Environment International 145 (2020) 106092

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Is PM_1 similar to $PM_{2.5}$? A new insight into the association of PM_1 and $PM_{2.5}$ with children's lung function

Mo Yang[a], Yu-Ming Guo[b], Michael S. Bloom[a,c,d], Shyamali C. Dharmagee[e,f], Lidia Morawska[g], Joachim Heinrich[h,i], Bin Jalaludin[j,k,l,m], Iana Markevychd[n], Luke D Knibbsf[o], Shao Lin[c,d], Steve Hung Lan[p], Pasi Jalava[q], Mika Komppula[r], Marjut Roponen[s], Maija-Riitta Hirvonen[q], Qi-Hua Guan[s], Zi-Mian Liang[s], Hong-Yao Yu[a], Li-Wen Hu[a], Bo-Yi Yang[a], Xiao-Wen Zeng[a], Guang-Hui Dong[a,*]

[a] Guangdong Provincial Engineering Technology Research Center of Environmental Pollution and Health Risk Assessment, Department of Occupational and Environmental Health, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China
[b] Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia
[c] Department of Environmental Health Sciences, University at Albany, State University of New York, Rensselaer, United States
[d] Department of Epidemiology and Biostatistics, University at Albany, State University of New York, Rensselaer, United States
[e] Allergy and Lung Health Unit, Centre for Epidemiology and Biostatistics, School of Population & Global Health, The University of Melbourne, Melbourne, VIC 3010, Australia
[f] Murdoch Children Research Institute, Melbourne, VIC 3010, Australia
[g] International Laboratory for Air Quality and Health, Queensland University of Technology (QUT), GPO Box 2434, Brisbane, Queensland 4001, Australia
[h] Institute and Clinic for Occupational, Social and Environmental Medicine, University Hospital, LMU Munich, Ziemssenstraße 1, 80336 Munich, Germany
[i] Comprehensive Pneumology Center Munich, German Center for Lung Research, Ziemssenstraße 1, 80336 Munich, Germany
[j] Centre for Air Quality and Health Research and Evaluation, Glebe, NSW 2037, Australia
[k] Population Health, South Western Sydney Local Health District, Liverpool, NSW 2170, Australia
[l] Ingham Institute for Applied Medical Research, Liverpool, NSW 2170, Australia
[m] School of Public Health and Community Medicine, The University of New South Wales, Kensington, NSW 2052, Australia
[n] Institute of Psychology, Jagiellonian University, Poland
[o] School of Public Health, The University of Queensland, Herston, Queensland 4006, Australia
[p] Department of Geography and Resource Management, Stanley Ho Big Data Decision Analytics Research Centre, Institute of Environment, Energy and Sustainability, The Chinese University of Hong Kong, Shatin, China
[q] Department of Environmental and Biological Science, University of Eastern Finland, Kuopio, Finland
[r] Finnish Meteorological Institute, Kuopio, Finland
[s] Foshan Center for Disease Control and Prevention, 3 Yingyin Road, Chancheng District, Foshan, China

ARTICLE INFO

Handling editor: Xavier Querol

Keywords:
PM_1
Lung function
Children
China

ABSTRACT

Experimental data suggests that PM_1 is more toxic than $PM_{2.5}$ although the epidemiologic evidence suggests that the health associations are similar. However, few objective exposure data are available to compare the associations of PM_1 and $PM_{2.5}$ with children lung function. Our objectives are a) to evaluate associations between long-term exposure to PM_1, $PM_{2.5}$ and children's lung function, and b) to compare the associations between PM_1 and $PM_{2.5}$. From 2012 to 2013, we enrolled 6,740 children (7–14 years), randomly recruited from primary and middle schools located in seven cities in northeast China. We measured lung function including forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), peak expiratory flow (PEF), and maximal mid-expiratory flow (MMEF) utilizing two portable electronic spirometers. We dichotomized continuous lung function measures according the expected values for gender and age. The spatial resolution at which PM_1 and $PM_{2.5}$ estimated were estimated using a machine learning method and the temporal average concentrations were averaged from 2009 to 2012. A multilevel regression model was used to estimate the associations of PM_1, $PM_{2.5}$ exposure and lung function measures, adjusted for confounding factors. Associations with lower lung function were consistently larger for PM_1 than for $PM_{2.5}$. Adjusted odds ratios (OR) per interquartile range greater PM_1 ranged from 1.53 for MMEF (95% confidence interval [CI]: 1.20–1.96) to 2.14 for FEV1 (95% CI: 1.66–2.76) and ORs for $PM_{2.5}$ ranged from 1.36 for MMEF (95%CI: 1.12–1.66) to 1.82 for FEV1 (95%CI: 1.49–2.22), respectively. PM_1 and $PM_{2.5}$ had

* Corresponding author at: Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, Department of Preventive Medicine, School of Public Health, Sun Yat-sen University, 74 Zhongshan 2nd Road, Yuexiu District, Guangzhou 510080, China.
E-mail addresses: donggh5@mail.sysu.edu.cn, donggh512@hotmail.com (G.-H. Dong).

https://doi.org/10.1016/j.envint.2020.106092
Received 5 April 2020; Received in revised form 23 August 2020; Accepted 23 August 2020
Available online 08 September 2020

significant associations with FVC and FEV1 in primary school children, and on PEF and MMEF in middle school children. Long-term PM_1 and $PM_{2.5}$ exposure can lead to decreased lung function in children, and the associations of PM_1 are stronger than $PM_{2.5}$. Therefore, PM_1 may be more hazardous to children's respiratory health than $PM_{2.5}$ exposure.

1. Introduction

Air pollution is a global public health problem and an important environmental determinant of human respiratory health (Burki 2019). Atmospheric particulate matter (PM), is a major contributor to urban air pollution, especially $PM_{2.5}$ (particulate matter with an aerodynamic diameter of 2.5 μm or less) (Kirrane et al. 2019) and PM_1 (particulate matter with an aerodynamic diameter of 1.0 μm or less) (Li et al. 2019). Toxicological evidence suggests that smaller particle PM_1 is more hazardous than $PM_{2.5}$ on cytotoxic effects and inflammation (Jalava et al. 2015). However, epidemiological evidence to date indicates similar negative health associations for PM_1 and $PM_{2.5}$ with cardiovascular outcomes, stroke, and respiratory endpoints (Hu et al. 2018).

Long-term $PM_{2.5}$ exposure has been linked to impaired lung function in children (Guo et al. 2019), yet few studies are available on the respiratory associations of PM_1 exposure. There are several studies that have investigated the adverse associations of PM_1 exposure on lung function in children and adolescents (Ghozikali et al., 2018; Moshammer et al., 2006; Xing et al., 2020; Zhang et al., 2019; Zwozdziak et al., 2016). All the studies suggested that higher short and long-term PM_1 exposure were associated with poorer lung function. However, none of them compared the individual contributions and differences of PM_1 and $PM_{2.5}$ to lung function.

Lung function measurement provides an objective index for evaluating lung injury, which is of great value for the diagnosis and prediction of respiratory disease (Vos et al. 2017). Age and gender are important factors affecting lung function (Carey et al. 2007). Some birth-cohort studies have shown that pediatric lung function growth trajectories track into adult lung function (Belgrave et al. 2018). Therefore, obtaining childhood lung function data is very important for the subsequent assessment and diagnosis of respiratory health (Agusti and Faner 2019).

Across China, PM_1 comprises approximately 70% to 90% of the $PM_{2.5}$ mass, suggesting that PM_1 is the key driver of fine particulate air pollution (Chen et al. 2017). However, there is little information available to evaluate the difference in associations and few indicators of PM_1 and $PM_{2.5}$ toxicity. Therefore, our aim was to evaluate associations between long-term exposure to PM_1 and $PM_{2.5}$ with children's lung function, and to differentiate the associations of PM_1 from $PM_{2.5}$. We used data from the Seven Northeastern Cities study (Dong et al. 2014). We hypothesized that long-term PM_1 and $PM_{2.5}$ exposures would be associated with children's poorer lung function, and that associations for PM_1 would be larger than those for $PM_{2.5}$.

2. Material and methods

2.1. Study population and questionnaire

Study participants were recruited to the China Seven Northeastern Cities study from seven Liaoning Province cities (Shenyang, Dalian, Fushun, Anshan, Benxi, Dandong, and Liaoyang), located in northeastern China. We selected a total of 24 urban districts across the study cities to maximize contrasts of ambient air pollutant concentrations measured in 2009–2012. Each of the 24 districts had one municipal air quality monitoring station available. In each district, we randomly selected one or two primary schools (student age range 6–12 years) and middle schools (student age range 12–15 years) among the schools located within 2 km of the district air quality monitoring station. A total of 62 schools were included in the study. Within each school, we randomly selected one or two classrooms, depending on the class size from each grade level, to enroll study participants (i.e., all students in the selected classrooms). All students who had lived in the study district for at least two years and had resided within a 2 km radius from the air quality monitoring station were eligible. A detailed description of the random sampling procedure is described in eMethods1 in the Supplement. The study was conducted according to World Medical Association Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects and the Human Studies Committee of Sun Yat-sen University approved the study protocol. Written informed consent was obtained from all participants and their parents/guardians before starting data collection.

Principals in the selected schools distributed study questionnaires to teachers of each selected classroom. Teachers described the study during a parent's school visitation night, obtained informed consent, and distributed study questionnaires to the parents with return envelopes. Eligible children's parents could choose to complete the questionnaire during the school visitation night or to complete the form at home and return it in a sealed envelope the next day. Principals and teachers were instructed not to encourage or otherwise coerce the parents to participate. The study questionnaire, previously described by our group (Zeng et al. 2016), captured covariate information, including sociodemographic factors, lifestyle factors, residential factors, personal medical history, including a detailed history of respiratory health, and family medical history among other requested information. Trained nurses followed the standardized World Health Organization protocol for measuring the height (at 0.1 cm) and weight (at 0.1 kg) of children and calculated the body mass index (BMI) in kg/m^2. We dichotomized parents' education as having a high school education or not, and categorized annual family income ($\leq$4999, 5000–9999, 10000–29999, 30000–100000, or $>$ 100000 RMB). Children's passive tobacco smoke exposure was defined as cohabitation with a daily cigarette smoker, and home coal use was assessed as household use for cooking or space heating. Area of residence per person (m^2) was calculated by dividing the housing area by the number of household residents. We also queried the 'ever' presence of a house pet (i.e., dog, cat, bird, farm animals, and others). We defined family history of atopy as a clinical diagnosis of allergies. Doctor-diagnosed asthma was defined as an affirmative answer to the question "Has a doctor ever diagnosed asthma in this child?" Current asthma among previously asthma-diagnosed children was defined by an affirmative answer to the question "Has this child had an asthma attack in the last two years?" or an affirmative answer to the question "Does this child take medicine or treatment for asthma or asthmatic bronchitis?" We determined home renovation as a positive response to the question "Have you made any renovations in your home within the past 2 years?" We defined breastfeeding as having been mainly breast fed for more than three months. A detailed description of this information is provided in eMethods 2 in the Supplement.

2.2. Ambient particulate matter exposure assessment

We estimated daily PM_1 and $PM_{2.5}$ concentrations from 2009 to 2012, using a machine learning method at a spatial resolution of 10 km by 10 km, based on satellite remote sensing, meteorological data, and land use information. Four-year (2009–2012) mean PM_1 and $PM_{2.5}$ concentrations were calculated and assigned to each child as surrogates for long-term exposure. Daily PM_1 and $PM_{2.5}$ concentrations were estimated using a spatial statistical model with a machine learning method matched to the children's geocoded home addresses. Briefly,

each participant's home address was geocoded as a geographical longitude and latitude, and superimposed over predicted daily PM_1 and $PM_{2.5}$ concentration grids. The exposure parameters were then calculated by averaging the daily concentrations for PM_1 and $PM_{2.5}$ over the four-year period 2009–2012. The results of a 10-fold cross-validation showed coefficient of determination values for daily predictions were 55% for PM_1 and 86% for $PM_{2.5}$, and coefficient of determination values for annual predictions were 75% for PM_1 and 86% for $PM_{2.5}$. Detailed information regarding the analysis had been published (Chen et al. 2018), and is presented in eMethods 3 in the Supplement.

2.3. Lung function measurement

We conducted the children's health examinations between April 2012 and May 2013. Briefly, four measures of lung function, including forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), peak expiratory flow rate (PEF), and maximum mid expiratory flow rate (MMEF) were measured utilizing two portable electronic spirometers (Spirolab, MIR, Italy) (Mehrparvar et al., 2014). Spirometry was performed according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) standards. The child stood comfortably and wore a nose clip to prevent air from coming out from the nose during spirometry. After that, the values of total lung capacity (TLC) and residual volume (RV) were measured. FVC and FEV1 should be both the largest value obtained from any of three technically satisfactory curves, and the change in FVC and FEV1 values should not exceed 5% in at least two of the three curves. All testing processes were automatically corrected for body temperature and pressure water vapor saturated (BTPS). We used EpiData Entry for data entry and documentation. We dichotomized spirometry measures as impaired, based on the values predicted for children residing in northeastern China (Ma et al. 2013): lung function as FVC < 85% of reference (FVC < 85%), FEV1 < 85% of reference (FEV1 < 85%), maximum mid expiratory flow < 75% of reference (MMEF < 75%), or PEF < 75% of reference (PEF < 75%).

2.4. Statistical analysis and data calculation

We examined distributions and evaluated bivariate associations among the covariates. We evaluated the association of ambient air pollutants with continuous lung function measures using generalized linear regression models, adjusted for confounding variables, as previously described (Dong et al. 2013). Briefly, we used a two-level logistic regression model to estimate the relation between dichotomized lung function tests and ambient air pollutant concentrations. Children were the first-level units and districts were the second-level units. The details of this model are described in eMethods 4 in the Supplement. In brief, PM_1 and $PM_{2.5}$ were considered as predictor variables, expressed per interquartile range (i.e., difference between the 75th percentile and the 25th percentile). We first operationalized lung function measures as continuous outcomes to assess biological response. Next, we dichotomized lung function measures according to predicted values to assess clinical significance. At the district level, the random coefficients were regressed on district-specific air pollutant levels. Confounding variables were identified as age, body mass index (BMI), breast fed status, gender (for total sample only: we only adjusted the gender in the total population analysis), parental education, income, passive tobacco smoke exposure, home coal use, home renovation, and family history of atopy. Because, lung function varies with age, we also adjusted for standing height and gender (Carey et al. 2007). We entered cross-product terms between gender and air pollutants to test effect measure modification in regression models, and then stratified by gender to interpret the results (VanderWeele, 2009). Asthma, breast fed and smoke are all important factors affecting children's lung function. We also analyzed the associations of PM_1 and $PM_{2.5}$ as predictors of lung impairment in children, overall and stratified by gender and current asthma, gender and breast fed, and by gender and passive tobacco smoke exposure. We further interrogated heterogeneity of PM_1 and $PM_{2.5}$ associations according to participant age, defined as primary school vs. middle school, using the same approach. *P*-values < 0.05 and 0.10 were considered statistically significant for two-tailed tests of main associations and interactions, respectively. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina). As PM_1 is a constituent of $PM_{2.5}$, $PM_{2.5}/PM_1$ concentration ratio should equal $\log(aOR_{pm1})/\log(aOR_{pm2.5})$ under ideal conditions, given that $PM_{2.5}/PM_1 = \log(aOR_{pm1})/\log(aOR_{pm2.5})$; where $y = \beta_1 \times PM_1$ and $y = \beta_2 \times PM_{2.5}$, and $aOR_1 = 10^{\beta 1}$ and $aOR_{2.5} = 10^{\beta 2}$, so $\beta_1 = \log(aOR_1)$ and $\beta_2 = \log(aOR_{2.5})$. That means $1 = \frac{\log(aOR1) \times PM1}{\log(aOR2.5) \times PM2.5}$, so $PM_{2.5}/PM_1 = \log(aOR_{pm1})/\log(aOR_{pm2.5})$.

Table 1
Distribution of sociodemographic, lifestyle, clinical, and exposure factors among 6740 Chinese children, overall and by gender.

Characteristics	Total (n = 6740) *n* (%)	Boys (n = 3382) *n* (%)	Girls (n = 3358) *n* (%)
Age (year), Mean (SD)	11.6 (2.1)	11.6 (2.1)	11.5 (2.0)
Height (cm)[a]	154.0 (12.6)	155.6 (14.0)	152.3 (10.8)
Weight (kg)[a]	48.4 (15.6)	51.2 (17.3)	45.7 (13.2)
BMI, Mean (SD)[a]	20.0 (4.7)	20.7 (5.3)	19.3 (3.9)
Exercise time per week (hour), Mean (SD)[a]	7.6 (7.8)	7.8 (7.6)	7.3 (7.9)
Area of residence per person (m^2), Mean (SD)[a]	22.7 (9.8)	23.1 (10.0)	22.4 (9.6)
Breast fed[a]	4751 (70.5)	2312 (68.4)	2439 (72.6)
Personal education > high school	4211 (62.5)	2101 (62.1)	2110 (62.8)
Family income			
< 4999 RMB	758 (11.3)	375 (11.1)	383 (11.4)
5000–9999 RMB	876 (13.0)	431 (12.7)	445 (13.3)
10,000–29,999 RMB	2394 (35.5)	1197 (35.4)	1197 (35.7)
30,000–100,000 RMB	2437 (36.2)	1250 (37.0)	1187 (35.4)
> 100,000 RMB	275 (4.1)	129 (3.8)	146 (4.4)
Passive tobacco smoke exposure	3281 (48.7)	1623 (48.0)	1658 (49.4)
House coal use	676 (10.0)	357 (10.6)	319 (9.5)
House pet	1435 (21.3)	694 (20.5)	741 (22.1)
House renovation	2416 (35.9)	1197 (35.4)	1219 (36.3)
Family history of atopy	1390 (20.6)	669 (19.8)	721 (21.5)
Asthma diagnosis[a]	460 (6.8)	275 (8.1)	185 (5.5)
Lung function			
FVC (mL), Mean (SD)[a]	2626.0 (755.1)	2817.7 (843.9)	2432.9 (594.2)
FEV1 (mL): Mean (SD)[a]	2463.5 (699.6)	2628.9 (775.7)	2296.8 (566.8)
PEF (mL/s): Mean (SD)[a]	4777.7 (1415.0)	5163.5 (1534.6)	4389.2 (1160.4)
MMEF (mL/s): Mean (SD)[a]	3349.7 (1048.5)	3490.9 (1153.9)	3207.6 (908.6)
Lung function impairment			
FVC < 85% predicted[a]	759 (11.3)	350 (10.4)	409 (12.2)
FEV1 < 85% predicted	578 (8.6)	303 (9.0)	275 (8.2)
PEF < 75% predicted[a]	458 (6.8)	186 (5.5)	272 (8.1)
MMEF < 75% predicted[a]	634 (9.4)	287 (8.5)	347 (10.3)
Air pollutant levels ($\mu g/m^3$), Mean (SD)			
PM_1	47.5 (6.5)	47.6 (6.5)	47.3 (6.5)
$PM_{2.5}$	54.6 (6.1)	54.7 (6.2)	54.4 (6.1)

Note: RMB, Chinese Yuan. FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; PEF, peak expiratory flow rate; MMEF, maximum mid expiratory flow rate.

[a] $P < 0.05$ for difference between boys and girls using Chi square for categorical variables and *t*-test for continuous variables.

3. Results

3.1. Study population characteristics and air pollution exposure

Participant characteristics are shown in Table 1. A total of 6740 children with complete data were included in this analysis. We excluded n = 279 with missing data (< 4%), although with similar characteristics to the included participants (eTable 1). Boys had higher BMI than girls, they exercised more frequently and resided in larger residences on a per person basis. However, boys were less likely to have been breast fed than girls. All lung function measures were better for boys compared to girls. The prevalence of impaired lung function ranged from 5.5% (PEF) to 10.4% (FVC) of the study population. Girls were more likely to have higher FVC, PEF, and MMEF impairment than boys. The distribution of air pollutants and lung function are shown in eTable 2 in the Supplement. Table 1 also shows the distribution of four-year average PM_1 and $PM_{2.5}$ concentrations, overall and by gender. The mean predicted concentration and standard deviation were 47.5 (6.5) $\mu g/m^3$ for PM_1 and 54.6 (6.1) $\mu g/m^3$ for $PM_{2.5}$. The mean $PM_1/PM_{2.5}$ ratio was 0.87 and it exceeded 0.85 for 77% of children. There was a significant and strong positive correlation between PM_1 and $PM_{2.5}$ (r_{Sp} = 0.94). $PM_{2.5\text{-}1}$ concentration is shown in eTable 3 in the Supplement.

3.2. Associations between air pollution exposure and dichotomized lung function

Table 2 shows the associations between ambient air pollutants and dichotomized lung function outcomes, and the results of $\log(aOR_{pm1})/\log(aOR_{pm2.5})$. The ratio of $\log(aOR_{pm1})/\log(aOR_{pm2.5})$ in total children, boys, and girls range from 1.3 to 1.6, 1.3 to 1.7, and 1.3 to 1.5, respectively. All t $\log(aOR_{pm1})/\log(aOR_{pm2.5})$ were greater than $PM_{2.5}/PM_1$ (i.e., 1.15). We consistently found positive associations between air pollutant exposure and the odds of lung function impairment. Among lung function measures, FEV1 association estimates were larger and weaker for MMEF. Among pollutants, association estimates were larger for PM_1 exposure, in which each increase in interquartile range (IQR) concentration was associated with and aOR of 2.1 (95% CI: 1.7, 2.8) for FEV1 impairment in total children, adjusted for confounding. Each $PM_{2.5}$ increase in IQR concentration was associated with an aOR of 1.8 (95% CI: 1.5, 2.2) for FEV1 impairment in total children. We also detected statistically significant interactions with respect to gender for FEV1 and MMEF with PM_1 and $PM_{2.5}$ exposures (Table 2). We found that associations of FEV1 with PM_1 and $PM_{2.5}$ were larger in girls than in boys. We also identified larger associations of MMEF with PM_1 and $PM_{2.5}$ in girls than in boys. Associations between $PM_{2.5\text{-}1}$ and lung function are shown in eTable 4 in the Supplement. There was no statistically significant association between $PM_{2.5\text{-}1}$ and lung function. Unadjusted estimates of ambient air pollutants in relation to lung function impairment are shown in eTable 6 in the Supplement. In addition, the associations between ambient air pollutants and lung impairment among Chinese children, overall and stratified by gender and asthma, and by gender and breast fed, are shown in eTable 8 and 9 in the Supplement. The results of passive tobacco smoke exposure with respect to lung function among children overall and by gender are shown in eTable 10 in the Supplement.

Fig. 1 shows the results of regression models to assess interactions between participant age and PM exposure associated with lung function impairment. The difference in associations between PM_1 and $PM_{2.5}$ was more significant in young children. In primary school children (mean ± SD = 10.2 ± 1.5 years of age) and middle school children (mean ± SD = 13.3 ± 1.2 years of age), the ratio of $\log(aOR_{pm1})/\log(aOR_{pm2.5})$ ranged from 1.5 to 1.8 and 0.8 to 1.2, respectively. All $\log(aOR_{pm1})/\log(aOR_{pm2.5})$ ratios were more than the $PM_{2.5}/PM_1$ (1.15) ratio in primary school children. Associations of PM_1 and $PM_{2.5}$ with FVC impairment and FEV1 impairment were significantly larger among primary school children than among middle school children. In addition, PM_1 and $PM_{2.5}$ had statistically significant associations with FVC and FEV1 (large airways) in primary school children, and on PEF and MMEF (small airways) in middle school children.

3.3. Associations between air pollution exposure and lung function measures

Table 3 shows the results of multiple linear regression analysis to estimate relationships between ambient air pollutants and continuous

Table 2
Adjusted OR (95% CI) of PM_1 and $PM_{2.5}$ concentrations ($\mu g/m^3$) in relation to lung impairment and $\log(aOR_{pm1})/\log(aOR_{pm2.5})$ among Chinese children, adjusted for confounding variables, overall and by gender (n = 6740).

Air pollutants	Total[a]		Boys[a]		Girls[a]		$P_{interaction}$[c]
	aOR[b]	95% CI	aOR[b]	95% CI	aOR[b]	95% CI	
FVC < 85% predicted							
PM_1	2.0	1.5, 2.5	1.9	1.4, 2.5	2.1	1.5, 2.8	0.54
$PM_{2.5}$	1.6	1.3, 1.9	1.5	1.1, 1.9	1.6	1.3, 2.1	0.36
log (aOR_{pm1})/log($aOR_{pm2.5}$)	1.6	–	1.7	–	1.5	–	–
FEV1 < 85% predicted							
PM_1	2.1	1.7, 2.8	1.8	1.3, 2.5	2.6	1.9, 3.6	0.06
$PM_{2.5}$	1.8	1.5, 2.2	1.6	1.3, 2.0	2.1	1.6, 2.7	0.06
log (aOR_{pm1})/log($aORpm_{2.5}$)	1.3	–	1.3	–	1.3	–	–
PEF < 75% predicted							
PM_1	1.6	1.3, 2.1	1.6	1.2, 2.3	1.6	1.2, 2.2	0.93
$PM_{2.5}$	1.4	1.1, 1.7	1.4	1.1, 1.9	1.4	1.1, 1.8	0.77
log (aOR_{pm1})/log($aOR_{pm2.5}$)	1.4	–	1.3	–	1.5	–	–
MMEF < 75% predicted							
PM_1	1.5	1.2, 2.0	1.2	0.9, 1.6	2.0	1.5, 2.6	0.003
$PM_{2.5}$	1.4	1.1, 1.7	1.1	0.9, 1.4	1.6	1.3, 2.1	0.01
log (aOR_{pm1})/log($aOR_{pm2.5}$)	1.4	–	1.4	–	1.4	–	–

Note: CI, confidence interval; aOR, adjusted adds ratios; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; PEF, peak expiratory flow rate; MMEF, maximum mid expiratory flow rate.

[a] Adjusted for age, body mass index (BMI = weight (kg) / height (m^2)), breast fed status, gender (for total sample only), parental education, income, smoking exposure, home coal use, house renovation, and family history of atopy.

[b] OR were scaled to the interquartile range (25th to 75th percentile of district-specific concentrations) for each pollutant (12.9 $\mu g/m^3$ for PM_1, 10.0 $\mu g/m^3$ for $PM_{2.5}$).

[c] *p*-Value for test of gender × air pollutant in regression models.

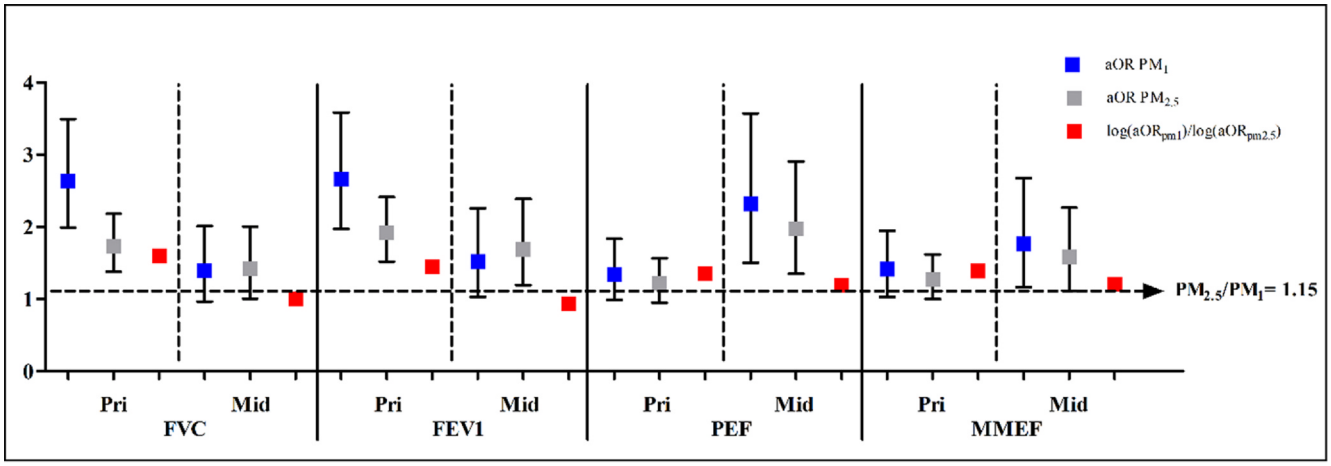

Fig. 1. Associations of PM_1 and $PM_{2.5}$ with lung function and $\log(aOR_{pm1})/\log(aOR_{pm2.5})$ in Chinese Children. aOR, adjusted adds ratios; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; PEF, peak expiratory flow rate; MMEF, maximum mid expiratory flow rate. Pri, Primary school students; Mid, Middle school students. The associations were adjusted for age, body mass index (BMI = weight (kg) / height $(m)^2$), breast fed status, gender, parental education, income, passive tobacco smoke exposure, home coal use, house pet, house renovation, and family atopy. Association estimate scaled to the interquartile range (25th to 75th percentile of district-specific concentrations) for each pollutant (12.9 μg/m^3 PM_1 and 10.0 μg/m^3 $PM_{2.5}$). $PM_{2.5}/PM_1$ = 1.15: the concentration ratio of $PM_{2.5}$ and PM_1 is 1.15.

measures of lung function. We consistently detected statistically significant and inverse associations between concentrations of air pollutants and lung function measures. Association estimates were largest for PEF and smallest for MMEF, adjusted for confounding. Association estimates were largest for PM_1 exposure, in which each increase in IQR concentration was associated with a −243.6 mL (95% CI: −307.0, −180.2) PEF (Table 3). We also detected statistically significant interactions with gender for all associations (Table 3). PM_1 associations among boys were stronger than among girls for FEV1. Yet, the PM_1 associations among girls were stronger than those among boys for PEF and MMEF. Still, association estimates were consistently largest for PEF and for PM_1 overall. The associations between $PM_{2.5\text{-}1}$ and continuous lung function measures are shown in eTable 5 in the Supplement, although there was no statistically significant association. The results of unadjusted estimates in lung function measures associated with ambient air pollutants are shown in eTable 7 in the Supplement.

4. Discussion

The results of this large, population-based investigation showed that long-term exposure to PM_1 and $PM_{2.5}$ were associated with poorer lung function and greater odds of lung function impairment in Chinese children. The associations were consistently stronger for PM_1 than for $PM_{2.5}$ exposure and varied according to children's gender and age. We found the largest overall associations for FEV1 impairment followed by FVC, and more modest associations for PEF and MMEF. Thus, our results suggest that PM_1 and $PM_{2.5}$ exert adverse associations with lung function in children, although the vulnerability may vary by gender and age, and PM_1 may be more hazardous to children's respiratory health than $PM_{2.5}$ exposure.

Our study appears to be the first comparison of children's lung function damage in association with both long-term PM_1 exposure and $PM_{2.5}$ exposure. Unlike previous epidemiologic studies, we found not only that greater long-term PM_1 exposure was associated with children's lung function, but also that the association estimates were

Table 3
Mean difference (95% CIs) in lung function measures associated with PM_1 and $PM_{2.5}$ concentrations (μg/m^3) among Chinese children, adjusted for confounding variables, total and by gender (n = 6740).

Air pollutants	Total[a,b]		Boys[a,b]		Girls[a,b]		$P_{Interaction}$[c]
	β	95% CI	β	95% CI	β	95% CI	
FVC							
PM_1	−163.0	−194.9, −131.0	−163.2	−212.8, −113.6	−148.1	−185.2, −111.1	0.07
$PM_{2.5}$	−136.7	−164.0, −109.3	−133.3	−175.5, −91.2	−127.7	−159.5, −95.9	0.03
FEV1							
PM_1	−123.9	−151.8, −96.1	−119.4	−161.7, −77.0	−116.4	−149.7, −83.1	0.02
$PM_{2.5}$	−102.9	−126.7, −79.1	−96.4	−132.3, −60.4	−99.1	−127.7, −70.5	0.01
PEF							
PM_1	−243.6	−307.0, −180.2	−175.6	−269.1, −82.1	−279.9	−359.5, −200.2	0.001
$PM_{2.5}$	−194.6	−248.8, −140.4	−140.4	−219.7, −61.1	–223.3	−291.7, −154.9	0.003
MMEF							
PM_1	−96.5	−144.4, −48.6	−38.6	−109.9, 32.7	−134.1	−194.5, −73.7	< 0.001
$PM_{2.5}$	−76.1	−117.1, −35.2	−27.6	−88.1, 32.9	−109.4	−161.1, −57.6	< 0.001

Note: β, association estimate; CI, confidence interval. FVC, forced vital capacity; FEV1, forced expiratory volume in 1 s; PEF, peak expiratory flow rate; MMEF, maximum mid expiratory flow rate.

[a] Adjusted for age, body mass index (BMI = weight (kg) / height $(m)^2$), breast fed status, gender (for total sample only), parental education, income, passive tobacco smoke exposure, home coal use, house pet, house renovation, and family atopy.

[b] Association estimate scaled to the interquartile range (25th to 75th percentile of district-specific concentrations) for each pollutant (12.9 μg/m^3 for PM_1, 10.0 μg/m^3 for $PM_{2.5}$).

[c] *p*-Value for test of gender × air pollutant in regression models.

stronger than for $PM_{2.5}$. PM_1 is the mainly part of $PM_{2.5}$. In this study, PM_1 accounts for 87% of $PM_{2.5}$, this means $PM_1 = 0.87 \times PM_{2.5}$. If $y = \beta1 \times PM_1$, and $y = \beta2 \times PM_{2.5}$, so $\beta2 \times PM_{2.5} = \beta1 \times 0.87 \times PM_{2.5}$. That means $\beta1/\beta2 = 1/0.87$, because $aOR_{pm1} = 10^{\beta1}$ and $aOR_{pm2.5} = 10^{\beta2}$, so $\beta1 = \log(aOR_{pm1})$ and $\beta2 = \log(aOR_{pm2.5})$. Therefore, log(aORpm1)/ log (aORpm2.5) = 1.15. Under ideal conditions, the association of PM_1 in $PM_{2.5}$ should be equal to the concentration proportion of PM_1 in $PM_{2.5}$ [$\log(aOR_{pm1})/\log(aOR_{pm2.5}) = PM_{2.5}/PM_1$]. However, if $\log(aOR_{pm1})/\log(aOR_{pm2.5}) > PM_{2.5}/PM_1$, that means the actual association of PM_1 is higher than the concentration proportion effect of PM_1 in $PM_{2.5}$, PM_1 has additional associations and PM_1 is stronger than $PM_{2.5}$. In our study, the $\log(aOR_{pm1})/\log(aOR_{pm2.5})$ in lung function ranged from 1.3 to 1.6 in children, higher than the ratio of $PM_{2.5}/PM_1$ (1.15). In addition, the $PM_{2.5\text{-}1}$ concentration was only 13% of $PM_{2.5}$, and $PM_{2.5\text{-}1}$ has no significant association with children's lung function in this study. PM_1 is the main hazardous component in $PM_{2.5}$. Therefore, because the association of $PM_{2.5\text{-}1}$ was null, the role of PM_1 was stronger than $PM_{2.5}$. These results showed that PM_1 had stronger associations with children's lung function than $PM_{2.5}$.

We reviewed the literature and found five children's studies (Ghozikali et al., 2018; Moshammer et al., 2006; Xing et al., 2020; Zhang et al., 2019; Zwozdziak et al., 2016) that assessed the associations of PM_1 and $PM_{2.5}$ with lung function, but they did not compare the associations of PM_1 and $PM_{2.5}$. A 2013 study by Xing et al (Xing et al. 2020), found that PM_1 and $PM_{2.5}$ concentrations were significantly associated with lung function impairment for normal weight, overweight, and obese children, especially in overweight and obese children. A 2013 study by Zhang et al (Zhang et al. 2019), found that breastfeeding could decrease the risk of lung function impairment among Chinese children exposed to PM_1, $PM_{2.5}$ and other air pollutants, especially in younger children. Several prior studies investigated associations between short-term PM_1 exposure and lung function measures in children or young adults. A 2001 panel study of 163 children 7–10 years of age, reported that the most sensitive indicator for acute combustion-related pollutant associations was a change in maximal expiratory flow in the small airways ($MEF_{50\%}$ and $MEF_{25\%}$) after PM_1 and $PM_{2.5}$ exposure (Moshammer et al. 2006). A more recent 2017 panel study of 23 asthmatic and 23 non-asthmatic Iranian students 15–18 years of age, reported inverse associations between greater ambient PM_{10}, $PM_{2.5}$, and PM_1 exposure, measured using personal air monitoring, with FVC and FEV1 (Ghozikali et al. 2018). Another recent 2010 panel study of 141 secondary school students 13–14 years of age, reported modest but statistically significant differences in FVC, FEV1, PEF, and MEF25 per interquartile range greater $PM_{2.5}$ and PM_1 exposure (Zwozdziak et al. 2016). In our study, we add new evidence to the literature by suggesting that long-term PM_1 and $PM_{2.5}$ exposure may increase the risk of lung function impairment, and the association of PM_1 is stronger than that of $PM_{2.5}$.

Smaller size particles have higher surface area to volume ratio than larger size particles, thus having greater potential for deleterious biological interactions with respiratory tissues and risks for adverse health outcomes (Mei et al. 2018). $PM_{2.5}$ has the ability to penetrate deeper into the respiratory tract than PM_{10}, where the particles can more easily penetrate the air-blood barrier (Polichetti et al. 2009). The greatest health risks may be associated with PM_1 exposure, not only because it can access the gas-exchange region of the lungs, but also because it contains a relatively large proportion of organic carbon that serves as a universal carrier of toxic organic compounds (Cassee et al. 2013). Fine particles contained greater concentrations of organic pollutants, such as polycyclic aromatic hydrocarbons (PAHs), polychlorinated dibenzo-p-dioxins and furans (PCDD/Fs), and other chemicals known to be associated with adverse health effects than larger particles (Degrendele et al. 2014). Toxicological experiments and human studies indicate that smaller particle sizes elicit greater toxicity. An experimental study of mature mice exposed to different PM granularities (i.e., $PM_{0.49}$, $PM_{0.95}$, and $PM_{0.95\text{-}1.5}$) found that PM exposure induced oxidative stress, peribronchiolar inflammation, and immune imbalance, and that PM $_{0.95}$ μm had a far more aggravating effect on asthma development than $PM_{0.95\text{-}1.5}$ (Mei et al. 2018). A 2007–2012 study of hospital admissions for respiratory diseases (Xiong et al. 2015) found stronger positive associations between respiratory hospital admissions in Beijing and exposure to $PM_{0.3}$ and $PM_{0.3\text{-}0.5}$, than for exposure to $PM_{0.5\text{-}1.0}$. In our study, associations with lung function measures were consistently stronger for PM_1 than for $PM_{2.5}$.

We also found stronger associations of PM_1 exposure with FVC and FEV1 in younger children than in older children, possibly indicating a modifying association of age on these parameters. In contrast, associations for PM_1 and $PM_{2.5}$ exposures with PEF were weaker in younger children than in older children. FEV1 represents the mechanical properties of large and medium-sized airways and FVC reflects lung size (Sullivan et al. 2019). Changes in FEV1 and FVC usually occur in the early stage of lung injury, whereas PEF and MMEF are used to confirm small airway obstruction and monitor the diagnosis following abnormal results from other measurements, such as asthma for example (Shrine and Guyatt 2019). Therefore, PEF and MMEF usually changes when the lungs develop deceases. Additional work is needed to characterize age-related vulnerabilities more definitively for different lung function indicators.

We found that girls had significantly lower lung function levels than boys and that they were more sensitive to PM_1. Gender differences on lung function in response to air pollution or other environmental stimuli may be present due to sex-related differences in lungs and airway development (Carey et al. 2007). A reason is that lungs in males tend to be larger than in females, with a greater number and surface area of alveoli at birth. Some studies suggest that greater estrogen synthesis in adolescence elevates pulmonary disease risk in girls, compared to boys (Keselman and Heller 2015). However, Carey et al., found that males' pulmonary airway growth lags behind females', resulting in narrower airways prior to adulthood (Carey et al. 2007), which might make boys more susceptible to the deleterious associations of air pollution exposure at younger ages. Thus, the gender-related associations with air pollution-lung function associations in children may be further modified by age, but additional investigation is necessary to test this hypothesis.

Our study offers many strengths although it also has several important limitations. The large sample size allowed us to detect modest associations with increased precision and to interrogate gender and age as potential modifiers of air pollution-lung function associations. Given the cross-sectional nature of our study design, we were unable to establish a temporal relationship in which PM exposure preceded the onset of lung function. Thus, we cannot rule out 'reverse causality,' although we believe this to be unlikely given that all participants resided in urban areas of Liaoning Province and the context of our hypothesis (i.e., for children with poorer lung function to relocate to areas with greater ambient air pollution). We enrolled participants from 24 of 27 urban districts across study cities based on air quality data. While this strategy enhanced statistical power, we cannot rule out the possibility for a selection bias if study district was independently related to children's lung function. We assessed for effect measure modification on the multiplicative scale. Yet multiplicative measures alone are insufficient to fully assess the relevance of exposure modification and so additional investigation should be conducted on the additive scale (Mathur and Tyler, 2018; Prentice, 2011). Furthermore, we were unable to generate multivariable PEF models among girls due to the small number asthma events (n = 18) (eTable 8).

We used a comprehensive, validated, satellite-based model to assign air pollutant exposures to children's home addresses, which may have misclassified exposure for some participants. Nevertheless, we estimated PM_1 and $PM_{2.5}$ concentrations using a machine learning method at a spatial resolution of 10 km by 10 km. The PM concentration of all home addresses in the same 10 × 10 km grid is the same. Therefore, the

misclassification is unlikely to have varied by study outcome, producing a bias towards the null hypothesis. In addition, small variations in PM_1 and $PM_{2.5}$ (< 10 μg/m^3) may have compromised our statistical power to detect modest associations. Yet, we detected statistically significant associations despite the limited range of exposure in the study population, further underscoring the relevance of PM_1 and $PM_{2.5}$. Furthermore, Chinese statute mandates attendance at local schools, and the average time walking to school was about 11.6 min from the home. Thus, our exposure assessment also captured school exposure in part, and so provides more robust conclusions than other similar investigations. In addition, we were unable to assess PM composition, including different proportions of constituent chemicals, metals, and ions in different areas. We used spirometry to capture an objective measure of lung function not prone to recall bias in all children, minimizing outcome misclassification. Finally, although we adjusted for a range of confounding variables, we were unable to capture data for additional, potential environmental confounders, such as time-activity patterns for study participants, and thus, residual confounding is possible.

5. Conclusions

PM_1 and $PM_{2.5}$ levels were associated with poorer lung function in children with stronger associations for PM_1 compared to $PM_{2.5}$. To the best of our knowledge, our results are the first to compare the associations of PM_1 and $PM_{2.5}$ exposure with children's lung function measures. Our results provide further support for previously published findings linking higher ambient air pollution concentrations to poorer lung function in children. Although preliminary, our results suggest the importance of regulating finer PM fractions (PM_1) and mitigating the adverse associations.

CRediT authorship contribution statement

Mo Yang: Conceptualization, Data curation, Formal analysis, Investigation, Validation, Visualization, Writing - original draft, Writing - review & editing. **Yu-Ming Guo:** Conceptualization, Data curation, Formal analysis, Software. **Michael S. Bloom:** Methodology, Writing - original draft, Writing - review & editing. **Shyamali C. Dharmagee:** Methodology, Software, Writing - original draft. **Lidia Morawska:** Writing - original draft. **Joachim Heinrich:** Software, Writing - original draft. **Bin Jalaludin:** Writing - original draft. **Iana Markevychd:** Software, Writing - original draft. **Luke D Knibbsf:** Writing - original draft. **Shao Lin:** Methodology, Software, Writing - original draft. **Steve Hung Lan:** Writing - original draft. **Pasi Jalava:** Writing - original draft. **Mika Komppula:** Writing - original draft. **Marjut Roponen:** Writing - original draft. **Maija-Riitta Hirvonen:** Writing - original draft. **Qi-Hua Guang:** Writing - original draft. **Zi-Mian Liang:** Writing - original draft. **Hong-Yao Yu:** Investigation, Project administration, Resources, Supervision. **Li-Wen Hu:** Funding acquisition, Investigation, Project administration, Resources, Supervision, Writing - original draft. **Bo-Yi Yang:** Funding acquisition, Investigation, Project administration, Resources, Supervision, Writing - original draft. **Xiao-Wen Zeng:** Funding acquisition, Investigation. **Guang-Hui Dong:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing.

Declaration of competing interest

The authors declare they have no actual or potential competing interests.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (grant numbers 81872583, 81872582, and 81972992), the National Key Research and Development Program of China (grant numbers 2018YFE0106900 and 2018YFC1004300), the Guangdong Provincial Natural Science Foundation Team Project (grant number 2018B030312005), the Science and Technology Planning Project of Guangdong Province (grant numbers 2019A050510017 and 2018B05052007), the Science and Technology Planning Project of Guangzhou (grant numbers 201803010054 and 201807010032), the Fundamental Research Funds for the Central Universities (grant number 19ykjc01), and Science and Technology Program of Zhongshan (grant number 2019B1110). The sponsor or funding organization had no role in the design or conduct of this research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.106092.

References

Agusti, A., Faner, R., 2019. Lung function trajectories in health and disease. Lancet Respirat. Med. 7, 358–364. https://doi.org/10.1016/S2213-2600(18)30529-0. PMID: 30765254.

Belgrave, D.C.M., Granell, R., Turner, S.W., Curtin, J.A., Buchan, I.E., Le Souef, P.N., et al., 2018. Lung function trajectories from pre-school age to adulthood and their associations with early life factors: A retrospective analysis of three population-based birth cohort studies. Lancet Respirat. Med., 6, 526–534, PMID: 29628377, https://doi.org/10.1016/S2213-2600(18)30099-7.

Burki, T.K., 2019. The innovations cleaning our air. The Lancet Respiratory medicine 7:111–112. PMID 30638907. https://doi.org/10.1016/S2213-2600(19)30002-5.

Carey, M.A., Card, J.W., Voltz, J.W., Arbes, S.J., Jr., Germolec, D.R., Korach, K.S., et al., 2007. It's all about sex: Gender, lung development and lung disease. Trends in endocrinology and metabolism: TEM 18, 308–313, PMID: 17764971, https://doi.org/10.1016/j.tem.2007.08.003.

Cassee, F.R., Heroux, M.E., Gerlofs-Nijland, M.E., Kelly, F.J., 2013. Particulate matter beyond mass: Recent health evidence on the role of fractions, chemical constituents and sources of emission. Inhalation Toxicol. 25, 802–812, PMID: 24304307, https://doi.org/10.3109/08958378.2013.850127.

Chen, G., Li, S., Zhang, Y., Zhang, W., Li, D., Wei, X., et al., 2017. Effects of ambient pm1 air pollution on daily emergency hospital visits in china: An epidemiological study. Lancet Planet. Health 1, e221–e229, PMID: 29851607, https://doi.org/10.1016/S2542-5196(17)30100-6.

Chen, G., Knibbs, L.D., Zhang, W., Li, S., Cao, W., Guo, J., et al., 2018. Estimating spatiotemporal distribution of pm1 concentrations in china with satellite remote sensing, meteorology, and land use information. Environ. Pollut. (Barking, Essex : 1987) 233, 1086–1094, PMID: 29033176, https://doi.org/10.1016/j.envpol.2017.10.011.

Degrendele, C., Okonski, K., Melymuk, L., Landlová, L., Kukučka, P., Čupr, P., et al., 2014. Size specific distribution of the atmospheric particulate pcdd/fs, dl-pcbs and pahs on a seasonal scale: Implications for cancer risks from inhalation. Atmos. Environ. 98, 410–416. https://doi.org/10.1016/j.atmosenv.2014.09.001.

Dong GH, Qian ZM, Liu MM, Wang D, Ren WH, Bawa S, et al. 2013. Breastfeeding as a modifier of the respiratory effects of air pollution in children. Epidemiology (Cambridge, Mass) 24:387-394, PMID: 23429406, https://doi.org/10.1097/EDE.0b013e3182877eb8.

Dong, G.H., Qian, Z.M., Trevathan, E., Zeng, X.W., Vaughn, M.G., Wang, J., et al., 2014. Air pollution associated hypertension and increased blood pressure may be reduced by breastfeeding in chinese children: The seven northeastern cities chinese children's study. Int. J. Cardiol. 176, 956–961, PMID: 25186732, https://doi.org/10.1016/j.ijcard.2014.08.099.

Ghozikali, M.G., Ansarin, K., Naddafi, K., Nodehi, R.N., Yaghmaeian, K., Hassanvand, M. S., et al., 2018. Short-term effects of particle size fractions on lung function of late adolescents. Environ. Sci. Pollut. Res., 25, 22, 21822–21832, PMID: 29796884, https://doi.org/10.1007/s11356-018-2264-z.

Guo, C., Hoek, G., Chang, L.Y., Bo, Y., Lin, C., Huang, B., et al., 2019. Long-term exposure to ambient fine particulate matter (pm2.5) and lung function in children, adolescents, and young adults: A longitudinal cohort study. Environ. Health Perspect. 127, 127008, PMID: 31873044, https://doi.org/10.1289/EHP5220.

Hu, K., Guo, Y., Hu, D., Du, R., Yang, X., Zhong, J., et al., 2018. Mortality burden attributable to pm1 in zhejiang province, china. Environ. Int. 121, 515–522. https://doi.org/10.1016/j.envint.2018.09.033.

Jalava, P.I., Wang, Q., Kuuspalo, K., Ruusunen, J., Hao, L., Fang, D., et al., 2015. Day and night variation in chemical composition and toxicological responses of size segregated urban air pm samples in a high air pollution situation. Atmos. Environ. 120, 427–437. https://doi.org/10.1016/j.atmosenv.2015.08.089.

Keselman, A., Heller, N., 2015. Estrogen signaling modulates allergic inflammation and contributes to sex differences in asthma. Front. Immunol. 6, 568. https://doi.org/10.

3389/fimmu.2015.00568.
Kirrane, E.F., Luben, T.J., Benson, A., Owens, E.O., Sacks, J.D., Dutton, S.J., et al., 2019. A systematic review of cardiovascular responses associated with ambient black carbon and fine particulate matter. Environ. Int. 127, 305–316. https://doi.org/10.1016/j.envint.2019.02.027.
Li, N., Chen, G., Liu, F., Mao, S., Liu, Y., Hou, Y., et al., 2019. Associations of long-term exposure to ambient pm1 with hypertension and blood pressure in rural chinese population: The henan rural cohort study. Environ. Int. 128, 95–102. https://doi.org/10.1016/j.envint.2019.04.037.
Ma, Y.N., Wang, J., Dong, G.H., Liu, M.M., Wang D, Liu YQ, et al. 2013. Predictive equations using regression analysis of pulmonary function for healthy children in northeast china. PloS one 8:e63875, PMID: 23667682, https://doi.org/10.1371/journal.pone.0063875.
Mathur, Maya B., Tyler J., 2018. VanderWeele. R function for additive interaction measures. Epidemiology 29.1: e5, PMID: 28901974, http://doi.org/10.1097/EDE.0000000000000752.
Mehrparvar, A.H., Sakhvidi, M.J., Mostaghaci, M., Davari, M.H., Hashemi, S.H., Zare, Z., 2014. Spirometry values for detecting a restrictive pattern in occupational health settings. Tanaffos 13, 27–34 PMID: 25506373.
Mei, M., Song, H., Chen, L., Hu, B., Bai, R., Xu, D., et al., 2018. Early-life exposure to three size-fractionated ultrafine and fine atmospheric particulates in beijing exacerbates asthma development in mature mice. Particle Fibre Toxicol. https://doi.org/10.1186/s12989-018-0249-1.
Moshammer, H., Hutter, H.P., Hauck, H., Neuberger, M., 2006. Low levels of air pollution induce changes of lung function in a panel of schoolchildren. Eur. Respirat. J. 27, 1138–1143. https://doi.org/10.1183/09031936.06.00089605.
Polichetti, G., Cocco, S., Spinali, A., Trimarco, V., Nunziata, A., 2009. Effects of particulate matter (pm10, pm2.5 and pm1) on the cardiovascular system. Toxicology 261, 1–8. https://doi.org/10.1007/s11356-019-05546-8.
Shrine, N., Guyatt, A.L., 2019. New genetic signals for lung function highlight pathways and chronic obstructive pulmonary disease associations across multiple ancestries. Nat. Genet., 51(3), 481–493, PMID: 30804560, https://doi.org/10.1038/s41588-018-0321-7.
Sullivan, P.W., Ghushchyan, V.H., Marvel, J., Barrett, Y.C., Fuhlbrigge, A.L., 2019. Association between pulmonary function and asthma symptoms. J. Allergy Clin. Immunol. In Practice 7, 2319–2325. https://doi.org/10.1016/j.jaip.2019.04.019.
VanderWeele, T.J., 2009. On the distinction between interaction and effect modification. Epidemiology, 20, 6, 863–871, PMID: 19806059 http://doi.org/10.1097/EDE.0b013e3181ba333c.
Vos, T., Abajobir, A.A., Abate, K.H., Abbafati, C., Abbas, K.M., Abd-Allah, F., et al., 2017. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: A systematic analysis for the global burden of disease study 2016. The Lancet 390, 1211–1259, PMID: 28919117, https://doi.org/10.1016/S0140-6736(17)32154-2.
Xing, X., Hu, L., Guo, Y., Bloom, M.S., Li, S., Chen, G., et al., 2020. Interactions between ambient air pollution and obesity on lung function in children: The seven northeastern chinese cities (snec) study. Sci. Total Environ. 699, 134397, PMID: 31677469, https://doi.org/10.1016/j.scitotenv.2019.134397.
Prentice, R.L., 2011. Empirical evaluation of gene and environment interactions: methods and potential. J. Natl. Cancer Inst. 17, 103, 16, 1209–1210, PMID: 21791675, http://doi.org/10.1093/jnci/djr279.
Xiong, Q., Zhao, W., Gong, Z., Zhao, W., Tang, T., 2015. Fine particulate matter pollution and hospital admissions for respiratory diseases in beijing, china. Int. J. Environ. Res. Publ. Health 12, 9, 11880–11892, PMID: 26402691, https://doi.org/10.3390/ijerph120911880.
Zeng, X.-W., Vivian, E., Mohammed, K.A., Jakhar, S., Vaughn, M., Huang, J., et al., 2016. Long-term ambient air pollution and lung function impairment in chinese children from a high air pollution range area: The seven northeastern cities (snec) study. Atmos. Environ. 138, 144–151. https://doi.org/10.1016/j.atmosenv.2016.05.003.
Zhang, C., Guo, Y., Xiao, X., Bloom, M.S., Qian, Z., Rolling, C.A., et al., 2019. Association of breastfeeding and air pollution exposure with lung function in chinese children. JAMA Network Open 2https://doi.org/10.1001/jamanetworkopen.2019.4186.e194186–e194186 PMID: 31125097.
Zwozdziak, A., Sowka, I., Willak-Janc, E., Zwozdziak, J., Kwiecinska, K., Balinska-Miskiewicz, W., 2016. Influence of pm1 and pm2.5 on lung function parameters in healthy schoolchildren-a panel study. Environ. Sci. Pollut. Res. Int. 23, 23892–23901. https://doi.org/10.1007/s11356-016-7605-1.