Association between greenness and allergic respiratory diseases in European children: A systematic review

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Abstract

Background The presence of asthma and allergic rhinitis in children significantly adds to the overall burden of illness worldwide. In Europe, the prevalence of asthma in children is more than 10% and continues to rise. Research conducted earlier has established a relationship between the prevalence of asthma and allergic rhinitis among children and the availability of green spaces in their residential surroundings. However, it is still uncertain whether the presence of green spaces is a protective factor or a cause of exacerbation. The objective of this systematic review was to evaluate the current evidence on the correlation between exposure to green environments and the development of allergic respiratory diseases in European children.

Methods Four databases were searched for primary studies relevant to the association between greenness and asthma or allergic rhinitis in children. After removing duplicates and applying exclusion criteria, 16 articles remained from a total of 20 156 search results.

Results Different methodologies were applied to measure greenness in the living environment. Some indices unselectively measured vegetation, others used geographical inventories of green areas, water zones, agricultural and urban spaces or tree canopy cover, or considered the representation of different fauna species in the living environment (Species Richness Index). Distance to greenspace was also evaluated as a variable. Seven out of the 16 included articles used the Normalised Difference Vegetation Index (NDVI) to measure greenness, which makes the NDVI the most used parameter in this systematic review. For almost all indices, conflicting results are reported between the occurrence of respiratory symptoms in children and the greenness of the living environment. Sometimes trends were observed, some of which were statistically significant under very strict conditions (e.g. considering distance to green).

Conclusion There is no conclusive evidence on the association between greenness and respiratory outcomes in European children based on current findings.

Abstract (Nederlands)

Context Astma en allergische rinitis dragen in belangrijke mate bij tot de wereldwijde ziektelast bij kinderen. In Europa is de prevalentie van astma bij kinderen meer dan 10% en blijft nog steeds stijgen. Eerder uitgevoerde studies hebben een verband aangetoond tussen de prevalentie van astma en allergische rinitis bij kinderen en de aanwezigheid van groene ruimte in hun woonomgeving. Het is echter nog niet duidelijk of de aanwezigheid van groen een beschermende factor is of juist bijdraagt aan verergering van de ziekte.
Onderzoeksvraag Het doel van deze systematische review was om het huidige bewijsmateriaal te evalueren met betrekking tot de correlatie tussen blootstelling aan groene omgeving en de ontwikkeling van allergische luchtwegaandoeningen bij Europese kinderen.
Methode Er werd in vier databanken gezocht naar primaire studies relevant voor de associatie tussen groene ruimte en astma of allergische rinitis bij kinderen. Na het verwijderen van duplicaten en toepassen van exclusiecriteria, werden van een totaal van 20 156 resultaten 16 studies geïncludeerd in deze review.
Resultaten Er werden verschillende methodieken gebruikt om de aanwezigheid van groen in de leefomgeving te definiëren. Door sommige parameters werd vegetatie op een niet selectieve manier gemeten. Andere methoden maakten gebruik van geografische inventarissen van groene ruimte, waterzones, landbouw en stedelijke ruimte of boomkroonbedekking. Bepaalde studies bekeken ook de representatie van verschillende faunasoorten in de leefomgeving (Species Richness Index). De afstand tot groene ruimte werd mede bestudeerd als variabele. Zeven van de 16 geïncludeerde studies gebruikten de 'Normalised Difference Vegetation Index' (NDVI) om de groene ruimte te evalueren, wat maakt dat de NDVI de meest gebruikte parameter was in deze systematische review. Voor bijna alle meetmethoden worden tegenstrijdige resultaten gerapporteerd tussen het voorkomen van luchtwegklachten bij kinderen en de groenheid van de leefomgeving. Soms werden er trends waargenomen, waarvan sommige statistisch significant waren onder zeer strikte voorwaarden (bijvoorbeeld rekening houdend met de afstand tot groen).
Conclusie De huidige bevindingen over de associatie tussen het voorkomen van groene ruimte en de uitkomst van respiratoire aandoeningen bij Europese kinderen blijven inconclusief.

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Introduction

Asthma and allergic rhinitis are significant contributors to the global burden of childhood illness. Among chronic diseases in children, asthma is the most prevalent. **(1)** Standardised methods have shown an increase in asthma prevalence worldwide between the mid-1990s and mid-2000s. The International Study of Asthma and Allergies in Childhood (ISAAC) has revealed differences in prevalence by global region, country as well as socioeconomic gradients. Similarly the World Health Organization (WHO) reports that the prevalence of asthma among children varies greatly across different countries and regions, ranging from 3.7% to 26.8%. **(2)** In Europe, the prevalence of asthma is over 10% in children and continues to rise. **(3)** In Flemish general practice prevalence rates of asthma were slightly lower, particularly 65 per 1000 children in the global practitioner population in 2021 (coded as ICPC R96), based on data from Intego. **(4) (Figure 1 and 2)**

Diagnosing asthma in early childhood can be difficult, primarily relying on clinical judgement and an assessment of symptoms and physical findings. Before the age of 3, over a third of children experience at least one episode of expiratory wheezing, usually in conjunction with or following viral upper respiratory tract infections. However, more than half of these children no longer exhibit symptoms by age 6. **(5)** Although around 20% of children diagnosed with asthma at age 7 will no longer have symptoms by the time they reach puberty, approximately 80% will continue to experience asthma later in life, with half experiencing periodic symptoms. **(6)**

Respiratory conditions can have a detrimental impact on children's health-related quality of life by causing insomnia, decreased levels of daytime physical activity, and by affecting school and social performance. According to the Global Initiative for Asthma (GINA) guidelines, achieving and maintaining disease control is the main goal of asthma management. **(7)** This involves working with healthcare professionals to develop an individualised asthma management plan, which may include medication, monitoring of symptoms, and avoidance of triggers.

Recent research suggests that access to or exposure to greenspaces can impact human health significantly via various pathways. **(8, 9)** Previous studies have linked the prevalence of asthma and allergic rhinitis in children to the presence of green areas in their residential surroundings. It is still uncertain whether the presence of greenness serves as a protective element or contributes to the worsening of a situation. The underlying reasons for this could be attributed to various confounding factors related to greenspace exposure, including but not limited to vegetation biodiversity, environmental microbiome, human behaviour, or geographical location **(10, 11)**.

Asthma is a common condition in Belgium, and environmental exposures can play a role in asthma control and exacerbations. As primary care physicians, general practitioners have an important role in preventive medicine and can help inform patients about the potential impact of environmental exposures on respiratory health. If there is a link between exposure to greenness and the prevalence of asthma or allergic rhinitis in children, family doctors can provide patients with advice on how to minimise exposure to potential triggers. For example, they can recommend that families avoid spending time outdoors during peak pollen seasons or avoid certain types of vegetation that may trigger respiratory symptoms. Gaining a more profound understanding of how asthma prevalence relates to exposure to different types of greenspaces can enable well-informed urban planning

choices and promote the creation of healthier habitats. Overall, primary care physicians can play an important role in promoting respiratory health and reducing the burden of asthma by educating patients about the potential impact of environmental exposures and providing guidance on how to minimise exposure to potential triggers.

Our objective was to conduct a review of the existing evidence to assess the current state of knowledge and identify any gaps in information regarding the correlation between children's exposure to greenness and the development of allergic respiratory diseases in Europe.

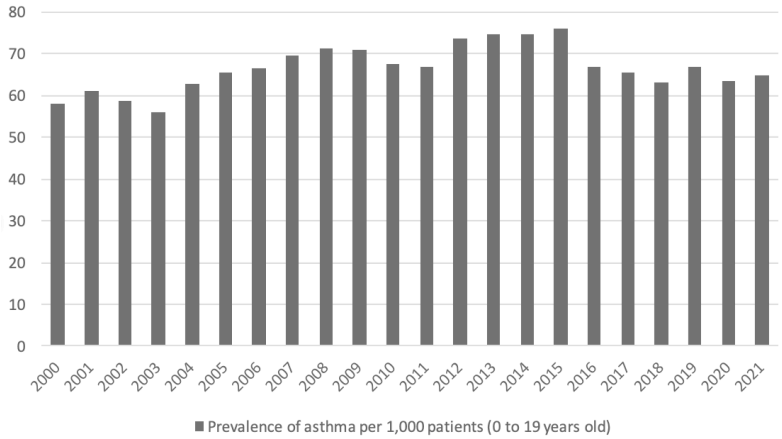


Figure 1: Prevalence rates of ICPC-96 code asthma per 1000 patients ranging from 0 to 19 years old in Belgium general practice population. Data from INTEGO. **(4)**

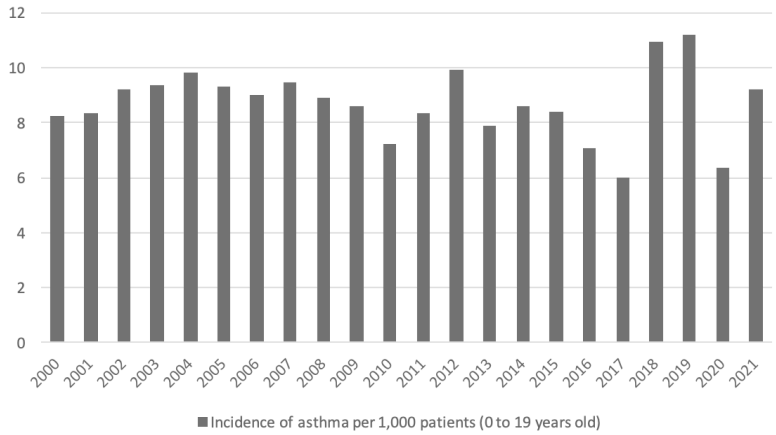


Figure 2: Incidence rates of ICPC-96 code asthma per 1000 patients ranging from 0 to 19 years old in Belgium general practice population. Data from INTEGO. **(4)**

Methods

Design

Inclusion criteria were studies published since 2018 (the last 5 years) that are relevant to the association between greenness and asthma or allergic rhinitis in children (under the age of 18) living in Europe. The included studies had to be written in English and a full text must be available.

Systematic reviews were excluded in this review because not all the separated studies included in these reviews met the inclusion criteria.
The search strategy was constructed from four concepts that met the search criteria: children, green space, asthma and allergic rhinitis. The MeSH terms for these concepts were used to build up the search strategy for PubMed. **(Appendix 1)** This search query was adjusted to the other databases. The search strategy was conducted in four databases (Pubmed, Embase, Cochrane Library and Web Of Science Core Collection) and gave a total of 20 156 records. All these records were collected in the reference management program EndNote. A total of 16 718 records were removed before screening: 4 183 were duplicates and 12 535 were published before 2018.

After screening on title and abstract, 16 studies were included in this review. These search results are shown in the PRISMA 2020 Flow Diagram. **(Figure 3)**

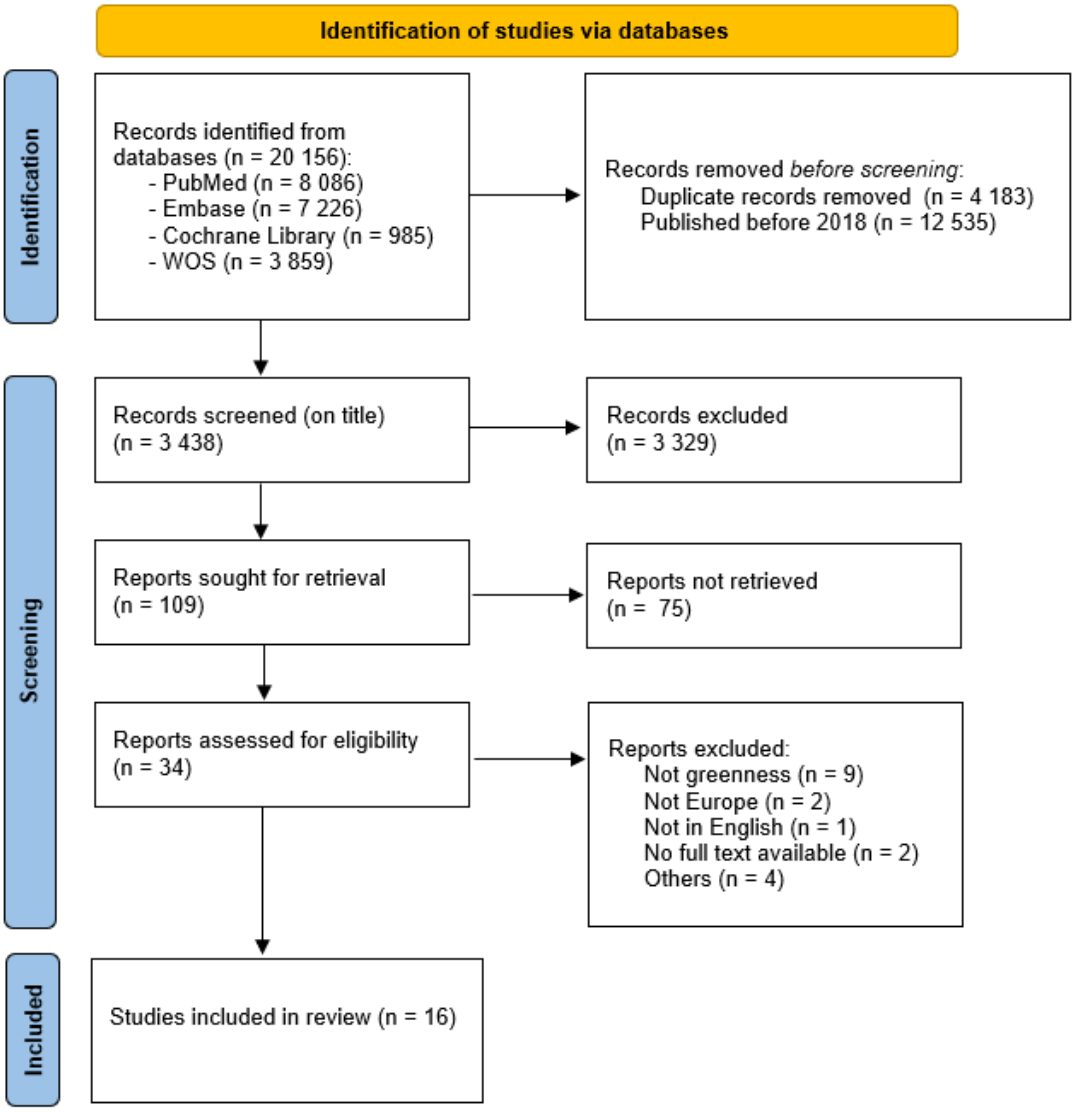


Figure 3: PRISMA Flow Diagram representing literature search results. **(12)**

Analytic strategy

The included studies were summarised in a table to give an overview of the study design and sample, study objective, study methods and statistical analysis, outcome variable, greenness measurements and relevant findings. **(Table 1)**

Authors (Year)	Study design & Sample	Study objective	Study methods & Statistical Analysis	Outcome variable	Greenness measurement	Relevant findings
Cilluffo et al. (2022)	Cohort; 179 asthmatic children (5-16 years); Palermo, Italy; September 2015 – December 2018	To evaluate the association between asthma control and exposure to greenness and other outdoor or indoor environmental factors.	SIDRIA questionnaire; skin prick tests; C-ACT and ACT; spirometry Logistic regression model	Asthma control	CORINE land-cover classes; NO_2 Concentrations; NDVI	Low NDVI exposure was a risk factor for uncontrolled asthma (OR: 2.662, 95% CI (1.043-6.799))
Dzhambov et al. (2021)	Cross-sectional; 1251 schoolchildren (8-12 years); Alpine valleys in Austria and Italy; 2004/2005	To investigate the association between different characteristics of residential and school environment and allergic symptoms in schoolchildren	Children's mothers completed a self-administered, standardised questionnaire (ISAAC) Logistic regression	Allergic symptoms	NDVI; Tree canopy cover; Agricultural cover; Imperviousness cover; Industrial cover; Distance to Nature (D2N)	Schoolchildren residing in places with lower naturalness and higher greyness may be more likely to have allergic rhinitis and possibly asthma

Authors (Year)	Study design & Sample	Study objective	Study methods & Statistical Analysis	Outcome variable	Greenness measurement	Relevant findings
Winnicki et al. (2022)	Cohort; 40 249 Danish individuals born between 1995 and 2015	Does childhood exposure to biodiverse greenspace reduce the risk of developing asthma?	Use of asthma medicines and hospital diagnosis of asthma Cox univariate and multivariate regression models	Asthma	The Danish Biodiversity Map; BaseMap (land-cover data) 2km circular buffer around the homes	High levels of greenspace cover are linked to increased risk of developing asthma, but may reduce the risk of severe asthma. Density of urban greenspace is associated with a decreased risk of asthma.
Aerts et al. (2021)	Tree inventory datasets of 18 urban green spaces (5940 trees; 278 taxa; 93 ha) Brussels, Belgium	To examine tree pollen allergy risks in urban green spaces in the Brussels Capital Region, Belgium, and changes in allergy risks associated with green space interventions, potential changes in tree allergenic potential and increased pollination duration.	Tree pollen allergy risk of each urban green space was calculated for the present situation (baseline IUGZA). Then IUGZA was calculated repeatedly for 13 scenarios that represented potential changes in tree species composition, allergenic potential, and pollen season duration. Linear mixed models	Tree pollen allergy risk	IUGZA	The allergic risk (AR) increased by 11 - 27% in increased allergenic potential scenarios, and by 44% in the increased pollen season duration scenario. AR increased by 99 - 111 % in combined scenarios despite preventive tree removal.

Authors (Year)	Study design & Sample	Study objective	Study methods & Statistical Analysis	Outcome variable	Greenness measurement	Relevant findings
Aerts et al. (2020)	Observational Retrospective cohort study Children aged 6 - 18 years (n = 1872) Belgium Study period 2010 - 2014	To investigate if residential exposure to different types of green space is associated with childhood asthma prevalence in Belgium.	Asthma medication sales Generalised log-linear mixed effects models with repeated measures.	Asthma	Land cover data were provided by the Belgian National Geographic Institute (NGI-IGN). Green space types and their relative cover were extracted from the Top10Vector database	Living close to areas with high grass cover may negatively impact child respiratory health (increased asthma medication sales).
Bednarek et al. (2019)	Cohort 176 hospitalised children with newly-diagnosed IgE-dependent asthma Lublin, Poland Study period: 2014 - 2015	Assess the impact of the living environment on the basic demographic and clinical parameters of preschool children with IgE-dependent asthma.	Peak expiratory flow (PEF) measurement Skin prick tests Serological evaluation (IgE, selenium and calcium) The Spearman correlation coefficient	Asthma	Place of residence (urban area or rural area)	Urban children with asthma were treated with antibiotics significantly more often ($p<0.05$) during hospitalisation, while the OR value (5.08) indicated that the rural environment necessitates a more frequent use of OGCs during hospitalised therapy of asthma. Residence does not determine the clinical course of IgE-dependent asthma in preschool children.

Authors (Year)	Study design & Sample	Study objective	Study methods & Statistical Analysis	Outcome variable	Greenness measurement	Relevant findings
Cavaleiro Rufo et al. (2021)	Birth cohort 1050 children Porto, Portugal	To evaluate the effect of early-life exposure to greenness and species richness on the development of allergic diseases and asthma in children.	Self-reported questionnaire (ISAAC) Generalised linear mixed models	Asthma and allergy at age 4 and 7.	NDVI (within 100m, 200m and 300m from the child home) SRI	Children living in neighbourhoods surrounded by high levels of SRI were at a significantly higher risk developing allergic sensitization (OR (95% CI) = 2.00 (1.04; 3.86)) at age 4; 2.35 (1.20;4.63) at age 7). Living surrounded by greener environments was significantly associated with a lower prevalence of asthma and rhinitis at the age of 7 (0.41(0.18;0.97 and 0.37(0.15;0.93), respectively).
Cilluffo et al. (2018)	Cross-sectional 219 children (8–10 years) Palermo, Italy April, 2013	To simultaneously evaluate the association between indicators of urban-related environmental exposures, including those for “green”, “grey” and NO2 exposure, with respiratory/allergic and general symptoms	Questionnaires (SIDRIA) self-administered by parents and children. Multiple Logistic and Poisson ridge regression models	Asthma, rhino-conjunctivitis Respiratory and/or allergic symptoms	NDVI Residential Surrounding Greyness (RSG) CORINE land-cover classes	Participants lived near each other, so little variation in NDVI. No statistically significant relationships between NDVI ≤ 0.15 (1st quartile) and pulmonary symptoms (breathlessness, wheeze) [aOR = 0.98 95% CI (0.79, 1.21)]. A very low exposure to NDVI ≤ 0.15 (1ste quartile) had a higher odds of nasal symptoms (OR = 1.47, 95% CI [1.07-2.03].

Authors (Year)	Study design & Sample	Study objective	Study methods & Statistical Analysis	Outcome variable	Greenness measurement	Relevant findings
Paciencia et al. (2019)	Cross-sectional study 701 schoolchildren (7–12 years) Porto, Portugal	To assess the effect of the environment and the walkability surrounding schools on lung function, airway inflammation and autonomic nervous system activity.	Self-administered questionnaire (ISAAC-based) Spirometry with bronchodilation, exhaled level of nitric oxide, exhaled breath condensate (EBC), pupillometry, skin prick test (SPT), weight and height Mixed effect models	Lung function, airway inflammation and pH from exhaled breath condensate.	The land use near each school was calculated on the basis of the European Urban Atlas using a geographical information system (GIS)	Green school areas tended to be associated with higher lung volumes (FVC, FEV1 and $FEF_{25–75\%}$) compared with built areas.
Cavaleiro Rufo et al. (2020)	Cross-sectional study 845 schoolchildren Porto, Portugal January 2014 to March 2015	To understand how the exposure to different levels of species richness surrounding urban primary schools may influence the development of allergic diseases and asthma in children.	Spirometry with bronchodilation Exhaled level of nitric oxide (FeNO) Skin-prick tests (SPT) Questionnaire (ISAAC) Mixed models	Lung function and allergic disease development	SRI (100m radius surrounding primary schools)	A unitary increment in the SRI was associated with an average increase of approximately 2 and 3 mL in FEV1 and FVC, respectively. However, this increase in lung function was not associated with any clinically relevant protective effect on allergy and asthma development.
Molnar et at. (2021)	Cross-sectional study 3836 schoolchildren (6-12 years) Budapest, Hungary September 2019	To evaluate the prevalence of asthma and its associating environmental factors.	Parent-reported questionnaire (ISAAC)	Asthma (prevalence and severity)	Environmental risk factors	Children commuting from the suburbs had a lower risk of asthma than children living centrally in the city (OR = 0.64, CI: 0.43 - 0.93, p = 0.0236). The proximity of a weedy area was associated with higher asthma risk (OR = 1.39, CI: 1,15 - 1,69, p = 0,0007).

Authors (Year)	Study design & Sample	Study objective	Study methods & Statistical Analysis	Outcome variable	Greenness measurement	Relevant findings
Paciencia et al. (2021)	Longitudinal cohort study 730 children, 0 - 10 years Porto, Portugal	To assess critical periods of exposure as well as the effect of longitudinal trajectories of exposure to green and blue spaces on the development of allergic sensitization in children at the age of 10 years.	Interviews and questionnaires for parents Serum samples for specific IgE antibodies. Latent class linear mixed models	Allergic sensitization	NDVI (within 100 m, 250 m and 500 m of the child's residence at birth) Distance to the nearest blue space.	Residing in neighbourhoods surrounded by more vegetation at 10 years (HR (95% CI) = 0.095 (0.011, 0.823)), as well as lifetime exposure to a trajectory of higher levels of NDVI, were associated with a lower risk of allergic sensitization (HR (95% CI) = 0.539 (0.301 - 0.965)).
Tischer et al. (2018)	Birth cohort study (INMA; LISAplus; GINIplus; BAMSE) 15646 children Spain, Germany, Sweden	To disentangle and prospectively evaluate the association between indicators of urban-related indoor and outdoor environmental exposure characteristics with respiratory and allergic health outcomes in young children	Parental-completed questionnaires Random-effects meta-analyses and factor analysis	Wheezing, bronchitis, asthma and allergic rhinitis.	NDVI CORINE land-cover classes	No statistically significant associations for the outdoor related environmental scores in relation to any of the health outcomes tested.
Parmes et al. (2020)	9 European cohorts 8063 children, (3-14 years) Italy, France, Slovenia and Poland	To evaluate associations between surrounding residential land cover and childhood allergic and respiratory diseases.	Parental questionnaires Logistic regression models	Allergic and respiratory symptoms (wheeze, asthma, allergic rhinitis and eczema)	CORINE land-cover classes (500 m buffer centred on each child's residential address)	A 10% increase in green space coverage was significantly associated with a 5.9%-13.0% increase in the odds of wheezing, asthma and allergic rhinitis, but not eczema. Children living in areas with surrounding coniferous forests had significantly greater odds of reporting wheezing, asthma and allergic rhinitis.

Authors (Year)	Study design & Sample	Study objective	Study methods & Statistical Analysis	Outcome variable	Greenness measurement	Relevant findings
Squillacioti et al. (2019)	Cross-sectional study 187 children (10-13 years) Turin, Italy	To investigate the association between greenness and respiratory health.	SIDRIA questionnaire Spirometry Urinary cotinine and creatinine Logistic regression models	Respiratory health (respiratory symptoms and diseases)	NDVI	Higher exposure (3rd tertile vs. 1st tertile) to NDVI was associated to significantly lower ORs for asthma [0.13 CI 95% 0.02-0.7, p = 0.019], bronchitis [0.14 CI 95% 0.05-0.45, p = 0.001], and current wheezing [0.25 CI 95% 0.09-0.70, p = 0.008]. A significative positive association was found between greenness and FEF_{25-75}, since children exposed to the 2nd tertile of NDVI reported a significantly decreased FEF_{25-75} compared to those in the 3rd tertile [B: -2.40; C.I.95%: -0.48-0.01; p = 0.049].
Trabelsi et al. 2019	Ecological study Pre-schoolers (0-5 years) registered in Belgium in 2014.	To describe the spatial differences in asthma medication sales for children 0 to 5 years in Belgium, and to evaluate the correlations with socio-economic and environmental factors.	Prescribed and sold asthma medication Pearson correlations	Asthma medication sales	CORINE land-cover classes	The geographical distribution of purchases of prescribed asthma medication for pre-schoolers in Belgium is only weakly correlated with some environmental factors. This study found positive moderate correlations of prevalence of purchase with green spaces and pig density.

Table 1: Characteristics of the included studies

Abbreviations: SIDRIA, Studi Italiani sui Disturbi Respiratori nell'Infanzia e l'Ambiente; C-ACT, Childhood Asthma Control Test; ACT, Asthma Control Test; CORINE, Coordination of Information on the Environment; NO_2 , Nitrogen Dioxide; NDVI, Normalised Difference Vegetation Index; OR, Odds Ratio; CI, Confidence Interval; ISAAC, International Study of Asthma and Allergies in Childhood; IUGZA, Urban Green Zone Allergenicity Index; OGCs, Oral glucocorticosteroids; FVC, Forced Vital Capacity; FEV1, Forced Expiratory Volume in 1 second; FEF, Forced Expiratory Flow; SRI, Species Richness Index

Results

Different methods were used to assess greenness exposure in the included studies. We will discuss each of these methods and compare studies that used the same parameters.

NDVI

The most used parameter to measure greenness was the Normalised Difference Vegetation Index (NDVI). The density of vegetation is determined by analysing the contrast between near-infrared light, which is highly reflected by vegetation, and red light, which is generally absorbed by vegetation, through the Normalised Difference Vegetation Index (NDVI). The NDVI's range is from -1 to +1. When NDVI values are negative, the area is likely to be water, whereas an NDVI value close to +1 suggests the presence of dense green vegetation. An NDVI value near 0 indicates a lack of green leaves, which could indicate an urbanised area. **(13)**

The findings of a longitudinal cohort study involving 179 asthmatic children conducted in Palermo showed that a low exposure of NDVI (≤ 0.21) was significantly associated with uncontrolled asthma. **(14)** Cilluffo et al. conducted another cross-sectional study in Palermo which revealed that children with lower exposure to NDVI (≤ 0.15) had an increased likelihood to develop nasal symptoms. Nevertheless, there was no statistically significant association between NDVI and pulmonary symptoms. **(15)** A different cohort study with 1050 children discovered that there was a significant correlation between higher levels of neighbourhood greenness at birth (NDVI > 0.14) and a lower prevalence of allergic rhinitis and asthma at 7 years of age. However, this correlation was restricted to a 100-metre radius from the participants' homes, and it ceased to exist when examining radii of 200 and 300 metres. **(16)** Paciencia et al. found in their cohort study conducted in Porto that children who had higher exposure to green spaces at 10 years of age within 500 m of their residence had a decreased risk of allergic sensitization. **(17)**

In Turin, Squillacioti et al. carried out a cross-sectional study that involved 187 children. In this study, an association was observed between higher NDVI exposure and significantly lower odds ratios for asthma, bronchitis and current wheezing. Furthermore, children exposed to lower levels of NDVI reported lower values of FEF_{25-75} (forced expiratory flow rate 25 - 75%). **(18)**

The primary limitation of estimating greenspace quality through NDVI is its coarseness as an indicator. NDVI does not account for variations in vegetation composition and structure, which may result in incomplete capturing of the potential impacts on human health. Tischer et al. aimed to address these limitations of unidimensional greenness indicators. The researchers created two environmental scores: the first being the outdoor-green score, which relied on NDVI and CORINE, and the second being the outdoor-grey score, which factored in CORINE, NO2 levels, and distance to roads. However, their study conducted on 15 646 children from 4 European birth cohorts found no significant associations between the ‘outdoor-green environmental score’ and wheezing, bronchitis, asthma, or allergic rhinitis at different ages. **(19, 20)**

Dzhambov et al. investigated several commonly used indicators for measuring greenness exposure, such as NDVI, CORINE, tree canopy cover, agricultural cover, imperviousness cover, and industrial

cover. Additionally, they explored a novel landscape metric called 'distance to nature' (D2N), which provides a more comprehensive perspective on greenness exposure. They found lower D2N (OR 1.32; 95% CI 1.09-1.60) and less industrial cover in the 500m buffer (OR 1.33; 95% CI 1.04-1.71) was significantly associated with lower ever prevalence of AR symptoms. There was a slight correlation observed between NDVI, tree coverage, and a reduced prevalence of asthma and AR symptoms. **(20)**

CORINE

The CORINE Land Cover (CLC) is a standardised map of land cover across Europe that spans a large time scale. This map offers several advantages, as it combines geo-spatial environmental information from national databases and satellite images to provide 44 land cover classes. These classes comprise various types of artificial surfaces, agricultural land, forests, wetlands, and water bodies. This database is operationally available for most areas of Europe. **(21)**

Parmes et al. used the CLC to determine the percentage of green, blue, agricultural, and grey spaces surrounding the residence of 8 063 children from nine European cohorts. According to this study, a 10% increase in green space cover was significantly associated with an increase in the likelihood of experiencing current and lifetime wheezing, with +5.9% and +13.0% respectively, as well as with lifetime and current asthma, +9.2% and +12.1%, and allergic rhinitis, + 8.1%. The study revealed that the connections between green space and health outcomes were consistent across various age groups and between males and females, suggesting that exposure to green spaces did not interact with sex or age regarding the studied outcomes. Furthermore, the study suggested that exposure to trees or tree pollen may raise the chances of developing asthma. As indicated by the study, children who lived in close proximity to forests had a 26% greater likelihood of experiencing current wheezing compared to those residing further away (OR = 1.26; 95% CI: 1.01-1.56; p = 0.039). **(22)**

Trabelsi et al. analysed the geographical distribution of asthma medication prescribed to preschool children in Belgium. In essence, this study discovered that green areas located far from urban and polluted regions had a higher prevalence of medication purchase. **(23)**

In a cross-sectional study, Cilluffo et al. identified three classes from the CORINE land cover classes: CUF (continuous urban fabric), DUF (discontinuous urban fabric) and “coniferous forests with continuous canopy”. This study found that children residing in CUF regions displayed a greater likelihood of experiencing ocular (OR = 1.49, 95% CI [1.10-2.03]) and general symptoms (OR = 1.18, 95% CI [1.00-1.48]) compared to those who lived in DUF areas. **(15)**

SRI

Two of the included studies, both from Cavaleiro Rufo et al., considered the effect of the species richness index (SRI). **(16, 24)** This index represents the number of different species (amphibians, birds, reptiles and small mammals) in a determined landscape. It can be an interesting parameter because it can give additional information on top of other more frequently used measurements of greenness (for example NDVI). Assuming that the quality of their habitat is optimal, small green spaces have the potential to support a significant number of species.

The cross-sectional study of Cavaleiro Rufo et al. found that a higher SRI was associated with an increase in lung function. Nevertheless, the improvement in lung function did not provide any

clinically significant protection against the development of asthma and allergies. **(24)** According to a longitudinal study of 1050 children in Porto, residing in a greener environment during early life provides protection against the onset of allergies and asthma at age 7. On the other hand, there seems to be a higher risk of developing asthma, allergies and wheezing among children living in communities with a high concentration of fauna species. **(16)**

OTHER PARAMETERS TO MEASURE GREENSPACE

Aerts et al. conducted a study in Belgium which investigated the risks of tree pollen allergies in urban green spaces, as well as changes in allergy risks resulting from green space interventions. In scenarios where allergenic potential was increased, the risk of allergies (AR) rose by 11-27%. Additionally, in the scenario where the duration of pollen season was increased, the risk of allergies rose by 44%. AR increased by 99 - 111 % in combined scenarios despite preventive tree removal. **(25)**

A longitudinal ecological study in Belgium examined childhood asthma medication sales by analysing the correlation between reimbursed medication sales for obstructive airway disease (OAD) and residential exposure to grassland, gardens, and forests. This study found a significant association between OAD medication sales and relative covers of grassland and gardens. The findings indicate that residing in proximity to regions with high grass coverage, such as permanent grasslands, hay meadows, lawns and residential gardens, may have a negative impact on the respiratory health of children. **(26)**

Lung function can also be affected by exposure to greenspaces outside of the home, such as those present in schools. According to an additional study conducted on 701 children attending 20 primary schools in Porto (Portugal), it was found that those who went to schools with more green areas had slightly higher values of FVC, FEV1, and FEF_{25-75}. However, these increases were not statistically significant. **(27)** In a study involving 40 249 Danish children, similar findings were reported. Specifically, this study found that a higher density of urban greenspace was linked to a lower risk of asthma. **(28)** Similarly, Molnar et al. found that the proximity of a weedy area was associated with a higher risk of asthma (OR = 1.39, CI: 1.15-1.69, p = 0.0007). **(29)** On the other hand, Bednarek et al. conducted a cohort study of 176 hospitalised preschool children with newly-diagnosed IgE-dependent asthma and found that their residence did not determine the clinical course of their respiratory disease. **(30)**

Discussion

The aim of this systematic review was to investigate the impact of exposure to urban green spaces within residential areas on the prevalence of allergic respiratory diseases in young individuals. Although there are some indications of a possible association between early-life exposure to urban greenery and the onset of allergic respiratory illnesses during childhood, the existing evidence is not yet completely conclusive.

For this review, 16 articles were selected that differed in terms of their research design, health outcomes, and approaches to evaluating exposure to green spaces. These differences may account for the inconsistencies noted in the published findings. Differences in study design, such as using cross-sectional versus longitudinal studies, may explain discordant results. Longitudinal studies tend to have greater statistical power and can estimate cause and effect, whereas cross-sectional studies may not be as powerful and only provide a snapshot of data at one point in time. In addition, there were only 2 researchers leading the entire study so inter-rater reliability may be lower.

Most of the included studies used (self-reported or parent-reported) questionnaires to evaluate allergic symptoms and asthma control. Certainly, it can be a limitation because there is the possibility of introducing self-reporting bias. However, the questionnaires were standardised (ISAAC or SIDRIA) which makes them more reliable to compare between studies. A more objective method to evaluate asthma control is measuring lung function by spirometry. In this systematic review, only five out of the 16 included studies used spirometry parameters.

The term 'green space' may contribute to the inconsistencies observed in the literature as it encompasses various types of land cover, ranging from uniform grass fields to diverse forests. The term 'green space' has up to six different meanings in the literature, with two major categories: naturally vegetated areas and urban green spaces. **(31)** Although both categories fall under the term 'green space', they may have different impacts. Most studies investigating respiratory health use NDVI as an indicator of green space, which includes both natural vegetation and urban green spaces. However, NDVI values fluctuate throughout the year based on vegetation growth and seasonal effects. Even with the use of annual averages, achieving consistent calibrated NDVI values in broad area studies that span across various years and seasons can be challenging. **(22)** On the other hand, CLC can differentiate between agricultural, forest, and grass areas, both within and among them. An additional parameter to look at greenness is the species richness index (SRI) which is a measure for the total number of species in a defined region and therefore does not look only at the amount of green space.

This review on the relationship between green spaces and asthma-like symptoms has yielded inconsistent results, indicating that this relationship is complex. The concept of green spaces encompasses a range of both protective factors and risk factors, making it challenging to draw straightforward conclusions. One widely accepted theory for how green spaces may improve respiratory health is through their ability to increase environmental biodiversity and decrease exposure to air pollution. **(32, 33, 34)** Additionally, green spaces may promote physical activity and help prevent overweight and obesity, which could also contribute to improved respiratory health. **(35)** In comparison to adults, children are typically more physically active and spend more time

outdoors. Additionally, children have a higher respiratory rate and inhale a greater amount of air relative to their body weight. **(36)** Green spaces have the potential to negatively impact respiratory health as they can emit volatile organic compounds (VOCs), produce pollen and mould, and release aerosols. These factors have been linked to the development of respiratory health problems and allergies. **(37, 38)**

The findings of a longitudinal ecological study conducted in Belgium indicates that the respiratory health of children may be negatively affected by residing near areas with a high concentration of grass cover, such as permanent grasslands, hay meadows, lawns, and residential gardens. Additionally, decreased exposure to environmental biodiversity may also play a role in the development of asthma. One potential solution to reduce the burden of childhood asthma could be to reduce the prevalence of grass in public and private green spaces. This could decrease exposure to allergens and improve air quality. However, it's important to note that reducing grass in green spaces must be done in a responsible and sustainable manner, as it may have unintended consequences on the ecosystem and wildlife. **(26)**

Furthermore several environmental challenges on a global scale are expected to augment the amount and the allergenic potency of airborne pollen, consequently raising the risk of allergies. Climate change and the urban heat island effect, traffic-related air pollution, elevated concentrations of carbon dioxide (CO_2), and nutrient deposition (such as nitrogen) are factors that may lead to longer and more intense pollen seasons, increasing the amount and potency of airborne allergenic pollen and thereby raising the risk of allergies. **(39, 40)**

The "biodiversity hypothesis" is a theory that suggests that limited exposure to natural environments and biodiversity during the early years of life can disrupt immune system development, making individuals more susceptible to allergens and abnormal immune responses to common epitopes later in life. **(41)** Conversely, the theory proposes that early exposure to a variety of microbiological agents can contribute to preventive immunomodulation, inducing tolerance to allergens through adaptive and innate immune mechanisms. **(42)** As a result, limited access to green spaces in urban environments may be impeding immunomodulation in young children and contributing to a higher prevalence of allergy and asthma.

Europe

The strength of this review is that all the included studies were conducted in Europe. A systematic review of Hartley et al. aimed to combine research results concerning the impact of green surroundings on asthma in children, which is about the same purpose as ours. This review incorporated a total of seven articles. All of these studies were published between 2017 and 2019 and were conducted in very different countries (two in Europe, others in the USA, Australia or New Zealand). The conclusion was that the presence of green spaces may not have a direct impact on childhood asthma, but it could potentially provide protection by altering individual and community-level risk factors. **(43)**

In Europe, the luxury effect has been observed in various studies, with more affluent individuals and households generally having greater access to biodiversity and green spaces than those with lower socioeconomic status. **(44)** This is partly due to factors such as housing location, education level, and income. For example, a study conducted in the UK found that people living in more affluent areas had access to more green space and higher quality green space than those living in less affluent areas. **(45)** More affluent individuals may also have the financial resources to travel to more remote areas or participate in outdoor recreation activities. Additionally, they may have higher levels of education and awareness about the importance of biodiversity and conservation, which can lead to greener lifestyles.

Conclusion

The present review aimed to synthesise studies on residential urban greenness and its association with the development of allergic and respiratory diseases in children. However, inconsistent results were found and made the challenge in drawing a conclusive interpretation difficult due to several factors, including the difficulty in measuring greenness accurately and consistently, the potential for confounding variables and the complex interplay between environmental factors and individual susceptibility. To address this issue, future studies should focus on the identified gaps in this review (e.g. different methods for measuring greenness, different research designs, evaluating asthma control with questionnaires) and investigate the underlying mechanisms of the complex relationship between urban greenness and respiratory health. Additionally, developing international consensus, particularly regarding objective measures of greenness exposure, is recommended to enhance the quality of research methodology in this area.

The impact of environmental changes, such as climate change and urbanisation, on allergenic plant species, pollen production, and pollen distribution is complex and can vary based on regional and local factors. It is important for future studies to consider the potential effects of environmental changes on the relationship between green spaces and allergy risks. This includes investigating the impact of changing climate and land use patterns on pollen counts, identifying the most allergenic plant species in urban green spaces, and assessing how these factors may vary across different regions and populations. A more comprehensive understanding of the current and potential future allergy risks posed by urban green spaces can inform urban planning decisions, guide management of green spaces, and assist patients with pollen allergies in avoiding environmental triggers during the airborne pollen season.

Therefore, further research is necessary to better comprehend the complex relationship between exposure to greenspaces and respiratory health, while considering various confounding factors and potential mechanisms of action.

The current findings on the association between greenness and respiratory outcomes remain inconclusive.

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Appendices

Appendix 1: The search query for PubMed

("Child"[Mesh] OR “Child*” [tiab] OR “infant*”[tiab] OR “junior*”[tiab] OR “adolescen*”[tiab] OR “teen*”[tiab] OR “youth*”[tiab] OR “newborn”[tiab] OR “neonat*”[tiab] OR “juvenile*”[tiab] OR “kid”[tiab] OR “pediatric*”[tiab] OR “toddler*”[tiab] OR “young*”[tiab] OR “puber*”[tiab]) AND ("Environment"[Mesh] OR “green*” [tiab] OR “Urban park*” [tiab] OR “Forest*” [tiab] OR “woodland*”[tiab] OR “natur*” [tiab] OR “park*”[tiab] OR “recreational park” [tiab] OR “urban park” [tiab] OR “forested area*” [tiab] OR “garden*” [tiab] OR “wilderness”[tiab] OR “blue space*”[tiab] OR “natural environment”[tiab] OR “wild land”[tiab] OR “vegetation*”[tiab] OR “roof garden*”[tiab] OR “recreation resource”[tiab] OR “national park*”[tiab] OR “community park*”[tiab] OR “forestland*”[tiab] OR “public land”[tiab] OR “open land”[tiab] OR “open space”[tiab] OR “wild area”[tiab] OR “municipal land*”[tiab] OR “municipal space*”[tiab]) AND (("Bronchial Diseases"[Mesh] OR “asthma*” [tiab] OR “bronchial asthma” [tiab] OR “status asthmaticus” [tiab] OR “chronic asthma” [tiab] OR “childhood asthma” [tiab] OR “bronchial hyperreactivity”[tiab] OR “bronchial spasm”[tiab] OR “bronchospasm*”[tiab] OR “respiratory hypersensitivity”[tiab] OR “obstructive lung disease*”[tiab] OR “lung allergy”[tiab] OR “bronchus asthma” [tiab] OR “lung asthma”[tiab] OR “obstructive pulmonary disease*”[tiab]) OR ("Nose Diseases"[Mesh] OR “Allergic rhinitis” [tiab] OR “Allergic Rhinitides” [tiab] OR “allergic rhinopathy” [tiab] OR “eosinophilic rhinitis” [tiab] OR “hay fever”[tiab] OR “nasal polyp*” [tiab] OR “nasal obstruction*” [tiab] OR “sinusitis” [tiab] OR “pollen allergy” [tiab] OR “pollen allergies” [tiab] OR “seasonal allergic rhiniti*” [tiab] OR “Pollinosis”[tiab] OR “Pollinoses”[tiab]))

Appendix 2: Goedgekeurd protocol



Geachte professor Gijs Van Pottelbergh,
Beste student Eline Vingerhoets, Dorien Mannens,

Betreffende masterproef ""Wat is het verband tussen de aanwezigheid van groen en respiratoire aandoeningen bij kinderen in de Europese Unie?" Een systematisch literatuuronderzoek binnen het overkoepelende project "Impact van milieublootstellingen op gezondheid"." (MP018588)

De verstrekte informatie toont aan dat het onderzoek in het kader van de masterproef een zuivere literatuurstudie betreft en dat er op geen enkele wijze gebruik wordt gemaakt van proefdieren, proefpersonen of menselijk lichaamsmateriaal.

Dit type onderzoek vereist geen goedkeuring van een gemachtigde commissie voor medische ethiek.

Onder voorbehoud van de volledigheid en correctheid van de door u verstrekte gegevens, krijgt u hierbij het akkoord om het onderzoek in het kader van de masterproef te starten. Deze mail dient als bewijs van goedkeuring mocht u uw onderzoek wensen te publiceren.

Wij willen u erop attent maken dat u zelf verantwoordelijk blijft voor uw onderzoek. Bovendien doet elke wijziging aan de door u verstrekte gegevens omtrent de onderzoeksopzet deze goedkeuring vervallen. U dient in dat geval een amendement te maken aan uw huidig dossier.

Veel succes!

Appendix 3: Persoonlijke reflectie

<u>Verloop van het groepsproces en persoonlijk aandeel</u>

Voor het schrijven van onze masterproef zijn we gestart met 8 HAIO's met als gemeenschappelijk thema "De impact van milieublootstellingen op gezondheid", kaderend binnen het doctoraatsonderzoek van Simon Beerten over het effect van urbanisatiefactoren (hittestress, geluidsoverlast, luchtvervuiling en de aanwezigheid van groen) op (mentale) gezondheid in Vlaanderen. Dit globale thema werd onderverdeeld in 4 subonderwerpen die per 2 verder werden uitgewerkt. Deze verdeling vond plaats in november 2020 (eerste jaar HAIO).
Ik heb mijn masterproef samen geschreven met Eline Vingerhoets over het verband tussen de aanwezigheid van groen en respiratoire aandoeningen bij kinderen. Wij zijn gestart met het opstellen van een "PICO" zodat we een duidelijke onderzoeksvraag konden formuleren voor de start van ons systematisch literatuuronderzoek. In samenspraak met co-promotor Simon Beerten werd er de volgende onderzoeksvraag geformuleerd: "Wat is het verband tussen de aanwezigheid van groen en het voorkomen van astma en allergische rinitis bij kinderen in Europa?" (mei 2021). Aan de hand van deze onderzoeksvraag konden we een zoekstrategie opstellen. We bekeken allebei de opgenomen video over de opbouw van een zoekstrategie die voorhanden is op Toledo. Verder namen we in juni 2021 met de volledige groep van 8 HAIO's deel aan een extra online meeting met Krizia Tuand (biomedische informatie specialist van de bibliotheek) waar onze zoekstrategie werd overlopen en verder uitgewerkt.
We werkten eerst een zoekstrategie uit voor PubMed en lieten deze nakijken door co-promotor Simon Beerten (maart 2022). Nadat de zoekstrategie voor PubMed goedgekeurd werd, konden we deze aanpassen naar de andere databanken (Embase, Cochrane Library en Web Of Science Core

Collection). Onze zoekstrategie leverde in totaal 20 156 zoekresultaten op. Om al deze resultaten te kunnen ordenen, maakten we gebruik van het software programma EndNote. Via dit programma werden eerst de duplicaten en studies die gepubliceerd werden na 2018 verwijderd waardoor er nog 3 438 studies overbleven voor verdere screening. De screening gebeurde eerst op titel en later op basis van abstract. Ik en Eline deden deze selectie elk apart in EndNote om zo veel mogelijk bias te vermijden. Uiteindelijk werden er 16 studies geïncludeerd in ons systematisch literatuuronderzoek. De selectie van deze 16 studies uit de meer dan 20 000 zoekresultaten gebeurde in oktober en november 2022. We stelden een PRISMA flow diagram op over het selectieproces.
De 16 geïncludeerde studies hebben we samengevat in een tabel op basis van verschillende kenmerken (auteurs en jaar van publicatie, studiedesign, doel van de studie, methoden en statistische analyse, uitkomst variabele, meetmethoden van groene ruimte en belangrijkste bevindingen). We verdeelden deze 16 artikels in twee zodat we elk de helft van de artikels in de tabel konden samenvatten. Nadien keken we elkaars samenvattingen na en pasten we deze aan zo nodig. De samenvattende tabel was eind december 2022 klaar en werd via mail naar Simon Beerten gestuurd ter nazicht.
In januari 2023 kwamen Eline en ik samen om te bespreken hoe we het schrijven van onze masterproef gingen aanpakken en verdelen. Een concrete indeling werd bepaald (inleiding, methoden, resultaten, discussie en conclusie) en we bespraken wat er in welk onderdeel vermeld zou moeten worden. Om dit vlot te laten verlopen, maakten we een 'Google Doc' aan waar we beiden in konden schrijven. Hierdoor konden we elkaars aanpassingen gemakkelijk volgen. Eline startte met het schrijven van een inleiding en ik nam het stuk over methoden voor mijn rekening. Verder schreef ik het grootste deel van de resultaten, Eline schreef het grootste deel van de discussie en de conclusie. In maart 2023 was een eerste versie van onze masterproef klaar zodat we deze konden doorsturen naar de Simon Beerten. We gingen aan de slag met zijn feedback en voerden de nodige aanpassingen door. Ten slotte schreef ik nog een abstract (in het Engels en Nederlands) en maakte het titelblad.

Over het algemeen vond ik het een erg vlotte samenwerking met Eline Vingerhoets, de afgesproken deadlines werden mooi nagekomen en we hebben elk een gelijkwaardig aandeel in het schrijven van de masterproef.

<u>Persoonlijke visie op wat het werk nu betekent voor het werkveld</u>

Binnen de huisartsengeneeskunde heb ik een bijzondere interesse in de pediatrische patiëntenpopulatie. Tijdens mijn HAIO-opleiding heb ik de kans gekregen om 6 maanden mee te werken op de afdeling pediatrie in AZ Turnhout waardoor deze interesse nog verder is gegroeid. Ik vind het daarom erg boeiend dat onze masterproef zich focust op kinderen.
Astma en allergische rinitis zijn aandoeningen die we als huisarts heel frequent tegenkomen in de praktijk, astma is zelfs de meest voorkomende chronische aandoening bij kinderen. Het is voor mij, als toekomstig huisarts, een meerwaarde dat ik me via deze masterproef heb kunnen verdiepen in de impact van groene omgeving op het voorkomen van deze aandoeningen. Als huisarts heb je een belangrijke preventieve rol waardoor het een meerwaarde is om (ouders van) patiënten te kunnen informeren over de mogelijke impact van groene omgeving op de respiratoire aandoeningen. Verder woon en werk je vaak in dezelfde omgeving als de patiënten waardoor je ongeveer aan dezelfde groene omgeving bent blootgesteld.
Het is echter jammer dat onze masterproef geen duidelijke conclusie laat zien, waardoor er geen eenduidig advies voorhanden is om mee te geven aan de patiënten. Gezien de toenemende prevalentie van allergische luchtwegaandoeningen, zullen er in de toekomst wellicht nog meerdere studies verschijnen in de literatuur.