Acute effects of ambient PM$_{2.5}$ on lung function among schoolchildren

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Previous studies have found that fine particulate matter (PM$_{2.5}$) air pollution is associated with decreased lung function. However, most current research focuses on children with asthma, leading to small sample sizes and limited generalization of results. The current study aimed to measure the short-term and lag effects of PM$_{2.5}$ among school-aged children using repeated measurements of lung function. This prospective panel study included 848 schoolchildren in Zhejiang Province, China. Each year from 2014–2017, two lung function tests were conducted from November 15th to December 31st. Daily air pollution data were derived from the monitoring stations nearest to the schools. A mixed-effects regression model was used to investigate the relationship between PM$_{2.5}$ and lung function. The effect of PM$_{2.5}$ on lung function reached its greatest at 1-day moving average PM$_{2.5}$ exposure. For every 10 $\mu$g/m$^3$ increase in the 1-day moving average PM$_{2.5}$ concentration, Forced Vital Capacity (FVC) of children decreased by 33.74 mL (95% CI: 22.52, 44.96), 1-s Forced Expiratory Volume (FEV$_1$) decreased by 32.56 mL (95% CI: 21.41, 43.70), and Peak Expiratory Flow (PEF) decreased by 67.45 mL/s (95% CI: 45.64, 89.25). Stronger associations were found in children living in homes with smokers. Short-term exposure to PM$_{2.5}$ was associated with reductions in schoolchildren's lung function. This finding indicates that short-term exposure to PM$_{2.5}$ is harmful to children’s respiratory health, and appropriate protective measures should be taken to reduce the adverse effects of air pollution on children’s health.

Air pollution is a major global concern and causes a variety of health problems, such as increased mortality, hospitalization, and outpatient visits, especially for cardiovascular and respiratory diseases$^{1–4}$. Fine particulate matter (PM$_{2.5}$) is one of the main components of air pollution. Because children are at a crucial stage of growth and development, they are particularly vulnerable to air pollution$^{5,6}$. The adverse effects of PM$_{2.5}$ air pollution on children’s health have been reported in many studies$^{6–8}$, with lung function serving as an effective indicator of early lung disease$^9$. By analyzing the relationship between PM$_{2.5}$ and lung function in children, we can better understand the effects of PM$_{2.5}$ air pollution on children’s respiratory health.

Previous studies have found an association between PM$_{2.5}$ air pollution and decreased lung function$^{10–13}$. However, most researchers have focused on children with asthma, creating a small sample size and limiting the extrapolation of results$^{10,12,14}$. In addition, these studies primarily have been carried out in developed countries with low levels of air pollution; developing countries with high levels of air pollution have been comparatively less studied. Another limitation of the current body of literature rests on the fact that most studies have focused on a single lung function indicator, not on multiple lung function indicators simultaneously$^{11,14,15}$. Finally, it must be noted that lung function is affected by various factors, such as age, gender, and disease state; however, the modification effects of these factors on the relationship between PM$_{2.5}$ and lung function remain ambiguous$^{10–12}$. Due to these shortcomings, it is possible to state that the impact of PM$_{2.5}$ pollution on lung function in children has yet to be fully and accurately understood.

This study sought to explore the short-term and lag effects of PM$_{2.5}$ among school-aged children using repeated measurements of lung function including Forced Vital Capacity (FVC), 1-s Forced Expiratory Volume (FEV$_1$), and Peak Expiratory Flow (PEF). We also considering the modification effects of other factors. These results can serve as a scientific basis demonstrating the harm of PM$_{2.5}$ to children’s respiratory health, creating a catalyst for protecting children’s health.

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Methods

Study population and design. This prospective panel study was conducted in Zhejiang Province, located in eastern China. Three cities were chosen for investigation: Jinhua, Lishui, and Zhoushan. Jinhua is located in the middle of Zhejiang Province and is hill-and-basin in landform. Lishui is located in the southwest of Zhejiang Province and is mainly in mountainous and hilly terrain. Zhoushan is an island city located in the northeast of Zhejiang Province. These three cities have good representation in Zhejiang Province. We selected 1–2 primary schools within 2 km of national air pollution monitoring stations before recruiting primary school students in grades 3–5 to fill in questionnaires and undergo lung function tests. In each school, 50 students were randomly selected from each grade, and a total of 150 students were surveyed each year. The questionnaires were completed by students and their parents. From 2014–2017, we conducted questionnaire surveys and lung function tests from November 15th to December 31st each year, during which time the particulate matter air pollution was serious. Table S1 indicates the number of participants and the number of lung function measurements in each city. Each year we recruited new students in grade 3, and students who progress to grade 6 left the study. So some students measured their lung function 6 times, while other students only measured it once or twice. We measured lung function on a total of 1,245 individuals one to six times and collected 3,418 lung function measurements. Because the lung function data involves repeated measurement, we used a linear mixed-effects regression model for data analysis and extracted data with more than 2 lung function measurements. Following this step, data analysis included 848 students with a total of 3,021 lung function measurements.

Ethics statement. The study was approved by the Medical Ethics Committee of the Zhejiang Provincial Center for Disease Control and Prevention. The research was conducted in accordance with the Declaration of Helsinki. Participants enrolled in this study and their parents gave written informed consent for participation.

Data collection. Lung function measurement. Lung function tests were performed in schools, and the rooms used for testing were relatively independent, quiet, bright, clean, and temperature-friendly. Tests were conducted by local medical staff who are responsible for lung function measurement in hospitals or physical examination centers using the same electronic spirometer (SPirOAnalyzer ST-75, FUKUDA SANGYO, Japan). From November 15th to December 31st each year, lung function was measured twice in Jinhua and Lishui, once in November and once in December; in Zhoushan, lung function was measured once during this period each year, because Zhoushan is an island city, less air pollution. All lung function tests were conducted in the morning and according to published standards16. Before measuring lung function, the electronic spirometer was calibrated according to changes in temperature, humidity, and atmospheric pressure. Then, the children's parameters were put into the electronic spirometer, including age, sex, height, and weight. With the participant standing and wearing a nose clip, pulmonary function tests were repeated in order to obtain at least three reproducible forced expiratory flow curves. Lung function indicators included FVC, FEV1, and PEF.

Air pollution data. Daily air pollution data from January 1, 2014 to December 31, 2017 were derived from the fixed-site monitoring stations of the National Air Pollution Monitoring System. We selected the monitoring stations nearest to the schools (Fig. 1). Air pollution indicators included PM2.5, sulfur dioxide (SO2), nitrogen dioxide (NO2), carbon monoxide (CO), and daily 8-h maximum ozone (O3–8h).

Covariates. Participants’ basic information, including family situation, lifestyle, living environment, and disease history, was obtained via questionnaires completed by the students and their parents. To control for the influence of meteorological factors on lung function, we also obtained data regarding the daily mean temperature and relative humidity from January 1, 2014 to December 31, 2017. We collected this information for each city from China’s Meteorological Administration’s data network. Our analysis included the following covariates: age (continuous), sex (boys, girls), height (continuous), weight (continuous), passive smoking status (yes, no), asthma (yes, no, we determined asthma status through question “Have you been diagnosed with asthma by a doctor?” in the questionnaire.), father’s education level (primary school and below, junior high or high school, college and...
above), whether the family uses natural gas for cooking (yes, no), whether the family uses air purifiers at home (yes, no), temperature (continuous), and relative humidity (continuous).

**Statistical analysis.** We used a mixed-effects regression model with study participants and districts as random effects in order to investigate the relationship between PM$_{2.5}$ and lung function\textsuperscript{17}. The effect estimates were expressed as the increase in lung function per 10$\mu$g/m$^3$ increase in PM$_{2.5}$ concentration. The mixed-effects model was constructed using Eq. (1).

$$Y_{ijk} = \beta_0 + \beta_1 \text{PM}_{2.5} + \beta_2 X_{1ijk} + \cdots + \beta_n X_{njik} + \xi_j + \xi_k + e_{ijk};$$

where $Y_{ijk}$ represents the lung function indicators (FVC, FEV$_1$, PEF); $\beta_0$ is the overall intercept; $\beta_1$ is the regression coefficient for PM$_{2.5}$; $\beta_2$ ... $\beta_n$ are the regression coefficients for the covariates in the model; $\xi_j$ is the random effect for the study participant; $\xi_k$ is the random effect for the study district; $j$ represents the study participant; $k$ represents the study district; $i$ identifies the workday; and $e_{ijk}$ is the residual error term.

Using the model, we measured exposure to PM$_{2.5}$ concentration at the current day (lag0) and at period lags (lag01, lag02, lag03, lag04, lag05). For example, lag01 would be the 1-day moving average PM$_{2.5}$ exposure (the average PM$_{2.5}$ concentration of the current day and 1 day before lung function measurement). Two-pollutant models were used to adjust for the potential confounding effects of co-pollutants. After correlation analysis, CO or O$_3$–8h was adjusted for in the two-pollutant models.

We also performed stratified analyses by sex (boys, girls), smoking at the child’s home (yes, no), asthma (yes, no), whether the family uses natural gas for cooking (yes, no), and whether the family uses air purifiers at home (yes, no) in order to explore the association between 1-day moving average PM$_{2.5}$ exposure and lung function indicators.

The following statistical formula was used to calculate whether or not the differences between groups were statistically significant ($P < 0.05$, Eq. 2).

$$ (b_1 - b_2) \pm 1.96 \times \sqrt{SE_1^2 + SE_2^2}; $$

Where $b_1$ and $b_2$ are the effect estimates of the two groups, and $SE_1$ and $SE_2$ are the standard errors of the two effect estimates, respectively.

Sensitivity analyses were performed to test the robustness of the results. We added a confounding factor (whether the participant’s home had pets) in the analysis model. In addition, we restricted data analysis to participants who did not have asthma and who did not use an air purifier at home.

All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant. Data analysis was performed using R version 3.5.1 software and the lme4 package.

**Results**

**Characteristics of study participants.** Table 1 illustrates the characteristics of the study population. A total of 848 participants and 3,021 lung function measurements were included in data analysis. The average age of the students was 9.74 years, with boys and girls accounting for 53.30% and 46.70% respectively. The percentage of children exposed to second-hand smoke was high at 59.28%. Households using natural gas accounted for 14.98%, and a few households used air purifiers, accounting for only 9.91%. There were very few students with asthma, only 2.12%.

**Results of descriptive data analysis and correlation analysis.** The results of our descriptive analysis, including lung function, daily air pollution, and daily meteorological data were shown in Table 2. The table
presents the means, standard deviations, minimums, quartiles, medians, and maximum measurements for lung function indicators, air pollution data, and meteorological data. The PM2.5 concentration was 67.58 ± 41.76 μg/m³, it is much higher than the World Health Organization’s ambient air quality guidelines for 24-h average PM2.5 of 25 mg/m³, but lower than the Chinese ambient air quality guidelines of 75 mg/m³. The minimum and maximum concentration was 9.00 μg/m³ and 156.00 μg/m³, respectively. Descriptive statistics on air pollution data for each city are shown in Table S2.

Table S3 shows the correlation coefficients between daily mean measures of outdoor air pollution, temperature, and relative humidity. There were high positive correlations between PM 2.5, SO2, and NO2, and the correlation coefficient between PM2.5 and SO2 was the largest at 0.85 (P < 0.001). O3–8h was negatively correlated with these pollutants. The correlation coefficient between temperature, relative humidity, and these air pollutants was small (P > 0.05).

Effects of PM2.5 on lung function. Figure 2 shows the changes in lung function per 10μg/m³ increase in PM2.5 concentrations on the current day as well as the moving average exposure. A 10μg/m³ increase in the current day PM2.5 concentration corresponded to a decrease in 25.45 mL (95% CI: 14.94, 35.96) FVC, 22.01 mL (95% CI: 11.55, 32.47) FEV1, and 37.96 mL/s (95% CI: 17.80, 58.13) PEF. When exposed to the 1-day moving average PM2.5 concentration before lung function measurement, children demonstrated the largest changes in lung function, with a 33.74 mL (95% CI: 22.52, 44.96) decrease in FVC, a 32.56 mL (95% CI: 21.41, 43.70) decrease in FEV1, and a 67.45 mL/s (95% CI: 45.64, 89.25) decrease in PEF.

Results of two-pollutant models. Table 3 shows the results of the two-pollutant modes. The correlation coefficients between PM2.5 and SO2, and between PM2.5 and NO2 were very high, which may indicate problems of multi-colinearity. As a result, we only included CO and O3–8h in the two-pollutant model for data analyses. In two-pollutant models with CO or O3–8h, the PM2.5 effect remained significant (P < 0.05), and the effect values changed little when compared to those of the single-pollutant model.
Results of stratified analyses. Figure 3 presents the results of stratified analyses. The results stratified by sex revealed that PM$_{2.5}$ more strongly affected FVC and FEV$_1$ for boys than for girls. The effect on PEF was weaker on boys than girls, but these differences were not statistically significant. When stratified by passive smoking status, no significant PM$_{2.5}$ effects were observed for the non-passive smoking group. However, for children who are exposed to second-hand smoke, there was a reduction of 53.12 mL (95% CI: 33.76, 72.49) in FVC, a reduction of 54.80 mL (95% CI: 35.61, 73.98) in FEV$_1$, and a reduction of 110.12 mL/s (95% CI: 75.36, 144.89) in PEF for each increase of 10 $\mu$g/m$^3$ in the 1-day moving average PM$_{2.5}$ concentration. The differences between the two groups (exposed to passive smoking and not) were statistically significant ($P < 0.05$). When stratified by asthma status, no significant PM$_{2.5}$ effects were observed for FVC and FEV$_1$ in the group of asthmatics, but there was a greater effect for PEF compared to the group of non-asthmatics. When we stratified based on the use of natural gas and air purifiers, we found no significant differences between these subgroups in terms of PM$_{2.5}$ effects ($P > 0.05$).

Results of sensitivity analyses. The results of sensitivity analyses were shown in Table S4. When we added the confounding factor (whether the participant’s home had pets) into the analysis model, the effect value of PM$_{2.5}$ on lung function was similar to the result found in the primary model analysis. When restricting data analysis to participants who did not have asthma and who did not use an air purifier at home, the effect value also changed little compared to the main model. These results indicate stability in our main model.

Discussion

Based on repeated lung function measurements among primary school students in Zhejiang, we found that short-term exposure to PM$_{2.5}$ was associated with reductions in lung function indicators. In addition, the effects of PM$_{2.5}$ on lung function had significant lag effects, with the largest effect occurring on the 1-day moving average PM$_{2.5}$ exposure. Based on the stratified analyses, our results indicate that children exposed to second-hand smoke were more sensitive to the effects of PM$_{2.5}$. Sex, asthma status, the use of natural gas, and air purifiers did not affect the relationship between PM$_{2.5}$ and lung function.

Our study found that an increase in the current day PM$_{2.5}$ concentration was associated with a statistically significant decrease in lung function indicators, indicating that PM$_{2.5}$ can affect children’s lung function in a short amount of time. Similar findings have been found in previous studies. A panel study with 309 children conducted in Brazil found that, for an increase of 10 mg/m$^3$ in same-day PM$_{2.5}$ exposure, there was an average reduction of 0.26 l/min (95% CI: 0.49, 0.04) in the PEF. Another Japanese study found that increased 24-hour mean concentrations of PM$_{2.5}$ were associated with a decrease in both morning and evening PEF.
two-pollutant models with O3, NO2, and SO2. In our study, the correlations between PM2.5 and SO2, and between
in Seattle reported adverse effects from centrally-monitored PM2.5 on the FEV1 of children with asthma, but
results by noting that asthmatic subjects may take medication when air quality deteriorates11. A study conducted
lag1 day demonstrated less significant effects on lung function than lag1 day13, results that mirror the current study.
lag2 day exposure of particulate matter and FVC, FEV1, and maximum mid-expiratory flow (MMEF). The lag2
day demonstrated less significant effects on lung function than lag1 day11, results that mirror the current study.
In our two-pollutant models with CO or O3, the PM2.5 effect remained statistically significant (p<0.05),
meaning that PM2.5 demonstrated a robust effect on lung function. Previous studies have demonstrated sim-
lar results10,12,13,14. These studies all showed that the association between PM2.5 and lung function persisted in
two-pollutant models with O3, NO2, and SO2. In our study, the correlations between PM2.5 and SO2, and between
PM2.5 and NO2 were very high and there may be multi-collinearity; as such, we only adjusted CO or O3, in the
two-pollutant models.

In our study, we found that children exposed to second-hand smoke were more sensitive to the effect of PM2.5
on lung function. Sex, asthma status, the use of natural gas, and the use of air purifiers did not affect the relation-
ship between PM2.5 and lung function. Our results suggest that second-hand smoke increases the vulnerability of
children to air pollution, severely affecting children's lung function. Regarding the modification effects of these
factors, previous studies have provided mixed results. For the sex comparison, a Canadian study reported similar
findings to ours, noting no significant differences between genders. A study in Shenyang, China also reported
similar findings9. However, research from southern California found significantly stronger associations between
FEV1 and PM in boys than in girls. Inferences from this study remain somewhat limited because the researchers
compared responses of five girls to those of 14 boys12. For asthma’s modification effect, Jacobson et al. found a
reduction in PEF ranging from 0.38l/min (95% CI: 0.63, 0.13) to 0.53l/min (95% CI: 0.90, 0.16) for each increase of
10 mg/m³ in PM2.5 in the subgroup of non-asthmatic children. However, the researchers found no significant
effect in the group of asthmatic children when analyzed separately. They offered a possible explanation for these
results by noting that asthmatic subjects may take medication when air quality deteriorates11. A study conducted
in Seattle reported adverse effects from centrally-monitored PM2.5 on the FEV1 of children with asthma, but
only if they were not receiving anti-inflammatory medications20. Therefore, our results also may reflect the use
of drugs in children with asthma, leading to no apparent effects of PM2.5 exposure on asthmatic lung function.
Unfortunately, we did not collect information regarding students’ use of medications. Few studies have focused on
the modification effects of passive smoking, the use of natural gas, or the use of air purifiers, making it difficult to
calculate our findings to previous studies. It is recommended that future studies analyze the modification effects
of these factors.

This study has several advantages. First, our panel study recruited a large sample of 848 students and collected
3,021 lung function measurements. The large number of lung function measurements increased the power of
our statistical analysis, rendering our results more stable. Second, we used multiple lung function indicators to
investigate the effects of short-term PM2.5 exposure on lung function, while previous studies primarily relied on a
single lung function indicator10,13,13,14. Third, we performed a mixed-effects regression model to analyze repeated
measurement data and to control for a variety of possible confounding factors, resulting in a highly reliable analy-
sis of results. Meanwhile, the repeated measurement analysis helped to reduce the impact of individual and other
factors that may influence the relationship between PM2.5 and lung function. Fourth, our stratified analyses based
on several factors assisted in observing the modification effects of these factors on the relationship between PM2.5
and lung function. These findings may help to inform us regarding vulnerable populations that may be more
susceptible to decreased lung function due to air pollution.

This study also has some unavoidable limitations. First, we used outdoor rather than indoor or personal air
pollution data; the data were obtained from the monitoring station nearest each school. In addition, the students’
 exposure to air pollution away from school was not measured. However, there exists a school district division pol-
icy in China, and students must study near their homes. Therefore, the monitoring stations closest to the schools
likely provide sound assessments of both school and home exposure to outdoor air pollution. In addition, Janssen
et al. reported that the median Pearson correlation coefficient between personal and outdoor concentrations of
PM10 was 0.71 when not exposed to second-hand smoke, indicating that changes in outdoor levels reflect per-
sonal changes21. Second, we did not collect information regarding student medications and thus could not analyze
the effects of medications on the relationship between PM2.5 and lung function. However, we conducted a strati-
fied analysis based on asthma and obtained the effect of PM2.5 on the lung function of healthy students. Because
there were very few students with asthma (18 students), this omission would have little impact on our findings.
Conclusions
Based on repeated lung function measurements among primary school students in Zhejiang, we found that short-term exposure to PM$_{2.5}$ was associated with reductions in lung function indicators, with the largest effect occurring on the 1-day moving average PM$_{2.5}$ exposure. In addition, children exposed to second-hand smoke were more sensitive to the effects of PM$_{2.5}$. Our results suggest that short-term exposure to PM$_{2.5}$ is harmful to children's respiratory health, and appropriate protective measures should be taken to reduce the adverse effects of air pollution on children's health. Our research thus is of great significance for the control of air pollution and the protection of children.

Data availability
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions
D.X., X.L., Z.C. and X.W. made contributions to the conception and design of the study. D.X., Y.Z., J.L. and X.Y. collected the survey data. D.X., Y.C., L.W., S.H. and P.X. prepared and cleaned the data. D.X. did the statistical analysis and drafted the article. All authors contributed interpreting the results and revised the draft critically.

Competing interests
The authors declare no competing interests.

Additional information
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