PM_{2.5}$ exposure and asthma mortality in Jiangsu Province, China: What's the role of neighborhood characteristics?

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ABSTRACT

Background: Evidence suggests that particulate matter (PM) with smaller particle sizes (such as PM_1, PM with an aerodynamic diameter≤1 μm) may have more toxic health effects. However, the short-term association between PM_1 and asthma mortality remains largely unknown.

Objective: This study aimed to examine the short-term effects of PM_1 and $PM_{2.5}$ on asthma mortality, as well as to investigate how neighborhood characteristics modified this association.

Methods: Daily data on asthma mortality were collected from 13 cities in Jiangsu Province, China, between 2016 and 2017. A time-stratified case-crossover design was attempted to examine the short-term effects of PM_1 and $PM_{2.5}$ on asthma mortality. Individual exposure levels of PM_1 and $PM_{2.5}$ on case and control days were determined based on individual's residential addresses. Stratified analyses by neighborhood characteristics (including green space, tree canopy, blue space, population density, nighttime light and street connectivity) were conducted to identify vulnerable living environments.

Results: Mean daily concentrations of PM_1 and $PM_{2.5}$ on case days were 33.8 μg/m^3 and 54.3 μg/m^3. Each 10 μg/m^3 increase in three-day-averaged (lag02) PM_1 and $PM_{2.5}$ concentrations were associated with an increase of 6.66% (95%CI:1.18%,12.44%) and 2.39% (95%CI: 0.05%–4.78%) asthma mortality, respectively. Concentration-response curves showed a consistent increase in daily asthma mortality with increasing PM_1 and $PM_{2.5}$ concentrations. Subgroup analyses indicated that the effect of PM_1 appeared to be evident in neighborhood characteristics with high green space, low urbanization level and poor street connectivity.

Conclusion: This study suggested an association between short-term PM_1 and $PM_{2.5}$ exposures and asthma mortality. Several neighborhood characteristics (such as green space and physical supportive environment) that could modify the effect of PM_1 on asthma mortality should be further explored.

1. Introduction

Asthma is a major public health problem that affects approximately 300 million people of all ages worldwide (Busse et al., 2020). Accounting for 0.82% of total deaths worldwide, 460,000 asthma deaths were reported in 2019, as suggested from the Global Burden of Disease Study 2019 (GBD, 2019 Risk Factors Collaborators 2020). Therefore, novel and comprehensive preventive measures are urgently required. While asthma is influenced by multiple factors, there is growing evidence that the living environment may have a considerable impact, such

Abbreviations: PM, particulate matter; PM_1, PM with an aerodynamic diameter≤ 1 μm; $PM_{2.5}$, PM with an aerodynamic diameter≤ 2.5 μm; STET, space-time extremely randomized trees; NDVI, Normalized Derived Vegetation Index; NTL, nighttime light; MT, mean temperature; RH, relative humidity; SO_2, sulfur dioxide;; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone;; BIC, Bayesian Information Criterion.

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as air pollution, which poses a major threat to global public health.

On September 22, 2021, WHO published its latest "Global Air Quality Guidelines", which further raised the standard for $PM_{2.5}$ (PM with diameters ≤2.5 μm) (namely, from 10 μg/m^3 to 5 μg/m^3), highlighting the serious risk to human health from PM exposure. As the most significant air pollutant, PM is the fourth leading global risk factor for mortality and contributes significantly to the burden of disease, especially in developing countries (like China) (GBD, 2019 Risk Factors Collaborators 2020; Bu et al., 2021; Yang et al., 2020).

Particle size is considered to be one of the key determinants in terms of the health effects of PM (Kim et al., 2015; Tian et al., 2020). However, most existing studies have focused mainly on $PM_{2.5}$ or PM_{10} (PM with diameters ≤10 μm). More recently, PM_1 (PM with diameters ≤1 μm) has attracted increasing research attention as it is the major component of $PM_{2.5}$ (accounting for more than 50%) and is considered particularly harmful because of its smaller particle size, greater abundance of harmful substances and more widespread lung deposition, as confirmed by toxicological evidence (Guak et al., 2017; Zou et al., 2017). Furthermore, a number of epidemiological studies, albeit small in number (as PM_1 is not a routinely monitored pollutant over a wide area), have reported the potential for PM_1 to act as a major contributor to the harmful effects of $PM_{2.5}$, with more significant harmful effects on health (for example, on all-cause mortality, emergency department visits, hospitalizations of ischemic stroke and pneumonia) (Chen et al., 2017, 2020; Hu et al., 2018; Lin et al., 2016; Liu et al., 2021; Wang et al., 2021a, 2021b). However, the limited evidence linking asthma mortality to PM_1 has largely hindered insights into PM-related asthma effects. To our knowledge, only one study (Zhu et al., 2021) was conducted, and this was a single-city design with only 1 PM_1 monitoring station and small sample size (129 asthma deaths). Thus, the results should be further validated. Multi-city data and individual-level exposure measurements of PM_1 are greatly required, and their applications could reduce exposure misclassification and improve statistical power.

Understanding whether and how neighborhood characteristics can alter the short-term impact of PM_1 on asthma mortality is also essential, as urban planners need epidemiological evidence to design cities to maximize health benefits and people with asthma need to better manage themselves. Especially, residential greenness has attracted increasing attention as more and more evidence hints at its health benefits (Rojas-Rueda et al., 2019; Dong et al., 2021; Zeng et al., 2020). However, the role of greenness in allergies and respiratory diseases such as asthma is complex, probably because of the complex role played by air pollution (Fuertes et al., 2021). On the one hand, air pollution levels tend to be lower in areas with high greenness. On the other hand, air pollutants may interact with inhale allergens (like pollen) to influence the association with asthma. A recent study in China even found that in areas with high levels of PM_1 (>55 μg/m^3), children attending schools surrounded by more greenness had poorer lung function compared with those with less greenness (Zhou et al., 2021). Therefore, the question of whether living in a highly green neighborhood exacerbates or mitigates the short-term effects of PM on mortality in asthmatic patients is worth exploring.

The objectives of this study were to (1) quantify the effects of PM_1 and $PM_{2.5}$ on asthma mortality in 13 Chinese cities, and (2) verify whether and how the PM_1-asthma mortality association could be modified by neighborhood characteristics including green space, blue space, population density, nighttime light and street connectivity.

2. Methods

2.1. Study area and population

Jiangsu province is located in the Yangtze River Delta and has 80.29 million population living in 13 cities in 2017. It is recognized as one of the most densely populated (population density: 749 persons/km^2) and developed provinces in China. The basic characteristics for each city are listed in Table S1. In the present study, all the cities included have the death data between 2016 and 2017, except for Huai'an with the data only in 2016. This study was approved by the Ethical Committee of Anhui Medical University.

2.2. Study design

Short-term effects of PM_1 and $PM_{2.5}$ on asthma mortality were evaluated based on a time-stratified case-crossover design, which has been extensively employed in environmental epidemiological research (Liu et al., 2019; Xu al., 2019). In this study, this design compared the PM exposure concentrations of the identical person on the case day (i.e., the day of death) and on the control days (i.e., the same days of the week in the same year and month). For instance, an asthma death occurred on Wednesday, May 17, 2017, and then all other Wednesdays in May, 2017 were selected as control days (i.e., May 3, May 10, May 24 and May 31). Thus, the confounders of time-invariant (e.g., ages, genders and educational levels) and time-dependent (e.g., seasonality, long-term trends and days of the week) could be automatically controlled (Carracedo-Martínez et al., 2010).

2.3. Outcome

Daily death data on asthma in all cities of Jiangsu province during the study period were obtained from Death Registration System in Jiangsu Provincial Center for Diseases Prevention and Control. For individuals that died from asthma (international Classification of diseases, ICD-10 codes: J45, J46) as the underlying cause, the information regarding their date of death, date of birth, residential address, and gender was acquired. Fig. 1 displayed the spatial distribution of the cases.

2.4. Exposure evaluation

Daily exposures to PM_1 and $PM_{2.5}$ at the individual level were determined based on their residential addresses. The processed spatial daily time-series data (spatial resolution: 1 km * 1 km) were derived from a high-resolution and high-quality dataset of ground-level air pollutants in China (CHAP, available at https://weijing-rs.github.io/product.html). The ChinaHighPM_1 and ChinaHigh$PM_{2.5}$ data were generated using our space-time extremely randomized trees (STET) model with multiple input variables, including CAWNET and MEE PM_1 and $PM_{2.5}$ observations, satellite MODIS MAIAC AOD products, MEIC emission inventories, land use information, road networks, topographic characteristics, and nighttime light (Wei et al., 2019, 2020, 2021). Table S2 summarized the data sources used for PM_1 estimation. A STET model was developed to estimate PM_1 levels, which considers the spatial autocorrelation and has a high computational efficiency and good training capability. Briefly, the STET model strongly enhances randomness in both attribute and cut-point selection when partitioning the tree nodes. More important variables from all of them (Table S2) were selected to build the final PM_1 estimation model, which has the best overall accuracy. Finally, the PM_1 predictions were reliable, with high cross-validation R^2 values of 0.74–0.77, showing a small mean absolute error of 5.9–8.7 μg/m^3 and a root-mean-square error of 9.5–14.5 μg/m^3 on a daily basis. A detailed description of the PM_1 estimates could be found in Wei et al. (2019).

2.5. Neighborhood characteristics measurement

Table S3 listed the neighborhood characteristics included in this study. These features were selected based on a review of the available literature and data availability. Based on the latitude and longitude of the residential address conversion, the following individual-level neighborhood characteristics for each subject were extracted.

(1) Green and blue space: In order to reflect the greenness of a

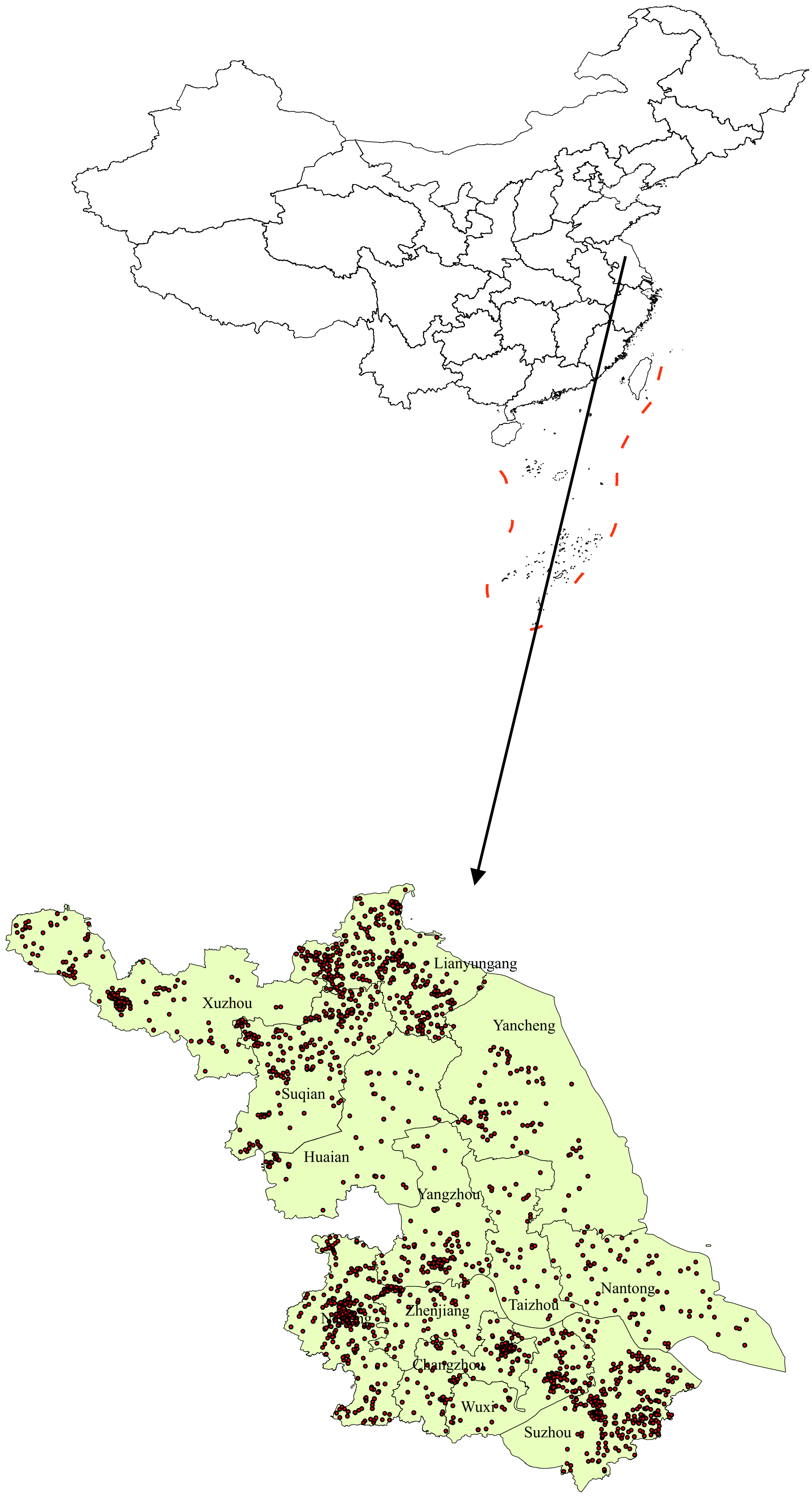

Fig. 1. Location of study area (Jiangsu province, China) and spatial distribution of the cases.

residence, the NDVI (Normalized Derived Vegetation Index) was used. NDVI values ranged from − 1 to 1, with higher values indicating higher greenness. The NDVI data were collected from the MODIS (Moderate-Resolution Imaging Spectroradiometer) database regularly released by NASA (National Aeronautics and Space Administration, https://modis.gsfc.nasa. gov/) at a spatial resolution of 250 m * 250 m, and a temporal resolution of 16 days. The 500 m buffer of NDVI was selected as the primary exposure range as it is almost equivalent to a 15-minute walk laps and has been used in previous studies applied (Zhou et al., 2021; Dong et al., 2021). NDVI averages for cloud-free images were calculated in spring and summer, the greenest period of the year, to reflect the average level of greenness exposure. In addition, the canopy cover, defined as the percentage of the surface covered by woody vegetation above 5 m, was measured. Canopy cover data (30 m resolution) was obtained from the University of Maryland Land-Cover/Land-Use Change Program (https://lcluc. umd.edu/metadata/ global-30-m-landsat-tree-canopy-version-4). For blue space, the distance to the nearest blue space from their home was calculated for each case by employing the Land use map of GlobeLand30 (http://www.global-landcover. com/).

(2) Nighttime light (NTL): As a direct representation of population density, economic growth, residents' income and socio-economic conditions, night light images can provide an objective and comprehensive picture of a city's level of urbanization. The DMSP/OLS nighttime light data in 2016/2017 used in our study were obtained from the NOAA NGDC (https://ngdc.noaa.gov/).

(3) Population density: It refers to the number of inhabitants per square kilometer around the residential address. The dataset format for China as Geotiff at a resolution of 1-km for 2016 and 2017 are available from WorldPop (https://www.world pop.org/ project).

(4) Street connectivity: This is an important neighborhood-built environment characteristic related to individual physical activity, based on available evidence (Jia et al., 2021; Leonardi et al., 2017), and was defined as the number of street intersections (at least three legs) within the buffer zone, divided by the (km^2) area of the buffer zone. Information on roads in the study area was obtained from Open-StreetMap (www. open streetmap.org/). Consistent with the buffer of NDVI here, a 500 m buffer of street connectivity was also selected as the primary exposure. Moreover, this selection has been extensively applied in existing studies (Timmermans et al., 2021; Hinckson et al., 2017).

2.6. Other variables

(1) Meteorological variables: Daily mean temperature (MT) and relative humidity (RH) for case days and control days were taken to adjust for the effect of meteorological variables in the statistical model. Data originated from the China Meteorological Data Sharing Service System (http://data.cma.cn).

(2) Air pollutants: The data of other main air pollutants were also collected, which comprised daily mean concentration of sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO) and daily maximum 8-h average concentration of ozone (O_3). All the information of the mentioned air pollutants was acquired from the National Air Pollution Monitoring System.

2.7. Statistical analysis

Spearman correlation analysis was conducted to assess the correlation between PM and various air pollutants. Conditional logistic regression models were adopted to analyze the effect of short-term PM_1 and $PM_{2.5}$ exposures on asthma mortality, including several steps. (1) Linear or non-linear model: The first step was to assess any potential non-linearity in the exposure-response association. Exposure to PM was included in the model as a natural cubic spline function (3 degrees of freedom (df)) and a linear function, respectively. According to existing studies (Xu et al., 2019; Buckland et al., 1997), lower values of the Bayesian Information Criterion (BIC) indicate better model performance. On the basis of the results of this study, the linear model had lower BIC values for both PM_1 and $PM_{2.5}$, which demonstrated that the correlation between the short-term exposure of PM_1 and $PM_{2.5}$ on asthma mortality tended to be linear. Therefore, PM was included as a linear function in the final model. (2) Lag structure of PM: The single-day lag model (from the current day (lag 0) to the previous 5 days (lag 5)) and the moving-average lag model (lag 01, lag 02, lag 03, lag 04, lag 05) were initially used. For instance, the 1-day moving average of exposure was defined as lag01, which suggested the average of daily exposures on the day of death and the previous day. The maximum lag day of PM was set at 5 days, as existing studies (Liu et al., 2019; Hu et al., 2018; Lin et al., 2016) had observed a significant effect of short-term PM_1 and $PM_{2.5}$ exposures on mortality during lags of 0–5 days. Likewise, the lag period that produced the lowest BIC value, indicating the best model fit, was then used in the main analyses. (3) Covariates: Daily mean temperature (MT), relative humidity (RH) and public holidays were controlled for in the main model. Following previous studies, the daily MT and RH were adjusted using the natural cubic spline functions (df=6 and 3, respectively), while public holidays were adjusted as the binary variable (1 =public holidays, 0 =non-public holidays) in all models. In addition, the lagged effect of temperature was considered by using lag 0–21(Vicedo-Cabrera et al., 2020; Gasparrini et al., 2015). The percentage changes ((odds ratio-1) * 100%) were reported in daily asthma mortality per 10 $\mu g/m^3$ increase in PM_1 and $PM_{2.5}$ concentrations.

Subsequently, several stratified analyses were conducted for age group (<65 years, ≥65 years), gender (male, female), season (warm season: May-October, and cool season: November-April), as well as the neighborhood characteristics (that is, high (above median) and low (below median) group), including NDVI, tree canopy, blue space, NTL, population density and street connectivity. Next, within-group differences were tested by 2-sample z-tests (Altman et al., 2003).

In order to verify the robustness of the results of this study, a sensitivity analysis was conducted as follows. (1) Two-pollutant models: to avoid model collinearity, pollutants with PM correlation coefficients below 0.5 were included in the two-pollutant model. (2) The df of MT and RH were changed. (3) In addition to MT and RH, the rainfall was also adjusted in our model.

All statistical analyses were performed by using R software (version 3.6.3, R Foundation for Statistical Computing, Vienna, Austria). P-value< 0.05 was considered to be statistically different.

3. Results

3.1. Data description

A total of 2519 asthma deaths (1335 males and 1164 females), and 8543 controls were recruited. The mean age of the cases was 79.22 years or older. There were 1448 (57.5%) and 1071(42.5%) deaths from asthma in the cool and warm seasons, respectively (Table S4). Data on air pollutants and meteorological conditions on case and control days were presented in Table 1. The daily mean concentrations of $PM_{2.5}$ and PM_1 on case days were 54.3 $\mu g/m^3$ and 33.8 $\mu g/m^3$, respectively. As indicated from the spearman correlation analysis, a strong correlation was observed between PM_1 and $PM_{2.5}$ ($r = 0.97$, P-value<0.05) and they were both positively correlated with NO_2, SO_2 and CO with correlation coefficients ranging from 0.59 to 0.71. However, PM_1 and $PM_{2.5}$ were negatively and weakly correlated with O_3 ($r = -0.11$ and -0.08) (Fig. S1).

3.2. PM-asthma mortality associations

As shown in Fig. 2, exposures to PM_1 (lag 2, lag 02, lag 03) and $PM_{2.5}$ (lag 02) were significantly associated with asthma mortality. Based on the corresponding BIC values, a 3-day moving average of PM_1 exposures

Table 1
Characteristics of air pollutants and meteorological conditions.

	Mean (SD)	Percentile				
On case days (n = 2519)		5th	25th	50th	75th	95th
PM_1 ($\mu g/m^3$)	33.8(15.1)	15.6	23.4	30.8	41.6	62.0
$PM_{2.5}$($\mu g/m^3$)	54.3(33.2)	16.0	29.0	46.1	71.4	118.1
SO_2($\mu g/m^3$)	20.6(11.6)	8.0	12.0	18.0	26.0	44.0
O_3($\mu g/m^3$)	100.0(45.0)	41.0	67.0	91.0	127.0	188.0
NO_2($\mu g/m^3$)	40.1(19.6)	15.0	26.0	37.0	51.0	78.0
CO($\mu g/m^3$)	1.0(0.4)	0.5	0.7	0.9	1.2	1.8
MT (°C)	15.0(9.8)	0.7	6.3	14.8	23.5	30.6
RH (%)	71.8(15.0)	45.0	61.0	73.0	83.0	95.0
On control days (n = 8543)						
PM_1 ($\mu g/m^3$)	33.2(14.8)	15.5	23.2	30.0	40.6	61.8
$PM_{2.5}$($\mu g/m^3$)	52.8(32.8)	16.0	29.0	44.9	68.5	116.0
SO_2($\mu g/m^3$)	20.4(11.6)	8.0	12.0	18.0	26.0	43.0
O_3($\mu g/m^3$)	99.6(43.3)	42.0	67.0	92.0	127.0	183.0
NO_2($\mu g/m^3$)	39.4(19.2)	14.0	25.0	36.0	50.0	75.0
CO($\mu g/m^3$)	1.0(0.4)	0.5	0.7	0.9	1.2	1.8
MT (°C)	14.9(9.6)	0.9	6.3	14.8	23.2	30.2
RH (%)	71.7(15.2)	45.0	61.0	73.0	84.0	94.2

SD: Standard Deviation; MT: mean temperature; RH: relative humidity; PM2.5: particulate matter with an aerodynamic diameter≤ 2.5 μm; PM1: particulate matter with an aerodynamic diameter≤ 1 μm; SO2: sulfur dioxide. CO: carbon monoxide; NO2: nitrogen dioxide; O3: ozone;
* 24-h average concentration for $PM_{2.5}$($\mu g/m^3$), PM_1($\mu g/m^3$), SO_2($\mu g/m^3$), NO_2($\mu g/m^3$), and CO ($\mu g/m^3$); maximum 8-h average concentration for O_3 ($\mu g/m^3$).

was used in the main analysis in this study. It was found that each 10 $\mu g/m^3$ increase in 3-day moving average (lag02) PM_1 and $PM_{2.5}$ concentrations displayed a correlation with the increase of 6.66% (95%CI: 1.18%, 12.44%) and 2.39% (95%CI: 0.05%,4.78%) asthma mortality, respectively. Fig. S2 presented the exposure-response correlations of short-term exposure to $PM_{2.5}$ and PM_1 with asthma mortality. The PM_1-asthma correlations showed a linear and positive slope correlation with increasing concentrations. As shown in Table 2, the effect of PM_1 on asthma mortality was significant in females (95%CI: 8.01%, 0.02%,17.2%), in the cool season (7.65%, 95%CI: 1.31%,14.92%), and in the elderly population (6.59%, 95% CI: 0.80%,12.67%).

3.3. *Modification effects of neighborhood characteristics*

Among neighborhood features (Table 2), when grouped by the NTL levels, a significant effect of short-term PM_1 exposure was found for asthma patients living in neighborhoods with low NTL (10.46%, 95%CI: 2.02%,18.36%). However, those who living in surrounding high NTL levels were not affected by PM_1 exposure (3.04%, 95%CI: −4.89%,11.56%). Similarly, significant effects were seen in neighborhoods with low population density (6.16%, 95%CI:0.09%,12.22%), whereas nonsignificant effects were observed in neighborhoods with high population density (6.16%, 95%CI: −1.59%,14.5%). In terms of green space, the short-term effect of PM_1 on asthma mortality was found to be significant for residents living in high NDVI (9.25%, 95%CI: 1.57%,17.50%) and tree canopy (9.37%, 95%CI: 1.71%,18.01%) areas, but not in low areas. Besides, asthmatics living in neighborhoods with low street connectivity (9.92%, 95%CI: 2.12%, 18.21%) might be affected by acute PM_1 exposure, while asthmatics living in environments with good street connectivity (3.04%, 95%CI: −4.89%,11.34%) would not be affected.

3.4. *Sensitivity analyses*

The results of the sensitivity analysis confirmed the robustness of the findings of this study (Fig. S3). For instance, after adjusted for rainfall, each 10 $\mu g/m^3$ increase in 3-day moving average (lag02) PM_1 displayed a correlation with increases of 6.67% (95%CI:1.18%,12.45%) and 2.39% (95%CI: 0.04%,4.78%). The estimates were also not significantly different in the two-pollutant model ($P > 0.05$).

4. Discussion

To the best of the authors' knowledge, this study conducted the first comprehensive analysis of short-term PM_1 exposure and asthma mortality by using multi-city data and individual-level exposure measures. It was found that short-term exposure to PM_1 and $PM_{2.5}$ was associated with an increased risk of asthma mortality in China, with a greater effect of PM_1, emphasizing the importance of giving more attention to PM_1. Furthermore, the fitted correlations tended to be linear, suggesting that asthma mortality could be influenced by PM_1 even at low concentrations. Moreover, the effect of PM_1 on asthma mortality observed in this study appeared to be evident in neighborhoods with low levels of urbanization, more green space, and poor physical supportive environments, which should be noted.

Consistent with the results of the present study, a study (Liu et al., 2019) in Hubei province, China also observed a significant correlation between $PM_{2.5}$ and asthma mortality, and their estimate estimates were close to the results of the present study. However, there are fewer studies on the short-term effects of PM_1 on asthma mortality. Given the high spatial and temporal variability of PM_1 exposure, this study employed individual exposure measurements by our satellite-derived methods (Wei et al., 2019), rather than city-level air pollution concentrations. Compared with other products (Chen et al., 2018; Zang et al., 2019), our product had a higher spatial resolution (namely 1 km), which is vital for assessing individual exposure information when studying

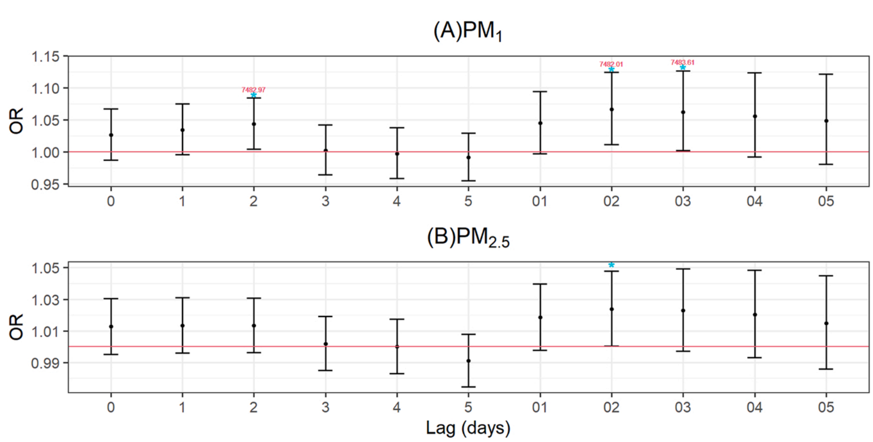

Fig. 2. Odds ratios (OR) with 95% CI for asthma mortality at different lag days, associated with per 10 $\mu g/m^3$ increase of (A)PM_1 and (B)$PM_{2.5}$ (*: $P < 0.05$; the numbers marked in read were the corresponding BIC values).

Table 2
Subgroup analysis of estimated percentage change in asthma mortality associated with a 10 μg/m^3 increase in PM_1, and $PM_{2.5}$ concentrations (lag02).

	PM_1		$PM_{2.5}$	
	Percent Change (95% CI)	P for difference	Percent Change (95% CI)	P for difference
Overall	6.66 (1.18–12.44)	–	2.39 (0.05–4.78)	–
Gender				
Male	5.72(−1.71,13.73)	–	2.56(−0.67,5.89)	–
Female	8.01(0.02,17.2)	0.697	2.30(−1.09,5.85)	0.915
Age				
< 65	10.11(−6.64,29.89)	–	5.60(−1.73,13.45)	–
≥ 65	6.59(0.80,12.67)	0.723	2.22(−0.30,5.11)	0.401
Season				
Warm	6.27(−6.22,20.47)	–	2.02(−4.03,8.40)	–
Cool	7.65(1.31,14.92)	0.856	2.84(0.20,5.11)	0.813
NDVI				
Low	4.01(−3.68,12.31)	–	1.57(−1.80,5.06)	–
High	9.25(1.57,17.50)	0.363	3.18(−0.05,6.53)	0.507
Tree canopy				
Low	3.04(−4.12,11.45)	–	1.31(−1.98,4.07)	–
High	9.37(1.71,18.01)	0.269	3.25(−0.10,6.69)	0.455
Blue Space				
Low	4.07(−3.93,12.67)	-	1.51(−1.88,5.01)	-
High	9.37(1.00,17.2)	0.372	3.04(−1.00,6.16)	0.550
Night light				
Low	10.46(2.02,18.36)	–	3.04(0.01,7.22)	–
High	3.04(−4.89,11.56)	0.211	1.00(−1.98,5.11)	0.425
Population density				
Low	6.16(0.09,12.22)	–	2.02(−0.01,4.73)	–
High	6.16(−1.59,14.5)	0.999	2.02(−1.98,5.74)	0.999
Street connectivity				
Low	9.92(2.12,18.21)	–	3.04(−1,60.160)	–
High	3.04(−4.89,11.34)	0.239	1.00(−1.98,1.92)	0.328

PM2.5: particulate matter with an aerodynamic diameter≤ 2.5 μm; PM1: particulate matter with an aerodynamic diameter≤ 1 μm; NDVI: normalized difference vegetation index.

PM_1-associated health effects. At the same time, the satellite-derived approach provided full-coverage PM_1 estimates, which could compensate for the sparsity and unevenness of ground-based air quality monitoring stations (Faridi et al., 2019). Based on our hypothesis that smaller sized PM would have a greater toxic effect on health, this study observed a greater effect of PM_1 than $PM_{2.5}$ on asthma. Similarly, in Zhejiang Province, China, PM_1 was indicated to exert a greater short-term effect on all-cause, stroke and COPD mortality than $PM_{2.5}$ and PM_{10} (Hu et al., 2018). In Guangzhou China, Lin and his colleagues reported that PM_1 contributed significantly to cardiovascular disease deaths associated with $PM_{2.5}$ (Lin et al., 2016). Each 10 μg/m^3 increase in PM_1 was associated with a 10.28% increase in the risk of hospitalization for pneumonia, compared with 1.21% for each 10 μg/m^3 increase in $PM_{2.5}$ (Wang et al., 2021a). Notably, given the high correlation between PM_1 and $PM_{2.5}$, it was difficult to distinguish their effects on asthma mortality and more advanced statistical techniques would be required in the future.

The biological mechanisms underlying the observed association were not fully understood. Several possible mechanisms have been proposed, mainly the inflammatory response and oxidative stress (Chatkin et al., 2021). Furthermore, from a biological point of view, smaller respirable particles indicated a greater impact on health. First and foremost, smaller particles could remain in the air for longer, thus increasing exposure. Secondly, compared with $PM_{2.5}$, PM_1 had a higher surface area-to-mass ratio, which could reach the alveoli and activate various pathophysiological processes. During the exercise, it was estimated that the respiratory deposition doses in the alveolar region were significantly higher in PM_1 than $PM_{2.5}$ (Gupta et al., 2017). Thirdly, PM_1 had a larger specific surface area and could carry more harmful substances, such as organic compounds and heavy metals, resulting in considerable adverse effects related to oxidative stress and inflammation, even at extra-pulmonary sites (Wang et al., 2020). In the vitro study (Zou et al., 2017), PM_1 exposure was suggested to induce more extensive cytotoxicity effects than $PM_{2.5}$ exposure, attributed to the combined effects of particle size and chemical composition (enriched in hazardous metals). Epidemiologically, a panel study (Chen et al., 2015) indicated stronger positive association between short-term exposure to smaller sized PM and biomarkers of inflammation, coagulation, and vasoconstriction (such as C-reactive protein, tumor necrosis factor-α and endothelin-1). However, the mechanisms between PM and asthma had not been fully understood, and more studies were required to reveal the exact biological pathways, particularly for PM with smaller matters (like PM_1).

To the best of our knowledge, this study preliminarily explored whether greenness could modify the short-term effects of PM on asthma mortality. Subgroup analyses by both NDVI and tree canopy both indicated that individuals living in high green space regions rather than in low green space regions were significantly impacted by PM_1. Though high greenness has many benefits (such as enhance physical activity and alleviate stress), it also increases the chance to inhale allergens (like pollen) for asthma patients (Fuertes et al., 2021). This complex interaction rendered the available evidence on the relationship between high greenness and asthma inconclusive. Several studies have reported a negative correlation between high greenness and asthma risk (Zeng et al., 2020; Sbihi et al., 2015), and a harmful effect of high greenness on asthma was observed (Andrusaityte et al., 2016). Meanwhile, non-significant relationship was also reported (Kuiper et al., 2020; Dadvand et al., 2014). These studies suggested regions exhibiting different levels of air pollution and region-specific characteristics (for example, the dominant types of vegetation) might achieve different results (Zhou et al., 2021; de Keijzer et al., 2017). Additionally, considering several shortcomings of this study, follow-up studies with advanced techniques are still needed. First, although NDVI refers to a generic index reflecting the degree of greenness, it could not distinguish between vegetation types (as for example, parks and farm). Second, the exposure assessment in this study matched the participants' home addresses, while time spent elsewhere (workplaces) failed to be accounted for. Third, this study was unable to determine the daily time spent outdoors for each participant, which may reduce the accuracy of the results. In summary, the role of greenness on PM_1-related asthma mortality should be further explored, particularly with more detailed vegetation measures (such as types, quality and use) and in more regions (including developed countries).

From our findings, individuals living in areas with low NTL rather than high NTL were significantly affected by PM_1, suggesting that asthmatics living in low-urbanization areas may be more susceptible to the effects of PM_1. This may be related to several factors such as air pollution levels, economic status and medical resources between different urbanized areas. Likewise, a national study in China also demonstrated that rural residents were more sensitive to the effect of air pollution on mortality than urban residents (Zhao et al., 2021). Besides, it should be noted that our results also implied that asthmatics living in environments with high street connectivity tend to be less affected by PM_1. Street connectivity, as a proxy for neighborhood walkability, has been suggested to influence individual physical activity (Jia et al., 2021; Leonardi et al., 2017). Physically supportive neighborhood environments may promote physical activity in people with asthma, which could help cope with PM_1 exposure, as emerging evidence pointed out that high physical activity may be beneficial in improving asthma symptoms, control and quality of life (Lang et al., 2019; Nyenhuis et al., 2018).

The results of this study have a number of public health implications. In this study, significant short-term effects of PM_1 and $PM_{2.5}$ on asthma mortality were observed, highlighting the importance of focusing on PM pollution for people with asthma. Notably, the findings of this study, as well as the existing literature (Chen et al., 2017, 2020; Hu et al., 2018; Lin et al., 2016; Liu et al., 2021; Wang et al., 2021a, 2021b), suggested a greater health impact of PM_1, emphasizing the importance of regular monitoring of PM_1 levels, particularly in China. More importantly, it was also observed that a number of neighborhood characteristics (including urbanization, green space, and street connectivity) might modify the short-term effects of PM_1 on asthma patients, which provided evidence to asthma patients to select a healthy neighborhood environment to mitigate acute PM_1 effects. In the future, more high-quality studies (like multi-country) are required to further explore the PM_1-related health effects in both developed and developing countries. Particularly, it is highly anticipated that PM_1 exposure could be included in Global Burden of Disease Study, which could help us to understand PM_1-associated disease burden globally, regionally and temporally. In addition, given the growing evidence that not only particle size but also chemical composition plays an important role in the health effects associated with PM (Wang et al., 2022), there is an urgent need for research into the composition of PM_1, which could contribute to the understanding of the health effects of various PM_1 components.

There are several limitations to this study that should be stated. First, due to the study design, no causal relationships could be inferred. Second, although the case-crossover design was effective in controlling for temporal variables (including ages and genders), some unmeasurable time-variant factors (like physical activity and alcohol consumption) might have confounded the results. Third, this study was conducted in only one province in China, with a relatively small sample size, which might limit the generalizability of the findings. Fourth, the stratified analyses to examine the effects of neighborhood characteristics were not good enough as this analysis was not adjusted for other potential confounding factor. More appropriate statistical methods are required in future research. Fifth, due to the data availability, we could not be able to explore other possible important modifiers, such as smoking status, education level, dietary habits and other concomitant diseases (such as cardiovascular diseases). Future studies are needed to find susceptible populations for more precise preventive measures.

5. Conclusions

In conclusion, the stronger correlation between the short-term exposure of PM_1 and asthma mortality highlighted the importance to give more attention to this important component of PM. Moreover, the effects of PM_1 appeared to be evident in neighborhood characteristics by a low urbanization level, high green space, and poor physical supportive environment.

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CRediT authorship contribution statement

All authors contributed to the final version of the manuscript and have approved the final article. Their contributions to the article were: **Jian Song, Zhen Dingc, Hao Zheng:** Conceptualization, Methodology, Data curation, Formal analysis, Writing - original draft. **Zhiwei Xu, Jian Cheng:** Methodology, Data curation. **Rubing Pan, Weizhuo Yi:** Data curation, Formal analysis, Visualization. **Hong Su, Jing Wei:** Conceptualization, Supervision, Writing - review & editing.

Patient consent for publication

Not required.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Hong Su reports financial support was provided by National Natural Science Foundation of China.

Data availability statement

Data are available upon reasonable request. The CHAP dataset is available at https://weijing-rs.github.io/product.html.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2022.113765.

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