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# Ambient particulate matter (PM<sub>1</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>) and childhood pneumonia: The smaller particle, the greater short-term impact?

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ABSTRACT

HIGHLIGHTS

## GRAPHICAL ABSTRACT

- We examined PM<sub>1</sub>, PM<sub>2.5</sub>, PM<sub>10</sub> effects on childhood pneumonia hospitalizations.
- The highest increase in pneumonia hospitalizations was from PM<sub>1</sub>, followed by PM<sub>2.5</sub> and PM<sub>10</sub>.
- PM<sub>1</sub> had larger effects on children by sex, age, and season than did PM<sub>2.5</sub> and PM<sub>10</sub>.
- We observed a linear exposureresponse curve for PM<sub>1</sub> and pneumonia hospitalization.

## ARTICLE INFO

Article history: Received 30 September 2020 Received in revised form 25 January 2021 Accepted 25 January 2021 Available online 1 February 2021 *Background:* Smaller sizes of ambient particulate matter (PM) can be more toxic and can be breathed into lower lobes of a lung. Children are particularly vulnerable to PM air pollution because of their adverse effects on both lung functions and lung development. However, it remains unknown whether a smaller PM has a greater short-term impact on childhood pneumonia.

-1 1 3 5 7 9 11 13 15 17

PM1 O PM25 O PM10

Percent change

6 82 (3 85-9 88)

0.93 (0.23-1.64

0.76 (0.23-1.3)

6.6 (3.71-9.57)

0.72 (0.19-1.26

1.1 (0.44-1.76)

P-value

<0.001

0.005

<0.001

~0.00

0.00

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*Keywords:* Particulate matter Pneumonia Children China Aims: We compared the short-term effects on childhood pneumonia from PM with aerodynamic diameters  $\leq 1 \mu m$  (PM<sub>1</sub>),  $\leq 2.5 \mu m$  (PM<sub>2.5</sub>), and  $\leq 10 \mu m$  (PM<sub>10</sub>), respectively.

*Methods*: Daily time-series data (2016–2018) on pneumonia hospitalizations in children aged 0–17 years, records of air pollution (PM<sub>1</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, and gaseous pollutants), and weather conditions were obtained for Hefei, China. Effects of different PM were quantified using a quasi-Poisson generalized additive model after controlling for day of the week, holiday, seasonality and long-term time trend, and weather variables. Stratified analyses (gender, age, and season) were also performed.

*Results:* For each 10 µg/m<sup>3</sup> increase in PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> concentrations over the past three days (lag 0–2), the risk of pneumonia hospitalizations increased by 10.28% (95%CI: 5.88%–14.87%), 1.21% (95%CI: 0.34%–2.09%), and 1.10% (95%CI: 0.44%–1.76%), respectively. Additionally, both boys and girls were at risk of PM<sub>1</sub> effects, while PM<sub>2.5</sub> and PM<sub>10</sub> effects were only seen in boys. Children aged ≤12 months and 1–4 years were affected by PM<sub>1</sub>, but PM<sub>2.5</sub> and PM<sub>10</sub> were only associated with children aged 1–4 years. Furthermore, PM<sub>1</sub> effects were greater in autumn and winter, while greater PM<sub>2.5</sub> and PM<sub>10</sub> effects were evident only in autumn.

*Conclusion:* This study suggests a greater short-term impact on childhood pneumonia from  $PM_1$  in comparison to  $PM_{2.5}$  and  $PM_{10}$ . Given the serious PM pollution in China and other rapid developing countries due to various combustions and emissions, more investigations are needed to determine the impact of different PM on childhood respiratory health.

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# 1. Introduction

Children's respiratory health is particularly vulnerable to particulate matter (PM) air pollution (World Health Organization, 2005). As one of most common respiratory diseases and the leading cause of death in children worldwide, a number of studies have reported the short-term association between PM and pneumonia (Li et al., 2018; Nhung et al., 2017; Walker et al., 2013). However, most of these studies explored PM with aerodynamic diameter  $\leq 2.5 \ \mu m (PM_{2.5})$  and  $\leq 10 \ \mu m (PM_{10})$ . So far, evidence is limited on the effects of PM with an aerodynamic diameter  $\leq 1 \ \mu m (PM_1)$  on childhood pneumonia (Nhung et al., 2018).

PM<sub>1</sub> could be comprised of primary organic aerosols, sulfate, ammonium, nitrate and chloride (Niu et al., 2020), whereas PM<sub>2.5</sub> and PM<sub>10</sub> were also related to dusts and hazes (Gao et al., 2015). These chemical components of PM1 could be from traffic, cooking emissions, and coal combustions (Niu et al., 2020; Zhang et al., 2018). Because PM1 is a part of PM<sub>2.5</sub> and PM<sub>2.5</sub> is a part of PM<sub>10</sub>, PM<sub>1</sub> could be more toxic in comparison with other components of PM<sub>2.5</sub> and PM<sub>10</sub> such as PM<sub>1-2.5</sub> and PM<sub>75</sub> (Lin et al., 2016; Chen et al., 2017b; Zhang et al., 2020a). Furthermore, the size (in diameter) of  $PM_1$  is much smaller than  $PM_{25}$  and PM<sub>10</sub>, which enables the pollutant to reach lower lobes of a lung and may cause a larger damage to respiratory health. In other words, parts of PM<sub>2.5</sub> and PM<sub>10</sub> components also go deep into respiratory system. However, despite the fact that PM<sub>1</sub> is supposing to have a great threat on human health, the health impact of this air pollutant was still underestimated. To date, most of the PM<sub>1</sub> studies were focused on the long-term effects (years of exposure) on community health risk (Chen et al., 2018; Li et al., 2019; Yang et al., 2018b; Yang et al., 2019). These studies suggested that several years of PM<sub>1</sub> exposure increased the risk of autism spectrum disorder, hypertension, cardiovascular disease, and metabolic syndrome. Some studies also assessed the short-term effects (days of exposure) of PM<sub>1</sub> on various health outcomes, suggesting elevated risk of mortality (all-cause and cardiovascular disease), emergency department visits, and respiratory hospitalizations (include pneumonia and chronic obstructive pulmonary diseases) within days after exposure (Chen et al., 2017b; Yin et al., 2020; Zhang et al., 2020a, 2020b; Lin et al., 2016). However, there are no studies examining whether the short-term effects of PM1 on pneumonia in children were larger than PM<sub>2.5</sub> and PM<sub>10</sub> effects in countries or regions that are heavily polluted by particulate matter such as China, Iran, Poland and South America (Nhung et al., 2017; Hadei et al., 2020; Badyda et al., 2017; Gouveia and Fletcher, 2000).

In order to further explore whether the smaller particle could contribute to the greater short-term impact on human health, the present study sought to examine and compare the impacts of PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> on childhood pneumonia in Hefei, China. Stratified analyses

by sex, age, and season were also performed to identify sensitive subgroups and exposure-time-window to the PM effects.

#### 2. Material and methods

#### 2.1. Data collection on pneumonia hospitalizations

Daily count of pneumonia patients (age: 0-17) from January 1, 2016 to December 31, 2018 were obtained from the computerized hospitalization database in Anhui Provincial Children's Hospital, which is a grade A tertiary hospital and the only children's hospital in Hefei (http://www.ahetyy.com/spinfo\_1.html). Selection of this hospital is in line with previous studies looking at childhood respiratory disease such as asthma in Hefei (Pan et al., 2019; Zhang et al., 2019). Meanwhile, childhood pneumonia hospitalizations have obvious seasonal pattern with a peak in summer and trough in summer, which has also been noted in previous investigation of pneumonia hospitalizations of all ages in Hefei (Xie et al., 2019). Causes of diseases of all patients were coded based on the International Statistical Classification of Diseases and Related Health Problems (ICD-10). Based on ICD classification, patients with primary diagnosis coded as "[12-[18" were extracted as pneumonia cases. For each pneumonia case, date of hospital admission, sex, age, and residential address were reported. Based on residential address, we selected all pneumonia cases living in the urban area of Hefei city as our analytic dataset. The residential locations of these patients were covered by air pollution monitoring network operated during the study period.

With the use of our analytic dataset, we aggregated pneumonia cases to a series of daily time-series data based on age and sex: 1) daily count of childhood pneumonia hospitalizations (in total), 2) daily hospitalization of pneumonia (boy), 3) daily hospitalization of pneumonia (girl), 4) daily hospitalization of pneumonia (age  $\leq$  12 months), 5) daily hospitalization of pneumonia (age:1–4 years), and 6) daily hospitalization of pneumonia (age: 5–17 years). This age classification was motivated by previous studies to identify which subgroups were more vulnerable to environmental risk exposure (Barnett et al., 2005; Xu et al., 2014).

#### 2.2. Data collection on air pollution

We then matched all data with daily concentrations of air pollutants based on the date of hospital admission. Particularly, we aggregated daily concentrations of PM<sub>2.5</sub>, PM<sub>10</sub>, ozone (O<sub>3</sub>), nitrogen dioxide (NO<sub>2</sub>), and sulfur dioxide (SO<sub>2</sub>) from air quality information retrieved from National Urban Air Quality Real-time Publishing Platform including a number of ground monitoring stations that constitute the National Air Pollution Monitoring System. Since January 2013, China's Ministry of

Environmental Protection begun to display the air pollution data at the official website (http://106.37.208.233:20035/). This online platform reports real-time (hourly) concentrations of the above-mentioned air pollutants, including 10 monitoring stations with air quality information in Hefei during the study period (Fig. S1). By averaging hourly concentrations within a day across all monitoring stations, we obtained daily values of each air pollutant (i.e., one mean value of  $PM_{2.5}$  and  $PM_{10}$  concentrations for each day) (Chen et al., 2017a; Tian et al., 2019).

Different from ground-monitored PM<sub>2.5</sub> and PM<sub>10</sub> data, information of PM<sub>1</sub> concentration was not reported in the above-mentioned platform, therefore, we additionally collected daily information of PM<sub>1</sub> from China Atmosphere Watch Network (CAWNET). Since CAWNET only had one station in Hefei and the data from this location may not be able to represent the entire city, we thus used the processed spatial time-series data (resolution: 1 km) based on CAWNET from a recent study (Wei et al., 2019). These spatial time-series data are daily estimation of PM<sub>1</sub> derived from an ensemble learning model based on air guality information from 153 stations of CAWNET, MAIAC AOD Product, MEIC Emission Data, land use information, road network, topographic characteristics, and night-time light (Wei et al., 2021). Briefly, a spacetime extremely randomized trees model was performed in the above estimation with a high accuracy (R<sup>2</sup>: 0.74–0.77, root-mean-square error: 9.5–14.5  $\mu$ g/m<sup>3</sup>, mean absolute error: 5.9–8.7  $\mu$ g/m<sup>3</sup>). The ChinaHighPM1 dataset is available at https://weijing-rs.github.io/ product.html. Based on an urban boundary, we averaged each pixel (1 km) of spatial time-series data to a daily mean of PM<sub>1</sub> in Hefei, which enhances the spatial representative of air pollution data.

## 2.3. Data collection on weather conditions

Daily records of meteorological information (mean temperature, relative humidity, wind speed, and air pressure) were retrieved from the China Meteorological Data Sharing Service System (http://data.cma.cn/) in order to control for the influence of weather when fitting the PM-pneumonia association (Tian et al., 2019).

# 2.4. Two-stage data analysis

This study consisted of two-stage analysis. In the first stage, we decomposed the daily-level time-series data of pneumonia hospitalizations and three PM fractions to identify their long-term trend and seasonality. Following previous literature (Cheng et al., 2019b), a loess method was used to decompose the time-series data, which was split into three key components: long-term trend, seasonality, and residuals (also refers to noise or random component). We then visually check whether there was an obvious long-term trend and seasonality in the returned plots.

The second stage analysis was then applied to fit the PM-pneumonia associations, based on a generalized additive model with a quasi-Poisson to account for overdispersion (Cheng et al., 2019b; Tian et al., 2019; Chen et al., 2017a). Potential confounders included: (1) meteorological factors including mean temperature and relative humidity, each using a nature cubic spline with three degrees of freedom (df = 3), (2) day of week as a categorical variable, (3) holiday as a binary variable, and (4) long-term trend and seasonality using year and month as a factor. Furthermore, we examined the short-term effects up to a lag of two days due to an evidence of acute and delayed PM effects on pneumonia (Tian et al., 2019). Given that the model with a single-day lag may underestimate the adverse effects of PM pollution, we follow previous studies to apply a 3-day moving-window to estimate associations between PM and pneumonia hospitalizations within lag 0-2 days (Tian et al., 2019; Chen et al., 2017a). This model was further validated by a sensitivity analysis as detailed below as well as by checking residuals of each model, suggesting an approximate normal distribution and the random fluctuation over time. PM effects were reported as percentage change in pneumonia hospitalizations associated with each 10  $\mu$ g/m<sup>3</sup>

increase in PM concentration using the equation: *Percentage change* = (RR - 1) \* 100%; RR is the relative risk. We repeated this analysis for different sex and age groups to identify potential sensitive subgroups.

## 2.5. Examination of the shape of exposure-response association

To check the shape of exposure-response curves for PM and pneumonia hospitalizations, we applied a non-linear smoothing function to the regression model. Specifically, a thin plate regression spline with three degrees of freedom for each particulate matter was used to allow for non-linear change in the risk of pneumonia hospitalizations associated with changes in PM concentration. We then plotted the relative risk of pneumonia hospitalizations against the change in PM concentration.

## 2.6. Sensitivity analysis

To check the robustness of our findings, we carried out several analyses. First, we utilized a two-pollutant model that controlled for the influence of gaseous pollutants to replace the single-pollutant model. Second, as an alternative of quasi-Poisson model, we also used a Poisson model. Third, we altered the strategy to adjust for long-term trend and seasonality by using a natural cubic spline for time with six to eight degrees of freedom per year. Fourth, in addition to temperature and relative humidity, we additionally adjusted for wind speed and air pressure. We performed all data analyses and plots making in R software (version: 3.6.3). Two-side *p*-value <0.05 was considered statistically significant.

# 3. Results

A total of 15,683 pneumonia hospitalizations from 2016 through 2018 were recorded and included for data analysis. On average, there were 14 pneumonia cases (range: 0–43) per day, with more cases in boys than in girls, and in 1–4-year age group than in age groups of <1 year and 5–17 years (Table 1). During the 3-year study period, the daily mean concentrations of PM<sub>1</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, temperature and relative humidity were 31  $\mu$ g/m<sup>3</sup>, 53  $\mu$ g/m<sup>3</sup>, 82  $\mu$ g/m<sup>3</sup>, 17 °C, and 75%, respectively.

Spearman correlations between air pollutants and weather variables were shown in Table 2.  $PM_1$  were positively associated with  $SO_2$  ( $\rho =$ 

 Table 1

 Summary statistics of data on daily children

Summary statistics of data on daily childhood pneumonia and particulate matter in Hefei, China, 2016–2018.

Variables	Min	25th percentile	50th percentile	Mean	75th percentile	Max
Pneumonia (count)						
Total	0	10	14	14	18	43
Boys	0	6	8	9	11	27
Girls	0	3	5	6	7	22
<12 months	0	3	4	5	7	17
1-4 years	0	5	7	8	10	31
5–17 years	0	0	1	1	2	7
Air pollutants (µg/m <sup>3</sup> )						
PM <sub>1</sub>	13	22	28	31	39	81
PM <sub>2.5</sub>	6	30	45	53	67	228
PM <sub>10</sub>	11	52	75	82	105	327
O <sub>3</sub>	8	43	63	66	84	188
SO <sub>2</sub>	2	8	10	11	13	58
NO <sub>2</sub>	10	30	39	44	55	134
Weather factors						
Mean temperature (°C)	-6	9	18	17	25	36
Relative humidity (%)	33	68	76	75	85	98

PM<sub>1</sub>: particulate matter with aerodynamic diameter of  $\leq 1 \mu m$ ; PM<sub>2.5</sub>: particulate matter with aerodynamic diameter of  $\leq 2.5 \mu m$ ; PM<sub>10</sub>: particulate matter with aerodynamic diameter of  $\leq 10 \mu m$ ; O<sub>3</sub>: ozone; SO<sub>2</sub>: sulfur dioxide; NO<sub>2</sub>: nitrogen dioxide.

0.48, *p*-value<0.05) and NO<sub>2</sub> ( $\rho = 0.56$ , *p*-value<0.05) but negatively associated with O<sub>3</sub> ( $\rho = -0.49$ , p-value<0.05), temperature ( $\rho = -0.78$ , *p*-value<0.05) and relative humidity ( $\rho = -0.09$ , *p*-value<0.05). Similar results were also observed for PM<sub>2.5</sub> and PM<sub>10</sub>.

Fig. 1 presents the results of time-series decomposition for pneumonia hospitalizations and concentrations of PM1, PM2.5, and PM10. Pneumonia hospitalizations had an apparent seasonality, with more hospitalizations in winter and less hospitalizations in summer. A similar seasonal pattern was also observed for PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub>. Details of the median value of daily pneumonia hospitalizations and particulate matter within 3-year study period are displayed in Table S1. Besides, there was a rising trend in the number of pneumonia hospitalizations but a declining trend of the concentrations of PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> over the study period. Increasing pneumonia hospitalizations could be attributed to a number of factors such as changes in the population size of children, hospital bed's managing strategy, and popularity of the selected hospital. The continuous reduction in particulate matter concentrations over years could be explained by the implication of Air Pollution Prevention and Control Action Plan (APPCAP) across China since 2013, which has been proven to be an effective measure in mitigating the air pollution level (Huang et al., 2018).

Fig. 2 shows the estimated percentage changes in the risk of pneumonia hospitalizations associated with each 10  $\mu$ g/m<sup>3</sup> increase in the concentrations of PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> at different lag days. In general, PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> were all associated with increases in pneumonia hospitalizations at lag 0, 1, 2, and 0-2 days. Notably, PM<sub>1</sub>, PM<sub>25</sub>, and PM<sub>10</sub> had the largest effect at lag 0. Meanwhile, the effects of PM<sub>1</sub> were seven to ten times larger than that of PM<sub>2.5</sub> and PM<sub>10</sub>. For example, at lag 0-2, we estimated an increase in pneumonia hospitalizations of 10.28% (95%CI: 5.88%-14.87%) for PM<sub>1</sub>, followed by PM<sub>2.5</sub> (1.21%, 95% CI: 0.34%-2.09%), and PM<sub>10</sub> (1.10%, 95%CI: 0.44%-1.76%). Similar findings were also observed when estimating the percent change in the risk of pneumonia hospitalizations associated with each IQR increase in the concentrations of PM1, PM2.5, and PM10 (Fig. S2). For each IQR increase in  $PM_1$ ,  $PM_{2.5}$ , and  $PM_{10}$  concentrations, the largest increase in the risk of pneumonia hospitalizations at lag 0 was 11.94% (95%CI: 6.67%-17.48%), 3.45% (0.83%-6.14%), and 4.05% (1.21%-6.98%), respectively.

Table 3 displayed the results of stratified analyses by sex, age, and season. Both boys and girls were vulnerable to PM<sub>1</sub> effects, with an estimated percentage increase of 8.85% (95%CI: 3.85%-14.1%) and 12.58% (95%CI: 5.99%-19.57%), respectively. Comparatively, PM<sub>2.5</sub> and PM<sub>10</sub> seemed to only affect boys and have a smaller effect, with the estimated percentage increase of 1.36% (95%CI: 0.35%-2.38%) and 1.28% (95%CI: 0.52%-2.06%), respectively. Among different age groups, PM<sub>1</sub> was associated with increased pneumonia hospitalizations in age groups of <12 months (9.0%, 95%CI: 2.29%-16.15%) and 1-4 years (10.16%, 95% CI: 4.71%-15.88%). However, increased pneumonia hospitalizations associated with PM<sub>2.5</sub> and PM<sub>10</sub> were only seen in 1-4 years age group. In four different seasons, greater increases in pneumonia hospitalizations associated with PM<sub>1</sub> were seen in autumn and winter, whereas

 $\ensuremath{\text{PM}_{2.5}}$  and  $\ensuremath{\text{PM}_{10}}$  appeared to increase pneumonia hospitalizations only in autumn.

The potential non-linear exposure-response relationships of pneumonia hospitalizations with  $PM_1$ ,  $PM_{2.5}$ , and  $PM_{10}$  were shown in Fig. 3.  $PM_1$ -pneumonia relationship had a linear and positive slope associated with increase in concentration. There was also a linear and positive trend in  $PM_{2.5}$ -pneumonia relationship when concentration was below around 100 µg/m<sup>3</sup>, after which the relationship remained stable.  $PM_{10}$ -pneumonia relationship was slightly non-linear, with a linear and positive slope at concentration not exceed about 80 µg/m<sup>3</sup>, then a stable slope at concentration of around 80-150 µg/m<sup>3</sup>, and finally a linear and positive slope at concentration above 150 µg/m<sup>3</sup>.

We performed three sensitivity analyses by running two-pollutant models (Table S2), replacing Poisson models with quasi-Poisson models (Table S3), adopting different strategies to adjust for long-term trend and seasonality (Table S4), and adjusting for wind speed and air pressure (Table S5). These sensitivity analyses in general generated similar results, suggesting the robustness of our findings. For example, before and after controlling for O<sub>3</sub>, each 10  $\mu$ g/m<sup>3</sup> increase in PM<sub>1</sub> concentration was associated with 10.28% (95%CI: 5.88%–14.87%) and 10.77% (95%CI: 6.15%–15.58%) increase in the risk of childhood pneumonia hospitalizations (Table S2). Although PM<sub>1</sub> effect was reduced after using a natural cubic spline for time with six to eight degrees of freedom per year to adjust for long-term trend and seasonality, the effect difference was not statistically significant (*p*-value>0.05) (Table S4).

## 4. Discussion

This study investigated the role of PM sizes (PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub>) in influencing childhood pneumonia hospitalizations. This study yielded some interesting findings. First, we found positive associations of childhood pneumonia hospitalizations with 3 PM examined. PM<sub>1</sub> had the largest impact on pneumonia hospitalizations, followed by PM<sub>2.5</sub>, and PM<sub>10</sub>. Second, stratified analyses by sex, age, and season not only verified the greater effects of PM<sub>1</sub> but also revealed detrimental PM<sub>1</sub> effects in more subgroups and seasons. Third, the shape of exposure-response curve for PM<sub>1</sub> and pneumonia hospitalization is approximately linear, suggesting no threshold for the adverse PM<sub>1</sub> effects on pneumonia.

The results regarding short-term effects of  $PM_{2.5}$  and  $PM_{10}$  on pneumonia hospitalizations are somewhat consistent with previous studies (Barnett et al., 2005; Cheng et al., 2019a; Li et al., 2018; Tian et al., 2019). For example, Tian et al. (2019) conducted a nationwide study in mainland China. This study reported a positive association between PM and pneumonia hospitalizations. Specifically, a 10 µg/m<sup>3</sup> increase in 3-day moving average of PM<sub>2.5</sub> and PM<sub>10</sub> concentrations were associated with 0.31% and 0.19% increase in adult pneumonia hospitalizations, respectively (Tian et al., 2019). Comparatively, a study in Ningbo, China (Li et al., 2018) and the present study found larger PM<sub>2.5</sub> and PM<sub>10</sub> effects on childhood pneumonia hospitalizations. Researchers also found harmful effects of PM<sub>2.5</sub> and PM<sub>10</sub> air pollution on childhood pneumonia in many regions such as Taiwan, China, Australia and New Zealand

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Spearman correlation coefficients between air pollutants and weather variables

·F								
	$PM_1$	PM <sub>2.5</sub>	PM <sub>10</sub>	03	NO <sub>2</sub>	SO <sub>2</sub>	Mean temperature	Relative humidity
PM <sub>1</sub>	1							
PM <sub>2.5</sub>	0.73*	1						
PM <sub>10</sub>	0.58*	0.86*	1					
O <sub>3</sub>	$-0.49^{*}$	-0.21	-0.03	1				
NO <sub>2</sub>	0.56*	0.65*	0.72*	$-0.28^{*}$	1			
SO <sub>2</sub>	0.48*	$0.52^{*}$	0.57*	-0.15	$0.54^{*}$	1		
Mean temperature	$-0.78^{*}$	$-0.45^{*}$	$-0.27^{*}$	0.67*	$-0.39^{*}$	$-0.29^{*}$	1	
Relative humidity	$-0.09^{*}$	-0.21	$-0.47^{*}$	$-0.34^{*}$	$-0.31^{*}$	$-0.39^{*}$	0.06*	1

PM<sub>1</sub>: particulate matter with aerodynamic diameter of  $\leq 1 \mu m$ ; PM<sub>2.5</sub>: particulate matter with aerodynamic diameter of  $\leq 2.5 \mu m$ ; PM<sub>10</sub>: particulate matter with aerodynamic diameter of  $\leq 10 \mu m$ .

\* *p*-Value < 0.05.



**Fig. 1.** The decomposition of daily time-series data for pneumonia hospitalizations (A) and three types of particulate matters (B–D) in Hefei, China, 2016–2018. PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> are particulate matters with an aerodynamic diameter  $\leq 1 \mu m$ , 2.5  $\mu m$ , and 10  $\mu m$ , respectively. A seasonal-trend decomposition procedure based on loess smoothing method was used to decompose daily time-series data including long-term trend, seasonality, and residuals (or irregular fluctuation) (Cheng et al., 2019b).



Fig. 2. The estimated percentage changes in childhood pneumonia hospitalizations per  $10 \ \mu g/m^3$  increase in PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> concentrations at different lag days.

(Cheng et al., 2019a; Barnett et al., 2005). Meanwhile, these studies suggested that  $PM_{2.5}$  had a slightly larger pneumonia effect than did  $PM_{10}$ . However, none of previous studies have investigated the effect of smaller PM such as  $PM_1$  on pneumonia occurrence in children.

Specifically, one key finding of this study is that  $PM_1$  was found to pose a greater short-term impact on childhood pneumonia hospitalizations than did  $PM_{2.5}$  and  $PM_{10}$ . As stated above, there was a lack of studies with similar research context. Therefore, it is difficult to directly compare our findings with previous research. Although short-term relationship between  $PM_1$  and childhood pneumonia occurrence is underestimated to date, a recent study has found a greater impact of  $PM_1$  than  $PM_{2.5}$  on pneumonia hospitalizations for all ages (Zhang et al., 2020a), which could somewhat support our hypotheses and findings. Several studies also documented greater short-term effects of  $PM_1$  than larger sizes PM ( $PM_{2.5}$  and  $PM_{10}$ ) on all-cause total, cardiovascular and respiratory mortality/morbidity (Chen et al., 2017b; Yin et al., 2020; Zhang et al., 2020a).

In term of toxicology, the impact of PM<sub>1</sub> is hard to determine simply based on our statistical analysis. However, several studies (Sun et al., 2013; Niu et al., 2020) documented that PM<sub>1</sub> was mainly formed by organic aerosol (OA), In particularly, PM1 related OA could be mainly contributed from primary OA such as hydrocarbon-like OA, cooking OA, coal combustion OA (Křůmal et al., 2013). For example, a study in Beijing found that primary OA dominates PM1-related OA during wintertime (69%) (Sun et al., 2013). As a major component of PM<sub>1</sub>, longterm exposure to polycyclic aromatic hydrocarbons (PAHs) with high molecular weight could be associated with respiratory diseases, bronchitis and pneumonia, especially to carcinogenic PAHs such Ind, BbkF, DahA, BaP, and BghiP (Agudelo-Castañeda et al., 2017). These may be the factors causing short-term effects of oxidative stress as well as inflammation and resulting childhood pneumonia, while more studies regarding the environmental-health mechanism should be further investigated.

Regarding the impact of different PM on childhood pneumonia hospitalizations in subgroups by sex and age, we also observed a larger increase in hospitalizations due to PM<sub>1</sub> in all subgroups in comparison to PM<sub>2.5</sub> and PM<sub>10</sub>. Likewise, previous studies showed a slightly higher risk of total respiratory disease and asthma associated with PM<sub>1</sub> than PM<sub>2.5</sub> in different sex and age groups (Zhang et al., 2020a; Yang et al., 2018a). Besides, PM<sub>1</sub> in this study was found to affect boys and girls as well as age groups of <12 months and 1–4 years. However, PM<sub>2.5</sub> and PM<sub>10</sub> seemed to affect only boys and 1-4-year-old children. One potential reason for the age and sex differences in PM<sub>2.5</sub> and PM<sub>10</sub> effects may be related to different behaviors. In general, older children and boys are more active and play more time outdoors, thereby increasing their exposure to PM. Infants or children younger than 12 months in China tend to be kept more time indoors by parents or guardians. Meanwhile, breastfeeding could protect infants from being less affected by PM<sub>2.5</sub> and  $PM_{10}$  (Dong et al., 2013). The difference of the results from various PM highlighted that girls and age groups of <12 months should also be protected in order to minimize the adverse effects on respiratory health across the study area. While the consequences of the effect of PM<sub>1</sub> could not clearly been shown from our analysis, one of the possible assumptions could be the toxic composition of PM<sub>1</sub>, which might be more sensitive to newborn baby with a weak lung. Particularly, younger children (age < 4 years) should have spent more time to stay at home. Therefore,

Table 3

Estimated percentage change (%) in childhood pneumonia hospitalizations associated with a 10 µg/m<sup>3</sup> increase in PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> concentrations (lag 0–2), stratified by sex, age, and season.

	PM <sub>1</sub>		PM <sub>2.5</sub>		PM <sub>10</sub>	
	Percentage change (95% CI)	p-Value	Percentage change (95% CI)	p-Value	Percentage change (95% CI)	p-Value
Sex						
Boys	8.85 (3.85 to 14.1)	< 0.001	1.36 (0.35 to 2.38)	0.009	1.28 (0.52 to 2.06)	0.001
Girls	12.58 (5.99 to 19.57)	< 0.001	0.97 (-0.33 to 2.28)	0.144	0.79 (-0.18 to 1.78)	0.113
Age						
<12 months	9.0 (2.29 to 16.15)	0.008	0.50 (-0.82 to 1.83)	0.461	1.02 (0 to 2.05)	0.050
1-4 years	10.16 (4.71 to 15.88)	< 0.001	1.65 (0.54 to 2.77)	0.003	1.18 (0.35 to 2.02)	0.005
5-17 years	13.29 (-0.05 to 28.42)	0.051	1.23 (-1.34 to 3.88)	0.352	0.79 (-1.1 to 2.72)	0.417
Season						
Spring	0.85 (-6.77 to 9.10)	0.832	-0.25 (-2.65 to 2.22)	0.844	0.60 (-0.48 to 1.68)	0.278
Summer	5.56 (-9.09 to 22.57)	0.479	0.25 (-3.79 to 4.45)	0.907	1.18 (-1.59 to 4.04)	0.408
Autumn	18.84 (7.63 to 31.21)	< 0.001	6.85 (3.99 to 9.79)	< 0.001	2.43 (0.22 to 4.69)	0.032
Winter	7.47 (1.07 to 14.26)	0.023	0.63 (-0.51 to 1.78)	0.281	0.15 (-0.93 to 1.23)	0.790

 $PM_1$ : particulate matter with aerodynamic diameter of  $\leq 1 \mu m$ ;  $PM_{2.5}$ : particulate matter with aerodynamic diameter of  $\leq 2.5 \mu m$ ;  $PM_{10}$ : particulate matter with aerodynamic diameter of  $\leq 10 \mu m$ ; CI: confidence interval.

Bold figures indicate statistically significant findings.



**Fig. 3.** Exposure-response curves for the associations of childhood pneumonia hospitalizations with  $PM_1$ ,  $PM_{2.5}$ , and  $PM_{10}$  concentrations. Solid lines indicate the relative risk and dashed lines are the corresponding 95% confidence interval.

they could have a high chance to be exposed to cooking OA and coal combustion OA. Considering that PM pollution is a ubiquitous threat to childhood respiratory health around the world, more investigations on ultra-fine PM and pneumonia including the mechanism behind the PM-health relationship are needed in other settings. This is because the results might be influenced by geographical disparities of background pollution level and socioeconomic status, therefore, resulting in a variation of sex- and age-specific effects of PM on childhood pneumonia across regions (Li et al., 2018; Qiu et al., 2014; Zhang et al., 2020a).

Partly due to the varying levels, sources, and chemical compositions of PM pollution in different seasons, PM effects on respiratory diseases have been reported to be greater in cold season than in warm season (Li et al., 2018; Zhang et al., 2020a). In the present study, we further divided a year into four seasons and found harmful PM<sub>1</sub> effects on

childhood pneumonia in both autumn and winter, whereas harmful PM<sub>2.5</sub> and PM<sub>10</sub> effects were evident only in autumn. In spite of the highest pollution level of PM in winter, local people in China have had an awareness of adverse health effects of particulate matter and take active protective measures such as wearing masks and stay at home in highly polluted days in winter, which could largely reduce or avoid the exposure to PM<sub>2.5</sub> and PM<sub>10</sub>. However, the adverse health effects of PM<sub>1</sub> have not been well perceived by people because there were a lack of relevant health research and no real-time reporting platform for PM<sub>1</sub> air pollution. Therefore, these preventive measures for PM<sub>2.5</sub> and PM<sub>10</sub> might not be relevant to PM<sub>1</sub>. Based on the evidence from the studies of source appointment and chemical compositions (Sun et al., 2013; Niu et al., 2020), staying at home might actually induce a higher risk of PM<sub>1</sub> because of coal combustions for heat as well as cooking. Compared with PM<sub>2.5</sub> and PM<sub>10</sub>, there may be a much easier migration of PM<sub>1</sub> from the ambient air into the interior space, increasing the exposure frequency to PM<sub>1</sub>. Conversely, the temperature in autumn is more comfortable than in winter, which motivates children to spend more time outside and expose themselves more frequently and longer to PM air pollution. As a negative health consequence, the risk of childhood pneumonia would be much higher in autumn than winter, as shown in this study. It is also possible that the sources for PM<sub>1</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> are different between autumn and winter, leading to inconsistent effects of particulate matter on childhood pneumonia hospitalizations. However, this hypothesis needs to be tested in future investigations.

We also observed an approximately linear relationship between PM<sub>1</sub> concentration and childhood pneumonia hospitalizations. This finding implies that childhood pneumonia can be affected by PM<sub>1</sub> not only at high concentrations but also at low concentrations. In reality, the distribution of daily PM<sub>1</sub> concentration is left skewed, suggesting there are more days with low PM<sub>1</sub> concentration than days with high PM<sub>1</sub> concentration. Therefore, it is necessary to take proactive measures to protect children's respiratory health even in low-level PM1 polluted days. Particularly, a previous study has found that even a low level of PM1 related carcinogenic PAHs (BaP and DahA) could result in longterm respiratory risk (Agudelo-Castañeda et al., 2017). This further implies the need of protecting short-term risk of respiratory health among children from days with low-level of PM<sub>1</sub>. In China, the government has already enacted air guality standards for PM<sub>2.5</sub> and PM<sub>10</sub> pollution and undertaken a series of measures (e.g. 2013 Air Pollution Prevention and Control Action Plan) to improve air quality, which plays an important role in lowering PM<sub>2.5</sub> and PM<sub>10</sub> concentration and mitigating associated health effects (Huang et al., 2018; Tian et al., 2019). Additionally, the China Atmosphere Watch Network (CAWNET) has established a routine monitoring network for PM<sub>1</sub> pollution across China. Based on this foundation, air quality standards as well as warning system could be set up based on the retrieved information from CAWNET in order to develop further action plans to improve air quality. Establishment of warning systems and air quality standards could also be based on accumulating evidence of deleterious PM1 effects on respiratory health (e.g., pneumonia and asthma) and other health outcomes (e.g. emergency department visits, cardiorespiratory mortality) (Zhang et al., 2020a, 2020b; Yin et al., 2020).

Unlike the linear expose-response association between  $PM_1$  and childhood pneumonia hospitalizations, the observed associations for  $PM_{2.5}$  and  $PM_{10}$  are somewhat non-linear. The reasons behind this heterogeneity may be multifaceted including but not limited to the differences in the population awareness or behaviors of protecting themselves in days polluted by different particulate matter, exposure level, and sources and toxicity of different particulate matters. In the case of the association of childhood pneumonia hospitalizations with  $PM_{10}$ , a similar exposure-response association shape was also found in a nationwide investigation of  $PM_{10}$  and adult pneumonia hospitalizations in China (Tian et al., 2019). We hypothesized that the increasing trend of  $PM_{10}$  effects at relatively low concentrations could be a result that

people did not perceive the risk of low-level of  $PM_{10}$  concentration. Before the  $PM_{10}$  concentration rose up to around 150 µg/m<sup>3</sup>,  $PM_{10}$  effects were stable, which may be due to a series of protection measures such as wearing masks and house ventilation. The rebound of  $PM_{10}$  effects (increasing trend) seemed to be related to the sporadic occurrence of heavily polluted days by  $PM_{10}$  (above 150 µg/m<sup>3</sup>) as shown in Fig. 1. The sudden occurrence of heavily polluted days by  $PM_{10}$  did not leave people enough time to take timely response actions, consequently contributing to increased risk of childhood pneumonia.

This study has several limitations. First, this is a single city research, which limits the extrapolation of our findings to other cities/regions with different characteristics. For instance, previous investigations revealed varied short-term PM effects on pneumonia hospitalizations by regional characteristics such as the background pollution level, economic and demographic patterns, and weather conditions (Tian et al., 2019). Second, as with many previous time-series studies, the ecological study design cannot prove the causal association between particulate matters and pneumonia hospitalizations (Tian et al., 2019; Xu et al., 2014). Third, we used air pollution data from fixed air pollution monitors and geographical interpolation technique to measure exposure level at the city-level, which may not be able to reflect PM exposure at individual-level. Thus, uncertainty of the exposure measurement cannot be excluded. Meanwhile, different data sources for PM<sub>1</sub>, PM<sub>25</sub>, and PM<sub>10</sub> may have caused uncertainties in comparing the effects of different PM fractions. More reliable comparison results could be achieved if data on PM<sub>1</sub>, PM<sub>2</sub>, and PM<sub>10</sub> could be from the same source such as the National Urban Air Quality Real-time Publishing Platform. Fourth, due to the issue of data availability, we were unable to examine the effects of chemical compositions of particulate matters, which warrants further investigation. Fifth, we only considered a limited number of confounders in regression model. Several potential confounders such as the influenza epidemics could be risk factors of pneumonia (Shrestha et al., 2015). The results of this study may be influenced after taking into account more confounders in the model. Sixth, due to the issue of data availability, we only collected data from one hospital. Future studies are needed to prove our findings using data from more hospitals.

## 5. Conclusion

Overall, this study suggests a larger impact of  $PM_1$  on childhood pneumonia than  $PM_{2.5}$  and  $PM_{10}$ . In addition, compared with  $PM_{2.5}$ and  $PM_{10}$  effects,  $PM_1$  effects appeared to be evident in more subgroups including boys and girls, children aged 4 years or younger as well as in more months within a year including autumn and winter. In view of persistent high or increasing level of PM pollution in China and many other rapid developing countries, it is necessary to further examine the effects of different PM, particularly the ultra-fine PM such as  $PM_1$ on childhood pneumonia.

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## **CRediT authorship contribution statement**

Xu Wang: Software, Formal analysis, Investigation, Resources, Writing – original draft. Zhiwei Xu: Investigation, Resources, Writing – original draft, Writing – review & editing. Hong Su: Project administration, Funding acquisition, Writing – review & editing. Hung Chak Ho: Formal analysis, Visualization, Writing – review & editing. Yimeng Song: Data curation, Writing – review & editing. Hao Zheng: Visualization, Writing – review & editing. Mohammad Zahid Hossain: Visualization, Writing – review & editing. Md Alfazal Khan: Visualization, Writing – review & editing. Daniel Bogale: Visualization, Writing – review & editing. **Heng Zhang:** Visualization, Writing – review & editing. **Jing Wei:** Methodology, Supervision, Data curation, Writing – review & editing. **Jian Cheng:** Conceptualization, Methodology, Data curation, Supervision, Project administration, Funding acquisition, Writing – review & editing.

# **Declaration of competing interest**

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

# Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.scitotenv.2021.145509.

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