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Medium-term exposure to size-fractioned particulate matter and asthma exacerbations in China: A longitudinal study of asthmatics with poor medication adherence

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A R T I C L E I N F O

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A B S T R A C T

Background: Studies have shown that short- and long-term exposure to particulate matter (PM) can increase the risk of asthma morbidity and mortality. However, the effect of medium-term exposure remains unknown. We aim to examine the effect of medium-term exposure to size-fractioned PM on asthma exacerbations among asthmatics with poor medication adherence.

Methods: We conducted a longitudinal study in China based on the National Mobile Asthma Management System Project that specifically and routinely followed asthma exacerbations in asthmatics with poor medication adherence from April 2017 to May 2019. High-resolution satellite remote-sensing data were used to estimate each participant's medium-term exposure (on average 90 days) to size-fractioned PM (PM_1, $PM_{2.5}$, and PM_{10}) based on the residential address and the date of the follow-up when asthma exacerbations (e.g., hospitalizations and emergency room visits) occurred or the end of the follow-up. The Cox proportional hazards model was employed to examine the hazard ratio of asthma exacerbations associated with each PM after controlling for sex, age, BMI, education level, geographic region, and temperature.

Results: Modelling results revealed nonlinear exposure-response associations of asthma exacerbations with medium-term exposure to PM_1, $PM_{2.5}$, and PM_{10}. Specifically, for emergency room visits, we found an increased hazard ratio for PM_1 above 22.8 μg/m^3 (1.060, 95 % CI: 1.025–1.096, per 1 μg/m^3 increase), $PM_{2.5}$ above 38.2 μg/m^3 (1.032, 95 % CI: 1.010–1.054), and PM_{10} above 78.6 μg/m^3 (1.019, 95 % CI: 1.006–1.032). For hospitalizations, we also found an increased hazard ratio for PM_1 above 20.3 μg/m^3 (1.055, 95 % CI: 1.001–1.111) and $PM_{2.5}$ above 39.2 μg/m^3 (1.038, 95 % CI: 1.003–1.074). Furthermore, the effects of PM were greater for a longer exposure window (90–180 days) and among participants with a high BMI.

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Conclusion: This study suggests that medium-term exposure to PM is associated with an increased risk of asthma exacerbations in asthmatics with poor medication adherence, with a higher risk from smaller PM.

1. Introduction

Asthma is a chronic respiratory disease mainly controlled by long-term and regular treatments or avoiding exposure to risk factors (von Mutius and Smits, 2020). Particulate matter (PM) air pollution is a well-recognized risk factor for asthma attacks and can significantly increase asthma morbidity and mortality in asthmatic populations (Chatkin et al., 2022; Orellano et al., 2017).

Nevertheless, no investigations so far have specifically assessed the effect of PM on asthmatics with poor medication adherence. It is estimated that there are approximately 300 million asthmatics worldwide (Busse et al., 2020); but a large proportion of asthmatics do not take their control medication as prescribed, especially in low- and middle-income countries (García-Marcos et al., 2023). Besides, the focus of existing literature on air pollution and asthma is mainly on the effects of short-term (days to weeks) and long-term (years) PM exposure. For instance, a national study found that short-term exposure to PM significantly increased asthma mortality in China (Liu et al., 2022). In addition, a multinational study found that long-term exposure to PM could also be a significant risk factor for asthma exacerbations (Ai et al., 2019). However, no studies to date have specifically explored the effect of medium-term (months) exposure to PM on asthma exacerbations, especially in asthmatics with poor medication adherence. Considering the higher PM concentrations in certain months of a year that may trigger persistent inflammatory responses in the body (Tripathy et al., 2021; van Donkelaar et al., 2021), we hypothesized that medium-term exposure to PM may be associated with an increased risk of asthma exacerbations.

In addition, existing evidence on the association between PM air pollution and the risk of asthma exacerbations is primarily limited to commonly monitored air pollution (e.g., $PM_{2.5}$ and PM_{10}: particulate matter with an aerodynamic diameter ≤ 2.5 μm and 10 μm) around the world (World Health Organization, 2021). Uncommonly monitored air pollutants such as ultra-fine PM (e.g., PM_1: particulate matter with an aerodynamic diameter ≤ 1 μm) remain a significant health threat and have been increasingly found to increase the risk of respiratory disease (Chen et al., 2021). Nevertheless, few studies have examined the effects of ultra-fine particles on asthma attacks. We assumed that size-fractioned PM, such as PM_1, $PM_{2.5}$, and PM_{10}, may have different toxic effects on asthmatics. Compared with $PM_{2.5}$ and PM_{10}, smaller PM such as PM_1 can reach lower lobes of the lungs, leading to an inflammatory response in respiratory tract and causing greater damage to respiratory health (Gupta and Elumalai, 2017). Additionally, PM_1 is mainly formed from organic aerosols and comes from traffic, cooking emissions, and coal combustion, possibly leading to differential effects on asthma attacks from $PM_{2.5}$ and PM_{10} (Khan et al., 2021).

To address above-mentioned knowledge gaps on PM and asthma exacerbations in asthmatics with poor medication adherence, we conducted a nationally representative longitudinal study in China, aiming to examine and compare the effects of medium-term exposure to size-fractioned PM on the risk of asthma exacerbations.

2. Materials and methods

2.1. Study population

The study population was based on the National Mobile Asthma Management System project, a prospective national longitudinal survey that routinely tracks morbidity status among asthmatics with poor medication adherence. All eligible participants met the enrollment criteria: (1) age ≥ 18 years; (2) did not change their residential address; (3) following the diagnostic criteria of the GINA 2016 guidelines; (4) poor medication adherence [Score on the Medication Adherence Report Scale for Asthma (MARS-A) < 4.5]; (5) asthma was not being well controlled [Asthma Control Test (ACT) score < 20]. Excluded participants were those with other pulmonary diseases, physical and mental illnesses (e.g., cardiovascular or psychiatric), and those who had received specific treatments (e.g., tracheal intubation or antimicrobial medications).

From April 2017 to May 2019, 858 asthmatics with poor medication adherence from 28 provinces and municipalities in China were enrolled and completed the follow-ups in this national dynamic cohort (Figure S1). Each participant underwent five follow-up visits, including one month, three months, six months, nine months, and twelve months after enrollment. Considering that participants may have experienced multiple asthma exacerbations and the number of follow-up visits varied between participants, we included participants who completed at least one follow-up visit and used the first asthma exacerbation after follow-up as the outcome to capture the effect of medium-term exposure to PM. This study was approved by the Ethics Committee of China-Japan Friendship Hospital (approval number: 2015–99).

2.2. Study design

We conceived a time-to-event study design by linking each participant's baseline to the follow-up information from five follow-up visits to generate the final longitudinal data (Zhang et al., 2021). Person-days of follow-up were calculated as the interval from the date of initial survey until the date of follow-up recording asthma exacerbations (e.g., hospitalizations and emergency room visits) or the end of follow-up, whichever occurred first. Each participant's medium-term exposure window was measured as the time interval between the follow-up date when asthma exacerbations occurred or the end of the follow-up and the time of the previous follow-up (Fig. 1). To ensure homogeneity of the study population, we excluded participants who experienced asthma exacerbations within one year before the follow-up began and quit after the follow-up. Following previous definition for medium-term PM exposure (Lee et al., 2022), we further excluded participants with exposure exceeding six months (180 days). Final data analysis included 499 participants. The detailed inclusion-exclusion process is shown in Fig. 2.

2.3. Exposure assessment

Individual-level PM exposure assessment consisted of three steps: (1) geocoding the residential address with longitude and latitude; (2) calculating the medium-term exposure window for each participant; (3) linking geocoded residential address to high-resolution (1 km × 1 km) satellite remote sensing data to estimate the average PM concentrations for each participant during the medium-term exposure window.

Satellite remote sensing data, including PM_1, $PM_{2.5}$, and PM_{10}, were obtained from the China High Air Pollutants (CHAP) online dataset (https://weijing-rs.github.io/product.html). This CHAP dataset used artificial intelligence technology to generate daily PM_1, $PM_{2.5}$, and PM_{10} concentrations from big data (e.g., ground-based measurements, satellite remote sensing products, atmospheric reanalysis, and the space-time extremely randomized trees models) by considering both environmental and human factors of air pollution (Wei et al., 2021b, 2021a, 2019). This data has been widely used to study the health effects of PM air pollution in China because of its long-term, full cover, and high spatial and temporal resolution (Li et al., 2023; Song et al., 2022; Wang et al., 2021). Considering the influence of meteorological factors, we also obtained daily ambient temperature from the European Centre for Medium-Range Weather Forecasts Global Climate Reanalysis dataset (https://cds.climate.copernicus.eu/cdsapp#!/dataset/reanalysis-era5-land?tab=overview).

2.4. Statistical analysis

We used a Cox proportional hazards model combined with a distributed lag nonlinear model to estimate the exposure-response association between medium-term exposure to PM and asthma exacerbations. In the crude model, asthma exacerbation was included as a dependent (dichotomous) variable, and the concentration of each size-fractioned PM was included as an independent variable. Similar to previous literature (Chen et al., 2019; Hao et al., 2020; Lin et al., 2018), adjusted model included three types of covariates, including (1) demographic characteristics (e.g., age, sex, and body mass index (BMI)); (2) Social environmental factors (e.g., educational level, geographic region (north or south, defined by the Qinling-Huaihe Line in China)); and (3) meteorological factors: (e.g., temperature). Based on the variance inflation factor, the model's collinearity issue was not a concern (Table S1).

In our initial data exploration, we used a natural cubic spline to model the non-linear PM-asthma association, and the optimal parameter (e.g., the degree of freedom) in the model was chosen according to the Akaike Information Criterion (Table S2). There was a nonlinear association was observed between three size-fractioned PM and the risk of asthma exacerbations (Figure S2). We further divided asthma exacerbations into hospitalizations and emergency room visits (ERVs) to quantify and compare the effects of three size-fractioned PM on different asthma exacerbation outcomes. Specifically, we first used the minimum risk concentration in the PM-asthma association as a reference concentration to estimate the hazard ratio (HR) of asthma exacerbations

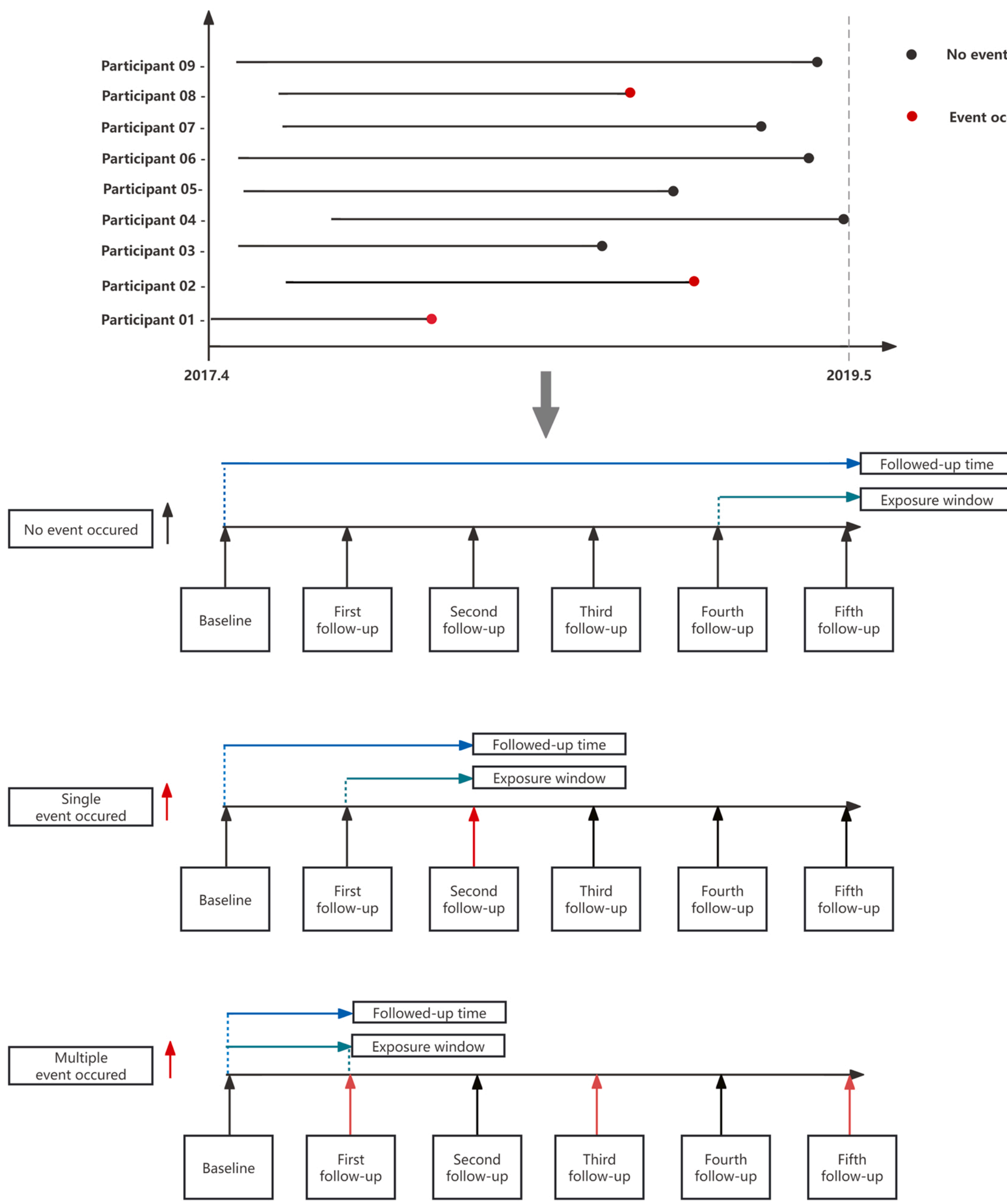

Fig. 1. Diagram of the time to event study design.

(Cheng et al., 2022). We then reported the HR of asthma exacerbations associated with each 1 μg/m^3 increase from reference concentration to the 95th percentile of PM concentrations (Table S3) (Wu et al., 2022). Differences between size-fractioned PM effects were tested using the Z-test (Altman and Bland, 2003).

We observed the inconsistent medium-term exposure window across participants (Figure S3), which was divided into two durations to explore the potentially sensitive exposure window. Specifically, in line with the seasonal variation in PM concentrations, we chose 90 days (three months) as the threshold to determine a short exposure window (≤ 90 days) and a long exposure window (90–180 days). We also performed several subgroup analyses stratified by gender, age (< 45 and ≥ 45 years), educational level (below undergraduate degree and undergraduate or above), BMI (< 24 and ≥ 24 kg/m^2), and geographic region (north or south). The Z-test was used to examine PM effects difference between subgroups (Altman and Bland, 2003).

Several sensitivity analyses were conducted to test the robustness of our findings. First, we considered PM exposure one year before the occurrence of asthma exacerbations in the model to control for the effect of long-term PM exposure. Second, we incorporated extra adjustments for relative humidity in the model and opted for a two-pollutant model instead of a single-pollutant model. Third, we used a binary logistic regression model instead of the Cox proportional hazards model and used the 90th and 99th percentiles of PM concentrations instead of the 95th percentile.

All data analyses and visualization were implemented in R software 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria), with the "survival" package for fitting Cox models and the "dlnm" packages for fitting regression models. A two-sided p-value < 0.05 was considered statistically significant.

3. Results

3.1. Statistical description

During the one-year follow-up period for 499 asthmatics with poor medication adherence, we observed 19 hospitalizations and 27 ERVs for asthma exacerbations (Table S4). Included participants were older than 18 years, with 281 (56.3 %) being female and 280 (56.1 %) living in Southern China. In addition, asthma exacerbations occurred more frequently in Northern China, and most hospitalized asthmatics tend to be older.

Table S5 depicts the basic PM statistics during the exposure window. For ERVs, the average concentrations were 21.13 μg/m^3 for PM_1, 36.25 μg/m^3 for $PM_{2.5}$, and 71.39 μg/m^3 for PM_{10}. For hospitalizations, the average concentrations of PM_1, $PM_{2.5}$, and PM_{10} were 21.05 μg/m^3, 35.98 μg/m^3, and 71.11 μg/m^3, respectively. Additionally, Spearman correlation analysis found a negative correlation between PM and temperature (Tables S6-S7).

3.2. Association between medium-term exposure to PM and asthma exacerbations

Fig. 3 shows a J-shaped concentration-response association between exposure to three size-fractionated PM and the risk of asthma exacerbations in asthmatics with poor medication adherence. Notably, there was a significant increase in the risk of asthma-related hospitalizations and ERVs when PM concentrations exceeded a specific threshold.

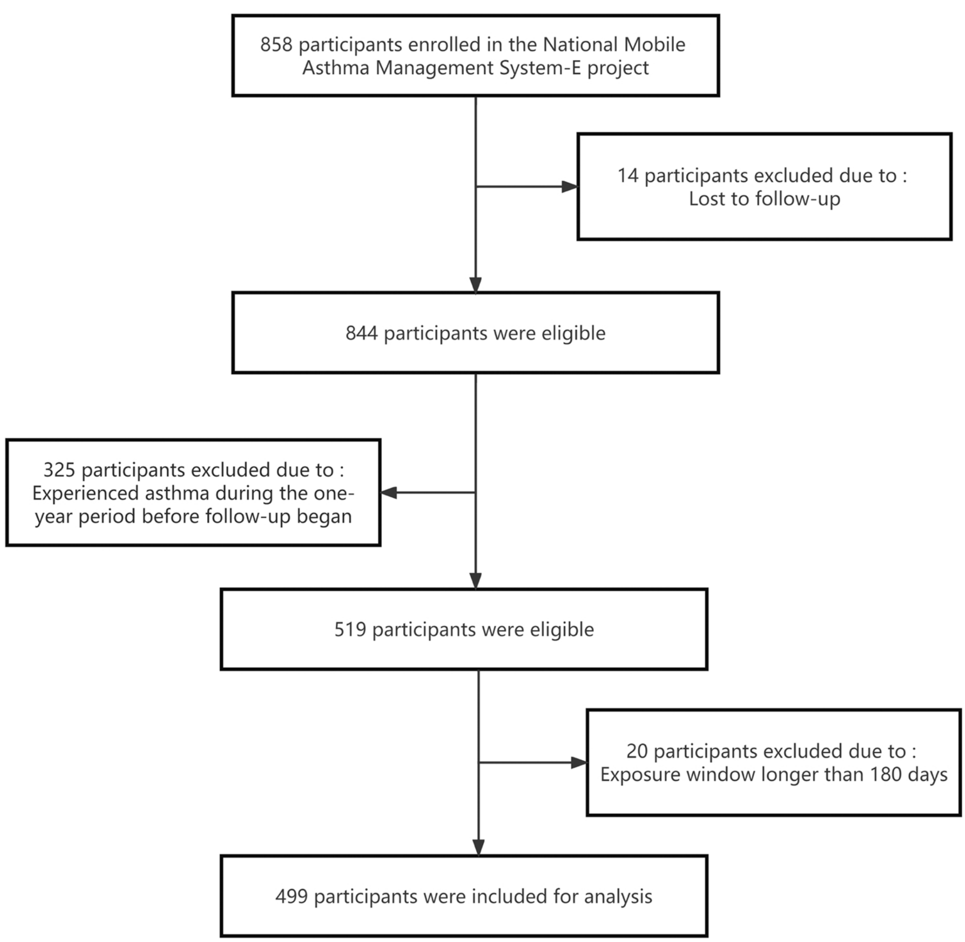

Fig. 2. Flow chart of the participants' selection.

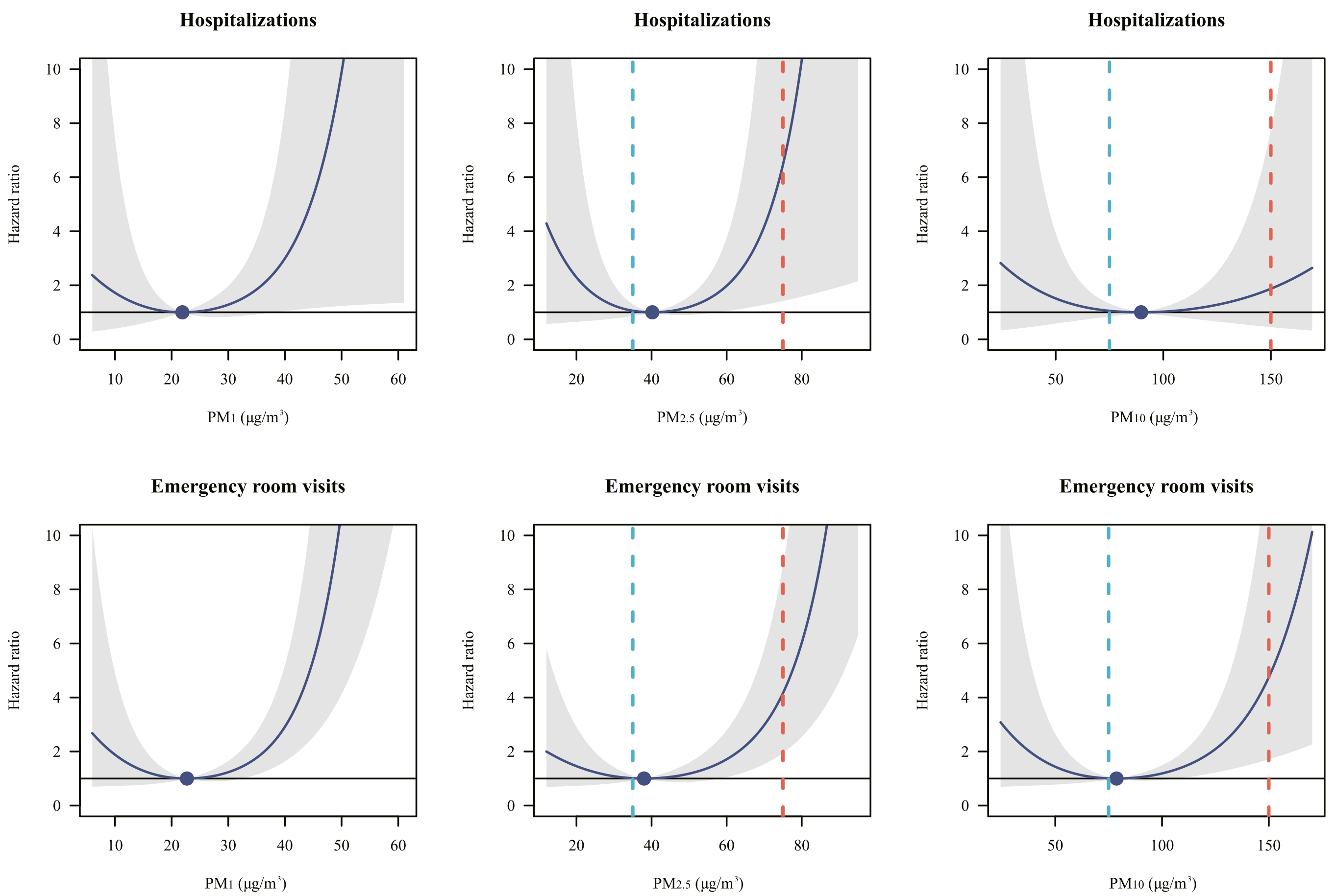

Fig. 3. Estimated concentration-response association between medium-term exposure to PM_1, $PM_{2.5,}$ and PM_{10} and the risk of asthma exacerbations in asthmatics with poor medication adherence. The blue and orange lines represented annual and daily average concentration limits for current the Chinese National Ambient Air Quality Standards Grade II; PM_1: particulate matter with an aerodynamic diameter ≤ 1 μm; $PM_{2.5}$: particulate matter with an aerodynamic diameter ≤ 2.5 μm; PM_{10}: particulate matter with an aerodynamic diameter ≤ 10 μm.

Specifically, the thresholds for the association of hospitalizations with PM_1, $PM_{2.5}$ and PM_{10} were 20.3 μg/m^3, 39.2 μg/m^3, 87.1 μg/m^3, while the thresholds for the association of ERVs were 22.8 μg/m^3, 38.2 μg/m^3, and 78.6 μg/m^3, respectively. Moreover, all thresholds for the association with $PM_{2.5}$ and PM_{10} were slightly above the annual average concentration limits for current Chinese National Ambient Air Quality Standards (CNAAQS) Grade II (35 μg/m^3 and 70 μg/m^3) but far below the daily standards (75 μg/m^3 and 150 μg/m^3).

Table 1 shows the effect of medium-term exposure to three size-fractioned PM on asthma-related hospitalizations and ERVs. Notably, both the crude and adjusted models indicate that PM_1 had the largest effect, followed by $PM_{2.5}$ and PM_{10}. For ERVs, estimated HRs were 1.060 (95 % CI: 1.025–1.096), 1.032 (95 % CI: 1.010–1.054), and 1.019 (95 % CI: 1.006–1.032), for each 1 μg/m^3 increase in PM_1, $PM_{2.5}$, and PM_{10} above the corresponding thresholds, respectively. For hospitalizations, we only observed the effects of PM_1 (HR, 1.055, 95 % CI: 1.001–1.111, per 1 μg/m^3 increase) and $PM_{2.5}$ (HR, 1.038, 95 % CI: 1.003–1.074, per 1 μg/m^3 increase).

Table 1
Estimated effects of medium-term exposure to PM_1, $PM_{2.5,}$ and PM_{10} on asthma exacerbations in asthmatics with poor medication adherence.

Exposures	Hospitalizations		Emergency room visits	
	HR (95 % CI)	*P*-value	HR (95 % CI)	*P*-value
Crude model				
PM_1	1.075 (1.031–1.120)	0.01	1.066 (1.041–1.092)	< 0.01
$PM_{2.5}$	1.045 (1.016–1.074)	0.07	1.032 (1.017–1.048)	0.30
PM_{10}	1.014 (0.996–1.032)	reference	1.022 (1.011–1.033)	reference
Adjusted model				
PM_1	1.055 (1.001–1.111)	0.10	1.060 (1.025–1.096)	0.03
$PM_{2.5}$	1.038 (1.003–1.074)	0.13	1.032 (1.010–1.054)	0.31
PM_{10}	1.007 (0.988–1.026)	reference	1.019 (1.006–1.032)	reference

Abbreviations: HR: hazard ratio; CI: confidence interval; PM_1: particulate matter with an aerodynamic diameter ≤ 1 μm; $PM_{2.5}$: particulate matter with an aerodynamic diameter ≤ 2.5 μm; PM_{10}: particulate matter with an aerodynamic diameter ≤ 10 μm; Crude mode: included particulate matter; Adjusted model: included particulate matter, age, sex, body mass index, educational level, geographic region, and temperature; *P*-value represents the difference between size-fractioned particulate matter.

3.3. Stratified analysis by medium-term exposure window

Fig. 4 and Table S8 show the effects of PM on asthma exacerbations stratified by medium-term exposure window. The risk of asthma-related hospitalizations and ERVs was significantly higher for a longer exposure window than for a shorter one. For instance, for longer exposure to PM_1, $PM_{2.5}$, and PM_{10}, the HRs of ERVs were 1.094 (95 % CI: 1.023–1.171), 1.052 (95 % CI: 1.014–1.092), and 1.026 (95 % CI: 1.005–1.047),

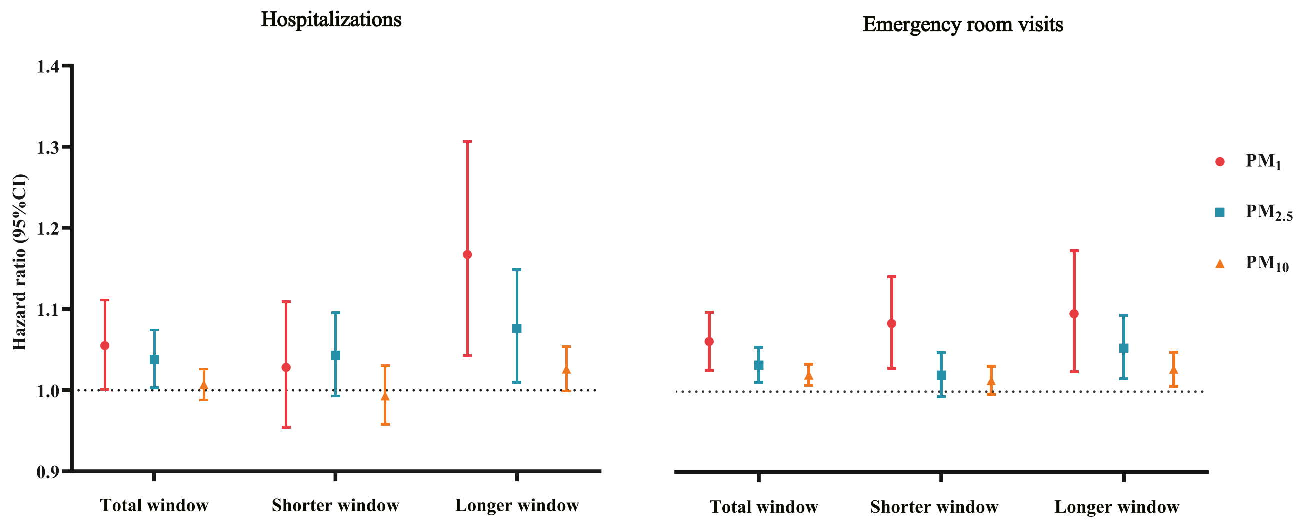

Fig. 4. Estimated effects of PM_1, $PM_{2.5}$, and PM_{10} in different exposure windows on asthma exacerbations in asthmatics with poor medication adherence. Total window: exposure period < 180 days; Shorter window: exposure period ≤ 90 days; Longer window: exposure period between 90 and 180 days; CI: confidence interval; PM_1: particulate matter with an aerodynamic diameter ≤ 1 μm; $PM_{2.5}$: particulate matter with an aerodynamic diameter ≤ 2.5 μm; PM_{10}: particulate matter with an aerodynamic diameter ≤ 10 μm.

respectively. While shorter exposure to PM_1, $PM_{2.5}$, and PM_{10}, the HRs of ERVs were 1.082 (95 % CI: 1.027–1.139), 1.019 (95 % CI: 0.992–1.046), and 1.012 (95 % CI: 0.995–1.030), respectively.

3.4. Subgroup analysis by age, sex, education, BMI, and area

Fig. 5 demonstrates subgroup-specific risks of asthma exacerbations associated with three size-fractioned PM. Generally, PM_1 still had the largest effect on asthma exacerbations in all subgroups compared to $PM_{2.5}$ and PM_{10}. In addition, PM effects appeared to be higher in males aged < 45 years, those with a high BMI, and in Southern China. Among different educational subgroups, HRs for asthma-related hospitalizations associated with exposure to PM were larger in higher education participants, whereas HRs for asthma-related ERVs associated with exposure to PM were larger in lower education participants. (Tables S9-S10).

3.5. Sensitivity analysis

Table S11-S12 show the effect estimates of medium-term exposure to PM_1, $PM_{2.5}$, and PM_{10} after controlling for long-term PM exposure and relative humidity in the main model. Table S13 shows the effect estimates by using a two-pollutant model approach. Table S14 shows the effect estimates using a binary logistic regression model approach. Table S15 shows the effect estimates using the 90th or 99th percentile of PM. Results of these sensitivity analyses were generally similar to the main model (Table 1), suggesting that our findings were robust.

4. Discussion

Medication nonadherence is one of the most prevalent and frustrating problems in treating asthmatics, and exposure to PM air pollution for several months (e.g., medium-term exposure) may be a significant but neglected risk factor for asthma exacerbations in asthmatics with poor medication adherence. Therefore, we conducted a longitudinal study based on high-resolution satellite remote sensing data to explore the effect of medium-term PM exposure on asthmatics with poor medication adherence. This study demonstrated that medium-term exposure to PM_1, $PM_{2.5}$, and PM_{10} was harmful, with PM_1 having the largest effect, followed by $PM_{2.5}$ and PM_{10}. Additionally, stratified analysis found that the risk of asthma exacerbations associated with PM appeared to be higher in a longer exposure window (90–180 days) and in participants with a high BMI.

The asthmogenic role of PM has been demonstrated in previous studies in many countries such as Australia, China, the USA and others; those studies found a significant association between PM and an increased risk of asthma occurrence (Ai et al., 2019; Altman et al., 2023; Cheng et al., 2022; Lu et al., 2020). Nevertheless, existing studies have merely focused on the effects of PM in the general population, while our study further found that asthmatics with poor medication adherence were also affected by PM. Common mechanisms of asthma caused by PM are related to inflammation and reduced defense capacity, which increases susceptibility (Zou et al., 2020). However, asthmatics with poor medication adherence may be more sensitive to PM, which is due to uncontrolled symptoms leading to recurrent episodes that cause epithelial damage to the airway walls and exacerbate airway inflammation (Tiotiu et al., 2020). Therefore, risk factors such as air pollution should be further explored in asthmatics with poor medication adherence.

In addition, previous studies have mainly focused on the short-term effects (days of exposure) and long-term effects (years of exposure) of PM on asthma attacks. For example, a national study from Italy showed that daily increases in ambient PM levels were positively associated with respiratory diseases, particularly asthma (Renzi et al., 2022). Moreover, one European cohort study found that long-term exposure to PM was also associated with asthma attacks (Liu et al., 2021). However, there are significant seasonal variations in PM concentrations, which are higher in certain months of the year and may cause a greater risk due to persistence and accumulation (van Donkelaar et al., 2021). Additionally, current guidelines for the prevention of asthma exacerbations focus on reducing the effects of daily and yearly exposure to PM air pollution, which is unable to capture the effects of several months of PM exposure (Brunekreef et al., 2015; Guan et al., 2016). To the best of our knowledge, this study is the first research hitherto investigating the effect of medium-term (months) exposure to PM on asthma exacerbations and found that PM above a specific concentration threshold could have adverse effects. This finding suggests a non-linear association between medium-term exposure to PM and asthma exacerbations, which is similar to previous studies focusing on short-term and long-term PM exposure and asthma attacks (Li et al., 2011; Zhao et al., 2020). However, many previous studies have reported an approximately linear exposure-response relationship between short-term and long-term exposure to PM and asthma morbidity (Ai et al., 2019; Zhang et al., 2020); moreover, the adverse effects of PM still exist even at levels

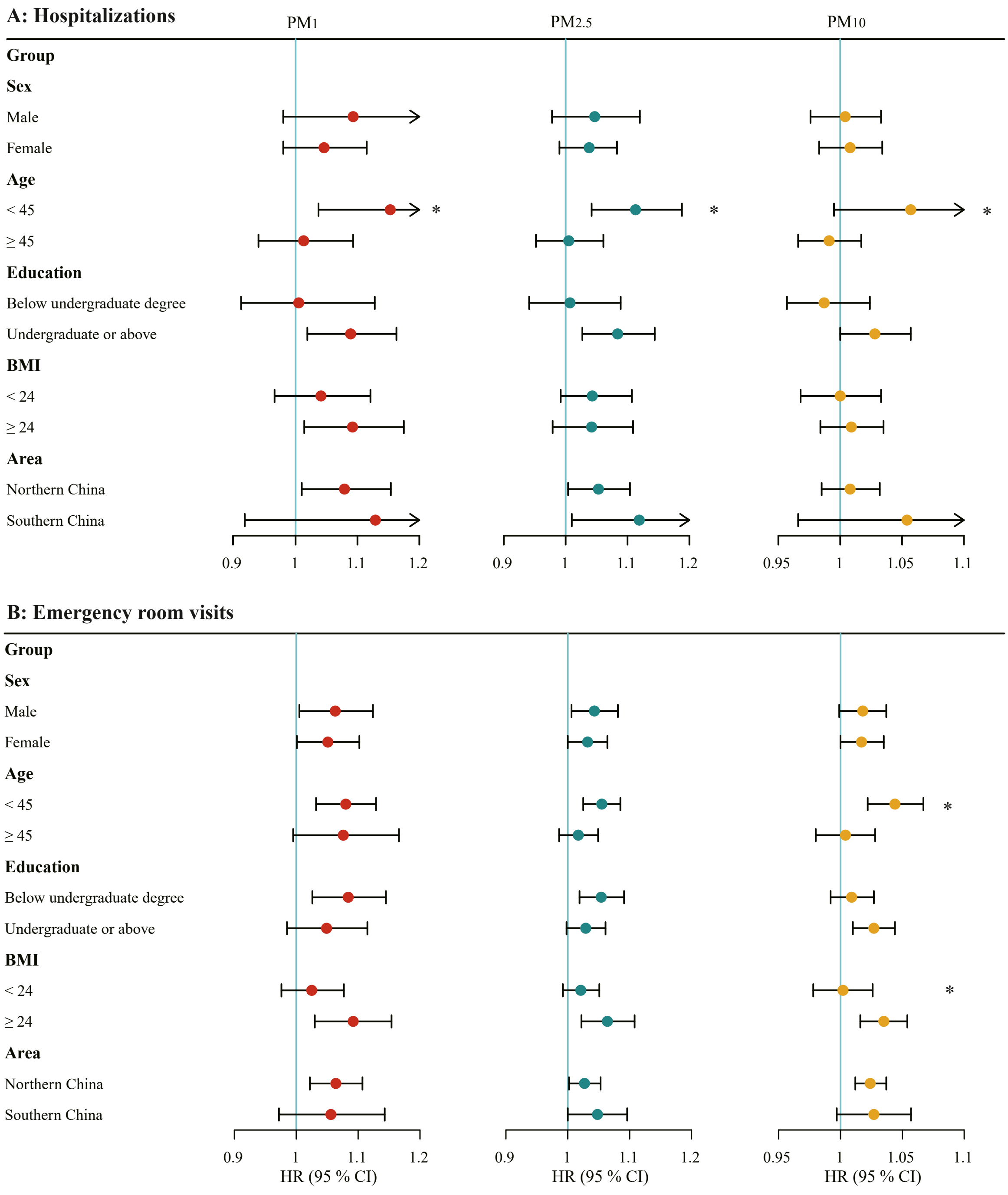

Fig. 5. Estimated effects of PM_1, $PM_{2.5}$, and PM_{10} in different subgroups on asthma exacerbations in asthmatics with poor medication adherence. HR: hazard ratios; CI: confidence interval; PM_1: particulate matter with an aerodynamic diameter ≤ 1 μm; $PM_{2.5}$: particulate matter with an aerodynamic diameter ≤ 2.5 μm; PM_{10}: particulate matter with an aerodynamic diameter ≤ 10 μm; * indicates *P*-difference < 0.05.

below the air quality standards (Liu et al., 2021, 2022). The heterogeneous shape of the exposure-response association between PM and asthma attacks in existing literature may be due to multiple factors, such as the differences in study region and population, PM air pollutant levels, and PM composition. Thus, the effects of PM on asthma might vary geographically, and more work is necessary to clarify the characteristics of localized PM-asthma association.

Notably, the identified thresholds for medium-term $PM_{2.5}$ and PM_{10} were higher than the annual and daily WHO air quality standard of PM but fell between the CNAAQS. More importantly, we found a lower threshold for PM_1 than $PM_{2.5}$ and PM_{10}. However, we were unable to compare PM_1 to the CNAAQ or WHO air quality standard due to the lack of a real-time reporting platform and measurement standards for PM_1 pollution. These findings mean that in addition to focusing on daily (short-term) and yearly (long-term) air pollution levels, monthly or seasonal (medium-term) PM pollution is worthy of being considered in the prevention of asthma attacks. Therefore, future studies are needed to investigate the effect of medium-term exposure to PM on asthma attacks.

Another important finding of this study is that PM_1 had a greater effect on asthma exacerbations than $PM_{2.5}$ and PM_{10}. It is possible that the smaller particle size of PM_1 could be deposited deeper in the airways or cross the alveolar cell membranes and enter the bloodstream, whereby triggering a series of reactions that exacerbate the existing diseases (Hu et al., 2022; Mazzarella et al., 2012). In addition, PM_1 mainly derives from the burning of fossil fuels (e.g., coal, volatile organic compounds), which leads to the generation of toxic components such as polycyclic aromatic hydrocarbons and metals; these toxins can lead to lung damage and even cancer (Niu et al., 2021). Nevertheless, more epidemiological and experimental research is still needed to differentiate the role of size-fractioned PM exposure in asthma exacerbations.

In the stratified analysis based on PM exposure window, we found that longer exposure (90–180 days) to PM had a significantly larger effect on asthma exacerbations than shorter exposure ($\leq$ 90 days). One potential reason is that longer exposure to PM can cause harmful substances to build up in the body, leading to chronic inflammation and lasting respiratory damage, making them more vulnerable to asthma exacerbations (Tripathy et al., 2021). Besides, we also found that PM had a stronger effect on obese individuals, which may be because, with higher BMI, more fatty adipose tissue accumulates in the airway walls. While this excess fat not only takes up space in the airways, it can also increase inflammation in the lungs, which restricts airflow in and out of the lungs and exacerbates asthma symptoms (Palma et al., 2022; Reyes-Angel et al., 2022).

This study has several limitations. First, our study included only adults, whereas children and adolescents also account for a large proportion of asthmatics with poor medication adherence. Second, due to the issue of data availability, some important confounding factors (e.g., smoking, economic level, indoor pollution) were not included in the data analysis. Third, we have only considered the effects of different size-fractioned PM, while PM from different sources and its chemical components also need to be explored. Fourth, this study included asthma cases from hospitalizations and emergency room visits, which did not consider cases from the outpatients that also account for a proportion of asthma exacerbation events.

5. Conclusion

In conclusion, this national longitudinal study in China provides new evidence that medium-term exposure to PM_1, $PM_{2.5}$, and PM_{10} can increase the risk of asthma exacerbations in asthmatics with poor medication adherence, with smaller PM having a greater effect. Nevertheless, more research is still needed to unravel the effect of medium-term exposure to size-fractioned PM on asthmatics to inform better prevention measures.

Ethics approval

This study was approved by the Ethics Committee of China-Japan Friendship Hospital (approval number: 2015-99).

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CRediT authorship contribution statement

Yufan Feng: Writing – original draft, Visualization, Software, Methodology, Formal analysis, Data curation. **Wenyi Zhang:** Writing – review & editing, Conceptualization. **Jing Wei:** Software, Resources. **Dingyuan Jiang:** Methodology, Formal analysis. **Shilu Tong:** Writing – review & editing, Supervision. **Cunrui Huang:** Writing – review & editing, Supervision. **Zhiwei Xu:** Writing – review & editing, Supervision. **Xiling Wang:** Writing – review & editing, Supervision. **Junwen Tao:** Writing – review & editing. **Zhiwei Li:** Writing – review & editing. **Jihong Hu:** Writing – review & editing. **Yongming Zhang:** Writing – review & editing, Conceptualization. **Jian Cheng:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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.

Data availability

The authors do not have permission to share data.

Acknowledgments

The longitudinal data used for this study cannot be shared due to ethical restrictions. Particulate matter datasets are available from https://weijing-rs.github.io/product.html and Meteorological data from https://cds.climate.copernicus.eu/cdsapp#!/dataset/reanalysis-era5-land?tab=overview.

Declaration of competing interest

All the authors declared no conflict of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2024.116234.

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