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The effect of residential urban greenness on allergic respiratory diseases in youth: A narrative review

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ABSTRACT

Background: Environmental exposures across the life course may be a contributor to the increased worldwide prevalence of respiratory and allergic diseases occurring in the last decades. Asthma and rhinoconjunctivitis especially contribute to the global burden of disease. Greenness has been suggested to have beneficial effects in terms of reduction of occurrence of allergic respiratory diseases. However, the available evidence of a relationship between urban greenness and childhood health outcomes is not yet conclusive. The current review aimed at investigating the current state of evidence, exploring the relationship between children's exposure to residential urban greenness and development of allergic respiratory diseases, jointly considering health outcomes and study design.

Methods: The search strategy was designed to identify studies linking urban greenness exposure to asthma, rhinoconjunctivitis, and lung function in children and adolescents. This was a narrative review of literature following PRISMA guidelines performed using electronic search in databases of PubMed and Embase (Ovid) from the date of inception to December 2018.

Results: Our search strategy identified 2315 articles; after exclusion of duplicates (n = 701), 1614 articles were screened. Following review of titles and abstracts, 162 articles were identified as potentially eligible. Of these, 148 were excluded following full-text evaluation, and 14 were included in this review. Different methods for assessing greenness exposure were found; the most used was Normalized Difference Vegetation Index. Asthma, wheezing, bronchitis, rhinoconjunctivitis, allergic symptoms, lung function, and allergic sensitization were the outcomes assessed in the identified studies; among them, asthma was the one most frequently investigated.

Conclusions: The present review showed inconsistencies in the results mainly due to differences in study design, population, exposure assessment, geographic region, and ascertainment of outcome. Overall, there is a suggestion of an association between urban greenness in early life and the occurrence of allergic respiratory diseases during childhood, although the evidence is still inconsistent. It is therefore hard to draw a conclusive interpretation, so that the understanding of the impact of greenness on allergic respiratory diseases in children and adolescents remains difficult.

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INTRODUCTION

Environmental exposures across the life course may be a contributor to the increased worldwide prevalence of respiratory and allergic diseases occurring in the last decades.[1,2] Asthma and rhinoconjunctivitis especially contribute to the global burden of disease, with prevalence data in childhood ranging from <5 to >20% and from 0.8 to 39.7%, respectively.[3-6]

It has been recently suggested that access or exposure to green spaces can significantly influence human health through many different pathways which may promote health, sustain healthy lifestyle, and decrease environmental factors such as air pollution, thereby contributing to reduce the risk of adverse health outcomes.[7-9] In this view, people living in urban contexts may benefit from proper planning of green areas, which could mitigate the negative effects of urbanization especially recognizable in children.[10] Greenness has been suggested to have beneficial effects in terms of reduction of occurrence of allergic respiratory diseases, and the underlying biological mechanisms are not yet clear. Green areas are generally characterized by biological diversity, which encompasses the variety of species (animals, plants, and microorganisms) as well as the variety of ecosystems in which the species reside. There is evidence that many observed associations between exposure to green environments and human health are mediated by different ecosystem services. One of the potential mechanisms involves the well-known hygiene hypothesis, since early-life exposure to biodiverse green spaces may indirectly (e.g. modulation of the immune system by environmental microbiota) influence health outcomes, including allergies and asthma during childhood.[11,12] Greenness could also have potential short-term benefits on respiratory outcomes, for example vegetation may improve air quality by removing air pollutants.[13] The health effects of green spaces are a relatively new research topic in environmental epidemiology. Available evidence of a relationship between urban greenness and childhood health outcomes is not yet conclusive. Indeed, published reviews on the association between exposure to urban greenness and health in youth reported so far are still inadequate, with insufficient quality of studies, lack of consistency and/or lack of statistical power precluding a conclusion regarding the presence or absence of a relationship with respiratory health.[13-16] In particular, a recent systematic review assessing the association between surrounding greenspace and allergic respiratory diseases in children and adolescents found inconsistent results.[17] In order to summarize the state of knowledge and identify information gaps, we aimed to review the current state of evidence exploring the relationship between children's exposure to residential urban greenness and development of allergic respiratory diseases, jointly considering health outcomes and study design.

METHODS

Search strategy

The search strategy was designed to identify studies linking residential urban greenness exposure to asthma, allergic rhinoconjunctivitis, and lung function in children and adolescents. This was a narrative review of literature following PRISMA guidelines performed using electronic searches in databases of PubMed and Embase (Ovid) from the date of inception to December 2018. No date limits were applied to the search strategy. Two reviewers (FA and MDS) searched the electronic databases. Studies identified from searching electronic databases were combined, duplicates removed, and papers screened for relevance to the review based on the information contained in the title and abstract. Further articles were found using citations from the publications included.

Searching in the databases was made using a search strategy reported in Supplementary material.

Inclusion criteria

Studies were evaluated by two reviewers (GC and GF) and included if (1) age of the participants was up to 18 years; (2) urban greenness was the main exposure variable or effect modifier of another environmental exposure; (3) outcomes of interest were asthma, rhinoconjunctivitis, respiratory diseases and symptoms, lung function, allergy; (4) primary evidence from both experimental and observational epidemiological study design were considered; (5) articles were in English

language. Studies on animals, studies with only abstracts (e.g. conference proceedings) and reviews were excluded.

Study identification and data collection

The full text of references identified as potentially relevant were obtained: papers that could not be rejected with certainty were assessed through discussion and consensus between reviewers (GC and GF). Data extracted from each article included: authors, year of publication, country, sample size, study design, exposure metric, age at outcome, outcome definition and ascertainment, and adjustment factors.

Word cloud from title of selected articles was produced using the statistical software R (3.5). All words were transformed to lower case; plural were transformed to singular. Common words (e.g. prepositions, transition words) and numbers were removed. The size of the words was scaled according to their frequency. Colors and position were assigned randomly and without specific meaning. Network visualization was computed using Gephi © (https://gephi.org/) which allows

Fig. 2 Word cloud of the most common title words.

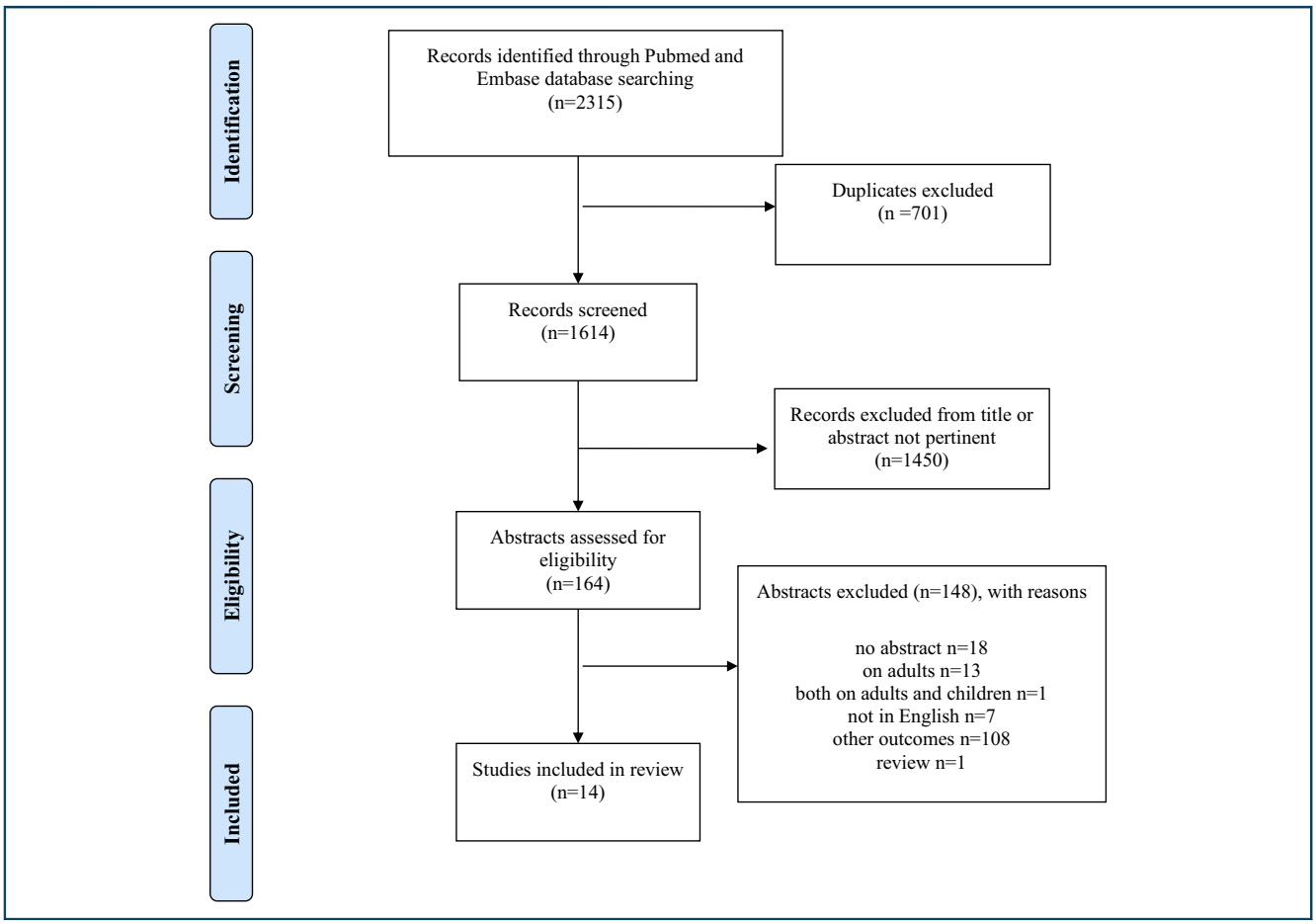

Fig. 1 Study flow from identification to inclusion.

Author (year)	Country	Sample size	Study design	Exposure metric	Age at outcome	Ascertainment	Adjustment factors	Result
Protective effect								
Lovasi et al. (2008)	USA	5857 asthmatic children aged 4–5 years; 9891 children and adolescents aged 0–14 hospitalized for asthma	Cross-sectional study	Street tree density	0–15 years	Disease registry	Population density, demographic and socioeconomic characteristics (percentages of residents below the poverty line, of African American residents and of Latino residents) and proximity to pollution sources	An increase in tree density of 1 standard deviation (SD, 343 trees/km^2) was associated with a lower prevalence of asthma (RR, 0.71 per SD of tree density; 95% CI, 0.64 to 0.79).
Feng et al. (2017)	Australia	4447 children	Cross-sectional study	Green-space land-cover	6–7 years	Parental face-to-face interviews	Age, gender, maternal education, household income, geographic remoteness, area disadvantage and green space quantity	The association between heavy traffic and asthma was significantly lower for participants living in areas with over 40% green space coverage (OR for interaction 0.32, 95% CI 0.12 to 0.84).
Sbihi (2017)	Canada	65254 children	Birth cohort study	NDVI	0–10 years	Disease registry	Sex, parity, breastfeeding initiation, birth weight, delivery mode, maternal smoking and educational attainment, and	Prenatal residential greenness exposure showed a modest effect on children with transient phenotypes (RRR

							household income	0.88, 95% CI 0.88–1).
Eldeirawi et al. (2018)	USA	1915 children and adolescents	Cross-sectional study	NDVI	4–18 years	Questionnaire/ telephone interview	Age, gender, country of birth, place child was born or lived during 1st year of life, family history of asthma or allergies, number of siblings, child attended pre-school or day-care, access to a regular doctor or clinic, child had an ear infection during 1st year of life, child had a viral infection during 1st year of life; child took antibiotics during 1st year of life; child ever breast-fed; current exposure to cats and/or dogs; smoker present in the home at the time of child's birth; current smoker in the home; and proximity to traffic, population density, neighborhood	A protective effect of greenness exposure within 100 m from residential address was observed for lifetime wheezing (OR, 0.82; 95% CI, 0.69–0.96). Increased greenness was associated with lower odds of lifetime asthma among children with current Environmental Tobacco Smoke exposure (100 m: OR, 0.43; 95% CI, 0.22–0.87; 250 m: OR, 0.39; 95% CI, 0.18–0.84; 500 m: OR, 0.48; 95% CI, 0.26–0.90).

(continued)

Author (year)	Country	Sample size	Study design	Exposure metric	Age at outcome	Ascertainment	Adjustment factors	Result
							deprivation, percentage of residents who identify as Mexican, and number of total crimes reported in 2004.	
Harmful effect								
Lovasi et al. (2013)	USA	549 children	Birth cohort study (CCCEH)	LiDAR imagery	5 and 7 years	Questionnaire and IgE antibody response to specific allergens	Sex, age at the time of outcome measurement, ethnicity, maternal asthma, previous birth, other previous pregnancy, Medicaid enrollment, tobacco smoke in the home, active maternal smoking, and the following characteristics of 0.25-km buffers: population density, percent poverty, percent park land, and estimated traffic volume	Tree canopy coverage did not significantly predict outcomes at 5 years of age.
Davdand et al. (2014)	Spain	3178 children	Cross-sectional study	NDVI and Residential proximity to green spaces	9–12 years	Questionnaire	Indicators of individual level socioeconomic status, area-level SES using	Living close to parks was associated with a 60% higher relative

							quintiles of the Urban Vulnerability index, Sex, age, exposure to tobacco smoke at home, older siblings, type of school (public vs. private), parental education, and parental history of asthma.	prevalence of current asthma.
Andrusaityte et al. (2016)	Lithuania	1489 children	Case-control study	NDVI and Residential proximity to green spaces	4–6 years	Questionnaire	Parental asthma, maternal education, age at childbirth, smoking during pregnancy, breastfeeding, antibiotic use during the first year of life, keeping a cat during the past 12 months, living in a flat, time spent in green space, $PM_{2.5}$ and NO_2.	An interquartile range increase in NDVI-100 m increased the risk of asthma (OR 1.43, 95% CI 1.10 to 1.85) with stronger associations for children with higher surrounding greenness (NDVI-100 $>$ median), compared to NDVI-100 $\leq$ median (OR 1.47, 95% CI 0.56 to 3.87).
Feng et al. (2017)	Australia	4447 children	Cross-sectional study	Green-space land-cover	6–7 years	Parental face-to-face interviews	Age, gender, maternal education, household income, geographic remoteness, area disadvantage and green space quantity	Among children exposed to high traffic volumes and areas with 0–20% green space quantity, the OR of asthma was 1.87 (95% CI 1.37 to 2.55).

(continued)

Author (year)	Country	Sample size	Study design	Exposure metric	Age at outcome	Ascertainment	Adjustment factors	Result
Tischer et al. (2017)	Spain	2472 children	Birth cohort study (INMA)	NDVI/Green-space land-cover	4 years	Questionnaire	Sex, cohort, maternal education, maternal smoking during pregnancy, any breastfeeding, season of birth, maternal allergy, pets at home at birth, passive smoking at home at 4 years, area SES and time.	In the Euro-Siberian region, higher residential surrounding greenness was associated with increased risk of asthma (2nd tertile *vs* 1st tertile: OR 2.46, 95% CI 1.01–6.00).
No effect								
Lovasi et al. (2008)	USA	5857 asthmatic children aged 4–5 years; 9891 children and adolescents aged 0–14 hospitalized for asthma	Cross-sectional study	Street tree density	0–15 years	Disease registry	Population density, demographic and socioeconomic characteristics (percentages of residents below the poverty line, of African American residents and of Latino residents) and proximity to pollution sources	An increase in tree density of 1 standard deviation (SD, 343 trees/km^2) was not associated with hospitalizations for asthma (RR, 0.89 per SD of tree density; 95% CI, 0.75 to 1.06).
Lovasi et al. (2013)	USA	549 children	Birth cohort study (CCCEH)	LiDAR imagery	5 and 7 years	Questionnaire and IgE antibody response to specific allergens	Sex, age at the time of outcome measurement, ethnicity, maternal asthma,	Tree canopy coverage did not significantly predict outcomes at 5 years of age.

							previous birth, other previous pregnancy, Medicaid enrollment, tobacco smoke in the home, active maternal smoking, and the following characteristics of 0.25-km buffers: population density, percent poverty, percent park land, and estimated traffic volume	
Davdand et al. (2014)	Spain	3178 children	Cross-sectional study	NDVI and Residential proximity to green spaces	9–12 years	Questionnaire	indicators of individual level socioeconomic status, area-level SES using quintiles of the Urban Vulnerability index, Sex, age, exposure to tobacco smoke at home, older siblings, type of school (public vs. private), parental education, and parental history of asthma.	An interquartile range increase in residential surrounding greenness was not associated with current asthma. Residential proximity to forests was not associated with current asthma.
Feng et al. (2017)	Australia	4447 children	Cross-sectional study	Green-space land-cover	6–7 years	Parental face-to-face interviews	Age, gender, maternal education, household	No association between asthma and green space coverage was

(continued)

Author (year)	Country	Sample size	Study design	Exposure metric	Age at outcome	Ascertainment	Adjustment factors	Result
							income, geographic remoteness, area disadvantage and green space quantity	observed for children not exposed to heavy traffic.
Sbihi (2017)	Canada	65254 children	Birth cohort study	NDVI	0–10 years	Disease registry	Sex, parity, breastfeeding initiation, birth weight, delivery mode, maternal smoking and educational attainment, and household income	No associations of prenatal residential greenness exposure on children with chronic asthma.
Tischer et al. (2018)	Spain, Germany, Sweden	15646 children	Birth cohort study (INMA; LISAplus; GINIplus; BAMSE)	NDVI plus green-space land-cover	1 and 6–8 years	Questionnaire	Sex, cohort, maternal allergy, maternal smoking during pregnancy, maternal education, breastfeeding, dampness at home 1st year, exposure to passive smoke 1st year, and environmental dimensions	No significant associations with the "outdoor-green environmental score".

Table 1. (Continued) Effects of greenness exposure on asthma. *CI: confidence interval; LiDAR: Light Detection and Ranging; NDVI: Normalized Difference Vegetation Index; OR: odds ratio; RR: relative risk; RRR: relative risk ratios.*

visualization of network maps. To produce network maps of exposure metrics and the health outcomes, nodes and their attributes were imported directly into Gephi from the associated spreadsheet, while edges were imported from another spreadsheet using line by line "co-occurrences" of the exposure metrics and the health outcomes thus representing interrelationships between nodes.

RESULTS

Our search strategy identified 2315 articles; after exclusion of duplicates (n = 701), 1614 articles were screened. Following review of titles and abstracts, 162 articles were identified as potentially eligible. Of these, 148 were excluded following full-text evaluation (18 were abstracts, 13 were performed on adults, 1 included both children and adults, 7 were not in English, 108 focused on other different outcomes and/or did not use an objective validated indicator of greenness exposure and 1 was a review article), and 14 were included in this review (Fig. 1). The title word cloud (Fig. 2) showed clear overrepresentation of asthma over other disease terms; greenness was the second term more frequently used.

All the papers included were published in the last 10 years. Six studies were performed on birth cohorts;[18-23] 6 had a cross-sectional design;[18,24-28] 1 was an intervention study;[29] and 1 was a case-control study.[30] Twelve studies involved children of age ≤12 years,[19-27,29-31] and only two included children and adolescents.[18,28] Most of the studies were conducted in Europe,[19,23,24,27,30] 2 in Australia,[21,25,26,28] 4 in North America,[18,31] 1 in Asia,[29] and 1 based on data from Swedish, Dutch, German, Australian, and Canadian birth cohorts.[20]

Exposure assessment

There were 5 different methods for assessing greenness exposure. The Normalized Difference Vegetation Index (NDVI), used by 10 articles[19-24,26-28,30], is a validated tool assessing vegetation cover in order to quantify the amount of vegetation derived from publicly available satellite images. NDVI is based on land surface reflectance, ranging from 0 to 1, where 0 means no vegetation and values close to 1 (0.8–0.9) indicate the highest possible density of green leaves.[32] Two of these studies also evaluated residential proximity to green spaces, whether the child's residential address was located within 300 m separately from an urban park or a forest[24] or within 1000 m from a park, having a green space within a 15 minute walk from home.[30] One study evaluated the quantity of green space available as a percentage of land-use through specific land cover databases.[25] One study used both NDVI and greenspace land-cover,[22] whereas another used NDVI and green land use to construct a composite score.[23] One article applied a combination of high-resolution Light Detection and Ranging (LiDAR), color infrared aerial imagery and ancillary vector data to assess the proportions of tree canopy cover around the home.[31] One study used the street trees count considering street tree density as the total number of trees divided by land area.[18] Lastly, the single intervention study examined changes after a short-term forest trip.[29]

Outcome assessment

Asthma, wheezing, bronchitis, rhinoconjunctivitis, allergic symptoms, lung function, and allergic sensitization were the outcomes assessed in the identified studies. Among them, asthma was included in 9 studies,[18,21-25,28,30,31] generally using data from questionnaires and/or parental interviews. Table 1 summarizes evidences related to effects of greenness exposure (protective/harmful/no) on asthma. One study considered local data of asthma prevalence and related hospitalizations,[18] whereas Sbihi et al. used linked administrative databases of medical visits.[21] Two studies also included the atopic status as evaluated through Immunoglobulin E (IgE) antibody response to specific allergens,[23,31] 4 studies also included wheezing,[22,23,28,31] and 2 of them also included bronchitis.[22,23] Two studies focused on lung function measured through spirometry[29] and forced oscillation technique (FOT).[26] Allergic rhinoconjunctivitis was included in 6 studies,[19,20,22-24,31] mostly using data from questionnaires. Lastly, 1 study referred to self-reported allergic symptoms by questionnaire.[27]

Study design

Birth cohort studies

The CCCEH birth cohort investigated a population of 459 children. Analysis based on the percentage of green spaces in the form of tree canopy cover around the home as measured by LiDAR related to development of asthma, wheeze, rhinitis, and allergic sensitization. Proportions of children with asthma, wheeze, or rhinitis did not appear to be related to quartiles of tree canopy coverage near the prenatal address. The authors found that for unit increase of tree canopy coverage the risk of asthma at 7 years increased by 17%, whereas tree canopy coverage did not significantly predict asthma at 5 years of age, nor wheeze at 5 or 7 years. Associations with rhinitis were not significant due to the low prevalence of this outcome. Moreover, tree canopy cover near the prenatal address was associated with higher prevalence of allergic sensitization to tree pollen.[31]

In the study by Fuertes et al., the pooled GINIplus and LISAplus birth cohorts were split according to study region with GINI/LISA South and its surrounding areas and GINI/LISA North. Greenspace was determined by NDVI at 500, 800, 1000 and 3000 m buffers around the birth, 6- and 10-year participant addresses. The authors found that risk estimates for mean greenness in a 500 m buffer around the 10-year home address were elevated for doctor diagnosed allergic rhinitis in GINI/LISA South (OR 1.16, 95% CI 0.99–1.36), whereas estimates for GINI/LISA North were significantly lower (OR 0.75, 95% CI 0.60–0.93).[19] Later, Fuertes et al. reported cohort-specific and combined associations of residential greenness measured by NDVI in a 500-m buffer around the home address of 13016 children with allergic rhinitis from multiple birth cohorts. Greenness was positively associated with allergic rhinitis in BAMSE (OR 1.42, 95% CI 1.13–1.79) and GINI/LISA South (OR 1.69, 95% CI 1.19–2.41) but inversely associated in GINI/LISA North (OR 0.61, 95% 0.36–1.01) and PIAMA (OR 0.67, 95% CI 0.47–0.95). Effect estimates in CAPPS and SAGE were also conflicting but not significant (OR 0.63, 95% CI 0.32–1.24 and OR 1.31, 95% CI 0.81–2.12, respectively).[20]

In a population-based birth cohort of 65254 children, prenatal residential greenness exposure measured by NDVI calculated for 100-m buffers around residential postal codes showed a modest effect on children with transient asthma. No

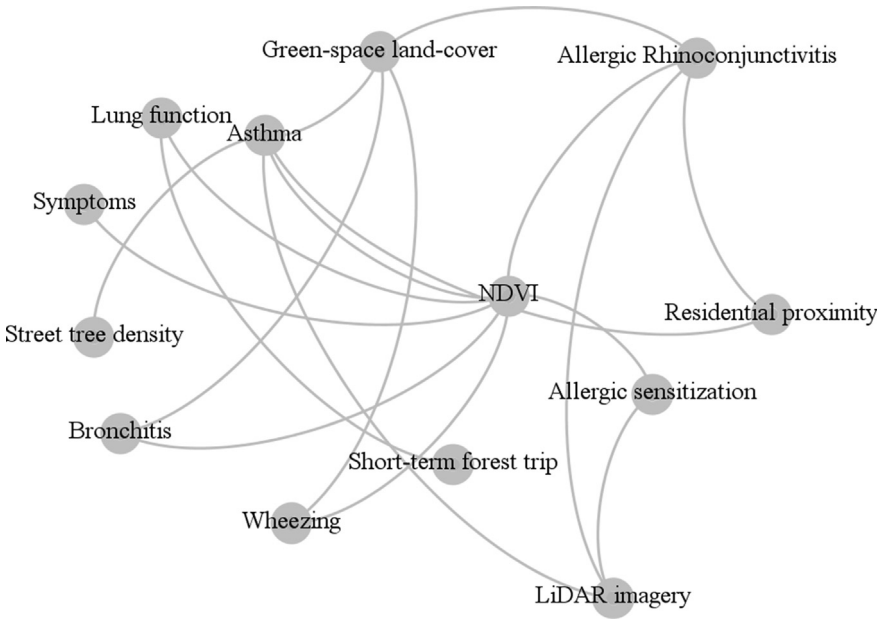

Fig. 3 Interrelations between the exposure metrics and the health outcomes. Lines indicate the investigated relation between exposure metrics and health outcomes in the fourteen studies included in the current review.

associations on children with early or late onset chronic asthma were found.[21]

A study on 2472 children from the INMA birth cohort calculated mean NDVI values in 300-m buffers around the place of residence at the time of birth and at age 4 years. Differently from the Mediterranean region, in the Euro-Siberian region, higher residential surrounding greenness was significantly associated with a lower risk of wheezing (adjusted odds ratio [aOR] 0.61, 95% CI 0.44–0.85) and increased risk of asthma (2nd tertile vs 1st tertile: aOR 2.46, 95% CI 1.01–6.00). Besides, the authors evaluated whether each child's residential address was located within 300 m of an urban green space by means of the Urban Atlas map developed by the European Environment Agency in 2007. Residential proximity to green spaces was negatively associated with wheezing in subjects in the Euro-Siberian region (aOR 0.67, 95% CI 0.45–0.99) and with doctor-diagnosed bronchitis among children in the Mediterranean region (aOR 0.77, 95% CI 0.61–0.98).[22]

A later study included 15646 children participating in 4 European birth cohorts. No significant associations with the "outdoor-green environmental score" (obtained from residential surrounding greenness measured by NDVI and neighborhood green land use measured by the CORINE land-cover classes developed by the European Environmental Agency) were found (OR 1.00, 95% CI 0.96–1.05 and OR 1.00, 95% CI 0.96–1.05 for wheezing and bronchitis at1st year; OR 1.00, 95% CI 0.84–1.19 and OR 1.01, 95% CI 0.89–1.15 for asthma and allergic rhinitis at 6–8 years).[23]

Cross-sectional studies

The study by Lovasi et al., based on data from 5857 asthmatic children and 9891 children hospitalized for asthma found that an increase in tree density of 1 standard deviation (SD, 343 trees/km^2) was associated with a lower prevalence of asthma (RR, 0.71 per SD of tree density; 95% CI, 0.64 to 0.79), but not with hospitalizations for asthma (RR, 0.89 per SD of tree density; 95% CI, 0.75 to 1.06).[18]

In a later cross-sectional study of a population-based sample of 3178 schoolchildren, residential surrounding greenness was measured as the average of satellite-derived NDVI in buffers of 100 m, 250 m, 500 m, and 1000 m around each home address. Residential proximity to green spaces was defined as living within 300 m of a forest or a park. An interquartile range increase in residential surrounding greenness was not associated with current asthma, nor residential proximity to forests, whereas living close to parks was associated with a 60% higher relative prevalence of current asthma. Current allergic rhinoconjunctivitis was not associated with NDVI, but was positively associated with residential proximity to a park or to a forest, although none of the associations was statistically significant.[24]

In a more recent study conducted on 4447 children, the OR of asthma was 1.87 (95% CI 1.37 to 2.55) for children exposed to high traffic volumes living in areas with 0–20% green space quantity. The association between heavy traffic and asthma resulted significantly lower for participants living in areas with over 40% greenspace coverage (OR 0.32, 95% CI 0.12 to 0.84) measured through the greenspace land-use metric.[25] In another study involving 360 children, surrounding green spaces within 100, 200, 300 and 500 m from home address were evaluated by means of NDVI. The Authors found no correlation between greenspace and children's lung function measured by FOT[26]

A recent cross-sectional study aimed to investigate the effect of greenness exposure on respiratory/allergic conditions and general symptoms in 219 schoolchildren. A very low exposure to NDVI $\leq$0.15 (1st quartile) was associated with a higher odds of self-reported nasal symptoms (OR = 1.47, 95% CI 1.07–2.03). The authors did not find significant associations between greenness exposure and ocular, pulmonary, and general symptoms.[27]

Finally, a cross-sectional study examined the association between surrounding greenness measured by NDVI within buffers of 100, 250 and 500 m of home address and parent-reported data of 1915 children. A protective effect of greenness within 100 m was observed for lifetime wheezing (aOR, 0.82; 95% CI, 0.69–0.96). For all buffer distances, increased greenness was associated with lower odds of lifetime asthma among children currently exposed to Environmental Tobacco Smoke (ETS) (100 m: aOR, 0.43; 95% CI, 0.22–0.87; 250 m: aOR, 0.39; 95% CI, 0.18–0.84; 500 m: aOR,

0.48; 95% CI, 0.26–0.90) and lower odds of current dry nocturnal cough among children with perinatal ETS exposure (100 m: aOR, 0.53; 95% CI, 0.31–0.92; 250 m: aOR, 0.55; 95% CI, 0.31–0.98; 500 m: aOR, 0.55; 95% CI, 0.35–0.87).[28]

Intervention studies

In the current review we selected a single intervention study involving 21 asthmatic children. Changes in lung function evaluated by means of spirometry were investigated before and after a short-term forest trip. Findings supported that forest trip may have beneficial effects since the mean forced vital capacity (FVC %predicted) was significantly increased after the forest trip (95.8 ± 13.3) than before (92.0 ± 11.3) ($p = 0.018$). No significant difference was observed in forced expiratory volume in 1 s (FEV_1% predicted) (92.9 ± 11.0 vs. 91.2 ± 9.9) ($p = 0.224$).[29]

Case-control studies

The single case-control study included in this review was conducted on 1489 children residing at their current address since birth. Surrounding greenness was measured as the average of the NDVI within the buffers of 100, 300, and 500 m from each child's home address, and the distance to a park was defined as the distance (m) to the nearest city park. An increase in the NDVI (>median) in buffers of 100, 300 and 500 m was associated with a slightly increased risk of asthma, while an IQR increase in NDVI-100 m significantly increased the risk of asthma (OR 1.43, 95% CI 1.10 to 1.85). The stratified analysis by surrounding greenness to distinguish NDVI and park effect and to assess their joint effect on the risk of asthma suggested higher risk among children with higher surrounding greenness (NDVI-100 > median) both in those living close (adjusted OR 1.27, 95% CI 0.56 to 2.86) and further away from parks (>1000 m) (OR 1.47, 95% CI 0.56 to 3.87), compared to NDVI-100 ≤ median and distant from a city park >1000 m; the risk of asthma increased by 27% for children living at a distance ≤1000 m to a park but increases were not statistically significant.[30]

Detailed characteristics of included studies are shown in Supplementary material (Table S1).

Interrelations between the exposure metrics and the health outcomes are shown in Fig. 3. NDVI resulted the exposure metric used for assessing the effect of greenness on all of the health outcomes considered in the fourteen studies included in the current review.

DISCUSSION

The current narrative review was aimed at assessing the effect of exposure to residential urban greenness on allergic respiratory diseases in youth. Overall, there is a suggestion of an association between urban green in early life and the occurrence of allergic respiratory diseases during childhood, although the evidence is still inconsistent. We selected 14 articles, different with regard to study design, health outcomes, and method of assessment of greenness exposure, which can explain somewhat lack of consistency in the published findings.

With special regard to asthma, which was the most frequently assessed outcome in the studies included in the current review, different effects were found according to the different exposure methodologies, even when the same exposure metric was considered. Studies were different in regard to the sample size, time windows of greenness exposure, and age ranges. Four of the selected studies were cross-sectional[18,24,25,28] and covered different geographic regions such Australia, Europe and USA. Studies were also different with regard to the sample size and age ranges, with 2 studies including both children and adolescents.[18,28] NDVI was the exposure metric most commonly used; 2 studies based on other greenness exposure measurements, such as street tree density[18] and green-space land-cover.[25] Notably, the study by Davdand et al., which evaluated greenness exposure by using both NDVI and residential proximity to green spaces, went to conflicting results. This could be suggestive for some potential differences in the living environment in terms of degree of urbanity and/or air pollution levels, as well as to differences in terms of quality of greenness. Namely, a difference between forest and park flora and relative to composition of ambient pollen concentrations and their allergenicity could partly explain variations in the observed

findings.[24] Moreover, these findings could be ascribed to biological diversity within different green areas, which has been suggested to influence the pathogenesis of asthma through the exposure to different microbial stimuli that modulate the immune system.[33] The single case-control study included in this review reported a significant association between increased NDVI and the risk of asthma, suggesting that high exposure to greenness may increase the risk of allergic conditions such asthma, possibly through the related exposure to pollens. Stronger associations were found in children exposed to higher surrounding greenness than for those living close to city parks and these results did not change after adjusting for other variables, including fine particulate matter and nitrogen dioxide, suggesting that residential greenness has an impact on children asthma prevalence.[30] On the contrary, Lovasi et al. provided an assessment of the urban tree canopy coverage using LiDAR. In this study the measurement of greenness exposure primarily included street trees and urban park/gardens. However, this metric does not allow to distinguish the importance of particular types of vegetation, making not possible to determine the specificity of the association at the level of tree species.[31] In general, uncertainty persists over the appropriate scale for accurately measuring greenness exposures. Nonetheless, approaches combining large-scale NDVI or land cover-based analysis with on-site mapping and surveys may be most informative in unpacking the relationship between greenness exposure and respiratory health.[13] With regard to study design, we found 4 birth cohort studies covering 7 cohorts (mostly located in Europe).[21–23,31] A clear protective association of greenness with asthma/wheezing has been observed in one of the selected studies,[28] whereas controversial results were observed in the cross-sectional study by Lovasi et al.,[17] as well as in 1 of the birth cohort studies.[22] In a cross-sectional study, a protective effect of greenness was found only in children exposed to heavy traffic.[25] Conversely, an increased risk of asthma was observed in the birth cohort study by Lovasi et al.,[31] and in the case-control study by Andrusaityte et al.[30] A higher prevalence of current asthma was found by Davdand et al. only in children living close to parks,[24] whereas a modest effect on children with transient asthma phenotype was observed in the birth cohort study by Sbihi et al.[21] Lastly, no associations were reported with the "outdoor-green environmental score" developed by Tischer et al.[23]

Concerning lung function, the only intervention study included in this narrative review showed a significant increase in FVC assessed by spirometry after a short-term forest trip. Notably, no significant difference was observed in FEV_1, probably because most of the enrolled children had mild-to moderate well-controlled asthma and their baseline lung function was near normal.[29] In another Australian study on children living on the outskirts of a heavy industrial area, surrounding green spaces within 100, 200, 300 and 500 m from home address were cross-sectionally evaluated by means of NDVI. The Authors found no correlation between green space and children's lung function measured by FOT[26]

In regard to allergic rhinitis, we found 1 cross-sectional study[24] and 4 birth cohort studies.[19,20,22,23] Only 1 study investigated the effect of greenness exposure on rhinoconjunctivitis showing not association with NDVI; residential proximity to a park or to a forest increased the risk of this disease, although none of the associations was statistically significant.[24] The other studies assessed allergic rhinitis. In particular, in the study by Fuertes et al., risk estimates for mean greenness in a 500 m buffer around the 10-year home address were elevated for doctor diagnosed allergic rhinitis in GINI/LISA South, whereas estimates for GINI/LISA North were significantly lower than one.[19] Later, Fuertes et al. reported that greenness was positively associated with allergic rhinitis in BAMSE and in GINI/LISA South but inversely associated in GINI/LISA North and in PIAMA. Effect estimates in CAPPS and SAGE were also conflicting but not significant.[20] Conversely, Tischer et al., in 2 birth cohort studies did not find significant association between NDVI/green space and allergic rhinitis.[22,23] Overall, despite the relevant contribution of these findings to the body of literature focusing on the effects of urban greenness on respiratory health in children and adolescents, it is hard to draw a conclusive interpretation. Interestingly, even when many

cohorts, which were fairly homogeneous in terms of exposure assessment, geographic area, and confounder control, were analyzed, findings were discordant.[20] This could be relative to residual confounding by socio-economic status or to quality of greenspace.

About self-reported allergic symptoms, only 2 studies investigated the effect of greenness exposure, using NDVI. In the birth cohort study by Fuertes et al., elevated associations for eyes and nose symptoms in the urban GINI/LISA South area and significantly below 1 in rural GINI/LISA North area were found.[19] In a recent cross-sectional study conducted in Southern Italy on schoolchildren, a very low exposure to NDVI $\leq$0.15 (1st quartile) was associated with a higher odds of self-reported nasal symptoms. The authors did not find significant associations between greenness exposure and ocular, pulmonary and general symptoms.[27] Although in both studies the same metric of exposure was used (NDVI), a conclusive interpretation cannot be drawn due the scant number of available studies on this topic and to the different study design.

In light of the available evidence, it is still unclear how much and what type of urban greenness is needed to determine benefit on respiratory health of children and adolescents. At this purpose, studies should be designed to provide further information on type and quality of the green space within the urban context. Furthermore, since exposure estimates are traditionally assigned to the residential address, it may be of interest to assign green space estimates to other places where children spend most time of the day, such as schools. Children within a cohort who change residence could be suitable to study the impact of greenness on respiratory health, allowing estimates of longitudinal effects.[34] Noteworthy, the effects of greenness exposure on health should be adjusted for environmental pollutants, which may influence the results; notably, only four of the studies included in the present review provided adjusted results for these confounders.[18,24,27,30] In our opinion, the lack of the adjustment for pollutants may have contributed to heterogeneous effects showed in the current review. In addition, atopic status should be considered as a complex condition including allergic comorbities as well as an interaction factor with both the greenness and environmental exposures. Future research should include a comprehensive assessment of different pieces, such as climatic zone, seasonality, meteorological and aerobiological data, as well as indoor chemical and toxic elements mainly derived from cigarette smoke.[35]

Overall, evidence on the impacts of urban greenness on respiratory health in low- and middle- income countries is scanty, and the findings obtained in high income countries might not be generalizable due to socioeconomic and cultural factors. Indeed, another factor that limits the interpretation of the results obtained by the different studies evaluated in the current review is that these were conducted in different countries with different urban development.[16] This highlights the inter-dependency between socioeconomic and environmental factors and the health outcomes, emphasizing that the effect of urban greenness on allergic respiratory health of children and adolescents should be further investigated across longitudinal studies evaluating the composition of green spaces, as well as air quality, in different population groups.[13] In particular, variables related to deprivation, lower socioeconomic status, and educational status have been demonstrated to be negatively related to health outcomes.[36] There is also evidence showing differential access to green spaces among vulnerable groups, such as socioeconomically disadvantaged or racial/ethnic minorities. Green spaces are often unequally distributed between white and racial/ethnic minority communities, and limited amount of green areas have been reported in the socioeconomically deprived residential areas.[37,38] Racial/ethnic minorities travel longer distances and visit less frequently green spaces.[39] Noteworthy, the presence of a nearby park does not mean that people will use it for recreation, especially in urban suburbs, where collapsing park budgets coincided with general declines in maintenance and use. Therefore, the disadvantage in green space access on the poor minorities deserves more research studies. A group of particular interest may be racial/ethnic minorities moving into cities, for whom there are little data.

CONCLUSIONS

The current review, aimed at qualitatively synthesizing studies on residential urban greenness and development of allergic and respiratory diseases in childhood, showed inconsistencies in the results mainly due to differences in study design, population, exposure assessment, geographic region, and ascertainment of outcome. It is therefore hard to draw a conclusive interpretation, so that the understanding of the impact of greenness on allergic respiratory diseases in children and adolescents remains difficult. Future studies should focus on the gaps we identified in this review, as well as on understanding the mechanisms underlying the complex relationship between urban greenness and respiratory health. Furthermore, the development of international consensus especially targeted on objective measures of greenness exposure is advisable in order to improve the quality of study methodology in this field of research.

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GF, FA, GC and MDS reviewed the data from the literature, contributed to the concept development and wrote the manuscript. PM and SLG were major contributors to the critical revision of the manuscript and the intellectual content within the paper. All authors read and approved the final manuscript.

Declaration of Competing Interest
The authors declare that they have no competing interests.

Appendix A. Supplementary data
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