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Greenness alleviates the effects of ambient particulate matter on the risks of high blood pressure in children and adolescents



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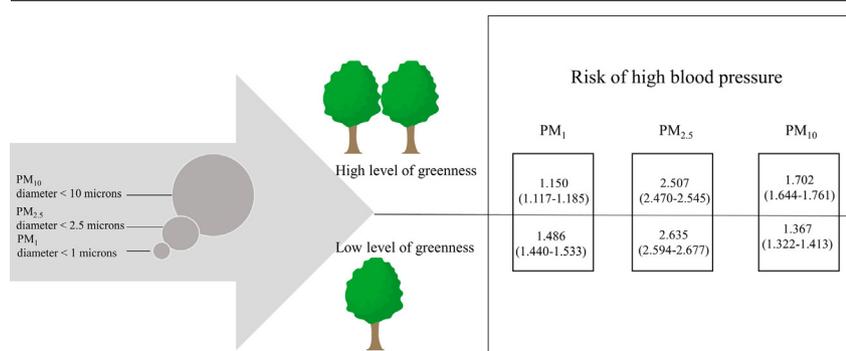
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HIGHLIGHTS

- Lower ambient particulate matter and higher greenness were associated with a lower risk of high blood pressure
- Higher greenness alleviated the adverse effects of ambient PM₁ and PM_{2.5} on the high blood pressure onset among children and adolescents.
- Reducing particulate matter concentration could gain more benefits in the schools with low level of greenness.

GRAPHICAL ABSTRACT



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ABSTRACT

Both ambient particulate matter (PM) and decrease of greenness have been suggested as risk factors for high blood pressure (HBP) in children and adolescents. But most evidence were from cross-sectional studies with limited data from prospective cohorts. In this cohort study, we included 588,004 children and adolescents aged 7 to 18 years without HBP from 2005 to 2018 in Beijing (240,081) and Zhongshan (347,923) city of China. The cumulative incidence of HBP was 32.04%, and incidence rate was 14.86 per 100 person-year. After adjustment for confounders, the ten-unit increase in PM₁, PM_{2.5}, and PM₁₀ exposure was significantly associated with 43%, 70%, and 43% higher risks of HBP, respectively, but the 0.1-unit increase in NDVI exposure was significantly associated with a 25% lower risk of HBP. The HRs of PM₁ on the HBP risk were 1.486 and 1.150 in the low and the high-level of greenness, and they were 2.635 and 2.507 for PM_{2.5}, and for PM₁₀ 1.367 and 1.702 in the two groups. The attributable fraction (AFs) of PM₁, PM_{2.5}, and PM₁₀ on HBP incidents were 13.74%, 40.08%, and 15.47% in the low-level of greenness, which simultaneously was higher than those in the high-level of greenness (AF = 4.62%, 17.28%, and 9.96%). The exposure to higher ambient PM air pollution and lower greenness around schools were associated with a higher risk of HBP in

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1. Introduction

Cardiovascular diseases (CVD) have become a major public health issue over the past decades and have accounted for 18.6 million deaths globally per year (Roth et al., 2020). Currently, more than 330 million in China were estimate to suffer from CVD (National Center for Cardiovascular Diseases, 2019), imposing huge health and economic burdens on families and societies. Among a range of CVD subtypes, hypertension or high blood pressure (HBP) was the one with highest disease burden (Poulter et al., 2015; Zhou et al., 2019). Previous studies found that HBP can be progressive throughout childhood into adulthood and was also a strong predictor for adulthood's hypertension (Lona et al., 2021; Aatola et al., 2017; Tirosh et al., 2010; Chen and Wang, 2008), despite rare prevalence among children and adolescents. Thus, exploring the risk factors associated with the onset of HBP in childhood and adolescence could help to provide potential and appropriate approaches to prevent the adverse outcomes of CVD in adulthood.

Fine particulate matter (PM) is one of the key global pollutants affecting human health (Combes and Franchineau, 2019; Miller et al., 2012). Evidence from experimental studies have showed the deleterious effects of PM on specific tissues, organs and systems, and the cardiovascular system was considered as the main target affected by PM (Thurston et al., 2017; Shkirkova et al., 2020; Lederer et al., 2021). A number of epidemiological studies also corroborated that PM concentration is associated with an increased risk of HBP in a dose-dependent manner (Prabhakaran et al., 2020; Liu et al., 2017). A previous study from 272 cities in China during 2013 and 2015 found that the risk of CVD death increased by 0.27% for every 10 $\mu\text{g}/\text{m}^3$ increase of PM_{2.5} (Chen et al., 2017). The GDB study indicated that ambient air pollution ranked 7th among 87 mortality risk factors (DALYs and Collaborators, 2018; Collaborators, 2018, 2020). A prospective cohort in China also showed that the long-term exposure to PM_{2.5} was associated with an increased risk of HBP in adults, with an increase of 11% risk of HBP for every 10 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} concentration (Huang et al., 2019; Liang et al., 2019). Except for the adults' evidence, a meta-analysis combining 14 original studies found that both short-term and long-term exposure to some ambient air pollutants might increase BP values among children and adolescents (Huang et al., 2021a).

In contrast, the greenness, a proximity to green space, has been suggested a beneficial environmental factor (Nieuwenhuijsen and Khreis, 2017). Although the protective effect of increased greenness on HBP has been well documented, evidence remain scarce in the childhood population (Xiao et al., 2020). What's more, a mixture of multiple environmental factors with opposite effects may confer an additive, synergistic or antagonistic impact on population health, especially in children and adolescents who are more vulnerable to exogenous exposure. For instance, plants and vegetation could absorb PM and toxic gases from the surrounding air, leading to the removal of air pollutants (Tong et al., 2016; Baldauf, 2017). We, therefore, speculated that the better surrounding greenness of living environment has the potential to attenuate effect of air pollutants on the onset of HBP.

In this study, we analyzed a longitudinal and dynamic cohort of children and adolescents living in Beijing and Zhongshan city in China during 2005 and 2018, to investigate the associations of PM and greenness around schools with the risk of HBP, and to investigate the interaction effect of greenness and PM on HBP onset.

2. Methods

2.1. Design and study population

A longitudinal dynamic cohort of children aged 7–18 years old was recruited through annual physical examination survey conducted between

2005 and 2018. It covered all school-aged students in Beijing and Zhongshan city, China, and was performed at a level similar to the census of local children and adolescents except for the drop-outs. In addition to self-reported sociodemographic information (e.g. gender, date of birth, and school location) complete medical examinations and measurements were collected for all surveyed students by trained and qualified medical physicians. We excluded those with a history of HBP diagnosis at baseline, and followed participants until the earliest occurrence of outcome of interest (HBP), death, loss of follow-up, or end of study. Students with missing data (weight, height, birthday) were also excluded. Finally, a total of 588,004 eligible children were included for the subsequent analyses (Beijing: 240,081, Zhongshan: 347,923) (see the flow chart of Figs. 1 and S1). This study was approved by the Medical Research Ethics Committee of Peking University Health Science Center (Reference Number: IRB00001052-20033).

2.2. Anthropometric measurements and outcome definition

Height (cm) and weight (kg) were quantified following a standardized procedure defined by the 2006 WHO Child Growth Standards (<http://www.who.int/childgrowth/standards/en/>). Specifically, height was measured to the nearest 0.1 cm with portable stadiometers and weight to the nearest 0.1 kg with a standardized scale. Students were required to remove their shoes and stand on an altimeter with bare feet. The height and weight measurements were repeated twice, and the mean of two measurements was used as the final height and weight. The height and weight were recorded with one decimal (e.g., 123.9 cm and 35.9 kg). BMI was calculated as body weight (kg) divided by height (m) squared (kg/m^2).

Systolic blood pressure (SBP; in mmHg) and diastolic blood pressure (DBP; in mmHg) were measured using an auscultation mercury sphygmomanometer with an appropriate cuff for children and adolescents according to their age and size. Each participant was seated for at least 10 min before the first reading of measurements of BP in a sitting position. SBP was determined by the onset of the first Korotkoff sound (K1), and DBP was determined by the fifth Korotkoff sound (K5). An average of three serial BP measurements was calculated for each child. The systolic HBP (SHBP) and diastolic HBP (DHBP) were defined as the SBP and DBP equal or higher than the 95th percentiles of the reference population according to age, sex, and height (Chinese Children BP-CCBP reference) (Dong et al., 2017). HBP was defined as the presence of either SHBP or/and DHBP.

2.3. Fine particulate matter (PM_x) exposure assessment

PM_x of one-km-resolution including PM₁, PM_{2.5}, and PM₁₀ concentrations were predicted using satellite remote sensing, meteorology, and land use information as described previously (Wei et al., 2019, 2020, 2021). PM₁ concentrations during 2014–2018, PM_{2.5} concentrations during 2000–2018, and PM₁₀ concentrations during 2014–2018 were estimated accordingly. Briefly, all schools address in the two cities were first transformed into latitude and longitude data. Then, address-specific annual average concentrations of PM_x were calculated for each address. In this study, we calculated the annual average PM₁, PM_{2.5}, and PM₁₀ concentrations and used the figure averaging concentration of the PM_x in previous years as surrogate of long-term exposure to ambient PM air pollution. Children within a school were assigned to the same level of exposure.

2.4. Greenness assessment

We used the Normalized Difference Vegetation Index (NDVI) to measure the green intensity around schools. The NDVI was a satellite-image-

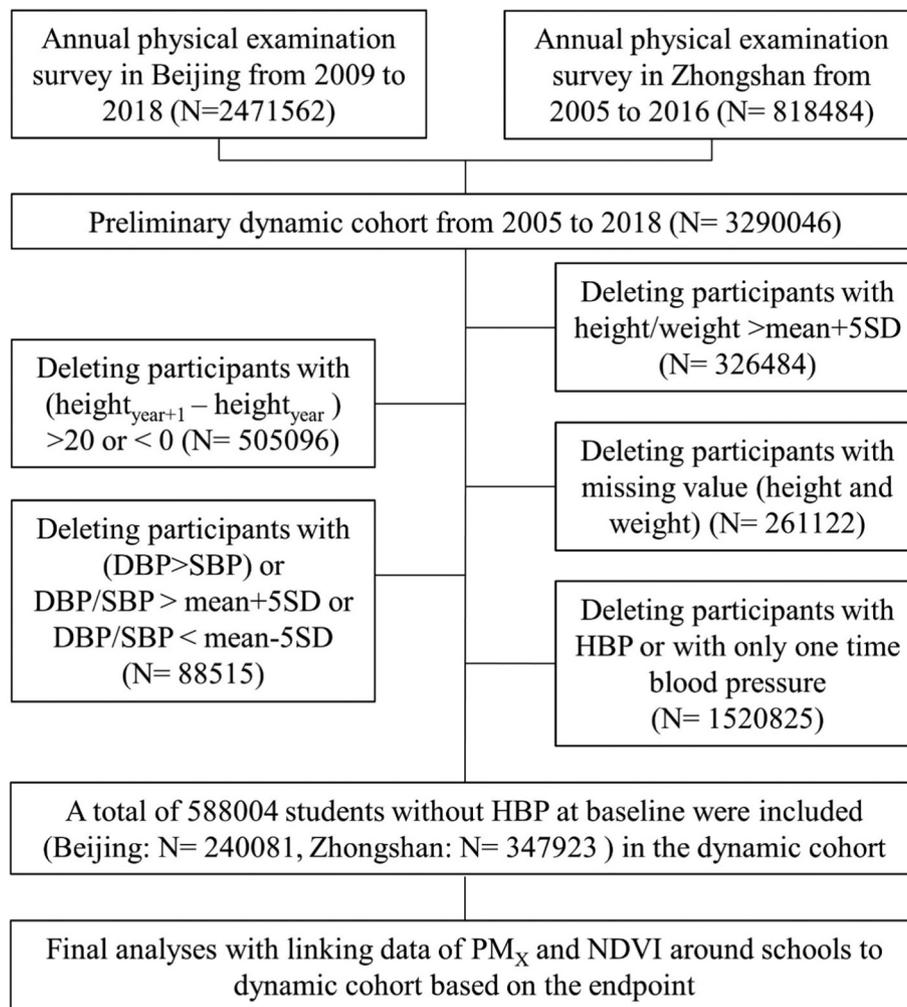


Fig. 1. Flow chart of data from the dynamic cohort in Beijing and Zhongshan from 2005 to 2018.

based vegetation index and derived from Landsat 5 Thematic Mapper satellite images at $30\text{ m} \times 30\text{ m}$ resolution (<http://earthexplorer.usgs.gov>). The NDVI was measured as the ratio of the difference between the spectral reflectance measurements in the near-infrared region and red regions of the electromagnetic spectrum and the sum of these two measures. Its values ranged from -1 to $+1$ with higher values indicating more greenness. $\text{NDVI} = \frac{\text{NIR}-\text{RED}}{\text{NIR}+\text{RED}}$, where NIR presented land surface reflectance of near-infrared, and RED presented the surface reflectance in red regions of the electromagnetic spectrum. The mean values of NDVI in 1000 m circular buffers around each school centroid were defined as greenness. The one-year mean NDVI (one year before the endpoint of each participant) was calculated and assigned to each participant in the corresponding school as the surrogate for greenness exposure. The NDVI values for circular buffers of 1000 m were used as a measure of the greenness around the school in the main analyses (Markevych et al., 2014a; Swinburn et al., 2019). The distribution of fine particulate matter (PM_x) exposure, greenness (NDVI) exposure, and school sites in Beijing and Zhongshan city were shown in Fig. 2.

2.5. Statistical analysis

Continuous variables were reported as the mean \pm standard deviation (SD) and the frequencies were calculated for categorical variables. The cumulative incidence of HBP was calculated using the formula as follows: $\frac{\text{Number of new HBP from 2005 to 2018}}{\text{Number of participants from 2005 to 2018}}$. The incidence rate of HBP was calculated using the formula by: $\frac{\text{Number of new HBP from 2005 to 2018}}{\text{Total person time of participants from 2005 to 2018}}$.

We used a generalized estimation equation (GEE) adjusting for age, sex, height, weight, and city (Beijing and Zhongshan) to remove the correlation of repeated measurement of each individual. Also, we applied the proportional hazards model with restricted cubic spline (RCS) with 3 knots to derive overall hazard ratio (HR) and dose-dependent HRs. Stratification analysis was also performed among subgroups by sex.

Specifically, the continuous NDVI were categorized into two groups using 50th percentile as a cutoff point (the low-level group VS high-level group.). The cutoff values were $21.70\ \mu\text{g}/\text{m}^3$ for PM_{10} , $64.56\ \mu\text{g}/\text{m}^3$ for $\text{PM}_{2.5}$, $62.59\ \mu\text{g}/\text{m}^3$ for PM_{10} and 0.248 for greenness. We assessed the effects of each PM_x exposure (independent variable) on HBP (dependent variable) separately in the low-level group and the high-level group of NDVI (stratification variables) after adjustment of the confounders.

We calculated the attributable fraction (AFs) of HBP risks attributed to PM_x in the low-level and high-level NDVI group using the following algorithm: $\text{AF} = 1 - \frac{(1-S_0)}{(1-S_t)}$, where S_0 denoted the counterfactual survival function for the event if the exposure would have been eliminated from the population at baseline and S_t denoted the factual survival function (Chen et al., 2010; Sjolander and Vansteelandt, 2017). To estimate the AFs in the whole samples from the dynamic cohort, we used the following formula to calculate the weighted AFs: $\text{weighted AFs} = \frac{\sum(n_t \times \text{AF}_t)}{N}$, where n_t presented the number of participants who participated in the cohort on the t year; N presented the whole number of participants in the dynamic cohort accordingly; AF_t presented the AF value of specifying t year in the cohort

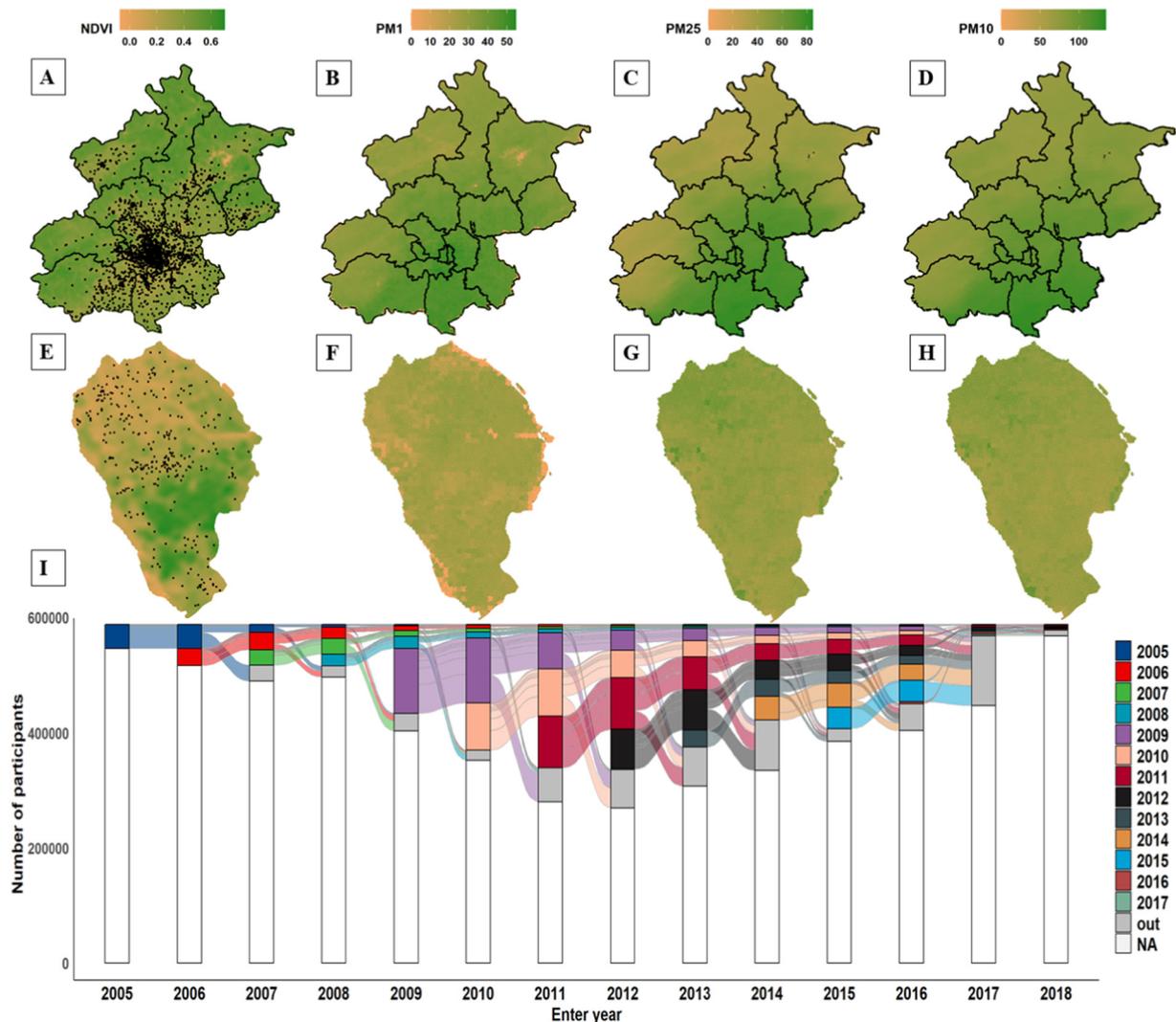


Fig. 2. Location of survey schools in Beijing and Zhongshan and their PM_x concentration distribution and mean NDVI levels, and participants' dynamic change in cohort. Note: Subfigure A and E represented the mean NDVI levels in 2015 from Beijing and Zhongshan, respectively. Black dots were the location of schools. Subfigure B (PM₁), C (PM_{2.5}), and D (PM₁₀) represented the PM_x concentration in 2015 in Beijing, and Subfigure F (PM₁), G (PM_{2.5}), and H (PM₁₀) represented the PM_x concentration in 2015 in Zhongshan, respectively. The subfigure I showed the flow of participants in this dynamic cohort study with integrating children from Beijing and Zhongshan. NA, Not Applicable; Out, participants who quitted the dynamic cohort study.

study. The 95% confidence interval of weighted AFs was calculated based on the Monte Carlo method. The original incidences of HBP were calculated from the observed data. Based on the weighted AFs, the expected number and rates of HBP were calculated to show the benefits of PM_x control in the reduction of HBP at different greenness levels.

R software (version 4.0.3) was used to perform all analyses in the study. The packages “gee”, “survival” and “rms” were used to fit the GEE model, Cox model, restrict the cubic spline model, respectively. The “AF” package was used to calculate the attributable fraction. Statistical significance was defined as a two-tailed *p*-value of less than 0.05.

3. Results

3.1. Baseline characteristic

The flow of participants in the dynamic cohort from 2005 to 2018 was shown in Fig. 2 (the characteristic of participants was shown in Table 1). Among 588,004 children and adolescents aged 7 to 18 years without HBP at baseline, a total of 188,204 students were identified with new HBP during the 14 years' follow-up. The cumulative incidence of HBP was 32.01%, and the incidence rate was 14.86 per 100 person-year.

3.2. Association of PM_x and greenness around school with the risk of HBP

As shown in Fig. 3 with nonlinear results, a significantly positive association was observed between PM_x and the risk of HBP onset after adjusting the cofounders. We found that the risk of HBP of children and adolescents increased with the increase in concentrations of PM₁, PM_{2.5}, and PM₁₀. However, a significantly negative association was observed between NDVI and the risk of HBP of children and adolescents, and the risk of HBP decreased with the increase in the levels of NDVI. Because the nonlinear analysis results were close to the linear relationship between them, the quantitative results showed that ten-unit (10 μg/m³) increase in PM₁, PM_{2.5} and PM₁₀ exposure was significantly associated with 0.67 (95% CI: 0.61, 0.73), 0.44 (95% CI: 0.40, 0.48) and 0.28 (95% CI: 0.24, 0.32) mmHg increases in SBP levels, and with 0.45 (95% CI: 0.41, 0.48), 0.31 (95% CI: 0.27, 0.35) and 0.27 (95% CI: 0.25, 0.29) mmHg increases in DBP levels, as well as 1.43 times, 1.70 times, and 1.43 times higher risk of HBP among children and adolescents. On the contrary, 0.1-unit increase in NDVI exposure was significantly associated with a −0.53 (95% CI: −0.59, −0.47) and −0.65 (95% CI: −0.67, −0.64) mmHg reduction in SBP and DBP levels, and a 25% (HR = 0.75, 95% CI: 0.74, 0.76) lower risk of HBP. The same results that the HBP risk was positively correlated

Table 1
Characteristic of participants of entering the dynamic cohort in Beijing and Zhongshan.

Characteristics	Beijing			Zhongshan		
	All	Non-HBP	HBP	All	Non-HBP	HBP
	N = 240,081	N = 211,293	N = 28,788	N = 347,923	N = 188,457	N = 159,466
Enter year						
2005	–	–	–	41,021 (11.79)	19,566 (47.70)	21,455 (52.30)
2006	–	–	–	29,992 (8.62)	11,434 (38.12)	18,558 (61.88)
2007	–	–	–	27,031 (7.77)	11,279 (41.73)	15,752 (58.27)
2008	–	–	–	20,687 (5.95)	7123 (34.43)	13,564 (65.57)
2009	66,178 (27.56)	57,074 (86.24)	9104 (13.76)	46,793 (13.45)	21,543 (46.04)	25,250 (53.96)
2010	55,175 (22.98)	49,626 (89.94)	5549 (10.06)	26,897 (7.73)	14,610 (54.32)	12,287 (45.68)
2011	58,855 (24.51)	51,124 (86.86)	7731 (13.14)	31,025 (8.92)	16,441 (52.99)	14,584 (47.01)
2012	44,655 (18.60)	40,309 (90.27)	4346 (9.73)	25,285 (7.27)	14,597 (57.73)	10,688 (42.27)
2013	4089 (1.70)	3439 (84.12)	650 (15.88)	25,408 (7.30)	17,167 (67.57)	8241 (32.43)
2014	–	–	–	41,251 (11.86)	28,904 (70.07)	12,347 (29.93)
2015	4379 (1.82)	3793 (86.62)	586 (13.38)	32,533 (9.35)	25,793 (79.28)	6740 (20.72)
2016	3579 (1.49)	3007 (84.02)	572 (15.98)	–	–	–
2017	3171 (1.32)	2921 (92.12)	250 (7.88)	–	–	–
Gender						
Girls	105,579 (44.0)	92,518 (87.6)	13,061 (12.4)	153,571 (44.1)	83,336 (54.3)	70,235 (45.7)
Boys	134,502 (56.0)	118,775 (88.3)	15,727 (11.7)	194,352 (55.9)	105,121 (54.1)	89,231 (45.9)
Age (mean, sd)	15.05 (2.00)	15.14 (1.98)	14.38 (2.04)	13.36 (2.98)	13.64 (3.06)	13.02 (2.84)
Height (mean, sd)	165.51 (9.82)	165.76 (9.71)	163.68 (10.37)	153.16 (14.54)	154.22 (14.46)	151.92 (14.53)
Weight (mean, sd)	59.89 (14.31)	59.12 (13.63)	65.52 (17.52)	43.83 (12.67)	43.97 (12.38)	43.67 (13.01)
BMI (mean, sd)	21.72 (4.15)	21.38 (3.91)	24.21 (4.98)	18.27 (2.97)	18.08 (2.79)	18.48 (3.16)
NDVI (mean, sd)	0.24 (0.05)	0.24 (0.05)	0.25 (0.06)	0.29 (0.08)	0.30 (0.09)	0.28 (0.08)
PM ₁ (mean, sd)	38.18 (7.75)	38.22 (7.88)	37.94 (6.81)	20.38 (4.08)	20.15 (4.08)	21.17 (3.98)
PM _{2.5} (mean, sd)	73.31 (12.33)	73.21 (12.36)	73.99 (12.06)	54.51 (15.04)	50.16 (15.07)	59.65 (13.28)
PM ₁₀ (mean, sd)	93.30 (10.67)	93.26 (10.91)	93.60 (8.85)	62.05 (9.06)	61.45 (8.64)	64.09 (10.10)

Notes: NDVI (mean, sd), PM₁ (mean, sd), PM_{2.5} (mean, sd), and PM₁₀ (mean, sd) represent the one-year mean NDVI, PM₁, PM_{2.5}, and PM₁₀ (one year before the endpoint of each participant), respectively.

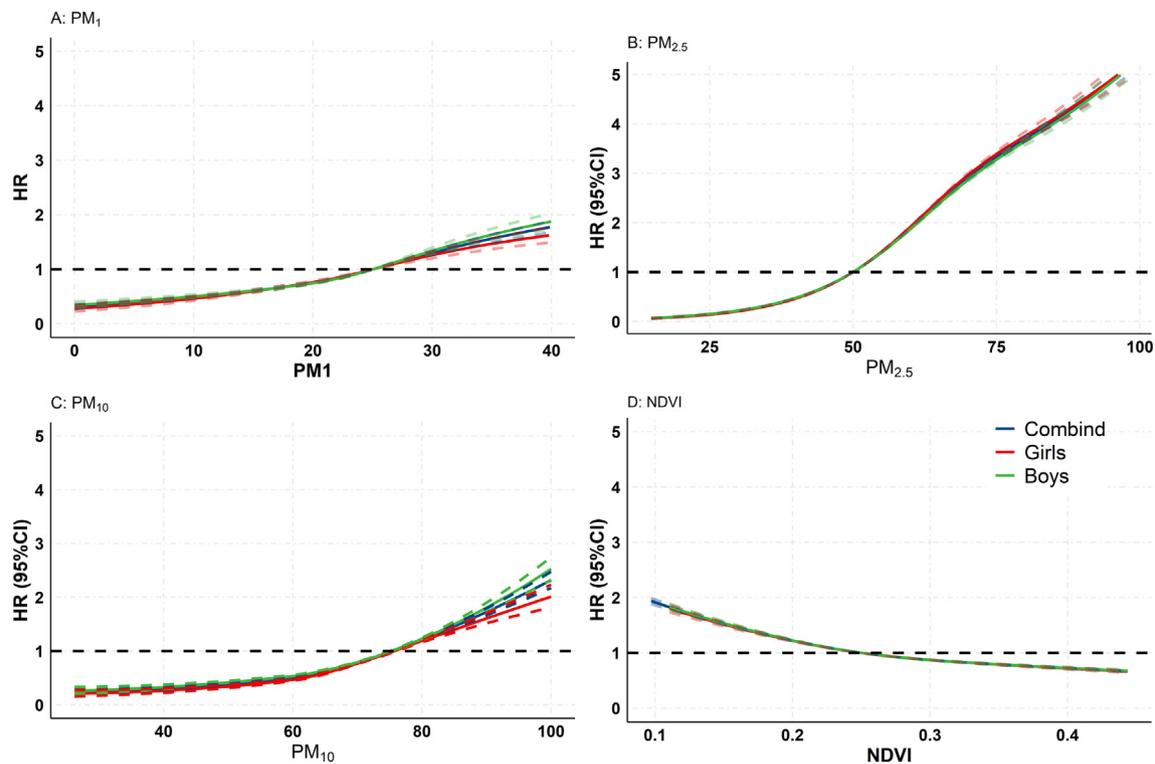


Fig. 3. Nonlinear association of PM_x (concentration of $\mu\text{g}/\text{m}^3$) and greenness around schools with HBP incident in both boys and girls. Note: The restricted cubic spline (RCS) with 3 knots combined with proportional hazards model (COX model) was used to assess the effects of PM_x (PM₁ for subfigure A, PM_{2.5} for subfigure B, PM₁₀ for subfigure C, and greenness for subfigure D) on HBP incident in boys (Green lines) and girls (red lines), and their combination (blue lines). The dotted lines represent 95% confidence intervals. HR, hazard ratio. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Association between PM_X (10 μg/m³) and BP (regression coefficient, β, 95% CI) and HBP risk (hazard ratio, HR, 95% CI) among children and adolescents in Beijing and Zhongshan, China.

Factor	Boys			Girls			Total		
	SBP (β)	DBP (β)	HBP (HR)	SBP (β)	DBP (β)	HBP (HR)	SBP (β)	DBP (β)	HBP (HR)
PM ₁									
Crude	0.44 (0.34, 0.54)	0.51 (0.46, 0.56)	1.45 (1.41, 1.49)	0.33 (0.23, 0.43)	0.13 (0.07, 0.19)	1.41 (1.37, 1.46)	0.36 (0.3, 0.42)	0.34 (0.30, 0.38)	1.44 (1.41, 1.47)
Adjusted	0.55 (0.47, 0.63)	0.57 (0.52, 0.62)	1.47 (1.43, 1.52)	0.79 (0.69, 0.89)	0.28 (0.22, 0.34)	1.44 (1.39, 1.49)	0.67 (0.61, 0.73)	0.45 (0.41, 0.48)	1.43 (1.40, 1.46)
PM _{2.5}									
Crude	0.65 (0.59, 0.71)	0.48 (0.44, 0.52)	1.56 (1.55, 1.56)	0.23 (0.15, 0.31)	0.31 (0.27, 0.35)	1.57 (1.56, 1.58)	0.44 (0.4, 0.48)	0.40 (0.38, 0.42)	1.56 (1.56, 1.57)
Adjusted	0.41 (0.35, 0.47)	0.45 (0.41, 0.49)	1.69 (1.68, 1.70)	0.44 (0.36, 0.52)	0.36 (0.32, 0.40)	1.71 (1.10, 1.72)	0.44 (0.4, 0.48)	0.31 (0.27, 0.35)	1.70 (1.69, 1.70)
PM ₁₀									
Crude	0.48 (0.42, 0.54)	0.32 (0.29, 0.35)	1.33 (1.31, 1.35)	0.23 (0.17, 0.29)	0.27 (0.24, 0.30)	1.33 (1.31, 1.35)	0.34 (0.3, 0.38)	0.29 (0.27, 0.31)	1.33 (1.32, 1.35)
Adjusted	0.22 (0.16, 0.28)	0.27 (0.24, 0.30)	1.42 (1.40, 1.44)	0.31 (0.25, 0.37)	0.28 (0.24, 0.31)	1.44 (1.41, 1.46)	0.28 (0.24, 0.32)	0.27 (0.25, 0.29)	1.43 (1.41, 1.45)
NDVI									
Crude	-1.08 (-1.12, -1.04)	-0.98 (-1.00, -0.95)	0.80 (0.79, 0.81)	-0.69 (-0.81, -0.57)	-0.84 (-0.86, -0.81)	0.81 (0.79, 0.82)	-0.87 (-0.93, -0.81)	-0.91 (-0.93, -0.89)	0.80 (0.80, 0.81)
Adjusted	-0.55 (-0.59, -0.51)	-0.66 (-0.69, -0.64)	0.74 (0.74-0.75)	-0.50 (-0.60, -0.40)	-0.64 (-0.66, -0.61)	0.75 (0.74, 0.76)	-0.53 (-0.59, -0.47)	-0.65 (-0.67, -0.64)	0.75 (0.74, 0.76)

Note SBP, systolic blood pressure; DBP, diastolic blood pressure; HBP, high blood pressure; HR, hazard ratio; CI, confidence interval; NDVI, normalized difference vegetation index. Greenness, measured by NDVI, was defined using a mean value of NDVI in 1000 m buffer around each of the participating schools. The regression coefficient of β was calculated using a generalized estimation equation after age, sex, height, weight, and city (Beijing and Zhongshan). The HR values were calculated using the COX model after adjusting for age, sex, height, weight, and city (Beijing and Zhongshan).

with PM_X concentrations and negatively correlated with NDVI levels were also presented in both boys and girls (Table 2).

3.3. Effects of PM_X on the risk of HBP modified by the greenness around schools

The interaction effects of PM and greenness were shown in Table S1, and the interaction effects were significant ($P < 0.01$). The visualization of interaction effects was shown in Figs. S2–S4. To enhance interpretability, the stratification analysis based on the low- and high-level of greenness was performed. The modified effects of PM_X on the risk of HBP by the greenness around schools were shown in Fig. 4. Stratification based on greenness, high concentrations of PM_X had an increased risk of HBP in children and adolescents. However, it was different for the effect strengths of different particle sizes of PM on the risks of HBP of children and adolescents by the stratification of greenness around schools.

Higher concentrations of PM₁ and PM_{2.5} had a higher increased risk of HBP in the low-level group of greenness than the high-level group of greenness. The HRs of the PM₁ on the risk of HBP were 1.486 (95% CI: 1.440–1.533) and 1.150 (95% CI: 1.117–1.185) in the low and the high-level group of greenness respectively, and they were 2.635 (95% CI: 2.594–2.677) and 2.507 (95% CI: 2.470–2.545) for the effects of PM_{2.5} on the HBP risk. Higher PM₁₀ concentrations appeared to have a stronger effect on the risk of HBP in the high-level group of greenness than the low-level group of greenness. The HRs of PM₁₀ on the HBP risks were 1.367 (95% CI: 1.322–1.413) and 1.702 (95% CI: 1.644–1.761) in the low and the high-level group of greenness, respectively. The similar results were also presented in both boys and girls (Fig. 5 and Table S2).

3.4. Benefits of the improvements of PM_X in reducing HBP risk in different NDVI groups

The AF values were used to assess the theoretical benefits of the improvements of PM_X in reducing HBP risk in the low-level group and the high-level group of greenness (Fig. 5). Reducing multiple PM_X led to a theoretical reduction in HBP, but such theoretical benefits seemed to be stronger in areas with low greenness around schools than that in high greenness areas, particularly for PM_{2.5}. For example, the AFs of PM₁ on HBP incident in the low-level group of greenness were 13.74% (95% CI: 12.75–14.73) than that in the high-level group (AF = 4.62%, 95% CI: 3.73–5.51), respectively. The risk of HBP in children and adolescents in low-level group and high-level group of green areas could theoretically be attributed to 13.74% and 4.62% of PM₁ around schools. Therefore, such results represented those children and adolescents in schools with low-level greenness could theoretically gain more benefits than those in high-green areas if there was a reduction of PM₁ from high levels to low levels. The AFs of the high-level group of PM_{2.5} and PM₁₀ on HBP incident were 40.08% (95% CI: 39.60–40.57) and 15.47 (95% CI: 14.00–16.94) in the low-level group of greenness respectively, which simultaneously were higher than those in the high-level group of greenness (AF for PM_{2.5} = 17.28%, 95% CI: 17.01–17.54; AF for PM₁₀ = 9.96%, 95% CI: 9.34–10.57). The same results were also shown in both boys and girls (Table S2).

4. Discussion

4.1. Key findings

To our knowledge, this is the first study that used a longitudinal, two-center, dynamic cohort in China to investigate the individual effect of PM₁, PM_{2.5}, and PM₁₀, as well as greenness around schools on the HBP risks among the children and adolescent's population. In addition, the modification effects of greenness on the association between the PM_X and HBP risks were analyzed. During the 14-year follow-up period for near 600,000 children and adolescents, we found that higher exposure to PM₁, PM_{2.5}, and PM₁₀ were associated with a higher risk of HBP, whereas the greenness surrounding schools with a lower risk. Furthermore, greenness could alleviate the adverse effects of PM₁ and PM_{2.5} on HBP among children and

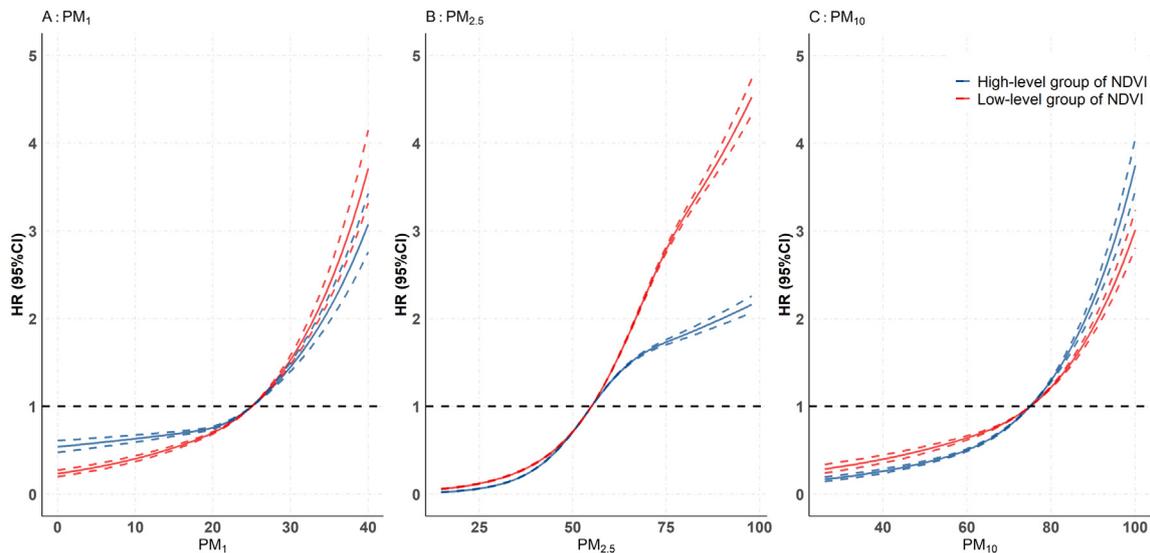


Fig. 4. Nonlinear association between PM_x (concentration of $\mu\text{g}/\text{m}^3$) and HBP incident in the low-level group and the high-level group of greenness. Note: The restricted cubic spline (RCS) with 3 knots combined with proportional hazards model (COX model) was used to assess the effects of PM_x (PM_1 for subfigure A, $PM_{2.5}$ for subfigure B, and PM_{10} for subfigure C) on HBP incident in the low-level group (Red lines) and the high-level group of greenness (blue lines). The dotted lines represent 95% confidence intervals. HR, hazard ratio. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

adolescents. Our findings were of great public health significance, informing the urgent need for effective air pollution mitigation strategies for the prevention of childhood HBP, such as by increasing the greenness areas around the schools to mitigate air pollution exposures.

Several cross-sectional studies shown that exposure to particulate matter was associated with the HBP prevalence among adults, especially in regions with high ambient PM concentration (Dong et al., 2014; B.Y. Yang et al., 2020; Cai et al., 2016; H.B. Yang et al., 2019), but this finding was not extensively exploited and validated among children and adolescents. For example, the long-term PM_{10} exposure was associated with increased BP levels and a higher prevalence of HBP in Chinese children and adolescents (Li et al., 2018; Zhang et al., 2019; Huang et al., 2021b), but no significant associations were found in German children (Liu et al., 2014). The possible explanations for the discrepancy could be different study design, PM concentration,

locations, and duration of PM exposure. In contrast, our study based on the longitudinal cohort with long term follow-up, multiple measurements of PM_x exposures in two distinct cities has the potential to provide more reliable evidence up to date. Although HBP among children and adolescents was a well-documented predictor for the risk of HBP and related CVD in adulthood (Chen and Wang, 2008; L. Yang et al., 2020), more studies were still warranted to elucidate the underlying mechanisms linking air pollutants exposure and HBP onset in children and adolescents such as oxidative stress, provocation of systemic inflammation, and dysfunction of vascular endothelium (Song et al., 2019; Bellavia et al., 2015; Zhong et al., 2015).

Several previous studies revealed that higher levels of residential greenness space were associated with a lower risk of HBP in adults (Xiao et al., 2020; Lane et al., 2017; Bijmens et al., 2017; B.Y. Yang et al., 2019; Dzhambov et al., 2018; Brown et al., 2016), and also

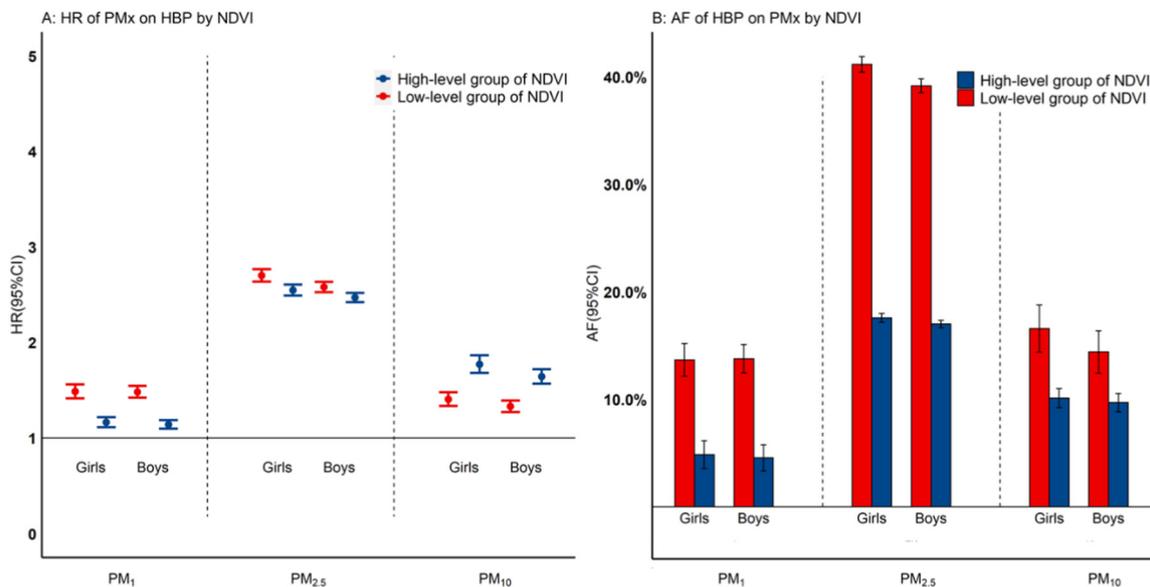


Fig. 5. The HR (Subfigure A) and AF (Subfigure B) of PM_x (concentration of $\mu\text{g}/\text{m}^3$) on HBP in the low-level group and the high-level group of greenness by sex. Note: AF, attributable fraction. HR of PM_x concentration on HBP risk was calculated using Cox models after adjusting confounders in the low-level group (red dot) and the high-level group of greenness (blue dot) by sex. We calculated the AF of HBP risks attributed to PM_x in the low-level (Red bar) and the high-level group (blue bar) of NDVI. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

reported a similar results among children and adolescents (Xiao et al., 2020; Warembourg et al., 2021), which were in line with our findings. Similarly, higher green space surrounding the maternal residence was associated with a lower risk of gestational HBP (Choe et al., 2018). One potential explanation could help to provide clue that exposure to higher greenness in childhood might lead to more active physical activity, a beneficial factor healthy cardiometabolic status (Nieuwenhuijsen et al., 2017; Nordbo et al., 2019). In addition, greenness was also hypothesized to decrease BP through stress reduction (Jendrossek et al., 2017). Thus, the locations, durations of greenness exposure, family socioeconomic status of children, and road traffic around schools or homes could underlie jointly to current findings.

We found that the association between PM and the onset of HBP was alleviated by greenness around schools. This finding was consistent with evidence for other diseases (Yitshak-Sade et al., 2019; de Keijzer et al., 2017; Kioumourtzoglou et al., 2016; Sun et al., 2020; Heo and Bell, 2019), such as ischemic stroke (Vivanco-Hidalgo et al., 2018), respiratory diseases (Sun et al., 2020), and total hospitalization (Heo and Bell, 2019). One study found an inverse association between residential greenness and BP in children regardless of ambient temperature and air pollution, noise annoyance, altitude, and level of urbanization, but our results shown that the greenness could offset the PM's harmful effects on BP to some extent. However, a few studies also found a composite effect of greenness and PM on HBP among children and adolescents. A prior study showed that greenness space attenuated the adverse effects of PM_{2.5} on cardiovascular mortality in neighborhoods of lower socioeconomic status, which was consistent with our study (Yitshak-Sade et al., 2019). We found that the effect of PM on the incidence of HBP was greater in low greening areas, and the benefits of environmental improvement were also greater in these areas, which highlights that better school greenness could alleviate the effect of PM_{2.5} on the onset of HBP. The finding suggested that the strengths of modification of greenness space around schools on the association between the PM concentration and HBP risks could depend on the aerodynamic diameters (James et al., 2015). In particular, children and adolescents are considered to be more vulnerable to air pollutants because of their unmaturing immune and respiratory systems and elevated level of outdoor activity.

Blood oxygen balance could be an important potential mechanism of greenness. According to a previous study, PM had a considerable acute effect on reducing blood oxygen saturation (Luttmann-Gibson et al., 2014; Goldberg et al., 2015). Low blood oxygen saturation at night was linked to nocturnal hypoxemia, which could be a risk factor for cardiovascular disorders including HBP (Zanobetti et al., 2010). Thus, greenery could decrease the negative effects of PM on HBP by reducing the acute effects of low blood oxygen saturation. However, the lack of information on the long-term effects of PM on blood oxygen saturation, as well as variations in oxygen saturation under varied levels of greenness, prevented us from delving more into the subject, which could be the subject of future research.

4.2. Implications

The main significance of the current study was that we provided evidence of environmental factors associated with the onset of HBP among children and adolescents, and a reasonable recommendation strategy of decreasing the adverse effects on HBP caused by PM through increasing school greenness. The intervention targeted at schools where students spent most of their time could enhance cost-effectiveness than that performed in the community. Therefore, the current findings provided a theoretical evidence basis for schools planning greenness policy. Reducing PM concentrations could be one of the most effective ways to reduce HBP risks among children and adolescents, but improving school greenness could be the practical way to alleviate the adverse effects of PM.

4.3. Strengths and limitations

The study has notable strengths including its comprehensive evaluation of PM and greenness around schools, its large sample size, and the repeated

measures of BP over a 14-year period. Our cohort consisted of entirely of school-aged children and adolescents surrounding by varying levels of greenness and air pollution from two Chinese cities, which makes stratified analyses by gender and greenness possible. Several potential limitations should also be noted. Firstly, the exposures measured by satellite with a low spatial resolution may be inaccurate. The indicator of NDVI could not distinguish the different types of vegetation and could be sensitive to atmospheric effects, clouds, and types of soil (Markevych et al., 2014b; Weier, 2000). However, satellite-driven environment assessment was a practical way to measure individual exposure in a large sample study. Secondly, the lack of data on participants' characteristics may lead to insufficient confounding adjustment such as physical activities, diet patterns, and family socioeconomic status. Also, the lack of students' home addresses limited the assessment of environmental exposure at home. However, it is expected that some behaviors, like physical activity levels, and breathing rate were relatively low at night in-home. Thirdly, we assumed no-transferring between different schools for students included in this study due to the lack of follow-on information on schools' switch. However, the inability to determine the outcome of the transferred students and accompanying their withdrawal of follow-up might lead to a misidentification of the level of HBP in our population and its relationship with various exposure factors, so their actual true association theoretically may be stronger. In addition, some environmental factors (NO_x, SO₂, and O₃), physical related risk factors of HBP (waist and hip circumference), and the traffic load around schools were not included in our study, therefore, we could not rule out the effects of these factors on the association between PM_x, greenness, and HBP among children and adolescents. Finally, this study only included data from two cities in China, which might be subject to the selection bias and limit the extrapolation of the findings. However, the prevalence of HBP among children and adolescents in Beijing and Zhongshan was 5% and 5.4% in 2014, respectively (Dong et al., 2018, 2019), which were the average level in China.

5. Conclusion

In conclusion, in this large longitudinal dynamic cohort of Chinese children and adolescents, we confirmed that the lower ambient PM and higher greenness around schools were associated with a lower risk of HBP, and higher greenness alleviated the adverse effects of ambient PM₁ and PM_{2.5} on the HBP onset among children and adolescents. Reducing PM concentration could benefit the schools with a low level of greenness than that with a high level of greenness. The observed antagonistic effect between PM and greenness on new HBP incidents could serve as evidence basis for policymakers to increase greenery around schools and communities, with an attempt to reduce the risks of HBP and its related CVD caused by air pollution.

CRedit authorship contribution statement

Dr. LC conceptualized and designed the study, completed the statistical analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Prof. MJ and YHD contributed to the conceptualization and design of the study, supervised the data collection, the statistical analyses and initial drafting of the manuscript, and reviewed and revised the manuscript; Dr. JQX, TM, MMC, DG, YHL, YM, BW, JJ, and XJW assisted with the statistical analyses and reviewed the manuscript. Dr. ZBZ, SC, LJW, XTL, XHG, SZH, and JW conducted the data collection, and reviewed and revised the manuscript. Dr. BD and YS reviewed and revised the manuscript. All authors read and approved the final version of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Availability of data and material

The datasets and result computational code used and analyzed during the current study are available from the corresponding author on reasonable request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2021.152431>.

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