Environment International 128 (2019) 103–108

Contents lists available at ScienceDirect

Environment International

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

Exposure to ambient particulate matter air pollution, blood pressure and hypertension in children and adolescents: A national cross-sectional study in China

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A R T I C L E I N F O

Handling Editor: Hanna Boogaard

Keywords:
Air pollution
Particulate matter
Blood pressure
Hypertension
Children
Adolescents

A B S T R A C T

Background: Air pollution has been associated with elevated blood pressure in adults. However, epidemiological evidence from children and adolescents is limited. We investigated the associations between long-term exposure to particulate matter (PM) air pollution and blood pressure in a large population of children and adolescents.
Methods: A cross-sectional analysis was performed in a nationally representative sample consisting of 43,745 children and adolescents aged 7 to 18 years in seven provinces in China. Exposure to ambient fine particles ($PM_{2.5}$) and thoracic particles (PM_{10}) was estimated using spatiotemporal models based on satellite remote sensing, meteorological data and land use information. Mixed-effects (two-level) linear and logistic regression models were used to investigate the associations between PM exposure and systolic blood pressure (SBP), diastolic blood pressure (DBP) and hypertension.
Results: After adjustment for a wide range of covariates, every 10 μg/m^3 increment in $PM_{2.5}$ and PM_{10} concentration was associated with 1.46 [95% confidence interval (CI): 0.05, 2.88] and 1.36 (95% CI: 0.34, 2.39) mmHg increases in SBP, respectively. PM_{10} was also associated with higher prevalence of hypertension [odds ratio per 10 μg/m^3 increment: 1.45 (95% CI: 1.07, 1.95)].
Conclusions: Long-term exposure to ambient PM air pollution was associated with increased blood pressure and higher prevalence of hypertension in children and adolescents. Our findings support air pollution reduction strategies as a prevention measure of childhood hypertension, a well-recognized risk factor of future cardiovascular health.

1. Introduction

Cardiovascular disease is a leading cause of death worldwide, responsible for around 17.8 million global deaths in 2017 according to the latest estimates of Global Burden of Disease Study (Roth et al., 2018). Hypertension is one of most important risk factors for cardiovascular disease because of its high prevalence and concomitant cardiovascular risks (Kearney et al., 2005). The etiology of hypertension is complex and its development involves various factors and their interactions, such as genetics, lifestyle and environmental factors including air pollution (Brook et al., 2009).

Air pollution is considered as the greatest environmental risk to health by the World Health Organization, responsible for > 7 million annual premature deaths worldwide (World Health Organization, 2019). Particulate matter (PM) is perhaps the most important pollutant which affects more people than any other pollutant (World Health

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https://doi.org/10.1016/j.envint.2019.04.036
Received 31 January 2019; Received in revised form 12 April 2019; Accepted 16 April 2019
Available online 03 May 2019

Organization, 2018). In recent decades, an increasing number of epidemiological studies have been conducted to investigate the associations between exposure, particularly long-term exposure, to PM air pollution and blood pressure and hypertension (Yang et al., 2018). Although most studies indicated a positive association between PM exposure and blood pressure and hypertension, controversy still remains (Yang et al., 2018). Moreover, the majority of previous epidemiological studies were conducted in adult populations and evidence from children is limited. Children are more vulnerable to the adverse effects of air pollutants because of the underdeveloped lungs and defending system and increased exposure due to higher minute ventilation and higher levels of physical activity (Kim and American Academy of Pediatrics Committee on Environmental Health, 2004). Only a few studies investigated the association between long-term PM exposure and blood pressure in child populations and the findings are inconsistent (Bilenko et al., 2015a; Bilenko et al., 2015b; Dong et al., 2014; Dong et al., 2017; Li et al., 2018; Liu et al., 2014).

Mounting evidence has shown that blood pressure tracks well from childhood to adulthood and elevated blood pressure in childhood is a good predictor of hypertension in adulthood (Chen and Wang, 2008). Elevated childhood blood pressure has also been associated with impaired cardiovascular health in adulthood (Magnussen et al., 2013). Identification of the health effects of PM air pollution on childhood blood pressure may provide insights into the prediction and early prevention of hypertension and related cardiovascular disease later in life. We therefore investigated the associations of long-term exposure to ambient fine particles (aerodynamic equivalent diameter < 2.5 μm; $PM_{2.5}$) and thoracic particles (aerodynamic equivalent diameter < 10 μm; PM_{10}) with blood pressure and hypertension prevalence in children and adolescents in Mainland China, a region with high levels of PM air pollution and heavy disease burden of hypertension (Lu et al., 2017).

2. Methods

2.1. Study population

Study participants were from a national project which aimed to assess the effectiveness of a lifestyle intervention program targeting obesity in Chinese children and adolescents. The study protocol has been documented in detail elsewhere (Chen et al., 2015). Briefly, over 60,000 children and adolescents aged 7 to 18 years were recruited from 94 schools in seven provinces/municipalities (Chongqing, Hunan, Guangdong, Liaoning, Ningxia, Shanghai and Tianjin) in Chinain 2013 (Fig. 1), based on a multi-stage random cluster sampling. The random

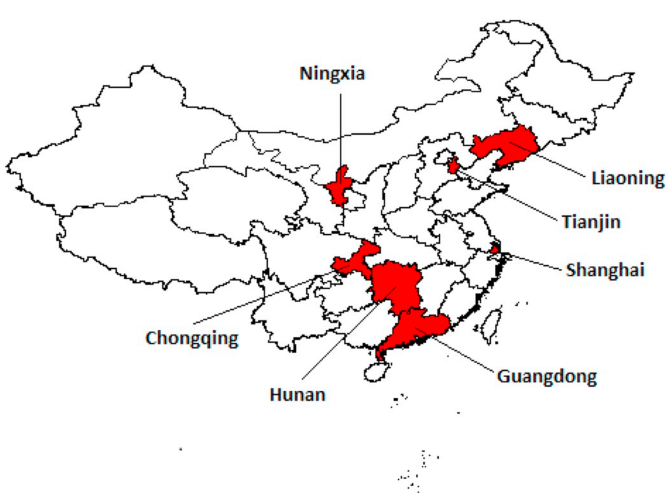

Fig. 1. Locations of the seven studied provinces/municipalities in China.

sequence was generated using computer and was stratified by school district, school grades (primary, secondary or high school) and school size in each province. All students who lived in the same area for at least 1 year were invited to participate and the response rate was higher than 95% in all schools. Participants and their parents/guardians gave written informed consent prior to their participation. The study protocol was approved by the Ethical Committee of Peking University Health Science Center (Reference No.: IRB0000105213034).

At baseline, participants underwent a series of physical examinations (e.g. height, weight and blood pressure measurements), blood tests and questionnaire survey. In the present study, we conducted a cross-sectional analysis using the baseline data. Blood pressure measurements were available for 599,59 participants. A total of 16,214 participants were excluded due to missing information on important potential confounders (e.g. lifestyle factors and parental smoking), leaving 43,745 participants in data analysis. (Fig. S1).

2.2. Air pollution exposure assessment

We used a machine learning method with Radom Forests Model for PM exposure assessment (Chen et al., 2018a; Chen et al., 2018b). The model combined satellite-derived aerosol optical depth (AOD) data, meteorological data and land use information to calculate daily concentrations of $PM_{2.5}$ and PM_{10} in Mainland China at a $0.1^\circ \times 0.1^\circ$ spatial resolution. The AOD data were combined from two types of Moderate Resolution Imaging Spectroradiometer (MODIS) algorithms, Dark Target and Deep Blue. The models showed good predictive ability when validated against ground-measured monitoring data in China. For $PM_{2.5}$, the R^2 and root mean squared error (RMSE) of 10-fold cross-validation were 83% and 18.1 μg/m^3, 86% and 10.7 μg/m^3 and 86% and 6.9 μg/m^3 for daily, monthly and annual estimates, respectively (Chen et al., 2018b). For PM_{10}, the R^2 and RMSE were 78% and 31.5 μg/m^3, 82% and 19.3 μg/m^3 and 81% and 14.4 μg/m^3 for daily, monthly and annual estimates, respectively (Chen et al., 2018a).

The addresses of the 94 schools were transformed into latitude and longitude data. Afterwards, address-specific annual average concentrations of $PM_{2.5}$ and PM_{10} were calculated. In the present study, we calculated the annual average $PM_{2.5}$ and PM_{10} concentrations of 2012 (the year prior to the baseline survey) as surrogates of long-term exposure to ambient PM air pollution. In addition to PM measurements, we also estimated annual average concentration of nitrogen dioxide (NO_2), which was used as a covariate to examine its potential influence on the effects of PM exposure on blood pressure. A spatial-temporal model was used for NO_2 estimation. The details of the model have been documented elsewhere (Zhan et al., 2018). Briefly, a hybrid model random-forest and spatiotemporal kriging model was developed to estimate the daily ambient NO_2 concentrations across China during 2013–2016 based on the satellite retrievals and geographic covariates. The model showed good prediction performance. The R^2 and RMSE were 62% and 13.3 μg/m^3 for daily NO_2 predictions in cross-validation.

2.3. Blood pressure measurement

The details of blood pressure measurement have been described previously (Chen et al., 2015; Dong et al., 2017). Briefly, seated blood pressure was measured after 10-min rest using an auscultation mercury sphygmomanometer (Model XJ1ID, Shanghai Medical Instruments Co. Ltd., China). An appropriate cuff for children was used. The cuff was placed around 2 cm above the crease of the right arm elbow. Systolic blood pressure (SBP) was determined by onset of the first Korotkoff sound (K1) and diastolic blood pressure (DBP) was determined by the fifth Korotkoff sound (K5). Blood pressure measurement was carried out twice and the average of the two readings was used in data analysis. All measurements were carried out by trained technicians based on standard protocols. The equipment was calibrated regularly.

2.4. Covariates

Covariates were selected a priori, mainly based on literature review of previous studies. In addition to blood pressure, weight and height were also measured with participants wearing light clothing and no shoes. Body mass index (BMI) was then calculated as weight (kg) divided by the square of height (m).

A self-administered questionnaire was used to collect information on participants` demographic information and lifestyle factors. For children of grade 1–3, the questionnaire was completed by their parents/guardians. Exercise was classified into three levels based on the reported daily time spent on outdoor exercising: < 1 h/day, 1–2 h/day or ≥2 h/day. Information on fruit intake was collected by a question "In the past week, how many days did you eat fruits (at least one serving)?" and was classified into three groups: ≤ 3 days/week, 4–6 days/week or daily. A similar question was used for vegetable intake. Information on parental smoking (either parent: yes or no), parental education (highest degree of either parent: primary school or illiterate, secondary school, high school, or college/university or above) and parental hypertension (either parent: yes or no) was collected by a parental questionnaire.

We generated two geographical indicators including one for north vs south (south: Chongqing, Hunan, Guangdong and Shanghai; north: Liaoning, Ningxia and Tianjin), and another for rurality (rural vs urban). We also collected information on two region-level covariates including annual average temperature and gross domestic product (GDP) per capita, which were obtained from the China Meteorological Administration (http://www.cma.gov.cn) and National Bureau of Statistics of China (http://www.stats.gov.cn).

2.5. Statistical analysis

We used mixed-effects linear regression models to investigate the associations between blood pressure and PM air pollution. School was modelled as a random intercept to account for clustering within school. We developed four models with covariates being added gradually, including: Crude Model: with no adjustment; Model 1: adjusted for age (numeric variable), sex (categorical variable) and BMI (numeric variable); Model 2: further adjusted for exercise, fruit & vegetable intake, parental education and parental smoking and parental hypertension (all as categorical variables); Model 3: further adjusted for south vs north (categorical variable), rurality (categorical variable), temperature (numeric variable) and GDP per capita (numeric variable). Effect estimates were calculated as changes in SBP or DBP for each 10 $\mu g/m^3$ increment in PM concentrations. Because the 2 PM measures were highly correlated, we only used one-pollutant models.

We used mixed-effects logistic regression to examine the associations between PM exposure and hypertension. Odds ratios (ORs) of having hypertension were calculated in association with each 10 $\mu g/m^3$ increment in PM concentrations. Hypertension was defined according to the national references for Chinese children and adolescents aged 7–17 years (SBP or DBP ≥ age, sex-and-height specific 95th percentiles) (Dong et al., 2017). For participants aged 18 years, the cut-offs of 140/90 mmHg for adults were used.

We performed a subgroup analysis stratified by sex. The potential effect modification by sex was examined by adding an interaction term between sex and PM into the regression models. As two previous studies in China indicated that overweight/obesity may modify the effects of PM air pollution on blood pressure (Dong et al., 2015; Li et al., 2018), we also investigated the modifying effects of overweight/obesity in our study. Overweight/obesity was defined according to the age-and-sex specific BMI standards of the Working Group on Obesity in China (Ji, 2005).

We conducted a series of sensitivity analyses to examine the robustness of our results. (1) We added NO_2 as a covariate into the regression models to investigate its influence on the associations between PM and blood pressure and hypertension. (2) We used different time windows when calculating the PM concentrations. We used 2-year (2 years prior to baseline survey) average concentration and 3-year (3 years prior to baseline survey) average concentration instead of the 1-year average concentration used in original analysis. (3) We excluded grade 1 participants because they had a shorter admission period. (4) As previous studies found that the association between temperature and blood pressure in children was nonlinear (Li et al., 2016; Miersch et al., 2013), we included annual temperature in the regression models as natural cubic spline term instead of linear term in main analysis. The degree of freedom of the splines was determined according to Akaike's Information Criterion (AIC). (5)For comparison, we used fixed-effects regression models (standard models) instead of mixed-effects models.

Statistical analyses were conducted using R 3.4.3 (R Core Team, Vienna, Austria). A two-tailed P value of < 0.05 was considered statistically significant.

Table 1
General characteristics of study participants.

Characteristics	(N = 43,745)
Age (year)	11.3 (3.1)
Male	22,037 (50.4%)
Weight (kg)	41.1 (15.3)
Height (cm)	145.9 (16.3)
Body mass index (kg/m2)	18.6 (3.8)
Systolic blood pressure (mmHg)	104.6 (12.1)
Diastolic blood pressure (mmHg)	66.3 (8.7)
Hypertension	5783 (13.2%)
Outdoor exercise	
< 1 h/day	18,321 (41.9%)
1–2 h/day	16,103 (36.8%)
≥ 2 h/day	9321 (21.3%)
Fruit intake (days of having at least 1 serving per day)	
≤ 3 days/week	11,790 (27.0%)
4–6 days/week	13,575 (31.0%)
Daily	18,380 (42.0%)
Vegetable intake (days of having at least 1 serving per day)	
≤ 3 days/week	5435 (12.4%)
4–6 days/week	7039 (16.1%)
Daily	31,271 (71.5%)
Parental smoking	21,942 (50.2%)
Parental hypertension	3088 (7.1%)
Parental education (highest level)	
Primary school or illiterate	1540 (3.5%)
Secondary school	14,487 (33.1%)
High school	12,495 (28.6%)
College/university or above	15,223 (34.8%)

Data are presented as mean (SD) and number (percentage) for continuous and categorical variables, respectively.

3. Results

The general characteristics of the study participants are summarized in Table 1. The average age was 11.3 [standard deviation (SD): 3.1] years. The mean SBP and DBP was 104.6 (SD: 12.1) and 66.3 (SD: 8.7) mmHg, respectively and 5783 (13.2%) participants were classified as hypertensive.

Table 2 shows the distribution of the annual average concentrations of the $PM_{2.5}$, PM_{10} and NO_2 in 2012. The mean concentration was 60.1, 99.4 and 39.4 $\mu g/m^3$ for $PM_{2.5}$, PM_{10} and NO_2, respectively. The air

Table 2
Distribution of annual average concentrations of air pollutants in 2012.

Air pollutants	Mean	Median	Minimum	Maximum	IQR
$PM_{2.5}$ ($\mu g/m^3$)	60.1	63.1	46.6	76.0	14.1
PM_{10} ($\mu g/m^3$)	99.4	96.9	77.3	133.9	14.5
NO_2 ($\mu g/m^3$)	39.4	42.8	18.2	60.7	8.5

Table 3
Associations between exposure to particulate matter air pollution and blood pressure in Chinese children and adolescents.

BP (N = 43,745)	$PM_{2.5}$	PM_{10}
SBP (mmHg)	Coef (95% CI)	Coef (95% CI)
Crude model	1.86 (0.14,3.58)	2.39 (1.42,3.36)
Model 1	1.26 (−0.22,2.74)	1.71 (0.85,2.57)
Model 2	1.25 (−0.23,2.72)	1.70 (0.84,2.56)
Model 3	1.46 (0.05,2.88)	1.36 (0.34,2.39)
DBP (mmHg)	Coef (95% CI)	Coef (95% CI)
Crude model	0.94 (−0.27,2.15)	1.71 (1.04,2.38)
Model 1	0.59 (−0.61,1.78)	1.30 (0.61,2.00)
Model 2	0.57 (−0.62,1.76)	1.29 (0.60,1.98)
Model 3	0.78 (−0.39,1.95)	0.72 (−0.13,1.57)
Hypertension	OR (95% CI)	OR (95% CI)
Crude model	1.22 (0.83,1.79)	1.56 (1.25,1.95)
Model 1	1.11 (0.73,1.70)	1.48 (1.15,1.90)
Model 2	1.11 (0.72,1.69)	1.47 (1.14,1.89)
Model 3	1.31 (0.86,1.98)	1.45 (1.07,1.95)

Effect estimates are calculated for each 10 μg/m^3 increment in particulate matter concentrations.
Crude Model: no adjustment.
Model 1: Crude Model + age, sex, height, body mass index.
Model 2: Model 1 + exercise, dietary, parental education, parental smoking and parental hypertension.
Model 3: Model 2 + region (south vs north), rurality (urban vs rural), annual average temperature and GDP per capita.
Abbreviations: BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; OR, odds ratio; SBP, systolic blood pressure.

pollutants were significantly correlated, especially for $PM_{2.5}$ and PM_{10} (correlation coefficient = 0.74). (Table S2) The 43,745 participants included in data analysis and the all 59,959 participants generally had a similar distribution of demographic and anthropometric measures, as well as PM exposure. (Table S1).

Table 3 shows the results of the associations between PM exposure and blood pressure. In Crude Model, both $PM_{2.5}$ and PM_{10} were associated with increased SBP levels. After adjustment for a wide range of covariates, the positive associations remained statistically significant. Every 10 μg/m^3 increment in $PM_{2.5}$ and PM_{10} concentration was associated with 1.46 [95% confidence interval (CI): 0.05, 2.88] and 1.36 (95% CI: 0.34, 2.39) mmHg increases in SBP, respectively. For DBP, we found no significant associations with either $PM_{2.5}$ or PM_{10}. In logistic regression analysis, PM_{10} was associated with higher prevalence of hypertension and the association was robust across different models. The fully adjusted odds ratio (OR) was 1.45 (95% CI: 1.07, 1.95) for every 10 μg/m^3 PM_{10} increment. No significant association was found for $PM_{2.5}$.

In stratified analysis, the positive associations between PM_{10} and SBP and hypertension were found in all subgroups stratified by sex or weight status. No significant effect modification by sex was observed. For obesity, we did not find a consistent pattern as a stronger association of PM_{10} with SBP, but a weaker association with hypertension were detected among obese participants. For DBP, no significant associations between PM_{10} and DBP were found in any subgroups. For $PM_{2.5}$, no significant modifying effects by overweight/obese were found. (Table 4).

Our sensitivity analyses generally generated similar results. (Table S3) Additional adjustment for NO_2 did not change the results materially. Similar results were found when 2-year or 3-year average PM concentrations were used. The results also remained stable after exclusion of grade 1 participants. Treating annual temperature as spline term did not substantially change the results, either. When standard regression models were used, the positive associations of $PM_{2.5}$ and PM_{10} with DBP became statistically significant.

4. Discussion

To our best knowledge, this is the largest epidemiological study to date to investigate the associations between long-term exposure to $PM_{2.5}$ and PM_{10} air pollution and blood pressure and hypertension in Chinese children and adolescents. In this large nationally representative sample, we found that exposure to $PM_{2.5}$ and PM_{10} was associated with increased SBP. PM_{10} was also associated with higher prevalence of hypertension.

In the past decades, there have been an increasing number of epidemiological studies which examined the health effects of long-term exposure to PM air pollution and blood pressure mainly among adults, and only a few studies were conducted in child populations. The Seven Northeastern Cities Chinese Children's Study found that among 9354 children, long-term PM_{10} exposure (4-year average) was associated with increased SBP and DBP and higher prevalence of hypertension (Dong et al., 2014; Dong et al., 2015), which are in line with our findings. Another Chinese study also found that PM_{10} exposure was associated with higher SBP and DBP levels in children (Li et al., 2018). The PIAMA birth cohort study in the Netherlands reported positive associations between DBP and $PM_{2.5}$ absorbance (a measure of black carbon) and certain PM_{10} components (iron, silicon and potassium), but the associations were only significant among children who lived at the same address since birth and no significant associations were detected for SBP (Bilenko et al., 2015a; Bilenko et al., 2015b). In a German study of 2368 children, no significant associations were found between blood pressure (neither SBP nor DBP) and $PM_{2.5}$, PM_{10}, or $PM_{2.5}$ absorbance (Liu et al., 2014). The inconsistency of current findings may be attributable to the differences in PM concentrations and compositions in different regions, for example, the PM levels reported in the three European studies were much lower than those reported in the studies in China, including our study. The heterogeneity of study population and study methodology may also play a part. For example, in our study, standard (fixed effects) model produced significant effect estimates, but random effects model did not for DBP and PM exposure. In our study, a multi-stage cluster sampling method was used and the sampling unit was school. The random effects model could account for the possibility that the patterns of health of participants from the same cluster (school) were more similar than for participants from other clusters and these patterns may not be completely explained by the variables included in the regression models. This method has also been extensively used in previous air pollution studies (Chen et al., 2016; Dong et al., 2014; Dong et al., 2015; Jerrett et al., 2013). Compared with fixed-effect models, our analysis based on random effects models controlled the possible within-cluster effects and therefore, may have provided more accurate results. More studies from different regions are warranted.

The biological mechanisms linking PM air pollution and blood pressure are not fully understood. One possible pathway is that PM exposure can induce systemic inflammation and oxidative stress, which can affect vascular function and, therefore, influence hemodynamic responses and ultimately lead to arterial remodeling (Boos and Lip, 2006; Brook et al., 2009; Brook et al., 2010; Giorgini et al., 2016). Another hypothesized mechanism is that inhaled PM may lead to changes in autonomic nervous system favoring sympathetic nervous system mediated arterial vasoconstriction (Giorgini et al., 2016). In addition, some constituents of PM (e.g. ultrafine particles and soluble metals) may have the potential to pass through the alveolar capillary membrane and penetrate into the circulation system and directly affect the blood vessels (Furuyama et al., 2009).

Obesity is another pressing global public health concern and a well-recognized risk factor for hypertension (Kotchen, 2010). It is hypothesized that obesity and air pollution may have synergistic effects on blood pressure because both of them can induce systemic inflammation (Dong et al., 2015), which plays an important role in the development of hypertension (Boos and Lip, 2006). Two Chinese studies found the associations between air pollution, including PM, and blood pressure/

Table 4
Associations between exposure to particulate matter air pollution and blood pressure in Chinese children and adolescents in stratified analysis.

Subgroup		$PM_{2.5}$		PM_{10}	
SBP (mmHg)		Coef (95% CI)	$P_{interaction}$	Coef (95% CI)	$P_{interaction}$
Sex	Male	1.55 (0.20,2.89)	0.33	1.41 (0.44,2.38)	0.06
	Female	1.44 (−0.03,2.91)		1.36 (0.30,2.42)	
Weight status	Normal-weight	1.62 (0.27,1.62)	–	1.38 (0.41,2.36)	–
	Overweight	1.26 (−0.36,2.89)	0.07	1.49 (0.33,2.65)	0.09
	Obese	1.19 (−0.56,2.94)	0.49	1.53 (0.29,2.78)	< 0.001
DBP (mmHg)		Coef (95% CI)	$P_{interaction}$	Coef (95% CI)	$P_{interaction}$
Sex	Male	0.76 (−0.41,1.93)	0.003	0.63 (−0.23,1.48)	< 0.001
	Female	0.84 (−0.31,1.99)		0.83 (−0.002,1.66)	
Weight status	Normal-weight	0.89 (−0.23,2.02)	–	0.76 (−0.07,1.58)	–
	Overweight	0.53 (−0.75,0.53)	0.01	0.66 (−0.27,1.59)	0.71
	Obese	0.50 (−0.87,1.86)	0.08	0.77 (−0.21,1.76)	< 0.001
Hypertension		OR (95% CI)	$P_{interaction}$	OR (95% CI)	$P_{interaction}$
Sex	Male	1.36 (0.91,2.04)	0.37	1.47 (1.10,1.97)	0.39
	Female	1.31 (0.87,1.97)		1.45 (1.08,1.94)	
Weight status	Normal-weight	1.42 (0.89,2.26)	–	1.53 (1.10,2.14)	–
	Overweight	1.24 (0.83,1.86)	0.16	1.43 (1.06,1.91)	0.45
	Obese	1.29 (0.89,1.85)	0.75	1.41 (1.08,1.83)	< 0.001

Effect estimates are calculated for each 10 μg/m^3 increment in particulate matter concentrations.
Abbreviations: CI, confidence interval; DBP, diastolic blood pressure; OR, odds ratio; SBP, systolic blood pressure.

hypertension were stronger in overweight/obese children than in normal-weight children (Dong et al., 2015; Li et al., 2018), which supports this hypothesis. However, in the present study, we did not find consistent evidence supporting the effect modification of overweight/obesity on the associations between PM exposure and blood pressure and hypertension, especially for $PM_{2.5}$. Results from adult studies, including our previous study in Taiwan, were also inconsistent (Fuks et al., 2011; Schwartz et al., 2012; Zhang et al., 2018). Current evidence on this issue is still scarce as most studies were not specifically designed to examine the interactions between air pollution and obesity. More studies are required to better elucidate the joint effects of PM air pollution and obesity on hypertension, which may provide insights on more effective strategies for hypertension prevention, especially in overweight and obese subjects.

A major strength of the present study is its large sample size, which enabled us to investigate the associations between PM exposure and blood pressure in a more statistically precise manner. The wide geographical coverage and the multi-stage random sampling method generated a sample with good representativeness of Chinese children and adolescents (Chen et al., 2015). Other strengths of the present study include the collection of information on a wide range of potential confounders, the standard methods used for blood pressure measurement, and the state-of-the-art method used for PM exposure estimation.

It is also worth noting that we performed a variety of sensitivity analyses and the results were generally similar with the original results, indicating the robustness of our findings. For example, in addition to PM, we also estimated NO_2 levels, another criteria pollutant. The additional adjustment for NO_2 did not substantially change our overall findings, suggesting the health effects of PM on blood pressure and hypertension are likely independent of NO_2. Rather than 1-year average concentrations of $PM_{2.5}$ and PM_{10}, we also used 2-year and 3-year average concentrations and similar results were found, indicating the 1-year average concentration is a good indicator of long-term PM exposure.

However, our study also has some limitations. First, our findings have limited capability for the inference on cause and effects relationship because of the cross-sectional nature. Second, the PM concentrations were estimated at participants' school address. This community-level exposure assessment may have resulted in nondifferential exposure misclassification and consequently lead to underestimated effects of PM air pollution (Shy et al., 1978). However, we think the school-based estimates could be a good surrogate of children's long-term exposure to PM air pollution because they spent a considerable amount of time at school. Also, children generally do not live far away from their schools because of the residence-related school assignment policies in China. Therefore, the school-based exposure assessment should not bring in substantial exposure misclassification. Third, a proportion of participants were excluded because of missing information on the covariates and this may have led to selection bias. However, the participants included in data analysis is generally comparable with the whole study population in terms of demographics, anthropometric measures and PM levels, indicating that the distribution of PM is likely to be nondifferential in included and excluded participants. Therefore, the exclusion of the participants with incomplete information should not seriously bias our results. Another limitation is that, like the vast majority of previous studies, we only estimated the mass concentrations of PM and information on compositions was not available. Both size and composition are important determinants of the adverse effects of ambient PM (Pope III and Dockery, 2006; Zou et al., 2017). This limitation may also contribute to the inconsistent findings from previous studies and future studies should consider including analysis on PM compositions to provide more suggestive evidence.

5. Conclusions

In conclusion, in this large population of Chinese children and adolescents, we found that long-term exposure to ambient PM air pollution was associated with increased blood pressure and higher prevalence of hypertension. Considering the high levels of PM air pollution and high prevalence of hypertension in both children and adults in China, (Dong et al., 2017; Lu et al., 2017), our findings are of great public health significance, supporting the urgent need of effective air pollution mitigation strategies for the prevention of childhood hypertension, which is also a well-recognized risk factor of future cardiovascular health in adulthood.

Acknowledgements

This study was supported by the Research Special Fund for Public Welfare Industry of Health of the Ministry of Health of China (201202010). Bin Dong was supported by the Excellent Talents Fund Program of Peking University Health Science Center (BMU2017YJ002). Yuming Guo was supported by the Career Development Fellowship of Australian National Health and Medical Research Council (#APP1107107 and #APP1163693). Shanshan Li was supported by the Early Career Fellowship of Australian National Health and Medical

Research Council (#APP1109193). We would like to thank the school teachers and principals, the students and their parents/guardians for their support to our study.

Conflict of interest

The authors declare they have no competing interests related to this manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.04.036.

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