



## POPULATION STUDY ARTICLE

# The association of ambient PM<sub>2.5</sub> with school absence and symptoms in schoolchildren: a panel study

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**BACKGROUND:** Children are a susceptible population to exposure of ambient fine particulate air pollution (PM<sub>2.5</sub>), and the associated symptoms are sensitive prevalent indicators of morbidity. However, few studies to date investigate the association between PM<sub>2.5</sub> exposure and school absence and symptoms.

**METHODS:** In a panel study including 20,291 observations in 615 schoolchildren 8–13 years of age, we asked the participants to record their school absence and symptoms on every school day from 17 November to 31 December 2014 in Jinan, China. We used the generalized linear mixed effects models to examine the adverse effects of ambient PM<sub>2.5</sub> on school absence and symptoms, adjusting for covariates including meteorological and individual factors.

**RESULTS:** The 3-day moving average of PM<sub>2.5</sub> was significantly associated with school absence (1.37; 95% CI: 1.07–1.74) and increases in symptoms of the throat (1.03; 95% CI: 1.00–1.05), nose (1.03; 95% CI: 1.01–1.06), and skin (1.09; 95% CI: 1.06–1.12). High PM<sub>2.5</sub> exposure also increased the risks of individual symptoms, especially for cough (1.02; 95% CI: 1.00–1.04), sneezing (1.03; 95% CI: 1.00–1.07), and stuffy nose (1.09; 95% CI: 1.02–1.17).

**CONCLUSION:** High PM<sub>2.5</sub> exposure is a risk factor for the health of schoolchildren. Allocation of medical resources for children should take into account the ambient PM<sub>2.5</sub> concentrations and be proportioned accordingly.

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## INTRODUCTION

Fine particulate air pollution (PM<sub>2.5</sub>) is associated with many acute adverse health effects, such as increased mortality, hospitalization, emergency, and outpatient rates, especially in respiratory and cardiovascular systems.<sup>1–3</sup> Children are a susceptible population, and existing studies have observed increases in adverse effects on children's respiratory systems.<sup>4–7</sup> Furthermore, compared to other vulnerable populations, such as patients with chronic respiratory disease, children are in the early stages of life and constitute a much larger proportion of the population. Thus, the health of children has a greater impact on health as a whole. However, most existing time-series and case-crossover studies lack individual-level data,<sup>4,5</sup> and the outcomes are often generalized, such as hospital admissions, lung function, and exhaled nitric oxide (FeNO).<sup>4–7</sup> Children with mild symptoms may not even have hospital records, and symptoms can vary daily, making them more sensitive prevalent indicators of morbidity than disease prevalence.<sup>8,9</sup> Panel studies of acute symptoms associated with PM<sub>2.5</sub> can be useful for establishing causal relationships, which makes these studies particularly important and relevant for public health.<sup>8,10</sup>

Several recent panel studies have focused on investigating the association between PM<sub>2.5</sub> exposure and absence or related symptoms in populations other than children, such as COPD patients.<sup>11,12</sup> Although some panel studies are focused exclusively on children, most of these studies only focus on children with

asthma.<sup>8,13</sup> Furthermore, the results from such studies are not consistent. Positive associations were found between PM<sub>2.5</sub> exposure and school absence in one study,<sup>14</sup> but most studies found null effects of PM<sub>2.5</sub>.<sup>8,11,12</sup> In addition, most of these studies reported cases in the United States and Europe, with relatively low concentrations and narrow ranges of PM<sub>2.5</sub>.<sup>8,11,14</sup> In comparison, PM<sub>2.5</sub> concentrations in China can be of the order of magnitudes higher than that of the Western countries,<sup>15</sup> such as 27–298 µg/m<sup>3</sup> observed in Jinan from 01 November to 31 December, 2014. As some of the studies were conducted with relatively small sample sizes, they may lack statistical power and their predictabilities may be restricted.<sup>8,11,12</sup> The outcomes of these studies were usually focused on respiratory symptoms, such as cough, sore throat, and sputum,<sup>8,11,12</sup> without concern for other more sensitive symptoms such as itchy skin. The statistical models used in most of the studies were generally appropriate and effective.<sup>8</sup>

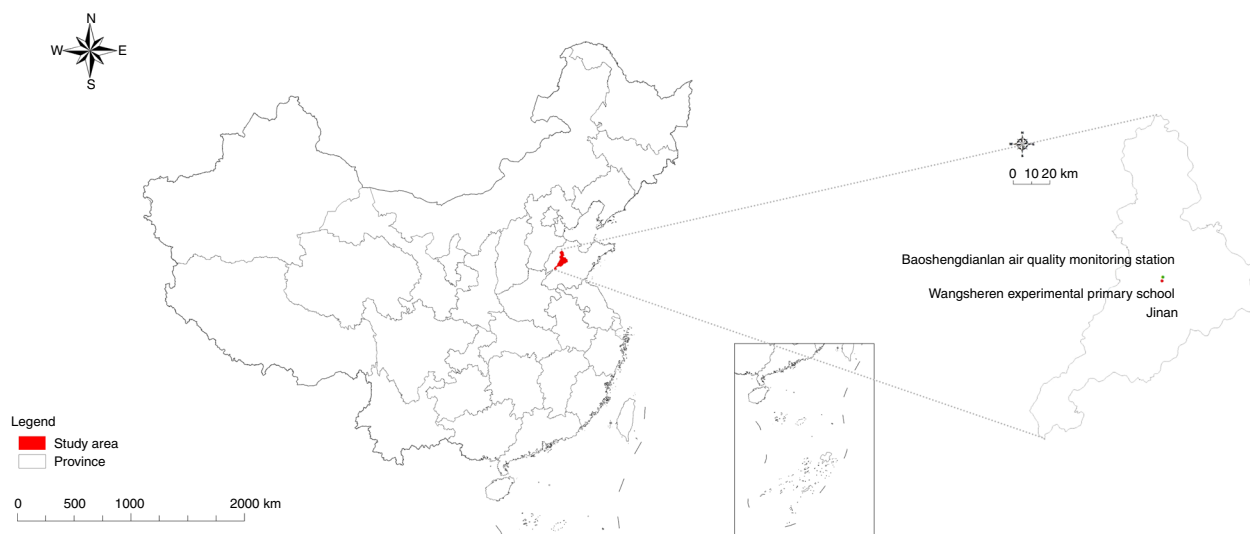
The key aim of this study is to conduct a panel study in an area with high PM<sub>2.5</sub> concentration, and explore the association between PM<sub>2.5</sub> exposure and respiratory (throat and nasal cavity)/skin/eye symptoms, fever, and school absence of children (primary school students). The results of this study will provide evidence of the adverse effects associated with PM<sub>2.5</sub> among schoolchildren and will also provide clues to choices of symptoms for improving symptom surveillance in primary school under high PM<sub>2.5</sub> pollution scenarios.

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**Fig. 1** Map of the study area, including the location of the air quality monitoring site and the school

## METHODS

### Subject and health outcome data collection

We conducted an individual-level panel study (longitudinal study) involving exposure and related symptom monitoring over a 6-week period from 17 November to 31 December 31, 2014, on school days at Wangsheren Experimental Primary School located in Jinan City, China. The school was more than 150 m away from the main traffic intersections (two-way four lanes) and had not been renovated in the last 5 years.

Study participants were recruited through classroom presentations in Grades 3–5. There are 649 children in the three grades (12 classes) in total. Each child's legal guardian provided informed consent, and the children who had a written assent from their guardians were recruited. The children completed a basic information questionnaire and daily diaries under the guidance of their guardians. Every week, the teachers delivered the diaries to each child. Every evening, the children filled the diaries and handed them to their teachers on the following day. If the child was absent the next day, he/she would hand over the diaries as soon as they returned to school. They were given a gift (worth about 50 CNY) at the end of the diary period.

Baseline information was collected before the completion of the daily diaries, which included sex, birth date, height, weight, second-hand smoke exposure, pet keeping, use of purifiers, asthma status, etc. Daily dairies included questions on absence, fever, cough, sputum, sore throat, tears, sore/red/itchy eyes, runny/itchy/stuffy nose, nose bleed, sneeze, rash, and itchy skin.

### Air quality and meteorological data collection

We obtained hourly ambient PM<sub>2.5</sub>, ozone, SO<sub>2</sub>, and NO<sub>2</sub> concentrations from Baoshengdianlan Air Quality Monitoring Station, which was specifically selected because it was near the study location (2.3 km). Daily ambient temperature and humidity data were obtained from the Jinan Municipal Bureau of Meteorology. We converted the hourly PM<sub>2.5</sub>, ozone, SO<sub>2</sub>, and NO<sub>2</sub> concentrations into daily average values. Most children lived around the school (mean ± SD: 1.9 ± 2.0 km) and are also not far from the air quality monitoring station (mean ± SD: 3.8 ± 1.9 km). The location of the air quality monitoring station and the school is shown in Fig. 1.

### Statistical analysis

We performed statistical modeling using the lme4 package in R version 3.2.3; the results with  $p < 0.05$  were considered statistically

significant, except the test for normality ( $p < 0.10$ ). Daily symptom sums were added by category. For example, individual symptoms of the throat included cough, sputum, and sore throat. If any of these symptoms occurred, it would be recorded as 1, and the sum of throat symptoms would be the sum of all individual symptoms. Observations from all grades were combined. A generalized linear mixed effects model was used to estimate the magnitude of association between PM<sub>2.5</sub> concentrations and the symptoms or absence incidence.<sup>8</sup> The symptoms were matched with pollutants and meteorological data by date. Subjects were included in the models as random intercept terms to control the random effect of repeated measurements. Because of the temporal correlation among outcomes within subjects, the autoregressive covariance variables were made and included in the models. We selected additional covariates based on an extensive review of the literature and group discussion. Other considered covariates included daily temperature (continuous variable),<sup>6,14</sup> daily humidity (continuous variable),<sup>6</sup> day of the week (categorical variable),<sup>14</sup> sex (binary variable),<sup>6</sup> age (continuous variable),<sup>6</sup> body mass index (BMI) (continuous variable),<sup>6</sup> second-hand smoking (binary variable),<sup>16</sup> pet keeping (binary variable),<sup>17</sup> and use of purifiers (binary variable).<sup>18</sup> Because the study period was only in the winter, we introduced temperature into the model without using a spline function. Since previous studies have reported the effects of PM<sub>2.5</sub> not only on the same day but also on several following days,<sup>12</sup> the effects at multiple lags of exposure from the same day (lag0) and 3-day moving averages (lag0–3) were examined. Odds ratios (ORs) and 95% confidence intervals (CIs) associated with a 10- $\mu\text{g}/\text{m}^3$  increase in PM<sub>2.5</sub> concentration were reported.

After establishing the main models, we sequentially introduced 8-h average ozone concentration, SO<sub>2</sub>, NO<sub>2</sub>, kitchen ventilator, and asthma into the regression model one by one as sensitivity analysis.

## RESULTS

Summary characters for exposure and study population data During the study period, the daily average PM<sub>2.5</sub> concentrations ranged from 29 to 191  $\mu\text{g}/\text{m}^3$ . Daily mean temperature ranged from -2.9 to 12.6 °C (Table 1).

A total of 615 children (94.8%) were recruited into the panel study, including 46.3% girls. A total of 20,291 daily diaries were completed, among which 613 children filled 33 diaries continuously (except Saturday and Sunday), and the other two children

**Table 1.** Summary statistics of the daily average of the air pollution and meteorological data

Variables	Mean	SD	Min	P25	P50	P75	Max
Temperature (°C)	3.85	4.32	-2.9	0.2	3	6.9	12.6
Humidity (%)	42.8	17.8	21	31	39	48	94
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	86.2	37.5	29	58	82	103	191
O <sub>3</sub> (µg/m <sup>3</sup> )	20.6	12.1	6	13	18	24	60
SO <sub>2</sub> (µg/m <sup>3</sup> )	86.7	32.4	31	63	88	108	163
NO <sub>2</sub> (µg/m <sup>3</sup> )	68.1	17.6	28	58	66	80	113

**Table 2.** Study population characteristics

Variables	N	Mean ± SD or percent
Sex	615	100.0
Boy	330	53.7
Girl	285	46.3
Age	614	9.6 ± 0.9
BMI	615	18.9 ± 4.7
Second-hand smoking	615	100.0
YES	158	25.7
NO	457	74.3
Pet at home	615	100.0
YES	74	12.0
NO	541	88.0
Purifier in home	615	100.0
YES	74	12.0
NO	541	88.0

filled 31 diaries. The completion rate of the diaries is 99.98%. The children were aged 8–13 years (Table 2).

During the study period, 5.69% of the subjects and 0.26% diaries reported absence, and 67.64% of the subjects and 13.87% diaries reported at least one of the symptoms. More than half of the subjects reported throat or nose symptoms (59.84% and 55.61% of the subjects reported at least 1 throat and nose symptom over the entire study period, respectively), among which cough was the most frequently reported symptom. About 57.56% of the subjects reported cough at least once (Table 3). As the sums of symptoms in certain categories increased, the number of children in those categories decreased (Table 3).

#### Associations between ambient PM<sub>2.5</sub> and health outcomes

The 3-day moving average of PM<sub>2.5</sub> was significantly associated with absence, with an OR of 1.37 (95% CI: 1.07–1.74) per 10 µg/m<sup>3</sup>. However, the association between PM<sub>2.5</sub> and fever was null (1.04; 95% CI: 0.90–1.19) (Fig. 2).

The increase in the 3-day moving average of PM<sub>2.5</sub> per 10 µg/m<sup>3</sup> was significantly associated with symptoms of the nose (1.05; 95% CI: 1.00–1.09). The 3-day moving average of PM<sub>2.5</sub> was also significantly associated with the increase in the symptoms of throat (1.03; 95% CI: 1.00–1.05), nose (1.03; 95% CI: 1.01–1.06), and skin (1.09; 95% CI: 1.06–1.12) (Fig. 2). However, there was no statistically significant association between PM<sub>2.5</sub> and the symptoms of the eye (0.99; 95% CI: 0.92–1.08).

A 10-µg/m<sup>3</sup> increase in the same-day average PM<sub>2.5</sub> concentration was associated with cough (1.02; 95% CI: 1.00–1.04) and sneezing (1.03; 95% CI: 1.00–1.07) (Fig. 2). The 3-day moving average of PM<sub>2.5</sub> was significantly associated with stuffy nose, with an OR of 1.09 (95% CI: 1.02–1.17). However, there was no

**Table 3.** Summary of study outcomes

Variable	Number of persons (n)	Percent	Number of reports (n)	Percent
Absence	35	5.69	52	0.26
Symptom	416	67.64	2812	13.86
Symptoms category				
Fever	56	9.11	142	0.70
Throat sums				
1	316	51.38	1432	7.06
2	164	26.67	614	3.03
3	63	10.24	220	1.08
Nose sums				
1	292	47.48	1035	5.10
2	183	29.76	636	3.13
3	87	14.15	252	1.24
4	28	4.55	109	0.54
5	5	0.81	12	0.06
Eye sums				
1	66	10.73	224	1.10
2	14	2.28	52	0.26
Skin sums				
1	16	2.60	62	0.31
2	1	0.16	8	0.04
Specific symptoms				
Throat	368	59.84	2266	11.17
Cough	354	57.56	2102	10.36
Sputum	176	28.62	797	3.93
Sore throat	128	20.81	421	2.07
Nose	342	55.61	2044	10.07
Runny	294	47.80	1652	8.14
Itchy	81	13.17	321	1.58
Stuffy	154	25.04	638	3.14
Bleed	44	7.15	85	0.42
Sneeze	190	30.89	863	4.25
Eye	68	11.06	276	1.36
Tears	48	7.80	170	0.84
Others (sore/red/itchy)	37	6.02	158	0.78
Skin	16	2.60	70	0.34
Rash	2	0.33	13	0.06
Itchy	15	2.44	65	0.32

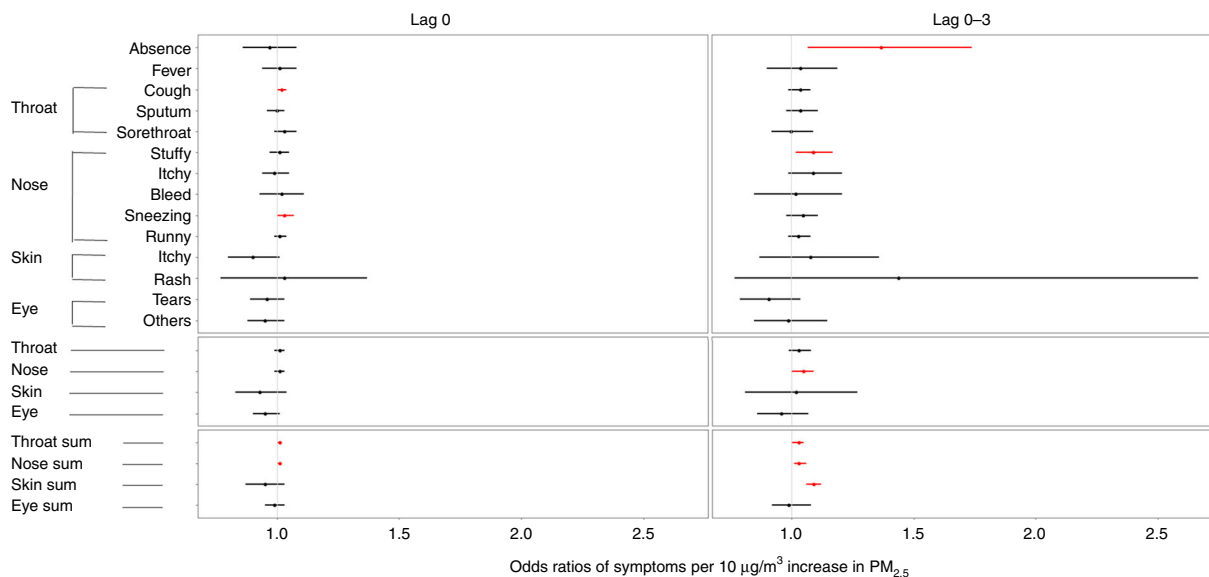
statistically significant association between PM<sub>2.5</sub> and sputum, sore throat, itchy nose, nose bleed, runny nose, itchy skin, skin rash, tears, and other symptoms of the eye. The stratification analysis result focusing on boys and girls is shown in the Supplemental file (Table S1).

#### Sensitivity analysis

When we introduced the 8-h average ozone concentration, SO<sub>2</sub>, NO<sub>2</sub>, kitchen ventilator, and asthma one by one into the main regression models, we found that all models produced similar effect estimates (Supplemental file, Table S2 and Table S3).

#### DISCUSSION

Our study focused on the risk of symptoms among children due to PM<sub>2.5</sub> in the context of the elevated levels of air pollution currently



**Fig. 2** Estimated ORs with 95% CI for symptoms with 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration at various lags of exposure. The effects with the red color are statistically significant

in China. To our best knowledge, this is the first study of PM<sub>2.5</sub> to focus on the symptoms related to the skin and eye, in addition to respiratory symptoms. Furthermore, by calculating the symptom sums of different categories, we aimed to examine the severity of these effects. We found adverse effects of PM<sub>2.5</sub> on absence and related symptoms in children. The effects of PM<sub>2.5</sub> were significant for cough and stuffy nose, and the adverse effects lasted for several days.

There are no reports for the association between absence and related symptoms under the high exposure of PM<sub>2.5</sub> in children. However, our findings regarding the association between absence and 3-day moving average PM<sub>2.5</sub> are consistent with the study by Hales et al., which demonstrated that school absence is associated with PM<sub>2.5</sub> exposures in populations not limited to schoolchildren.<sup>14</sup> However, their estimated OR (1.062; 95% CI: 1.060–1.063) was lower than that of our results. Since we use data from a panel study other than the surveillance data of absence in the study of Hales, we controlled a number of confounders, including sex, age, BMI, exposure to second-hand smoking, pet keeping, and the use of purifiers. This may be the reason of the inconsistency between their result and ours. There is another study similar to ours that focused on high school students with a relatively narrow range of PM<sub>2.5</sub> concentration (4.5–49 µg/m<sup>3</sup>), and their findings are null. This may be due to the low levels of air pollutants in the U.S. In our study, the association between PM<sub>2.5</sub> and sum of the symptom categories suggests that the increase in PM<sub>2.5</sub> concentration might cause more severe symptoms of the throat.<sup>8</sup>

Additionally, we found associations between PM<sub>2.5</sub> and stuffy nose, which was another important symptom of the respiratory system missed in other studies. Based on the association for sum of the symptom category in our study, the increase in PM<sub>2.5</sub> concentration was associated with more severe symptoms of the throat, nose, and skin. The null findings for associations with specific skin symptoms may be attributable to low incidence as well as recall bias, which are the common limitations of the survey data for children panels. Our studies also monitored eye symptoms, which had no statistically significant association with PM<sub>2.5</sub>.

Several mechanisms may explain why the increase in PM<sub>2.5</sub> concentration is related to the risk of school absence and related

symptoms in children. PM<sub>2.5</sub> is a mixture of constituents from multiple sources, including but not limited to black, elemental and primary and secondary organic carbon, secondary inorganic aerosols, transition metals, and metal compounds.<sup>19</sup> These components of PM<sub>2.5</sub> could stimulate the respiratory tract and the eye mucosa, leading to acute inflammatory response.<sup>20–23</sup> PM<sub>2.5</sub> is associated with inflammatory cytokines, and stimulates the overexpression of transcription factor genes and inflammation-related cytokine genes, which also leads to inflammatory response.<sup>24</sup> PM<sub>2.5</sub> also directly induces inflammation, leading to an increase in the number of neutrophils.<sup>25,26</sup> Existing studies found that PM<sub>2.5</sub> affected the human alveolar macrophages expressing high levels of M1-associated cytokines and low levels of M2-associated cytokines.<sup>27–29</sup> M1 polarized alveolar macrophages are mainly induced by Th1-type cytokines (IL-12, IFN-γ) and pathogens *in vivo*, and promote inflammation. M2 polarized alveolar macrophages are closely related to Th2-type cytokines (IL-4 and IL-13) and immunoregulatory cytokines (IL-10), and primarily inhibit inflammation.<sup>30</sup> In addition, PM<sub>2.5</sub> disrupts intracellular calcium homeostasis. Calcium is one of the important secondary messengers that mediate and regulate the physiology and pathology of the cellular functions. Abnormally high calcium concentrations activate a series of inflammatory responses that cause inflammation and cell damage.<sup>31</sup> Furthermore, ROS-mediated regulation of intracellular Ca<sup>2+</sup> concentration may be one of the mechanisms of PM<sub>2.5</sub>-induced cell damage.<sup>32</sup> There were lag effects on the absence and symptoms because inflammation is a process that takes time to recover.

Because PM<sub>2.5</sub> concentration is associated with school absence and symptoms among schoolchildren, there are several suggestions for the authorities. First and foremost, authorities should concentrate on reducing the exposure levels of PM<sub>2.5</sub>. In addition, more strategies will be necessary to protect schoolchildren, such as health education for protection from PM<sub>2.5</sub> pollution, delivering free masks for children, and installing fresh air systems in schools. Furthermore, since more children would have symptoms on and after the days of PM<sub>2.5</sub> pollution and some may go to clinics and hospitals, the medical resources for children should be increased accordingly with the increase in PM<sub>2.5</sub> concentration, especially more number of pediatric pulmonary physicians. The increase can be achieved by mobilizing doctors from other types of hospitals to

children's hospitals or related departments, or by providing additional training for general practitioners. Finally, to improve absence surveillance in primary schools, in addition to considering respiratory symptoms, skin symptoms should be considered as well.

Our study has several strengths. First, we used a longitudinal panel study design to repeatedly measure PM<sub>2.5</sub> and health outcomes. Each subject served as his or her own control, thus the confounding from between-subject differences such as genetic susceptibility was minimized, and the statistical power to detect the health effects was high. Second, our study focused on children, a susceptible population with some of the highest potential impacts from air pollution. Third, the health outcomes of our study were symptoms, which are more sensitive than disease morbidity and would be undetected at clinical levels. Fourth, our study was the first to monitor the symptoms of the skin and eye, and the results provide initial insights into the adverse effects of PM<sub>2.5</sub> on other body systems in addition to the respiratory system. Fifth, the ambient PM<sub>2.5</sub> concentration observed in the study was high and allowed us to detect more significant effects.

Our study also has a number of limitations. First, PM<sub>2.5</sub> concentration data were obtained from an outdoor monitor station rather than based on individual exposure, and therefore the exposures of the children were assumed to be the same. However, we controlled the factors that may have caused the exposure to vary by introducing second-hand smoking, purifier use, and pet keeping into the model. Second, we do not have PM<sub>2.5</sub> component data available, which would provide more detailed analysis of the adverse effects. Third, the survey was from one school, and the generalizability of the findings may be limited. However, we recruited almost all students in the school from Grade 3 to 5, and the large number of subjects may attenuate this limitation. Fourth, the children were not asked to fill in the daily diaries on Saturday and Sunday, and it avoided recall bias but undermined the continuity of the study. Additionally, we modified the impact of missing values of the weekend by introducing 3-day autocorrelations of the symptoms into the model. Fifth, we did not collect the information of medication use in our survey. However, we did consider asthma as a covariate, and introduced it as a binary variable into our main model as part of our sensitivity analysis. In this model, the estimated value of the OR is similar to that of the main model.

## CONCLUSION

High PM<sub>2.5</sub> exposure is a risk factor for adverse symptoms of schoolchildren. PM<sub>2.5</sub> was associated with school absence and symptoms of the respiratory system. The adverse effects were present in the throat and nose, and cough and stuffy nose were the common symptoms. The increase in PM<sub>2.5</sub> concentration may cause more severe symptoms in children. Under high PM<sub>2.5</sub> exposure, more strategies will be necessary to protect schoolchildren. In addition, medical resources for children should be increased accordingly with the increase in PM<sub>2.5</sub> concentration. To improve symptoms surveillance in primary schools, in addition to the respiratory symptoms, skin symptoms should be considered as well. Future studies should focus on individual exposure in different seasons and consider the multi-center studies for better generalizability of the results.

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## ADDITIONAL INFORMATION

The online version of this article (<https://doi.org/10.1038/s41390-018-0004-1>) contains supplementary material, which is available to authorized users.

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