

Vegetation, Air Pollution, and Asthma and Allergy: A Narrative Review

Iana Markevych, PhD

Institute of Psychology, Jagiellonian University, Krakow, Poland

ABSTRACT

Vegetation may benefit asthma and allergy, but null and detrimental associations were also reported. One explanation can be the impact of air pollution. The author aimed to narratively review published epidemiological studies that considered both vegetation and air pollution in relation to asthma, rhinitis, sensitization, and eczema. Search of peer-reviewed original studies was performed in PubMed. Additional articles were identified from the reference lists, the author's personal records, and new publication alerts. Among 18 identified studies, two indicate that vegetation reduces air pollution and is therefore protective against asthma. Results of three studies indicate that protective effects of vegetation on asthma are due to absence of pollution. Four studies identified varying interaction between vegetation and air pollution with allergic outcomes. The remaining studies reported no interplay between vegetation and air pollution in relation to allergy. Combined effects of air pollution and vegetation on allergic outcomes need to be further tested. (BRN Rev. 2021;7(1):47-61)

Corresponding author: Iana Markevych, iana.markevych@uj.edu.pl

Key words: Allergy. Asthma. Epidemiology. Greenness. Greenspace.

Correspondence to:

Dr. Iana Markevych

Institute of Psychology, Jagiellonian University

Ingardena 6

30-060 Krakow, Poland

E-mail: iana.markevych@uj.edu.pl

Received in original form: 18-01-2021

Accepted in final form: 25-02-2021

DOI: 10.23866/BRNRev:2020-0003

www.brnreviews.com

INTRODUCTION

Asthma is a prevalent chronic inflammatory disease characterized by airway obstruction and recurring episodes of bronchospasm, and its symptoms include wheezing, shortness of breath and tightness in the chest¹. It has been estimated that over 339 million people in 2016 suffered from asthma globally and that asthma is the 16th leading cause of years lived with disability². Asthma- and allergy-related socioeconomic costs are high³. In particular, a meta-analysis based on 15 studies indicated that asthmatics and their caregivers have decreased physical, psychological and social functioning compared to their counterparts⁴. Allergy, especially allergic rhinitis, is a known risk factor of asthma. Allergy and asthma started to increase in 1960s⁵, and remain on the rise, especially in middle-to-high-income countries¹.

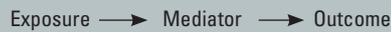
The pathophysiology of allergy is complex. There is a consensus that susceptibility to asthma and allergy is a combination of genetic predisposition, environmental influences, and gene-environment interactions⁶. Exposure to outdoor air pollution has been listed among the culprits of airway allergy occurrence and severity⁷. The results of cellular and animal models' studies support the notion that particulate and gaseous air pollutants generate reactive oxygen species, which results in oxidative stress and inflammatory responses⁸. The results of one recent study demonstrate that parental early-life exposure to particulate air pollution and ozone even in relatively clean Norway and Sweden increased the risk of asthma and hay fever in future offspring, which points out towards transgenerational effects of air pollution on allergy⁹.

Air pollution abatement is commonly presented as the key role of urban vegetation¹⁰. One would thus expect that people who reside in “greener” places will be less likely to suffer from allergies. But vegetation is also a source of biogenic volatile organic compounds, which are ozone precursors, and produce allergenic pollen¹⁰. Exposure to allergenic pollen exacerbates allergic outcomes, as is summarised by two recent systematic reviews^{11,12}. Indeed, exposure to vegetation has been repeatedly shown to correlate with asthma and allergic endpoints, but presence and direction of the association greatly differed across published studies¹³. Apparently, mechanistic links behind the association between vegetation and allergy are less straightforward than just due to lower air pollution in more vegetated places. One explanation is a complex interplay between air pollutants, vegetation, and other relevant factors. First, more vegetated places are less polluted (confounding). Alternatively, air pollution can be actively reduced by vegetation (mediation). Finally, there can be an interaction effect between air pollution and vegetation in relation to allergy, possibly driven by pollen mechanisms (effect modification). Brief explanations on confounder, mediator, and effect modifier variables are provided in Box 1.

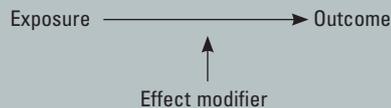
The aim of this article is to narratively review published epidemiological studies that considered both vegetation (commonly labelled as “greenspace” in epidemiological literature) and air pollution in relation to asthma and allergic endpoints, specifically, rhinitis, eczema, and atopic sensitization, and to discuss how these two factors can relate to each other and to allergy. The studies considering specifically plant and fungal pollen were outside of the

Box 1. Confounding, mediation, and effect modification

Confounder is a variable that is related to both an independent variable (exposure) and a health outcome but is not on a causal pathway between an exposure and an outcome.
E.g., smoking is a confounder in the association between coffee consumption and pancreatic cancer and should be adjusted for.



Mediator is a variable that is on a causal pathway between an exposure and an outcome. A mediation model seeks for a mechanistic explanation of an observed association.
E.g., happiness (outcome) is observed to be related to higher school grades (exposure). The possible explanation is that higher school grades increase self-esteem. Self-esteem is on the pathway between school grades and happiness and is therefore a mediator in this association.



If an association differs between different subgroups, it is effect modification. Here, an **effect modifier** is a variable for a subgroup.
E.g., exposure to asbestos (exposure) is related to lung cancer (outcome). This association is much stronger in smokers. Thus, smoking is an effect modifier of the association.

scope as they were summarised by the previous systematic review¹².

METHODS

Search strategy

The literature search of peer-reviewed studies for this narrative review was performed in PubMed end of May 2020 with no time restrictions. The author used a combination of keywords of synonyms for “greenspace” (e.g., “greenness”, “tree*”, “green space”), and “allergy” (e.g., “hayfever”, “asthma”, “allergic disease”) (Box 2).

Titles and abstracts of identified studies were screened, and full texts of candidate original and review articles were retrieved and checked for eligibility. Additional articles were identified from the reference lists of the candidate studies, personal records of the author, and new publication alerts.

Eligibility criteria

Only original quantitative epidemiological studies of any design in English language

Box 2. PubMed search used for the review

```

((greenspace[Title/Abstract] OR green space*[Title/Abstract]
OR greenness[Title/Abstract] OR NDVI[Title/Abstract] OR
greenery[Title/Abstract] OR tree*[Title/Abstract]))
AND
(allerg*[Title/Abstract] OR allergic disease[Title/Abstract]
OR asthma[Title/Abstract] OR eczema[Title/Abstract] OR
rhinitis[Title/Abstract] OR atopy[Title/Abstract] OR
sensitization[Title/Abstract] OR hayfever[Title/Abstract]
OR hay fever[Title/Abstract])
  
```

that considered greenspace metrics, air pollution metrics, and asthma or allergic endpoints were included. If greenspace was the main exposure, air pollution had to be treated as a confounder, a mediator, or an effect modifier. If air pollution was the main exposure, vegetation had to be treated as a confounder, a mediator, or an effect modifier. Studies with any analysis unit and any greenspace and air pollution metrics were eligible. Studies without data on human subjects (e.g., modelling studies), studies with only abstracts (conference abstracts), and reviews were excluded.

Data charting

Data on the following study characteristics were extracted: name of the first author and

the publication year; study design; number of participants, country; age of participants; allergic outcomes; air pollution metrics; green-space metrics; and reporting of results.

RESULTS

Characteristics of included studies

The author identified 18 epidemiological studies that considered co-exposures to greenspace and air pollution in relation to allergic endpoints (Table 1). The studies were published during the last seven years, between 2014¹⁴ and 2021¹⁵. Eight studies were cross-sectional¹⁵⁻²², four studies were longitudinal^{14,23-25}, one study was a combination of cross-sectional and longitudinal design²⁶, three studies were case-control²⁷⁻²⁹, and the remaining two studies^{30,31} were ecological. Sample sizes of the included studies ranged from 174 zip codes³⁰ to over 65,000 children²⁹.

Eight studies were conducted on European data^{14,15,19,24-27,31}, four studies were of North American origin^{16,17,29,30}, three studies originated from Asia^{18,20,28}, two studies were based on Australian and New Zealand data^{21,23}, and finally, one study combined data from Europe, North America, and Australia²².

All included studies treated greenspace metrics as main exposures. In the majority of analyses (n = 11), air pollution was considered to be a confounder of greenspace-allergy relationships, while one study analysed both confounding and mediating effects of air pollution²⁰ and three studies treated air pollution as a confounder and as an effect modifier^{21,22,31} (Table 1). Two studies analysed

only effect modification of air pollution^{14,25} and one study treated air pollution as only a mediator¹⁵.

Outcomes

Asthma and asthma-like symptoms were the most commonly studied outcome – 15 out of 18 studies focussed on it as the only health endpoint or one of the endpoints^{15,16,18-21,23-31}. Rhinitis and allergic rhinitis were considered as one of several outcomes by nine studies^{14,15,17-19,22,24-26}. Four studies also included sensitization^{14,17,22,25}. The least studied was eczema^{15,18,24}.

Vegetation metrics

Exposure to vegetation can be measured using various methods, and the included studies are very heterogenous in this respect. In 13 of the studies, satellite-derived general level of vegetation (i.e., greenness), as defined by the Normalised Difference Vegetation Index (NDVI) or Soil-Adjusted Vegetation Index (SAVI), was utilised as a single or one of the exposure metrics^{14,15,17-23,25-29}. Greenness is the most convenient vegetation metric, as it is rather easily derived from satellite imagery, which is available for all continents and free of charge unless it has a very high resolution; hence, there is no surprise that greenness was the most used. Nine studies used land use- or land cover-derived data on availability of structured green space^{15-19,21,24,26,27,31}. One study used a novel naturalness index, Distance to Nature (D2N)¹⁵, which is an attempt to take into account both built and natural environments. Finally, two studies have

TABLE 1. Characteristics and results of included epidemiological studies

#	Authors (year)	Design	Country	Age	Sample size	Outcome	Air pollution metric	Greenspace metric	Results
Confounding/initial co-adjustment									
1	Alcock et al. (2017) ³¹	Cross-sectional ecological	England, UK	Presumably all ages	26,455 urban residential areas	Standardised hospitalisation rates for asthma in Lower-layer Super Output Areas	NO ₂ , SO ₂ and PM _{2.5}	(1) Percentage of green space and percentage of gardens and (2) Tree density	Models were initially adjusted for NO ₂ /SO ₂ or PM _{2.5} /SO ₂ (impact of confounding was not specifically checked). Reduced asthma hospitalisation was observed in relation to all green exposures
2	Andrusaityte et al. (2016) ²⁷	Nested case-control study	Lithuania	4-6-year-olds	1,489 children	Asthma ever	PM _{2.5} , NO ₂	(1) Normalised Difference Vegetation Index (NDVI) in 100-m, 300-m and 500-m buffers around current home address, (2) Presence of park of 1 ha within 1000-m from the current home address	Greenness was a risk factor for asthma. After additionally adjusting for air pollutants, effect estimates became stronger for children residing close to city parks in areas with low exposure to greenness (before additional adjustment the opposite was true)
3	Donovan et al (2018) ²³	Longitudinal study within routinely collected data and semi-individual exposure assessment	New Zealand	18-year-olds	49,956 children	Asthma ever	Road density in meshblock, NO ₂ in meshblock	(1) Mean meshblock NDVI, (2) Vegetation diversity defined by number of natural, native, and non-native land cover types	Models were initially adjusted for air pollution and road density (impact of confounding was not specifically checked). Greenness and vegetation diversity were protective against asthma, some non-native vegetation land cover classes increased risk of asthma
4	Douglas et al. (2019) ¹⁶	Cross-sectional ecological study	USA	Presumably all ages	2,347 census tracts	Asthma emergency department visits (AEDV)	Diesel particulate matter (DPM)	Min-max normalised acres of parks and open space (PPOS) per census tract	Models were initially adjusted for DPM and PPOS (impact of confounding was not specifically checked), DPM was associated with increased AEDV while PPOS was related to decreased AEDV
5	Feng and Astell-Burt (2017) ²¹	Cross-sectional study	Australia	6-7-year-olds	4,447 children	Asthma according to ISAAC definition	Parent-reported perceptions of traffic volume within close proximity of the household	Quantity of green space available as a percentage of land-use within the SA2 of residence	Living in places with perceived heavy traffic was a risk asthma for asthma. Effect estimates of traffic perception did not change after additional adjustment for green space quantity
6	Fuertes et al. (2016) ²²	Multicentre cross-sectional study	Australia, Canada, Germany, The Netherlands and Sweden	6-8-year-olds and 10-12-year-olds	13,016 children	Allergic rhinitis (doctor diagnosis or symptoms) and aeroallergen sensitization	NO ₂ or distance to major road	NDVI in a 500-m buffer around the current home address	Very heterogenous associations between NDVI and allergic outcomes were observed, and this pattern was not clarified by co-adjusting for NO ₂

(Continues on next page)

TABLE 1. Characteristics and results of included epidemiological studies (*Continuation*)

#	Authors (year)	Design	Country	Age	Sample size	Outcome	Air pollution metric	Greenspace metric	Results
7	Gernes et al. (2019) ¹⁷	Cross-sectional study	USA	7-year-olds	478 children	Outdoor aeroallergen sensitisation (overall, to grasses, and to trees) ever and current allergic rhinitis	Traffic related air pollution (TRAP)	(1) NDVI, tree cover and grass/shrub cover in 400-m buffers around current home address	Models were initially adjusted for TRAP, but crude estimates also shown, and they were similar to the estimates from the main models. Grass coverage was associated with an increased risk of sensitization to grass pollens, trees tended to have an opposite, albeit non-significant effects
8	Hsieh et al. (2019) ²⁸	1:1 matched case-control study with semi-individual exposure assignment	Taiwan	0-18-years-olds	7,040, with 3,520 asthmatics and 3,520 controls	Ever diagnosed asthma	CO, PM _{2.5} and NO ₂	Coverage by the mean NDVI above 0.4 on the township level treated as categories of 0-20%, 21-40%, 41-60%, 61-80%, and 81-100%	Models were initially adjusted for air pollutants (impact of cofounding was not specifically checked), and residing at townships with more greenness was related to occurrence of asthma, but not at the highest tertile
9	Lai and Kontokosta (2019) ³⁰	Cross-sectional ecological study	USA	Presumably all ages	174 zip codes	Asthma hospitalization and emergency department visit rates	PM _{2.5}	Relative allergenicity (measured as the proportion of trees with severe pollen allergen divided by the total number of street trees in a given area)	Models were initially adjusted for PM _{2.5} (impact of cofounding was not specifically checked), and relative allergenicity was related to increased asthma emergency department visits
10	Li et al. (2019) ¹⁸	Cross-sectional study	China	12-15-years-olds	5,643 children	Current asthma, ever asthma, ever eczema, and ever rhinitis	PM _{2.5}	(1) NDVI in 100-m, 200-m, 500-m and 1,000-m around current home address and (2) distance to the nearest park in quartiles from the current home address	Living closer to parks was related to lower odds of current and ever asthma, and these results did not change after additional adjustment for PM _{2.5}
11	Parnes et al. (2019) ²⁴	Multi-centre longitudinal study	Italy, France, Slovenia, and Poland	3-14-years-olds	8,063 children	Current wheeze, lifetime asthma, current asthma, lifetime allergic rhinitis, and eczema	NO ₂ /PM ₁₀	CORINE-derived green space cover (and also specifically agricultural space, forest cover, coniferous forests, deciduous forests and mixed forests) in 100-m, 300-m, 500-m, and 1,000-m buffers around residential addresses	More green space and more coniferous forests were related to increased odds of asthma, wheeze, and allergic rhinitis. Further adjustment of the analyses for residential outdoor air pollution did not change the estimates for the associations between land cover features and outcomes
12	Sbihi et al. (2015) ²⁹	1:5 matched case-control study	Canada	0-5 years-olds and 6-10-years-olds	More than 65,000 children	Incident asthma in pre-school (0-5 years) and school age (6-10 years)	NO, NO ₂ , PM _{2.5} , black carbon	NDVI in the 100-m buffer around postal code at birth	Higher perinatal greenness was related to lower incidence of asthma in preschool age. Accounting for contemporaneous co-exposures to air pollutants enhanced the effect of greenness on incident asthma

(Continues on next page)

TABLE 1. Characteristics and results of included epidemiological studies (Continuation)

#	Authors (year)	Design	Country	Age	Sample size	Outcome	Air pollution metric	Greenspace metric	Results
13	Tischer et al. (2018) ¹⁹	Multicentre cross-sectional study	Spain, Germany, Sweden	4-years-olds	14,364 children	Asthma, allergic rhinitis, and wheeze	NO ₂ and distance to the major road	Combination of lifetime residential mean NDVI and presence of green space in 300-m buffer together with air pollution markers	The factor described by "outdoor exposure" (NO ₂ , distance to major road, greenness, and green land use) significantly increased the risk for bronchitis within the first year
14	Tischer et al. (2017) ²⁶	Cross-sectional for asthma and allergic rhinitis, and repeated measurements for wheeze	Spain	4-year-olds	2,472 children	Asthma, allergic rhinitis, and wheeze	NO ₂	NDVI and presence of green space in 300-m buffer around a current address	After additional adjustment for NO ₂ exposure at the first year of life, the association between exposure to higher residential surrounding greenness and wheezing was found to be slightly stronger in the Euro-Siberian region
15	Zeng et al. (2020) ²⁰	Cross-sectional	China	Schoolchildren with mean age 10.3 ± 3.6 years	59,754 children	Current asthma and current wheeze	PM ₁₀ , NO ₂	(1) NDVI in 30-m, 100-m, 300-m, 500-m and 1000-m around current school address and (2) Soil-Adjusted Vegetation Index (SAVI) n 30-m, 100-m, 300-m, 500-m and 1000-m around current school address	Effect estimates did not change after the additional individual adjustment for NO ₂ and PM ₁₀ . Greenness was protective against asthma and wheeze
Mediation									
1	Dzhambov et al. (2020) ¹⁵	Cross-sectional	Austria and Italy	8-12-years-olds	1,251 children	Current asthma symptoms, ever asthma symptoms, ever allergic rhinitis (AR) symptoms, and ever eczema symptoms	NO ₂	(1) NDVI, (2) tree canopy cover, (3) agricultural cover, (4) presence of domestic garden and (5) naturalness index (Distance to Nature, D2N) in 500-m buffer around a current home address and in 100-m buffer around a current school address	Higher naturalness and greenness, as measured by different indicators, were associated with lower prevalence of current asthma symptoms through lower NO ₂ levels
2	Zeng et al. (2020) ²⁰	Cross-sectional	China	Schoolchildren with mean age 10.3 ± 3.6 years	59,754 children	Current asthma and current wheeze	PM ₁ , PM _{2.5} , PM ₁₀ , NO ₂	(1) NDVI in 30-m, 100-m, 300-m, 500-m and 1000-m around current school address and (2) SAVI n 30-m, 100-m, 300-m, 500-m and 1000-m around current school address	Reduced air pollution, especially PM _{2.5} and PM ₁₀ mediated the inverse associations between school greenness and asthma (up to 95% of associations) but not wheezing in schoolchildren

(Continues on next page)

TABLE 1. Characteristics and results of included epidemiological studies (*Continuation*)

#	Authors (year)	Design	Country	Age	Sample size	Outcome	Air pollution metric	Greenspace metric	Results
Effect modification									
1	Alcock et al. (2017) ³¹	Cross-sectional ecological	England, UK	Presumably all ages	26,455 urban residential areas	Standardised hospitalisation rates for asthma in LSOAs	NO ₂ , SO ₂ and PM _{2.5}	(1) Percentage of green space and percentage of gardens and (2) Tree density	Increases in tree density were associated with greater reductions in asthma hospitalisation when NO ₂ , PM _{2.5} and SO ₂ were higher and had no benefit when they were very low. In contrast, there was some (limited) evidence that increases in green space and gardens were associated with greater reductions in asthma hospitalisation when NO ₂ and PM _{2.5} exposure were lower.
2	Feng and Astell-Burt (2017) ₂₁	Cross-sectional study	Australia	6-7-year-olds	4,447 children	Asthma according to ISAAC definition	Parent-reported perceptions of traffic volume within close proximity of the household	Quantity of green space available as a percentage of land-use within the SA2 of residence.	Among children considered to be exposed to high traffic volumes and areas with 0 to 20% green space quantity, the odds ratio of asthma was 1.87 (95% CI 1.37 to 2.55). However, the association between heavy traffic and asthma was lower for participants living in areas with over 40% green space coverage (odds ratio for interaction 0.32, 95% CI 0.12 to 0.84). No association between asthma and green space coverage was observed for participants not exposed to heavy traffic
3	Fuertes et al. (2016) ²²	Multicentre cross-sectional study	Australia, Canada, Germany, The Netherlands and Sweden	6-8-year-olds and 10-12-year-olds	13,016 children	Allergic rhinitis (doctor diagnosis or symptoms) and aeroallergen sensitization	NO ₂ or distance to major road	NDVI in a 500-m buffer around the current home address	Very heterogenous associations between NDVI and allergic outcomes were observed, and this pattern was not clarified by stratifying for NO ₂
4	Fuertes et al. (2014) ¹⁴	Longitudinal cohort with repeated measurements on allergic outcomes	Germany	10-year-olds	5,803 children	Allergic rhinitis, eyes and nose symptoms and aeroallergen sensitisation	PM _{2.5} and NO ₂	NDVI in a 500-m buffer around different addresses, including birth and current address	In the urbanized area, risk estimates increased from null to significantly elevated with increasing PM _{2.5} tertiles. For the rural area, risk estimates increased with increasing PM _{2.5} tertiles, but from significantly protective to null. Risk estimates were significantly below one in the lowest NO ₂ strata for this area
5	Markevych et al. (2020) ²⁵	Longitudinal cohort with repeated measurements on allergic outcomes	Germany	15-year-olds	631 children	Asthma and allergic rhinitis, sensitization to aeroallergens and food allergens	NO ₂ and ozone	(1) NDVI in 500-m buffer around birth address, (2) Number of all trees from the tree registry around birth address, and (3) Number of allergenic trees (two definitions) around birth address	Trees and allergenic trees were associated with a higher prevalence of allergic rhinitis when NO ₂ levels were comparatively high or ozone was comparatively low

CI: confidence interval; NO₂: nitrogen dioxide; ISAAC: International Study of Asthma and Allergies in Childhood; PM: particulate matter; SA2: statistical local areas level 2; SO₂: sulphur dioxide.

employed information on allergenic trees^{25,30}, although they used different approaches to decide on tree allergenicity.

Air pollution metrics

Quality of air pollution is characterized by concentrations of various pollutants, or by using traffic proxies. Most of the included studies considered at least two metrics ($n = 12$) and only 6 studies operated on only one air pollution metric (Table 1). Most of studies ($n = 13$) have employed nitrogen dioxide (NO_2) as one of or the only air pollution metrics^{14,15,19,20,22-29,31} and one study also considered nitrogen oxides (NO)²⁹. Eight studies used particulate matter with aerodynamic diameter $< 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$)^{14,18,20,27-31}. Four studies utilised objectively measured or perceived traffic indicators as proxies for air pollution^{19,21-23}. Two studies included particulate matter with aerodynamic diameter $< 10 \mu\text{m}$ (PM_{10}) as one of the air pollution indicators^{20,24}. One per pollutant study has also considered: diesel particulate matter¹⁶, traffic-related air pollution without specification¹⁷, carbon monoxide (CO)²⁸, black carbon²⁹, sulphur dioxide (SO_2)³¹, particulate matter with aerodynamic diameter $< 1 \mu\text{m}$ (PM_1)²⁰, and ozone²⁵.

Confounding studies

Out of 15 studies that considered air pollution to be a confounder in relationship with allergy, nine studies explicitly checked how effect estimates changed after additional adjustment for air pollutants^{17,18,20-22,24,26,27,29}. In three studies in Lithuania²⁷, Canada²⁹ and Spain²⁶ additional adjustment enhanced identified protective

associations of greenspace on asthma or asthma-like symptoms. Six other studies from diverse world regions reported no change in association when simultaneous adjustment for air pollution and greenspace was considered^{17,18,20-22,24}.

The remaining six studies (Table 1) initially corrected their models for air pollution concentrations, and impact of confounding by air pollution is unknown in those cases. In two studies, prevalence of asthma outcomes was lower in greener settings^{16,23}, while four other studies reported higher allergic risk among residents of more vegetated areas^{19,24,28,30}.

Figure 1 shows more details on these results, separately for every group of outcomes. When rhinitis, sensitization, or eczema were considered, no confounding was observed, or the impact of confounding was not checked specifically. Vegetation tended to be not associated with these outcomes or show harmful effects. In the case of asthma, vegetation tended to be a beneficial exposure. Air pollution was a confounder in three studies.

Mediation studies

Only two studies – one in China²⁰ and another in Austria and Italy¹⁵ – considered air pollution a variable on the pathway between greenspace and asthma, and both found that air pollution partially mediated this association. While the Austrian-Italian study checked mediation only by NO_2 , the Chinese study employed four air pollutants, and all four of them were reported to mediate the association with asthma, but not with wheezing. No mediation for rhinitis or

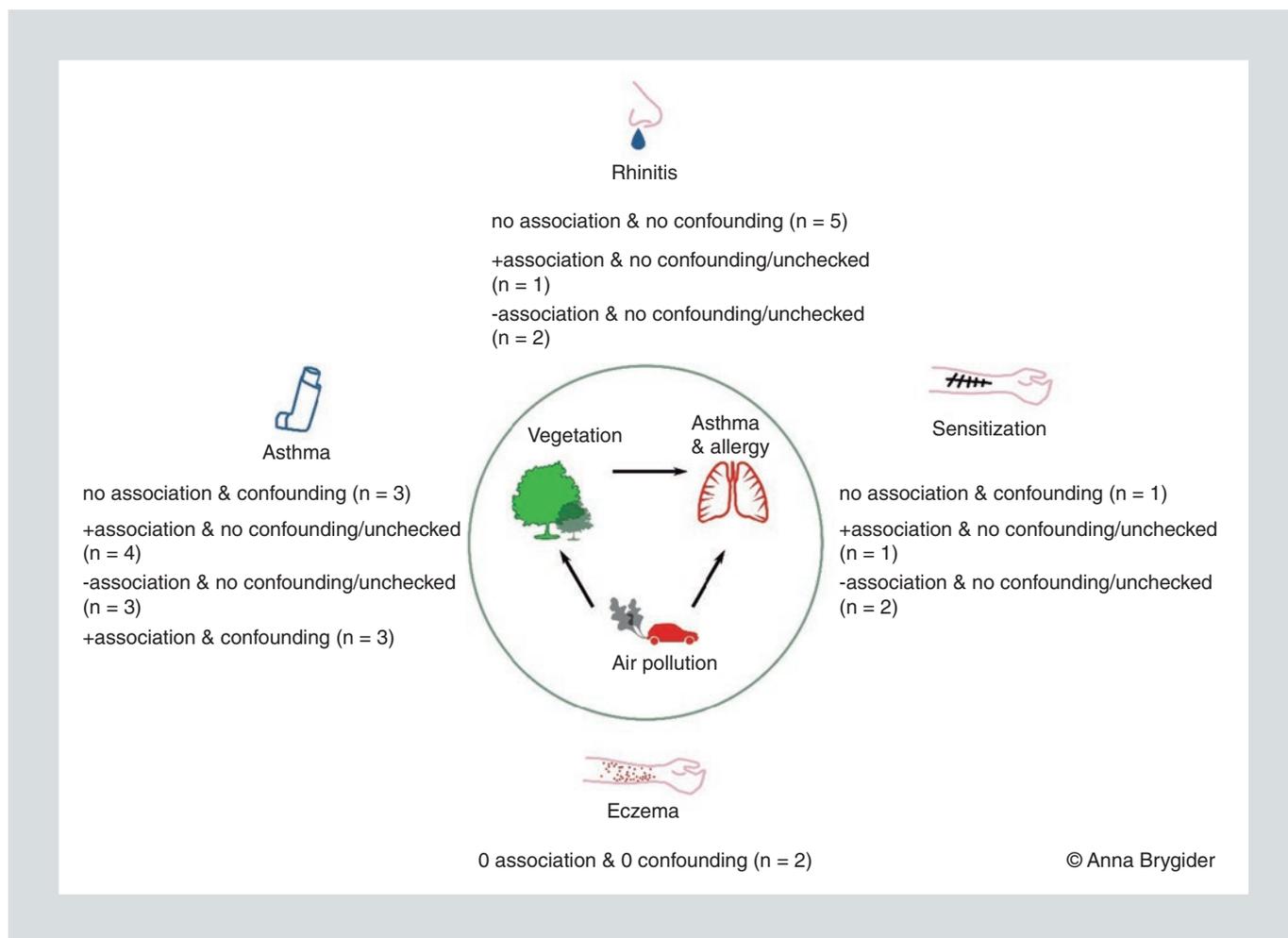


FIGURE 1. Summary of the findings from the **confounding** studies.

“+association” refers to a “beneficial association”, “-association” refers to a “detrimental association”.

eczema was observed in the study of Dzhambov et al.¹⁵ (Fig. 2).

Effect modification studies

Perhaps, the most informative were studies that considered interaction effects of vegetation and air pollution. In the two-centre German study by Fuertes et al.¹⁴, longitudinal associations between greenness and allergy differed depending seemingly on the area urbanicity. When effect modification by particulate matter with diameter < 2.5 μm ($\text{PM}_{2.5}$) was

considered, the associations between greenness and all considered allergic endpoints were more detrimental in more polluted settings. Just in the urbanized Munich area, the associations shifted from null in the residents of the lowest $\text{PM}_{2.5}$ tertile to detrimental in the highest $\text{PM}_{2.5}$ tertile, while in the rural Wesel area, the associations were protective in the lowest $\text{PM}_{2.5}$ tertile and null in the highest $\text{PM}_{2.5}$ tertile. Interestingly, this trend was not present when NO_2 was considered instead of $\text{PM}_{2.5}$. In another German study²⁵, the direction of effect modification depended on the considered air pollutant. While NO_2 enhanced

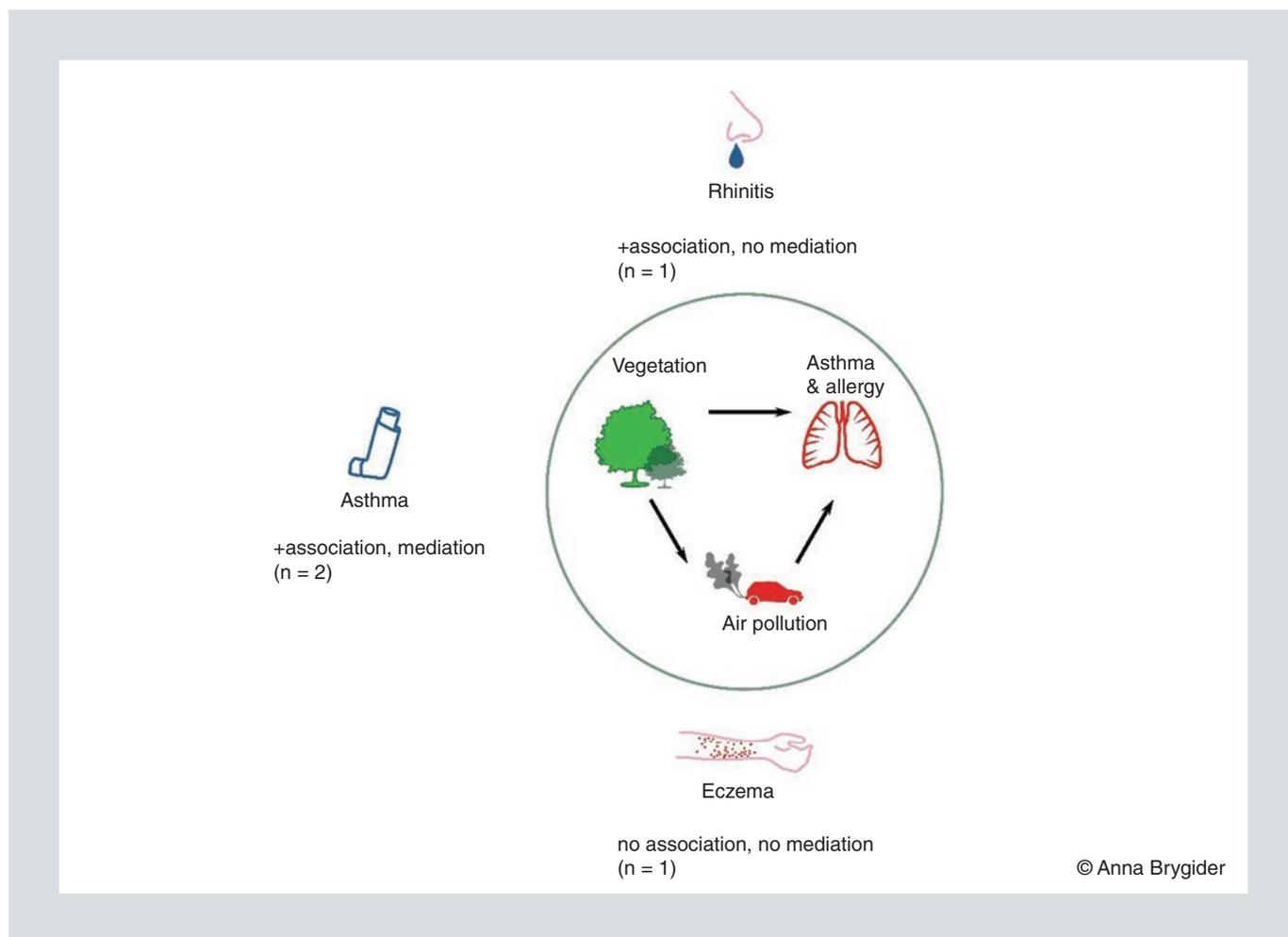


FIGURE 2. Summary of the findings from the **mediation** studies. “+association” refers to a “beneficial association”.

detrimental associations between trees and allergenic trees and allergic rhinitis, the opposite trend was evident for ozone.

In one Australian study²¹, no association was observed between residing in areas with higher green cover in the general population. Children from the least green areas exposed to heavy traffic volumes were at higher risk of having asthma, while children exposed to heavy traffic but living in green areas, had a lower risk of asthma. This observation was partially in line with an England-based study³¹ where greater reductions in asthma hospitalisations

were observed in more polluted with NO_2 , $\text{PM}_{2.5}$ and SO_2 urban areas.

The multicentre study by Fuertes et al.²² observed mixed associations between living in more vegetated areas and odds of having allergic rhinitis or aeroallergen association, which seemingly depended on urbanisation. However, statistical tools in hand could not clarify this trend, including the check of potential effect modification by air pollution levels.

Figure 3 is an attempt to generalise the complicated findings above for each of the outcomes.

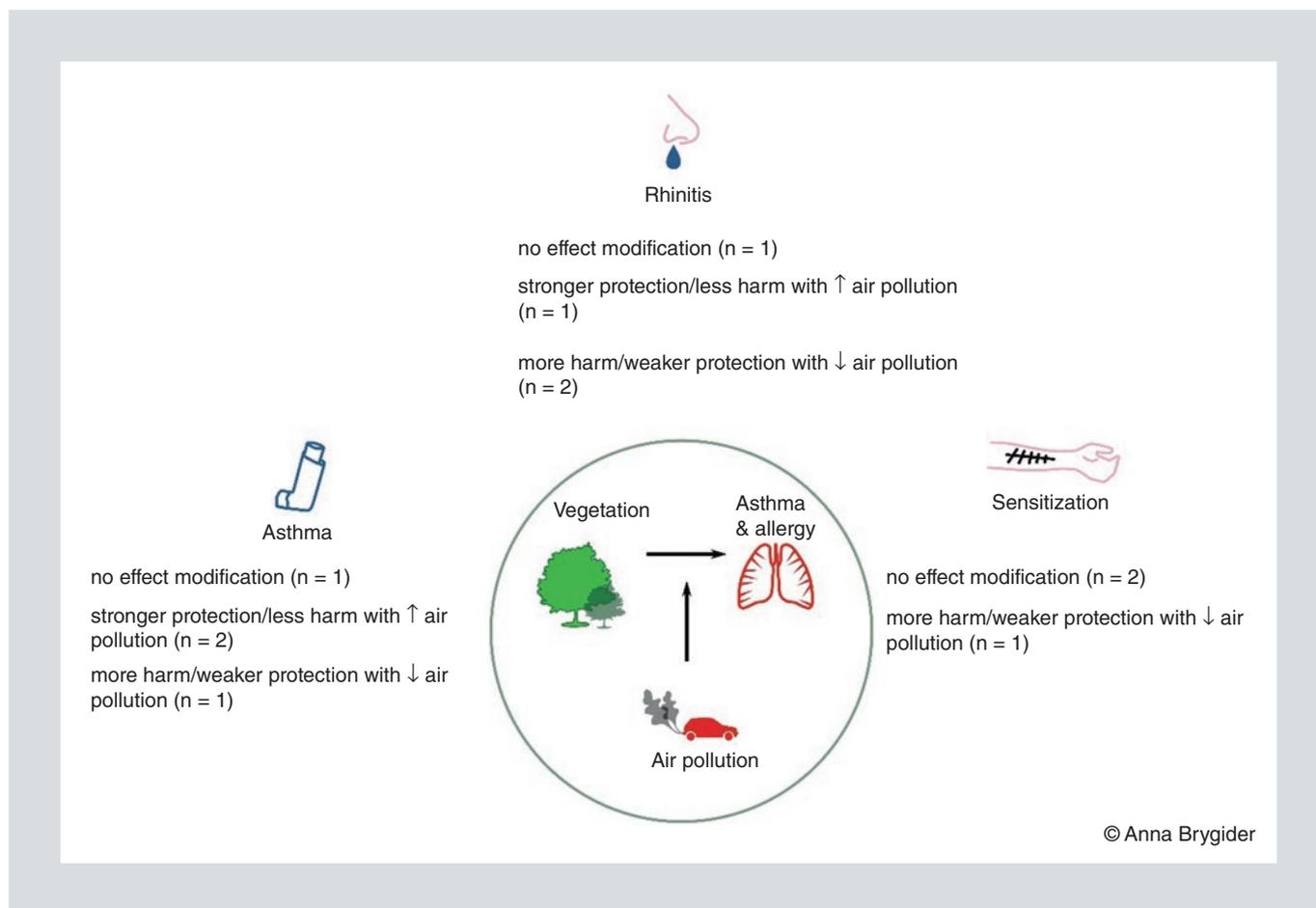


FIGURE 3. Summary of the findings from the **effect modification** studies.

Stronger beneficial or weaker harmful effects of vegetation on asthma and allergic outcomes were observed in three studies. Weaker beneficial or stronger harmful effects of vegetation on asthma and allergic outcomes were observed in four studies. Four studies did not reveal any pattern.

DISCUSSION

Among the identified 18 studies, two studies indicate that vegetation reduces air pollution and is therefore protective against asthma (mediation). The results of three studies indicate that the protective effects of vegetation

on asthma are due to the absence of pollution (confounding). Four studies identified varying patterns of effect modification between greenspace and air pollution with allergic outcomes. The remaining studies reported no interplay between vegetation and air pollution in relation to allergy.

Although there is consensus on the interrelation between air pollution and vegetation, the nature of it is a matter of scientific dispute across various disciplines. One group of scientists claim that the reported associations between greenspace and allergy, as reported by many studies, are non-existent per se and reflect an inverse spatial correlation between

vegetation and air pollution³². Indeed, there are typically no traffic arteries or industries in parks, gardens, or other highly vegetated areas. Summarising the evidence from **confounding** studies included in this review, it is hard to agree that associations between greenspace and allergy can be explained by air pollution. Air pollution seems to either not affect the greenspace-allergy link, or to even enhance it (the so-called positive confounding). Yet, most of the studies in this review did not compare effect estimates prior to and after adjustment by air pollution; therefore, it is hard to be certain.

Mainly driven by modelling studies, another group of scientists support the notion that vegetation actively reduces concentrations of air pollutants³³. Theoretically, this reduction can occur by the deposition of air pollutants on leaf surfaces and the subsequent uptake by leaf stomata, as well as by modification of air circulation, but a few existing experimental studies do not always support this¹⁰. For instance, trees may well trap air pollutants in street canyons, thus, the spatial arrangement of vegetation is not to be neglected¹⁰. Among the identified literature included in this review, two studies formally tested mediation by air pollution of the greenspace-asthma relationship, and both reported partial **mediation**. Perhaps, even if vegetation can actively remove only a very little portion of air pollution³⁴, this can still explain part of the greenspace-allergy relationship. More mediation studies to validate this assumption are needed.

Apparently, not only the residential amount of vegetation plays a role in developing allergic conditions, but also species composition,

most of all, their allergenicity^{10,25}. Air pollutants can modify the viability, germination, and chemical composition of pollen grains³⁵. Molecular studies have reported that allergenicity of the many common species, as tested by Immunoglobulin E (IgE) reactivity, increased after treatment by NO₂, and there is some evidence for ozone as well³⁶. Yet only three reviewed studies^{23,25,30} attempted to disassemble the association between allergenic vegetation and allergy from the effects of all vegetation on allergy. Only one of the above studies²⁵ explored interaction between allergenic vegetation and air pollution and detected it in the expected direction – that detrimental effects of allergenic vegetation on the development of allergic rhinitis were stronger in more polluted with NO₂ settings. This finding was partially in line with only one another included study¹⁴. The rest of the **effect modification** studies revealed differing patterns. Overall, if to assume pollen-air pollution interactions as a driving mechanism here, one would expect more harmful or less beneficial effects of vegetation on asthma and allergy in more polluted settings. But this was the case in only one third of the associations. I might only speculate that the four out of five included effect modification studies did not operate on any specific definitions of vegetation and were conducted in settings with different urbanicity. In Markevych et al.²⁵ we observed that a big fraction of the tree vegetation of the city of Leipzig was allergenic, in comparison to rural surroundings of the city. Definitely, effect modification by air pollution of the association between greenspace and allergy should be further explored, and studies should preferably use more specific data on vegetation and its allergenicity. Interestingly, the recent

review on air pollution and pollen interactions in relation to respiratory health also concludes on the weak evidence for this interaction in epidemiological studies¹².

The current review includes very heterogeneous studies on interplay between vegetation and air pollution in relation to asthma and allergic outcomes. One difficulty identifying relevant studies was that commonly, confounding, mediation, and effect modification checks are considered to be additional analyses in epidemiological studies. Thus, these results are not mentioned in the Abstract, and often are only briefly mentioned in the Results section with the effect estimates being provided in the Supplement, if at all. All texts of potentially relevant studies had to be attentively checked manually but it is very likely that not all studies were identified. The systematic search only happened in PubMed, and only by one person, each of which increases the risk of overlooking relevant studies. Checks in personal records and following publication alerts could not compensate for this. It is not to mention that likely, the authors of the included studies checked more ways of air pollution and vegetation to interplay than what they reported (e.g., confounding and mediation were both checked but only mediation results ended up in the final publication). If confounding, mediation or effect modification was tested but findings were null, these were likely to be not reported either, which could have led to a publication bias towards the existence of interplay between vegetation and air pollution in relation to asthma and allergy. This review was limited to asthma and allergic outcomes only and did not include studies on respiratory but not allergic outcomes. Also, studies on pollen

and air pollution were outside of the scope. Finally, since this narrative review was meant to map the existing evidence rather than quantitatively assess it, no formal assessment of the risk of bias of the included studies was performed.

CONCLUSION

Exposure to vegetation tends to be protective against asthma, but the findings are mixed for allergic outcomes. Surprisingly, the role of air pollution in this association has been rarely researched in epidemiological studies. Based on the scarce available evidence it is premature to make any definite conclusions yet. More studies testing confounding, mediative, and effect modifying effects of air pollution on the association of interest are needed.

FUNDING

Iana Markevych is supported from the “NeuroSmog: Determining the impact of air pollution on the developing brain” (Nr. POIR.04.04.00-1763/18-00) which is implemented as part of the TEAM-NET programme of the Foundation for Polish Science, co-financed by EU resources, obtained from the European Regional Development Fund under the Smart Growth Operational Programme.

DISCLOSURES

Dr. Markevych has nothing to disclose.

REFERENCES

1. Ferrante G, La Grutta S. The Burden of Pediatric Asthma. *Front Pediatr.* 2018;6:186.

2. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; 390:1211–59.
3. Nunes C, Pereira AM, Morais-Almeida M. Asthma costs and social impact. *Asthma Res Pract.* 2017;3:1.
4. Silva N, Carona C, Crespo C, Canavarró MC. Quality of life in pediatric asthma patients and their parents: a meta-analysis on 20 years of research. *Expert Rev Pharmacoecon Outcomes Res.* 2015;15:499–519.
5. Platts-Mills TA. The allergy epidemics: 1870–2010. *J Allergy Clin Immunol.* 2015;136:3–13.
6. Han Y, Jia Q, Jahani PS et al. Genome-wide analysis highlights contribution of immune system pathways to the genetic architecture of asthma. *Nat Commun.* 2020;11:1776.
7. Khreis H, Kelly C, Tate J, Parslow R, Lucas K, Nieuwenhuijsen M. Exposure to traffic-related air pollution and risk of development of childhood asthma: A systematic review and meta-analysis. *Environ Int.* 2017;100:1–31.
8. Huang SK, Zhang Q, Qiu Z, Chung KF. Mechanistic impact of outdoor air pollution on asthma and allergic diseases. *J Thorac Dis.* 2015;7:23–33.
9. Kuiper IN, Markevych I, Accordini S et al. Associations of Preconception Exposure to Air Pollution and Greenness with Offspring Asthma and Hay Fever. *Int J Environ Res Public Health.* 2020;17:5828.
10. Eisenman TS, Churkina G, Jarilawa SP et al. Urban trees, air quality, and asthma: An interdisciplinary review. *Landscape and Urban Planning* 2019; 187:47–9.
11. Erbas B, Jazayeri M, Lambert KA et al. Outdoor pollen is a trigger of child and adolescent asthma emergency department presentations: A systematic review and meta-analysis. *Allergy.* 2018;73:1632–41.
12. Lam HCY, Jarvis D, Fuertes E. Interactive effects of allergens and air pollution on respiratory health: A systematic review. *Sci Total Environ.* 2021;757:143924.
13. Ferrante G, Asta F, Cilluffo G, De Sario M, Michelozzi P, La Grutta S. The effect of residential urban greenness on allergic respiratory diseases in youth: A narrative review. *World Allergy Organ J.* 2020;13:100096.
14. Fuertes E, Markevych I, von Berg A et al. Greenness and allergies: evidence of differential associations in two areas in Germany. *J Epidemiol Community Health.* 2014;68:787–90.
15. Dzhambov AM, Lercher P, Rüdiger J, Browning MHEM, Markevych I. Allergic symptoms in association with naturalness, greenness, and greyness: A cross-sectional study in schoolchildren in the Alps. *Environ Res.* 2020 (In press) DOI:10.1016/j.envres.2020.110456.
16. Douglas JA, Archer RS, Alexander SE. Ecological determinants of respiratory health: Examining associations between asthma emergency department visits, diesel particulate matter, and public parks and open space in Los Angeles, California. *Prev Med Rep.* 2019;14:100855.
17. Gernes R, Brokamp C, Rice GE et al. Using high-resolution residential greenspace measures in an urban environment to assess risks of allergy outcomes in children. *Sci Total Environ.* 2019;668:760–7.
18. Li L, Hart JE, Coull BA, Cao SJ, Spengler JD, Adamkiewicz G. Effect of Residential Greenness and Nearby Parks on Respiratory and Allergic Diseases among Middle School Adolescents in a Chinese City. *Int J Environ Res Public Health.* 2019;16:991.
19. Tischer C, Dadvand P, Basagana X Et al. Urban upbringing and childhood respiratory and allergic conditions: A multi-country holistic study. *Environ Res.* 2018;161:276–83.
20. Zeng XW, Lowe AJ, Lodge CJ et al. Greenness surrounding schools is associated with lower risk of asthma in schoolchildren. *Environ Int.* 2020;143:105967.
21. Feng X, Astell-Burt T. Is Neighborhood Green Space Protective against Associations between Child Asthma, Neighborhood Traffic Volume and Perceived Lack of Area Safety? Multilevel Analysis of 4447 Australian Children. *Int J Environ Res Public Health.* 2017;14:543.
22. Fuertes E, Markevych I, Bowatte G et al. Residential greenness is differentially associated with childhood allergic rhinitis and aeroallergen sensitization in seven birth cohorts. *Allergy.* 2016;71:1461–71.
23. Donovan GH, Gatzolis D, Longley I, Douwes J. Vegetation diversity protects against childhood asthma: results from a large New Zealand birth cohort. *Nat Plants.* 2018;4:358–64.
24. Parmes E, Pesce G, Sabel CE et al. Influence of residential land cover on childhood allergic and respiratory symptoms and diseases: Evidence from 9 European cohorts. *Environ Res.* 2019:108953.
25. Markevych I, Ludwig R, Baumbach C et al. Residing near allergenic trees can increase risk of allergies later in life: LISA Leipzig study. *Environ Res.* 2020;191:110132.
26. Tischer C, Gascon M, Fernández-Somoano A et al. Urban green and grey space in relation to respiratory health in children. *Eur Respir J.* 2017:49.
27. Andrusaityte S, Grazuleviciene R, Kudzyte J, Bernotiene A, Dedele A, Nieuwenhuijsen MJ. Associations between neighbourhood greenness and asthma in preschool children in Kaunas, Lithuania: a case-control study. *BMJ Open.* 2016;6:e010341.
28. Hsieh CJ, Yu PY, Tai CJ et al. Association between the First Occurrence of Asthma and Residential Greenness in Children and Teenagers in Taiwan. *Int J Environ Res Public Health.* 2019;16:2076.
29. Sbihi H, Tamburic L, Koehoorn M, Brauer M. Greenness and Incident Childhood Asthma: A 10-Year Follow-up in a Population-based Birth Cohort. *Am J Respir Crit Care Med.* 2015;192:1131–3.
30. Lai Y, Kontokosta CE. The impact of urban street tree species on air quality and respiratory illness: A spatial analysis of large-scale, high-resolution urban data. *Health Place.* 2019;56:80–7.
31. Alcock I, White M, Cherrie M, Wheeler B, Taylor J, McInnes R, Otte Im Kampe E, Vardoulakis S, Sarran C, Soyiri I, Fleming L. Land cover and air pollution are associated with asthma hospitalisations: A cross-sectional study. *Environ Int.* 2017;109:29–41.
32. Markevych I, Schoierer J, Hartig T et al. Exploring pathways linking greenspace to health: Theoretical and methodological guidance. *Environ Res.* 2017;158:301–17.
33. Franchini M, Mannucci PM. Mitigation of air pollution by greenness: A narrative review. *Eur J Intern Med.* 2018;55:1–5.
34. Xing Y, Brimblecombe P. Role of vegetation in deposition and dispersion of air pollution in urban parks. *Atmos Environ.* 2019;201:73–83.
35. Sénéchal H, Visez N, Charpin D et al. A Review of the Effects of Major Atmospheric Pollutants on Pollen Grains, Pollen Content, and Allergenicity. *ScientificWorldJournal.* 2015;2015:940243.
36. Frank U, Ernst D. Effects of NO₂ and Ozone on Pollen Allergenicity. *Front Plant Sci.* 2016;7:91.