Greenness around schools associated with lower risk of hypertension among children: Findings from the Seven Northeastern Cities Study in China

Xiang Xiao, Bo-Yi Yang, Li-Wen Hu, Iana Markevych, Michael S. Bloom, Shyamali C. Dharmage, Bin Jalaludin, Luke D. Knibbs, Joachim Heinrich, Lidia Morawska, Shao Lin, Marjut Roponen, Yuming Guo, Steve Hung Lam Yim, Ari Leskinen, Mika Komppula, Pasi Jalava, Hong-Yao Yu, Mohammed Zeeshan, Xiao-Wen Zeng, Guang-Hui Dong



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4	C. Dharmage ^{e,f} , Bin Jalaludin ^{g,h} , Luke D. Knibbs ⁱ , Joachim Heinrich ^{b,j} , Lidia Morawska ^k ,
5	Shao Lin ^d , Marjut Roponen ¹ , Yuming Guo ^m , Steve Hung Lam Yim ^{n,o} , Ari Leskinen ^{p,q} , Mika
6	Komppula ^p , Pasi Jalava ^l , Hong-Yao Yu ^a , Mohammed Zeeshan ^a , Xiao-Wen Zeng ^a , Guang-Hui
7	Dong ^{a,*}
8	^a Guangdong Provincial Engineering Technology Research Center of Environmental Pollution
9	and Health Risk Assessment, Department of Occupational and Environmental Health, School
10	of Public Health, Sun Yat-sen University, Guangzhou 510080, China
11	^b Institute and Clinic for Occupational, Social and Environmental Medicine, University
12	Hospital, LMU Munich, Ziemssenstraße 1, 80336 Munich, Germany
13	^c Institute of Epidemiology, Helmholtz Zentrum München - German Research Center for
14	Environmental Health, Ingolstädter Landstraße 1, 85764 Neuherberg, Germany
15	^d Departments of Environmental Health Sciences & Epidemiology and Biostatistics,
16	University at Albany, State University of New York, Rensselaer, New York 12144, USA
17	^e Allergy and Lung Health Unit, Centre for Epidemiology and Biostatistics, School of
18	Population and Global Health, The University of Melbourne, Melbourne, Vic 3004, Australia
19	^f Murdoch Children Research Institute, Melbourne, VIC 3010, Australia
20	^g Centre for Air Quality and Health Research and Evaluation, Glebe, NSW 2037, Australia
21	^h IIngham Institute for Applied Medial Research, University of New South Wales, Sydney

Greenness around Schools Associated with Lower Risk of Hypertension among Children: 1

Xiang Xiao^{a,1}, Bo-Yi Yang^{a,1}, Li-Wen Hu^{a,1}, Iana Markevych^{b,c}, Michael S. Bloom^{a,d}, Shyamali

Findings from the Seven Northeastern Cities Study in China 2

22 2170, Australia

- ⁱSchool of Public Health, The University of Queensland, Herston, Queensland 4006, Australia
- 24 ^jComprehensive Pneumology Center Munich, German Center for Lung Research,
- 25 Ziemssenstraße 1, 80336, Munich, Germany
- ²⁶ ^kInternational Laboratory for Air Quality and Health, Queensland University of Technology
- 27 (QUT), GPO Box 2434, Brisbane, Queensland 4001, Australia
- 28 ¹Department of Environmental and Biological Sciences, University of Eastern Finland,
- 29 Kuopio FI 70211, Finland
- ^mDepartment of Epidemiology and Preventive Medicine, School of Public Health and
- 31 Preventive Medicine, Monash University, Melbourne, VIC 3004, Australia
- ^aDepartment of Geography and Resource Management, The Chinese University of Hong
- 33 Kong, Shatin N.T., Hong Kong, China
- ^oStanley Ho Big Data Decision Analytics Research Centre, The Chinese University of Hong
- 35 Kong, Shatin N.T., Hong Kong, China
- ⁹Finnish Meteorological Institute, Kuopio 70211, Finland.
- ^qDepartment of Applied Physics, University of Eastern Finland, Kuopio 70211, Finland.

38 *Address correspondence to:

- 39 Guang-Hui Dong, MD, PhD, Professor, Guangdong Provincial Engineering Technology
- 40 Research Center of Environmental Pollution and Health Risk Assessment, Department of
- 41 Occupational and Environmental Health, School of Public Health, Sun Yat-sen University, 74
- 42 Zhongshan 2nd Road, Yuexiu District, Guangzhou 510080, China. Phone: +862087333409;

- 43 Fax: +862087330446. Email: donggh5@mail.sysu.edu.cn
- ¹ These authors contributed equally to this work and should be list as the first author.

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45 Abstract

Evidence suggests that residential greenness may be protective of high blood pressure, but 46 there is scarcity of evidence on the associations between greenness around schools and blood 47 48 pressure among children. We aimed to investigate this association in China. Our study included 9,354 children from 62 schools in the Seven Northeastern Cities Study. Greenness 49 around each child's school was measured by NDVI (Normalized Difference Vegetation Index) 50 51 and SAVI (Soil-Adjusted Vegetation Index). Particulate matter $\leq 1 \mu m$ (PM₁) concentrations were estimated by spatiotemporal models and nitrogen dioxide (NO₂) concentrations were 52 collected from air monitoring stations. Associations between greenness and blood pressure 53 were determined by generalized linear and logistic mixed-effect models. Mediation by air 54 pollution was assessed using mediation analysis. Higher greenness was consistently 55 associated with lower blood pressure. An increase of 0.1 in NDVI corresponded to a reduction 56 57 in SBP of 1.39 mmHg (95% CI: -1.86, -0.93) and lower odds of hypertension (OR= 0.76, 95% CI: 0.69, 0.82). Stronger associations were observed in children with higher BMI. Ambient 58 PM₁ and NO₂ mediated 33.0% and 10.9% of the association between greenness and SBP, 59 respectively. In summary, greater greenness near schools had a beneficial effect on blood 60 pressure, particularly in overweight or obese children in China. The associations might be 61 partially mediated by air pollution. These results might have implications for policy makers to 62 63 incorporate more green space for both aesthetic and health benefits.

64 *Keywords*: greenness; blood pressure; hypertension; modification; mediation

65 Capsule

- 66 Greater greenness near schools was associated with lower blood pressure among children,
- 67 which might have implications for policy makers to incorporate more green space.

68

69 Abbreviations

- 70 BMI, body mass index; BP, blood pressure; CI, confidence interval; DBP, diastolic blood
- 71 pressure; NDVI, normalized difference vegetation index; NO₂, nitrogen dioxide; OR, odds
- ratio, PM₁, particles with diameters \leq 1.0 µm; SAVI, soil adjusted vegetation index; SBP,

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73 systolic blood pressure;

74 Introduction

The global urban population has increased dramatically, from approximately 751 million in 75 1950 to 4.2 billion in 2018, and now accounts for 55% of the world's population (United 76 77 Nations 2018). As one of the global health challenges being confronted in the 21st century (Giles-Corti et al. 2016), rapid urbanization has resulted in alterations to the urban 78 environment (Zhou et al. 2018), including changes in the amount of urban green space. More 79 80 attention is drawn to green space due to recent findings about its public health impacts (Nieuwenhuijsen and Khreis 2017). A growing number of studies have demonstrated that 81 proximity to green space, measured as "greenness", has many beneficial health effects 82 (Nieuwenhuijsen et al. 2017), such as alleviating psychological stress (Gariepy et al. 2015; 83 84 Pun et al. 2018; Van Aart et al. 2018), supporting normal body weight (Lachowycz and Jones 2011), reducing blood lipids levels (Yang et al. 2019) and lowering cardiovascular disease risk 85 86 (Lane et al. 2017; Yitshak-Sade et al. 2017).

To date, few epidemiological studies have investigated the relationship between greenness 87 and blood pressure. Raised blood pressure is the leading risk factor for cardiovascular 88 diseases (Gillespie et al. 2013; WHO 2013), which has caused 9.4 million premature deaths 89 and accounted for 7% of the global disease burden in 2010 (WHO 2014). Although thought to 90 be less common in children, hypertension often originates in childhood (Feber and Ahmed 91 92 2010; Gupta-Malhotra et al. 2015) and may track into adolescence and adulthood (Chen and Wang 2008), possibly resulting in early vascular and heart damage (Gupta-Malhotra et al. 93 2015). 94

95 Only one study has investigated the impact of residential greenness on blood pressure in children (Markevych et al. 2014), which observed inverse association between residential 96 greenness and blood pressure. To our knowledge, these findings have not been replicated in 97 98 other childhood populations. Furthermore, the greenness around a child's school may be particularly important to children, given one of the mechanisms suggested for this link is 99 increased physical activity (Jia et al. 2018), maintaining healthy body weight (Sander et al. 100 101 2017), stress relief and other recreational activities (Herrera et al. 2018; Van Aart et al. 2018). The other suggested mechanisms are reducing air pollution levels (Dadvand et al. 2012b; 102 Thiering et al. 2016), which is itself a documented risk factor for hypertension (Yang et al. 103 2018b). However, the specific pathways linking greenness to blood pressure are not well 104 105 understood.

106 Therefore, we aimed to contribute new information to help address this knowledge gap, and 107 hypothesized that (1) higher greenness is associated with lower blood pressure among urban 108 children; and (2) the associations between greenness and children's blood pressure occur via 109 lower air pollution levels.

110 Methods

111 Design and study populations

From April 2012 to June 2013, the Seven Northeastern Cities (SNEC) study was conducted in
Liaoning Province, China, to explore the health effects of exposure to environmental factors
in children. The details of the study have been described previously (Dong et al. 2015; Zeng
et al. 2017). Briefly, we randomly selected 24 study districts in seven cities: Shenyang, Dalian,

116 Anshan, Fushun, Benxi, Liaoyang and Dandong. From each of the study districts we 117 randomly selected one or two primary and one or two middle school (62 schools in total). From each grade of the schools we randomly selected one or two classes. All children in the 118 119 selected classes, and their parents or guardians, were invited to participate in the study, provided that they had lived in the study district for at least two years. Participating children 120 completed a physical examination, and participants' parents or guardians completed a study 121 122 questionnaire to capture data about demographic information and environment exposure. A total of 10,428 children from the 62 random selected schools were invited and 9,567 123 participated in the study (response rate: 91.7%). After excluding 213 children who had not 124 resided in their current district for more than two years, the final sample for our analysis 125 comprised 9,354 children from 4.3 to 17.8 years of age (Figure 1). All children and their 126 parents or guardians provided written informed consent. This study was approved by the 127 128 Human Studies Committee of Sun Yat-sen University.

129 Blood pressure measurements

Blood pressure was measured according to the American Academy of Pediatrics guidelines 130 (National High Blood Pressure Education Program Working Group on High Blood Pressure in 131 and Adolescents 2004). All research personnel completed a training program to facilitate a 132 133 standardized approach for blood pressure measurement. Study participants were asked not to drink coffee or tea, and to abstain from physical activity for at least 30 minutes prior to blood 134 pressure measurements. After resting for five minutes in a quiet and temperate room, 135 participants were seated with back support, feet on the floor, right arm supported and an 136 appropriate cuff for children was placed around 2cm above the crease of the right arm elbow. 137

138 Trained nurses measured the brachial artery blood pressure at the upper right arm using a standardized mercury-column sphygmomanometer. Systolic blood pressure (SBP) was 139 determined by the onset of the Korotkoff sounds (K1), and the fifth Korotkoff sound (K5) 140 141 determined diastolic blood pressure (DBP). This was done three times at 2-minute intervals and we used the average of the three measurements in all analyses. Hypertension was defined 142 as systolic (SBP) and/or diastolic blood pressure (DBP) \geq 95th percentile for sex, age, and 143 144 height (National High Blood Pressure Education Program Working Group on High Blood Pressure in and Adolescents 2004). 145

146 Greenness exposure assessment

Greenness was assessed using two indices of satellite-derived vegetation measures -147 Normalized Difference Vegetation Index (NDVI) and Soil-Adjusted Vegetation Index (SAVI). 148 NDVI was calculated as the ratio of the difference between the reflectance of near-infrared 149 150 region light and red region light by chlorophyll in plants, to the sum of these two measures (Tucker 1979). Compared with NDVI, SAVI includes a correction factor to suppress soil 151 pixels (Huete 1988). Both indices range from -1 to +1, with -1 referring to water, values close 152 to zero indicating barren soil and values close to +1 representing a high density of greenness. 153 We used two cloud-free Landsat 5 Thematic Mapper satellite images from August 2010, at a 154 spatial resolution of 30 m x 30 m (http://earthexplorer.usgs.gov), to derive NDVI and SAVI 155 156 values at the school addresses. We calculated mean values of NDVI and SAVI values for circular buffers of 100m, 500m and 1000m around each school to assess exposure over 157 differing proximities to the school. These calculations were performed using ArcGIS 10.4 158

(ESRI, Redlands, CA, USA). Similar methods have been used previously (Casey et al. 2016;
Lane et al. 2017; Markevych et al. 2014).

161 *Covariates and mediators*

We selected the following covariates: age (years), gender (boy, girl), annual family income 162 (RMB yuan), family history of hypertension (yes/no), premature birth (yes/no), environmental 163 tobacco exposure (yes/no), home coal use (yes/no), parental education level (primary school 164 165 or lower vs. middle school or higher), personal living area (m^2 /person) and the season when BP was measured. Additionally, we used concentrations of air pollutants as possible mediators 166 in our mediation analyses. BMI was calculated as measured body weight divided by height 167 168 squared (kg/m²). BMI higher than the 85th percentile based on gender, age, and height was considered to be overweight. 169

Blood pressure is reported to be associated with both ambient air pollution and urban 170 greenness (Dadvand et al. 2012a; Yang et al. 2018b). We chose particulate matter with an 171 aerodynamic diameter $\leq 1 \mu m$ (PM₁) and nitrogen dioxide (NO₂) as two proxies of air pollution. 172 Four-year (2009-2012) average PM₁ concentrations were predicted by using spatiotemporal 173 models based on PM₁ concentrations from air monitoring stations, satellite-based aerosol 174 175 optical depth (AOD), meteorology and land use information. In brief, two types of Moderate 176 Resolution Imaging Spectroradiometer (MODIS) Collection six aerosol optical depth (AOD) data—Dark Target (DT) and Deep Blue (DB)—were combined to generate the spatiotemporal 177 models. Four-year average ground-monitored NO₂ concentration was used. (Supplementary 178 File). The details have been described in previous studies (Yang et al. 2018c). 179

180 Statistical analysis

As multiple levels (both individual and school) of data existed in our study, we applied generalized linear mixed-effects regression models (lmer and glmer function in R package) to investigate associations between greenness and blood pressure or childhood hypertension (Supplementary File). We used city and school as random effect in the models. Similar statistical models were used in our previous study (Zeng et al. 2017).

186 We implemented two sets of models for each endpoint: (1) crude mixed effect model, without adjustment for covariates; (2) adjusted mixed effect model, adjusted for age, gender, parental 187 education, income, and season. In line with previous studies, we used the 500m buffer NDVI 188 and SAVI values for the main analyses (Dzhambov et al. 2018a; Markevych et al. 2014; Yang 189 et al. 2018a). Finally, we evaluated effects in the adjusted models for NDVI and SAVI 190 averaged over 100m and 1000m buffers in a sensitivity analysis to assess the stability of our 191 192 results. We also excluded participants with a family history of hypertension from the adjusted models in sensitivity analysis to assess the impact of a family history of hypertension. In 193 another sensitivity analysis, in order to investigate if there is any study that were so 194 195 heterogeneous that can bias the overall effect estimates, seven additional sensitivity analyses were also conducted in which we excluded one city at a time in each analysis. 196

We performed stratified and interaction analyses by using age, sex, BMI, family income and parental education levels as modifiers to investigate the potential difference of effect of residential greenness among different subgroups. For these analyses, age ($\leq 11 \text{ vs} > 11 \text{ years}$) and family income level ($\leq 30000 \text{ vs} > 30000 \text{ yuan per year}$) were split at the median. The 201 interaction effect was estimated by significance of the corresponding interaction item202 (greenness×modifier) additionally added in the models.

We followed the Baron-Kenny's step for mediation analyses to examine whether air pollutants 203 concentrations could be modes or mechanisms through which greenness affected blood 204 pressure and hypertension (Baron and Kenny 1986). Briefly, we first constructed a full model 205 that includes the exposure, mediator and all covariates. Then we constructed a mediate model 206 207 that mediator was regressed on the exposure and all covariates. Last, the exposure effect in first model was compared with the counterpart in the second model. These results were 208 generated by bootstrapping (500 simulations) using the function mediate implemented in the 209 210 R package 'mediation' (Imai et al. 2010)

All statistical analyses were performed using R version 3.5.1. All statistical tests used
two-tailed P <0.05 to indicate statistical significance.

213 Results

214 Baseline characteristics

Study participants were 10.9 years of age on average (ranging from 4.3 to 17.8 years), just under half (49%) were girls, and 41.5% lived in a family with an annual income greater than 30000 yuan (Table 1). The average systolic and diastolic blood pressures were (111.0 \pm 14.1) mmHg and (64.5 \pm 9.8) mmHg, respectively, and 13.8% were hypertensive. Compared to normotensive children, participants with hypertension were older (P<0.05), had higher BMI (P<0.05), were more likely to be exposed to environmental tobacco smoke (P<0.05) and to

have a family history of hypertension (P<0.05). Greenness levels varied markedly across different schools (Supplementary Materials, Figure S1, Table S1). For example, NDVL_{500m} levels ranged from -0.09 to 0.77, with a median value of 0.31, whereas SAVL_{500m} levels ranged from 0.00 to 0.47 with a median value of 0.18. The greenspace indices were also strongly positively inter-correlated (r_s : 0.63 to 0.99), while their inverse correlations with air pollutant concentrations were comparatively weaker (r_s : -0.15 to -0.33).

227 Associations between greenness and blood pressure

Associations of greenness with systolic and diastolic blood pressure and with hypertension, are presented in Table 2. In the adjusted model, a 0.1-unit increase in NDVI_{-500m} exposure was significantly associated with a -1.39 (95% CI: -1.86, -0.93) mmHg reduction in SBP and a 24% (OR= 0.76, 95% CI: 0.69, 0.82) lower odds of hypertension, similarly, a 0.1-unit increase in SAVI_{-500m} exposure was significantly associated with a -2.16 (95% CI: -2.93, -1.38) mmHg reduction in SBP and a 37% (OR= 0.63, 95% CI: 0.55, 0.73) lower odds of hypertension. We did not observe any significant association with DBP in adjusted model.

235 Sensitivity analyses

The direction and significance of our results were consistent when participants with a family history of hypertension were excluded (Supplementary file, Table S2), when participants exposed to environmental tobacco were excluded (Supplementary file, Table S3), when 100m and 1000m buffers were used to calculate NDVI and SAVI values (Supplementary file, Table S4) and when the participants from each one of the seven cities were excluded (Supplementary file, Table S5 and Table S6).

242 Effect modification

We also evaluated modification of the greenness-blood pressure associations according to the 243 key factors shown in Table 3. We found statistically significant interactions for BMI, in which 244 245 stronger associations for both NDVI (P<0.0001) and SAVI (P<0.0001) with SBP were observed among overweight/obese participants compared to those with normal weight (Table 246 4). The 3D response surface and the 2D contour plots are graphical representations of the 247 regression equation (Figure 2). Each contour curve represents an infinite number of 248 combinations of greenness and BMI. Greenness showed a negative association with SBP 249 when the BMI level was fixed. There was a linear increase in SBP with an increase in BMI, 250 but a decrease in greenness level. We also detected statistically significant interactions of 251 252 NDVI (P<0.0001) and SAVI (P<0.0001) with sex, in which higher levels of greenness was associated with higher DBP in boys, but with lower DBP in girls. No interaction with SES 253 254 factors (family income and parental education levels) was observed.

255 Mediation analyses

We found that 33.0% and 10.9% of the effects of greenness on SBP was mediated by lower ambient levels of PM_1 and NO_2 , respectively (P <0.0001). It is important to note that road traffic is a source of both of these pollutants (PM_1 and NO_2), therefore there is usually an association between their concentrations in close proximity to a roadway. However, we did not detect significant mediation effects for exercise time (data not shown). The mediation analysis results were similar for the associations between greenness and hypertension (Table 5). We used BMI as potential moderators in the mediation models (Supplementary file, Table 263 S7). The mediation effect of air pollutants varied remarkably by BMI quantiles.

264 Discussion

265 Key findings

Higher exposure to greenness surrounding school, as measured by NDVI and SAVI, was
significantly associated with lower SBP and lower odds of hypertension in children living in
Northeast China. The relationship was stronger among overweight/obese children.
Furthermore, ambient PM₁ and NO₂ concentrations might be mediating variables in the
associations between greenness and SBP and greenness and hypertension.

271 Comparison with other studies and interpretations

To our knowledge, only one previous study has investigated the associations between 272 greenness and blood pressure in children. In that study, Markevych et al. (2014) found 273 beneficial associations between lower greenness levels (calculated as NDVI) and higher SBP 274 and DBP in 10-year-old German children, which are in line with our results. However, a 275 number of studies have reported associations on greenness and blood pressure in adults. 276 277 Dzhambov et al. (2018a) conducted a study in residents of an Alpine valley in Austria and observed that an interquartile range (IQR = 0.16) increase in greenness was associated with 278 279 lower odds (OR=0.64 95% CI: 0.52, 0.78) of hypertension and a 2.84 mmHg decrease in SBP. 280 A twin cohort study carried out in Belgium reported that an interquartile increase (IQR = 46%change) in residential greenness in early life resulted in a decrease of 3.59 mmHg and 4.0 281 mmHg in night-time SBP and DBP respectively (Bijnens et al. 2017). Jendrossek et al. (2017), 282 however, detected no effect of greenness on maternal hypertension assessed by questionnaire. 283

284 A recent meta-analysis pooling most previously published studies indicated that the current evidence generally supports a relationship between higher greenness levels and lower blood 285 pressure levels (Twohig-Bennett and Jones 2018). Collectively, our results, combined with 286 287 previous studies, support an inverse relationship between greenness and SBP levels and importantly, the overall observed associations in adults can also be detected at much younger 288 ages. However, given the cross-sectional nature of the studies addressing the influence of 289 290 greenness on children's blood pressure, future longitudinal studies in children are needed to 291 confirm our findings.

292 Effects modification and mediation

In stratified analyses, we found a statistically significant interaction between greenness and 293 sex. To the best of our knowledge, this study is the first reporting on the interaction between 294 greenness and sex, so it is difficult for us to compare the results and discuss the possible 295 296 explanations. And the interaction showed only on DBP, so this result should be interpreted cautiously. It is likely that psychological and endocrine factors may contribute to the 297 differences of the effect. We also found a stronger association between NDVL_{500m} and SBP 298 among children with higher BMI. As far as we are aware, only one previous study showed a 299 300 similar result (Dzhambov et al. 2018a). In our data, under or normal weight children and overweight or obese children exercised for 7.5 hours/week and 7.8 hours/week on average 301 302 (data not shown), respectively (P=0.17). Thus, children with higher BMI levels might benefit more from increasing greenness than those with lower BMI given the same physical activity 303 304 level. Unfortunately, we did not collect information about individual greenspace use and so

305 future studies that include such data may provide more definitive answers. Notably, our results indicated that family income and parental education level did not modify the 306 relationship between greenness and blood pressure, while previous studies have shown that 307 308 the relationship between greenness with health outcomes was stronger in lower income groups (Browning and Rigolon 2018; Dzhambov et al. 2018a). The inconsistency could be 309 attributed in part to differences in the study populations – children in our study and adults in 310 311 the previously reported studies, different greenness exposure – school-based versus residential, and differences in ethnic groups. Also, our study population resided in a region dominated by 312 heavy industry, and so the industrial influence and economic development status may be quite 313 different to those studies conducted in developed countries (Dzhambov et al. 2018a; 314 315 Jendrossek et al. 2017). For example, participants with lower income were surrounded by higher greenness (average NDVI_{-500m} is 0.34 in the lower income versus 0.32 in the higher 316 317 income group, P < 0.05), contrary to other studies in which lower income residents were surrounded by lower greenness (Astell-Burt et al. 2014; Bell et al. 2008). 318

We found that higher levels of greenness were significantly associated with lower air pollution, and mediation analyses showed that both airborne particles and gaseous pollutants might partially explain the associations between greenness and blood pressure. Previous studies have suggested that the concentration levels of urban ambient air pollutants can be reduced by vegetation (Hirabayashi and Nowak 2016; Nowak et al. 2013; Uni and Katra 2017). Green areas, which are barriers between the pollution source and receptors, can remove some particles and gaseous pollutants, although the efficacy is likely to be limited

326 (Gómez-Moreno et al. 2019; Markevych et al. 2017; Xing and Brimblecombe 2019). Regardless of the ability of greenness to act as a filter of air pollution, its presence may reflect 327 a relative absence of pollutant sources and also can increase the distance between the source 328 329 and the receptor (Richmond-Bryant et al. 2018), enabling greater dilution. In addition, some studies have also speculated that people were more likely to engage in physical activities 330 when exposed to higher green space (Markevych et al. 2017), which in turn may be protective 331 against hypertension (Huai et al. 2013; Lagisetty et al. 2016). Jia et al. (2018) found that 332 physical activity accounted for a 55% reduced risk of hypertension in adults when exposed to 333 higher greenness. However, based on our data, we did not find that the greenness association 334 with blood pressure was mediated through physical activity levels (data not shown). One 335 336 possible explanation for the discrepancy could be that children's exercise time in schools is usually scheduled and consequently would be independent of greenness levels around schools. 337 338 Nevertheless, our results were consistent with previous study (Markevych et al. 2014) which also reported that the effect on children's blood pressure was independent of physical activity. 339 It should be noticed that even though greenness around school may not affect the time of 340 children's exercise but rather, greenness may affect the environmental quality of the place 341 where they exercise or engage in other recreational activities, through lowering stress and 342 increasing social engagement (Herrera et al. 2018; Markevych et al. 2017). More interestingly, 343 344 BMI tended to moderate or modify the greenness-air pollution-blood pressure process instead of mediating the association directly. Among participants with higher BMI, less effect of 345 346 greenness could be explained by air pollution.

347 Implications for policy makers

As children usually spend lots of time in school and most of their outdoor activities (taking exercise, reading a book outside, or doing other recreational activity) may happen in school, school-based greenness is important to children. This study suggests a beneficial effect for greenness surrounding schools on children's blood pressure. This finding may have important implications for policy makers to plan more greenspace around schools for not only the aesthetic benefits but also the health effect that may influence all children in the school.

354 Strengths and limitations

Our study is the largest to date to evaluate the association between greenness and childhood 355 blood pressure and hypertension. It was based on a large sample size and we achieved a high 356 participation rate (91.7%), minimizing the likelihood for selection bias and strengthening the 357 external validity of our results. We leveraged two widely recognized, valid and reliable 358 indices to assign greenness exposure, the NDVI and SAVI, and we captured a comprehensive 359 profile of covariates to adjust for confounders. Several sensitivity analyses were also 360 conducted to validate the robustness of the associations. We also examined interactions 361 according to the most likely effect modifiers and conducted mediation analyses to determine 362 the contribution of ambient PM₁ and NO₂, as well as physical activity and BMI to the 363 greenness-BP associations. In addition, our study is the first to date to evaluate the health 364 365 effect of school-based greenness on children given that children usually spend much time participating in a wide range of outdoor activities in school. 366

367 Our study also had some limitations and therefore the results should be interpreted cautiously.

368 First, we may not capture greenness exposure from other non-school places (such as home). However, due to a Chinese policy restricting children from attending trans-regional schools, 369 our data showed that the average walk time from their homes to schools was about 12 minutes, 370 371 and thus the school-based greenness exposures are very likely to represent residential greenness exposure to a large extent. The latter was also confirmed when we generated 372 similar results using a larger buffer (1000m exposure buffer instead of the 500m exposure 373 374 buffer) and found that the results were consistent. The major limitation of exposure assessment in our study was that we could not differentiate greenness within the premises of 375 the schools form the buffered greenness so that we could not determine how much of the 376 exposure was contributed by the greenness within schools as this could vary depending the 377 area of each school. Some studies showed slight differences between the effect of greenness 378 within and around school boundaries, which should be considered in further study. Second, 379 380 although we adjusted for the most likely confounders in our analysis, we cannot rule out the possibility of unmeasured confounding due to other factors that co-vary with greenness and 381 have been shown to impact blood pressure, including noise (Dzhambov et al. 2018b), 382 walkability (James et al. 2017) and psychological status (Herrera et al. 2018; Van Aart et al. 383 2018). We were also unable to adjust our analyses for neighborhood socioeconomic status 384 because we did not have such data, either. Third, although we tried to explore the mediation 385 effect of air pollution by using model predicted PM₁ and NO₂ from air monitoring stations, 386 the deviation of air pollution assessment brought by inherent limitation of model prediction 387 was inevitable, thus the results of mediation analysis should be interpreted with caution. Forth, 388 the cross-sectional design of our study prevented us from inferring temporality, in that we 389

cannot be sure if greenness exposure preceded blood pressure values in time. Still, we believe
it unlikely for children's blood pressure to have impacted the distribution of greenness around
their homes and schools. However, for mediation analyses, we cannot rule out the possibility
that greener schools were located in regions where air pollution levels were lower, thus
temporality of the mediation process cannot be inferred, either.

395 Conclusion

Higher levels of greenness near schools was associated with lower systolic blood pressure and lower odds ratio of hypertension in school children from Northeastern China, especially in children with higher BMI. Air pollutants might partly mediate the associations. Further well-designed longitudinal studies with more specific assessment of individual greenness exposure are needed to confirm our results. If confirmed in future studies, this effect could have implications for policy makers and public health authorities to build more greenery, not only for its aesthetic benefits but also for better health.

403 **Declaration of interests**

404 None.

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567 Figure legends

568 Figure 1. Children recruitment flow chart of the Seven Northeastern Cities Study

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- Figure 2. The 3D response surface and 2D contour plots showing interactive effects of BMI
- and greenness (500m buffer) on blood pressure

- Footnote: Panel A for SBP-NDVI-BMI, Panel B for DBP-NDVI-BMI, Panel C for
- SBP-SAVI-BMI, Panel D for DBP-SAVI-BMI.

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		Mean \pm SD, n (%)	
	Total	Non-hypertension	Hypertension
Characteristic	(<i>n</i> = 9354)	(<i>n</i> = 8065)	(<i>n</i> = 1289)
Age (years) ^a	10.9 ± 2.6	10.8 ± 2.6	11.9 ± 2.5
Sex			
Boys	4771 (51.0%)	4112 (51.0%)	659 (51.1%)
Girls	4583 (49.0%)	3953 (49.0%)	630 (48.9%)
BMI $(kg/m^2)^a$	19.6 ± 4.3	19.2 ± 4.1	21.7 ± 5.2
Family income per year			
\leq 5000 yuan	1032 (11.0%)	891 (11.0%)	141 (10.9%)
5000-10000 yuan	1211 (12.9%)	1023 (12.7%)	188 (14.6%)
10000-30000 yuan	3230 (34.5%)	2778 (34.4%)	452 (35.1%)
30000-100000 yuan	3441 (36.8%)	2994 (37.1%)	447 (34.7%)
> 100000 yuan	440 (4.7%)	379 (4.7%)	61 (4.7%)
Parental education level ^a			
Primary school or lower	3595 (38.4%)	3066 (37.9%)	529 (41.0%)
Middle school or higher	5759 (61.6%)	4999 (62.1%)	760 (59.0%)
Family history of hypertension ^a			
No	5755 (61.5%)	5024 (62.3%)	731 (56.7%)
Yes	3599 (38.5%)	3041 (37.7%)	558 (43.3%)
Environment tobacco exposure ^a			
No	4868 (52.0%)	4264 (52.9%)	604 (46.9%)
Yes	4486 (48.0%)	3801 (47.1%)	685 (53.1%)
Home coal use ^a			
No	8466 (90.5%)	7328 (90.9%)	1137 (88.2%)
Yes	888 (9.5%)	737 (9.1%)	151 (11.8%)
Season of measurements ^a			
Spring	3622 (38.7%)	3048 (37.8%)	574 (44.5%)
Summer	1055 (11.3%)	858 (10.6%)	197 (15.3%)
Fall	1135 (12.1%)	866 (10.7%)	269 (20.9%)
Winter	3542 (37.9%)	3293 (40.8%)	249 (19.3%)
Average exercise per week (hours)	7.6 ± 7.8	7.6 ± 7.0	7.7 ± 8.6
Person living area (m ²)	22.7 ± 10.2	22.7 ± 9.8	22.3 ± 12.5
Temperature (°C) ^a	147+60	150+58	128+65
Systolic blood pressure (mmHg) ^a	111.0 + 14.1	108.1 + 12.1	129.1 + 11.5
Diastolic blood pressure (mmHg) ^a	64.5 + 9.8	62.7 + 8 3	75.6 + 11.2

577 **Table 1** Characteristics of participants from the Seven Northeastern Chinese Cities Study

578 Abbreviations: BMI, body mass index

 $^{a}P < 0.05$ for difference between hypertension and non-hypertension groups.

		β	/ OR (95% CI) for NE	β / OR (95% CI) for SAVI			
	Greenness	SBP (β)	DBP (β)	Hypertension (OR)	SBP (β)	DBP (β)	Hypertension (OR)
	Buffer 500m						
	Crude	-2.68 (-3.82, -1.53)	-0.84 (-1.28, -0.41)	0.70 (0.63, 0.77)	-4.12 (-5.98, -2.26)	-1.34 (-2.05, -0.62)	0.56 (0.47, 0.66)
	Adjusted ^b	-1.39 (-1.86, -0.93)	-0.41 (-0.87, 0.05)	0.76 (0.69, 0.82)	-2.16 (-2.93, -1.38)	-0.64 (-1.39, 0.11)	0.63 (0.55, 0.73)

Table 2 Associations of greenness indices^a (per 0.1-unit increase) with blood pressure and hypertension (n = 9354)

581 Abbreviations: BMI, body mass index. CI, confidence interval. DBP, diastolic blood pressure. NDVI, normalized difference vegetation index.

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582 OR, odds ratio, SAVI, soil adjusted vegetation index. SBP, systolic blood pressure.

^aGreenness defined using a 500m buffer around each of the participating schools.

^bAdjusted for age, sex, parental education, income and season.

		β	(95% CI) f	or NDVL _{500m}		β	(95% CI) f	for SAVI.500m	
Subgroup	n	SBP	P _{interaction}	DBP	P _{interaction}	SBP	P _{interaction}	DBP	P _{interaction}
Sex									
Boys	4771	-1.20 (-1.81, -0.59)	0.846	-0.04 (-0.59, 0.50)	< 0.0001	-1.89 (-2.88, -0.90)	0.692	-0.10 (-0.98, 0.79)	< 0.0001
Girls	4583	-1.52 (-2.01, -1.04)		-0.78 (-1.23, -0.34)		-2.31 (-3.12, -1.49)		-1.19 (-1.91, -0.46)	
Age									
≤ 11 years	4545	-1.25 (-2.08, -0.43)	0.060	-0.63 (-1.29, 0.03)	0.229	-1.92 (-3.18, -0.65)	0.104	-0.94 (-1.95, 0.07)	0.202
> 11 years	4809	-2.12 (-2.85, -1.38)		-0.73 (-1.17, -0.29)		-3.23 (-4.49, -1.97)		-1.23 (-1.96, -0.50)	
BMI									
Normal	6323	-1.18 (-1.65, -0.72)	< 0.0001	-0.50 (-0.95, -0.05)	< 0.0001	-1.83 (-2.60, -1.06)	< 0.0001	-0.79 (-1.51, -0.06)	< 0.0001
Overweight/obese	3031	-1.45 (-2.15, -0.75)		-0.16 (-0.78, 0.46)		-2.27 (-3.40, -1.14)		-0.28 (-1.27, 0.72)	
Family Income									
\leq 30000 yuan	5473	-1.38 (-1.95, -0.81)	0.850	-0.40 (-0.91, 0.12)	0.951	-2.14 (-3.08, -1.19)	0.995	-0.61 (-1.44, 0.22)	0.982
> 30000 yuan	3881	-1.34 (-1.94, -0.74)		-0.42 (-0.89, 0.06)		-2.00 (-2.97, -1.04)		-0.66 (-1.41, 0.09)	
Parental education									
\leq Primary school	3595	-1.66 (-2.31, -1.02)	0.285	-0.63 (-1.16, -0.09)	0.065	-2.57 (-3.65, -1.49)	0.326	-0.99 (-1.86, -0.12)	0.082
> Middle school	5759	-1.19 (-1.67, -0.70)		-0.32 (-0.78, 0.15)		-1.84 (-2.61, -1.07)		-0.52 (-1.26, 0.22)	

Table 3 Associations of greenness indices (per 0.1-unit increase) and blood pressure, stratified by demographic factors (n = 9354)^a

587 Abbreviations: BMI, body mass index. CI, confidence interval. DBP, diastolic blood pressure. NDVI, normalized difference vegetation index.

588 SAVI, soil adjusted vegetation index. SBP, systolic blood pressure.

^a Adjusted for age, sex, parental education, income and season. (unless stratified by the respective factor).

590 Note: The P-values for interaction were calculated by adding a corresponding interaction item (greenness×modifier) in the model

		OR (95% CI) for	NDVI.500m	OR (95% CI) for	OR (95% CI) for SAVI.500m	
Subgroup	n	Hypertension	P _{interaction}	Hypertension	$P_{\text{interaction}}$	
Sex						
Boys	4771	0.81 (0.74, 0.89)	0.279	0.71 (0.61, 0.83)	0.259	
Girls	4583	0.72 (0.65, 0.80)		0.59 (0.49, 0.70)		
Age						
≤ 11 years	4545	0.82 (0.72, 0.92)	0.200	0.73 (0.61, 0.87)	0.008	
> 11 years	4809	0.73 (0.66, 0.80)		0.59 (0.49, 0.70)		
BMI						
Normal	6323	0.78 (0.69, 0.87)	< 0.0001	0.67 (0.55, 0.81)	< 0.0001	
Overweight/obes		0.74 (0.64, 0.95)		0(1(0.49, 0.76))		
e	3031	0.74 (0.64, 0.85)		0.61 (0.48, 0.76)		
Family Income						
\leq 30000 yuan	5473	0.77 (0.70, 0.85)	0.912	0.65 (0.55, 0.77)	0.948	
> 30000 yuan	3881	0.74 (0.67, 0.82)		0.62 (0.53, 0.73)		
Parental education						
\leq Primary school	3595	0.73 (0.64, 0.83)	0.197	0.59 (0.47, 0.74)	0.237	
> Middle school	5759	0.78 (0.71, 0.86)		0.67 (0.57, 0.78)		

592 **Table 4** Associations between greenness indices (per 0.1-unit increase) and hypertension, 593 stratified by demographic factors (n = 9354)^a

594 Abbreviations: BMI, body mass index. CI, confidence interval. DBP, diastolic blood pressure.

NDVI, normalized difference vegetation index. OR, odds ratio. SAVI, soil adjusted vegetation
 index. SBP, systolic blood pressure.

^a Adjusted for age, sex, parental education, income, exercise time and season. (unless
 stratified by the respective factor).

Note: The P-values for interaction were calculated by adding a corresponding interaction item(greenness×modifier) in the model.

601	Table 5 Mediation of the association between greenness (NDVL _{500m}) and SBP/hypertension
602	explained by air pollutants, BMI, and exercise time ^a

Outcome	Mediator	Proportion Mediated (95% CI) /%	Р
SBP			
	PM_1	33.0 (25.6, 44.0)	< 0.0001
	NO_2	10.9 (5.4, 18.0)	< 0.0001
Hypertension			
	PM_1	11.7 (8.0, 17.0)	< 0.0001
	NO_2	12.2 (5.5, 23.0)	< 0.0001

Adjusted for age, sex, parental education, income, exercise time and season.

e and rval. NDV Abbreviations: BMI, body mass index. CI, confidence interval. NDVI, normalized difference vegetation index. SBP, systolic blood pressure.



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Highlights

- Evidence on the association between greenness and blood pressure among children is scarce.
- We are the first to explore this topic based on school surrounding greenness exposure.
- Attending schools with higher greenness showed beneficial effects on blood pressure.
- The beneficial effects were stronger in children with higher BMI levels.
- Air pollution might partially mediate the effects of greenness on blood pressure.

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Declaration of interests

 \square 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.

□The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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