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Review article

# Different greenness exposure in Europe and respiratory outcomes in youths. A systematic review and meta-analysis

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ABSTRACT

The existing evidence on the association between greenness and respiratory outcomes remains inconclusive. We aimed at systematically summarizing existing literature on greenness exposure and respiratory outcomes in European children and adolescents, with a preliminary attempt to qualify the distribution of dominant tree species across different geographical areas and bioclimatic regions. Overall, 4049 studies were firstly identified by searching PubMed/MEDLINE, EMBASE, Scopus, Web of Science, GreenFile and CAB direct, up to 29 August 2023. Eighteen primary studies were included in the systematic review and six were meta-analyzed. No overall significant association was observed between the Normalized Difference Vegetation Index, assessed within 500-m buffers (i.e. NDVI-500), and the odds of asthma for 0.3-increase in the exposure (OR: 0.97, 95% CI from 0.53 to 1.78). Similarly, an overall exposure to the NDVI-300 highest tertile, as compared to the lowest tertile, was not significantly associated with asthma (OR: 0.65, 95% CI from 0.22 to 1.91): heterogeneity among studies was significant ($p = 0.021$). We delineated some key elements that might have mostly contributed to the lack of scientific *consensus* on this topic, starting from the urgent need of harmonized approaches for the operational definition of greenness. Additionally, the complex interplay between greenness and respiratory health may vary across different geographical regions and climatic conditions. At last, the inconsistent findings may reflect the heterogeneity and complexity of this relationship, rather than a lack of scientific *consensus* itself. Future research should compare geographical areas with similar bioclimatic parameters and dominant or potentially present vegetation species, in order to achieve a higher inter-study comparability.

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## 1. Introduction

An accumulating body of evidence supports the beneficial effects of exposure to greenness (i.e. green spaces, parks and green infrastructures) over several health outcomes (Yang et al., 2021). Exposure to greenness has been previously associated with improved mental health and well-being (Frumkin et al., 2017), reduced mortality (Vienneau et al., 2017), obesity (Kondo et al., 2018), and cardiovascular diseases (Seo et al., 2019), or improved immune system (Rook, 2013) and birth outcomes (Hystad et al., 2014). However, data on respiratory health remain inconsistent or inconclusive, as highlighted by recent systematic reviews (Cao et al., 2023; Fyfe-Johnson et al., 2021; Hartley et al., 2020; Islam et al., 2020; Lambert et al., 2017; Liu et al., 2023; Mueller et al., 2022; Sprague et al., 2022; Ye et al., 2022). Some studies reported that living closer to parks or being more exposed to greenness is protective against asthma and respiratory outcomes (Alasauskas et al., 2020; Cavaleiro Rufo et al., 2021; Cilluffo et al., 2022a; Dzhambov et al., 2021; Squillacioti et al., 2019; Tang et al., 2023; Wang et al., 2022) or, similarly, that low exposure to greenness is a risk factor for lack of

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asthma control (Cilluffo et al., 2022b). Other studies found the opposite (Andrusaityte et al., 2016; Dadvand et al., 2014; Markevych et al., 2020; Parmes et al., 2020) or reported no association (Cilluffo et al., 2018).

Chronic respiratory diseases are among the most prevalent illnesses worldwide, affecting both adults and youths, and being responsible, in 2019, for 71.1 million (95% Uncertainty Intervals 64.7–77.0) Years of Life Lost and 32.4 million (26.1–38.5) Years Lived with a Disability (IHME, 2019). Asthma is the most common non-communicable disease among children (Poole, 2014; Ferrante and La Grutta, 2018). Its prevalence is high in childhood, predominantly in boys before puberty, with a relatively high remission rate during adulthood (Sears et al., 2003). Risk factors for asthma and respiratory diseases range from environmental exposures to individual characteristics, such as sex, age, and genetic make-up (Trivedi and Denton, 2019). A multi-factorial model, emphasizing the interplay between both genes and environment, has been recently proposed to acknowledge factors contributing to the onset of respiratory allergic diseases, like asthma and rhinitis (Ferrante et al., 2022). In addition, the increasing urbanization degree has put the spotlight on some emerging environmental factors, including gray spaces, which have been associated with the allergic status (Maio et al., 2022) and greenness.

Greenness favorably contributes to respiratory health through the following potential pathways. First, plants can remove pollutants from air (Diener and Mudu, 2021) and improve air quality by the mitigation of outdoor air pollution, a recognized risk factor for many respiratory diseases (De Matteis et al., 2022; Maio et al., 2023). Second, the early-life exposure to biodiverse vegetated areas may support the immunomodulatory capacity of children by influencing their microbiota (Rook, 2013). Finally, the access to parks and green spaces may also reduce obesity and sedentary behavior by encouraging physical activity, with positive effects on general and respiratory health (Yang et al., 2021). Sparse evidence from cross-sectional studies has also recently suggested that living in greener areas is associated with lower oxidative stress levels in children (De Petris et al., 2021; Squillacioti et al., 2022). Despite these pathways possibly involved in preventing or ameliorating pre-existing diseases, greenness may also adversely affect respiratory health by exposing individuals to aeroallergens and harmful chemicals, such as pollens (Dellavalle et al., 2012; Lovasi et al., 2013), fungal spores (Bartra, 2009; De Linares et al., 2010), pesticides (Corsini et al., 2013), or biogenic volatile compounds (Ciccioli et al., 2023).

The complexity of the potential mechanistic links between vegetation and respiratory health is even more intricate when considering the different scientific approaches and operational choices adopted by different authors. Indeed, the lack of consistency among previous studies may be attributable to several elements, including study designs, population characteristics, exposure/outcomes assessment, and the geographical area where primary studies were implemented. The latter entails climatic differences able to influence the distribution of prevalent vegetation species and air pollution levels, both identified as potential confounders or effect modifiers in the complex association between greenness and respiratory outcomes (Fuertes and Jarvis, 2021), but not always considered. In addition, the generic definition of greenness fails to differentiate between botanical species and types of vegetation. Further, greenness metrics can be based on satellite-derived vegetation indexes, like the Normalized Difference Vegetation Index (NDVI) and the Soil Adjusted Vegetation Index (SAVI), or on land use-derived percentage or distance to different green coverages/infrastructures (Ekkel and de Vries, 2017). However, none of the aforementioned metrics can qualify the type of vegetation.

Despite the vast amount of recent scientific literature on this topic, a knowledge gap still exists, in terms of both scientific *consensus* and methodology harmonization. The present systematic review was designed with the specific goal of trying to partly overcome the issues related to the high degree of heterogeneity already highlighted by previous research in this field. Among numerous key issues previously identified, the exposure assessment has been recurrently pointed out as one of the main issues potentially affecting the consistency of available findings. Therefore, we aimed to systematically summarize the existing literature on greenness exposure and respiratory outcomes in European youths (0–18 years old), by adding further insights through the contextualisation of the existing results in terms of biogeographical and climatic regions, as they can strongly influence the type of vegetation. We focused on European youths considered as a susceptible population prone to respiratory outcomes linked to environmental exposures, without the influence of many other variables, including occupational exposures, to which adults may be additionally exposed. The geographical restriction to European residents was intended to support a preliminary attempt to qualify the distribution of prevalent vegetation species across bioclimatic regions, in order to 1) ensure a higher degree of homogeneity among the aforementioned elements; 2) ease the management of our additional elaborations that included the use of tools such as Corine Land Cover (CLC), Nomenclature of territorial units for statistics (NUTS) that are currently Europe-based and 3) avoid a total overlapping with the existing systematic reviews that are mostly based on evidence from worldwide with no geographical restrictions.

## 2. Materials and methods

The current systematic review has been conducted following a protocol registered on the “International prospective register of systematic reviews” (PROSPERO ID: CRD42022312603) and reported according to the “Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines” (Page et al., 2021).

### 2.1. Search strategy and study eligibility criteria

Primary studies were searched in the following electronic databases: PubMed/MEDLINE, EMBASE, Scopus, Web of Science, GreenFile and CAB direct, up to 29 August 2023. The full search strings are available in Appendix A.

Cross-sectional studies, case-control studies, non-randomized trials, Cluster Randomized Trials (CRTs), Randomized Controlled Trials (RCTs), quasi-experimental studies, before-after controlled studies, interrupted time-series, and cohort studies were deemed eligible for inclusion, without time restriction. The target population included children and adolescents (0–18 years old) from Europe, as defined by the World Health Organization (WHO, 2016).

Respiratory and allergic health outcomes of interest were asthma, rhino-conjunctivitis, bronchitis, respiratory symptoms, and lung function measurements, either assessed by clinicians or self-reported by questionnaires.

Exposure to greenness encompassed quantitative (e.g. vegetation indexes, number of trees, etc.), qualitative (e.g. vegetation cover type percentage, etc.), proximity and accessibility metrics (e.g. proximity to parks/gardens, etc.). We only considered exposures assessed at individual level (residential address) or, alternatively, referred to postal code or census area (i.e. cluster of subjects).

### 2.2. Screening and data extraction

All original studies identified by the search strings were screened for duplicates using Mendeley software. Two independent reviewers (GS and SF) screened titles and abstracts for identifying articles that potentially met the inclusion criteria. Then, they independently assessed the selected full texts for individuating the primary studies to be included and used for data extraction. All the exclusion reasons were recorded. The relevant information was extracted in a specific spreadsheet. If any discrepancy arose, a third reviewer’s opinion was collected to solve the differences through discussion.

The WebPlotDigitizer online software (https://apps.automeris.io/wpd/) was used to extract data that were originally presented only through a figure. In case of missing information, the corresponding author or co-authors were asked to provide such information.

### 2.3. Risk of bias (quality) assessment

Two reviewers (GS and SF) independently assessed the risk of bias of the included studies, by using a validated checklist, the Johanna Briggs Institute critical appraisal tools (Moola et al., 2020), according to the design of the study. Selection and information bias, confounders, blinding, data analysis methods were the main domains checked for the risk of bias. An overall risk of bias was reported for each study, then normalized to 100 and expressed as "low", "medium" and "high" (first, second and third tertile, respectively).

### 2.4. Data synthesis and analysis

Study and participants characteristics were summarized in tabular form, according to how they were originally reported in primary studies. We retrieved the European Local Administrative Units (LAUs) from the Urban Audit 2020 dataset (Eurostat, 2023), in order to present the results by study areas. LAUs are the building blocks of the NUTS and comprise the municipalities of the European Statistical System. Five study areas were not identifiable as municipalities (e.g. Asturias, Alpine valleys, etc.) and we approximated them with the corresponding NUTS (level 3) (Brus et al., 2012).

If three or more studies were identified as homogenous and comparable in terms of operational choices (i.e., same greenness metrics, respiratory outcomes, and measures of association), their reported effect measures were pooled through meta-analysis. Given the expected differences among populations and vegetation species, a random-effect meta-analysis was performed using the DerSimonian-Laird estimator (Borenstein et al., 2021). In case of effect measures expressed as different exposure increments between studies, they were converted and expressed in terms of the same exposure increment (Chen and Hoek, 2020).

Statistical heterogeneity of the effect measures between studies was assessed through the Cochran's Q test and the $I^2$ statistic, i.e., the ratio of true heterogeneity to total variance across the observed effect estimates. $I^2$ values of 25%, 50% and 75% were taken as indicative of low, moderate and high degree of heterogeneity, respectively (Woodward, 2013). The R program package 'metafor' was used for computations. Figures were created using GraphPad Prism version 9.4.1 for Windows, GraphPad Software, San Diego, California USA, www.graphpad.com.

We further retrieved maps from the biogeographical regions' dataset 2016 (European Commission – Eurostat/GISCO https://sdi.eea.europa.eu/catalogue/idp/api/records/c6d27566-e699-4d58-a132-bbe3fe01491b (accessed Feb 20, 2023), containing the official delineations used in the Habitats Directive (92/43/EEC). Within study-specific NUTS or LAUs, we calculated the coverage percentage of dominant tree species, available from 1x1-km tree species maps, showing the distribution of 20 tree species over Europe (Brus et al., 2012).

Spatial analyses were performed using QGIS 3.16.2 (QGIS Development Team (2020). QGIS Geographic Information System. Open Source Geospatial Foundation Project. http://qgis.osgeo.org).

Additionally, to provide a more comprehensive synthesis on the existing results on this topic, we selected and briefly synthetized (Table S3) all the systematic reviews found by the search string that have been published within the same time span of the studies included in the present systematic review.

## 3. Results

### 3.1. Study and participants' characteristics

Overall, 4049 studies were identified at the beginning. After duplicate exclusion, 1671 articles were screened for eligibility, 75 full-texts were sought for retrieval, and 18 were finally included in the systematic review (Fig. S1). The reasons for exclusion encompassed the place where the recruitment was carried out (outside Europe), the lack of explicit reference to respiratory outcomes or greenness, the involvement of adult subjects and/or the lack of quantitative/original data.

Eighteen articles were included in the qualitative synthesis (Alasauskas et al., 2020; Almeida et al., 2022; Andrusaityte et al., 2016; Cavaleiro Rufo et al., 2021; Cilluffo et al., 2018; Cilluffo et al., 2022a; Cilluffo et al., 2022b; Dadvand et al., 2014; Dzhambov et al., 2021; Fuertes et al., 2016; Fuertes et al., 2014; Markevych et al., 2020; Müller-Rompa et al., 2018; Parmes et al., 2020; Squillacioti et al., 2019; Tischer et al., 2017, 2018, Winnicki et al., 2022), and six of them were included in the meta-analysis (Andrusaityte et al., 2016; Dzhambov et al., 2021; Markevych et al., 2020; Müller-Rompa et al., 2018; Squillacioti et al., 2019; Tischer et al., 2017). Detailed study and participants characteristics are summarized in Table S1. Briefly, the included studies covered a large time span, ranging from 1991 to 2018. Eight of them (44.4%) used a cross-sectional design, while nine were cohort or multi-cohort studies. One report was a meta-analysis including three cohort studies, one longitudinal study and three cross sectional studies. Sample sizes ranged from 179 to 54,310, while male/female ratio was almost balanced, with few exceptions. Most of the human participants were children (<12 years old), with some reports including adolescents (12–18 years old). The studies covered a relatively small European area, mostly referring to urbanized locations in North-central Europe. None of them explored greenness effects in low- or middle-income countries (Fig. S2).

The outcome of the risk-of-bias assessment is reported in Table 1. Most studies were considered with low risk of bias. The major concern about the study quality was the definition of participants' eligibility criteria, especially in the cross-sectional studies.

### 3.2. Metrics of greenness, respiratory outcomes, and meta-analysis

Exposure to greenness was mostly assessed by the NDVI, calculated within buffers centered on the residential or school address of the participants (78% of the included studies) (Table 1). Four studies (Alasauskas et al., 2020; Andrusaityte et al., 2016; Dadvand et al., 2014; Winnicki et al., 2022) used proximity measurements, such as distance from parks or forest, and around a third of the studies (Almeida et al., 2022; Cilluffo et al., 2022a; Cilluffo et al., 2022b; Dzhambov et al., 2021; Müller-Rompa et al., 2018; Parmes et al., 2020; Tischer et al., 2017) assessed greenness, as the percentage of the green coverage within fixed buffers, approximating residence surroundings. One study (Tischer et al., 2018) used a combination of greenness metrics to derive a green score, while six authors (Almeida et al., 2022; Andrusaityte et al., 2016; Dadvand et al., 2014; Dzhambov et al., 2021; Müller-Rompa et al., 2018; Winnicki et al., 2022) adopted more than one metric, once at a time, in the same study.

Beyond their intrinsic differences, all the metrics were often poorly comparable across studies, because of different operational choices adopted by the authors. For example, NDVI buffers ranged between 15 and 1000 m in radius size, with 300-m and 500-m buffers being the most commonly used (reported in 43% and 50% of the studies, respectively) and 150-m and 200-m buffers the least (both only in one study). Around 36% of the included studies assessed exposure to greenness within 100-m buffers and 14.3% of them within 1000-m. The spatial resolution of the satellite images, used for the NDVI calculations, was more homogenous (30 × 30 m), as the vast majority of the studies (86%) used images from the Landsat satellite operated by the NASA and USGS (National Aeronautics and Space Administration and United States Geological Survey agencies). Only two studies (Cilluffo et al., 2018; Cilluffo et al., 2022b) used images from the NASA-operated Advanced Spaceborne Thermal Emission and Reflection Radiometer (ASTER), reaching a higher spatial resolution (15 × 15 m).

With reference to the measurement of green coverage percentage, three studies (Cilluffo et al., 2022a; Parmes et al., 2020; Tischer et al.,

**Table 1**
Associations between exposure to greenness and respiratory outcomes among the included studies. The Risk of bias was evaluated according to the Johanna Brigg Institute (JBI) critical appraisal tools, study-design specific.

| Study reference | Exposure | Outcome | Statistical analysis and confounders | Greenness effect on the respiratory outcomes | Risk of bias evaluation | Study location |
|---|---|---|---|---|---|---|
| Alasauskas et al., 2020 | Distance from trees/bushes | Asthma | Multivariable logistic regression adjusted by age, sex, $NO_2$, $PM_{10}$, $PM_{2.5}$,BaP | Protective | High | Vilnius (LT) |
| Almeida, 2022 | Spring-Summer NDVI-100-250-500 (Landsat 5–8 TM), proximity (distance), accessibility (yes/no), and number of urban green spaces within 400 and 800 m from the residence | $FEV_1$, FVC, FEF 25-75% | Linear regression models adjusted for sex, age, maternal education, household monthly income, population density, neighborhood socioeconomic deprivation, change of residence's address, residential mobility, birthweight | Protective | Medium | Porto (PT) |
| Andrusaityte et al., 2016 | NDVI-100-300-500 (Landsat 5 TM), distance from parks (Urban Atlas) | Asthma | Multivariable logistic regression adjusted by 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 | Negative effect | High | Kaunas (LT) |
| Cavaleiro Rufo et al., 2021 | NDVI-100-200-300 (Landsat 8) | Allergy, asthma, dry cough, rhinitis, wheezing | Multilevel multivariable logistic regression adjusted by sex, neighborhood deprivation, distance to major roads, maternal history of asthma, crowding and maternal education | Protective | Medium | Porto (PT) |
| Cilluffo et al., 2018 | NDVI-15 (ASTER) | Pulmunary and nasal symptoms | Logistic Ridge multi-exposure regression adjusted by discontinuous/continuous urban fabric, residential surrounding greyness, high traffic roads, $NO_2$, sex, age, family socio-economic status, atopy, diagnosed asthma, parental history of allergy and preterm birth. | Children with a very low exposure to NDVI (1st quartile) had a higher odds of nasal symptoms | High | Palermo (IT) |
| Cilluffo et al. 2022a | Green coverage (%) (CLC) | $FEV_1$, FVC, $FEV_1$/FVC FEF 25-75% | Quantile regression adjusted by age, sex, height, obesity, smoke exposure, mold exposure, parental history of asthma, indoor sensitization, outdoor sensitization, crowding index, physical activity, eczema, high vehicular traffic | Protective | High | Palermo (IT) |
| Cilluffo et al. 2022b | NDVI-15 (ASTER) | Asthma control | Multilevel multivariable logistic regression adjusted by CLC-derived artificial surfaces, $NO_2$ $\geq 40\ \mu g/m^3$, high traffic roads within 200m, passive smoke, mold exposure, pet exposure, crowding index, comorbidity, persistent asthma, atopy, parental education <8 years | Protective | Medium | Palermo (IT) |
| Dadvand et al., 2014 | NDVI-100-150-250-1000 (Landsat 4–5 TM), distance from parks and forest (Urban Atlas) | Asthma, allergic rhinoconjunctivitis | Multilevel multivariable logistic regression adjusted by sex, age, passive tobacco smoke at home, older siblings, type of school (public vs. private), parental education, and parental history of asthma | Negative effect | High | Sabadell (ES) |
| Dzhambov et al., 2021 | NDVI-500 (Landsat 4–5 TM), residential tree cover (%) (Landsat VCF) | Allergic rhinitis, asthma | Multivariable logistic regression adjusted by age, sex, maternal education, low birth weight, maternal smoking during pregnancy, breastfeeding duration, cumulative risk of passive smoking/pneumonia/bronchitis in the 1st year of life, n° of green months during pregnancy, geographic region | Protective | High | Wipp and Lower Inn Alpine valleys (AT) (IT) |
| Fuertes et al., 2014 | NDVI-500 (Landsat 5 TM) | Allergic rhinitis | Generalized Estimating equations with logit link and | Protective in children from GINI/LISA North (Ruhr, | High | Germany (DE) |

(continued on next page)

**Table 1** (*continued*)

| Study reference | Exposure | Outcome | Statistical analysis and confounders | Greenness effect on the respiratory outcomes | Risk of bias evaluation | Study location |
|---|---|---|---|---|---|---|
| | | | exchangeable correlation structure adjusted by age, sex, parental history of atopy, older siblings, maternal smoking during pregnancy, passive tobacco smoke (1–4 years), parental education, cohort | Wesel), negative effect for those from GINI/LISA South (Munich) | | |
| Fuertes et al., 2016 | NDVI-500 (Landsat 5 TM) | Allegic rhinitis | Multivariable logistic regression adjusted by sex, age, parental atopy, older siblings, maternal smoking during pregnancy, current passive tobacco smoke, socioeconomic status. | Protective in children from GINI/LISA North (Ruhr, Wesel) and PIAMA (NL), negative effect for those from GINI/LISA South (Munich) and BAMSE (SE) | Medium | Netherlands (NL)<br>Germany (DE)<br>Sweden (SE) |
| Markevych et al., 2020 | NDVI-100-300-500-1000 (Landsat 5 TM) | Allerigc rhinitis, asthma | Generalized Estimating Equations adjusted by age, sex, season of birth, parental atopy and parental education | Negative impact | High | Leipzig (DE) |
| Müller-Rompa et al., 2018 | NDVI-500, tree cover (Landsat VCF) | Asthma | Multivariable logistic regression adjusted by exposure strata of children living or not close to farms | Not associated | High | Bavaria (DE) |
| Parmes et al., 2020 | Green coverage (%) (CLC) | Allergic rhinitis, asthma, eczema, wheezing | Multivariable logistic regression adjusted by sex, age, BMI, parental history of allergy, maternal education, parental smoking | Negative impact for pooled analyses. Negative effect in children from EDEN (FR) and Fumane (IT). | Not applicable | Ljubljana (SI)<br>Lodz (PL)<br>Nancy (FR)<br>Pisa (IT)<br>Poitiers (FR)<br>Turin (IT)<br>Verona (IT) |
| Squillacioti et al., 2019 | NDVI-300 (Landsat 5 TM) | Allergic cold, asthma, asthmatic bronchitis, bronchitis, cough, phlegm, skin redness, sneezing, wheezing, $FEV_1$, FVC, $FEV_1$/FVC, FEF 25-75% | Multivariable logistic regression adjusted by age, sex, BMI and urinary cotinine (tobacco smoking exposure); Generalized linear models adjusted by age, sex, BMI, cigarettes/day, and exposure to $PM_{10}$ | Protective | High | Turin (IT) |
| Tischer 2017 | NDVI-300 (Landsat 4–5 TM) + residential proximity to green space (Urban Atlas) | Allergic rhinitis, asthma, bronchitis, wheezing | Generalized Estimating Equation models (wheezing and bronchitis) or logistic regression (asthma and allergic rhinitis) adjusted by 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 socioeconomic status and time (in case of wheezing and bronchitis only) | Not associated in pooled analyses. Protective against wheezing yet a risk factor for asthma in children from Asturia and Gipuzkoa. | High | Asturias (ES)<br>Gipuzkoa (ES)<br>Sabadell (ES)<br>Valencia (ES) |
| Tischer 2018 | Green score (NDVI-300 (Landsat 4–5 TM) + green coverage % (CLC)) | Allergic rhinitis, asthma, bronchitis, wheezing | Multivariable logistic regression adjusted by sex, cohort, maternal allergy, maternal smoking during pregnancy, maternal education, breastfeeding, dampness at home 1st year, exposure to passive smoke 1st year | No association in pooled analyses. Negative effect in children from BAMSE (SE) | High | Asturias (ES)<br>Gipuzkoa (ES)<br>Munich (DE)<br>Sabadell (ES)<br>Stockholm (SE)<br>Valencia (ES)<br>Wesel (DE) |
| Winnicki, 2022 | Green coverage (%) (BaseMap) | Asthma | Cox regression models adjusted by family history of asthma, income, education, age and sex | Protective in children growing up in highly urbanized settings and agaist the risk of developing severe asthma. Negative effect vs asthma in the overall population | High | Denmark (DK) |

Footnote. $PM_{10}$: particles with a diameter of 10 µm or less; $PM_{2.5}$: particles with a diameter of 2.5 µm or less; $NO_2$: Nitrogen dioxide; BaP: Benzo(a)pyrene; NDVI: Normalized Difference Vegetation Index calculated within circular buffers surrounding participant's residence and having 15-m, 100-m, 200-m, 250-m, 300-m, 500-m and 1000-m radius; ASTER: Advanced Spaceborne Thermal Emission and Reflection; CLC: Corine Land Cover; BMI: Body Mass Index; $FEV_1$: Forced Expiratory Volume in the 1st second; FVC: Forced Vital Capacity; $FEF_{25–75\%}$: Forced Expiratory Flow at 25–75%.

2018) employed the CLC, provided by the Copernicus Land Monitoring Service (CLMS) of the European Environment Agency (EEA). CLC uses a Minimum Mapping Unit (MMU) of 25 ha: it is organized in five main land cover groups, which – in turn-are divided into more than 40 classes of land cover, including coniferous forest, broadleaved forest, green urban area, etc. In two studies (Dzhambov et al., 2021; Müller-Rompa et al., 2018), the tree cover was assessed using The Landsat Vegetation Continuous Fields (VCF) tree cover layers, which estimate the percentage of horizontal ground in each 30-m pixel covered by woody vegetation greater than 5 m in height and is derived from Landsat-5 TM and Landsat- ETM+. One study (Winnicki et al., 2022) used the national BaseMap.

Proximity analyses were used as a surrogate for the access to greenness. Three studies (Andrusaityte et al., 2016; Dadvand et al., 2014; Tischer et al., 2017) based their proximity analyses on the Urban Atlas map, while another (Alasauskas et al., 2020) did not specify the methodology used. The Urban Atlas is a high-resolution land use map of urban areas provided by CLMS: it covers nearly 800 cities with more than 50,000 inhabitants, distributed across Europe.

As regard to respiratory outcomes, asthma was the most frequently investigated disease, reported by 72.2% of the included studies (Alasauskas et al., 2020; Andrusaityte et al., 2016; Cavaleiro Rufo et al., 2021; Cilluffo et al., 2022b; Dadvand et al., 2014; Dzhambov et al., 2021; Markevych et al., 2020; Müller-Rompa et al., 2018; Parmes et al., 2020; Squillacioti et al., 2019; Tischer et al., 2017, 2018; Winnicki et al., 2022). Seven out of 18 reports (Dzhambov et al., 2021; Fuertes et al., 2014, 2016; Markevych et al., 2020; Parmes et al., 2020; Tischer et al., 2017, 2018) focused on allergic rhinitis, the second most commonly assessed disease. Among several respiratory symptoms, wheezing was recurrently assessed. Only three studies (Almeida et al., 2022; Cilluffo et al., 2022a; Squillacioti et al., 2019) included pulmonary function measurements obtained from spirometry. Apart from spirometry parameters, all the respiratory outcomes were self-reported, mostly using validated questionnaires.

The association between greenness and respiratory outcomes was inconsistent across the included studies. Four out of eight cross-sectional studies reported a protective effect of greenness on respiratory outcomes (Alasauskas et al., 2020; Cilluffo et al., 2022a; Dzhambov et al., 2021; Squillacioti et al., 2019), whilst cohort studies highlighted a greater variability by reporting greenness as a protective factor (Cavaleiro Rufo et al., 2021; Cilluffo et al., 2022b), a risk factor (Markevych et al., 2020) or without reaching a conclusive result (Fuertes et al., 2016; Fuertes et al., 2014; Tischer et al., 2017, 2018; Cilluffo et al., 2018; Winnicki et al., 2022).

Six studies were eligible for meta-analysis (Andrusaityte et al., 2016; Dzhambov et al., 2021; Markevych et al., 2020; Müller-Rompa et al., 2018; Squillacioti et al., 2019; Tischer et al., 2017). Three of them (Andrusaityte et al., 2016; Dzhambov et al., 2021; Müller-Rompa et al., 2018) were included in a meta-analysis for pooling the association between NDVI-500 and asthma (Fig. 1A). The overall association was expressed as ORs for 0.3-increase in the exposure, and was not statistically significant (OR: 0.97, 95% CI from 0.53 to 1.78). Heterogeneity between studies was moderate ($I^2 = 54\%$) and not statistically significant ($p = 0.113$). The other three studies (Markevych et al., 2020; Squillacioti et al., 2019; Tischer et al., 2017) were included in a meta-analysis for pooling the association between NDVI-300 and asthma (Fig. 1B). The overall effect was expressed as ORs for exposure to the high (third) tertile, as compared to the low (first) tertile, and was not statistically significant (OR: 0.65, 95% CI from 0.22 to 1.91). Heterogeneity between studies was high ($I^2 = 74\%$) and statistically significant ($p = 0.021$).

### 3.3. *Dominant tree species across geographical areas*

Hints of peculiar associations of dominant tree species can be appreciated over each geographical area (Fig. 2, Table S2), and its specific biogeographic region (Fig. S3), reflecting different climatic conditions. A protective effect of exposure to greenness and asthma and/or allergic rhinitis was found in children from Boreal-Continental, Atlantic-Mediterranean, Mediterranean, Atlantic, Alpine and Continental-Alpine biogeographic regions (Table 2, Fig. 3). *Pinus sylvestris* was the most frequent tree species, identified as dominant in around 20% of the studies reporting a positive effect of greenness. Fig. 3 summarizes both statistically significant and not significant (NS) associations observed across different climatic regions. Studies located in Continental biogeographic region seemed more likely to highlight a negative effect of greenness exposure on respiratory outcomes, or at least to not remark a significant association. Miscellaneous Pinus genera (*Pinus misc*) and broadleaved trees (*Broad-leaved misc*) were more frequently distributed as dominant trees in these studies. Additionally, *Quercus robur* and *Quercus petrea* were dominant among studies that reported both a positive and a negative association between greenness and various respiratory outcomes.

## 4. Discussion

### 4.1. *Key findings and limitations of the existing evidence*

Despite the growing research interest in the effects of greenness on human health, existing evidence regarding its association with respiratory outcomes remains inconclusive. In this study, we aimed to summarize the available literature systematically, by focusing on primary research on European youths. Additionally, we explored the dominant tree species and biogeographic regions to provide new insights into vegetation characteristics and geographical factors to achieve a higher inter-studies comparability. Our systematic review confirmed that a harmonized approach to investigate greenness effects on respiratory health has not yet been achieved. The main critical pitfalls that might have contributed to the lack of a scientific *consensus* are summarized below.

Firstly, the studies had different designs, sample sizes and methodologies, which could have affected the reliability and validity of their findings and the extent of inter-studies comparability. We observed that cross-sectional studies were more likely to highlight a positive effect of greenness on respiratory health, while longitudinal designs drew mixed conclusions, with many authors reporting no associations or opposite results, depending on the geographical area. The sample sizes varied widely, and many studies did not report any formal calculations for

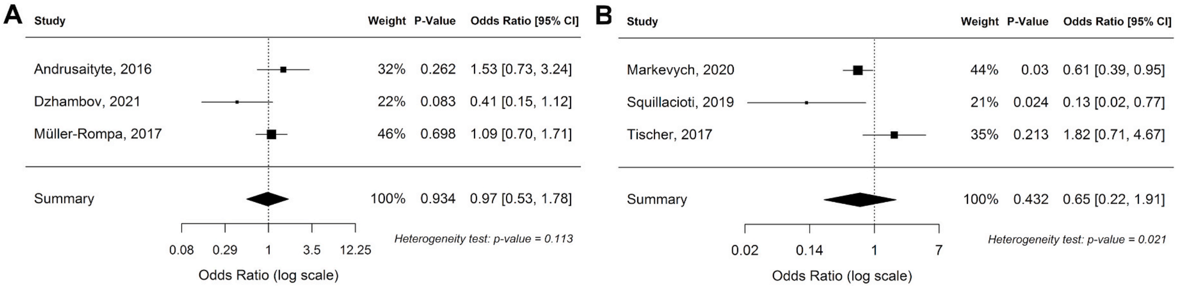

**Fig. 1.** Pooled associations between exposure to greenness and asthma among youths. Panel A: ORs for 0.3-increase in NDVI-500. Panel B: ORs for exposure to the high vs. low tertile of NDVI-300.

Footnote. ORs: odds ratios; NDVI-500: Normalized Difference Vegetation Index calculated within circular buffers with 500-m radius; NDVI-300: Normalized Difference Vegetation Index calculated within circular buffers with 300-m radius.

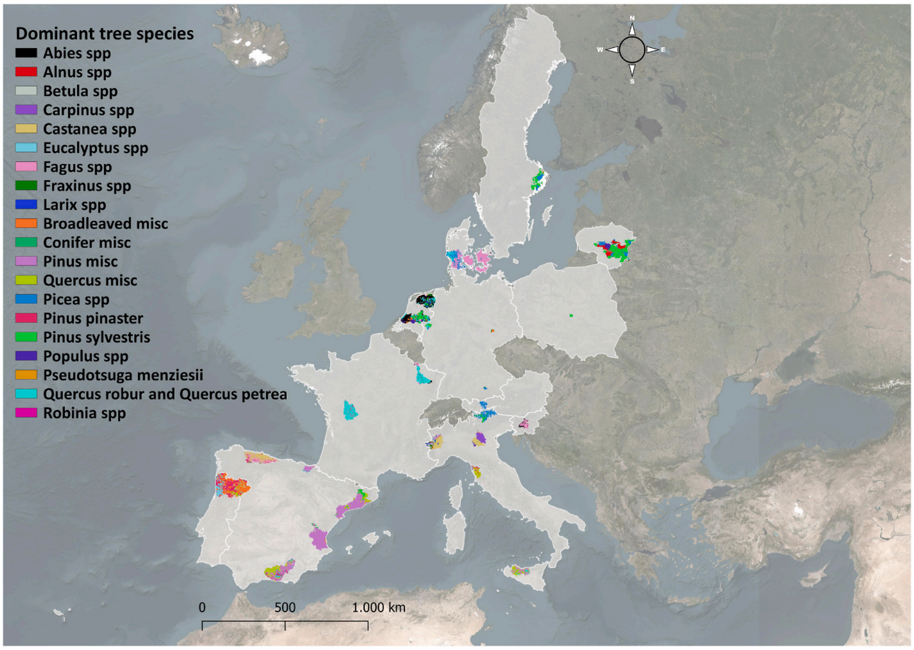

**Fig. 2.** Dominant tree species across study locations approximated to the smaller European NUTS (level 3).

sample size. This may be due to the recently emerging need of studying the effect of greenness from an epidemiological perspective. This approach is relatively new and, in some cases, involves conducting secondary analyses on pre-existing data that had not been collected with the intention of analyzing the effects of greenness on population health.

Secondly, the studies differed in the operational definitions of greenness exposure. Beside the use of satellite-based or proximity analyses that capture different aspects of greenness and cannot be directly comparable, even the operating range (e.g. buffer size) of the same metric can considerably affect the outcome (Browning and Lee, 2017). We observed that NDVI, i.e. the most widely used metric, varied widely in buffer size across different studies. The "optimal" buffer size for NDVI calculations would be able to capture different aspects of greenness exposure, and would strongly depend on the research question, the characteristics of the population, the location scale and the spatial resolution of the satellite images used.

Depending on their socio-economic status and geographic area, newborns and preschoolers may spend a significant amount of time indoors, especially at homes or childcare centers (Pickett and Bell, 2011), which together define the major sources of their environmental exposures. In this case, smaller buffer sizes (up to 1000-m radius) may be suitable for approximating their habitual environment and a local-scale effect of greenness. School-aged children and adolescents may have an increasingly higher level of mobility, compared to young children. Indeed, they may commute to school or to after-school activity venues and, depending on the urbanization level, age and socio-economic status, their mobility patterns may become more complex. Under these circumstances, larger buffer sizes may be an option that, however, remains a poor approximation, although they can capture a higher spatial heterogeneity of greenness as well as the interactions with land use and air quality.

In order to try to overcome these issues related to the Modifiable Area Unit Problem (MAUP), some authors suggested multisite exposure assessments or network buffers along walking routes or different destinations (Amoly et al., 2014; Browning and Lee, 2017; Squillacioti et al., 2022), whilst others proposed the use of GPS-enabled tracking systems to identify the activity space of individuals (Su et al., 2019). A convenient option might be to explore multiple buffer sizes of impact, to identify whether their associations with respiratory health are sensitive to the size of the buffer through sensitivity analyses. In this case, future research should include at least the most widely used buffer sizes range of 100–1000 m, encompassing buffers already used in previous studies (e.g. 100-m, 200-m, 300-m, 500-m and 1000-m), and possibly adding other study-specific measures.

In our systematic review, we observed that the spatial resolution of the satellite images used across the included studies was quite homogenous (30 m); only two studies (Cilluffo et al., 2018; Cilluffo et al., 2022b) used imagery with higher spatial resolution (15 m). Additionally, all the meta-analyzed studies used the same spatial resolution. We, therefore, hypothesize that this may not represent a large source of variability among studies. However, especially in urban areas with a high degree of spatial heterogeneity, higher spatial resolutions might be preferable for NDVI calculations to mitigate the mixed pixel problem, although previous authors detected similar associations with physical health by using different spatial resolution satellite data (Su et al., 2019).

As a third pitfall, the studies may not account for confounding factors, such as air pollution, socio-economic status, and lifestyle factors, that can affect both greenness exposure and respiratory health outcomes. Exceptions to these limitations are three studies (Cilluffo et al., 2018; Cilluffo et al., 2022a,b), in which models were adjusted, respectively, for a total score of Family's Socio-Economic Status (FSES) (categorized using the 1st quartile as the threshold) and for physical activity (>3 times per week). Overall, failure to account for these factors can lead to biased or spurious associations between greenness and respiratory health, contributing to the inconclusive results observed in our meta-analysis on asthma and in previous research, and confirming how mandatory a more harmonized approach is.

Additionally, although questionnaires have been shown to be useful and reasonably valid epidemiological tools, questionnaire-based assessment of respiratory outcomes may be susceptible to misclassification such as recall bias, especially when parents are asked to provide information on behalf of their children (Kuiper et al., 2018). Indeed, in this review, clinical examination (spirometry), assessing lung function outcomes, was only performed in two studies (Cilluffo et al., 2022a; Squillacioti et al., 2019).

At last, the complex interplay between greenness and respiratory health may vary across different geographical regions and climatic

**Table 2**
Dominant tree species and biogeographic regions referred to the study areas.

| Study reference | Specific location | Study design | Sample size referred to location-specific result | Age | Biogeographic region | Dominant tree species | Result on the effect of greenness |
|---|---|---|---|---|---|---|---|
| Positive effect of greenness exposure on respiratory outcomes | | | | | | | |
| Alasauskas et al., 2020 | Vilnius (LT) | Cross-sectional | 54,310 | 7 to 17 | Boreal, Continental | *Pinus sylvestris, Picea* spp | Protective vs asthma |
| Almeida, 2022 | Porto (PT) | Cohort study Generation XXI (G21) | 3278 | 4, 7 and 10 | Atlantic, Mediterranean | *Eucalyptus* spp, *Broadleaved misc* | Protective vs lung function |
| Cavaleiro Rufo et al., 2021 | Porto (PT) | Cohort study Generation XXI (G21) | 1050 | 0 to 7 | Atlantic, Mediterranean | *Eucalyptus* spp, *Broadleaved misc* | Protective vs asthma and allergic rhinitis |
| Cilluffo et al., 2018 | Palermo (IT) | Cross-sectional | 219 | 8.98 (0.9) | Mediterranean | *Pinus misc, Quercus misc* | Protective vs nasal symptoms |
| Cilluffo et al. 2022a | Palermo (IT) | Cross-sectional | 2082 | 12.58 (0.94) | Mediterranean | *Pinus misc, Quercus misc* | Protective vs lung function |
| Cilluffo et al. 2022b | Palermo (IT) | Cohort study CHASER | 179 | 8.70 (2.64) | Mediterranean | *Pinus misc, Quercus misc* | Protective vs asthma control |
| Dzhambov et al., 2021 | Wipp and Lower Inn Alpine valleys (AT) (IT) | Cross-sectional | 1251 | 9.36 (0.65) | Alpine | *Picea* spp, *Fagus* spp, *Pinus sylvestris* | Protective vs asthma and allergic rhinitis |
| Fuertes et al., 2014 | Wesel (DE) | Multi-cohort study | GINI/LISA North: 2497 | 0 to 10 | Atlantic | *Pinus sylvestris, Quercus robur & Quercus petraea* | Protective vs allegic rhinitis |
| Fuertes et al., 2016 | Netherlands (NL) | Multi-cohort study | PIAMA: 3339 | 0 to 12 | Atlantic | *Abies* spp, *Quercus robur & Quercus petraea, Pinus sylvestris* | Protective vs allegic rhinitis |
| Squillacioti et al., 2019 | Turin (IT) | Cross-sectional | 187 | 11.5 (0.8) | Continental, Alpine | *Castanea* spp, *Larix* spp | Protective vs asthma, bronchitis and wheezing |
| Tischer 2017 | Asturias Gipuzkoa (ES) | Cohort study | 2472 | 1 and 4 | Atlantic | *Castanea* spp, *Fagus* spp, *Pinus pinaster, Pinus misc, Quercus robur & Quercus petraea* | Protective vs wheezing yet a risk factor vs asthma |
| Winnicki, 2022 | Fanø, Greve, Lolland, Nyborg, Solrød, Tårnby (DK) | Cohort study | 40,249 | 0 to 2 | Continental, Atlantic | *Fagus* spp | Protective vs the risk of developing severe asthma |
| Negative effect of greenness exposure on respiratory outcomes | | | | | | | |
| Andrusaityte et al., 2016 | Kaunas (LT) | Cross-sectional | 1489 | 4 to 6 | Boreal | *Broadleaved misc, Alnus* spp | Negative effect vs asthma |
| Dadvand et al., 2014 | Sabadell (ES) | Cross-sectional | 3178 | 9 to 12 | Mediterranean | *Pinus misc* | Negative effect vs asthma |
| Fuertes et al., 2014; Fuertes et al., 2016 | Munich (DE) | Multi-cohort studies | 2531 | 0 to 10 | Continental | *Picea* spp, *Betula* spp | Negative effect vs allergic rhinitis |
| Markevych et al., 2020 | Leipzig (DE) | Cohort study | 631 | 0 to 15 | Continental | *Broadleaved misc, Fraxinus* spp | Negative effect vs allergic rhinitis |
| Parmes et al., 2020 | Fumane (IT) | Cross-sectional | 748 | 3 to 14 | Continental, Alpine | *Carpinus* spp | Negative effect vs asthma, allergic rhinitis and wheezing |
| Parmes et al., 2020 | Nancy (FR) | Cohort study | <877 | 3 to 8 | Continental | *Abies* spp, *Quercus robur & Quercus petraea* | Negative effect vs asthma and allergic rhinitis |
| Tischer 2017 | Valencia, Granada (ES) | Cohort | 1364 | 4 | Mediterranean | *Pinus misc, Quercus misc* | Negative effect vs bronchitis |
| Tischer 2018 | Stockholm (SE) | Cohort study | 4089 | 8 | Boreal | *Pinus sylvestris* | Negative effect vs asthma |
| Winnicki, 2022 | Fanø, Greve, Lolland, Nyborg, Solrød, Tårnby (DK) | Cohort study | 40,249 | 0 to 2 | Continental, Atlantic | *Fagus* spp | Negative effect vs the risk of developing asthma |
| No association | | | | | | | |
| Müller-Rompa et al., 2018 | Bavaria (DE) | Cross-sectional | 2265 | 8 | Continental | *Picea* spp | NOT ASSOCIATED |
| Parmes et al., 2020 | Pisa (IT) | Cross-sectional | 135 | 8 to 14 | Mediterranean | *Pinus misc* | NOT ASSOCIATED |
| Parmes et al., 2020 | Viadana (IT) | Cross-sectional | 3771 | 3 to 14 | Continental | *Populus* spp, *Castanea* spp | NOT ASSOCIATED |
| Parmes et al., 2020 | Łódź (PL) | Cohort study | 78 | 7 | Continental | *Pinus sylvestris* | NOT ASSOCIATED |
| Parmes et al., 2020 | Ljubljana (SL) | Cohort study | 168 | 7–8 | Continental, Alpine | *Fagus* spp, *Abies* spp | NOT ASSOCIATED |
| Tischer 2017 | Valencia, Granada (ES) | Cohort | 1364 | 4 | Mediterranean | *Pinus misc, Quercus misc* | NOT ASSOCIATED |

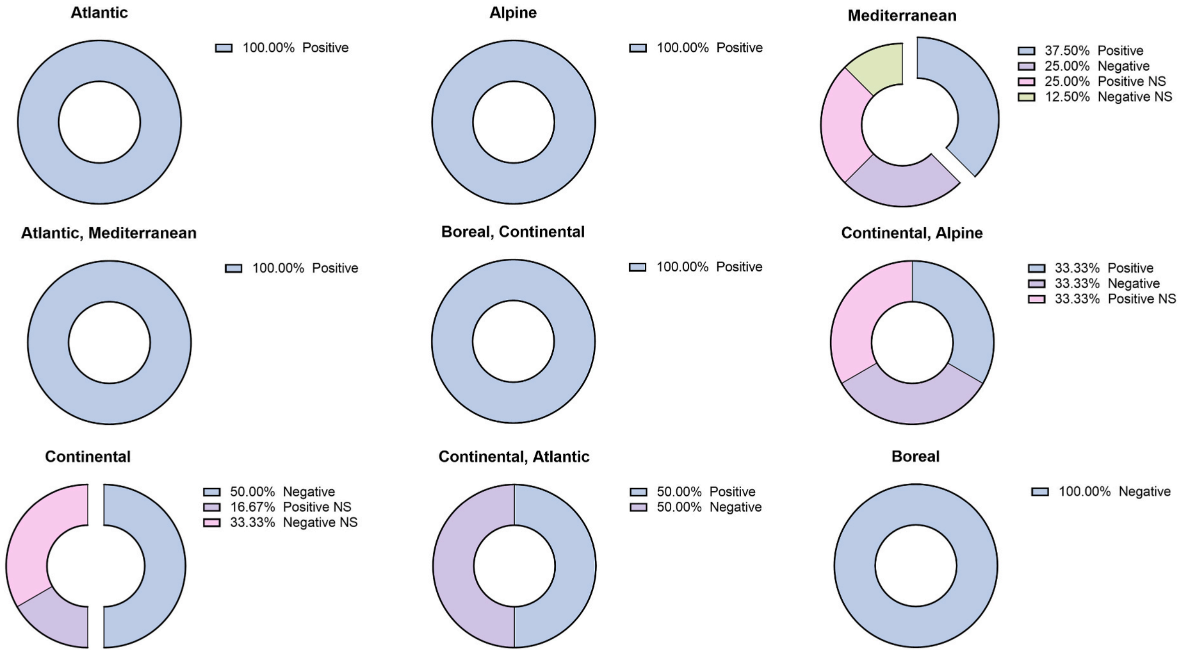

**Fig. 3.** Percentage of studies reporting positive, negative or not significant (NS) associations between exposure to greenness and respiratory outcomes, by climatic region.

conditions. Therefore, the inconsistent findings may reflect the heterogeneity and complexity of this relationship, rather than a lack of scientific *consensus*.

To emphasize this aspect, we conducted some preliminary analyses on dominant tree species and biogeographic regions. Of note, the maps used for this purpose are not solely based on the probability of a particular tree species being distributed throughout the European territory. Instead, they provide data on the distribution of twenty dominant tree species, considering the composition of the soil and other bioindicators derived from temperature and precipitation data (Brus et al., 2012). Our analysis showed that *Pinus sylvestris* was recurrent in the study areas where a protective effect of greenness on respiratory health was observed. In contrast, *Quercus robur* and *Quercus petraea* were equally common in studies that showed a positive association and in those that showed opposite results. This analysis cannot contribute substantially to the urgent need to qualify the type of vegetation. However, it stimulates further considerations on the need of standardizing the exposure assessment through the harmonization of operational choices, potentially including a few elements on dominant or potentially present species in a given geographic area.

The comparison of studies that vary by locations, vegetation patterns and climatic conditions may not be optimal, as the effect of greenness on respiratory health may intrinsically depend on the local characteristics of climate and vegetation. Another aspect, not specifically addressed in this review but equally important, is air quality, which differs between locations and is fundamental to understand the complex interplay between greenness and respiratory health, as already stated by other authors (Fuertes and Jarvis, 2021). The locations of the studies considered cover a relatively small portion of the European territory, usually in urban areas, and may not reflect the numerous potential effects of greenness on respiratory outcomes.

#### 4.1.1. *Future perspectives*

Further research assessing the association between greenness and respiratory health is highly warranted. This should encompass harmonized operational definitions of greenness and studies in different locations, thereby enabling comparisons between geographical areas with similar vegetation patterns, climate and air quality. To date, only a relatively small proportion of the European territory has been investigated and no data are available for many areas including Eastern and Southern Europe.

Greater efforts are needed to develop more accurate metrics able to capture exposure to greenness, both in terms of quantity and quality (e.g. species and/or vegetation type). This might require combined metrics that integrate several sources of information (e.g. by combining data from vegetation indexes, land use maps, GPS, etc.) at a higher spatial resolution. The involvement of experts from different fields, such as ecology, geomatics, botany, etc., could warranty the multidisciplinary approach required for such an arduous task. Not less important, data provided by local administrations could integrate the exposure assessment. Finally, strategies already used in different disciplines might be explored in epidemiology. A good example comes from image interpretation in photogrammetry. It exploits the characteristic reflectance of each object, the spectral signature, to classify vegetation and other surfaces, and this approach may support greenness calculations in future studies.

Additional research is needed to analyze greenness effect in urban and rural contexts, also including low- and middle-income countries, insofar as health associations with greenness may be modified by socioeconomic status, as well as by other relevant potential confounders, effect modifiers and mediators of the association between greenness and respiratory outcomes. They should be tested in future research, with particular attention to geographical characteristics and air pollution.

#### 4.1.2. *Strengths and limitations*

This is the first systematic review that comprehensively synthesizes respiratory health outcomes, focusing on European youths, associated with greenness exposure. As the main strength, we summarized operational choices and pitfalls potentially affecting the exposure assessment and potentially responsible for inconclusive results. We also derived prevalent dominant tree species by using available official maps, in order to speculate further on the influence of geographical location and the importance of studies comparability that should also encompass bioclimatic and vegetation characteristics. We outlined specific suggestions by exploring the relationship between greenness and respiratory health in children and adolescents for supporting future research on this topic.

Some limitations should be acknowledged. We were unable to perform a meta-analysis including all the included studies, because of a substantial heterogeneity among exposures and outcomes. Although we acknowledge the importance of some variables, such as the age, as the associations may differ or even be reversed among younger children (Lin et al., 2022), subgroup analyses could not be conducted given the paucity of the meta-analyzed studies. However, the pooled quantitative effects of NDVI on asthma were calculated in two groups of three primary researches. The analysis on the dominant tree species should be considered as preliminary, and cannot overcome the urgent need of qualifying the type of vegetation in greenness research. Finally, our findings should be approached with caution as our approach was only able to overcome some of the numerous issues potentially affecting the comparability and synthesis among previous studies.

## 5. Conclusions

In the present study, we summarized and delineated some key elements that might have mostly contributed to the lack of scientific *consensus* on the association between respiratory health outcomes and exposure to greenness in youths. An urgent need of harmonized approaches for the operational definition of greenness is imperative. Additionally, the complex interplay between greenness and respiratory health may vary across different geographical regions and climatic conditions: the inconsistent findings may reflect the heterogeneity and complexity of this relationship, rather than a lack of scientific *consensus*. Future studies are needed to achieve a higher inter-study comparability, especially by comparing geographical areas with similar bioclimatic parameters and dominant or potentially present vegetation species.

## CRediT authorship contribution statement

**Giulia Squillacioti:** Conceptualization, Data curation, Methodology, Writing – original draft. **Salvatore Fasola:** Data curation, Formal analysis, Methodology, Writing – original draft. **Federica Ghelli:** Methodology, Writing – review & editing. **Nicoletta Colombi:** Methodology, Supervision, Writing – review & editing. **Alessandra Pandolfo:** Data curation, Formal analysis, Methodology. **Stefania La Grutta:** Project administration, Supervision, Writing – review & editing. **Giovanni Viegi:** Project administration, Supervision, Writing – review & editing. **Roberto Bono:** Conceptualization, Project administration, Supervision, Writing – review & editing.

## Declaration of competing interest

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

## Data availability

Data are available upon request to Authors who published the original studies (this is a systematic review)

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2024.118166.

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