The Effects of Short-Term PM$_{2.5}$ Exposure on Pulmonary Function among Children with Asthma—A Panel Study in Shanghai, China

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Abstract: Fine particulate matter (PM$_{2.5}$) has been reported to be an important risk factor for asthma. This study was designed to evaluate the relationship between PM$_{2.5}$ and lung function among children with asthma in Shanghai, China. From 2016 to 2019, a total of 70 Chinese children aged 4 to 14 in Shanghai were recruited for this panel study. The questionnaire was used to collect baseline information, and the lung function covering forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1) and peak expiratory flow (PEF) were carried out for each child more than twice during follow-up. Meanwhile, the simultaneous daily air atmospheric pollutants and meteorological data were collected. The linear mixed effect (LME) model was used to assess the relationship between air pollutants and lung function. A significantly negative association was found between PM$_{2.5}$ and lung function among children with asthma. In the single-pollutant model, the largest effects of PM$_{2.5}$ on lung function were found for lag 0–2, with FVC and FEV1 decreasing by 0.91% [95% confidence interval (CI): −1.75, −0.07] and 1.05% (95% CI: −2.09, 0.00), respectively, for each 10 µg/m$^3$ increase in PM$_{2.5}$. In the multi-pollution model (adjusted PM$_{2.5}$ + SO$_2$ + O$_3$), the maximum effects of PM$_{2.5}$ on FVC and FEV1 also appeared for lag 0–2, with FVC and FEV1 decreasing by 1.57% (95% CI: −2.69, −0.44) and 1.67% (95% CI: −3.05, −0.26), respectively, for each 10 µg/m$^3$ increase in PM$_{2.5}$. In the subgroup analysis, boys, preschoolers (<6 years old) and hot seasons (May to September) were more sensitive to changes. Our findings may contribute to a better understanding of the short-term exposure effects of PM$_{2.5}$ on lung function in children with asthma.

Keywords: PM$_{2.5}$; asthma; pulmonary function; children; panel study

1. Introduction

As a chronic disorder of the airways characterized by reversible airflow obstruction and airway inflammation, persistent airway hyper-reactivity, and airway remodeling [1], asthma is one of the most common diseases in children [2]. The prevalence of asthma is about 10.5% in 6- to 14-year-old children in 25 countries, and the prevalence rate is still rising [3]. The number of asthma patients worldwide reached 339.44 million in 2016 [4], and low and middle-income countries contributed 96% of global asthma-related deaths and 84% of global disability-adjusted life-years [5]. In China, the average prevalence of asthma in children under 14 years of age increased by 32.7% during 2000 to 2010 [6]. Therefore, it
is crucial to study the risk factors of asthma in children to reduce and prevent its risk to children’s health.

In addition to individual-related risk factors such as genetics and tobacco exposure [7], air pollutants, such as nitrogen dioxide (NO$_2$), sulfur dioxide (SO$_2$), ozone (O$_3$), fine particulate matter with aerodynamic diameter $\leq$ 2.5 $\mu$m (PM$_{2.5}$) and particulate matter with aerodynamic diameter $\leq$ 10 $\mu$m (PM$_{10}$) [8–12], were also considered to be related to the occurrence and development of asthma among children [13–15]. The most health-harmful pollutant is PM$_{2.5}$ which could penetrate deep into lung passageways [16] and may trigger an immune response and oxidative stress, which may lead to lung function decrease [17]. However, the results about the effect of PM$_{2.5}$ on asthma have not been consistent, and the biological mechanism of the relationship between the changes of lung function and PM$_{2.5}$ in children with asthma is still unclear [6,18–21].

A Japanese study showed that each 10 $\mu$g/m$^3$ increment in PM$_{2.5}$ corresponded to decreased peak expiratory flow (PEF, changes: $-2.96$, 95% confidence interval: $-4.55$, $-1.37$) [22]. Similarly, based on the Columbia Center for Children’s Environmental Health cohort (CCCEH) birth cohort study, PM$_{2.5}$ increase was significantly linked with a decrease in forced expiratory volume in 1 s (FEV$_1$, $\beta$: $-0.15$, 95% confidence interval: $-0.29$, $-0.01$) in children with asthma [23]. However, a California study showed that FEV$_1$ in children with asthma decrements were not significantly associated with increasing ambient PM$_{2.5}$ [24]. Additionally, the majority of the research that explored the relationship between lung function and PM$_{2.5}$ based on big data analysis and animal experiments was rarely based on panel study data. Furthermore, China is the largest developing country, with unprecedented socio-economic and urbanization changes, and these changes are associated with a rapidly increasing prevalence of asthma and a significant burden on the health care system [25,26]. Therefore, the effect of PM$_{2.5}$ on lung function in children with asthma needs further study.

Since Shanghai is one of the largest cities in China and has the highest prevalence of childhood asthma in China [27,28], it is necessary to design a panel study to explore the effects of PM$_{2.5}$ on lung function in children with asthma. Therefore, this study explores the relationship between PM$_{2.5}$ and lung function in children with asthma based on a panel study design in Shanghai. The linear mixed effect model was used to estimate these relationships, and subgroup analyses stratified by demographic season were conducted to identify potentially influencing factors. Expectations for providing a scientific basis for the prevention and control of asthma.

2. Materials and Methods
2.1. Design and Population

From January 2016 to December 2019, we recruited 117 asthmatic children from the Respiratory Department at Shanghai Children’s Medical Center. These participants were included based on the following criteria: (1) no history of chest surgery; (2) asthma cases were extracted from the hospital information systems according to the International Classification of Disease codes, Revision 10 (ICD-10, J45 and J46) or diagnosed by a professional doctor; (3) ages 4–14 years and parent-reported asthma or a history of symptoms including wheezing, cough or dyspnea. Finally, this study included a total of 70 children (39 boys and 31 girls, aged 4–14 years) with asthma for statistical analysis (Figure 1). This study was conducted in accordance with the Declaration of Helsinki. All participants in this study completed questionnaires, lung function measurement and received written informed consent and were approved by the Ethics Committee of Shanghai Children’s Medical Center (SCMCIRB-K2016037).
From January 2016 to December 2019, we initially recruited 117 children with asthma in Pudong, used standard questionnaires to investigate their basic conditions and began personal lung function monitoring.

**Inclusion criteria:**
1. No history of chest surgery;
2. Asthma cases were extracted from the hospital information systems according to the International Classification of Disease codes, Revision 10 (ICD-10, J45 and J46) or diagnosed by a professional doctor;
3. Ages 4–14 years and parent-reported asthma or a history of symptoms including wheezing, cough, or dyspnea.

**Exclusion criteria:**
1. Effects of exposure to outdoor air pollution and lung function indicators were not reported or could not be obtained from the information provided;
2. Loss of follow-up;
3. Children with less than 2 pulmonary function tests during the study;
4. Children with lost or incomplete personal information.

70 children completed questionnaires and lung function test more than 2 times.

We introduced the basic conditions of the standard questionnaire and analyzed the relationship between individual lung function and air pollutants.

**Figure 1.** The selection of the participants in this study.

### 2.2. Lung Function Test and Questionnaire

In this study, the spirometry was performed by experienced operators (medical doctors specialized in pediatric pulmonology) and the specific recommendations for spirometry in the pre-school age were considered [29]: (1) children were instructed how to perform the maneuvers, repeating them at least three times; (2) a training period was considered to familiarize them with the equipment and technician; (3) the operator observed the child closely to ensure there was no leak, and that the maneuver was performed optimally; and (4), to visibly examine volume–time curves and flow–volume curves in real time [30]. The adolescents were all in sitting position and no nasal clips were used in any of the operations.

With standard questionnaires (Supplementary Materials), the trained interviewers collected the data on basic demographic information, parents’ allergy history, allergy history, cigarette exposure and so on. In this study, the frequency of smoking in places where children often move or rest was classified into the following groups: 0 unit/day, <1 unit/day, 1–5 units/day and >5 units/day. The frequency of contact between smokers and children was classified into the following groups: 0 h/day, <1 h/day, 1–4 h/day, 4–8 h/day and >8 h/day. Body mass index (BMI) was calculated as weight (kg) divided by the square of the height (m).

### 2.3. Exposure

The data of daily fine particulate matter with aerodynamic diameter $\leq 2.5 \mu m$ (PM$_{2.5}$), particulate matter with aerodynamic diameter $\leq 10 \mu m$ (PM$_{10}$), nitrogen dioxide (NO$_2$),
sulfur dioxide (SO$_2$), carbon monoxide (CO), and ozone (O$_3$, maximum 8 h average concentration) was obtained from the Shanghai Environmental Monitoring Center. A total of 9 stations of Shanghai Environmental Monitoring Center were used, and the values of each element were taken as the average values of all stations. Daily meteorological data covering temperature (including mean, maximum, and minimum) and relative humidity were provided by the Shanghai Meteorological Bureau (Figure 2).

Figure 2. Location of environmental monitoring station and Shanghai Children’s Medical Center, Shanghai Jiao Tong University School of Medicine in Shanghai.

2.4. Statistical Analysis

We set up the questionnaire information database through EpiData (Version 3.0, Odense, Denmark) and used double input for quality control. In the descriptive analysis for baseline characteristics of the asthmatic children and exposure data for environmental factors, categorical variables were described as frequency and percentage, and continuous variables were given as means and standard deviations.

Because there were repeated measures for all participants, the linear mixed effect (LME) model was used to estimate the effects of PM$_{2.5}$ on lung function [30]. This model allows each subject to act as self-control of time and to explain the correlation between repeated measurements collected by each person by including the random effects of the subjects [31]. Due to the abnormal distribution of lung function, the measured values of lung function were transformed logarithmically. We controlled three-day moving average temperature (lag 0–3) and three-day moving average relative humidity (lag 0–3) for potential lagged meteorological confounders. In addition, the time of lung function tests, holidays and day of the week effects were adjusted in the model. The respiratory health indicators were regressed on moving average concentrations of exposure variables from 1 day to 7 days before the measurements to estimate the potential cumulative effects of the exposures. The mixed-effects model is as follows:

$$\log(Y_{ij}) = u + b_i + \beta_1 X_1 + \beta_2 X_2 \ldots + \beta_n X_n + \xi_{ij}$$

$\log(Y_{ij})$ represents the logarithmic value of the lung function index for study subject $i$ on measurement $j$; $u$ represents the fixed intercept; $b_i$ is individual-specific random intercept; $\beta_1$ through to $\beta_n$ represent the fixed effect variable coefficients for variables $X_1$ through $X_n$; and $\xi_{ij}$ represents the error for participant $i$ on measurement $j$. We reported
the results as the estimated percentage change in FVC, FEV1 and PEF with 95% confidence intervals (CI) with each 10 µg/m³ increase in air pollutants. The estimated percent changes were calculated as \[10^{(\beta \times 10)} - 1\] × 100%; with [95%CI[10^{(\beta \times 1.96 \times SE)} - 1\] × 100%; where \(\beta\) and SE are the effect estimate and its standard error [32].

We used the single-pollutant model and multi-pollutant model to test the consistency of exposure effects. Pollutants that were highly related to PM\(_{2.5}\) (\(r > 0.7\)) were excluded in order to reduce the collinearity among pollutants, last SO\(_2\) and O\(_3\) were included in the multi-pollutant model (Figure S1). To control for intra-participant variability, the subject was included in the LME model as random variables and adjusted for questionnaire information (atopic dermatitis, allergic rhinitis, food or drug allergies, mother’s or father’s history of allergies, frequency of smoking in places where children often move or rest and frequency of contact between smokers and children), age, sex, and BMI.

We conducted a subgroup analysis by sex (boy vs. girl), age (preschool children were defined as aged less than 6 years old vs. school-aged children defined as aged older than or equal to 6 years) and season (cold season was defined the period of November to March, and the hot season was defined as the period of May to September [20]) to control for potential modifying effects.

The mixed linear effect model was performed with the “lme4” package and “Matrix” package in R software (R Development Core Team; http://R-project.org) [33]. Other statistical analysis was achieved in SPSS 22.0 (IBM SPSS, Chicago, IL, USA), and \(p < 0.05\) (two-tailed) was considered statistically significant.

3. Results

3.1. Descriptive Analysis

Table 1 shows the basic demographic information of the study population. After the filtration of population information, we included 39 boys and 31 girls in this study, and their BMI was 16.55 ± 2.82; 87.14% of children with asthma had allergic rhinitis, 62.86% had atopic dermatitis and 87.14% of parents chose not to smoke in places where their children often had activities or rest. Table 2 shows the descriptive results of the meteorological variables, air pollutants, and lung function indicators. The daily average temperature and relative humidity were 19.17 °C and 74.86%, respectively. The daily average concentrations of PM\(_{2.5}\), PM\(_{10}\), O\(_3\), SO\(_2\), NO\(_2\) and CO were 34.15 µg/m³, 50.69 µg/m³, 107.34 µg/m³, 9.92 µg/m³, 40.38 µg/m³ and 663.23 µg/m³, respectively. The average of FVC, FEV1 and PEF were 1.63 L, 1.36 L and 3.03 L/s, respectively.

| Variable                  | n   | %    |
|---------------------------|-----|------|
| Sex                       |     |      |
| boy                       | 39  | 55.71|
| girl                      | 31  | 44.29|
| Age                       |     |      |
| <6                        | 40  | 57.14|
| ≥6                        | 30  | 42.86|
| BMI, Mean ± SD            | 16.55 ± 2.82 |
| Atopic dermatitis         |     |      |
| Yes                       | 44  | 62.86|
| No                        | 26  | 37.14|
| Allergic rhinitis         |     |      |
| Yes                       | 61  | 87.14|
| No                        | 9   | 12.86|
| Food or drug allergies    |     |      |
| Yes                       | 20  | 28.57|
| No                        | 50  | 71.43|
Table 1. Cont.

|                         | n | %     |
|-------------------------|---|-------|
| Mother’s history of allergies |   |       |
| Yes                     | 52| 74.29 |
| No                      | 18| 25.71 |
| Father’s allergy history |   |       |
| Yes                     | 52| 74.29 |
| No                      | 18| 25.71 |
| Frequency of smoking in places where their children often had activities or rest |   |       |
| 0 units/day             | 61| 87.14 |
| <1 unit/day             | 2 | 2.86  |
| 1–5 units/day           | 6 | 8.57  |
| >5 units/day            | 1 | 1.43  |
| Frequency of contact between smokers and children |   |       |
| 0 h/day                 | 43| 61.43 |
| <1 h/day                | 9 | 12.86 |
| 1–4 h/day               | 11| 15.71 |
| 4–8 h/day               | 3 | 4.29  |
| >8 h/day                | 4 | 5.71  |

Table 2. Description of basic meteorological pollutants and lung function indicators.

|                              | Mean   | SD    | Min   | Max    | IQR   |
|------------------------------|--------|-------|-------|--------|-------|
| Daily temperature (°C)       | 19.17  | 9.03  | −0.10 | 32.20  | 16.40 |
| Relative humidity (%)        | 74.86  | 11.73 | 37.00 | 97.50  | 18.30 |
| PM$_{2.5}$ (µg/m$^3$)        | 34.15  | 25.13 | 9.00  | 173.00 | 28.00 |
| PM$_{10}$ (µg/m$^3$)         | 50.69  | 26.46 | 13.00 | 166.00 | 34.00 |
| O$_3$ (µg/m$^3$)             | 107.34 | 48.04 | 32.00 | 251.00 | 67.00 |
| SO$_2$ (µg/m$^3$)            | 9.92   | 4.30  | 5.00  | 40.00  | 5.00  |
| NO$_2$ (µg/m$^3$)            | 40.38  | 19.84 | 13.00 | 118.00 | 26.00 |
| CO (µg/m$^3$)                | 663.23 | 236.13| 400.00| 1800.00| 200.00|
| FVC (L)                      | 1.63   | 0.52  | 0.57  | 3.85   | 0.62  |
| FEV1 (L)                     | 1.36   | 0.42  | 0.54  | 3.45   | 0.51  |
| PEF (L/s)                    | 3.03   | 1.61  | 1.05  | 21.80  | 1.43  |

SD, standard deviation; IQR, interquartile range; PM$_{2.5}$, fine particulate matter with aerodynamic diameter ≤ 2.5 µm; PM$_{10}$, particulate matter with aerodynamic diameter ≤ 10 µm; O$_3$, ozone; SO$_2$, sulfur dioxide; NO$_2$, nitrogen dioxide; CO, carbon monoxide; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; PEF, peak expiratory flow.

3.2. Regression Analysis

Figure 3 shows the changes in lung function of asthmatic children with each 10 µg/m$^3$ increase in PM$_{2.5}$ in a single-pollution or multi-pollution model. The changes of lung function in the single-pollution or multi-pollution model were similar, indicating that the model was stable. Delayed effects of PM$_{2.5}$ were significantly associated with FVC and FEV1 on lag 0, lag 0–1 and lag 0–2, both in single-pollution or multi-pollution models, with the largest effect observed on lag 0–2. Per 10 µg/m$^3$ increase in PM$_{2.5}$ on lag 0–2 corresponded with a 1.57% (95% CI: −2.69, −0.44) decreased FVC and 1.67% (95% CI: −3.05, −0.26) decreased FEV1 in the multi-pollution model (adjusted PM$_{2.5}$ + SO$_2$ + O$_3$). However, in the double-pollution model (adjusted PM$_{2.5}$ + O$_3$) and the single-pollution model, the delayed effect of PM$_{2.5}$ was significantly related to the effect on PEF on lag 0, with the largest effect of PEF on lag 0–3 in the single-pollution model. For each 10 µg/m$^3$ increase in PM$_{2.5}$ on lag 0–3, the PEF decreased 2.12% (95% CI: −4.18, −0.02).
Figure 3. Association between lung function and air pollutants in single- or multi-pollution models. Estimates are adjusted for questionnaire information, relative humidity, temperature, age, BMI, sex, holiday, day of week and times of the measurement. PM\textsubscript{2.5}, fine particulate matter with aerodynamic diameter ≤ 2.5 μm; O\textsubscript{3}, ozone; SO\textsubscript{2}, sulfur dioxide; FVC, forced vital capacity; FEV\textsubscript{1}, forced expiratory volume in 1 s; PEF, peak expiratory flow.

3.3. Subgroup Analysis

Figure 4 shows the gender difference in the relationship between lung function and PM\textsubscript{2.5} in the multi-pollution model (adjusted PM\textsubscript{2.5} + SO\textsubscript{2} + O\textsubscript{3}). For boys, the maximum effect of PM\textsubscript{2.5} on both FVC and FEV\textsubscript{1} occurred in lag 0–2, FVC and FEV\textsubscript{1} decreased by 3.65% (95% CI: −5.28, −1.98) and 3.12% (95% CI: −5.25, −0.95), respectively, for each 10 μg/m\textsuperscript{3} increase in PM\textsubscript{2.5}. In the girls’ group, the maximum effect of PM\textsubscript{2.5} on FEV\textsubscript{1} occurred on lag 0–4, FEV\textsubscript{1} decreased 2.33% (95% CI: −4.38, −0.24) for each 10 μg/m\textsuperscript{3} increase in PM\textsubscript{2.5}. These results were similar to other models (adjusted PM\textsubscript{2.5}, PM\textsubscript{2.5} + O\textsubscript{3}, PM\textsubscript{2.5} + SO\textsubscript{2} in Figures S2–S4).
Figure 4. Association between lung function and PM$_{2.5}$ in gender-stratified multi-pollution model (adjusted PM$_{2.5}$ + SO$_2$ + O$_3$). Estimates are adjusted for questionnaire information, relative humidity, temperature, age, BMI, holiday, day of week and times of the measurement. FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; PEF, peak expiratory flow.

Figure 5 shows the age difference in the relationship between lung function and PM$_{2.5}$ in the multi-pollution model (adjusted PM$_{2.5}$ + SO$_2$ + O$_3$). Each 10 µg/m$^3$ increase in PM$_{2.5}$ on lag 0–3 was associated with decreased FVC and FEV1 by 3.77% (95% CI: −5.72, −1.77) and 4.25% (95% CI: −6.62, −1.81) in preschool children. As for PEF, each 10 µg/m$^3$ increase of PM$_{2.5}$ on lag 0–6 was associated with a maximum effect decrease of 6.89% (95% CI: −10.55, −3.09), but for school-aged children, none of them were statistically significant. The results were similar to other models (adjusted PM$_{2.5}$, PM$_{2.5}$ + O$_3$, PM$_{2.5}$ + SO$_2$ in Figures S2–S4).

Figure 6 shows the season difference in the relationship between lung function and PM$_{2.5}$ in the multi-pollution model (adjusted PM$_{2.5}$ + SO$_2$ + O$_3$). No statistically significant
relationship between lung function and PM$_{2.5}$ was located in the cold season (November to March). During the hot season (May to September), both FVC and FEV1 had the largest decline when exposed to PM$_{2.5}$ on lag 0–2. For each 10 µg/m$^3$ increase of PM$_{2.5}$, FVC decreased by 2.56% (95% CI: $-4.74$, $-0.33$, and FEV1 decreased by 3.28% (95% CI: $-5.78$, $-0.72$). In the seasonal subgroup analysis, the results were not quite the same for different pollutant models (adjusted PM$_{2.5}$, PM$_{2.5}$ + O$_3$, PM$_{2.5}$ + SO$_2$ in Figures S2–S4). Among them, the results in the two-pollutants model controlling PM$_{2.5}$ and SO$_2$ (Figure S4) were similar to the multi-pollution model (adjusted PM$_{2.5}$ + SO$_2$ + O$_3$).

**Figure 6.** Association between lung function and PM$_{2.5}$ in a season-stratified multi-pollution model (adjusted PM$_{2.5}$ + SO$_2$ + O$_3$). Cold season refers to the period of November to March, and hot season means May to September [20]. Estimates are adjusted for questionnaire information, relative humidity, temperature, age, BMI, sex, holiday, day of week and times of the measurement. FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; PEF, peak expiratory flow.

**4. Discussion**

In this study, children’s lung function was repeatedly measured, and a linear mixed effect model was used to explore the relationship between air PM$_{2.5}$ and lung function in children with asthma. Mixed-effect models showed that exposure to PM$_{2.5}$ was related to decreases in forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1), respectively, and there is a cumulative lag effect. In contrast, peak expiratory flow (PEF) change was not associated with PM$_{2.5}$ concentrations. Generally, the change in lung function in boys was more obvious than that in girls. In the subgroup analysis, the changes in lung function in preschool children were more vulnerable to the effects of PM$_{2.5}$ than those in school-age children, and in hot seasons the changes were more obvious than in cold seasons. This study was based on a panel study, and the results may add new knowledge to the effects of PM$_{2.5}$ on lung function in children with asthma aspect.

Consistent with prior studies [34–37], we also found higher PM$_{2.5}$ was associated with decreased lung function. Xu, et al. [36] assessed the association of lung function with current day PM$_{2.5}$ and found that each 10 µg/m$^3$ increment of PM$_{2.5}$ exposure was associated with a 9.83 mL decrease [95% confidence interval (CI): 2.46, 17.19] in FVC and an 8.06 mL decrease (95% CI: 1.06, 15.06) in FEV1; however, associations with PEF were non-statistically significant. In Canada, researchers observed that an interquartile range (IQR) increase (6 µg/m$^3$) in the previous 24 h mean concentration of PM$_{2.5}$ was associated with a 0.54% (95% CI: 0.06, 1.02) decrease in bedtime FEV1 (Dales, et al., 2009). Similar results were reported in a Polish study reporting that an IQR increment of PM$_{2.5}$ was related to 2.1% decrease in FVC (95% CI: $-2.6$, $-1.6$) and 1.0% decrease in FEV1 (95% CI: $-1.4$, $-0.6$) [37]. However, some studies have reported inconsistent results. For example, a
systematic review reported that effects of PM$_{2.5}$ on PEF widely spread and more than those for PM$_{10}$ [38]. Epton et al. [35] assessed the association of lung function with air pollution and concluded that no significant correlation between lung function and pollution level could be detected, either in asthmatics or normal students. The inconsistencies among these studies may be attributed by heterogeneity in participants’ characteristics, statistical methodology, other air pollutants, area of study and/or exposure assessment methods. In this study, we used the multi-pollution model to explore the relationship between PM$_{2.5}$ and lung function in children with asthma, but the results were also stable.

These panel study findings imply that PM$_{2.5}$ adversely may affect asthmatic children’s lung function, but the underlying biological mechanism of the effects of PM$_{2.5}$ is still unclear. Some biological mechanisms have been recognized as reasonable ones. Firstly, inhaled PM$_{2.5}$ can trigger oxidative stress and systemic inflammation, which can affect lung function [39,40]. This oxidative stress may also be activating NF-κB and MAPK signaling pathways and promoting the expression of pro-inflammatory factors, which increases nasal mucus and decreases airway barrier function [16,41]. Secondly, a study has confirmed the cytotoxic effect of PM$_{2.5}$ on airway epithelial cells and may activate APCs and T-cells, which can contribute to the exacerbation of respiratory diseases such as asthma [42]. Thirdly, PM$_{2.5}$ exposure can disrupt antioxidant lung function [43], and due to PM$_{2.5}$ having a small diameter which leads to a larger surface area and greater allergen uptake [44], this is more likely to cause a decline in lung function in children with asthma. In this study, we suggested the adversary effects of PM$_{2.5}$ on lung function in children with asthma and the impact of PM$_{2.5}$ may further display potential mechanisms involved in the changes in lung function.

In the subgroup analysis, we found that gender and age may modify the effects of PM$_{2.5}$ on lung function. This study results coincide with the study of Gauderman et al. [45], where a stronger association between PM$_{2.5}$ and lung function change were found in boys. Similarly, the European Study of Cohorts for Air Pollution Effects (ESCAPE) reported that associations between with annual average PM$_{2.5}$ and lung function tended to be somewhat stronger in boys compared with girls [46]. Additionally, Kasamatsu et al. [47] reported that gender had no modification on the effects of PM$_{2.5}$ on PEF. Then, a study in Nanjing suggested that the acute effects of PM$_{2.5}$ on lung function indicators in girls were greater in boys [36]. The effects of modification of gender may be due to gender-linked estrogen [48,49]. This is probably because boys prefer and enjoy being involved in outdoor activities, which causes more frequent exposure to atmospheric pollutants than it does to girls [50]. Sex-related differences in lung function also could be due to the difference in sex hormones and the difference in the airway relative to lung size [51,52].

Additionally, we found a stronger association between lung function and the exposure to PM$_{2.5}$ in the group of preschool children (< 6 years old), which was consistent with other studies [53,54]. This may be explained by the more susceptible status of preschoolers to PM$_{2.5}$ due to their immature immune function and sensitive lung tissue [55,56]. Nevertheless, studies in China showed the effects of PM$_{2.5}$ in 5–14-year-olds were higher than 0–4-year-olds [57]. Additionally, a study in Hefei [58] found that school-aged children (> 6 years old) were more sensitive than preschoolers (< 6 years old) in the relationship between PM$_{2.5}$ exposure and asthma. This may be explained by the different area of air pollution, socioeconomic status and adaptive capacity of children at different locations.

Consistent with the results found in a meta-analysis including 87 studies [21] and a study in Shanghai [44], PM$_{2.5}$ had a greater impact on lung function in children with asthma during the hot season. This result can be explained from three aspects. Firstly, there are higher levels of aerosol molecules compared with the cold seasons, such as fungal spores and pollen, which may trigger more allergy attacks [59,60]. Moreover, a Shanghai study reported that the effects of PM$_{2.5}$ on asthma hospital visits was highest in summer [61]. This may be explained by the high pollution episodes of PM$_{2.5}$ being prone to occur in the eastern Yangtze River Delta of China in summer [62]. Thirdly, children spend more time outdoors and become involved in more physical activities in the warmer season,
which increases their per-minute ventilation, and thus they inhale more air pollutants. However, a study conducted in Shenzhen and a time-stratified case-crossover study in the Philadelphia metropolitan region showed that the risk was significantly greater in the cold season than the warm season [63,64]. This is likely to be related to factors such as the chemical composition and levels of ambient particulate matter, the exposure patterns of the local population and local climatic conditions [65,66].

This panel study had many strengths in explaining the association between lung function in children with asthma and short-term exposure to PM$_{2.5}$, but some limitations could not be avoided. Firstly, due to the lack of specific home addresses of participants, the data of air pollutants and meteorological factors from monitoring stations could not represent the specific exposure level for each participant. Secondly, this study only considered the effects of external atmospheric pollutants and meteorological factors, without regard to indoor pollution [13,14,67], which may lead to misclassification and bias. At the same time, one study has suggested that the characteristics of domestic housing conditions and indoor and outdoor pollutants are highly correlated, indicating that the use of outdoor detection data has certain research value [68] and the model also controlled for factors such as the frequency of smoking in places where their children often had activities or rest. What is more, this study did not analyze PM$_{2.5}$ components due to technical limits, which may result in an underestimate of the effect. Fourthly, the sample size was small; however, we performed at least two repeated measurements of lung function and analyzed the data using a mixed-effects model. Last but not least, the analysis of temperature in this study was in a subgroup analysis only, and the interaction between PM$_{2.5}$ and temperature was not considered, which may cause an underestimation of the results.

5. Conclusions

In summary, this panel study explored the relationship between atmospheric PM$_{2.5}$ concentrations and lung function in children with asthma. The single- and multi-pollutant models all suggested that the increase in PM$_{2.5}$ concentration was associated with the decline of lung function and short-term exposure to PM$_{2.5}$ may affect the health of lung function in children with asthma, particularly in boys, preschoolers (<6 years old) and in the hot seasons (May to September). The results suggest that more attention should be paid to the effect of PM$_{2.5}$ on the lung health of asthmatic children. In addition, the effects of PM$_{2.5}$ on lung function showed significant lag effects. The results suggested that the importance of protective measures after air pollution events, such as wearing masks, reducing non-essential going out and so on.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/ijerph191811385/s1, Figure S1: Pearson’s correlation coefficients between factors affecting lung function.; Figure S2: Association between each lung function index and PM$_{2.5}$ in the stratified analysis of PM$_{2.5}$ single pollution model; Figure S3: Association between each lung function index and PM$_{2.5}$ in a stratified analysis of a two-pollution model (adjusted PM$_{2.5}$+O$_3$); Figure S4: Association between each lung function index and PM$_{2.5}$ in a stratified analysis of a two-pollution model (adjusted PM$_{2.5}$+SO$_2$); Questionnaire.

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Data Availability Statement: The meteorological datasets and air pollutant datasets used and/or analyzed are available from the open-access websites. All data on children with asthma were obtained from the Shanghai Children's Medical Center.

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