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Greenness and its composition and configuration in association with allergic rhinitis in preschool children

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ABSTRACT

Background: Few studies focus on the associations of green space composition and configuration with children's allergic rhinitis (AR).

Methods: A multi-center population-based cross-sectional study was performed in 7 cities in mainland of China between 2019 and 2020, recruiting 36,867 preschool children. Information on the current AR symptoms and demographics were collected by questionnaire. Exposure to residential greenness was estimated by Normalized Difference Vegetation Index (NDVI, 1000 m buffer) around the residences. Greenness composition was estimated in 3 main categories: forest, grassland, shrubland. Configuration of each category and total greenness (a spatial resolution of 10 m × 10 m) was estimated by 6 landscape pattern metrics to quantify their area, shape complexity, aggregation, connectivity, and patch density. Exposure to daily ambient particulate matter (PM_1, $PM_{2.5}$ and PM_{10}, a spatial resolution of 1 km × 1 km) was estimated. Multilevel logistic regression models were applied to analyze the associations of greenness and its composition and configuration with AR, and mediation effects by PMs were examined by mediation analysis models.

Results: The prevalence of self-reported current AR in preschool children was 33.1%. Two indicators of forest, Aggregation Index of forest patches (AIforest) (odds ratio (OR):0.92, 95% Confidential Interval (CI): 0.88–0.97), and Patch Cohesion of forest (COHESIONforest) (OR: 0.93, 95% CI:0.89–0.98) showed significantly negative associations with AR symptoms. Mediation analyses found the associations were partially mediated by PMs. Age, exclusive breastfeed duration and season were the potential effect modifiers. The associations varied across seven cities.

Conclusion: Our findings suggest the inverse associations of the aggregation and connectivity of forest patches surrounding residence addresses with AR symptoms. Since the cross-sectional study only provides associations rather than causation, further studies are needed to confirm our results as well as the underlying mechanisms.

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1. Introduction

Allergic rhinitis (AR) is one of the most common diseases globally (Bousquet et al., 2008), which is defined as an inflammatory and IgE-mediated disease with the characteristics of nasal congestion, rhinorrhea (nasal drainage), sneezing, and/or nasal itching (Seidman et al., 2015). The prevalence of self-reported AR ranges from 2% to 25% in children (Asher et al., 2006) and 1% to over 40% in adults worldwide (Bousquet et al., 2008; Katelaris et al., 2012). In China, the prevalence of AR has increased rapidly in many regions for the past few years, especially in Shanghai, rising from 13.6% to 23.9% between 2005 and 2011 (Wang et al., 2016). AR influenced patients' life qualities and caused a huge burden of disease. In addition to the reduced work productivity and increased leave days due to AR sickness, the total annual direct medical cost of AR was $3.4 billion or thereabouts (Meltzer and Bukstein, 2011).

Rapid urbanization leads to population growth and destruction of natural environment as well as a consistent decline of urban green space (Chen et al., 2017a). However, green space provides residents with various health benefits including reducing harm (e.g. reducing exposure to air pollution, noise and heat), restoring capacities (e.g. attention restoration and physiological stress recovery) building capacities (e.g. encouraging physical activity and facilitating social cohesion) (Markevych et al., 2017), as well as maintaining urban biodiversity (Wheeler et al., 2015), which in turn is associated with improved health via multiple pathways, including but not limited to provision of medicines, food and clean water, and facilitating transcendent experiences (Marselle et al., 2021). Landscape pattern metrics (McGarigal and Marks, 1995), quantifying the spatial composition and configuration, are also used widely to relate spatial patterns to processes such as biodiversity, water quality, aesthetic preference (Uuemaa et al., 2013) which is related to psychological restoration (Dramstad et al., 2006; van den Berg et al., 2003), and air pollution level (Liu and Shen, 2014).

A widely used indicator of greenness is Normalized Difference Vegetation Index (NDVI) (Tucker, 1979) and it was applied in many studies to explore the association of residential greenness exposure with AR in China, Germany, Canada, USA and other countries (Chan-Yeung et al., 2000; Fuertes et al., 2014; Gernes et al., 2019; Li et al., 2019b). For example, a study in Europe found that increased residential NDVI had protective effects on AR symptoms (Dzhambov et al., 2021). Similarly, a study from eastern-northern cities in China indicated that residential NDVI was negatively associated with the risk of AR (Huang et al., 2022).

Few studies focus on the associations between AR and the composition and configuration of green space, aiming to characterize vegetation types as well as their connectivity, segregation, and shape (Li et al., 2019a). Among others, forest, grass and shrub are three typical types of green space which usually accounted for the largest proportion (Duncan and Boruff, 2023; Gong et al., 2019). Although cropland may also exhibit high NDVI values, it is generally expected to have low population densities (Bille et al., 2023). Specifically, forest areas were found to have potentially protective impact on AR (Dzhambov et al., 2021; Huang et al., 2022), while grass cover might aggravate AR symptoms because it can produce various allergenic pollen, some of which are the most frequently recognized aeroallergens worldwide (Bauchau and Durham, 2004; Scala et al., 2010). In the total green space and in each vegetation type, the green space configuration can be characterized by landscape pattern metrics such as percentage of green space (PLAND), mean area of green space patches (AREA_MN), area-weighted mean complexity of shape of green space (SHAPE_AM), connectivity of green space (COHESION), aggregation of green space (AI) and fragmentation of green space (PD) (McGarigal and Marks, 1995; Wang and Tassinary, 2019). Recent studies have indicated that specific green space configuration could promote health by improving mental health status (Ha et al., 2022), reducing suicide risk (Shen and Lung, 2018) and respiratory disease mortality (Jaafari et al., 2020), and further lowering all-cause mortality (He et al., 2021; Wang and Tassinary, 2019).

On the other hand, particulate matter (PM), a typical air pollutant, consists of solid particles and liquid droplets in the atmosphere and is composed of organic and inorganic compounds with various elements and ionic species (such as sulfate, nitrate, and ammonium ions) from multiple sources (Sompornrattanaphan et al., 2020). According to the aerodynamic diameter, respirable particles (PM_{10}) consist of $PM_{2.5\text{-}10}$, $PM_{2.5}$, and PM_1. PM_1, as a main part of $PM_{2.5}$, could account for 80% of $PM_{2.5}$ (Wang et al., 2015). Numerous epidemiological studies confirmed the harmful effects of PM on allergic respiratory diseases (Chu et al., 2019; Lin et al., 2021; Sompornrattanaphan et al., 2020).

Exposure to green space could be able to reduce the risk of AR via multiple pathways, including indirect effects via PMs (Mueller et al., 2022). In perspectives of green space composition and configuration, the concentrations of ambient particulate matters would be lower under circumstance of larger green space, higher shape complexity of green space, or higher connectivity of green space (Ren et al., 2022; Zhan et al., 2022). On the other hand, the more fragmented the forest was, the higher the fine PM concentration was (Lin and Chen, 2023). However, few studies investigated the roles of composition and configuration of green space on AR, and the mediation roles of PMs in these associations.

This study selected a series of landscape metrics to describe the composition and configuration of residential green space as well as NDVI, in order to make up for the deficiency resulting from single evaluation of NDVI. The objectives of our study were to test whether the composition and configuration of green space were associated with AR, how this association would be in comparison with NDVI and how it is mediated by PM exposure as potential mechanisms on AR. The findings will provide implications to further understand the relationship of greenness exposure and AR in children. It would also hint for city planning specialists in perspective of public health promotion.

2. Methods

2.1. Study design and subjects

A multi-center cross-sectional study was carried out from 2019 to 2020 in 7 cities, including 2 eastern cities (Shanghai and Nanjing), 3 mid-southern cities (Wuhan, Changsha and Chongqing) and 2 northern cities (Urumqi and Taiyuan), as the second phase of the China, Children, Homes and Health (CCHH) study (Lu et al., 2022). A questionnaire survey was performed in the study as described in previous publications (Chen et al., 2022). Briefly, a multistage cluster sampling method was used to select the surveyed kindergartens in these cities (more detailed information of the sampling method can be found in previous paper (Cai et al., 2019)) and we invited all children in these kindergartens to participate in the study. All questionnaires were handed out to children's parents or guardians through children's teachers. Parents or guardians answered the questionnaire on children's demographic characteristics, indoor environment, meteorological factors and AR symptoms. A total of 52,812 children were invited to participate in the survey, and the response rate was 88.05% (n = 46,502). Among them, 40,486 children were 3–6 years old. Finally, 36,867 children aged 3–6 years old who had complete information on covariates were included in the analyses (Fig. 1) (see Fig. 2).

2.2. Ethics statements

The study was approved by the Institutional Review Board of School of Public Health, Fudan University (IRB00002408&FWA00002399, IRB#2019-09-0778). Children's parents or guardians signed informed consents.

2.3. Questionnaire and health information

The core questions in the International Study of Asthma and Allergies in Childhood (ISAAC) (Asher et al., 2006) were adopted to obtain information on current AR symptoms. Current AR symptoms were defined by answering "Yes" on the following question: "Has the child ever had symptoms of sneezing, a runny or a blocked nose without a cold or flu during past 12 months?". The sensitivity and specificity for this item were 67% and 63%, respectively when compared with a gold standard of specialty-trained physician-diagnosed AR (Kim et al., 2012). The questionnaire was tested in a pilot study of 100 children in Chongqing in April 2010 before CCHH was carried out, and thereafter adjustments were made to enhance its readability (Zhang et al., 2013). Therefore, we believe the questionnaire data in this study is valid for analysis. Additionally, we adopted the description of disease symptoms rather than disease labels in this study (Asher et al., 2006). More details of the questionnaire could be seen in the previous study (Chen et al., 2022).

2.4. Exposure assessment

2.4.1. Assessment of exposure to residential greenness

We used NDVI to assess participants' exposure to residential surrounding greenness, which is a common indicator of green vegetation density ranging from −1 to 1 (Tucker, 1979). Higher values of NDVI represent higher density of green vegetation. Values close to zero correspond to bare surfaces or buildings and negative values of NDVI indicate water or snow. In our study, we omitted the negative NDVI values within buffers because only positive values contributed exposure to greenness. The original NDVI data of our study was extracted from the Terra Moderate Resolution Imaging Spectroradiometer (MODIS) Vegetation Indices (MOD13Q1) (https://ladsweb.modaps.eosdis.nasa) at a spatial resolution of 250m × 250 m and a temporal resolution of 16 day.

The cross-sectional study was performed between 2019 and 2020, and we initially retrieved 69 NDVI images for each city from January 01,

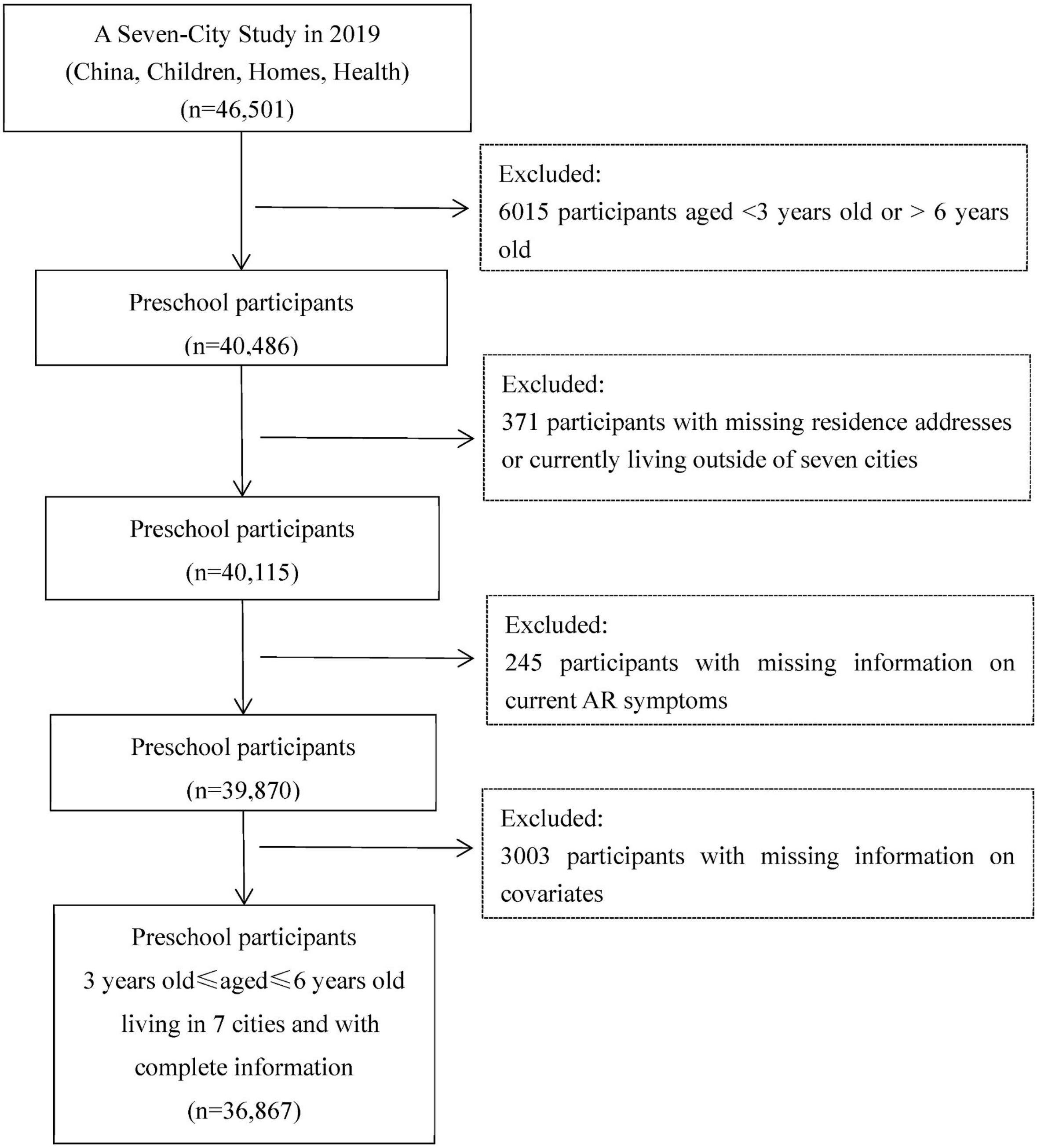

Fig. 1. Flow chart of the study subjects.

2018 to December 31, 2020 (but not all the images were applied for each participant). After geocoding the children's residence addresses in the WGS-84 coordinate system, we created circular buffers of 1000 m radius around each participant's residential address and averaged the NDVI values across the buffer to represent residential greenness exposure level ($NDVI_{1000m}$). This 1000 m buffer size was selected in main analysis based on several considerations: (1) the medium distance between children's residence and kindergartens was around 1101.6 m (the mean distance was 1823.4 m; the IQR was 434.05 m–2469.5 m). The map with labels of both kindergartens and home addresses was shown in Fig. S2. Thus, 1000 m could represent an average radius for children's home-kindergarten activities. (2) According to the handbook "Exposure Factors Handbook of Chinese Population (Children 0–5 years)", the average daily cumulative walking time for children aged 3–6 years is approximately 20 min (Wang and Duan, 2016), and their mean walking speed is about 0.99 m/s (Wang et al., 2023). Therefore, we estimated the children's daily walking distance was around 1.2 km, very close to 1 km (3) a recent systematic review suggested that larger buffer sizes may predict physical health better than smaller ones (Browning and Lee, 2017).

The questionnaire dates varied among participants. Temporally, we calculated the average $NDVI_{1000m}$ values in the 12 months preceding the questionnaire date for each child, the same time window as their current AR symptoms. This value represented their current residential greenness exposure level.

Moreover, based on the distribution of distances between homes and kindergartens, we observed that over 80% of children resided within 4 km of their homes. To cover their farthest activity area, we also assessed greenness exposure within 4000 m buffers around children's addresses in the same time window.

2.4.2. Assessment of greenness composition and configuration

We characterized the greenness composition and configuration surrounding children's residences using Finer Resolution Observation and Monitoring of Global Land Cover (FROM-GLC) at a 10 m × 10 m spatial resolution in 2017, which was the most recent year with publicly available data at the highest spatial resolution. The map has an overall

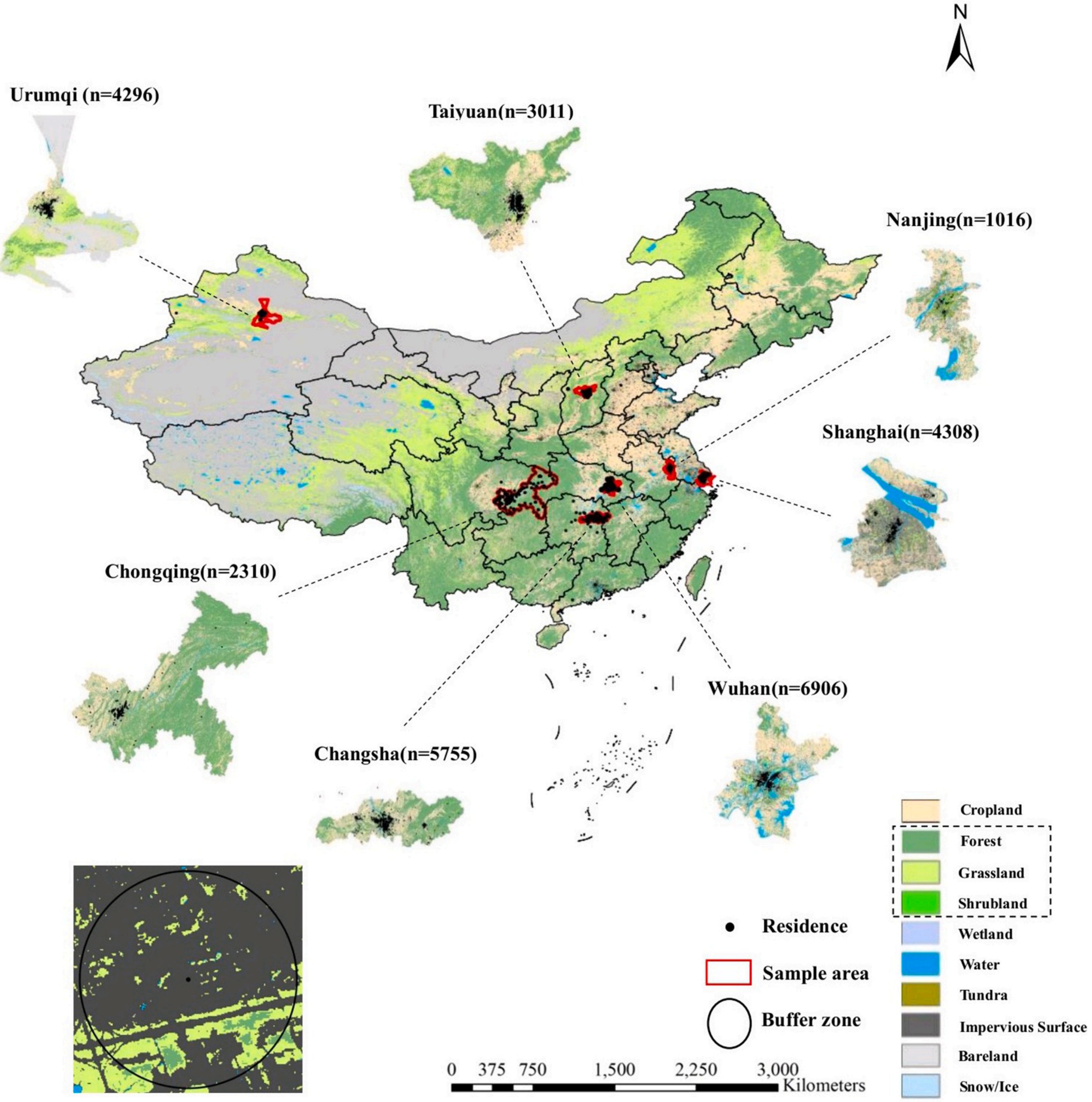

Fig. 2. Land cover map for different vegetation types with study subjects labeled in each of the 7 cities.
Note: In the left bottom corner, a participant's residence address point (the circle center in black) is displayed with a 1000 m radius buffer to show the size of the buffer area relative to the address.

accuracy of 72.76% (Gong et al., 2019). Land covers in the FROM-GLC were classified into ten classes: cropland, forest, grassland, shrubland, wetland, water body, tundra, impervious area, bare land and snow and ice. We considered forest, grassland and shrubland as 3 main vegetation types in the main analyses, excluding the cropland, as it rarely existed within the buffers surrounding the children in our study (Table S11). The results of analyses on the cropland can be found in Supplementary Materials (Table S12). To quantify the configuration characteristics in each vegetation type and in the total green space, six landscape pattern metrics were applied: percentage of landscape (PLAND), mean patch area (AREA_MN), patch density (PD), patch cohesion index (COHESION), aggregation index (AI), and area-weighted mean complexity of the shape (SHAPE_AM) (McGarigal and Marks, 1995). They were calculated in 1000 m and 4000 m radius buffers around participants' residences, respectively. Due to very slight variations of these indicators between years (Gong et al., 2019), we applied them as relatively constant data from 2017 till the questionnaire year of 2019. Fragstats 4.2 and QGIS 3.28.1 were used to perform this analysis. More details are provided in the Supplementary materials (Table S1).

2.4.3. *Assessment of exposure to ambient air pollution*

Concentrations of ambient PM_1, $PM_{2.5}$, and PM_{10} were obtained from the open-access China High Air Pollutants (CHAP) datasets (available at https://weijing-rs.github.io/product.html), which is a long-term, seamless, high-resolution and high-quality datasets of ground-level air pollutants for China. Detailed information on modeling methodology was shown in previous literature (Wei et al., 2019, 2021a, 2021b). Briefly, daily $PM_1/PM_{2.5}/PM_{10}$ concentrations at a 1 km × 1 km spatial resolution was obtained in the prediction model. The model was constructed by integrating ground-monitored $PM_1/PM_{2.5}/PM_{10}$ Data (PM_1 from the China Atmosphere Watch Network (CAWNET) of the China Meteorological Administration (CMA), $PM_{2.5}$ and PM_{10} from the China's National Environmental Monitoring Center (CNEMC)), multi-angle implementation of atmospheric correction aerosol optical depth (MAIAC AOD) derived from the National Aeronautics and Space Administration's (NASA) Terra and Aqua MODIS C6 MAIAC Level (L) 2 swath aerosol products (MCD19A2), meteorological data from the ERA-interim atmospheric reanalysis products, MEIC Emission Data from the multi-resolution emission inventory for China, and other auxiliary data such as land cover, topography, traffic, and population. All selected independent variables with potential effects on $PM_1/PM_{2.5}/PM_{10}$ estimations were input to the Space-Time Extra-Trees (STET) model. This new space-time extremely randomized trees model incorporated spatial and temporal information into the original extremely randomized trees (ERT) model consisting of hundreds to thousands of decision trees that can be used for addressing regression and classification issues. Cross-validation coefficients of determination (CV-R^2) were respectively 0.83, 0.92 and 0.90 for PM_1, $PM_{2.5}$, and PM_{10}, and root-mean-square errors (RMSE) were 9.5 $\mu g/m^3$, 10.76 $\mu g/m^3$, 21.12 $\mu g/m^3$ for PM_1, $PM_{2.5}$, and PM_{10}, respectively, suggesting high qualities for these datasets. The daily mean concentrations of PM_1, $PM_{2.5}$, and PM_{10} were assigned to every residence address, and then we calculated each child's average exposure to ambient air pollution within the past 12 months preceding the questionnaire dates, the same averaging time span with greenness exposure and health outcomes.

2.5. *Covariates*

Data on covariates was collected through questionnaire and in public database. Covariates which were constant across years such as children's sex, sibship, duration of exclusive breastfeeding, residential location, parental history of allergies (any positive report on either parent's history of asthma, allergic rhinitis or eczema) were obtained through questionnaire. Other covariates which may vary with years were collected in the last 12 months including municipal per capita income (1000RMB annual per capita, from China Statistical Yearbook, https://www.yearbookchina.com/), environmental tobacco smoke (ETS), home redecoration and home dampness (any positive report on visible mold, water stains, water leakage, or condensation on the floor, walls or ceiling, or any positive report on damp clothes and damp bedding) and municipal daily averages of temperature and relative humidity (from the China Metrological Data website, http://data.cma.cn). Moreover, we recorded the questionnaire date, and transformed it into a covariate named questionnaire survey season in the subsequent analysis.

2.6. *Statistical analysis*

Demographic characteristics, living environment, meteorological factors and exposure to green space were described in the total subjects and in two subgroups with and without current AR, respectively. T-test and chi-square test were applied to compare the differences between two groups for continuous and categorical variables, respectively. Spearman correlations between PMs, greenness, and greenness configuration and configuration were analyzed.

Considering the hierarchical structure of our data (kindergarten-individual), we adopted a two-level logistic regression model with kindergarten as a random intercept after examining the variance partition and composition of the multilevel logistic model (Table S9). Then, we applied three two-level logistic regression models to estimate the association between current AR symptoms and total greenness and its composition and configuration, including NDVI, PLAND, AREA_MN, SHAPE_AM, AI, COHESION and PD, respectively: (1) model 1: crude model without any adjustment; (2) model 2: model 1 additionally adjusted for age, gender, income per capita, residential area, and questionnaire survey season; (3) model 3 (main model): model 2 additionally adjusted for sibship, duration of exclusive breastfeeding, and parental history of allergies, as well as living environment variables including ETS, mold/dampness, decoration, relative temperature, and humidity in the past 12 months. We selected these covariates on the basis of their confounding effects on the associations of greenness and its composition and configuration with AR symptoms or a change in effect estimate of more than 10% (Vincent et al., 2014). We used generalized variance inflation factors (GVIFs) to quantify multicollinearity between covariates and exposure variables by the use of "car" package in R (Fox and Monette, 1992). The effect estimates were reported as odds ratios (ORs) with a 95% confidence interval (95% CI) per IQR increase of explanatory variables. Additionally, we performed Generalized Additive Mixed Models (GAMM) with kindergarten as a random-effect intercept to test the nonlinearity of the relationships between each greenness related variable and current AR symptoms (Wahba, 1983). We didn't discover the associations deviate from linearity. The main analysis was on current AR symptoms in association with greenness or its composition or configuration within 1000 m buffers around participants' residence addresses, since we believed that a radius of 1000 m could represent an average radius for children's home-kindergarten activities, and the median distance between children' addresses and kindergartens was approximately 1000 m (Fig. S2).

Furthermore, we investigated the mediation effects because we assumed causal relations between greenness (NDVI) and its composition and configuration and current AR symptoms through air pollution. We specified PM_1, $PM_{2.5}$ and PM_{10} as potential mediators. The mediation analyses were conducted separately to test whether it could be the mechanism underlying the associations between greenness (NDVI) and its composition and configuration and AR symptoms. Each mediation analysis model with kindergarten as a random-effect intercept controlled for the same covariates as illustrated above and we estimated the total effect, the direct effect, the mediated effect, and the mediation proportion respectively.

To examine the robustness of the results, we performed sensitivity analysis: (1) the association between greenness exposure and AR symptoms were examined by additionally adjusting for co-exposure to NDVI and each of ambient PM_1, $PM_{2.5}$, and PM_{10}, respectively, in the two-level logistic regression models, and the absolute Spearman Correlation coefficients between each exposure and adjusting variable were less than 0.7; (2) the associations between greenness exposure and its composition and configuration within 1000 m buffers and AR symptoms were examined in each city, and the multilevel logistic regression models with the city as the third level random-effect intercept (individual-kindergarten-city) were additionally performed, which could account for the city clustering of AR (Wu et al., 2020; Zhou et al., 2023); (2) the exposure to greenness and its composition and configuration within 1000 m buffers were replaced by their assessments within 4000 m buffers around participants' addresses, and the same co-exposure to NDVI and ambient PMs were adjusted for in the two-level logistic regression model; (3) subgroup analysis stratified by age, sex, singleton, duration of exclusive breastfeeding, parental history of allergies, ETS, income per capita, residence area, and questionnaire survey season, to evaluate the relationships between current AR symptoms and AI_{forest}, $COHESION_{forest}$, PD_{total}, and PD_{grass} in different populations. Additionally, we examined whether these variables modified the association of interest by introducing separate interaction terms between them and AI_{forest}, $COHESION_{forest}$, PD_{total}, and PD_{grass}. (4) similar regression models were performed in a subgroup of preschool children who had never changed their residence addresses.

The "lme4" and "mediation" packages in R were applied for the multilevel logistic regression analysis and mediation analysis. In all analyses, p values less than 0.05 (two-tailed) were considered statistically significant if not specifically stated. All statistical analysis were performed using R 4.1.2.

3. Results

3.1. Descriptive statistics

Children's demographic characteristics, living environmental, meteorological factors and questionnaire survey season are summarized in Table 1. In total, 36,867 participants were recruited. The average age was 4.8 ± 1.0 years, 52.0% of the participants were boys and 57.4% of the participants were non-sibships. A total of 12,190 children had self-reported current allergic rhinitis. The study population mostly resided in urban areas (79.2%), and 62.8% of them had more than 6 months of exclusive breastfeeding. Over a third had history of parental allergies (38.4%), and 34.3% and 12.2% of participants reported to have exposure to environmental tobacco smoke and home dampness, respectively. Around 9.8% of participants redecorated their homes in the past 12 months.

3.2. Exposure assessment

The mean area percentage of total green space ($PLAND_{total}$) within 1000 m buffers around the participants' addresses was 21.22%. It comprised mostly of grass (16.69%) and forest (4.45%) and less of shrub (0.08%). The patches of grass and forest were more aggregated (AI_{grass}: 68.70 and AI_{forest}: 56.95) and connected ($COHESION_{grass}$: 87.84 and $COHESION_{forest}$: 71.46) than those of shrub cover (AI_{shrub} 18.85 and $COHESION_{shrub}$: 17.27), and the shapes of grass patches ($SHAPE\_AM_{grass}$: 3.18) and forest patches ($SHAPE\_AM_{forest}$: 1.97) were more complicated than that of shrub patches ($SHAPE\_AM_{shrub:}$ 1.05). Besides, patch density of grass (PD_{grass}: 90.23) was the highest among three types of vegetation (PD_{forest}: 30.35 and PD_{shrub}: 4.81). The mean NDVI was 0.252 (Table S2). Cropland, sometimes considered as another green space type, seldom existed within 1000 m buffers around the participants' addresses (Table S11).

Between subjects with and without current AR symptoms, there were significant differences of exposure to greenness and its composition and configuration (Table 2). Individuals without current AR symptoms showed significantly higher levels of NDVI, as well as increased area percentage, mean patch area, and shape complexity in total green space, forest and grass vegetation types. Moreover, they exhibited higher levels of aggregation and connectivity, either in the total green space or in the forest vegetation type. However, these differences were almost non-significant in the shrub vegetation type.

For PMs, the daily averages of PM_1, $PM_{2.5}$ and PM_{10} during the past 12 months were 25.3 $\mu g/m^3$, 45.3 $\mu g/m^3$ and 77.5 $\mu g/m^3$, respectively. The detailed distributions of green space and ambient air pollutants (PM_1, $PM_{2.5}$, PM_{10}) in quartiles and range in the whole subjects are shown in Table S2.

3.3. Associations of greenness and its composition and configuration with AR symptoms

The associations between current AR symptoms and NDVI, green space composition and configuration around residence addresses are presented in Table 3. In the total green space, the results showed that the

Table 1

Demographic characteristics, living environment, meteorological factors and questionnaire survey season in the study participants.

Categories	Variables	Total (n = 36,867)	With current AR symptoms (n = 12,190)	Without current AR symptoms (n = 24,677)	p [c]
Demographic characteristics	Age, mean (SD)	4.8 (1.0)	4.8 (1.0)	4.8 (1.0)	0.189
	Male, n (%)	19,156 (52.0)	6752 (55.4)	12,404 (50.3)	<0.001
	No sibships, n (%)	21,169 (57.4)	7793 (63.9)	13,376 (54.2)	<0.001
	Urban, n (%)	29,209 (79.2)	10,002 (82.1)	19,207 (77.8)	<0.001
	Exclusive breastfeeding duration>6 months, n (%)	23,166 (62.8)	7340 (60.2)	15,826 (64.1)	<0.001
	History of parental allergy, n (%)	14,146 (38.4)	6833 (56.1)	7313 (29.6)	<0.001
	Income per capita [a], mean (SD,1000RMB)	32.79 (15.01)	34.61 (16.34)	31.89 (14.22)	<0.001
Living Environment [a]	Environmental tobacco smoke, n (%)	12,637 (34.3)	4491 (36.8)	8146 (33.0)	<0.001
	Home dampness [b], n (%)	4509 (12.2)	1905 (15.6)	2604 (10.6)	<0.001
	Home redecoration, n (%)	3610 (9.8)	1402 (11.5)	2208 (8.9)	<0.001
Meteorological factors [a]	Relative humidity, mean (SD, %)	71.6 (9.2)	72.6 (8.5)	71.0 (9.5)	<0.001
	Temperature, mean (SD, °C)	14.7 (5.5)	15.1 (5.1)	14.5 (5.7)	<0.001
Questionnaire survey season					<0.001
	Spring	3928 (10.7)	717 (5.9)	3211 (13.0)	
	Summer	4072 (11.0)	1044 (8.6)	3028 (12.3)	
	Autumn	20,821 (56.5)	7559 (62.0)	13,262 (53.7)	
	Winter	8046 (21.8)	2870 (23.5)	5176 (21.0)	

Notes: [a] These variables were assessed during past 12 months; [b] Home dampness: positive report on any of the s signs of home dampness in children's bedroom: mold, water stains, damp clothes and bedding, water leakage, condensation in the window and moldy smell. [c] Comparisons between subgroups with and without current AR symptoms.

Table 2

Comparisons of exposure to greenness and greenness composition and configuration within 1000 m buffers in the total subjects and in two subgroups with and without current AR symptoms, respectively.

Vegetation types	Exposure variables	Total (n = 36,867)	With current AR Symptoms (n = 12,190)	Without current AR symptoms (n = 24,677)	p [c]
Exposure to greenness, NDVI [a]		0.252 (0.077)	0.254 (0.068)	0.254 (0.082)	<0.001
Greenness composition and configuration [b]					
Total green space	**PLAND$_{\text{total}}$**, percentage of total green space cover, %	21.22 (12.94)	19.71 (12.28)	21.80 (13.19)	<0.001
	AREA_MN$_{\text{total}}$, mean patch area of total green space, hm^2	0.32 (0.51)	0.30 (0.53)	0.33 (0.50)	<0.001
	AI$_{\text{total}}$, Aggregation Index of total green space patches	74.86 (9.07)	74.01 (8.90)	75.28 (9.13)	<0.001
	COHESION$_{\text{total}}$, Patch Cohesion Index of total green space	90.71 (7.11)	90.19 (7.12)	90.97 (7.09)	<0.001
	SHAPE_AM$_{\text{total}}$, Area-weighted mean complexity of the shape of total green space patches	3.40 (1.64)	3.30 (1.58)	3.45 (1.66)	<0.001
	PD$_{\text{total}}$, Patch Density of total green space, n/100 hm^2	76.36 (23.85)	76.25 (23.79)	76.42 (23.88)	0.523
Forest	**PLAND$_{\text{forest}}$**, percentage of forest cover, %	4.45 (7.17)	3.74 (6.22)	4.80 (7.57)	<0.001
	AREA_MN$_{\text{forest}}$, mean patch area of forest, hm^2	0.15 (0.55)	0.12 (0.51)	0.16 (0.56)	<0.001
	AI$_{\text{forest}}$, Aggregation Index of forest patches	56.95 (18.73)	54.16 (18.51)	58.33 (18.68)	<0.001
	COHESION$_{\text{forest}}$, Patch Cohesion Index of forest	71.46 (19.72)	69.09 (19.89)	72.63 (19.52)	<0.001
	SHAPE_AM$_{\text{forest}}$, Area-weighted mean complexity of the shape of forest patches	1.97 (0.87)	1.89 (0.82)	2.00 (0.89)	<0.001
	PD$_{\text{forest}}$, Patch Density of forest, n/100 hm^2	30.35 (24.65)	29.82 (24.18)	30.62 (24.88)	0.004
Grass	**PLAND$_{\text{grass}}$**, percentage of grass cover, %	16.69 (9.75)	15.99 (9.26)	17.04 (9.97)	<0.001
	AREA_MN$_{\text{grass}}$, mean patch area of grass, hm^2	0.20 (0.19)	0.19 (0.16)	0.21 (0.20)	<0.001
	AI$_{\text{grass}}$, Aggregation Index of grass patches	68.70 (10.56)	68.57 (9.67)	68.76 (10.98)	0.105
	COHESION$_{\text{grass}}$, Patch Cohesion Index of grass	87.84 (9.64)	87.80 (8.65)	87.85 (10.09)	0.633
	SHAPE_AM$_{\text{grass}}$, Area-weighted mean complexity of the shape of grass patches	3.18 (1.39)	3.10 (1.31)	3.21 (1.43)	<0.001
	PD$_{\text{grass}}$, Patch Density of grass, n/100 hm^2	90.23 (34.94)	89.23 (34.36)	90.73 (35.21)	<0.001
Shrub	**PLAND$_{\text{shrub}}$**, percentage of shrub cover, %	0.08 (0.15)	0.08 (0.12)	0.08 (0.16)	0.324
	AREA_MN$_{\text{shrub}}$, mean patch area of shrub, hm^2	0.01 (0.01)	0.01 (0.01)	0.01 (0.01)	0.431
	AI$_{\text{shrub}}$, Aggregation Index of shrub patches	18.85 (18.24)	18.66 (17.35)	18.92 (18.56)	0.460
	COHESION$_{\text{shrub}}$, Patch Cohesion Index of shrub	17.27 (14.47)	17.20 (14.01)	17.30 (14.64)	0.699
	SHAPE_AM$_{\text{shrub}}$, Area-weighted mean complexity of the shape of shrub patches	1.05 (0.11)	1.05 (0.10)	1.05 (0.11)	0.049
	PD$_{\text{shrub}}$, Patch Density of shrub, n/100 hm^2	4.81 (5.63)	4.83 (5.35)	4.80 (5.73)	0.779

Notes: hm^2: square hectare.

[a] Refer to the average exposure to greenness during the past 12 months. The original NDVI data was at a spatial resolution of 250m × 250 m and a temporal resolution of 16 days.

[b] Characteristics of greenness composition and configuration were assessed from 10-m resolution global land cover in 2017 (FROM_GLC10_2017) and resumed to be constant till our survey in 2019.

[c] Comparisons between subjects with and without current AR.

patch density of total green space (PD$_{\text{total}}$) (OR: 1.05, 95%CI: 1.01–1.09) was significantly associated with higher prevalence of current AR symptoms after adjustment for covariates in the main model (Model 3).

When the above regression analyses were performed in each of the 3 vegetation types, the significant associations were observed in forest and grass (Table 3). The observed associations of AI$_{\text{forest}}$ and COHESION$_{\text{forest}}$ with AR symptoms were consistent in both crude models, parsimonious model, fully adjusted models, and even additional adjustments for PM$_1$, PM$_{2.5}$, PM$_{10}$, and NDVI$_{\text{1000m}}$. An IQR increase in AI$_{\text{forest}}$ and COHESION$_{\text{forest}}$ was associated with 8% (95%CI: 3%, 12%) and 7% (95%CI: 2%, 11%) lower odds for current AR symptoms in the main model, respectively. However, the patch density of grass (PD$_{\text{grass}}$) (OR: 1.06, 95%CI: 1.01–1.10) was significantly related to a higher prevalence of current AR symptoms in the main model.

The above regression analyses were further adjusted for PM$_{1.0}$, PM$_{2.5}$, PM$_{10}$, and NDVI, individually (Table 3). The aforementioned significant associations still remained significant, despite of being attenuated slightly after adjustment in some cases.

3.4. Mediation analyses

We explored whether PMs mediated relationships between greenness composition and configuration and current AR symptoms. Significant mediation effects by ambient PMs (PM$_{1.0}$ and PM$_{10}$) in the associations of AI$_{\text{forest}}$, COHESION$_{\text{forest}}$, PD$_{\text{total}}$, and PD$_{\text{grass}}$ with current AR symptoms were observed, while PM$_{2.5}$ only mediated the associations of AI$_{\text{forest}}$ with current AR (Table 4). The negative indirect effects via PMs on the associations between current AR symptoms and two configuration variables of forest showed that AI$_{\text{forest}}$ and COHESION$_{\text{forest}}$ reduced the concentrations of PMs through certain mechanism, while the directions of the indirect effects via PMs on the associations between current AR and patch density of two types of green space (PD$_{\text{total}}$ and PD$_{\text{grass}}$) were positive, indicating that fragmentation of these types of green space would aggravate air pollution.

Mediation analysis models showed that the indirect effects via PMs for many other indicators of greenness composition and configuration were significant, indicating their influence on the concentrations of PMs; however, their direct effects were not significant (Table S5).

3.5. Sensitivity analyses

The aforementioned associations of AI$_{\text{forest}}$, COHESION$_{\text{forest}}$, PD$_{\text{total}}$, and PD$_{\text{grass}}$ with current AR symptoms persisted among preschool children who have never changed their residence addresses since birth too (Table S4). These associations remained significant or marginally significant in the subgroups of younger (<5 years) and older children (≥5years), boys and girls, singletons or not, with longer (≥6months) or shorter (<6months) exclusive breastfeeding, with or without a parental history of allergies, with or without environmental tobacco smoking exposure during past 12 months, with higher (≥27.07 (1000RMB)) or lower (<27.07 (1000RMB)) income per capita, and residence in urban or suburban-rural area, respectively (Table S3). However, of particular note was that age, exclusive breastfeed duration, and questionnaire survey season were the effect modifiers for the associations between current AR symptoms and greenness composition and configuration (*P*-interaction<0.05). The positive associations between current AR symptoms and PD$_{\text{total}}$ and PD$_{\text{grass}}$ only existed in children under the age of five. The negative associations between current AR symptoms and

Table 3
Associations between current AR symptoms and greenness and its composition and configuration within 1000 m buffers.

Vegetation types	Variables	Model 1	Model 2	Model 3	Model 3 +PM$_1$	Model 3 +PM$_{2.5}$	Model 3 +PM$_{10}$	Model 3 +NDVI
NDVI		0.99 (0.93,1.04)	1.04 (0.98,1.10)	0.97 (0.91,1.02)	0.99 (0.93,1.05)	0.97 (0.92,1.03)	0.98 (0.92,1.04)	–
Greenness composition and configuration								
Total green space	PLAND$_{total}$	0.97 (0.93,1.01)	0.99 (0.95,1.04)	1.00 (0.95,1.04)	1.00 (0.96,1.05)	1.00 (0.96,1.04)	1.00 (0.96,1.05)	1.02 (0.96,1.07)
	AREA_MN$_{total}$	1.00 (0.99,1.01)	1.00 (0.99,1.01)	1.00 (0.99,1.02)	1.01 (0.99,1.02)	1.00 (0.99,1.02)	1.01 (0.99,1.02)	1.01 (0.99,1.02)
	AI$_{total}$	**0.96 (0.92,0.99)**	0.99 (0.95,1.03)	0.99 (0.95,1.03)	1.00 (0.95,1.04)	0.99 (0.95,1.03)	0.99 (0.95,1.03)	1.00 (0.96,1.05)
	COHESION$_{total}$	0.98 (0.95,1.01)	1.00 (0.97,1.03)	1.01 (0.97,1.04)	1.01 (0.98,1.04)	1.01 (0.97,1.04)	1.01 (0.97,1.04)	1.02 (0.98,1.05)
	SHAPE_AM$_{total}$	0.98 (0.95,1.01)	0.99 (0.96,1.02)	0.99 (0.96,1.02)	0.99 (0.97,1.02)	0.99 (0.96,1.03)	0.99 (0.96,1.02)	1.00 (0.97,1.03)
	PD$_{total}$	1.03 (0.99,1.07)	1.02 (0.98,1.05)	**1.05 (1.01,1.09)**	**1.05 (1.01,1.09)**	**1.05 (1.01,1.09)**	**1.05 (1.01,1.09)**	**1.05 (1.01,1.09)**
Forest	PLAND$_{forest}$	0.99 (0.97,1.01)	1.00 (0.98,1.02)	1.00 (0.98,1.02)	1.00 (0.98,1.02)	1.00 (0.98,1.02)	1.00 (0.98,1.02)	1.01 (0.98,1.03)
	AREA_MN$_{forest}$	1.00 (0.99,1.01)	1.00 (0.99,1.01)	1.00 (0.99,1.01)	1.00 (0.99,1.01)	1.00 (0.99,1.01)	1.00 (0.99,1.01)	1.00 (0.99,1.01)
	AI$_{forest}$	**0.89 (0.85,0.94)**	**0.92 (0.88,0.96)**	**0.92 (0.88,0.97)**	**0.94 (0.89,0.98)**	**0.93 (0.88,0.97)**	**0.93 (0.89,0.98)**	**0.93 (0.88,0.97)**
	COHESION$_{forest}$	**0.91 (0.87,0.95)**	**0.93 (0.89,0.98)**	**0.93 (0.89,0.98)**	**0.94 (0.90,0.98)**	**0.93 (0.89,0.98)**	**0.94 (0.90,0.98)**	**0.93 (0.89,0.98)**
	SHAPE_AM$_{forest}$	**0.96 (0.93,0.99)**	0.98 (0.95,1.01)	0.97 (0.94,1.00)	0.98 (0.95,1.01)	0.97 (0.94,1.00)	0.97 (0.94,1.00)	0.97 (0.94,1.01)
	PD$_{forest}$	0.98 (0.95,1.02)	1.00 (0.96,1.04)	1.00 (0.96,1.04)	1.00 (0.96,1.04)	1.01 (0.97,1.05)	1.00 (0.96,1.04)	1.01 (0.97,1.05)
Grass	PLAND$_{grass}$	0.97 (0.93,1.01)	0.99 (0.95,1.03)	1.00 (0.96,1.04)	1.00 (0.96,1.04)	1.00 (0.96,1.04)	1.00 (0.96,1.04)	1.01 (0.96,1.05)
	AREA_MN$_{grass}$	0.98 (0.96,1.00)	0.99 (0.97,1.01)	0.99 (0.97,1.01)	0.99 (0.97,1.01)	0.99 (0.97,1.01)	0.99 (0.97,1.01)	0.99 (0.97,1.01)
	AI$_{grass}$	0.99 (0.96,1.03)	1.00 (0.97,1.04)	1.02 (0.98,1.05)	1.01 (0.98,1.05)	1.01 (0.98,1.05)	1.01 (0.98,1.05)	1.02 (0.98,1.05)
	COHESION$_{grass}$	1.00 (0.97,1.03)	1.01 (0.98,1.03)	1.02 (0.99,1.05)	1.01 (0.99,1.04)	1.01 (0.99,1.04)	1.01 (0.99,1.04)	1.02 (0.99,1.05)
	SHAPE_AM$_{grass}$	0.97 (0.95,1.00)	0.98 (0.95,1.01)	0.98 (0.95,1.01)	0.98 (0.95,1.01)	0.98 (0.95,1.01)	0.98 (0.95,1.01)	0.98 (0.96,1.01)
	PD$_{grass}$	1.02 (0.98,1.06)	1.02 (0.98,1.06)	**1.06 (1.01,1.10)**	**1.05 (1.01,1.09)**	**1.06 (1.02,1.10)**	**1.05 (1.01,1.10)**	**1.06 (1.02,1.10)**
Shrub	PLAND$_{shrub}$	1.00 (0.98,1.02)	0.99 (0.97,1.02)	0.99 (0.96,1.02)	0.99 (0.97,1.02)	0.99 (0.96,1.02)	0.99 (0.96,1.02)	0.99 (0.96,1.02)
	AREA_MN$_{shrub}$	0.98 (0.94,1.02)	0.98 (0.94,1.02)	0.99 (0.95,1.03)	1.00 (0.96,1.04)	0.99 (0.95,1.03)	0.99 (0.95,1.03)	0.99 (0.95,1.04)
	AI$_{shrub}$	0.99 (0.95,1.03)	0.99 (0.95,1.02)	1.00 (0.96,1.04)	1.01 (0.96,1.05)	1.00 (0.96,1.04)	1.00 (0.96,1.04)	1.00 (0.96,1.04)
	COHESION$_{shrub}$	0.97 (0.90,1.05)	0.97 (0.90,1.05)	0.98 (0.90,1.07)	0.99 (0.91,1.08)	0.98 (0.90,1.07)	0.98 (0.90,1.07)	0.98 (0.90,1.07)
	SHAPE_AM$_{shrub}$	0.98 (0.95,1.00)	0.98 (0.95,1.01)	0.98 (0.95,1.01)	0.98 (0.95,1.01)	0.98 (0.95,1.01)	0.98 (0.95,1.01)	0.98 (0.95,1.01)
	PD$_{shrub}$	1.01 (0.97,1.05)	1.00 (0.96,1.04)	0.98 (0.94,1.03)	0.99 (0.95,1.03)	0.99 (0.94,1.03)	0.99 (0.94,1.03)	0.98 (0.94,1.03)

Notes: All ORs were estimated per IQR increase of exposure. Bold texts of ORs(95%CI) were statistically significant.
Model 1: crude model without any adjustment.
Model 2: adjusted for age, gender, income per capita, residential area, and questionnaire survey season.
Model 3: main model. Model 2 additionally adjusted for sibship, duration of exclusive breastfeeding, and parental history of allergies, as well as living environment variables including ETS, mold/dampness, decoration, relative temperature, and humidity in the past 12 months.
The Model 3 + PM$_{1.0}$, Model 3 + PM$_{2.5}$, Model 3 + PM$_{10}$, and Model 3+NDVI additionally adjusted for PM$_{1.0}$, PM$_{2.5}$, PM$_{10}$, and NDVI in Model 3, respectively.
Abbreviations: PLAND, percentage of the area of some type of green space; AREA_MN, mean patch area of some type of green space; AI, Aggregation Index of some type of green space patches; COHESION, Patch Cohesion Index of some type of green space; SHAPE_AM, Area-weighted mean complexity of the shape of some type of green space patches; PD, Patch Density of some type of green space.

Table 4
Mediating effects of particulate matters on the association between current AR symptoms and AI$_{forest}$, COHESION$_{forest}$, PD$_{total,}$ and PD$_{grass}$ within 1000 m buffers.

Predict variable	Mediator	Direct effect OR (95%CI)	Indirect effect OR (95%CI)	Total effect OR (95%CI)	Proportion % (95%CI)
AI$_{forest}$	PM$_1$	**0.987(0.978,0.996)**	**0.999(0.998,0.999)**	**0.986(0.977,0.995)**	**7.22(3.20,16.88)**
	PM$_{2.5}$	**0.984(0.974,0.995)**	**0.999(0.999,0.999)**	**0.984(0.974,0.995)**	**2.67(0.18,11.17)**
	PM$_{10}$	**0.987(0.976,0.996)**	**0.999(0.998,0.999)**	**0.986(0.975,0.994)**	**8.97(3.19,29.32)**
COHESION$_{forest}$	PM$_1$	**0.987(0.976,0.997)**	**0.999(0.999,0.999)**	**0.987(0.976,0.996)**	**5.03(1.97,17.07)**
	PM$_{2.5}$	**0.986(0.977,0.995)**	1.000 (0.999,1.000)	**0.985(0.976,0.994)**	3.02 (-0.20,8.81)
	PM$_{10}$	**0.986(0.977,0.996)**	**0.999(0.999,0.999)**	**0.985(0.976,0.995)**	**5.33(1.76,17.15)**
PD$_{total}$	PM$_1$	**1.008(1.001,1.016)**	**1.001(1.001,1.002)**	**1.010(1.003,1.017)**	**13.76(6.00,45.70)**
	PM$_{2.5}$	**1.009(1.002,1.015)**	1.000 (1.000,1.001)	**1.010(1.002,1.015)**	3.60 (-0.94,22.18)
	PM$_{10}$	**1.010(1.003,1.016)**	**1.001(1.001,1.002)**	**1.011(1.004,1.018)**	**10.53(4.03,34.88)**
PD$_{grass}$	PM$_1$	**1.009(1.001,1.016)**	**1.003(1.002,1.004)**	**1.012(1.004,1.019)**	**24.11(11.70,83.53)**
	PM$_{2.5}$	**1.012(1.005,1.018)**	1.000 (0.999,1.000)	**1.011(1.005,1.017)**	−2.07 (-7.52,0.26)
	PM$_{10}$	**1.010(1.004,1.018)**	**1.002(1.001,1.003)**	**1.012(1.006,1.020)**	**16.26(5.73,32.99)**

Notes: All ORs were estimated per IQR increase of exposure. Bold texts of ORs(95%CI) and mediation proportions were statistically significant. Each mediation analysis model adjusted for children's age, gender, income per capita, residential area, and questionnaire survey season, sibship, duration of exclusive breastfeeding, and parental history of allergies, as well as living environment variables including ETS, mold/dampness, decoration, relative temperature, and humidity in the past 12 months.
Abbreviations: AI$_{forest}$, Aggregation Index of forest patches; COHESION$_{forest}$, Patch Cohesion Index of forest; PD$_{total}$, Patch Density of total green space; PD$_{grass}$, Patch Density of grass.

AI$_{forest}$ and COHESION$_{forest}$ were found in children with exclusive breastfeeding durations longer than 6 months. In cold seasons, the association between COHESION$_{forest}$ and AR remained significantly negative, while COHESION$_{forest}$ was positively associated with the prevalence of AR in warm seasons (Table S3).

Besides, although the results of multilevel logistic regression model with city as the third level random-effect intercept were similar to those of the two-level logistic regression models (Table S7), the associations of AI_{forest} and $COHESION_{forest}$ with current AR symptoms only remained significantly inverse in Wuhan ($n = 9120$) accounting for the largest sample size among seven cities (Table S6). The negative associations of AI_{forest} and $COHESION_{forest}$ with AR persisted within 4000 m buffers (Table S14).

4. Discussion

In this multi-city study, we found forest aggregation and connectivity were negatively associated with the prevalence of AR symptoms, while patch density of total green space and grass land was positively associated with AR symptoms. The robust inverse association of forest configuration was independent of co-exposure to NDVI and ambient particulate matter ($PM_{1.0}$, $PM_{2.5}$, PM_{10}). Mediation analyses found the associations were partly mediated through $PM_{1.0}$, $PM_{2.5}$, and PM_{10}. Age, exclusive breastfeed duration and season were the potential effect modifiers. The associations were heterogeneous across cities.

33.1% of children had AR symptoms in our study (Table 1). The prevalence of AR increased rapidly in many regions (Asher et al., 2006; Bousquet et al., 2008; Katelaris et al., 2012), and the burden of allergic diseases was considerable according to the Global Asthma Network (García-Marcos et al., 2022). In Shanghai, it rose from 13.6% to 23.9% between 2005 and 2011 (Wang et al., 2016). In a 10-city survey (the CCHH Phase I study) in 2010–2012, the prevalence of current AR in children aged 3–6 years old varied from 24.0% to 50.8% (Zhang et al., 2013). On the other hand, when comparing the ISAAC core questions on current AR symptoms with a gold standard of physician-diagnosed AR, the sensitivity and specificity were 67% and 63%, respectively (Kim et al., 2012). This indicated that the prevalence of AR in our study might not accurately reflect the true prevalence of diagnosed AR. Heredity was a risk factor (Westman et al., 2013) and we did observe parents had a higher proportions of self-reported AR than 8 years ago, but it was not sufficient to account for this high prevalence of AR in children. Recently, a study showed there was an obvious increase of positive sensitization (serum IgE) to house dust mite, dog allergen, pollens and Artemisia (the last two in north China) both in children and adults in China from 2008 to 2018 (Wang et al., 2022). Sensitization is the immune basis to have allergic symptoms observed clinically. Climate change (potential increase of the allergenic pollen amounts), environment exposure from indoor and outdoor (i.e. home renovation, exposure to moisture and mold, and exposure to air pollution), and alterations in lifestyle such as lack of natural beneficial contact to stimulate healthy development of immunity were likely to drive the AR development (Zhang and Zhang, 2019). Despite lacking clinically verification in such a large-scale survey, we believed using questionnaire data was applicable for analysis which had actually been validated and widely applied in previous studies (Asher et al., 2006). Additionally, we adopted the description of disease symptoms rather than disease labels in this study (Asher et al., 2006).

Our study focused on a new perspective of greenness exposure by evaluating the greenness composition and configuration, not only the NDVI values. By quantifying the proportions of different vegetation classes, their aggregation, connectivity or fragmentation and their shape complexity, the exposure assessment could present more adequate information of green space morphology which mattered for health (Wang and Tassinary, 2019). NDVI provided evaluation of greenness depending on the visible light (R) and the near-infrared (NIR) light reflected by the vegetative growth (Malamardi et al., 2022), omitting the specific spatial configuration of vegetation. Many previous studies reported the association between NDVI and allergic respiratory diseases, whereas the association was not consistent. GINI/LISA North and PIAMA cohorts showed that exposure to greenness (NDVI) had an inverse association with risk of AR, BAMSE and GINI/LISA South cohorts showed that NDVI had a positive association with AR, and CAPPS and SAGE cohorts showed no significant association (Dzhambov et al., 2021; Fuertes et al., 2016; Huang et al., 2022; Kim et al., 2020; Ruokolainen et al., 2015).

In this study, we analyzed the associations of greenness composition and configuration and NDVI with children's current AR symptoms in the last 12 months. The results showed that the configuration of forest vegetation had pronouncedly negative associations with AR symptoms in preschool children, in particular forest aggregation and cohesion. These robust associations were independent of co-exposure to NDVI and ambient particulate matter ($PM_{1.0}$. $PM_{2.5}$, PM_{10}). Similar findings on the same direction of the association between forest and allergies had been reported. In 2015, a study from Finland and Estonia reported that the cover of forest within 2–5 km from the home was inversely associated with atopic sensitization (Ruokolainen et al., 2015). In 2019, Kim et al. reported that in Korea adults, the significantly inverse association of greenness with the risk of AR existed in participants surrounded with the highest percentage of green space (Kim et al., 2020). In 2021, a cross-sectional study in Alps reported that there were marginally negative associations between school and residential greenness (the percentage of tree cover) and the prevalence of AR symptoms among school children aged 8–12 years old (Dzhambov et al., 2021). Another study in Belgium in 2021 found a protective effect of forest cover for men on pollen allergy symptom (Stas et al., 2021). In 2022, a cross-sectional study in northern cities of China observed that exposure to green space, especially forest, was negatively associated with AR symptoms (Huang et al., 2022). However, evidence from nine European cohorts showed that children living close to a coniferous forest had greater odds of AR (Parmes et al., 2020). A German birth cohort suggested that planting trees in early life residences might increase the risk of AR later in life (Markevych et al., 2020). These inconsistences could be partially due to differences in tree species and their potential sensitization. Different tree species were distributed in different geographical regions (McInnes et al., 2017), however, certain species were sources of harmful BVOC emissions, allergenic pollen, and aerosols, all of which had been proved to be harmful for allergies and respiratory health problems (Gibbs, 2019; Schuler Iv and Montejo, 2019; Wise et al., 2023). Specifically, in Leipzig in Germany, there were 16 allergenic tree genera in streets and green space (Markevych et al., 2020), while in urban streets in China, there were only three highly allergenic tree genera, that is, *Populus*, *Salix*, and *Ailanthus altissima* (Wang et al., 2020; Yao et al., 2023). In the seven cities we studied, other common urban street tree species including *C. camphora*, *S. japonica*, *Ficus microcarpa*, *Fraxinus chinensis*, *L. lucidum*, and others (Wang et al., 2020), just had low or moderate degree of allergenicity according to the existing literature (Yao et al., 2023). Further studies are needed to investigate and provide more explicit understandings on the current findings.

The underlying pathways linking the configuration of forest to AR remain unclear. Several mechanisms may elucidate this finding. That AR could be aggravated by air pollution was a consensus (Chen et al., 2022; Naclerio et al., 2020). Our mediation analyses showed that the inverse associations of AI_{forest} and $COHESION_{forest}$ with AR were partially mediated by air pollution, as measured by PM_1, $PM_{2.5}$, and PM_{10} (Table 4). Additionally, our mediation analyses results suggested that total green space/forest area, mean patch area of total green space/forest, and shape complexity of total green space/forest had negative indirect effects through PMs, indicating that these characteristics contributed to lower concentration of PMs. On the other hand, patch density of total green space/grassland had positive indirect effects via PMs, suggesting that fragmentation of green space/grassland might exacerbate air pollution (Table S5). These findings were consistent with enormous previous research (Cai et al., 2020; Chen et al., 2017b; Lei et al., 2018; Liang et al., 2016; Lin and Chen, 2023; Liu and Shen, 2014; Liu et al., 2022; Lowicki, 2019; Piao et al., 2006; Ren et al., 2022; Wu et al., 2018; Zhan et al., 2022), where the mechanisms were mostly explained by the deposition effects of vegetation leaves (Laurent et al., 2019), changing the trajectory and velocity of ambient PMs' dispersions (Wu et al., 2023), vegetation leaf surface villi retardation and interception, stem adsorption, and stomatal absorption by plants (Chen et al., 2017b; Liang et al., 2016). However, these mechanisms lacked empirical evidence in our study which needed further verification. This warranted cautious interpretation and we noticed the observed indirect effects via PMs might be more linked with the following reasons: (1) the potential competitive land use between green space and sources of PMs might account for the indirect effect. That is, larger green space (positively related to the aggregation, connectivity, mean patch area, and shape complexity of total green space/forest in our study Fig. S1) might contribute to decreasing number of emitting sources (e.g., parking lots), and in turn reduced the air pollution concentrations (Klompmaker et al., 2019). Although this effect was causal, the indirect effect was not due to actual reduction in PMs by vegetation leaves. (2) greenspace and air pollution were most commonly operationalized using geographic variables (NDVI, LUR models), which were both contingent on common contextual factors such as urbanicity, and urban form and design (Dzhambov et al., 2020). To be specific, air pollution concentration was generally higher and greenness was lower in city centers of major cities, while the pollution was produced from sources of PMs far from the local surrounding whose impact couldn't be reduced by local green space (Klompmaker et al., 2019), hence, this strong spatial correlation might lead to indications of mediation by air pollution, although it could be an artifact in reality.

Moreover, a larger and more connected forest possibly offered opportunities for longer stays and a broader range of activities (Kaczynski et al., 2008; Sugiyama et al., 2010), making the utilization of beneficial natural elements more accessible to residents. It could enhance the duration, frequency, and intensity of residents' exposure to green space (Wang and Tassinary, 2024). Connected and aggregated greenspace/park were also reported to be associated with increased physical activity in cities such as Los Angeles, New York, Seattle, San Antonio, and Miami, while fragmented greenspace/park was linked to physical inactivity. Such configuration was proposed to provide a "continuous" natural experience compared to scattered green space, facilitating engagement in "linear" types of physical activities such as walking, biking, and jogging (Wang and Tassinary, 2024). In another American study, forest cover was positively associated with population physical activity as well, as it constituted green infrastructure essential for activity spaces such as parks and trails (Tsai et al., 2016). Meanwhile, increasing evidence suggested that greenness exposure protected from allergic disorders through exposure to microbial diversity (Rook, 2013). By collecting samples from three different countries, Selway et al. suggested that exposure to green space could increase skin and nasal microbial diversity and alter human microbiota composition (Selway et al., 2020). In 2021, LISA cohort study reported that a higher bacterial diversity was associated with lower risk of AR in childhood (Hyytiäinen et al., 2021). Some plant-derived metabolites, such as flavonoids, which possessed several protective health effects, have been found to potentially enhance respiratory health and reduce the occurrence of AR and other allergic conditions in indoor study (Sun et al., 2023; Sun et al., 2022; Zhang et al., 2023a), indicating that similar mechanisms could also be at play in outdoor forest. Extreme temperature would increase the frequency and severity of AR, resulting from the process that heat stress activated heat shock proteins, and then led to both epithelial barrier dysfunction and airway inflammation (Celebi Sozener et al., 2023), but several research found that the configuration of green space affected urban microclimate. Both higher aggregation and connectivity of green space/forest and reduced green space fragmentation contributed to reducing ambient temperature (Kong et al., 2014; Liu and Shen, 2014; Zhang et al., 2023b). Behavioral and psychological factors might also contribute to the negative association of forest configuration with AR. Plenty of previous research indicated inverse associations between physical activity, controlled stress, and the prevalence of AR symptoms (El Hennawi et al., 2016; Garcia-Marcos et al., 2007; Lind et al., 2014; Smith et al., 2016; Strom and Silverberg, 2016). Akpinar et al.'s study (2016) reported that forest-type greenspace rather than total green space significantly reduced psychological distress in the United States (Akpinar et al., 2016), as forests were complex enough to generate fascination, and the diverse vegetation within them contributed to a feeling of extent and being away, and also provided support for various activities (Van den Berg et al., 2014). Therefore, aggregated and connected forest patches would yield health benefits for AR, while fragmented green space/grassland was less able to.

The positive associations between current AR symptoms and PD_{total} and PD_{grass} only existed in children under the age of five (Table S3), which was probably because AR symptoms tended to become milder, and its incidence tended to decrease with increasing age (Simola et al., 1999; Suh et al., 2019). On the other hand, the inverse associations between current AR symptoms and AI_{forest} and $COHESION_{forest}$ were found in children with exclusive breastfeeding durations longer than 6 months. This was possibly attributed to the protective effects of prolonged breastfeeding against the development of AR and other allergic diseases (Hoang et al., 2022; Obihara et al., 2005), thereby enhancing the benefits of AI_{forest} and $COHESION_{forest}$ for AR. Season might modify the association between forest configuration and AR. In our study, the negative associations of forest aggregation and connectivity with current AR symptoms existed in cold seasons (autumn and winter), while it turned to be non-significantly even positively associated with AR in warm seasons (spring and summer). Trees might produce and emit allergenic pollen (Thompson and Thompson, 2003), which increased the risk of AR or other allergies (Wise et al., 2023), and some reported that arboreal pollen peaked in spring in Beijing, Shanghai, and Nanjing in China (Fang et al., 2018; Sun et al., 2017; Zhao et al., 2023; Zhaobin et al., 2024). However, the season of the questionnaire date might not align with the season of current AR symptoms occurrence. This temporal difference reminded us to approach our conclusions with caution.

The observed associations were heterogeneous across seven cities in our study (Table S6), where significant inverse associations of forest aggregation and forest connectivity with AR were only observed in Wuhan, accounting for the largest sample size. Similarly, Fuertes et al. (2016) reported that the direction of associations between residential greenness and childhood AR in seven birth cohorts varied by region. The author suggested that confounding by an unknown factor that varied between study areas or by several region-specific confounders might explain this heterogeneity (Fuertes et al., 2016). Besides, the heterogeneity might be attributed to the discrepant sample size across seven cities. Larger sample sizes enhanced the statistical power to reveal the associations between green space configuration and human health outcomes (Wang and Tassinary, 2024). Furthermore, our distinctions for vegetation types and current indicators of greenness configuration were not fine enough to derive individual-level measures of exposure to tree species and duration of exposure in each city. However, just like what Fuertes did (Fuertes et al., 2016), we chose to present the results of multilevel logistic regression models in total participants as they answered our original research question.

Our study had several strengths. First, to our knowledge, this study was the first to examine the associations of composition and configuration of green space with AR, instead of the commonly used greenness metrics (e.g, NDVI), indicating the importance of spatial distribution of green space. Second, we used a large population-based multi-city cross-sectional design to investigate the association between green space structure and AR, which had a good representativeness of children in urban areas. Third, the estimated greenness exposure based on individuals' residence addresses at high spatial resolution (10 m) helped to largely reduce miss-classification.

We acknowledged several limitations in our study. First, this was a cross-sectional study, thus we could only observe the association rather than causality. Further interventional studies are needed to assess the effect of greenness composition and configuration on AR and elaborate the underlying mechanisms. Second, we used a questionnaire to collect health information. Though it had been validated both internationally and nationally, it could still cause information bias. And we didn't collect information on perennial or seasonal AR symptoms. Third, the land use data (FROM_GLC 2017) was obtained from 2017 rather than a time-series data, in which the estimations of greenness composition and configuration was not from the same year of our questionnaire survey. However, only a tiny proportion of the territory (no more than 5%) in the world would change its land cover type annually due to human activities or natural forces such as wild fires, volcanoes, hurricanes, etc (Gong et al., 2019). From 2000 to 2016, the net increase in forest area in China was 441,461 ± 26,196 km^2, which was approximately 4.6% of the terrestrial area of China (Guo et al., 2022). Moreover, the 10 m spatial resolution of FROM_GLC2017 is highest among current free-available land cover maps, with the overall accuracy reaching 72.76%, well classifying categories with relatively pure spectral properties. Meanwhile, compared with FROM_GLC2015 at a 30m × 30 m resolution, FROM_GLC2017 could better distinguish forest from shrub or grassland classes (Gong et al., 2019). Thus, we believed the time gap between evaluation time of greenness composition and configuration and questionnaire survey date would not bring large bias on the exposure assessment and exposure-effect estimation. Furthermore, we conducted sensitivity analyses in children who never changed residence addresses since birth (Norbäck et al., 2018) and the results were similar to those in the whole subjects. Fourth, as discussed above, due to limitations in exposure data, we couldn't verify the mechanism behind the relationship between forest configuration and respiratory diseases, which was explained by the actual mitigation of air pollution by vegetation.

5. Conclusion

Our study showed the configuration and composition were important in the association of greenness with AR symptoms in preschool children. Forest, specifically, aggregated and connected forest, was associated with a lower prevalence of AR symptoms. The associations were partially mediated by air pollution. Our research findings are important in strengthening our understanding on the relationship of greenness exposure and AR in children. It would also hint for city planning specialists in perspective of public health promotion, in particular reducing AR risk in children. To be specific, building more large forest parks or expanding already existing forest parks near kindergartens, and linking fragmented forest patches by providing a large canopy may be beneficial for public.

CRediT authorship contribution statement

Han Chen: Writing – original draft, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Xia Meng:** Resources, Data curation, Conceptualization. **Yongfu Yu:** Methodology, Formal analysis. **Jin Sun:** Methodology, Data curation. **Zhiping Niu:** Methodology, Conceptualization. **Jing Wei:** Resources, Methodology. **Ling Zhang:** Resources, Investigation, Formal analysis. **Chan Lu:** Resources, Investigation, Formal analysis. **Wei Yu:** Resources, Investigation, Formal analysis. **Tingting Wang:** Resources, Investigation, Formal analysis. **Xiaohong Zheng:** Resources, Investigation, Formal analysis. **Dan Norbäck:** Resources, Investigation, Formal analysis. **Magnus Svartengren:** Resources, Investigation, Formal analysis. **Xin Zhang:** Supervision, Resources, Investigation, Formal analysis, Conceptualization. **Zhuohui Zhao:** Writing – review & editing, Supervision, Resources, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

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Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2024.118627.

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