Effect of Acute PM2.5 Exposure on Lung Function in Children: A Systematic Review and Meta-Analysis

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Abstract

Background: Long-term exposures to particulate matter 2.5 (PM2.5) impairing lung function in children, but the effect of acute exposure has not been clarified. The objective of this study was to conduct a systematic review and meta-analysis to identify the adverse effect of acute PM2.5 exposure on lung function in children.

Methods: Studies analyzing PM2.5 level and lung function in children were eligible. Effect estimates were quantified for peak expiratory flow (PEF) by using random effects models, for forced vital capacity (FVC)and forced expiratory volume in 1 s(FEV1) by using fixed effects models. Heterogeneity was investigated with Q-test and I^2 statistics. Subgroup analyses were conducted to determine the effects of acute PM2.5 exposure on children of different asthmatic status and different countries.

Results: A total of 11 studies with 4314 participants from Brazil, China and Japan were included finally. A 10 μg/m^3 increase of PM2.5 was associated with a 1.74L/min (95% CI: -2.68, -0.90) decrease in PEF. Children with severe asthma were more susceptible to PM2.5 exposure (-3.11 L/min per 10 μg/m^3 increase, 95 % CI -4.54, -1.67) than healthy children (-1.61 L/min per 10 μg/m^3 increase, 95 % CI -2.34, -0.91). The change of PEF in children of Brazil was -0.38 L/min(95 % CI -0.91, 0.15) per 10 μg/m^3 increase of PM2.5, which was slighter than that in China (-1.54 L/min, 95 % CI -2.33，-0.75) and Japan (-1.72 L/min, 95 % CI -3.82 , 0.36). Elevated PM2.5 exposure was also associated slight alteration of FVC and FEV1, with no significant difference presented.

Conclusions: Our results demonstrated that the acute PM2.5 exposure has an adverse impact on children's lung function, and children with severe asthma were more susceptible when PM2.5 concentration increases. The impact of PM2.5 varies among the three countries. More measures should be taken to protect lung function of children from PM2.5 exposure.

Background

Air pollution, a culprit of human respiratory problems, is challenging human health worldwide [1]. The components of air pollution are fine particulate matters of different aerodynamic diameters. Particulate matter 2.5 (PM2.5) is defined as tiny airborne particles or droplets of two and a half microns or less in width [2]. As an important source of pollutants, PM2.5 is characterized by small size, complex composition, allergen absorptivity and sensitization enhancing property [3]. The sources of PM2.5 include automobile emissions, urban constructions, smokestacks, power plants, industrial and biomass burning. PM2.5 not only penetrates the human respiratory system deeply due to its small size but also carries toxic and harmful substances such as transition metals and polycyclic aromatic hydrocarbons (PAHs) into human bodies [4]. PM2.5 is associated with a myriad of different adverse health effects, such as asthma [5], chronic obstructive pulmonary disease(COPD) [6], cardiovascular disease [7], and cancer [8]. Exposure to PM2.5 confers an increased risk of wheeze-associated disorders [9], asthma-related emergency room visits and hospital admissions in children [10].

Ambient air pollution is damaging the human respiratory system. Lung function is an early indicator to evaluate and quantify the effect of air pollution on respiratory system and a sub-clinical marker with clinical implications for lung health across the lifespan [11]. Children are more susceptible to air pollution because of their faster breath rate and immature immunity [12]. The grow phase of the lung is critical among the three phases of normal lung function trajectory [13]. Abnormal lung function in the growth phase is associated with future adverse clinical outcomes, such as propensity to develop respiratory diseases, and early multimorbidity [14]. Hence, it is urgent to investigate the effects of PM2.5 exposure on childhood lung function.

Previous meta-analyses indicated that both acute and long-term exposure to outdoor PM2.5 was significantly associated with decreased lung function in healthy and asthma adults [15, 16]. One meta-analysis based on European birth cohort study revealed that long-term exposure to PM2.5 resulted in decreased lung function in schoolchildren [17]. However, this study only focused on the relation between PM2.5 exposure and FEV1 alteration. Since acute and long-term PM2.5 exposure may have different impacts on health outcomes[15, 16] and few meta-analyses have clarified the association between acute exposure of PM2.5 and childhood lung function, the objective of this study was to quantify the effect of acute outdoor exposure of PM2.5 on the lung function of children by performing a comprehensive systematic review and meta-analysis.

Methods

Design

This study followed the Preferred Reporting in Systematic Reviews and Meta-Analyses (PRISMA) guidelines[18].

Literature search and selection

A comprehensive literature search was conducted to identify potential articles published on the acute effect of PM2.5 on children's lung function. We systematically searched Embase, PubMed, the Cochrane library, Web of Science, China biomedical literature database (CNKI), Chinese Biomedical Literature (CBM) databases for literature published before February 2022 and identified the studies describing the relationship between acute PM2.5 exposure and lung function in children up to 18 years old of age with no geographical or language restrictions. The PubMed search string used was as follows:

(PM2.5 OR Ultrafine Fibers OR Ultrafine Fiber OR Fiber, Ultrafine OR Airborne Particulate Matter OR Particulate Matter, Airborne OR Air Pollutants, Particulate OR Particulate Air Pollutants OR Ambient Particulate Matter OR Particulate Matter, Ambient OR Ultrafine Particulate Matter OR Particulate Matter, Ultrafine OR Ultrafine Particles OR Particles, Ultrafine OR Ultrafine Particle OR Particle, Ultrafine OR Particulate Matter*) AND (children OR Child*) AND (Function Test, Respiratory OR Function Tests, Respiratory OR Test, Respiratory Function OR Tests, Respiratory Function OR Pulmonary Function Tests OR Function Test,

Pulmonary OR Function Tests, Pulmonary OR Test, Pulmonary Function OR Tests, Pulmonary Function OR Lung Function Tests OR Function Test, Lung OR Function Tests, Lung OR Lung Function Test OR Test, Lung Function OR Tests, Lung Function OR Pulmonary Function Test OR Respiratory Function Tests*)

Detailed search strategies were presented in Additional file Table 1. In order to avoid bias, two reviewers independently assessed the eligible studies by examining the full text of articles based on the pre-defined eligibility criteria.

Table 1
Study characteristics.

Authors/year	Region/Country	Study type	Population (number)	Average age (years old)	Daily mean concentration of PM2.5 (μg/m3)	Lag (days)	Outcome: observed change (change per 10 μg/m3 PM2.5 increase in pollutant when applicable)	Statist model
Lu Ma/2008	Yotsukaido, Japan	cohort study	Children with severe asthma(19)	Mean age 12.9	22.6	lag0-1	PEF:-3.40L/min(95%CI:-6.47, -0.33)	Genera Estima Equati model
BingYu /2010	Taiwan,China	cohort study	Healthy, asthmatic, and allergic rhinitis school children (100)	Mean age 10.6	28.2	lag0-1	FVC:-0.16L (95%CI:-0.23, -0.08) FEV1:-0.12L (95%CI:-0.20, -0.05)	Mixed-effects models
Yamazak /2011	Yotsukaido, Japan	cohort study	Children with severe asthma(17)	8–15	Not reported	lag0-1	PEF:-2.96L/min (95%CI:-4.55, -1.37)	Genera Estima Equati
Ludmilla/2012	Amazon,Brazilian	cohort study	Healthy and asthmatic children(280)	Mean age 10.4	24.34	lag0-1	PEF:-0.29L/min (95%CI:-0.52, -0.07)	Mixed-effects models
Ludmilla/2014	Tangara,Brazil	cohort study	Healthy and asthmatic children(220)	Mean age 10.3	19.6	lag0-4	PEF: -0.54L/min (95%CI:-0.946, -0.137)	Mixed-effects models
Masanari/2016	Matsue,Japan	cohort study	Healthy,asthmatic,allergic rhinitis children(339)	10–12	Not reported	lag0-1	PEF: -1.72 L/min (95%CI:-3.82, 0.36)	Linear mixed model
Dandan Xu/2018	Nanjing, China	cohort study	Healthy School children(86)	Mean age 9	84.3	lag0-1	PEF:-1.76L/min (95%CI: -3.549, 0.024) FVC: -0.023L (95%CI: -0.033, -0.013) FEV1:-0.019 L (95%CI: -0.029, -0.009)	Mixed-effects regress mode
Liu Weiyan/2019	Hangzhou,China	cohort study	Healthy school children(1685)	Mean age 9.8	50	lag0-1	PEF:-2.34L/min (95%CI: -4.02, -0.72)	Linear mixed model
Dandan Xu/2020	Zhejiang, China.	cohort study	Healthy and asthmatic school children (848)	Mean age 9.7	67.58	lag 1	PEF:-4.02L/min (95%CI: -5.36, -2.73) FVC:-0.034L (95%CI: -0.045, -0.023) FEV1:-0.033L (95%CI: -0.044, -0.021)	Mixed-effects regress mode
Yang Xiaoyan/2020	Beijing, China	cohort study	Healthy school children(51)	9–12	57.75	lag4	PEF:-0.49L/min (95%CI:-2.84, 1.87) FVC:-0.033L (95%CI:-0.050, -0.015) FEV1:0.003L (95%CI:−0.015, 0.020)	Linear mixed effects model

Authors/year	Region/Country	Study type	Population (number)	Average age (years old)	Daily mean concentration of PM2.5 (μg/m3)	Lag (days)	Outcome: observed change (change per 10 μg/m3 PM2.5 increase in pollutant when applicable)	Statist model
WU Xingbin/2020	Jinan, China	cohort study	Healthy school children(484)	Not reported	90	lag0-1	PEF:-1.54L/min (95%CI:-2.33, -0.76) FVC: -0.008L (95%CI:-0.014, -0.003) FEV1:-0.008L (95%CI:-0.012,-0.003)	Multipl Linear regress model

Inclusion And Exclusion Criteria

Studies examining the relationship between acute (daily) exposure to outdoor air pollution PM2.5 and lung function in children were eligible for this review. The flow of the review process is shown in Fig. 1. Studies were included when meeting all the following criteria:(i)quantitatively analyzing the change of lung function index when 10 μg/m^3 PM2.5 increased;(ii)children up to 18 years old of age as study subjects;(iii) published in full-text;(iv) analyzing acute exposure to PM2.5.Studies were excluded if meeting any of the following criteria:(i)reviews, conference abstracts, editorial letters, or comments;(ii)not related to ambient PM2.5 (e.g. only related to indoor, passive smoking or other pollutions);(iii)no measurement of lung function in children;(iv)no quantitative results for the effects;(v)only analyzing long term exposure to PM2.5;(vi)with insufficient data.

Data Extraction

Two reviewers extracted the data from the eligible literature, including study time, study types, country, simple size, average age of population, daily mean concentration of PM2.5, controlled variables, lag days of exposure, and statistical analysis model. All effect measures were transformed to per 10μg/m^3 increase in PM2.5, assuming a linear relationship between the concentration of particulate matter and lung function. Some studies often reported assessing the effect of acute exposure to air pollution by different time periods (lag of 0, 1, or 2 days, etc.). In order to reduce the heterogeneity of the original studies, we recorded the effect noted at 1 day after exposure whenever possible. The reviewers then used a standardized data extraction format in Microsoft Office Excel 2019 to extract all the necessary data. A third person resolved the disagreement between the two reviewers. An extract of these collected data is presented in Table 1, using the Preferred Reporting Items for Systematic and Meta-analyses (PRISMA) guidelines[18].
(Table 1 location)

Study Quality Assessment

Two investigators independently performed quality assessment of the cohort studies using the Newcastle-Ottawa Scale (NOS) [19]. NOS contains 8 items, 9 was the highest score, and a maximum of 2 scores could be obtained for comparability. The scales and grading are presented in Additional file. Adjustment for confounding was based on three factors: a) asthma status, asthmatic medicinal usage, passive smoking; b) environmental parameters, such as temperature and humidity; c) individual factors, such as age, gender, BMI, height, and weight. A good control was considered for adjustment for all 3 factors, fair for adjustment for 2 factors and poor for adjustment for 1 or less factor. The quality of studies was categorized as poor, fair, and good.

Statistical analysis

To determine the effect of acute PM2.5 exposure on lung function in children, we conducted the meta-analysis separately for different indices such as PEF, FEV1and FVC. Effect estimates per 10 μg/m^3 were combined to calculate summary effect estimates using generic inverse variance method assuming a random effects model or a fixed effects model. A forest plot was used to assess visually the change of indicators of children's lung function and corresponding 95% confidence. If a confidence interval was presented, the corresponding standard error was calculated as (upper CI- lower CI)/(xn-x0 *3.92), where CI refers to confidence interval, xn denoted exposure at the level of group n, and x0 denoted exposure at the reference group. The standard error was calculated following the method recommended by published articles[20]. Heterogeneity among studies was statistically investigated with the Q-test and the I^2 statistics. When I^2 > 50%, the random effects model was used; when I^2<50%, the fixed effects model was used. Publication bias was assessed using funnel plot and Egger's linear regression method. Considering that the group of FEV1 and FVC only contained the data of Chinese healthy children and the data of children with severe asthma were not included, we performed a subgroup analysis to clarify the impact of asthmatic status on PEF of children. There are 2 studies including the children with severe asthma and 4 studies including healthy children. So, we performed subgroup analysis on these 6 studies. There are 4 studies including both asthmatic and healthy children which were not included in subgroup analysis. We also performed a subgroup analysis by dividing the children into three country groups: China, Japan and Brazil. All analyses were performed using the R computing framework (www.r-project.org).

Results

Literature search

We systematically searched PubMed, Embase, Web of Science, the Cochrane library, China biomedical literature database (CBM) and Chinese National Knowledge Infrastructure (CNKI) and identified 1123 studies in the initial search (Fig. 1). Among the 145 studies going through full-text review, 134 were excluded, and ultimately 11 studies were included in this meta-analysis[21–27][11, 12, 28, 29]. The primary reason for exclusion was the lack of quantitative results for the effects. Other reasons for exclusion included the lack of outdoor PM2.5 measurement or lung function.

Characteristics Of Included Studies

The characteristics of the 11 studies examining the association between acute exposure to outdoor PM2.5 and lung function in children are described in Table 1. Of these studies, ten studies examined the association between PEF and acute exposure to PM2.5[11, 12, 21, 23–29]. Data from 4129 individuals from three different countries were examined in these reports. Of the included studies, six were conducted in China, three in Japan, and two in Brazil. Two studies included children with severe asthma, three studies included both healthy and asthmatic children, two studies included healthy, asthmatic, allergic rhinitis school-age children, and four studies only included healthy children. All of the studies were about the acute exposure of PM2.5 and lung function in children.

Risk Of Bias Among Included Studies

The quality of included studies was assessed by the two authors. After By applying the NOS, study quality was appraised as follows: Eight studies were rated as good[11, 21–26, 28], and three were rated as fair [12, 27, 29]. Five studies that included both asthmatic and healthy children failed to provide the exact information about the quantitative lung function change of the two groups of children[22, 24–26, 28], so they were not considered as healthy or asthmatic group in subgroup analysis. The results for each item from each study are shown in Additional file Table 2.

Meta-analyses

The association between acute exposure to ambient PM2.5 and changes of lung function indicators in children is graphically displayed in Fig. 2. A significant association was found between PM2.5 exposure and the change of PEF(L/min) in children($P < 0.01$). A 10 μg/m^3 increase of PM2.5 was associated with a change in PEF of -1.74L/min (95% CI: -2.68, -0.90). In contrast, no statistically significant associations of a 10 μg/m^3 increase of PM2.5 with FVC and FEV1 were observed (-0.03L [95% CI: -0.08, -0.01] and – 0.02L [95% CI: -0.05, 0.00], respectively). There was substantial heterogeneity among studies included in the PEF analysis ($I^2 = 70.89\%$), but low heterogeneity among studies included in the FVC ($I^2 = 0.0\%$) and FEV1 ($I^2 = 0.0\%$) analyses, respectively. There was no statistical evidence of publication bias for any of the analyses (Egger's regression test: $p = 0.15$ for PEF, $p = 0.40$ for FVC, and $p = 0.52$ for FEV1). Forest plots of change in PEF, FVC, FEV1 per 10 ug/m^3 increase in PM2.5 level were showed in Fig. 2. Funnel plots for the publication bias are provided in Additional file Fig. 1–3.

Subgroup Analyses

Asthma status might modify the relationship between PM2.5 exposure and PEF in children, we conducted subgroup analyses of the studies that included children with severe asthma and healthy children. When the concentration of ambient PM2.5 showed a 10 μg/m^3 increase, there was a significant decrease in PEF (-1.61 L/min, -2.34, -0.91) in healthy subgroup, but a more significant decrease was found in severe asthmatic group (-3.11 L/min, -4.54, -1.67). We also conducted subgroup analyses of the studies excluding children with severe asthma in different countries. Studies in Brazil showed a PEF decrease of -0.38 L/min (-0.91, 0.15), while results in China and Japan showed PEF reduced by -1.54 L/min (-2.33, -0.75) and – 1.72 L/min (-3.82, 0.36), respectively. Relationship between acute PM2.5 exposure and PEF alteration indicated that asthma status and country of studies were both sources of heterogeneity. The results of subgroup analyses are described in Table 2.

Table 2
Subgroup analysis by asthma and country examining the relationship between PM2.5 and PEF in children.

Subgroups	Estimate(n)	Included studies	Change in PEF per 10μg/m^3 of PM2.5 (95% CI)	I^2
Asthma				
Severe Asthma group	2	Lu Ma/2008, Yamazak /2011	-3.11 L/min (-4.54, -1.67)	0%
Health group	4	Dandan Xu/2018, Liu Weiyan/ 2019, Yang Xiaoyan/2020, WU Xingbin/2020	-1.61 L/min (-2.34, -0.91)	0%
Country				
China	5	Dandan Xu/2020, Dandan Xu/2018, Liu Weiyan/ 2019, Yang Xiaoyan/2020, WU Xingbin/2020	-1.54 L/min(-2.33, -0.75)	53.6%
Japan	1	Masanari/2016	-1.72 L/min (-3.82, 0.36)	NA
Brazil	2	Ludmilla/2012, Ludmilla/2014	-0.38 L/min(-0.91, 0.15)	0%

Discussion

This study is, to our knowledge, the first meta-analysis assessing the effects of acute exposure to outdoor PM2.5 on lung function in children. We found that increased PM2.5 levels was significantly associated with decreases in PEF (-1.74L/min per 10μg/m^3 increase in PM2.5). Elevated PM2.5 exposure was also associated slight alteration of FVC and FEV1, with no significant difference presented.

The effect of acute PM2.5 exposure on PEF was more significant in children with severe asthma, suggesting that asthmatic children are more vulnerable to PM2.5 exposure than healthy ones. Zhang et al [30] showed that PM2.5 exposure induced higher variation in NOS2(Nitric Oxide Synthase2) in children with asthma, which contributing to greater alteration of lung function. In addition, patients with severe asthma produced more cytokines when exposed to PM2.5 than healthy ones[31]. In contrast, Ludmilla[24] indicated that PM2.5 exposure had little effect on asthmatic children. However, for non-asthmatic children there was a significant reduction of PEF for a 10 ug/m^3 increase of PM2.5. This discover may result from the fact that the asthmatic subjects tend to take medication when they perceive the deteriorating air quality according to the author. Previous studies showed that anti-inflammatory medication in asthmatic children could significantly alleviate the effect of PM2.5 exposure on PEF[32]. The impact of acute PM2.5 exposure was more obvious in studies involving children with severe asthma, suggesting that asthma status may amplify the effect of acute PM2.5 exposure on lung function.

PM2.5 exposure appeared to exert profounder effect on children's lung function than that of adults, suggesting that children are more vulnerable to PM2.5 exposure than adults. One meta-analysis found a 10 μg/m^3 increase of PM2.5 was associated with a 1.02L/min decrease of PEF in non-smoking asthmatic adults, while no decrease of PEF was found in smokers[4]. Ge Mu showed a 10 μg/m^3 increase of PM2.5 was associated with a 0.972 L/min decrease of PEF among 4697 urban adults[33]. The change of PEF in our finding was more obvious than these previous studies. In addition, Jingchun Fan's meta-analysis showed that the risk of asthma emergency department visits due to per 10 μg/m^3 increase in PM2.5 was much higher in children than in adults [34]. Sandra also revealed that younger children were more susceptible to air pollution [35]. Compared with adults, children have undeveloped lungs, higher baseline respiratory rates, more time spending outdoors, more frequent mouth-breathing, larger lung surface area per unit of body weight, all making them more vulnerable to PM2.5 exposure [36].

The reduction of lung function can be attributed to the inflammatory response, oxidative stress, and bronchial epithelium cell apoptosis caused by PM2.5. A previous study found pro-inflammatory response induced by airborne PM resulted in weakened pulmonary function in schoolchildren [26]. An in vivo study suggested that a variety type of cells might cause inflammation response through different pathways when exposed to PM2.5: Macrophages released proinflammatory mediators via the LPS/MyD88 pathway, while type II alveolar cells mainly caused oxidative stress-dependent inflammation[37]. Decreased lung function was related to not only proinflammatory mediators but also microRNAs. After PM2.5-inhalation, Balb/c mice showed decreased MiR-146a and miR-146b, and dramatically increased IL-6, INF-γ and TNF-α; miR-146a level was found negatively related to PEF[38]. Persistent endoplasmic reticulum stress caused by oxidative stress contributes to the lung damage induced by PM2.5 exposure[39]. An in vitro study demonstrated that PM2.5 could not only cause inflammatory responses and oxidative injury, but also trigger the autophagy-mediated apoptosis of mice bronchial epithelium cells via PI3K/AKT/mTOR pathway[40].

When stratified by geographical location, PM2.5 showed varied effects on PEF of children without severe asthma in different countries. The results indicated that PM2.5 exposure in different countries may have different physiologic consequences. Firstly, this phenomenon may result from different concentration, compositions, inflammatory chemotaxis of PM2.5 among countries[41–43]. The effect of air pollution may be less obvious in areas with low PM2.5 concentrations, so larger sample sizes are needed to illustrate the associations between PM2.5 exposure and lung function in different areas [41, 42]. The effects of PM2.5 exposure on lung function in children may depend more on the pro-inflammatory response to the PM composition than on the PM mass concentration[41, 42]. The different contents of allergens, polycyclic aromatic hydrocarbons, especially heavy metals in PM2.5 exposure can lead to various inflammatory responses [41, 42, 44]. Secondly, population susceptibility, gene polymorphisms and dietary habits may also contribute to different effects of PM2.5 exposure among countries. A cohort study in China found that gene-environment interaction of Sirtuin 1 (SIRT1) was associated with different mortality caused by PM2.5 exposure among the elder people[45]. DNA repair gene XPC might play a role in the pathogenesis of respiratory diseases, and children with the CC alleles of XPC polymorphisms were found to be more susceptible to the adverse effects of ambient air pollution[46]. People often eating antioxidant food such as fruits and vegetables may be less vulnerable to the adverse effects of PM[47]. Lastly, the distinct climate, temperatures and humidity may also contribute to the varied effects of PM2.5 exposure in different countries [48].

In the subgroup analysis, we found the alteration of PEF in children's pulmonary function was much slighter in Brazil than in China and Japan. The subgroup analysis was only restricted to the studies that excluded children with severe asthma, because these children had dramatically changed PEF. The reason for the slight PEF change in Brazil was that the PM2.5 concentration in Brazil was much lower than China. In our study, the PM2.5 concentration in China fluctuated between 50 and 90μg/m^3, while in Brazil, it ranged from 19.6 to 24.34μg/m^3. The relatively higher PM2.5 concentration in China is responsible for the bigger change of PEF in children. In addition, in the non-severe asthmatic children of Brazil, inhaling drugs such as corticosteroids during air pollution deterioration made the effect on PEF slighter. An explanation for the heterogeneity was that the proportions of asthmatic children was different among studies excluding individuals with severe asthma and the children couldn't be divided into asthmatic or healthy group due to incomplete information. Another explanation for the heterogeneity was that the studies were of different types and spanned over 20 years.

The alteration of FVC and FEV1 at PM2.5 exposure were slight in our study, showing no statistical significance. In contrast, Ge Mu found that each 10 μg/m^3 increase in the previous-day personal PM2.5 exposure was associated with significant decreases in FVC and FEV1[33]. Ralph J. Delfino[49] also revealed that FEV1 decrements were significantly associated with the increasing personal PM2.5 exposure, but not the ambient PM2.5. We speculate that the personal PM2.5 exposure might exert more significant impacts than ambient PM2.5 exposure on FVC and FEV1. Our result may also be influenced by the smaller sample size including FVC and FEV1 in children exposed to ambient PM2.5. Furthermore, the study of ESCAPE Project suggested[17] that long-term exposure to PM2.5 might result in reduced FEV1 in schoolchildren, indicating that the different effects of long-term and short-term PM2.5 exposure on FEV1.

Our meta-analysis had some limitations. First, the number of studies within each subgroup was small. The results of subgroup analysis should therefore be interpreted with caution. Second, the studies included in our meta-analysis were mainly on school-age children because the children of this age are more frequently exposed to PM2.5. It was impractical to perform subgroup analysis stratified by age due to the similar age of children in different studies. However, studies on children of other age groups are needed in further. Thirdly, we made an assumption of a linear relationship between PM2.5 exposures and lung function. We didn't know whether there was truly linear relationship between PM2.5 and lung function because of lack of data. But this method was also used by other meta-analyses about relationship between air pollution and lung function[5, 15]. Lastly, we discussed the effect of ambient PM2.5 exposure on children's lung function while the results may be different from those studies on personal PM2.5 exposure. Hence, more researches are needed in future work.

Despite the limitations, our meta-analysis also had some strengths. Firstly, as far as we know, it is the first meta-analysis about the association between acute PM2.5 exposure and lung function in children. Secondly, we attempted to reduce heterogeneity among studies by using a consistent lag time (one day) when possible and analyzing different subgroups by asthmatic status and countries. Thirdly,we also demonstrated the different effects of PM2.5 exposure on lung function in children among three countries. Lastly, we strived to address the issue of confounding and performed subgroup analysis on studies with severe asthmatic and healthy children, which demonstrated more obvious effects of acute PM2.5 exposure on children with severe asthma.

Conclusion

In summary, our results demonstrated that acute PM2.5 exposure was associated with reduced PEF in children. Acute PM2.5 exposure may induce more obvious effect on children with severe asthma. The impact of PM2.5 varies among the three countries. Further researches are required to better quantify this effect and compare the effects of different concentration of PM2.5.

Abbreviations

CI
95% confidence interval
PM2.5
particulate matter 2.5
PEF
peak expiratory flow
FVC
forced vital capacity
FEV1
forced expiratory volume in 1 s
PAHs
polycyclic aromatic hydrocarbons
COPD
chronic obstructive pulmonary disease
PRISMA
Preferred Reporting Items for Systematic Reviews and Meta Analyses
NOS
Newcastle-Ottawa Scale
NOS2
Nitric Oxide Synthase 2
Sirtuin 1
SIRT1.

Declarations

Consent to for publication

Not applicable.

Ethics approval and consent to participate

Not applicable here, as this is systematic review and meta-analysis.

Competing interests

The authors declare that there are no competing interests.

Availability of data and materials

All data used in this meta-analysis are freely and publicly available from the cited papers used in the analysis; the full citations are in the reference list.

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Authors' contributions

YMZ, ZXL, QYL conceived, designed the review and did the data collection analysis for the study. QYL and YMZ performed quality assessment of the studies.The manuscript was drafted by YMZ. ZXL reviewed the manuscript originally submitted and revised it following the reviewer's comments. ZLW and ZYG checked the final analysis and revised the manuscript. The authors read and approved the final manuscript.

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Figures

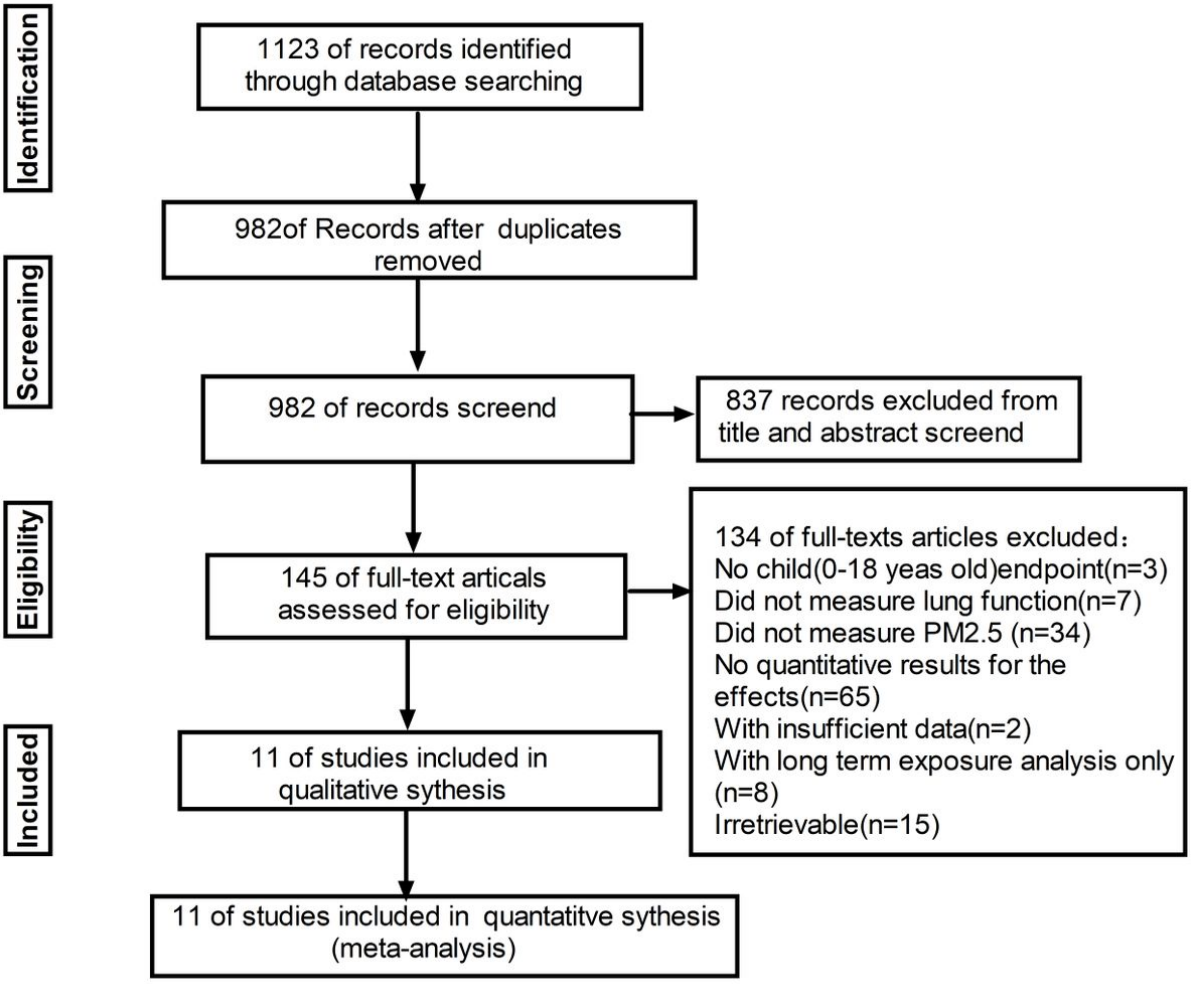

Figure 1

Flow diagram of the selection procedure of studies.

Legend: A PRISMA flow diagram that details the inclusion and exclusion of studies considered for this systematic review.

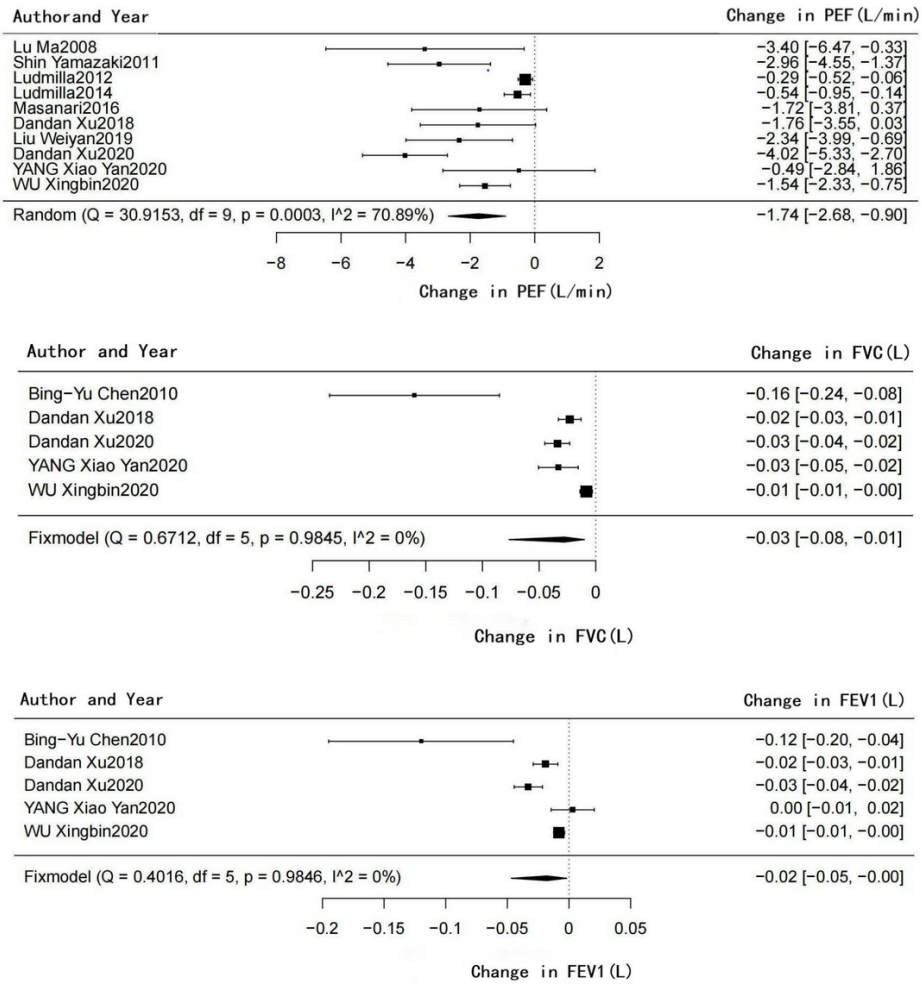

Figure 2

Forest plots of change in PEF, FVC, FEV1 per 10 ug/m^3 increase in PM2.5 level.

Legend: The summary estimates for PEF was calculated using a random-effects meta-analysis. The summary estimates for FVC, FEV1 were calculated using a fixed-effects meta-analysis.

Supplementary Files

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