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RespirIT

Assessing spatio-temporal relationships between respiratory health and biodiversity using individual wearable technology

COORDINATORS: SOMERS Ben (KU Leuven)
VAN ORSHOVEN Jos (KU Leuven)

PROMOTORS: DENDONCKER Nicolas (UNamur)
LINARD Catherine (UNamur)
HENDRICKX Marijke (Sciensano)
VAN NIEUWENHUYSE An (Sciensano)
NAWROT Tim (UHasselt)
DELCLOO Andy (IRM-KMI)
HAMDI Rafiq (IRM-KMI)
AERTS Jean-Marie (KU Leuven)

AUTHORS: AERTS Raf (Sciensano, KU Leuven & UHasselt)
BRUFFAERTS Nicolas (Sciensano)
DOCKX Yinthe (UHasselt)
DUJARDIN Sébastien (UNamur)
HOEBEKE Lucie (Sciensano)
STAS Michiel (KU Leuven)
VERSTRAETEN Willem (IRM-KMI)

belspo .be

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WTCIII

Simon Bolivarlaan 30 Boulevard Simon Bolivar

B-1000 Brussels

Belgium

Tel: +32 (0)2 238 34 11

http://www.belspo.be

http://www.belspo.be/brain-be

Contact person: Aline van der Werf

Tel: +32 (0)2 238 36 71

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TABLE OF CONTENTS

1. INTRODUCTION

1.1 Pollen allergy

In Belgium, 13.2% percent of the population was sensitized to tree pollen (*Alnus, Betula, Corylus)* and symptoms of allergic rhinitis were present in 9.7% (Blomme *et al.*, 2013). Over the past decades an increase in the prevalence of allergic disease has been observed (Lake *et al.*, 2017; Ring, 2012). Taking into account population growth, Neumann *et al.* (2019) predicted that emergency department visits for birch and grass pollen induced asthma exacerbations will increase with 14% by 2090. The observed trend of increasing prevalence of pollen allergy and asthma is expected to continue due to further urbanization, increasing emissions of air pollutants and climate change (D'Amato *et al.*, 2016; Lake *et al.*, 2017). The mechanisms behind these drivers of increased respiratory health problems are visualized in Figure 1.

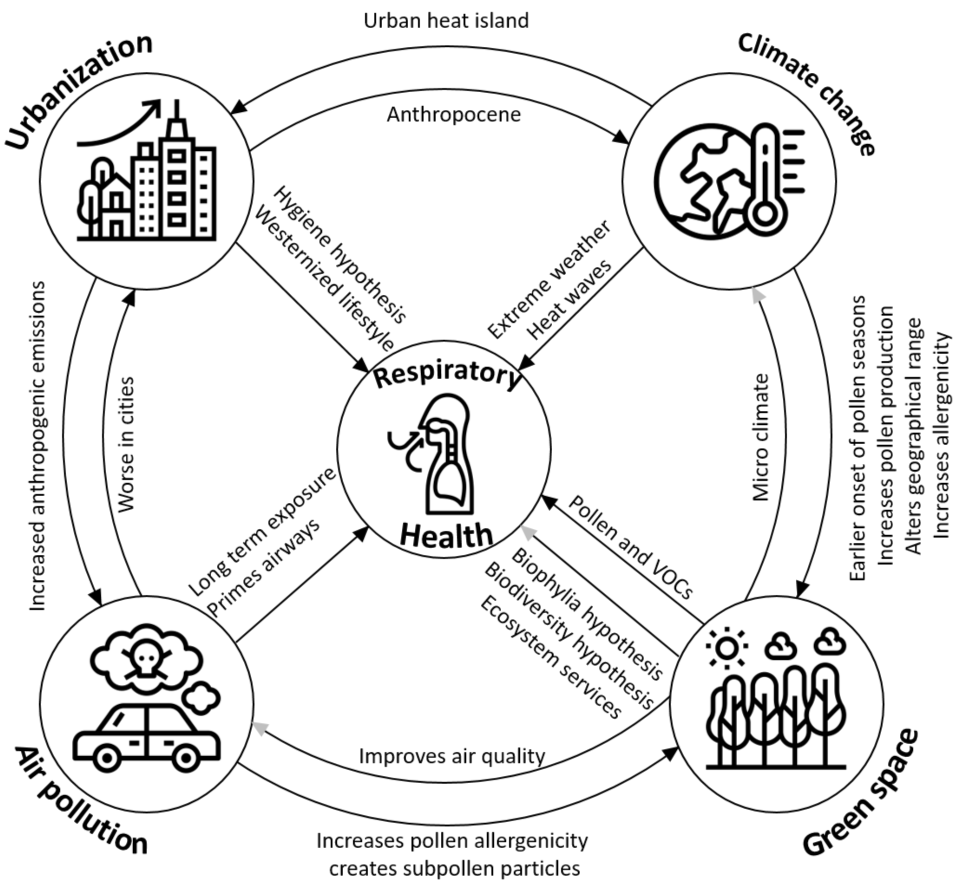

Figure 1: A structured overview of the interactions between urbanization, air pollution, climate change and green space, and their effects on respiratory health. A grey arrowhead indicates a direct or indirect health benefit, a black arrowhead indicates a direct or indirect health risk.

1.2 The impact of green space on respiratory health

An Australian study found that natural and biodiverse landscapes were associated to respiratory health benefits (Liddicoat *et al.*, 2018). And in a New Zealand birth cohort the risk of asthma development was lower for children growing up with more diverse natural land cover types (Donovan *et al.*, 2018). Although (urban) green spaces deliver ecosystem services and contribute to positive health outcomes, they also deliver ecosystem disservices by emitting pollen and VOCs (Grote *et al.*, 2016). Depending on the tree species present, certain urban green spaces can have a high allergenic potential (Cariñanos *et al.*, 2019; Velasco-Jiménez *et al.*, 2020). While urban green spaces could potentially decrease asthma and respiratory disease by improving air quality, there is currently limited evidence of this beneficial pathway for asthma and pollen allergy patients (Eisenman *et al.*, 2019).

A number of studies on residential green space exposure and respiratory health in children have emerged, but the results are heterogeneous (Lambert *et al.*, 2018). Residential proximity to green space and residential greenness have been associated with a reduced risk of bronchitis and wheezing (Tischer *et al.*, 2017). Other studies, however, find that children living with more green space around the residence suffer more wheezing and have an increased risk of allergic rhinitis (Parmes *et al.*, 2020) and asthma (Andrusaityte *et al.*, 2016). A first large scale study on adults in England found that the presence of more tree cover, gardens and green space in residential areas was associated with fewer asthma hospitalizations (Alcock *et al.*, 2017). The health benefits of green space remained when concentrations of air pollutants was high (Alcock *et al.*, 2017). Regarding allergic rhinitis in adults contradicting results on the effects of green space have been reported (Kim *et al.*, 2020; Kwon *et al.*, 2019). From these studies it is clear that green space has an effect on respiratory health. Whether this is a protective or a risk effect might be determined by confounders such as biodiversity, environmental microbiome or behaviour (Rufo *et al.*, 2019).

2. STATE OF THE ART AND OBJECTIVES

2.1 Studying short term exposure

The literature shows that effects of vegetation on the health of pollen allergy patients is heterogeneous (E. Fuertes et al., 2016; Tischer et al., 2017). This heterogeneity is not solely due to the complex environmental interactions but also due to the high variation in defining exposure (Nordbø *et al.*, 2018). Certain studies rely on self-reported nature experience (Doherty *et al.*, 2014), others derive greenness objectively from satellite images (Kwon *et al.*, 2019) or land cover maps (H. J. Kim et al., 2020). In addition, no uniform guidelines on scale effects of exposure are available (Labib *et al.*, 2020). In order to obtain reliable insights in health effects, there is a need to accurately study exposure both in thematic and spatiotemporal detail.

Plant species richness (Young *et al.*, 2020) or species specific effects (Guan *et al.*, 2017) have hardly been studied, even though these are of high importance for pollen allergy patients. Mapping of allergenic vegetation and source areas of pollen contributes to assessing respiratory health risks (Bogawski, Grewling, et al., 2019; McInnes et al., 2017). Belgium has regional datasets on forest species composition (Alderweireld *et al.*, 2015; Westra *et al.*, 2015) and for Flanders a biological valuation map (Vriens *et al.*, 2011) and validated observations of vascular plants (Florabank) (Van Landuyt *et al.*, 2012) are available. The available data can be used in species distribution models to develop a species richness map or a map of allergenic (tree) species, suitable to study exposure and associated health effects.

Besides green space the exposure to pollen and air pollutants needs to be assessed when studying health of allergy patients. In Belgium, air quality is monitored by Irceline (https://www.irceline.be/en) using a network of 111 sensors. Airborne pollen levels in Belgium are monitored by the Belgian Aerobiological Surveillance Network at 5 sampling locations (https://airallergy.sciensano.be/en). Volumetric Spore Samplers (Burkard Manufacturing Co. Ltd) located at rooftop level are used to measure airborne pollen levels for a radius of 20-30 km around the sampling location. The 5 stations of the Belgian Aerobiological Surveillance Network are part of a European network of more than 600 stations which use the standard Hirst monitoring method (https://ean.polleninfo.eu). Currently technologies are being developed to automate pollen monitoring, reducing the manual work load and allowing for near real-time online reporting (Chappuis *et al.*, 2020; Oteros *et al.*, 2015). Nevertheless, pollen measurements from rooftop-level samplers take place outside the human breathing zone and represent background concentrations of pollen (Galán *et al.*, 2014). However, personal exposure can differ from background concentrations because of local sources of pollen (Peel *et al.*, 2013). Although pollen can be transported over long distances (Bogawski, Borycka, et al., 2019), short-distance transport contributes to important pollen peak levels (Rojo & Pérez-Badia, 2015). The local scale effects of vegetation on airborne pollen composition relevant for human health studies have not been clearly defined.

Studies on environmental exposure have heterogeneous protocols using buffer sizes ranging from 30 to 8000 m (Labib *et al.*, 2020; Nordbø *et al.*, 2018). Nevertheless, residential green space exposure has been associated with mental health benefits (White *et al.*, 2013) and the development of pollen allergy (Parmes *et al.*, 2020). However, 35% (Dėdelė *et al.*, 2019) or 50% (MacKerron & Mourato, 2013) of the time is spent in non-home environments. Exposure beyond the residence contributes to the daily exposure that can cause pollen allergy symptoms. When in transport for example, individuals might be exposed to peak concentrations of NO_2 (Dons *et al.*, 2019). Even though transport made up only 8% of daily activities, Dons *et al.* (2011) identified transport (walking, cycling, car or public transport) as the largest contributor to personal air pollution exposure. Pollen and air pollutant levels have a high spatiotemporal variability and exposure is thus best studied using Global Positioning Systems (GPS) (Steinle *et al.*, 2015). Until now the use of GPS locations to study exposure to green space (Almanza *et al.*, 2012) and air pollution (Dėdelė *et al.*, 2019; Steinle *et al.*, 2015) has been limited. GPS tracking can be incorporated in mobile health (mHealth) applications that have already shown to be useful for pollen allergy symptom management and research (Matricardi *et al.*, 2020).

2.2 Studying long term exposure

As described in the hypothesis of Developmental Origins of Health and Diseases" (DoHaD), the environment may play a substantial role in intrauterine and early childhood development, resulting in health outcomes, such as respiratory diseases, later in life (Barker 2004, Barker and Thornburg 2013). Thus appropriate epidemiological studies are required to investigate the relationship between long-term environmental exposure and early-life health outcomes. Better understanding these underlying mechanisms are worth exploring because they could have potential lifelong implications.

The available studies on the effects of green space on childhood respiratory and allergic diseases are conflicting (Lambert, Bowatte et al. 2017). Both adverse (Dellavalle, Triche et al. 2011, Lovasi, O'Neil-Dunne et al. 2013, Dadvand, Villanueva et al. 2014, Fuertes, Markevych et al. 2016) as well as protective effects, have been reported (Lovasi, Quinn et al. 2008, Hanski, von Hertzen et al. 2012, Pilat, McFarland et al. 2012, Tischer, Gascon et al. 2017, Müller-Rompa, Markevych et al. 2018, Tischer, Dadvand et al. 2018). These contradicting results might reflect a complex relationship, involving green spaces, our respiratory health, and possible other mediating factors. On the one hand, there is a need to better understand what defines respiratory diseases, such as asthma, and their differences in evidence and prevalence between children and adults (Fuhlbrigge, Jackson et al. 2002, Dharmage, Perret et al. 2019). On the other hand, there is a need for detailed information on green space estimation and its interaction concerning our environment and health. Several studies try to investigate the possible mechanisms through which green space can influence our respiratory health. For instance, green space can release pollen and fungal spores related to an increased risk of chronic respiratory diseases (Bartra, Belmonte et al. 2009, De Linares, Belmonte et al. 2010, Dellavalle, Triche et al. 2011, Lovasi, O'Neil-Dunne et al. 2013). On the contrary, several studies link green spaces with an increase in environmental microbial diversity which is important in the development of the immune system, especially when investigating early-life exposure (Hanski, von Hertzen et al. 2012, Stiemsma, Reynolds et al. 2015, Tischer, Weikl et al. 2016, Weikl, Tischer et al. 2016, Dharmage, Perret et al. 2019). Additionally, green spaces can mitigate urban-related environmental hazards such as outdoor air pollutants, which have been associated with an increased risk on asthma (Dadvand, Rivas et al. 2015, Yang, Chu et al. 2018). Besides investigating the mechanisms through which green space can influence our health, there is also a need to look further into the green space assessment because the evidence supports the idea that types of vegetation and green spaces might also play a differential role in the relationship with childhood asthma (Dadvand, Villanueva et al. 2014).

Considering many of these studies showing that the environment can play a role in the development of respiratory diseases, as early as childhood, might urge us to look into the possibility that this relationship might already have its origins during fetal development. There is much research supporting the evidence that the prenatal maternal environment can influence the development of the fetus. There are, for instance, many studies that associate prenatal tobacco smoke exposure with an increased risk on childhood wheezing and asthma (Underner, Perriot et al. 2015). Additionally, maternal exposure to air pollutants can influence the fetal immune system and growth (Vieira 2015, Wong, Wais et al. 2015). Besides air pollution, there are also consistent results that associate surrounding greenness with fetal health outcomes, such as an increase in birth weight and head circumference (Dadvand, de Nazelle et al. 2012, Dadvand, Wright et al. 2014, Dzhambov, Dimitrova et al. 2014, Banay, Bezold et al. 2017). However, further research is needed to look into these complex relationships, particularly interesting are longitudinal epidemiological studies to validate results seen in early-life and relate them to subsequent health outcomes.

Furthermore, as described before, green spaces are not solely associated with respiratory conditions, but are also proven to be able to impact several other health outcomes, including mental well-being and cognitive development (Kahn 1997, Kellert 2002). Continually, we must recognize the prenatal and early postnatal periods as being vulnerable and important windows to the impacts of environmental exposures (Nieuwenhuijsen, Dadvand et al. 2013) and especially important for brain development (Grandjean and Landrigan 2014). Earlier studies were primarily focused on short-term effects of green space on mental well-being, in which they established, for instance, that the acute exposure to more green environments was related to a decrease in ADHD risk and symptoms in children (Taylor, Kuo et al. 2001, Kuo and Taylor 2004, Skounti, Philalithis et al. 2007, Taylor and Kuo 2009, van den Berg and van den Berg 2011, Schutte, Torquati et al. 2017). However, there is emerging evidence also supporting the relationship between chronic green space exposure and behavior and cognition in children. Long-term exposure to green space, for instance, was associated with a decreased risk in childhood-associated behavioral problems concerning emotion, conduct and hyperactivity (Amoly, Dadvand et al. 2014, Markevych, Tiesler et al. 2014, Aggio, Smith et al. 2015, Younan, Tuvblad et al. 2016, Zach, Meyer et al. 2016, Feng and Astell-Burt 2017, Bijnens, Derom et al. 2020) and associated with a lower risk of psychiatric disorders as found in a large-scale study covering more than 900.000 Danish individuals (Engemann, Pedersen et al. 2019).

Additionally, studies found that children residing in an environment surrounded with more green could better memorize, were more attentive and had a higher intelligence quotient (Dadvand, Villanueva et al. 2014, Dadvand, Tischer et al. 2017, Bijnens, Derom et al. 2020). These findings support the relationship between chronic exposure to green spaces and cognitive functioning and development. However, as explained before, some of the observed associations might have a preceding link with prenatal maternal green space exposure through fetal cognitive development. Unfortunately there is a significant lack of research on this important topic, considering the majority of studies focus primarily on the influence of maternal air pollution exposure on fetal cognitive outcomes (Perera, Jedrychowski et al. 1999, Sunyer and Dadvand 2019). Moreover, evidence support the relationship between prenatal maternal green space exposure and birth weight and head circumference, which are health outcomes related to cognitive functioning and school performance (Frisk, Amsel et al. 2002, Veena, Krishnaveni et al. 2010). This illustrates, that further research is required in this field.

2.3 Research objectives

In this project we use an innovative approach in which the whereabouts and symptom severity of individual patients is continuously tracked using individual wearable technology, and linked to spatially explicit information on plant diversity, pollen concentrations and air quality. This unique data assimilation concept allows to quantitatively, dynamically and spatially study plant diversity effects on allergic symptom severity.

In this study, we aim at exploring and understanding the spatial and temporal effects of plant diversity on respiratory health in general and allergic asthma and allergenic rhinitis more specifically. We aim at examining three aspects of this relationship:

(i) the chronic health effect: Does long term exposure to plant diversity impact on the risk of allergy or asthma prevalence?;

(ii) the acute health effect: Does recent exposure to plant diversity impact on the acute expression of pollen allergy symptom severity?;

(iii) possible future health effects: How will future changes in plant diversity, coupled to climate and land use changes, have an impact on (i) and (ii)?

In order to generate significant clinically relevant results in the framework of this 4 year project and given the diversity in allergenic pollen triggers, this study focused specifically on the allergenic response to three of the most allergenic tree species in Belgium, i.e. *Corylus*, *Alnus*, and *Betula* (Biedermann et al., 2019; G. D'Amato et al., 2007).

3. METHODOLOGY

The methods and results are discussed simultaneously in the results section.

4. SCIENTIFIC RESULTS AND RECOMMENDATIONS

WP1: Implementation of measurement equipment and data platform

Task 1.1 Wearable technology

The RespirIT monitoring system consisted of a Samsung Galaxy J1 smartphone with android operating software version 4.3 or newer. The location services of the smartphone were used to gather point locations. Smartphones use satellite navigation and triangulation from mobile connection for faster location services, referred to as assisted GPS (AGPS). In the course of this manuscript we will refer to this sampling as smartphone GPS-tracking (SGT), commonly used in scientific literature (Korpilo *et al.*, 2017). The gyroscopes in the smartphone were used to derive activity levels. Via Bluetooth the smartphone was connected to a Mio Alpha 2 sport watch (Figure 2). The sport watch was used to measure heart rate (beats per minute, BPM) by means of an optical sensor on the wrist. The sample frequency of the measurements was 1 HZ, i.e. one measurement per second. For the project 50 smartphones and sport watches were purchased to be delivered to participants with the most suitable profile. These participants reported to have their allergies confirmed by a skin prick test or blood test at some point in their life. They were allergic to *Alnus, Betula* and/or *Corylus* and not to pet dandruff or house dust mite.

The custom full app provided a user interface where measurements could be observed in real-time. Two questionnaires were integrated in the application: one to register acute symptoms during the day and one to register mood, medication intake and symptoms at the end of every day (symptom diary). A second similar app was developed to be used on a personal smartphone without the sport watch. This limited app allowed to recruit more than 50 people during the tree pollen seasons of 2017 and 2018. The limited app had the same user interface and acute and daily questionnaires. Only the functionality to connect to a sport watch via Bluetooth was unavailable in the limited app. Both apps were made freely available in the Google play store. However, only participants of the RespirIT project could activate and create a user account for the apps using a personal activation code. The app was not available for Apple smartphone users. Ultimately 189 users were monitored during the tree pollen season (January – May) of 2017 and/or 2018.

Whenever the smartphone and the app were connected to WIFI the data stored in the app would be synchronized with the cloud database. This data could be accessed by the researchers of the project to download anonymized data of the participants (Figure 2).

Figure 2: Schematic overview of the full RespirIT monitoring system.

Before the first measurement campaign in 2017 was launched the functionality of the monitoring system and the user friendliness of the limited app was tested. To test the accuracy of the point location measurements of the Samsung Galaxy J1 smartphone, static and dynamic tests were performed. During the static test the smartphone was held for five minutes above a geodetic point of the National Geographic Institute. The average horizontal error (difference between the measured location and the known location of the geodetic point) varied between 2 and 15 m depending on the conditions of the measurement. Obstruction of the GPS signal by tall buildings and keeping the smartphone in a trouser pocket contributed to larger inaccuracies.

For the dynamic analysis a trajectory passing under tree canopy and through street canyons was selected to be walked and cycled with the smartphone in the trouser pocket. The measured track was compared to the road segments of Open Street Map (OSM). Traveling speed (cycling vs. walking) did not affect the dynamic spatial accuracy. The location services of the smartphone continued to perform well in street canyons and under tree canopies. Overall 95% of the GPS points did not fall further than 10 m from the OSM street segments.

To evaluate the accuracy of the sport watch used to measure heart rate, we used data of the experiments of Dr. Deborah Piette. The heart rate of healthy individuals was measured during a cycling test and a rest period using a gold standard electrocardiogram (ECG) and the Mio Alpha 2 simultaneously. A Bland-Altman plot with mean difference and lower and upper limits of agreement (Wallen *et al.*, 2016) was used to quantify the agreement between the ECG and the Mio Alpha 2 measurements. The mean difference between the Mio Alpha 2 watch and the ECG was -1.19 BPM. The difference in accuracy during rest and during active behavior was negligible. Compared to the wearables tested by Wallen *et al.* (2016) the Mio Alpha 2 performs well (Figure 3).

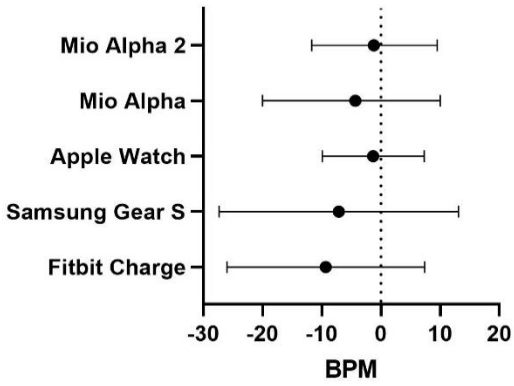

Figure 3: The results of the Mio Alpha 2 watch were added to the Bland-Altman plot of Wallen *et al.* (2016). The Mio Alpha 2 performs well compared to the other wearables tested.

The participants were asked to wear the smartphone on their body as often as possible to obtain accurate activity levels that are necessary to distinguish between active and motorized transport in Chapter 5. We determined the 5-minute average activity level during certain relevant activities (Table 1).

Table 1: Average measured activity levels ('counts') for various performed behaviors.

Activity	On Table	Sitting	Standing	Walking	Stairs	Cycling
Measured	0.0492	0.1497	0.1189	7.4504	5.4588	5.2157

During a test-campaign, 42 volunteers installed the limited RespirIT app on their personal smartphone for a week. The app worked on various devices and was deemed easy to use by the majority of the testers. The test period revealed some issues that could then be solved in due time for the launch of the actual campaign. We found that the app would shut down when permission to the location services was not granted. In the final version, the app would ask for permission instead of shutting down, guaranteeing continuous measurements. At the end of each day the application would give a reminder to fill out the symptom diary. Several testers mentioned that a reminder at the beginning of the day to start the measurements would be beneficial, thus this was included in the final app. Due to the high sampling frequency half of the testers reported that the battery life of their device was severely impacted by the constant activity of the app. This issue was not addressed in the optimization of the app as to not compromise the data-quality.

In conclusion, the spatial accuracy of the Samsung Galaxy J1 was of sufficient quality for the RespirIT mobile health study, which used environmental data with a minimal spatial resolution of 100 m. We expected that other smartphones would have a similar accuracy. The Mio Alpha 2 watch measured the heart rate accurately during rest and active periods. We characterized activity measures for various behaviors and recommend to use a threshold of 0.2 to distinguish stationary from active behavior. Based on a test campaign the already user friendly RespirIT app could be further improved before the start of the main campaign. We expected drop outs of participants using the limited app due to its effect on the battery life of the personal smartphones.

WP2: Spatio-temporal monitoring of respiratory allergic responses of individuals

Task 2.1 Sampling a birth cohort to study the relationship between early life exposure to plant diversity and atopic constitution

ENVIR*ON*AGE
Original data will be catalogued and stored in their original form that will be never altered. Copies of original data will be cleaned and prepared for the analysis according established standard operating procedures. Ambiguous values will be assessment by a trained operator. Data allowing personal identification will be separately stored from all the other data and linked through anonymized files accessible only to authorized team members. Biological samples are stored in the biobank. To prevent freezer failures the laboratory has an emergency generator to provide back-up power on a 24 hour alarm system. Hard copies of consent forms, study grant application, protocol, ethical approval are stored at Hasselt University. All measurements, samples and analyzes on the collected samples are encrypted and stored to protect privacy in accordance with the new GDPR standards. The encrypted data is stored on an encrypted Google Drive disk of the research group. The USB stick used to store and transport the data from the measurement devices to the corresponding Google Drive folders is kept in a locked cabinet in the research room. The data is transferred twice a month, after which the data is deleted from the stick. The personal details of the participants are stored separately in an encrypted Excel file. Additionally, databases released for research purpose come with an unique anonymous identifier.

To investigate the relationship between early life exposure to green space on health outcomes, we used samples and measurements from the participants of the ENVIR*ON*AGE (Environmental Influences on Early Aging) birth cohort. The ongoing ENVIR*ON*AGE birth cohort recruits mother-newborn pairs at arrival for delivery at the East-Limburg Hospital in Genk (Belgium). Only singletons, mothers without a planned caesarean section and able to fill out a questionnaire in Dutch are eligible for the cohort. Written informed consent was obtained from all participating mothers and the procedures were approved by the Ethical Committee of Hasselt University and East- Limburg Hospital. The overall participation rate of eligible mothers was 61%. Questionnaires with detailed information about demographic and lifestyle characteristics were collected, and perinatal parameters were obtained by birth records as previously described elsewhere (Janssen, Madhloum et al. 2017).

Task 2.2 Recruitment of allergy sensitive participants for spatio-temporal monitoring of allergic responses

For the RespirIT study on health effects of green on respiratory health adults sensitized to pollen of common hazel (*Corylus avellana*), alder (*Alnus* spp.) and/or birch (*Betula* spp.) were recruited from the general population of Belgium in 2016 and 2017. The study was approved by the Ethical Commission of the KU Leuven University Hospital (Belgian registration number B322201629692). After obtaining informed consent the patients used a smartphone to track their whereabouts and score and log their daily mood and allergy symptoms during the tree pollen season (January–May) of 2017 and/or 2018. One month after the start of the pollen season as defined by the Belgian Aerobiological Surveillance Network (Sciensano, www.airallergy.be), the patients completed a questionnaire providing detailed background information.

After finding our call in newspapers, newsletters and social media 225 persons showed interest in participating and 189 (84%) were included in the RespirIT study. Ultimately 32 participants dropped out and thus anonymized data from 157 (70%) participants were used in a cross-sectional study (residential exposure). The participants used the mobile app on 8423 person-days of which 4714 were symptom days used in the analysis.

For the case-crossover (Jaakkola, 2003) study (dynamic exposure) a patient is their own control. Thus, for each patient, case-days with severe allergy and control days without (or with mild symptoms) were selected. Severe allergy was defined as the 25% highest symptom severity scores experienced per patient (SSS > Q3). Every case-day was matched to a control day with a symptom severity score in the lowest 25% for that patient (SSS < Q1). Case days were bi-directionally 1:1 matched to control days on the same weekday within the same month. For the case-crossover analysis 45 participants were excluded for two reasons: (1) the diary entries did not allow to make matching case and control days, (2) no sufficient SGT data were gathered on selected case or control days. Ultimately 144 patients were included in the final analysis, providing 808 person-days equally split in case days and control days

WP3: Spatio-temporal monitoring of plant diversity and the environment

Task 3.1 Providing spatially explicit proxies for plant diversity

A. Generic tree diversity in Flanders

Potential tree diversity can be modelled by stacking individual species distribution models (SDMs) on top of one another to yield a total richness. Stacking of SDMs is most commonly done after thresholding the continuous probability output of the individual SDMs, a method known as binary stacking (Calabrese *et al.,* 2014). Nevertheless, discretizing continuous probabilities using fixed thresholds (for example considering all cases with a modelled probability of $p > 0.55$ as being present) is generally discouraged (Merow *et al.*, 2013). Instead, species-specific threshold rules can be applied (Cao *et al.*, 2013). Still, the literature suggests that binary stacking tends to overestimate species richness because biotic limitations are not accounted for (Calabrese *et al.*, 2014; Gavish *et al.*, 2017; Guisan and Rahbek, 2011). Nonetheless, combining binary SDMs is the most straightforward method to create potential species richness maps (Trotta-Moreu & Lobo, 2010).

The occurrence data of thirteen wind-pollinated tree genera were included in the study: *Aesculus* (horse chestnut), *Alnus* (alder), *Betula* (birch), *Carpinus* (hornbeam), *Corylus* (hazel), *Fagus* (beech), *Fraxinus* (ash), *Juglans* (walnut), *Platanus* (plane), *Populus* (poplar), *Quercus* (oak), *Salix* (willow) and *Tilia* (linden). Presence-records of these genera were extracted from Florabank1 (Van Landuyt & Brosens, 2017) available on GBIF.org. The Florabank is an open-access presence-only database of validated observations of vascular plants, from checklists, literature and herbarium specimen information. The observations are georeferenced and attributed to the centers of 14317 1km×1km IFBL grid cells (Van Landuyt *et al.*, 2012).

Soil texture class, soil drainage class, mean lowest and highest groundwater table depth, land cover type and habitat type were the environmental covariates used. In Belgium, natural plant communities are primarily determined by variation in soil nutrient content and soil moisture (Cornelis *et al.*, 2009). Thus, soil texture and drainage class were extracted as categorical soil variables from the Belgian soil map (Dondeyne *et al.*, 2014). Mean highest and lowest groundwater tables data were obtained from a soil hydrology raster (ECOPLAN, 2014). Land cover data were obtained from one of the base layers in the ECOPLAN ecosystem services information system Habitat data were obtained from the Biological Valuation Map (BVM), a geodataset of habitat types with attribute information on the ecological context and value of the delineated areas (Vriens *et al.*, 2011).

Probability models of the spatial distribution of each of the 13 genera were developed using MaxEnt version 3.3.3k. MaxEnt is a machine-learning algorithm highly suitable to develop models from presence-only data (Elith *et al.*, 2006; Phillips *et al.*, 2006). The algorithm is based on the principles of maximum entropy and finds an optimal probability distribution using a combination of occurrence data and environmental data (Elith *et al.,* 2011). MaxEnt is known to perform well even when environmental covariates are linearly correlated (De Marco and Nóbrega, 2018). The logistic output of MaxEnt is an attempt at expressing the raw output as a probability of presence (Elith *et al.*, 2011). A 10-fold cross validation was applied.

We applied the ‘10 percentile training presence’ rule on the MaxEnt-output (Ficetola *et al.*, 2009; Pearson *et al.*, 2006; Skowronek *et al.*, 2017), for every genus and model approach separately, resulting in a threshold value above which 90% of the training samples are correctly classified. Thus, a unique threshold value is used for every genus to create a binary output (0 = absence, 1 = presence). Binary stacking is the process of adding up the individual binary models, resulting in a generic tree diversity varying from 0 to 13 genera.

We found that binary stacking was a suitable method for an urbanized research area such as Flanders. The alpha diversity map of allergenic tree species (Figure 4) shows that the loamy south of Flanders is richer in taxa than the poor sandy soils in the north. The tree diversity is lowest in the polder region in the west of Flanders.

The model resulting from this study can be expanded by stacking more binary SDMs, by producing species-level models or by producing models of other plant groups. Abundance distributions can be obtained by combining the SDM output (based on widely available presence-only data) with a few inventories of tree abundance in a random forest model as presented in section 3.1.1 and 4.1.1).

Spatially-explicit biodiversity data are vital for emerging environmental health studies (McInnes *et al.*, 2017), for example to study relationships between residential and dynamic exposure and human health outcomes (Cox *et al.*, 2017; Shanahan *et al.*, 2016). The generic tree diversity map is used in the dynamic exposure study of the RespirIT project.

Landscape and urban planners could also use tree diversity maps to identify areas with low diversity and optimize the delivery of ecosystem services or decrease potential social inequalities in access to biodiverse green space by increasing biodiversity in focus areas (Wolch *et al.*, 2014). Finally, when subsets of models for allergenic species are used, diversity maps could be interpreted as allergy risk maps and inform pollen allergy patients about pollen allergy risks (McInnes *et al.*, 2017). For this last application we refer to the maps as produced in section 3.1.1.

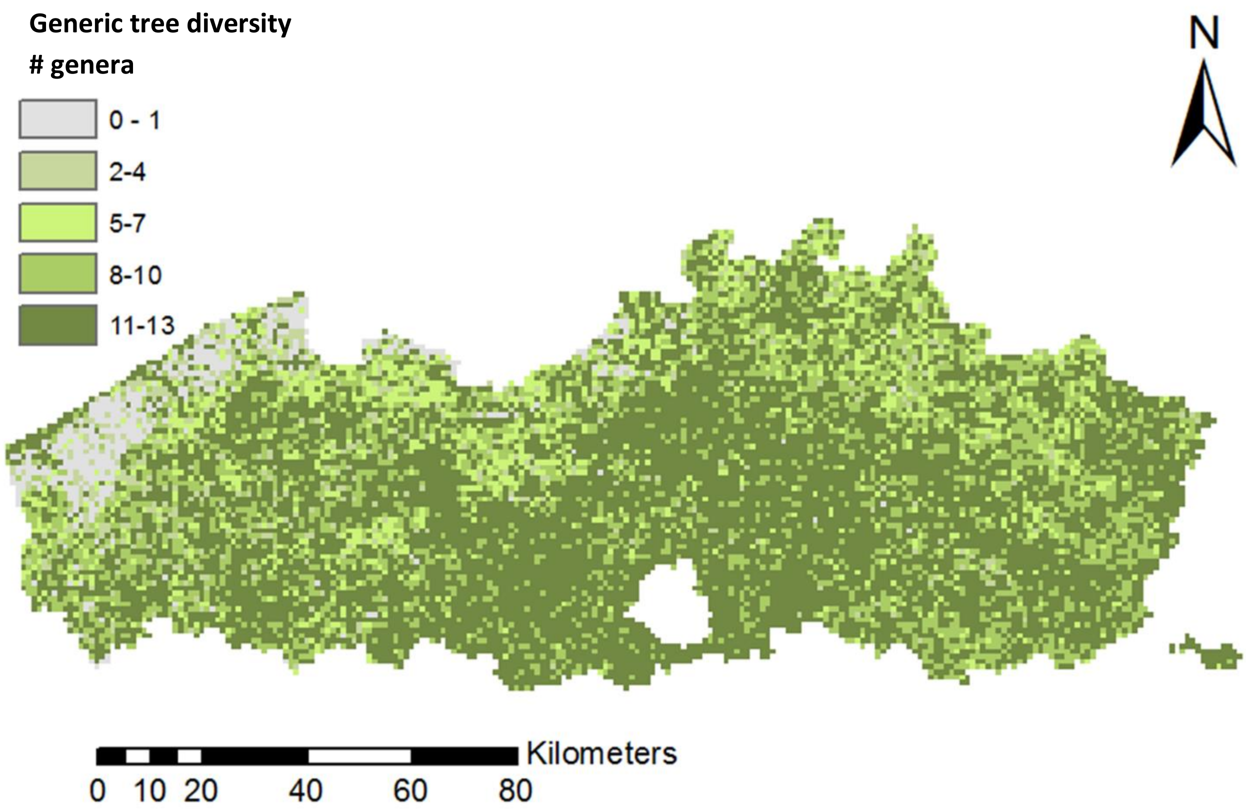

Figure 4: Alpha diversity of wind pollinated tree species in Flanders.

B. 3.1.1 Allergenic tree abundance

For the purpose of mapping the location of targeted allergenic trees species (task 3.1.1), we built a two-stage approach to both predict habitat suitability and species abundance. The main objective was to estimate the similarity of the conditions at any site to the conditions at the locations of known occurrence (and perhaps of non-occurrence) of allergenic trees and predict species ranges with environmental data as predictors. The methodological approach consists of constructing a dataset on the basis of sampling plots with detailed information on tree species and good data coverage for calibration, and then to extrapolate this relationship to a larger area by using statistical regressions. Our two-stage approach first uses Species Distribution Models (including Random Forest, GLM, GBM, and Maxent) to predict species habitat suitability, using environmental data as predictors (e.g. soil types, slope, temperature). This first predictive modelling approach is used as it is good at selecting relevant variables and working with presence-absence data to evaluate the predictions (Elith et al., 2006). The second stage then uses random forest regressions to model the relationships between abundance, the probability of occupancy predicted by the SDMs, and additional tree cover covariates, which we expect to be important for modelling tree abundance.

The first stage included two may steps. First, we used forest inventories data from Flanders and Wallonia in combination with open access data from the observations.org platform. This allowed for building a representative sample of allergenic tree observation records covering both forested and non-forested areas of Belgium. Then, we created a set of independent variables in order to predict habitat suitability. We downloaded and use data on a variety of ecological variables across Belgium from multiple sources. Pre-processing of layers were carried out in ArcGIS (ESRI 2014) to ensure identical extent, cell size, and coordinate system for use in species distribution modelling. All environmental covariates were used at 100m resolution: vector datasets were rasterized to 100 m resolution. Next, we first explored how to fit species distribution models (SDMs) to these data. SDMs use species records and environmental variables to fit models that describe the relationship of the species' distribution to the environmental variables, which can then be used to predict the occupancy probability or related measures across a wider landscape (Elith & Leathwick, 2009; Thuiller, 2003).
We selected around 15 environmental variables as covariates from the original set. We removed one of each pair of variables with a pairwise Pearson's correlation coefficient higher than 0.7, while retaining variables that are known to be important determinants of plant growth (Guisan et al., 2007; Prentice et al., 1992). Drawing upon the literature and previous studies (see Guisan et al. (2007); Hill et al. (2017); McInnes et al. (2017)), the final selection was: altitude, aspect, slope, direct incoming solar radiation, mean diurnal temperature range, temperature seasonality, annual precipitation, topsoil available water capacity, topsoil texture class, soil category, distance to water, distance to roads, land cover type, and ancient woodlands.

We ran the random forest (RF) algorithm 15 times for each species using the 13 environmental covariates, producing a total of (3 species × 1 algorithms × 15 repeats) = 45 models. Each model run is carried out using a randomly chosen 70% of the presence–absence data (Heikkinen, Marmion, & Luoto, 2012; Thuiller, 2003); the remaining 30% was used for cross-validation to assess the performance of each model using two model assessment criteria; area under the receiver operator curve (ROC) and the true skill statistic (TSS; Allouche, Tsoar, & Kadmon, 2006). For each species, we selected the best-performing models to build an ensemble distribution model (a mean of the raw model results, weighted by the model ROC scores). Finally, model results were projected as to show on a continuous grid map the habitat suitability for the 3 targeted allergenic tree species.

The second stage made use of random forest regressions to model the relationships between abundance (the dependent variable), the habitat suitability predicted by the SDMs, and additional tree cover covariates, which we expected to be important for modelling tree abundance (Breiman, 2001). A separate random forest regression was implemented for *Alnus*, *Betula* and *Corylus*. The habitat suitability maps for all species were included as variables for each species, so that the models would also capture interactions between species (such as competition). Potentially, this could also capture variation in other variables that are not included in that species' SDM, but which correlate with the distribution of other species. Abundance data for trees were also obtained from regional forest inventories. While forest inventories provide an elaborated measure of abundance named relative basal area (m²/ha), most studies within the literature measure the abundance of allergenic pollen vegetation in the form of percent cover, i.e. the number of hectares covered by a species per square kilometre. The model output variable produced here is thus a percentage cover per grid square as to serve the feeding of pollen dispersion models (Pauling et al. 2011) and woodland management and conservation studies (Hill et al. 2011).

Additional covariates where built based on the vectorised topographic map (Top10vGIS) provided by the National Geographic Institute. We built the following layers from the dataset's polygon features: coniferous woodland, predominantly coniferous mixed woodland, mixed woodland, predominantly broad-leaved mixed woodland, broad-leaved woodland, unspecified herbaceous vegetation with brushwood, and gardens. Besides, we derived the number of isolated trees and the length of edge rows per ha from the point and linear features dataset respectively. We then computed the average value of each metric per buffer of 1 km as to capture the broader environmental conditions surrounding the one by one hectare pixel. Normalized vegetation indices (min, max, and Long Term Average) for the 2008-2016 period were also added as to take into account for plant phenology and live green vegetation. All these layers were used as covariates in the random forest regression.

We used R version 3.2.3 for all modelling and data processing (R Core Team 2015). Random forest regressions took the following form:

$$\mathrm{Abundance}_{\mathrm{sp.A}} \sim P_{\mathrm{sp.B}} + P_{\mathrm{sp.C}} + \mathrm{C_F} + \mathrm{I_F} + \mathrm{L_F} + \mathrm{N_F}$$

where P is the predicted habitat suitability from the relevant SDM model, C_F are the land cover variables, I_F the proportion of edge rows, L_F the density of isolated trees, and N_F the vegetation indices. F indicates that the same covariate was used to model each of the 3 targeted allergenic tree species. We thus used these models to predict abundance of each species across the whole of Belgium at 1 ha resolution. We choose random forest regressions because it is insensitive to data distribution and therefore copes well with our data, which has a high percentage of zeros (e.g. arable lands). It can also take a large number of potentially collinear variables, and is robust to overfitting, making it extremely useful for prediction (Prasad, Iverson, & Liaw, 2006; Segal, 2004). We used root-mean-square error (RMSE) and mean absolute error (MAE), produced by k-fold cross-validation with 10-fold, to evaluate our models. These two commonly used evaluation metrics give interpretations of a model's average error when testing it against independent data, in this case, the 10% that will be left out of each run (Chai & Draxler, 2014). Lastly, we produced a single abundance map for each species that represents a robust estimate of an allergenic tree species' density in Belgium at 1 ha resolution (see Figure 5).

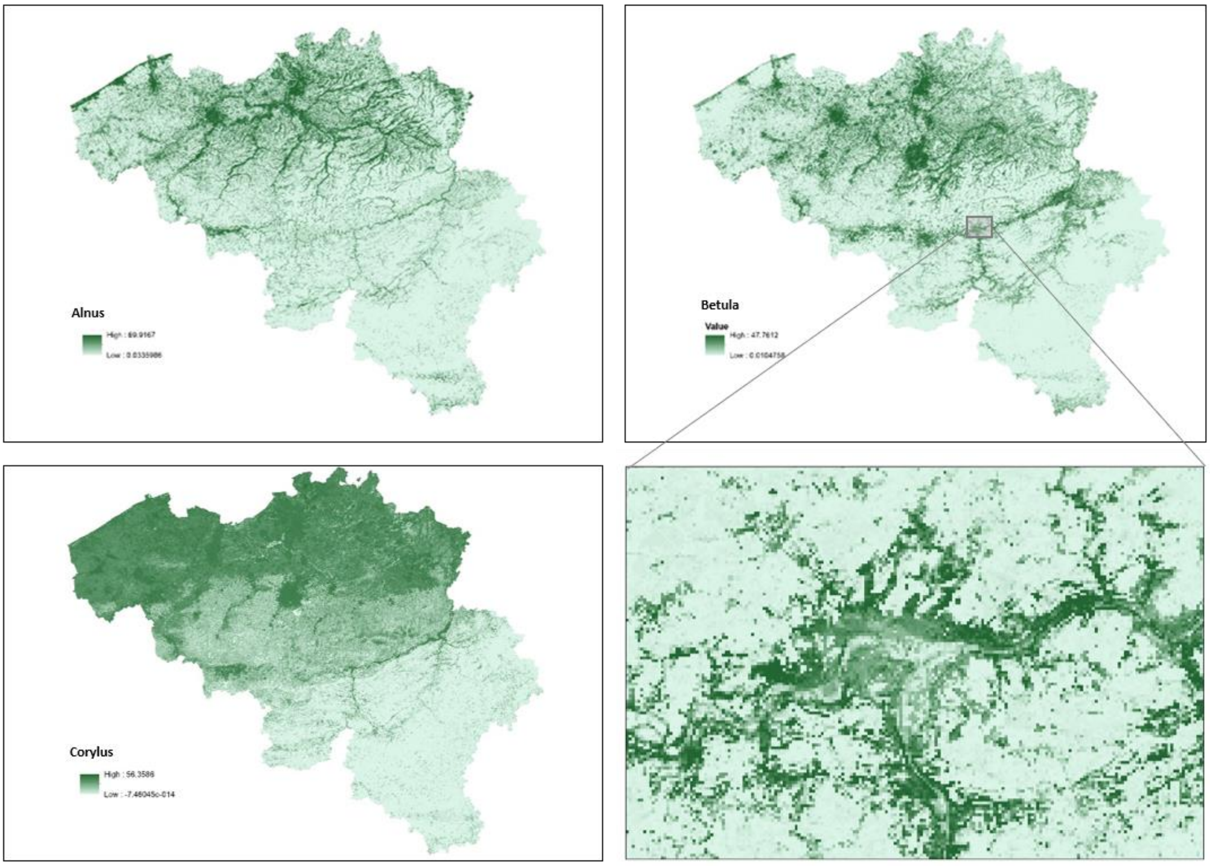

Figure 5: Tree density map for alnus, betula and corylus. These maps are produced from a combination of species distribution models and Random Forest regressions and show the spatial distribution of 3 targeted allergenic tree species across Belgium at a 100m x 100m resolution. A detailed view of the city of Namur is provided, showing intra-urban variation of Corylus density.

Four main limitations and opportunities for further research can be highlighted at the outcomes of this first mapping of allergenic tree species at the scale of Belgium.

- First, species with narrower elevation ranges and with slow growth rate are more likely to be modelled successfully (Elith et al. 2007). As allergenic species such as *Betula* and *Corylus* are fast growing species with weak competitive power, additional information on biotic variables should be gathered from forest inventories in order to improve the accuracy of models performed in stage 2. This means identifying a set of common trees present in forested areas that should also be modelled. The same approach should also be undertaken for areas outside forests.

- Second, observations from citizen science data often contain an important number of records along pathways and roads where opportunistic observations often occur. This is very useful to capture the presence of allergenic tree species in understudied areas where no systematic forest inventory was ever made. However, one species observed on a woodland edge will not necessarily be representative of the core of this woodland. The type of geographic distribution (core, satellite, see Collins et al. 1993) may affect model performance and should be further explored for each tree species.
- Third, information about the 'activity stage' such as flowering contained in the citizen science data could be used to build dynamic maps of allergenic tree species distributions. The specific time of flowering time could be identified during pollen season to identify which period is the most critical for pollen dispersion across the country.
- Fourth, data-points from forest inventories often fall within land use categories of mixed forest, deciduous forest and coniferous forest (i.e. 83,5% of the sample) according to the LULC map. The information about tree abundance, i.e. the dependent variable, is therefore highly contained to forested areas, while our covariates seek to describe the environmental conditions outside forests (e.g. distance to roads or proportion of residential areas). Future studies should integrate covariates that describe forest management practices and individual interventions both in the private and public spaces.

Task 3.2 Monitoring air quality

In Belgium, air quality is monitored by IrcelineIRCEL-CELINE (https://www.irceline.be/en)). During this project, they provided surface observations of anthropogenic air pollution across Belgium on a regular grid (resolution 4 km²). The following parameters were provided: ozone, NOx, PM10, PM2.5 and BC on an hourly basis (Janssens et al., 2008).

Task 3.3 Monitoring of tree species specific pollen concentrations

A. Silam pollen model

Pollen emission and transport models based on Chemistry Transport Models (CTM's) are an interesting tool to both quantify and forecast spatial and temporal distributions of airborne pollen levels near the surface provided that sufficient data on the pollen emission sources can be ingested. Pollen grains are biogenic aerosols with a diameter of typically 5-50 times larger than conventional atmospheric aerosols depending on vegetation species. The CTM SILAM (Sofiev et al. 2006, www.fmi.fi) is able to simulate the dispersion of pollen based on processes such as wind advection (transport with air masses), mixing due to turbulence, gravitational settling (dry deposition), and scavenging with precipitation (wet deposition) (Kouznetsov and Sofiev 2012).

Pollen modelling with SILAM is based on the temperature degree day approach or the thermal time flowering model (Sofiev et al. 2006). The parameterization of flowering follows a principle of two thresholds (start and end of the flowering season) for the temperature sum (Linkosalo et al. 2010; Sofiev et al. 2013), which assumes that the timing of birch flowering is mostly driven by accumulated ambient temperature during a certain period in time. The cumulative fraction of pollen released from the start of the pollen season until a certain period (to the end of the pollen season) is assumed piecewise linear and proportional to the temperature sum during the main flowering season. Short-term meteorological conditions such as wind speed, relative humidity and precipitation rate will affect the amount of pollen in the air. Precipitation and humidity inhibit the pollen release and threshold values are used to compute reduction factors. Typically, the lower and upper thresholds from relative humidity are 50% and 80%, respectively. For precipitation the lower and upper thresholds are 0 and 0.5 mm hr-1 (the grid cell average rate), respectively. At the saturation wind speed of 5 m s-1 the pollen release rate is maximal. At a wind speed around 1 m s-1, no pollen emissions will occur. The transport, emission and deposition in SILAM is driven by ECMWF ERA5 reanalysis meteorological data (grid-cell of 0.25° x 0.25°) (ECMWF) for the birch seasons of the period 2008-2018.

The simulation of birch pollen levels in the air requires the quantification of the spatio-temporal distributions of emission sources of birch pollen in the model domain. Stated otherwise, a map with the areal fractions of birch trees is fundamental as underlying data set or input. At the European scale, such a map was first compiled by Sofiev et al. (2006) and refined by (Sofiev et al, 2013). This general European map is updated for Belgium using Flemish and Walloon forest inventory data on a spatial resolution of 0.1°x0.1°. At each sampling plot the diameter at breast height (DBH) for individual birch (and other) trees were measured. 11.080 plots in the Walloon region and 2.147 plots in the Flemish region were used (observed over the period of 2008-2017 and 2009-2017 respectively). For each plot the DBH is scaled to basal area (m^2) per hectare (Dujardin et al. 2017). In the next step, a 0.1° x 0.1° grid was defined over Belgium that corresponds to the native SILAM grid. Based on the statistical relationship between DBH and birch tree canopy diameter (Hemery et al. 2005), the scaled areal fraction (percentage) at each grid-cell was assessed. The resulting updated areal fraction map of birch trees for Belgium was combined with the original MACCIII map if no birch data was available (i.e. no forest inventory data). In Figure 6 both the original and updated areal birch fraction maps are illustrated. The birch pollen levels near the surface are then modelled and compared using both the original as well as the updated birch fraction map. More details can be found in Verstraeten et al. (2019).

The 2008-2018-time series of birch pollen levels near the surface at daily basis were extracted from the SILAM output for each pollen monitoring station from Table 2 and compared with observations. In Figure 7 the time series of the pollen concentration from the SILAM run with updated areal fractions of birch trees are presented as well as the observed pollen concentrations for each station. The corresponding statistics (slope, intercept, R^2 of the SILAM versus observation data) are given in Table 3. The simulated daily pollen grains m^{-3} near the surface from the scenario with the updated emission source maps compared to the pollen observations have larger slopes closer to one, and in general better R^2 values than the MACCIII model scenario (Figure 7 upper versus lower panel). This indicates that the observed pollen magnitude is generally captured well by SILAM when the birch area fraction maps are updated. Similar results can be found for the 3-day averaged, 5-day averaged pollen concentrations as well as for the 5-day moving average of pollen concentrations. With respect to the pollen monitoring stations, SILAM can reproduce the pollen time series quite well for most stations with longer amount of observations (more than five seasons), except for De Haan at the sea side where the sharp sea-land boundary does not correspond to the geometry of the ECMWF and fraction map size. If 5-day averages of birch pollen concentrations would be used, then reasonable large R^2 values from 0.60 up to 0.88 are obtained. For the location at the coast, the best correspondence between SILAM and observations is obtained using 3-day averages. Compared to MACCIII input, the R^2 values between the time series of SILAM and the observed ones at the pollen monitoring stations increase in general with 13 to 47%, except for De Haan, Antwerp and Genk where a slight decrease or status quo is obtained. Similar results are found for the 3-day and 5-day averaged pollen concentrations.

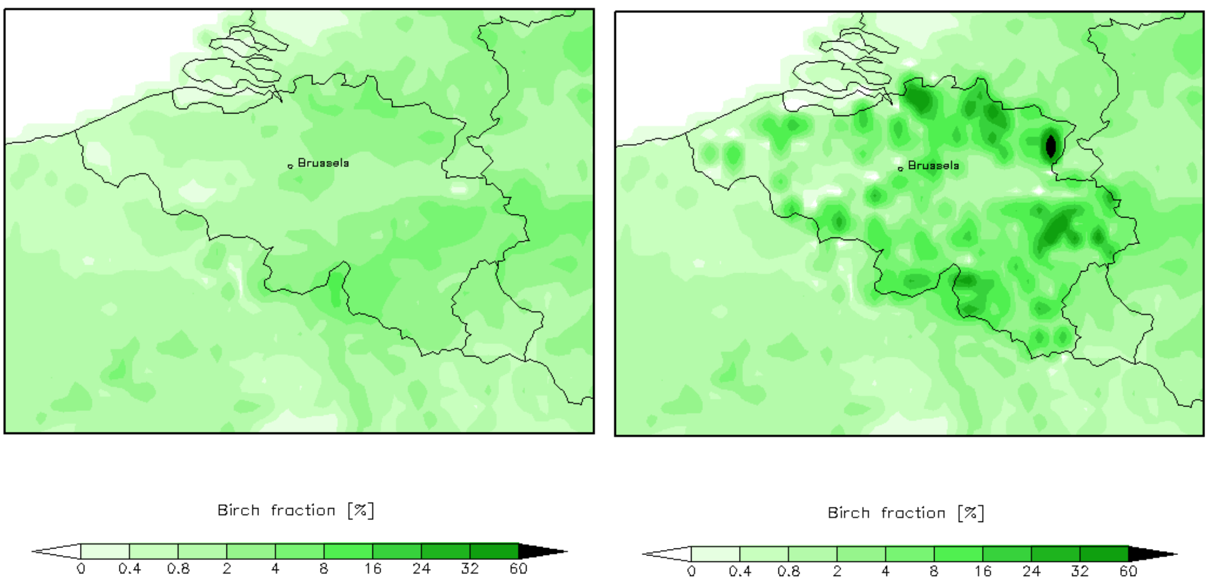

Figure 6: Spatial distribution of areal fractions (percentage) of birch trees in Belgium. Left panel (a) is the original (MACCIII) birch fraction map from Sofiev et al. (2006). Right panel (b) is the updated birch tree fraction map using forest inventory data.

Table 2: The location of the pollen monitoring stations of the Belgian aerobiological surveillance network and the corresponding observation periods available for this study. In total 50 birch pollen seasons were included

Pollen observation locations	Latitude / Longitude	Observation period
De Haan	51.274 N / 3.022 E	2008-2018
Tournai	50.614 N / 3.387 E	2013-2018
Brussels	50.825 N / 4.383 E	2008-2018
Antwerp	51.214 N / 4.393 E	2008-2010
Charleroi	50.405 N / 4.400 E	2008
Namur	50.468 N / 4.865 E	2010-2012
Marche-en-Famenne	50.200 N / 5.312 E	2012-2018
Genk	50.965 N / 5.495 E	2011-2018

Table 3: Airborne birch pollen concentration simulated with the SILAM model using the updated areal fraction map of birch trees compared to observations collected at eight pollen monitoring stations in Belgium. Slope, intercept and the determination coefficient (R^2) between modelled and observed birch pollen concentrations are given. Comparison is made for daily pollen concentration values, 3-day and 5-day average values, and for a 5-day moving average values

	De Haan	Tournai	Brussels	Antwerp	Charleroi	Namur	Marche-en-Famenne	Genk
Daily values								
Slope	0.55	0.90	0.80	0.64	0.54	0.36	1.07	1.14
Intercept	14.74	22.88	61.95	114.72	85.91	64.07	77.61	59.55
R²	0.30	0.57	0.40	0.33	0.29	0.33	0.59	0.49
3-day average								
Slope	0.84	1.10	1.03	0.92	0.69	0.51	1.27	1.41
Intercept	7.83	8.84	41.53	79.62	72.03	0.51	58.01	6.24
R²	0.76	0.75	0.56	0.56	0.43	0.54	0.75	0.65
5-day average								
Slope	0.74	1.16	1.18	1.18	0.98	0.52	1.20	1.87
Intercept	10.45	2.26	28.99	49.76	52.94	40.85	65.98	12.68
R²	0.49	0.83	0.63	0.75	0.65	0.58	0.77	0.84
5-day moving average								
Slope	0.83	1.17	1.13	1.07	0.79	0.52	1.24	1.41
Intercept	8.10	4.90	32.71	61.86	64.86	38.75	62.08	6.11
R²	0.68	0.79	0.65	0.66	0.53	0.61	0.78	0.68

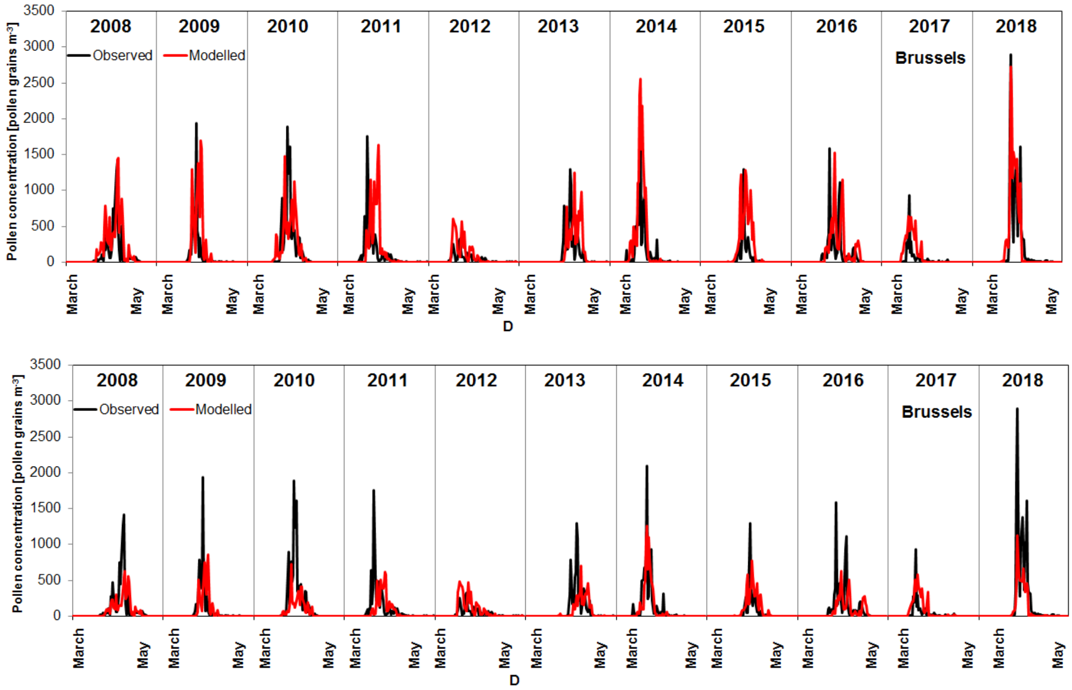

Figure 7: Upper panel. Time series of observed (red) and SILAM modelled (black) daily airborne pollen concentration (pollen grains m^{-3}at the surface for the period 2008-2018 for the Brussels monitoring station of the Belgian aerobiological surveillance network. SILAM uses the updated emission source map, i.e. areal birch fraction based on the forest inventory data of Flanders and Wallonia. Lower panel, same as upper panel, but SILAM simulations are based on MACCIII areal birch fractions.

The ability to detect either less or more than 80 pollen grains m^{-3} (the critical threshold above which the majority of sensitized patients is considered to develop allergy symptoms as used in Belgian aerobiological surveillance network) from the observations and the SILAM model using the updated birch fraction map is shown in Table 3, based on several statistics for dichotomous classification. The overall model accuracy (MA) represents the fraction of correct forecasts. The Probability of Detection (POD) is the fraction of high forecasts appeared to be correct. False alarms are quantified using the Probability of False Detection (POFD) which shows the fraction of low-concentration days predicted as high. The Odds Ratio (OR) shows how much higher are the chances to get the high than low day if the model prediction is high. The MA values of the pollen monitoring station is ~0.90 (0.82-0.93) for most stations, and the OR is 9.5 or higher (9.5-∞) indicating that SILAM is able to detect more than 80 pollen grains m^{-3} on days where more than 80 pollen grains m^{-3} are observed. Setting the exceeding threshold to 20 pollen grains m^{-3} results in OR values larger than 5.1. Null pollen levels (1-0 pollen grains m^{-3}), moderate pollen levels (10-100 pollen grains m^{-3}) and high pollen levels (100-1000) can be detected by SILAM with large probability (OR >2.8, 1.4 and 4.6 for all stations).

In conclusion: For Belgium we have performed a unique study that evaluates birch pollen levels near the surface retrieved from SILAM simulations using updated areal fraction maps of birch trees based on scaled forest inventory data. Multi-site evaluations of the simulated birch pollen concentrations were performed using daily observations at eight pollen monitoring stations corresponding to 50 birch pollen seasons. The odds ratio applied on the SILAM data set and the observations shows that the model is able to capture the probability of exceeding of the 80 pollen grains m-^{3} concentration near the surface. Finally, by introducing the updated map with birch pollen emission sources in Belgium, the correlation between the SILAM and observed time series of the pollen concentrations increases in general up to ~50% and the 5-day averaged pollen concentrations from SILAM have R^2 values between 0.49 and 0.84 at the pollen stations included in this study.

B. Local pollen composition

In European aerobiological networks, airborne pollen concentrations are monitored by the Hirst method at building roof-level, i.e. 10-20 meters above ground (Galán *et al.*, 2014), optimal for homogeneous measurements representative for an approximate 25 km radius area (Oteros *et al.*, 2019; Rojo *et al.*, 2019). Depending on the local landscape, topography and climate, the measured pollen composition can even be relevant for a 50 km radius area (Gehrig, 2019). Pollen can be transported over long distances, contributing to an extension of the pollen season (Bogawski *et al.*, 2019a). Short-distance transport, however, contributes to the most important pollen peaks (Rojo and Pérez-Badia, 2015). Nevertheless, standardized measurements are not taken in air layers at ground level, and as such outside the regular human breathing zone, potential local variations in pollen composition at lower height are poorly taken into account (Hjort *et al.*, 2016; Rojo *et al.*, 2019; Werchan *et al.*, 2017). Peel *et al.* (2013) have shown that the actual pollen-dose can differ strongly from the measured regional pollen concentration.

We aimed to measure local variations in airborne tree pollen composition by passive sampling at 2 m height above ground-level. We intended to identify the environmental factors of the surrounding landscape that drive the local airborne pollen composition and at which spatial scales the environment affects the local airborne tree pollen composition the most. These scales would be of relevance for exposure studies.

We placed passive samplers (Figure 8) at 14 sites in Flanders and the Brussels-capital region: Aarschot, Bornem, Brussels, Genk, Gent, Hasselt, Heusden-Zolder, Hoboken, Kessel-Lo, Mechelen, Neerpelt, Oplinter, Roosdaal, Sint-Truiden. We sampled airborne tree pollen between February and May 2017 under supervision of the Belgian Aerobiological Surveillance Network.

To characterize the local airborne pollen composition at each site, the total pollen count (per taxa) from passive sampling was divided by the number of sampling days and multiplied by 30 to obtain estimates of monthly pollen loads. The monthly average pollen taxa data were then log-transformed. Ordination of the sampling sites based on pollen taxa composition was obtained by Non-metric multidimensional scaling (NMDS). An initial exploratory run, testing one- to four-dimensional ordination, showed that a two-dimensional ordination resulted in an acceptable stress score of < 0.1 (Kenkel and Orloci, 1986). NMDS presents the sampling sites in two-dimensional space and based on Bray-Curtis distances a stress level is determined. The stress level quantifies the compositional dissimilarity between the original and current position of the sampling sites. The iterative process (set to a maximum of 100 iterations) aims to minimize the stress value (Clarke, 1993). Ordination was performed using the *vegan* package (Oksanen *et al.*, 2019) for R software (R Core Team, 2017).

The surrounding environment was characterized from two land cover data sources available for Flanders. The ECOPLAN dataset (Ecoplan, 2014) is a gridded land cover dataset with a spatial resolution of 5×5 m. The Biological Valuation Map (BVM) (Vriens *et al.*, 2011) is a vector-based dataset of habitats with information on the type and ecological value of the habitats. Polygon sizes range between 4 m² and 3236 ha. The mapped polygons are visited by experts in the field to survey the vegetation present to make specific habitat types. In addition, the presence of remarkable species can be reported as high ecological value. The area fractions (%) of the land cover classes were calculated within six radii (20 m, 200 m, 500 m, 1000 m, 2000 m, 5000 m) around the sampling site using ArcGIS 10.5.1 software (ESRI, 2011). The radii we studied correspond to the meso-gamma scale as proposed by Orlanski (1975), atmospheric processes relevant for pollen transport are studied at this scale (Romero-Morte *et al.*, 2018).

For the gradient analysis the site of Brussels was not included, because detailed land cover data was not available for the Brussels-Capital Region. We used the *envfit* function of the *vegan* package (Oksanen *et al.*, 2019) in the R software (R Core Team, 2017) to correlate (r^2) the area fractions with the ordination of the sampling sites. The gradients in the environment are unknown and inferred from the pollen compositions, i.e. an indirect gradient analysis. Correlations with a p-value smaller than 0.1 are considered significant.

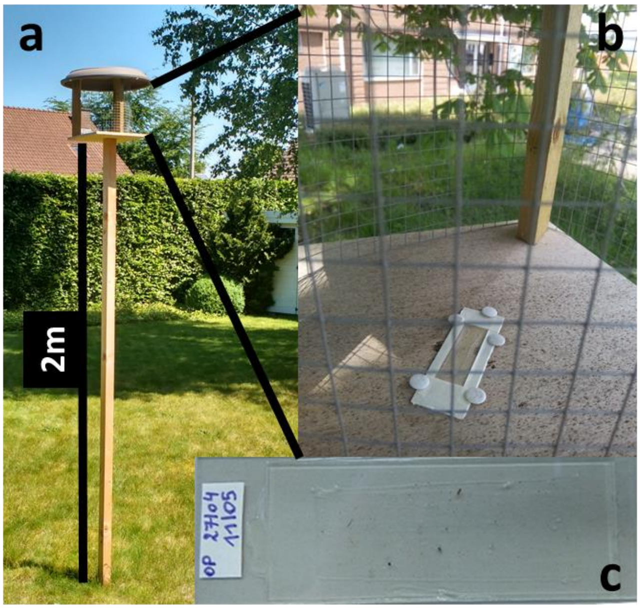

Figure 8: (a) Durham-type passive pollen sampling construction, mounted at 2 m height above ground level. (b) Sticky tapes were placed in the sampler for successive periods of two weeks per tape (c) The samples were mounted on glass slides and labeled before proceeding to pollen identification and counting by light microscopy.

Passive sampling of airborne tree pollen demonstrated that local variations in airborne tree pollen composition were driven by landscape characteristics at the meso-scale (1-5 km). Exposure studies (WP4) should thus prioritize exposure radii within this range of scales.

WP4: Assessment of spatio-temporal relationships between respiratory health of individuals and plant diversity

Task 4.1. Assessment of epigenetic biomarkers of wheezing susceptibility, exposure to green spaces and plant diversity (the chronic health effect)

We randomly selected 391 placental tissue samples collected from placenta's from mother-newborn pairs of the (Environmental Influences on Early Ageing) ENVIR*ON*AGE birth cohort recruited between February 2010 and May 2013. After isolation of genomic placental DNA with QIAamp DNA mini Kit (Qiagen, Hilden, Germany), the DNA was quantified using Thermo Scientific NanoDrop^{TM} 1000 spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA) and subsequently, DNA was treated with bisulfite to convert unmethylated cytosines into uracil using EZ DNA methylation-Gold^{TM} Kit (ZYMO RESEARCH CORPORA TION, Irvine, CA, USA.). The bisulfite- treated DNA was amplified via polymerase chain reaction (PCR) in accordance with the manufacturer's instructions (Pyromark PCR kit, QIAgen, Hilen, Germany) and PCR amplification success was quantified via post-PCR gel electrophoresis (Bio-Rad, Hercules, CA, USA). DNA methylation pattern was quantified via pyrosequencing using PyroMark Q48 Autoprep and PyroMark Q48 Advanced Reagents (Qiagen, Hilden, Germany). We investigated CpG sites in 2 serotonin-related genes: *SL6A4* and *HTR2A.* CpG sites were selected combining GRCh37/hg19 UCSC genome browser 2009 with literature. PyroMark Assay Design 2.0 was used to develop appropriate PCR- and sequence primers. These genes were selected because of their importance in serotonin-signaling, involved in fetal neurodevelopment (McKay 2011). The *HTR2A* gene encodes the G-protein coupled, 5-hydroxytryptamine (serotonin) receptor 2A and functions as a mitogen, affecting the placental implantation and mitogenesis (Oufkir and Vaillancourt 2011)· The solute carrier family 6 member 4 (*SLC6A4*) codes for a serotonin transporter that manages the placental uptake of serotonin (Hadden, Fahmi et al. 2017).

For green space exposure, we used the cumulative area (m^2) covered by gardens, grasslands and forests, derived from the Top10 Vector land cover geo-dataset for Belgium (National Geographic Institute (NGI), 2014) for two buffers surrounding the household (50m and 1000m).

Furthermore, we used four other types of green space variables (overall green space, low-growing, and high-growing green space, and natural area) within five buffers around the household (50m, 100m, 300m, 500m and 1000m). Here, the Geographical Information System (GIS) ArcGIS 10 software was used to calculate the green spaces surrounding the residential addresses of the participants, which were geocoded beforehand. We determined the exposure to overall green space based on the land cover data from the Green Map of Flanders (GF) 2012 (Agency for Geographic Information Flanders, AGIV) (Groenkaart Vlaanderen 2012). The GF contains high-resolution (1x1m) information about the physical attributes of the surrounding environment based on segment-based classification of 2012 satellite flight ortho-photographs (Agency for Nature and Forest, ANB). The overall green, including all non-agricultural vegetation, is further stratified in low-growing and high-growing green, depending on whether the vegetation is below or above 3 meters in height, respectively. For the exposure to natural area surrounding the household we used functional information about the landscape based on the Land-use Map of Flanders (LF) 2012 (Landsgebruikskaart Vlaanderen 2012). We created a new artificial classification ,"nature" described as the sum of the following 10 LF classes: thickets and bushes; poplars; deciduous, coniferous and alluvial forests, semi-natural grassland, heath, swamp, coastal dune, and bay mud.

We included maternal demographic characteristics such as maternal age, pre-pregnancy body mass index (BMI), maternal education and maternal smoking behavior, as well as newborn characteristics such as gestational age, sex and ethnicity. Additionally we adjusted for season at delivery and maternal exposure to $PM_{2.5}$-levels. Maternal education was defined as low (no diploma or primary school),

middle (high school), or high (college or university degree). Information about smoking behavior was divided in never smoked, stopped before pregnancy and current smoker. The ethnicity of the child was determined based on the native country of the grandparents and classified as European when at least two grandparents were European. We calculated the average ambient airborne $PM_{2.5}$ levels during the whole pregnancy using a spatiotemporal interpolation method that combines land cover data and data from monitoring stations as described before (Janssen, Dumont et al. 2008).
For the statistical processing we used the R environment.(R Development Core Team 2019). To examine the associations between the green space exposure and methylation of the *HTR2a* gene we used a generalized linear model, considering we only used one CpG site. After exclusion of samples with no methylation data (n = 61) and missing data of green space exposure (*n* = 1) or lifestyle characteristics (*n* = 2) statistical analyses were carried out for 327 subjects in the green space exposure models. To examine the associations regarding the *SLC6a4* gene we used mixed-effects models with the 7 different CpG sites treated as repeated measures. After exclusion of samples with no methylation data (n = 9) and missing data of green space exposure (*n* = 3), lifestyle characteristics (*n* = 2) statistical analyses were carried out for 377 subjects in the green space exposure models. We adjusted both models, for the aforementioned covariates, but including the batch for the *SLC6a4* statistical analysis. The results are presented as an absolute percentage change in placental DNA methylation for an interquartile range (IQR) increment in green space exposure. The exposure to forest cover (50m), and grassland cover (50m) however was stratified into a discrete variable of none versus some presence of green cover, to better deal with the low number of households with surrounding green. Statistical significance was defined as *p*-Value < 0.05.
On average, the mothers were 29 years old and had a median (± standard deviation, sd) pregestational BMI of 23.4 kg/m^2 (± 4.5 kg/m^2). Half of the mothers obtained a higher education and the majority (66.2 %) never smoked cigarettes. For the newborn population, approximately half (51.8 %) were boys and the majority were primiparous (51.2 %) or secundiparous (37.5 %). The mean gestational age was 39 ± 1.3 weeks.

The most abundant type of residential green space was low-growing green, followed by high-growing green, and then nature (Figure 9). The percentage of low-growing green decreased as the buffer size surrounding the participants residence increased, while the percentage of high-growing green showed the inverse effect. Similarly, the percentage of nature increases when the distance from the household increased.

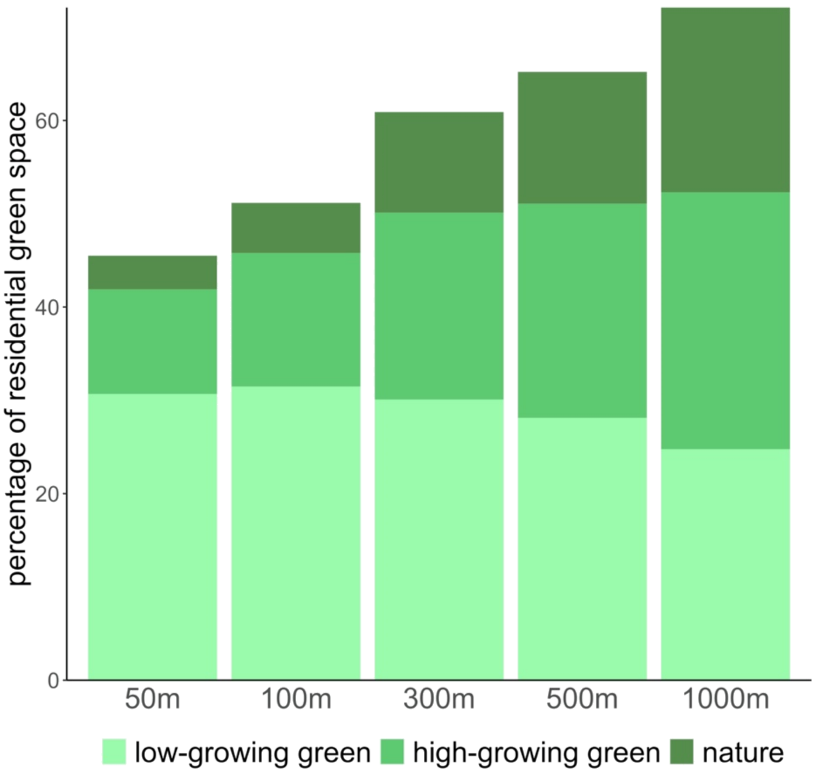

Figure 9: A stacked bar plot presenting the overall percentage of residential green space (low-growing green, high-growing green and nature) within five different buffers surrounding the participants household (50m, 100m, 300m, 500m, and 1000m).

In Figure 10 we show correlation coefficients (Spearman's rho) for all green space variables. As expected, the highest correlations were observed between high-growing green and forest (Spearman's rho of 0.96). The same high correlation was also observed concerning nature and high-growing green (rho = 0..92) and between nature and forest (rho = 0.94). The correlation between low-growing green and gardens was less pronounced but still positive (rho = 0.57). In contrast we notice a negative correlation between low-growing green and the variable grassland (rho = -0.08), which is probably due to the fact that low-growing green only included non-agricultural vegetation in its calculation.

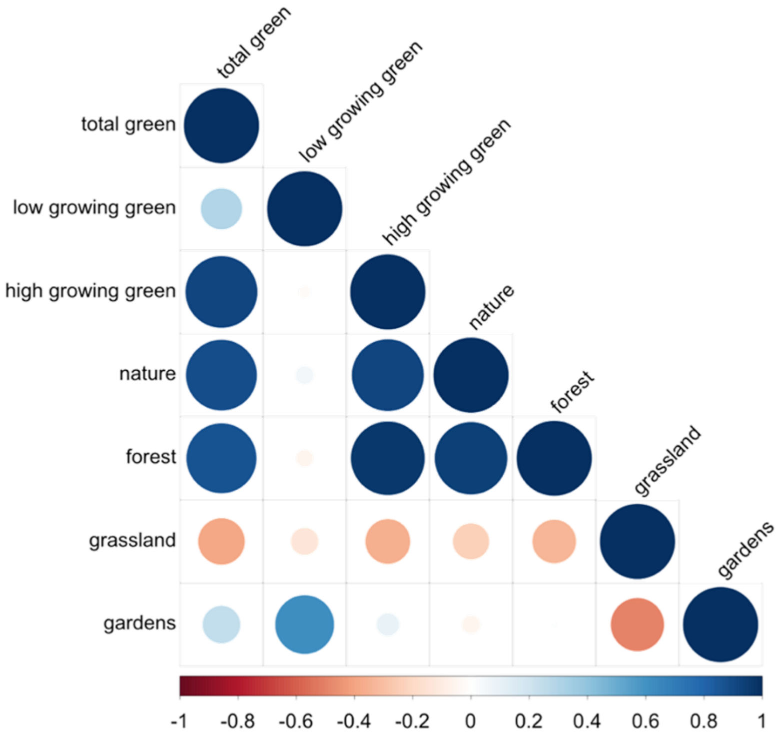

Figure 10: Spearmann correlation matrix of all calculated green space exposure variables (including GV-variables (total green, low-growing green, and, high-growing green), LG-variable (nature) and NGI-variables (gardens, grassland, and forest)) within a 1000m radius surrounding the participant's residence.

After adjustment for newborn sex, maternal age, maternal education, smoking status, gestational age, prepregnancy BMI and ambient airborne $PM_{2.5}$ concentrations, placental *HTR2A* methylation was significantly positively associated with an increase in residential greenness. With an IQR increment in residential nature exposure, DNA methylation was 0.006 % (95%CI: 0.001,0.011) and 1.389 % (CI: 0.660,2.119) higher within a 50m and 100m radius respectively. Moreover for an IQR increment in residential greenness exposure within a 1000m buffer the methylation of *HTR2A* was 1.472 % (95%CI: 0.168;2.776) higher. Other buffers did not alter the methylation in a significant way (Figure 11). Additionally the other green space variables derived from NGI were not statistically significant (Figure 12).

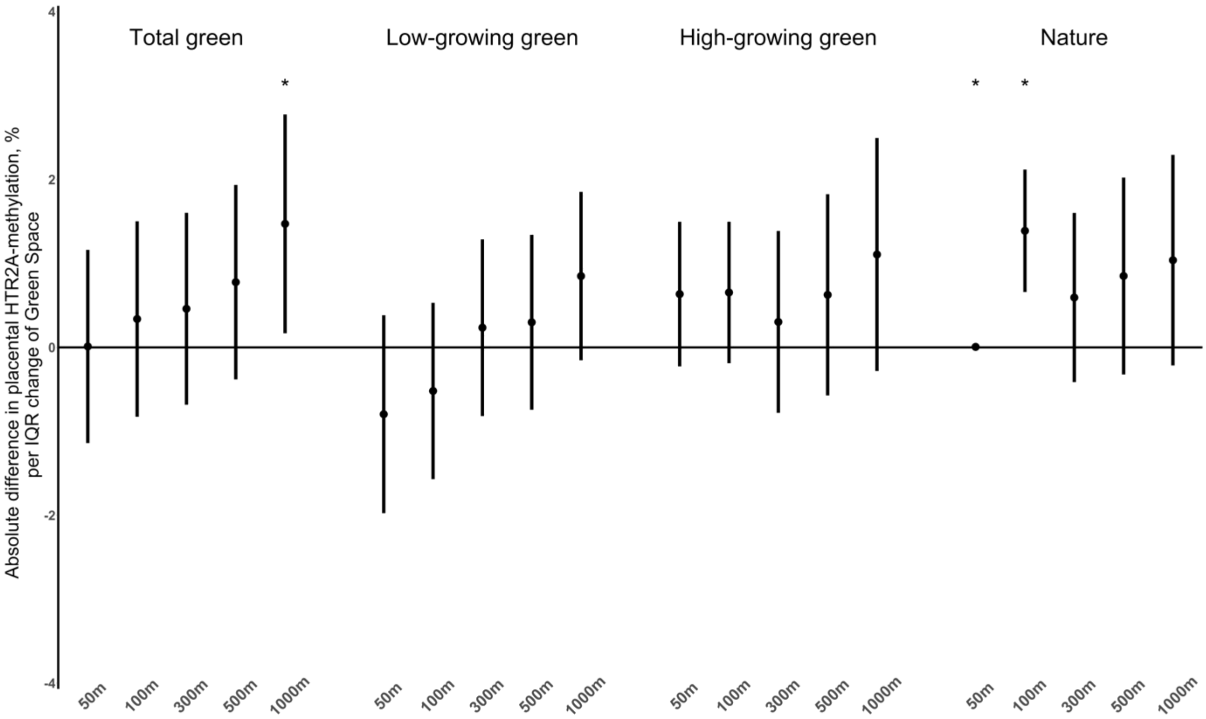

Figure 11: Estimates (with 95% CI) of 327 placental *HTR2A* DNA-methylation in association with green space exposure derived from GV (total green, low-growing green, and, high-growing green) and derived from LG (nature) for five buffer surrounding the residence (50m, 100m, 300m, 500m and 1000m). Model was adjusted for newborn sex, maternal age, maternal education, maternal smoking status, gestational age and pre-pregnancy BMI and ambient airborne $PM_{2.5}$ concentration.

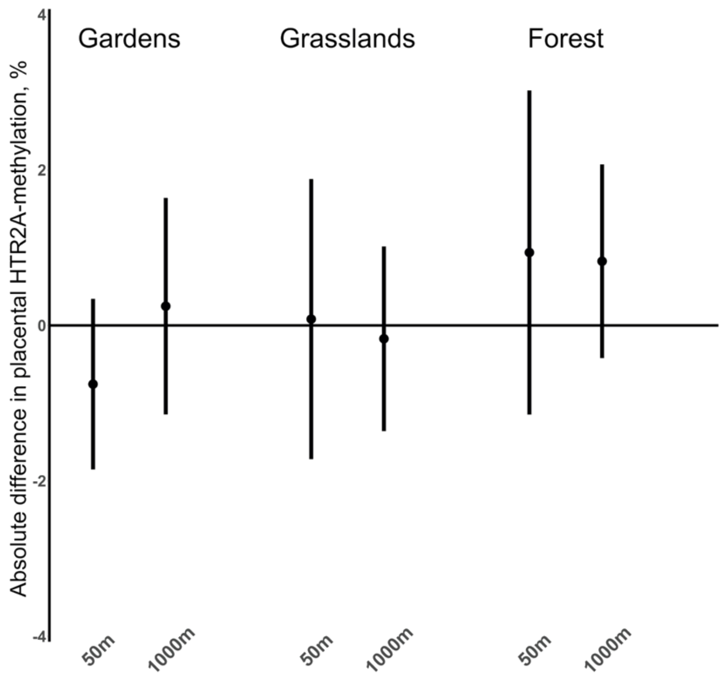

Figure 12: Estimates (with 95% CI) of 327 placental *HTR2A* DNA-methylation in association with green space exposure derived from NGI (gardens, grasslands and forest) for two buffer surrounding the residence (50m and 1000m). Variables with low amount of green within the buffers are recalculated as a discrete categorical variables (50m Forest and 50m Grassland). Model was adjusted for newborn sex, maternal age, maternal education, maternal smoking status, gestational age and pre-pregnancy BMI and ambient airborne $PM_{2.5}$ concentration.

We fitted a mixed-effects model to evaluate the association between the methylation levels in the *SLC6a4* promoter region of interest (individual CpG sites treated as repeated measures) and green space exposure. We adjusted for the same covariables as we did with the *HTR2A*-methylation, and added the plate used to measure the methylation on the different CpG sites. With an IQR increment in residential low-growing green, DNA methylation was 0.07 % (95%CI: -0.13 ,-0.01) lower within a 50m radius surrounding the household. Other buffers or other green space variables did not alter the methylation in a significant way (Figure 13 and Figure 14).

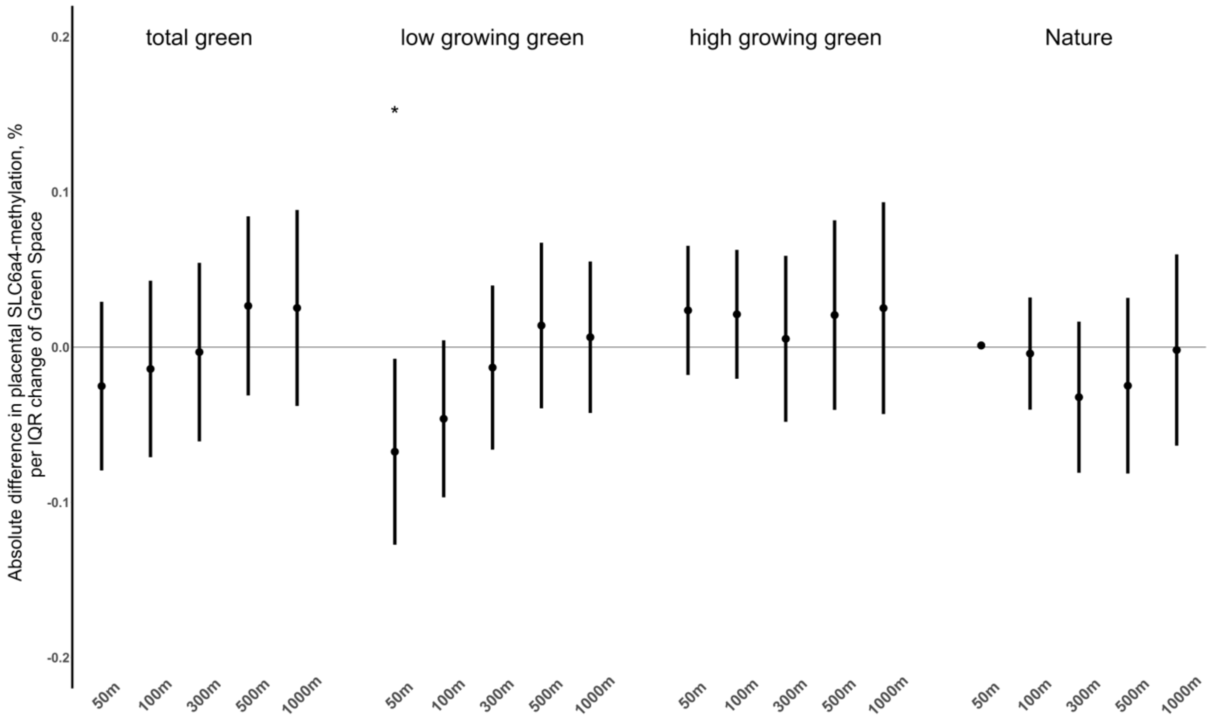

Figure 13: Estimates (with 95% CI) of 377 placental *SLC6a4* DNA-methylation in association with green space exposure derived from GV (total green, low-growing green, and, high-growing green) and derived from LG (nature) for five buffer surrounding the residence (50m, 100m, 300m, 500m and 1000m). Model was adjusted for newborn sex, maternal age, maternal education, maternal smoking status, gestational age and pre-pregnancy BMI and ambient airborne $PM_{2.5}$ concentration.

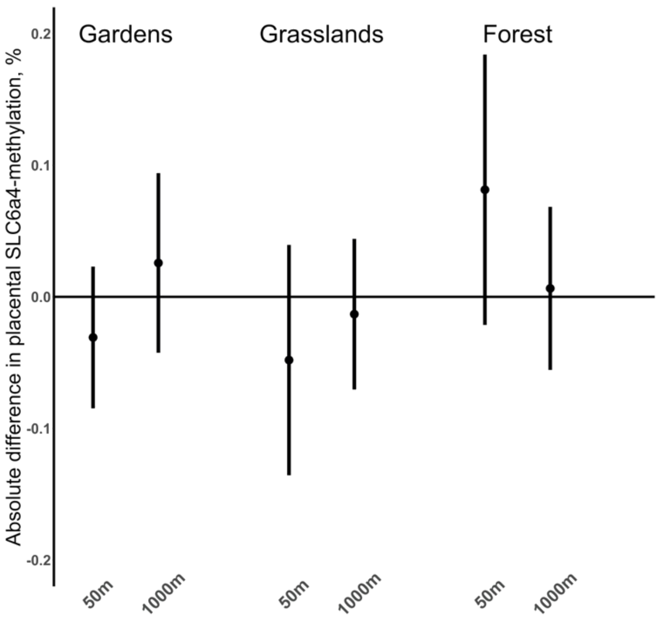

Figure 14: Estimates (with 95% CI) of 377 placental *SLC6a4* DNA-methylation in association with green space exposure derived from NGI (gardens, grasslands and forest) for two buffer surrounding the residence (50m and

1000m). Variables with low amount of green within the buffers are recalculated as a discrete categorical variables (50m Forest and 50m Grassland). Model was adjusted for newborn sex, maternal age, maternal education, maternal smoking status, gestational age and pre-pregnancy BMI and ambient airborne $PM_{2.5}$ concentrations.

This study has several strengths. First of all, we included a large number of mother-newborn pairs, which were representative for the gestational segment of population in Flanders, as described earlier (Janssen, Madhloum et al. 2017). Additionally, we used bisulfite-PCR-pyrosequencing to asses DNA methylation, which is a highly standardized technique with an excellent detection limit to obtain accurate results (Tost and Gut 2007, Dejeux, El abdalaoui et al. 2009). Moreover, we used high-resolution green exposure data to obtain detailed information on the type of green space, considering this might be an important contributing factor to the underlying mechanisms between green space exposure and health outcomes (Dadvand, Villanueva et al. 2014). Our results show that early-life green space exposure, expressed as overall green and nature, is associated with an increase in placental *HTR2a*-methylation. Epigenetic changes in genes involved in serotonin signaling, could results in changes to fetal neurodevelopment (Gaspar, Cases et al. 2003, Hadden, Fahmi et al. 2017). This research is an important first step to investigate the relationship between early-life prenatal green space exposure and fetal cognitive development. Furthermore, these findings are relevant for policymakers and important to take into consideration for future urban planning. However, further research is needed to assess the implications of these epigenetic changes on the cognitive functioning.

Task 4.2 Assessment of spatio-temporal relationship between allergic symptom severity and exacerbation risks and environmental conditions (the acute health effect)

A. Residential exposure

Participants to the RespirIT study reported their mood and allergy symptoms daily in the diary of the Dutch or French language smartphone application that was specifically created for this study (WP1) The user-manual encouraged the participants to fill in the diary at the end of every day as to have an idea of the overall mood and symptoms during the past day. In case the participants experienced symptoms that were not due to a regular cold or a flue they were asked to record these at the end of the day in the diary of the RespirIT app. The diary asked the question 'What symptoms are bothering you today and to what degree?', followed by a list of eleven symptoms related to seasonal pollen allergy: wheezing, dyspnea, coughing, sneezing, runny or stuffy nose, itching, fatigue, headache, bad sleep, difficulty concentrating, and irritation of the eyes. Under every symptom the participant could move a slider from 0 (never) to 4 (always), Figure 15. The daily symptom score was calculated by summing the individual values for the eleven symptoms resulting in a scale from 0 to 44, 0 corresponding to no allergy symptoms. We calculated the average symptom score on symptom days (AvgSy) multiplied by 10 and truncated to no decimals.

Daily mood was assessed on the same symptom days with one question 'How did you feel today?' and scored on a five-point rating scale represented by minimalist smileys (Figure XX). A score from 1 to 5 was assigned to the moods: 1) poor, 2) fair, 3) neutral, 4) good 5) excellent. We calculated the average mood score on symptom days (AvgMo) multiplied by 10 and truncated to no decimals.

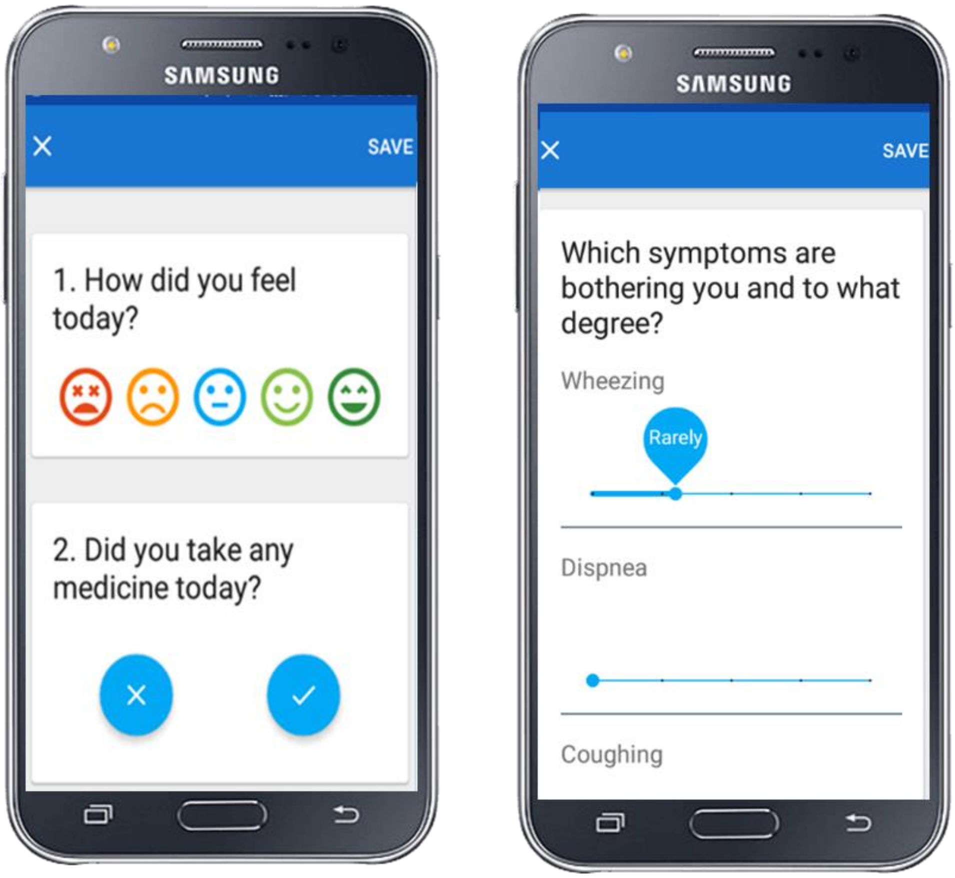

Figure 15: Two screenshots from the RespirIT app for android used by the participants to log their mood (left) and allergy symptoms (right) at the end of every day.

Two validated questionnaires were used to quantify mental health outcomes during the tree pollen season. The Dutch and French version of the standardized questionnaires were integrated in the follow-up questionnaire sent out to the participants during the pollen season. First, the 12-item General Health Questionnaire (GHQ-12) is a shorter version of the fully detailed 60-item General Health Questionnaire (https://www.gl-assessment.co.uk/products/general-health-questionnaire-ghq/). In the GHQ respondents were asked how their mental state during the past month differed from the usual state. The GHQ is sensitive to short-term psychiatric disorders and can be interpreted as a measure for psychological distress. To score the GHQ-12 we used the standard bimodal scoring method (0-0-1-1) resulting in a scale range of 0–12, a higher score meaning more distress. Second, the

Perceived Stress Scale (PSS) is a widely used validated questionnaire to measure the perception of stress over the past month (http://www.mindgarden.com/documents/PerceivedStressScale.pdf). The scale includes items about current levels of stress as well as items on stressful times during the past month. Questions are scored on a five-point rating scale (0-4). Four of the questions, however, are formulated in a positive way and needed to be scored in reverse. After summation of the scores the scale ranges from 0 to 40, where 0 is best.

Residential green space was objectively quantified from geodatasets for a 0.5, 1, 2 and 5 km radius around each of the 157 residences (Task 2.2). Using topological overlay between the corresponding circular zones and the Top10 Vector land cover geodataset for Belgium ("Soil cover and vegetation" dataset, version 1.1 2011, National Geographic Institute, equivalent scale level of 1:10,000), the cumulative cover (m^2) of three green space types (gardens, grassland and forest) was determined for the three radii. Gardens are included as a unique land cover type in the dataset. Grassland cover was calculated as the sum of permanent grassland or hay meadow and lawns. Forest cover was determined as the sum of all five forest-related land cover types in the geodataset: 1) coniferous forests, 2) mixed forests dominated by conifer species, 3) mixed forests, 4) mixed forests dominated by deciduous species, 5) deciduous forests. Garden, grassland and forest covers within each radius were then expressed in 10 ha units.

The Belgian forest inventory uses a regular grid of 0.5 × 1 km covering the entire area of Belgium. The grid points that occur in forested areas were visited by experienced surveyors who record the species type and circumference at 1.30 m above ground level of trees and woody vegetation in an 18 m radius around the point (Westra et al., 2015). From the circumference and the plot area we were able to calculate the basal area (m^2/ha) of the three main allergenic taxa *Alnus* (alder), *Betula* (birch), and *Corylus* (hazel) from the Belgian forest inventory. The total basal area of the allergenic trees can be interpreted as the density of allergenic trees in the forest.

We included the participant's sex and age as sociodemographic characteristics. Next, we included three indicators of physical fitness: body mass index (BMI), smoking behaviour (yes/no), and physical activity (at least 1 × /week 20 min of activity vs. less). Education level (higher education vs. no higher education) was included as indicator of socio-economic status of the participants. Higher education is defined as having obtained an academic degree through a tertiary education. Regarding the health status of the participants we included two items: medication use (antihistamines and/or corticosteroids: yes/no) and chronic disease (asthma and/or chronic respiratory disease: yes/no). Participants were asked to report whether hazel, alder and/or birch trees were present or absent in close proximity to their residence. The objective presence of these allergenic trees was not verified (outside forested areas). Therefore, the reported presence of allergenic trees is interpreted as perceived presence.

Generalized linear models based on the Poisson probability distribution for count data with log-link function were used to estimate the effects of residential green space exposure on allergy symptoms and mental health of participants. The unadjusted models included only objective green space predictors. In the fully adjusted model all the confounders were included at once. To test whether having more severe allergy symptoms may reduce a potential positive effect of exposure to forests on distress, we included allergy symptoms as additional explanatory variables in models for mental health. We calculated both unadjusted and confounder-adjusted estimates and their 95% Wald confidence intervals. Model performance was evaluated using Akaike's Information Criterion (AIC). Models were created and evaluated using IBM SPSS (Version 26) predictive analytics software.

The study population consisted of 95 women (60.5%) and 62 men (39.5%). All participants were adults aged between 21 and 67 years (median age 39, IQR 16). Over half of the patients had a normal body weight (58.6% normal BMI; median BMI 23.5 kg m^{-2}, IQR 5.5). The majority of the patients were non-smokers (96.2%), were physically active (≥ 20.min active/week: 91.1%) and had a higher education level (91.1%). Almost all of the allergy patients took medication (93.3%), with 52.9% of the allergy patients using antihistamines, 7.0% using corticosteroids, and 34.4% taking a combination of both. Some patients suffered from other chronic respiratory health issues besides pollen allergy, mostly asthma (28.6%).

The most prevalent green space types present around the residency was gardens, followed by grasslands, and then forests (Figure 16). As the distance from the residence increased the area fraction of gardens decreased, while the area fraction of grassland and forest increased. The density of allergenic trees in the forest increased with the increasing forest area fraction.

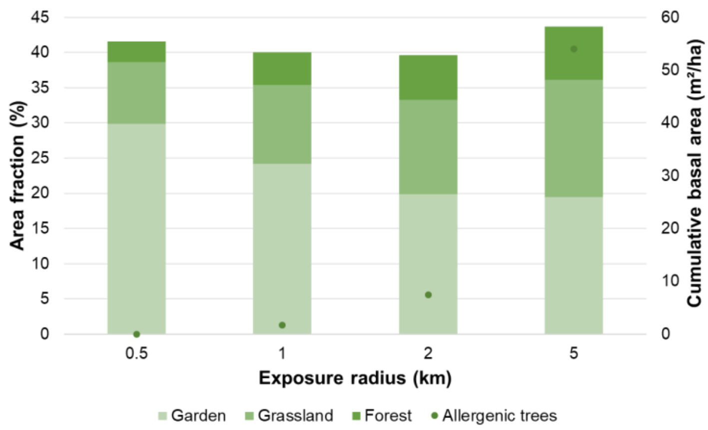

Figure 16: A stacked bar plot presenting area fractions of residential green space (garden cover, grassland cover and forest cover) within the four exposure radii (0.5, 1, 2 and 5 km) studied. The cumulative density of allergenic trees within the entire forest area fraction is presented as a dot.

In our cohort of 157 tree pollen allergy patients residing in Belgium, exposure to residential green space (gardens, grasslands and forests) had a protective effect on short-term mental distress (GHQ-12) and perceived stress (PSS) during the tree pollen season. However, the objective presence of allergenic trees in forests near the residence, in particular within a 2 km distance, was found to be a risk factor for short-term mental distress and perceived stress (Figure 17). More severe allergy symptoms were associated with worse mental health (Figure 17). Exposure to residential green space was associated with higher allergy symptom scores but did not affect daily mood. We did not find evidence that green space had a mitigating effect on respiratory health complaints of allergy patients during the tree pollen season (Figure 18).

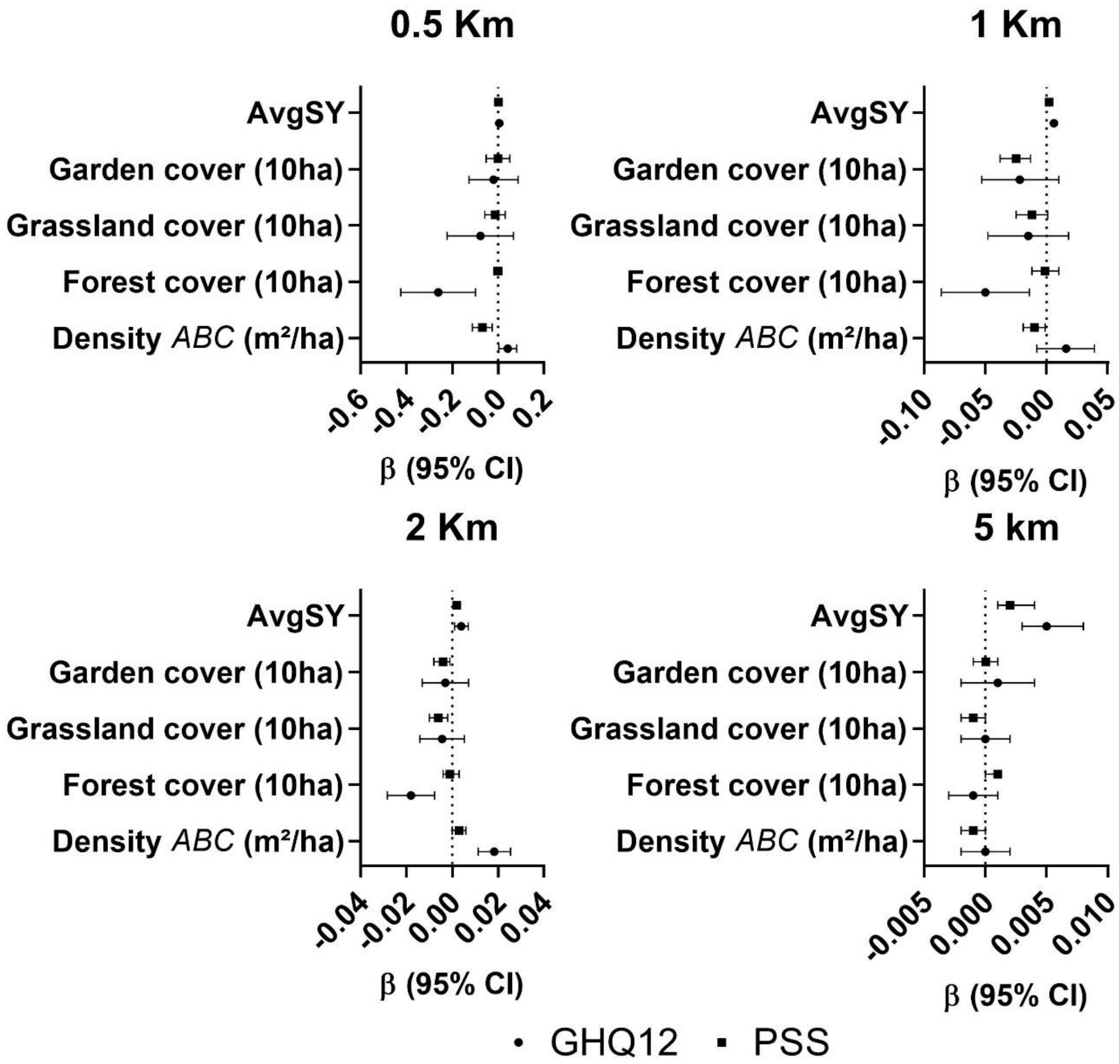

Figure 17: Association between exposure to green space and mental health (GHQ12 and PSS) adjusted for all confounders including average allergy symptom severity. Exposure to green space was determined for radii of 0.5 km, 1 km, 2 km and 5 km around the residence in a cohort of 157 tree pollen allergy patients in Belgium.

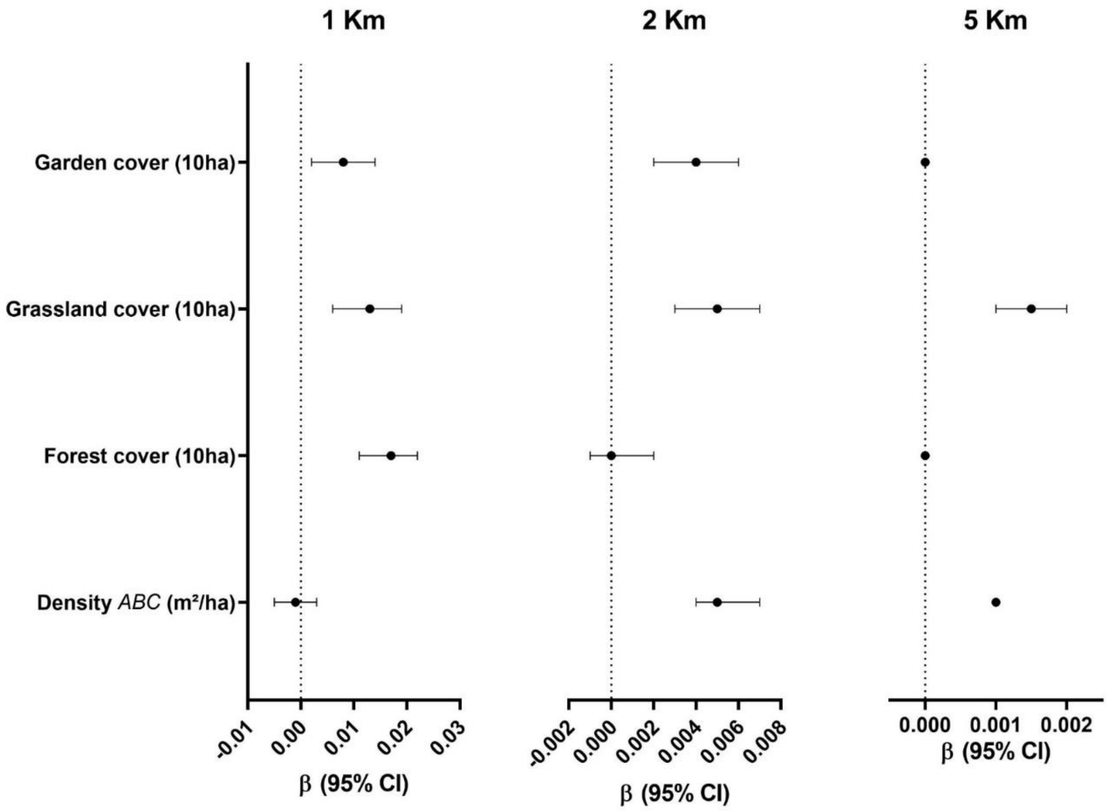

Figure 18: Associations (beta-coefficients with 95% confidence interval limits) between health outcomes and objective residential green space indicators in a 1 km, 2 km and 5 km radius around the residence in a cohort of 157 tree pollen allergy patients in Belgium. Parameter estimates are adjusted for sex, age, BMI, medication intake, chronic respiratory disease, smoking behaviour, higher education, physical activity and perceived presence of allergenic trees. The response variable is the average symptom score (Avg.Sy).

There are risks related to specific tree species for both mental and respiratory health during the pollen season which must be further elaborated into recommendations for design of allergy-friendly urban green spaces and other city greening (Aerts et al., 2021; Cariñanos et al., 2019; Jochner-Oette et al., 2018). Moreover, apart from residential green areas *sensu stricto* also more distant green areas should be taken into account (Jochner-Oette et al., 2018), since we find associations up to a distance of 5 km while pollen can travel over even larger distances.

B. Dynamic exposure

For the dynamic exposure study the health outcome of interest was the occurrence of a severe tree pollen allergy event defined by the symptom severity score provided by the participating patients. When the participants experienced symptoms that were not due to a regular cold or a flue, they were asked to record the allergy symptom severity in the diary of the Dutch or French language version of the mobile health app. The question asked in the diary was 'What symptoms have been bothering you today and to what degree?', followed by a list of eleven symptoms related to seasonal pollen allergy: wheezing, dyspnea, coughing, sneezing, runny or stuffy nose, itching, fatigue, headache, bad sleep, difficulty concentrating, and irritation of the eyes. Under every symptom the participant could move a slider along from 0 (never) to 4 (always), shown in Figure 15. The symptom severity score of each diary entry was the sum of the individual values for the eleven symptoms, resulting in a symptom severity score ranging from 0 to 44, 0 corresponding to no allergy symptoms. Severe allergy cases were defined as the 25% highest symptom severity scores recorded per patient.

Green space zones and types were extracted from the Top10 Vector land cover geo-dataset for Belgium (National Geographic Institute (NGI), 2014, cartographic reference scale 1:10,000). The vector dataset (consisting of points (e.g. individual trees), lines (e.g. hedgerows) and polygons (e.g. forest plots)) is the geometrically most accurate and thematically most detailed product of the NGI. We computed the area (m²) covered by the polygons of gardens, grasslands and forests within the cells of a 100 × 100 m reference grid. Grassland cover consisted of two land cover types: 1) permanent grassland or hay meadow and 2) lawns. Forest cover was determined as the total cover of five forest-related land cover types: 1) coniferous forests, 2) mixed forests dominated by conifer species, 3) mixed forests, 4) mixed forests dominated by deciduous species and 5) deciduous forests. Garden cover was included as a separate land cover type. Then, area fractions for each green space type were determined within a 1km buffer around each 100 × 100 m reference grid cell. We used a 1km buffer because associations between green space and health are often more relevant at larger scales beyond the direct surroundings (Browning and Lee, 2017).

The allergenic tree taxa of interest in this study were birch (*Betula* spp.), alder (*Alnus* spp.) and hazel (*Corylus avellana*), because these were the pollen taxa our participants were sensitized to. The development of the allergenic tree diversity is described in WP 3 – Task 3.1B. Then, similarly to the green space cover, average density for each taxa was determined within a 1km buffer around each 100 × 100 m raster cell.

Birch pollen levels are monitored at five measurement sites in Belgium by the Belgian aerobiological surveillance network (Sciensano, www.airallergy.be). These pollen concentrations were used to validate the birch pollen levels determined by the SILAM model as described in WP3 – Task3.3A. SILAM

provides daily birch pollen levels as grains/m³ at a spatial resolution of 10 km. Ultimately daily pollen concentrations were converted to 100 grains/m³ approximating the critical threshold above which the majority of sensitized patients experience allergy symptoms (80 grains/m³) as used by the Belgian aerobiological surveillance network (Hoebeke et al., 2018; Sofiev and Bergmann, 2013).
Ultimately, daily average concentrations for black carbon (BC), nitrogen dioxide (NO_2), ozone (O_3) and particulate matter smaller than 10µm (PM_{10}) were derived from the hourly result of the RIO model, WP3 – Task3.2.
We calculated dynamic exposure to the environmental features using GNSS tracks sampled at 1 second intervals. For annotation of the track with distinct behaviours, we down-sampled to 5 second intervals, which has shown to be a more suitable sampling frequency to successfully distinguish behaviors (Shen and Stopher, 2013). We defined three distinct behaviours: (1) stationary, when a person is sitting or standing; (2) active movement such as walking or bicycling; (3) motorized transport such as driving a car or using public transport. To distinguish stationary behavior from the two other types, we used a speed threshold of 3.6 km/h. This speed is lower than the threshold used by Hazlehurst et al. (2017) who define a speed larger than 5 km/h as being in a vehicle. In our classification, we wanted a threshold that was sensitive enough to detect walking. When the travelling speed was higher than 30 km/h the transport behavior was characterized as motorized transport. Transport slower than 30 km/h with an activity level higher than 0.2 was characterized as active transport. The activity level threshold was based on our own tests exploring the sensitivity of the gyroscopes in a Samsung Galaxy J1 smartphone. For an optimal classification of the transport behaviour, an appropriate dwell time should be applied (Hazlehurst et al., 2017; Shen and Stopher, 2013). A dwell time takes into account stopping at a traffic light or traffic jams during motorized transport. Using a dwell time of 60 seconds, a point with stationary or active transport behaviour would be set to motorized transport behavior when motorized transport was detected within 30 seconds before and after the behavior of that point (Hazlehurst et al., 2017).
To calculate dynamic exposure, values from the environmental rasters were extracted at the GNSS point locations using the extract function from the 'raster' package (Hijmans, 2020) of the R software (Core Team R, 2017). By extracting the raster values we determined the time spent exposed to a certain environment knowing that every GPS point corresponds to a 5 second time period. The total exposure is the sum of the time spent in a raster cell (t_i) multiplied by the value of that raster cell (r_i), i.e. $\sum_{t=1}^{t=n} t_i \times r_i$. The total exposure is then divided by the total time tracked to obtain an average exposure representative of that person day. In this way dynamic exposure to green space types, allergenic tree density, birch pollen and air pollution was determined for the total GNSS track and for

the three subsampled tracks: the stationary behaviour subsample, the active transport subsample, and the motorized transport subsample.

We used a case-crossover design (Jaakkola, 2003) to analyze the associations of dynamic exposure to green space cover, allergenic tree density, birch pollen levels and air pollutants (BC, NO_2, O_3 and PM_{10}) on the one hand with the occurrence of severe allergy symptoms on the other hand. Severe allergy was defined as the 25% highest symptom severity scores experienced per patient. Every case-day was matched to a control day with a symptom severity score in the lowest 25% for that patient. Case days were bi-directionally 1:1 matched to control days on the same weekday within the same month. For the case-crossover analysis 45 participants were excluded for two reasons: (1) the diary entries did not allow to make matching case and control days, (2) no sufficient GNSS data were gathered on selected case or control days. Ultimately 144 patients were included in the final analysis, providing 808 person-days equally split in case days and control days (WP2-Task2.2). We used Cox regression to estimate odds ratios with 95% confidence intervals. First models for exposure to green space types and density of allergenic trees were created (further termed unadjusted models), then the models were adjusted for dynamic exposure to birch pollen and air pollutants. We performed three stratified analyses to detect potentially different associations for subgroups of our participants. For a stratification by region (Brussels Capital Region, Flanders and Wallonia) tracks that crossed region boundaries were omitted and case days were matched to control days spent in the same region. For the tracks running through Flanders, we could calculate exposure to the generic tree diversity map developed in WP3-task3.1A. Ultimately, a sensitivity analysis was done considering cumulative dynamic exposure of the case day and one (lag 0-1) and two days (lag 0-2) before. When studying lag effects cumulative exposure is recommended as opposed to single-day lags (Hajat et al., 2001).

the cohort comprises more women (59.3%) than men (40.7%) with an average age of 40.4 (standard deviation of 9.9). There is no distinct difference in the total tracked time on case days (7.8 ± 4.6 hours) and control days (7.6 ± 4.8 hours). In addition, the time spent in the three behaviour types is approximately the same for case and control days: 82–83% stationary, 8% active transport and 9–10% motorized transport. Case days were characterized by high symptom severity scores with a median and inter quartile range (IQR) of 11 (8–16), while control days had a median symptom severity score of 0 (0–2). The exposure values indicate that participants were exposed to less grassland area fractions 11.8 % (7.3–17.5) and forest area fractions 6.4 % (2.9–14.0) on case days compared to control days [grassland 12.5 % (8.0–19.0); forest 7.0 % (3.0–14.8)]. On case days patients were also exposed to more pollen 193.9 grains/m³ (3.1–648.0) compared to control days 43.1 grains/m³ (0–240.0). Finally, case days are characterized by higher levels of air pollutants.

In our cohort of 144 tree pollen allergy patients residing in Belgium, the odds to experience severe tree pollen allergy symptoms were lower when participants were exposed to grassland or *Alnus* trees. However, exposure to *Betula* trees was a risk factor for severe pollen allergy symptoms (Figure 19). The stratified analysis by region included 678 person days with 193 case-control pairs in Flanders, 97 pairs in the Brussels Capital Region and 49 pairs in Wallonia. Only for the region of Flanders we found a protective effect of forest cover, We did not find an effect of exposure to the generic tree diversity (Figure 19). One and two days before the case day with severe allergy, fewer person-days were available because fewer tracks stretching over two or three consecutive days were available. There were 584 person-days for the calculation of cumulative exposure for lag 0-1 and 444 for lag 0-2. We found no significant associations with green in the unadjusted model for lag 0-1 and lag 0-2 (Figure 19).

Birch pollen and air pollutants (O_3 and PM_{10}) were found to be risk factors for severe allergy (Figure 19). We found that NO_2 was a risk factor for severe allergy during the motorized transport subsample of the track. The risk effect of O_3 was found for Flanders (Figure 20) and Wallonia, not in Brussels (Figure 21). In addition, birch pollen, O_3 and PM_{10} were identified as risk factors at lag 0-1 and lag 0-2 (Figure 22).

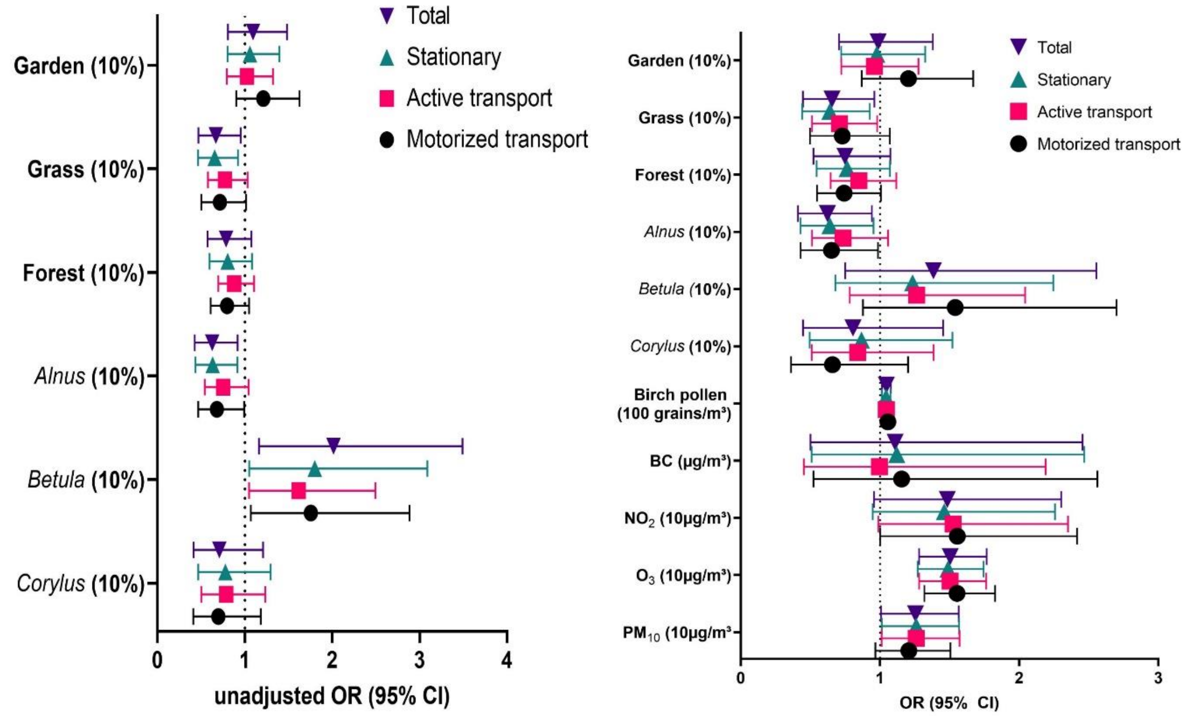

Figure 19: Associations (unadjusted (left) and adjusted (right) odds ratios (OR) with 95% confidence interval (CI) limits) between severe allergy and dynamic exposure to green space types and allergenic tree densities in a cohort of 144 tree pollen allergy patients in Belgium. Models were obtained from a case-crossover analysis and adjusted (right) for dynamic exposure to birch pollen and to air pollutants: black carbon (BC), nitrogen dioxide (NO_2), ozone (O_3) and particulate matter < 10µm (PM_{10}). The dynamic exposure was calculated for the total GNSS track and the stationary, active transport and motorized transport subsamples of the track.

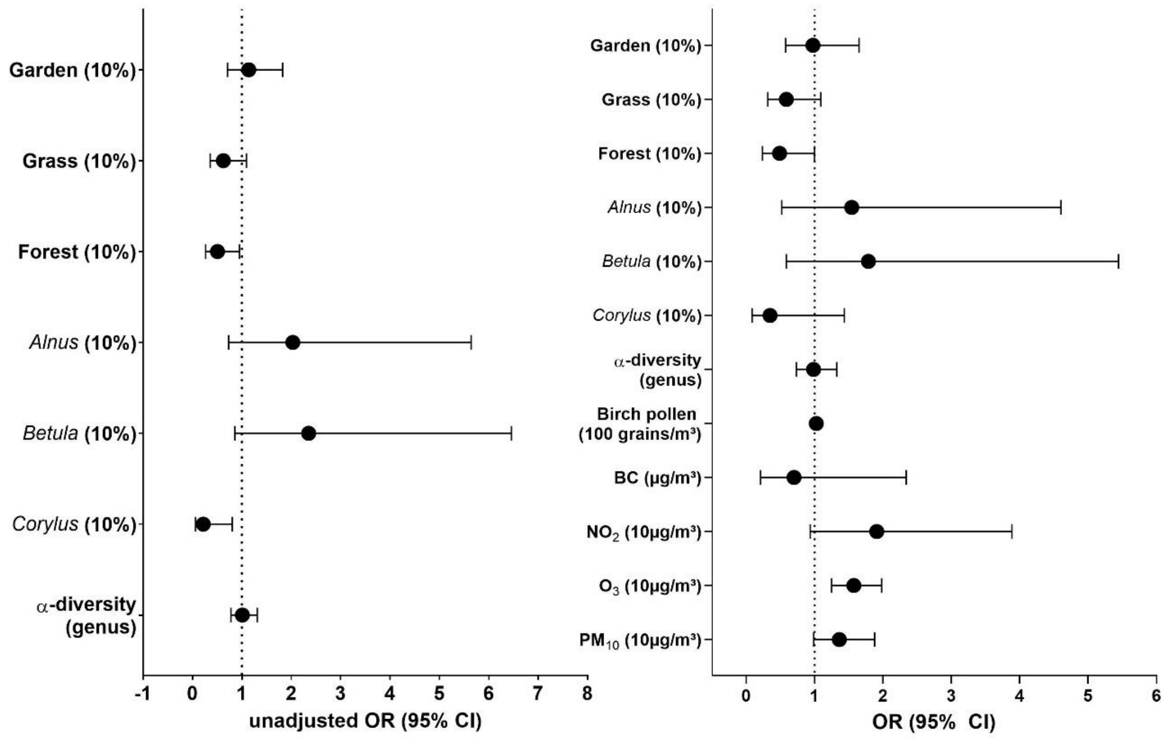

Figure 20: Associations, unadjusted (left) and adjusted (right) odds ratios (OR) with 95% confidence interval (CI) limits, between severe allergy and dynamic exposure to green space types and allergenic tree densities and α-diversity of tree genera in a cohort of tree pollen allergy patients in Flanders. In the right panel, models are adjusted for dynamic exposure to birch pollen and to air pollutants: black carbon (BC), nitrogen dioxide (NO_2), ozone (O_3) and particulate matter < 10 µm (PM_{10})

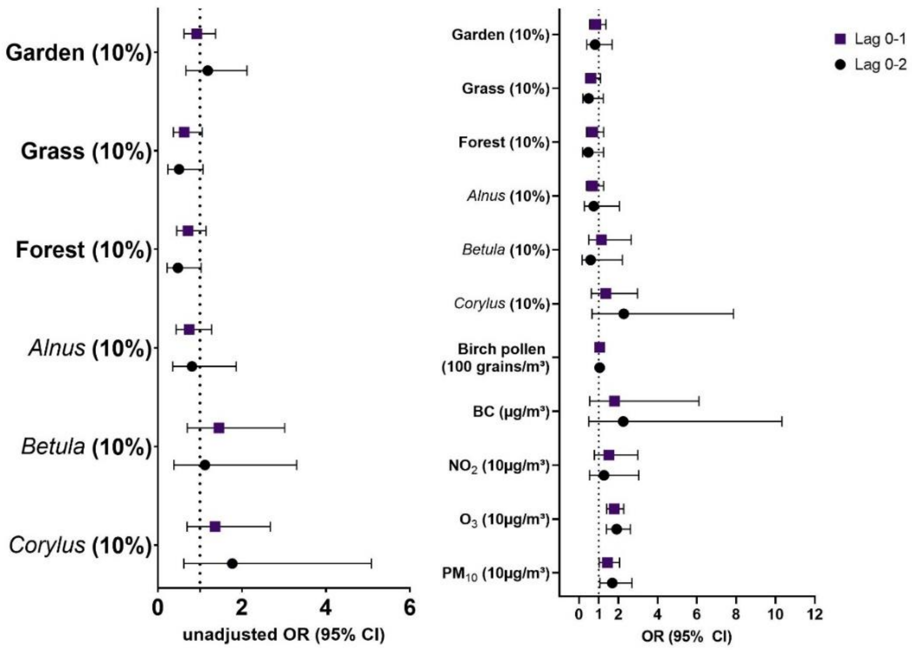

Figure 21: Associations (unadjusted odds ratios (uOR) (left) and adjusted odds ratios (OR) (right) with 95% confidence interval (CI) limits) between severe allergy and dynamic exposure to green space types and allergenic tree densities in a cohort of 144 tree pollen allergy patients in Belgium. Models were obtained from a case-crossover analysis and adjusted (right) for dynamic exposure to birch pollen and to air pollutants: black carbon (BC), nitrogen dioxide (NO_2), ozone (O_3) and particulate matter < 10µm (PM_{10}). The dynamic exposure is calculated for the total GPS track on the day of the severe allergy event and one (lag 0-1) and two (lag 0-2) days before.

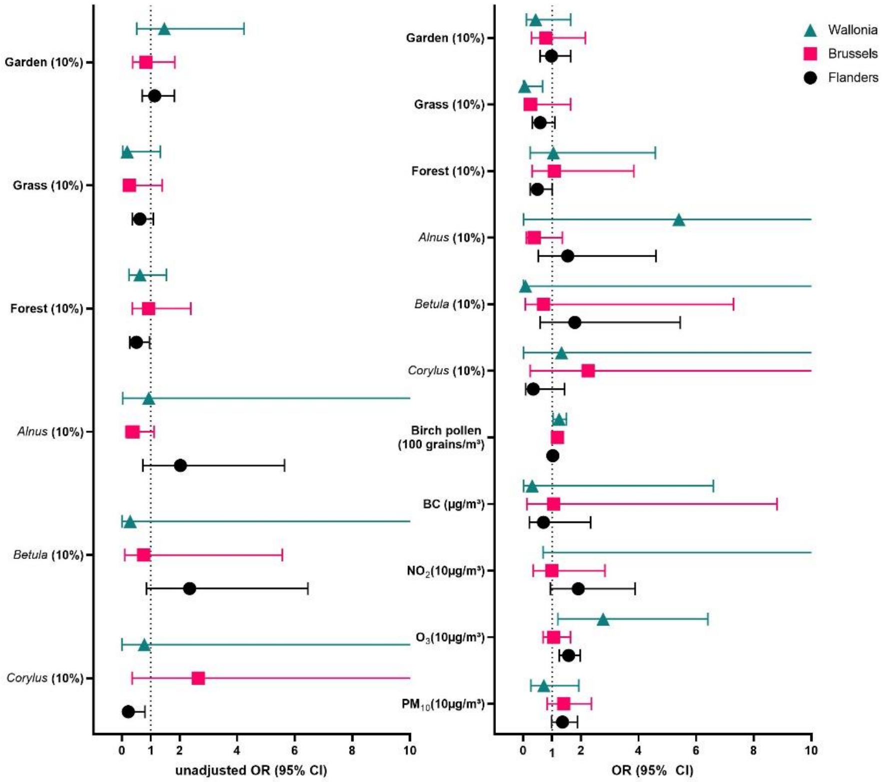

Figure 22: Associations (unadjusted (left) and adjusted (right) odds ratios (OR) with 95% confidence interval (CI) limits) between severe allergy and dynamic exposure to green space types and allergenic tree densities in a cohort of 144 tree pollen allergy patients in Belgium. Models were obtained from a case-crossover analysis *and* adjusted *(right)* for dynamic exposure to birch pollen and to air pollutants: black carbon (BC), nitrogen dioxide (NO_2), ozone (O_3) and particulate matter < 10µm (PM_{10}). The dynamic exposure is calculated for the total GPS track for the three Belgian regions Flanders, Brussels and Wallonia.

The main strength of this study is the spatio-temporal detail of the dynamic exposure calculated based on GNSS tracking. In addition, the temporal resolution (daily data) of the birch pollen model and the air pollutants model allowed to make personal exposure estimates at a spatial and temporal resolutions that have not been reported before.

The exposure to green space that we calculated is also very detailed using three distinct land cover types instead of satellite derived greenness indicators (i.e. NDVI). Additionally, we modeled densities of allergenic tree species at a high spatial resolution of 100 m. These species-specific exposures are of high importance for the participants in this cohort who are sensitized to the pollen emitted by these trees.

We calculated dynamic exposure on 808 person-days obtained from a cohort of 144 adults sensitized to tree pollen. We found that severe allergy was associated with birch pollen levels, O_3 and PM_{10} on the day of the severe allergy event and the two days before the event. Grass cover, forest cover, *Alnus* density and *Corylus* density were protective for severe allergy. However, increased densities of *Betula* trees was a risk factor.

Our results show that short-term exposure to green space has a protective effect on the physical health of pollen allergy sufferers. Tree pollen allergy sufferers can benefit from abundant green spaces at the condition that the density of allergenic trees is low. Spatio-temporal detail is important in environmental health studies on exposure to green space as well as pollen and air pollutants. We did not find protective effects of green space on the respiratory health of allergy sufferers when we did not take the spatio-temporal detail into account (WP4-Task4.2A: residential exposure).

WP5: Upscaling of spatio-temporal relationships between respiratory health and plant diversity to the regional scale

Task 5.2 Creating a relative risk GIS for allergy symptom severity and exacerbations for the Belgian Territory

In Task 4.2B we used a Cox regression model to determine the impact of exposure to green space, allergenic tree density and air pollutants on the health of allergy sufferers. We found that Exposure to grasslands and forests have a protective effect. Exposure to allergenic *Betula* (birch) trees, as well as air pollutants were risk factors. By taking the natural logarithm of the odds ratios described in Task 4.2B we obtained beta-parameters for a possible hazard model (Table 4). Odds ratios smaller than 1 correspond to negative beta-parameters, indicating a protective effect that contributes to a lower hazard level (Forest cover and Grassland cover). Odds ratios larger than 1 correspond to positive beta-parameters, indicating a risk effect that contributes to a higher hazard level.

Table 4: *Results from the Cox regression model for the total track on 808 person days from 144 participants to the RespirIT study. Beta-parameters are the natural logarithm of the odds ratio.*

	Beta-parameter	p-value	odds ratio	95% CI	
Alnus density	-0.474	0.025	0.622	0.411	0.942
***Betula* density**	**0.325**	0.298	1.384	0.750	2.554
Corylus density	-0.216	0.473	0.806	0.447	1.454
Forest cover	**-0.290**	0.115	0.748	0.521	1.074
Grassland cover	**-0.424**	0.030	0.655	0.446	0.960
Garden Cover	**-0.013**	0.937	0.987	0.706	1.380
Birch pollen	0.044	0.004	1.045	1.014	1.078
PM_{10}	**0.227**	0.043	1.255	1.007	1.565
O_3	**0.408**	0.000	1.504	1.281	1.766
NO_2	**0.395**	0.078	1.484	0.957	2.302
BC	1.028	0.800	2.795	0.001	7992.766

The following formula can be used to calculate the hazard level experienced given a certain exposure: $H(t) = H_0(t) * \exp(b_1 x_1 + b_2 x_2 + ... + b_p x_p)$. In this formula $H(t)$ is the hazard level, $H_0(t)$ is the baseline hazard, b_1-b_p these are the beta-parameter estimates, and x_1-x_p these are the covariates. The baseline hazard (H_0 (t)) is person-dependent, it can be omitted from the cox regression model when a person is used as its own control (which was the case in the case-crossover design used in Task 4.2B). Thus by calculating $\exp(b_1 x_1 + b_2 x_2 + ... + b_p x_p)$ we can estimate a general, environmental hazard for Belgium. However due to personal factors accounted for in the baseline hazard the experienced hazard can differ from the environmental hazard.

With the parameters given in Table XX the formula for the environmental hazard is the following: exp(-0.290 * Forest cover + (-0.424) * Grassland cover + 0.325 * Betula + 0.227 * PM_{10} + 0.408 * O_3 + 0.395 * NO_2). We use quintiles to obtain hazard maps with five hazard levels (Figure 23) the thresholds for these levels are presented in Table 5. The thresholds for 2018 are slightly higher than the thresholds for 2017, caused by higher concentrations of air pollutants in 2018. The differences between the hazard map of 2017 and 2018 are very subtle. When aggregating hazard levels at the municipality scale (Figure 24) there are no differences between both years (only 2017 is shown).

Table 5: *Limits of the quantiles that make op the five hazard levels used in the hazard maps.*

	Hazard 2017	Hazard 2018
Very low	<= 3.00	<= 4.66
Low	> 3.00 && <= 19.38	> 4.66 && <= 20.76
Medium	> 19.38 && <= 27.40	> 20.76 && <= 28.63
High	> 27.40 && <= 32.88	> 28.63 && <= 34.07
Very High	> 32.88	> 34.07

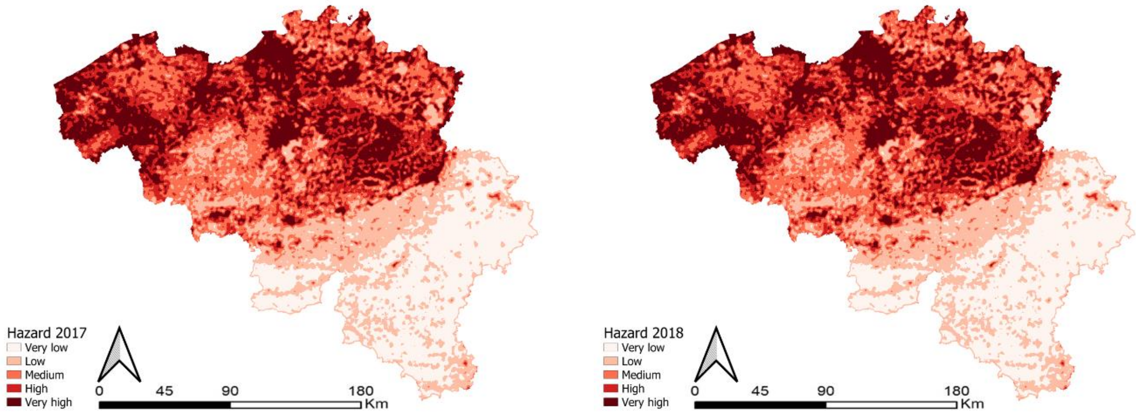

***Figure 23**: Hazard map for 2017 (left) and 2018 (right). Grassland and forest cover contribute to lower hazard levels, while* Betula *density and air pollutant (NO_2, O_3 and PM_{10}) concentrations contribute to higher hazard levels. Resolution of 100m.*

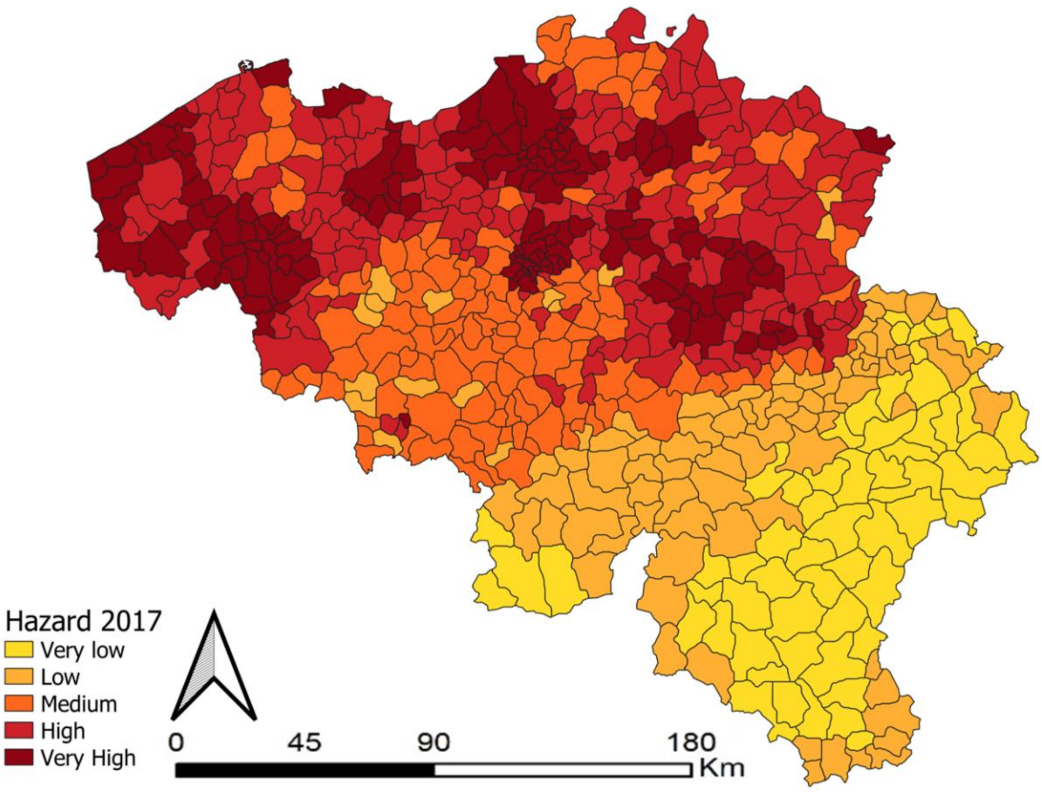

Figure 24: *Hazard level based on 2017 data (same result for 2018) based on the average hazard within a municipality.*

Hazard levels in Wallonia are lower than in Flanders, due to lower concentrations of air pollutants, lower densities of *Betula* trees and high cover of forests in Wallonia. Within Flanders The most urbanized areas are characterized by the highest hazard levels, probably due to higher concentrations of air pollutants. Surprisingly the coastal area of Belgium shows high hazard levels although the density of *Betula* is low in this region. Perhaps the low forest cover explains the lack of a protective effect in West-Flanders.

The maps generated here are developed using the daily average concentration of air pollutants. However, air pollutants can be monitored and modeled at hourly rates. There is a high application potential for hourly hazard maps to be incorporated in apps for the general public to monitor exposure and perhaps even suggest a healthiest route with the best air quality.

WP6: Scenario analyses for assessing the effect of plant diversity changes (in relation to climate and land use changes) on respiratory health (future health effects)

Task 6.1. Improving and downscaling air quality scenarios for the whole of Belgium

The future A1B scenario which has been used in this project is described in Hamdi et al., 2015.

While Global Climate Models or Regional Climate Models are able to describe the large-scale features of the climate fairly well, they fail to describe accurately the physical process at suitable high temporal and spatial resolution for urban areas (e.g. the Urban Heat Island, UHI). The urban downscaling technique has been developed by Hamdi et al. (2014) in order to examine how rural and urban areas respond to climate change. The regional climate simulations have been performed using the numerical weather prediction limited-area model ALARO, running at 4km resolution coupled with the state-of-the-art urban parameterization of Masson (2000), taking into account the Town Energy Balance (TEB) scheme. The physics parameterization package of ALARO has been specifically designed to be run at convection-permitting resolutions (10km ~ 4km). The TEB scheme is based on the canyon concept, where the buildings and roads are represented with roofs, roads, and two facing walls, . The advantage is that relatively few individual surface energy balance need to be resolved, radiation interactions are simplified, and therefore computation time is kept low. Then, in order to downscale further the regional climate projections to the urban scale, at 1km resolution, a stand-alone surface scheme was employed in offline mode and a 1km spatial resolution dataset over Belgium of temperature, relative humidity, has been produced in the course of the project.

Air quality simulations were conducted with the chemical transport model (CTM) CHIMERE (Vautard et al., 2001), using high resolution NWP model data from ALARO for Belgium (Delcloo et al., 2014). The period 2046-2055 was simulated, based on global climate simulations from the ARPEGE-Climate

(Gibelin and Déqué 2003) GCM from Météo-France. For these climate scenarios, we have been using the TNO/GEMS emissions (Visschedijk et al., 2007).

For this project we used the simulations for the year 2050.

Task 6.2. Land use and plant diversity scenarios for the whole of Belgium

The main goal of this analysis is to measure the potential impact of land use and climate change on future allergenic tree distributions and, in task 6.3, evaluate the trade-off for allergy risk. Specifically, we thus sought to map future *Betula* abundances by taking into account evolution of both land use and climatic conditions. Land uses constantly evolve and this has an effect on the proportion of greenness in a given neighbourhood. With the growth of urbanization and land artificialization, one may expect green spaces and associated allergenic trees to decrease. Yet, when considering that *Betula* and *Corylus* trees, for instance, are often planted in the vicinity of residential area, this could increase the abundance of such type of allergenic trees and allergy risk. A comprehensive analysis of this issue must consider how much these two factors may affect each other. Besides, when new residential areas are getting closer to forests containing an important proportion of *Betula* for instance, this also means people may be more exposed if they live closer to allergenic trees.

In order to measure the potential impact of land use and climate change on future allergenic tree distributions, we selected three main scenarii based on 3 plausible storyline that consider the future development of the Belgium economy and population trends. We started our analysis with using VITO's land use change simulations and retained 3 main scenarii, namely the Business As Usual scenario (BAU), the Global Economy (GE) scenario, and the Sustainability (SUST) (corresponding to VITO's Regional Community scenario).

The overall approach was based on the creation of a model that predicts, on a continuous grid map, the abundance of *Betula* for the current situation and then predicts what would be the abundance in the future using the present situation algorithm but with the corresponding covariate dataset for 2040. The selected covariates included LULC information, climate data (temperature and precipitation), soil types, topography, and the habitat suitability maps produced in WP3. While the land use and climate dataset covered both the current and future period, the soil types, topography and habitat suitability covariates were the same for present and future models.

For land use covariates, each scenario assumes a specific evolution of land use and land cover (LULC) across Belgium and associated green spaces in the future. They mainly picture an increase of artificial land (including residential, commercial and areas) and a decrease of agricultural and natural lands. Differences between scenarios resides in the amplitude of those changes with a stronger variation for the GE scenario and weaker changes for the GE; the BAU being the "middle-of the road" scenario. Land use maps are ready-to-use in the format of raster dataset. We extracted 10 categories of land use as to keep only the most relevant categories that best describe allergenic trees' distributions. These categories included: grassland, deciduous forest, coniferous forest, mixed forest, wetland, residential, commerce and services, industry, park, and water. Then, we computed the proportion of each land use category within a 1 km buffer. Zonal statistics were performed in R using the raster package. This allowed for converting the categorical variable into a continuous one that better describe the broader environmental conditions surrounding each survey points.

For climate change covariates, we needed to broaden our scale of analysis outside Belgium as to encompass the future climatic conditions that *Betula* may face in the future. We produced these maps using Maxent algorithm in order to specifically predict the habitat suitability of *Betula* for the current and future situation. First, we collected data from the Worldclim website where 19 bioclimatic variables are provided for the current situation (historical records for the 1970-200 period) as well as for the future situation (2021-2040 period). These bioclimatic provide a set of specific indicators of temperature and precipitation variations and vary depending on shared socio-economic pathways (SPPs) and the corresponding projections of future greenhouse gas emissions. We selected the SSP1-2.6, SSP2-4.5, and SSP5-8.5 as to match with our land use change storylines (SUST, BAU, and GE respectively). For each scenario, we collected outputs from 6 Global Circulation Models (GCM) available for download (BCC-CSM2-MR, CNRM-CM6-1, CNRM-ESM2-1, CanESM5, MIROC-ES2L, and MIROC6). All layers were provided with a spatial resolution of 2.5 minutes (~4km). Second, we collected *Betula* observation records from the GBIF database and created a presence-only dataset at the scale of Europe. We applied filters as to collect the most reliable observations, including the selection of data from the 2008-2018 period, the inclusion of *Betula pubesens* or *Betula pendula* species only, and setting a 1km spatial resolution threshold for coordinates uncertainty. We discarded non-verified data, data flagged with a spatial-resolution related issue, and data without XY coordinates. We ran Maxent using the *dismo* and *ENMeval* packages in R. We created 10.000 random background points and selected the 'checkboard2' method at a spatial grid of 3 by 3 degrees. Model parameters included RMvalues of 0.5,1.0,1.5,2.0 and Fc='L','LQ','LQH'. The best model selection was based on minimizing the AICc and maximizing the AUC. This procedure was replicated 6 times for the 6 Global Circulation Model and averaged as to keep only one map for our subsequent analysis. We used the MESS (multivariate similarity surface) to evaluate whether there are some areas where one or more variables are outside the range present in the training dataset. Maps showed that observation records across Europe covered the range of climatic conditions expected across Belgium by 2040.

Once all covariates (land use, climate suitability, topography, soil types, and habitat suitability) were set for modelling, we then reproduced the Random Forest (RF) regressions performed in WP3 as to model present *Betula* densities. Using basal area (m^2/a) as the dependent variable, we computed a new model using R studio. We followed a 15 folds cross-validations scheme using 70% of the data for training and the remaining 30% for testing the model performance. R squared reached 0.43 with a *mtry* of 2. Building upon this RF model, we finally ran the model for predicting future *Betula* densities and computed a continuous grid map showing predicted *Betula* abundance for three land use and climate change scenarios.

Climate suitability maps resulting from the Maxent modelling suggest that changes in temperature and precipitation may contribute to the reduction of climate suitability of *Betula* trees as this species prefers cold and humid weather. By 2040, our model suggest that climate suitability will be even lower within areas of higher altitudes, while lowland remain best suited for the development of *Betula* L. trees. Yet, maps did not show any distinguishable pattern between the three future greenhouse gas emission scenarii (Business As Usual – BAU, Global Economy – GE, and Sustainability – SUST). Only small, non-significant changes were observed when comparing climate suitability patterns between the BAU, GE, and SUST scenarios.

Results from the RF modelling follow a similar pattern to *Betula* densities observed in maps produced in WP3 with more detailed datasets. *Betula* is mainly distributed in the northern part of the country at lower altitudes. Densities tend be lower in agricultural areas and higher in areas covered by mixed land uses or forest cover. This similarity can be explained by the very high importance of the habitat suitability covariate used in this model. Indeed, variables importance figures places habitat suitability maps as the most important covariate; then, come altitude, forest cover (deciduous, mixed and coniferous), residential areas, slope and climate suitability in 8th position of importance. Meanwhile, such a low ranking of climate suitability suggests that temperature and precipitation play a lower role in predicting the abundance of *Betula* compared to land use variables such as forest cover.

Land use change may therefore be of higher importance for explaining the evolution of future *Betula* distribution, including the proportion of land dedicated to both residential land and forest cover. A comparison between scenarios does not show any distinguishable pattern between the three future greenhouse gas emission scenarios (Business As Usual – BAU, Global Economy – GE, and Sustainability – SUST). Only minor, non-significant changes of densities can be observed when comparing maps between the BAU, GE, and SUST scenarios.

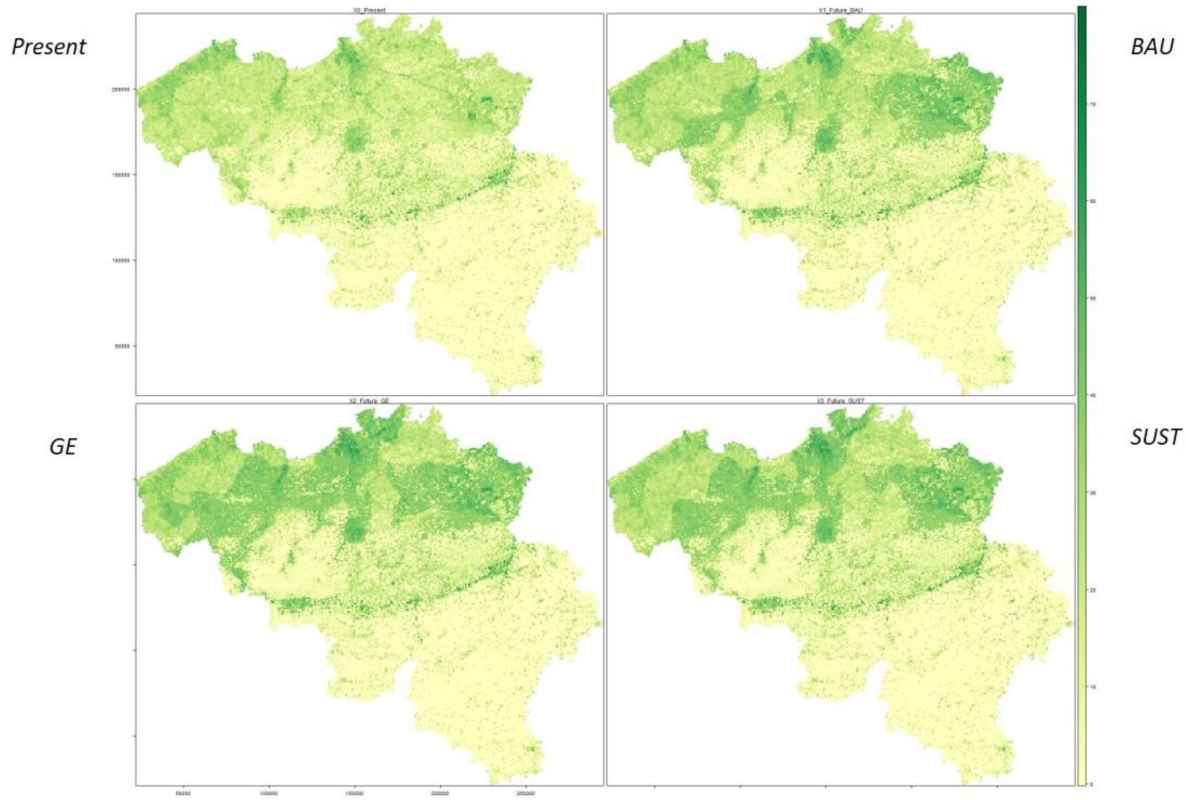

Figure 25: Maps showing the predicted abundance (% cover) of *Betula L.* across Belgium for present and three future land use and climate change scenarii (Business As Usual – BAU, Global Economy – GE, and Sustainability – SUST).

The main objective was to map the spatial distribution of allergenic tree species across Belgium for 2040. We designed and implemented a method that allowed for producing these maps but this task showed being rather challenging for several reasons. These reasons are detailed below and should be considered both as important limitations for the applications of the results presented in this work package and opportunities for future research.

a. Tree species selection. The selection of allergenic tree species for this research stopped at the genus level because it does not make any difference for allergy symptoms whether pollens responsible for allergies come from a *Betula pubescens* of *Betula pendula*. For understanding distributions of *Betula* tree species in the future, however, this proved being more problematic. *Betula pendula* is a very common species that adapts to many types of environments. On the opposite, *Betula pubescens*, grow in more specific habitats as it is mostly found in higher altitudes and harsher environments (higher humidity, colder temperatures, etc.). Aggregating those two species made it difficult to understand how species' abundance may be impacted by land use and climate change over time. In the stage of modelling climate suitability, interpretations came to be contradictory depending on whether we would consider *Betula pubesens* or *Betula pendula*.

b. The time horizon should be expanded further as to account for more significant land use and climate changes. The 2040 horizon is very near in the lifetime of a tree species. In 20 years' time, environmental conditions may not change significantly enough to affect species' distribution, especially in the case of *Betula pendula* which has a high capacity to adapt in many types of environments. On the one hand, patterns of greenhouse gas emissions are not clearly distinct when we look at the emission projection curves provided by the CMIP6 and SSPSs scenarios. On the other hand, the strong inertia of the built environment does make the artificialization of land significantly different between 2018 and 2040, especially in the norther part of the country where vacant lots are getting seldom. These factors partly explain why no clear pattern emerged between maps produced for each scenario. In this regard, additional land use change scenario should be produced and made available as to provide, for example, a scenario where the net change of artificial land is negative (by converting residential or industrial land into natural land) and therefore applying the principle of 'regreening cities'.

c. The covariates collected here were meant at characterizing the surrounding environmental conditions of *Betula* records. The metric chosen to represent abundance is a basal area (m^2/ha), i.e. a measure specifically elaborated by forest managers for the purpose of (among others) quantifying the available timber to be exploited. Yet, the covariates gathered in this research do not include factors pertaining to the management of forest and greenspaces. We did not take into account in this analysis any specific variable accounting for the reasons why some *Betula* stands are spontaneous, grown on purpose (e.g. for commercial use), or planted for ornamental reasons. No information on land tenure was included either (e.g. private domain, public forests, etc.). Yet this type of information would have a great explanatory power of *Betula* distributions. Further research should align covariates that better capture forest management practices and individual factors both in the private and public spaces.

In summary, the main objective was to map the spatial distribution of allergenic tree species across Belgium for the present (WP3) and future (WP6). In WP 3 we looked specifically at 3 main types of trees, i.e. *Alnus* (Alder), *Betula* (Birch), and *Corylus* (Hazelnut), while we focused only on *Betula* in WP6. In order to produce a continuous map, we used an advanced ecological modelling technique called "species distribution modelling". These techniques build upon a set of tree occurrence records to predict the probability of finding these trees at locations where no record exist. First, we collected tree occurrence records from forest inventories (Flanders & Wallonia) and the open citizen science data platforms (*observations .org* and *GBIF*) where anyone can share an observation of animals or plants on a volunteer basis. Second, we used several computer algorithm (Random Forest in WP3 and Maxent in WP6) to build a set of statistical relationships between the observed trees and the local environmental conditions (e.g. soil types, slope or precipitation, etc.). In WP3, this allowed producing a continuous map of *Alnus*, *Betula* and *Corylus* covering both urban and rural areas at a fine resolution of 1ha (100x100m). This method was then adapted for predicting *Betula* densities in 2040 under three climate and land use change scenarii (Business As Usual – BAU, Global Economy – GE, and Sustainability – SUST). Results showed that, in 20 years' time, climate change may contribute to the reduction of tree density of *Betula* trees as this species prefers cold and humid weather. However, land use and land cover factors showed being of higher importance, suggesting that future densities of allergenic tree will highly rely upon forest management practices and individual interventions both in the private and public spaces. Future research also need to focus on larger time period as 20 years ahead from now is very near in the lifetime of a tree species.

Task 6.3 Impacts of management and climate induced plant diversity changes on respiratory health risks

According to task 6.2 climate change may contribute to the reduction of tree density of *Betula* trees in Belgium in 2040. However, future densities of allergenic trees will highly rely upon forest and urban green management practices and individual interventions both in the private and public spaces. Future densities of allergenic trees as well as future emissions of pollutants will contribute to the environmental hazard levels that pollen-allergy sufferers are exposed to.

Complete eradication of birch trees is not a desired strategy since the genus is associated with many insects and fungi. When we modeled birch pollen in task 3.3 we found that even if there were no birch trees in Belgium there is pollen transport from neighboring countries. It could be possible to limit the amounts of birch trees in urban areas because they are unsuitable for the warm and dry urban climate. Nevertheless, the literature shows that high CO_2 concentrations and high temperatures result in the production of more pollen. Thus, even though future densities of birch trees might be lower they might produce more pollen contributing to similar hazard levels.

WP7 - Recommendations

We found that allergy symptom severity was associated with protective effects and risk factors in the environment. To improve the health of allergy patients and humans in general we suggest interventions that alter exposure in order to optimize health outcomes. First, green space management should focus on better (biological) air quality by reducing airborne allergenic pollen and pollutant levels. Second, personal exposure can be altered by lifestyle adjustments. These behavioural changes can be based on real-time information provided in a mobile health application. However, the responsibility should not be limited to the individuals with allergies. The proposed actions will only have a maximal effect when implemented under the 'One Health' approach (Zinsstag *et al.*, 2020). We need to continue to fight climate change and drastically reduce emissions of air pollutants to ensure healthier ecosystems and better public health.

Green space management

Large green spaces with a low density of allergenic trees should be promoted to guarantee health benefits that can also be enjoyed by tree-pollen allergy patients. Based on the findings of this research we propose guidelines for allergy-friendly green space management.

When planting new trees allergenic species such as *Betula, Alnus* and *Corylus* should be avoided. Additionally, exotic species are discouraged as they can prompt new allergies (Spellerberg *et al.*, 2006). However, entirely excluding non-native trees in urban forests might compromise the resilience of green spaces under climate change (Sjöman *et al.*, 2016). Trees such as *Platanus*, for example, that produces high amounts of pollen causing severe allergy symptoms in Southern-Europe (Asam *et al.*, 2015) might become a problem in Belgium. Pollen concentrations of *Platanus* have been observed to increase over the past 34 years (Hoebeke *et al.*, 2018) and might cause symptoms in certain areas in Belgium. Various studies abroad have identified novel allergenic trees based on skin prick tests (beech, maple, oak, pine, poplar, willow), yet they do not cause clinically relevant symptoms (Asam *et al.*, 2015). However, trees that are considered non-allergenic can still contribute to allergies due to cross-reactivity. Individuals allergic to birch pollen can also react to pollen emitted by other trees in the Fagales group, because these pollen carry chemically similar allergens (Biedermann *et al.*, 2019).

From the previous paragraph it may seem that the remaining list of possible tree species suitable to populate green spaces is very limited. However, we expect that negative effects of allergenic trees will be low when species richness within a green space is high (Cariñanos *et al.*, 2016). We suggest to increase biodiversity in order to prevent dominance or high densities of allergenic trees. High diversity will dilute the allergenic pollen cloud and structural diversity might contribute to obstruction of emitted pollen (Sánchez-Robles *et al.*, 2014). A tree diversity map as developed in Chapter 2 can be used to identify focus areas where biodiversity should be increased.

To help green space managers in quantifying the allergenicity of urban green spaces, Cariñanos *et al.* (2014) developed an urban green zone allergenicity index based on characteristics of the vegetation that is present. The allergenicity of a tree species is determined by intrinsic and biometric parameters. Intrinsic parameters, such as the allergenicity of the species, pollen emission strategy and the duration of the principal pollination period, cannot be altered. Trees with low allergenicity and a short pollination period should be favored (Cariñanos *et al.*, 2014). In his book on allergy-free gardening, Ogren (2000) coins the term 'botanical sexism' to refer to the preference for male dioecious trees in urban planting policy. Dioecious plants produce male and female flowers on different plants. Male flowers emit pollen to be captured by female flowers who produce seeds. In the past, male dioecious pollen-producing plants were preferred to avoid litter of seeds and seedpods. However, female dioecious trees do not produce pollen and will not produce seeds when they are not fertilized. For certain species, such as ash and willow, planting female trees can reduce pollen emissions for trees from the Fagales group this is unfortunately not an option.

For wind-pollinated species the amount of pollen emitted is related to the crown size. Pruning the crown appropriately will reduce the flowering intensity and thus reduce pollen emissions (Cariñanos *et al.*, 2017). Nevertheless, large crown volumes are associated with other ecosystem services such as deposition of air pollutants and management of micro climate (Samson *et al.*, 2017). As shown in Chapter 5, air pollutants contribute to severe allergy outcomes. Besides reducing pollen emissions, improving air quality should be a key ecosystem service of urban green spaces. In addition, trees can also capture biological particulate matter (including pollen grains) and thus mitigate pollen emissions of allergenic trees (Cariñanos *et al.*, 2017). The urban forest should perform multiple ecosystem services at once, to achieve this we should strive for taxonomic and functional diversity (Schwarz *et al.*, 2017).

Airborne pollen levels are related to the number of trees of a species in a certain area. A common indoor allergen avoidance strategy might be the removal of sources, such as carpets and molds (Cipriani *et al.*, 2017). Nevertheless, we do not propose to systematically remove birch trees. In the literature, one paper from New-Zealand argues in favor of birch tree removal as it is an exotic species causing allergies (Spellerberg *et al.*, 2006). In Europe *Betula* is a native tree, a host plant for 44 insect species (Van Gerven *et al.*, 2012) and known to form mycorrhizae with fungi (Fernández-Fuego *et al.*, 2017). Eradication of *Betula* trees will have effects on other trophic levels and this is never the goal in times of a biodiversity crisis (Leather, 2018). However, on unmanaged vacant lots exotic and pioneer species, such as birch, could be removed and replaced with other trees. Greening of vacant lots contributes to increased biodiversity in the city (Anderson *et al.*, 2014; Rega-Brodsky *et al.*, 2018) and positive behavioral and health outcomes (Cohen *et al.*, 2014; Hunter *et al.*, 2019; South *et al.*, 2015).

Ultimately, increasing biodiversity in urban green spaces is not only beneficial for human well-being, it is also beneficial for ecosystem well-being (van Heezik and Brymer, 2018).

Mobile health supported lifestyle adjustments

Reduced exposure to air pollutants and pollen can be achieved by lifestyle adjustments (D'Amato *et al.*, 2018). New mobile health applications relying on real-time location and environmental data can be developed to guide individual behavior with the goal of reducing exposure. Hazard maps can be developed based on the parameter estimates from the models tested in Chapter 5. Static maps of green spaces and densities of allergenic trees can be used to identify areas to be avoided by allergy patients. When hourly air pollution and pollen data are available real-time risks can be determined. A mobile health application linked to real-time risk maps can provide alarms for allergy patients when air pollution and pollen concentrations in their area are high. The alarm should come with suitable behavioral guidelines that can reduce exposure, such as 'avoid going outside' or 'wear sunglasses when outdoors'. However, an environmental health app can be of interest to a much larger user-base. Based on current conditions the application could determine the healthiest route to take to go from one place to another. When a part of the route inevitably passes through a polluted area the app can again provide appropriate advise for protective measures. To reduce exposure to peak concentrations of traffic-related air pollutants during motorized transport, air recirculation can be activated (Tartakovsky *et al.*, 2013). In the future real-time feedback by users (Mobile Crowdsensing) should also be able to improve the healthy routes that are suggested by such a mobile health application (Kalogiros *et al.*, 2018).

Long term exposure

We found that early-life exposure to green space was associated with epigenetic changes to genes involved in placental serotonin signaling, important in fetal cognitive development (Gaspar, Cases et al. 2003, Hadden, Fahmi et al. 2017). Serotonin is the key hormone that stabilizes our mood, feelings of well-being, and happiness. It is known that serotonin levels in placental are in conjunction with the fetal brain serotonin and plays an important role in fetal brain development (McKay 2011, Zeltser and Leibel 2011). As described in the hypothesis of Developmental Origins of Health and Diseases" (DoHaD), these epigenetic changes could result in long-lasting health outcomes later in life (Barker 2004, Barker and Thornburg 2013). Our study contributes to fundamental understanding of how green exposure might contribute to cognitive and mental health. Whether the epigenetic changes on serotonin signaling are persistent throughout childhood should be further investigated. Importantly, these results were independent of gestational exposure to air pollution. Our findings contribute to inform public health specialists, policymakers, and urban planners on the influence of green space during gestational life, which could help establish future guidelines concerning pregnant women.

5. DISSEMINATION AND VALORISATION

Conference presentations are traditional means of sharing research findings. As a task planned from the beginning, an end-project workshop was aimed to disseminate RespirIT results to the follow-up committee, the scientific community, stakeholders, health professionals, national policies, the study participants and more generally to any citizen interested by the topic of the project. Due to the restrictions imposed by the sanitary conditions from 2020 onwards, the workshop was finally organized as an online seminar (webinar) with open access (registration was possible on www.respirit.be). Advertisement of the event was organized at the universities of consortium, and on social media (AirAllergy twitter, etc.). Invitations were also sent by e-mail to all persons linked to the project, including the participants of the RespirIT cohort.
This webinar was held on Friday, February 12th 2021 from 13h to 15h on the *Cisco Webex Meetings* platform hosted by Sciensano. The agenda, including several Q&A sessions in order to interact on live as much as possible with the audience via the platform's chat, was as follows:

Timeslots	**Webinar presentations**
13:00 – 13:15	The RespirIT project: Introduction (Pr. Ben Somers, KU Leuven / Dr. Nicolas Bruffaerts, Sciensano)
13:15 – 13:30	The RespirIT cohort (Pr. Raf Aerts, Sciensano/KU Leuven)
13:30 – 13:35	First Q&A round
13:35 – 13:50	Distribution of allergenic tree species (Dr. Sébastien Dujardin, UNamur)
13:50 – 14:05	Spatio-temporal modelling of birch pollen levels in Belgium (Pr. Andy Delcloo, IRM)
14:05 – 14:10	Second Q&A round
14:10 – 14:25	Green space exposure and long-term health effects (Yinthe Dockx, UHasselt)
14:25 – 14:40	Acute health effects (Dr. Michiel Stas, KU Leuven)
14:40 – 14:50	RespirIT project wrap-up (Pr. Ben Somers, KU Leuven) Last Q&A round

The webinar was considered as successful, given the highly observed interactivity during the webinar, the final feedback of many attendees on the live chat and afterwards by e-mails, and also by the size of the audience who meanly reached about 40 people. The challenge of reaching the interest of an audience with a wide variety of backgrounds (including non-scientists) seems to have been met. The online format resulted particularly practical to gather such audience.

6. PUBLICATIONS

- Stas M., Aerts R., Hendrickx M., Bruffaerts N., Dendoncker N., Hoebeke L., Linard C., Nawrot T., Van Nieuwenhuyse A., Aerts J.-M., Van Orshoven J., & Somers B. (2021) Association between local airborne tree pollen composition and surrounding land cover across different spatial scales in northern Belgium. Urban Forestry & Urban Greening. https://doi.org/10.1016/j.ufug.2021.127082
- Stas, M., Aerts, R., Hendrickx, M., Dendoncker, N., Dujardin, S., Linard, C., Nawrot, T., Van Nieuwenhuyse, A., Aerts, J.-M., Van Orshoven, J., & Somers, B. Residential green space types, allergy symptoms and mental health in a cohort of tree pollen allergy patients. Landscape and Urban Planning, 210, https://doi.org/10.1016/j.landurbplan.2021.104070
- Stas, M., Aerts, R., Hendrickx, M., Delcloo, A. Dendoncker, N., Dujardin, S., Linard, C., Nawrot, T., Van Nieuwenhuyse, A., Aerts, J.-M., Van Orshoven, J., & Somers, B. Dynamic exposure to green space and tree pollen allergy symptom severity: a case-crossover study in Belgium Science of the Total Environment (under review)
- Aerts, R., Bruffaerts, N., Somers, B., Demoury, C., Plusquin, M., Nawrot, T., Hendrickx, M. with Aerts, R. (corresp. author) (2020). Tree pollen allergy risks and changes across scenarios in urban green spaces in Brussels, Belgium. *Landscape And Urban Planning*, *207*, Art.No. 104001. doi: 10.1016/j.landurbplan.2020.104001 Open Access
- Aerts, R., Dujardin, S., Nemery, B., Van Nieuwenhuyse, A., Van Orshoven, J., Aerts, J., Somers, B., Hendricks, M., Bruffaerts, N., Bauwelinck, M., Casas, L., Demoury, C., Plusquin, M., Nawrot, T. with Aerts, R. (corresp. author) (2020). Residential green space and medication sales for childhood asthma: a longitudinal ecological study in Belgium. *Environmental Research*, *189*, Art.No. 109914. doi: 10.1016/j.envres.2020.109914 Open Access
- Stas, M., Aerts, R., Hendrickx, M., Dendoncker, N., Dujardin, S., Linard, C., Nawrot, T., Van Nieuwenhuyse, A., Aerts, J., Van Orshoven, J., Somers, B. with Stas, M. (corresp. author) (2020). An evaluation of species distribution models to estimate tree diversity at genus level in a heterogeneous urban-rural landscape. Landscape And Urban Planning, 198, Art.No. 103770. doi: 10.1016/j.landurbplan.2020.103770 Open Access
- Aerts, R., Stas, M., Vanlessen, N., Hendrickx, M., Bruffaerts, N., Hoebeke, L., Dendoncker, N., Dujardin, S., Saenen, N.D., Van Nieuwenhuyse, A., Aerts, J-M., Van Orshoven, J., Nawrot, T.S., Somers, B. (2020). Residential green space and seasonal distress in a cohort of tree pollen allergy patients. INTERNATIONAL JOURNAL OF HYGIENE AND ENVIRONMENTAL HEALTH, 223 (1), 71-79. doi: 10.1016/j.ijheh.2019.10.004 Open Access

- Delcloo, A., Verstraeten, W.W., Dujardin, S. et al. 2019. Spatio-Temporal Monitoring and Modelling of Birch Pollen in Belgium. Air Pollution Modeling and its Application XXVI. DOI 10.1007/978-3-030-22055-6_12.
- Verstraeten, W.W., Dujardin, S., Hoebeke, L., Bruffaerts, N., Kouznetsov, R., Dendoncker, N., Hamdi, R., Linard, C., Hendrickx, M., Sofiev, M. & Delcloo, A.W., 2019. Spatio-temporal monitoring and modelling of birch pollen levels in Belgium. Aerobiologia. 35(4), 703-717. https://doi.org/10.1007/s10453-019-09607-w Open Access
- Dujardin, S, Linard, C & DENDONCKER, N 2017, Research note on mapping allergenic tree speciesdistributions in Belgium. UNamur Institutional Repository. pp. 51. https://pure.unamur.be/ws/portalfiles/portal/54066609/20210226_RespirIT_ResearchNote_data_UNamur_V2_PURE.pdf
- Dujardin, S, Linard, C & Dendoncker, N. 2021, Research note on mapping future abundance distributions of allergenic tree species for risk allergy prediction. UNamur Institutional Repository. pp.19. Available from: https://pure.unamur.be/ws/portalfiles/portal/54066549/20210226_RespirtIT_ResearchNote_data_UNamur_V1_PURE.pdf.

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REFERENCES

- Aerts, R., Bruffaerts, N., Somers, B., Demoury, C., Plusquin, M., Nawrot, T.S., Hendrickx, M., (2021). “Tree pollen allergy risks and changes across scenarios in urban green spaces in Brussels, Belgium”. Landsc. Urban Plan. 207, 104001. https://doi.org/10.1016/j.landurbplan.2020.104001
- Aggio, D., L. Smith, A. Fisher and M. Hamer (2015). "Mothers' perceived proximity to green space is associated with TV viewing time in children: the Growing Up in Scotland study." Prev Med 70: 46-49.
- Alcock, I., White, M., Cherrie, M., Wheeler, B., Taylor, J., McInnes, R., Otte im Kampe, E., Vardoulakis, S., Sarran, C., Soyiri, I., Fleming, L., (2017). “Land cover and air pollution are associated with asthma hospitalisations: A cross-sectional study”. Environ. Int. 109, 29–41. https://doi.org/10.1016/j.envint.2017.08.009
- Alderweireld, M., Burnay, F., Pitchugin, M., Lecomte, H., (2015). “Inventaire Forestier Wallon Résultats 1994-2012”. Jambes.
- Almanza, E., Jerrett, M., Dunton, G., Seto, E., Ann Pentz, M., (2012). “A study of community design, greenness, and physical activity in children using satellite, GPS and accelerometer data”. Heal. Place 18, 46–54. https://doi.org/10.1016/j.healthplace.2011.09.003
- Amoly, E., P. Dadvand, J. Forns, M. López-Vicente, X. Basagaña, J. Julvez, M. Alvarez-Pedrerol, M. J. Nieuwenhuijsen and J. Sunyer (2014). "Green and blue spaces and behavioral development in Barcelona schoolchildren: the BREATHE project." Environ Health Perspect 122(12): 1351-1358.
- Anderson, P.M.L., Avlonitis, G., Ernstson, H., (2014). “Ecological outcomes of civic and expert-led urban greening projects using indigenous plant species in Cape Town, South Africa”. Landsc. Urban Plan. 127, 104–113. https://doi.org/10.1016/j.landurbplan.2014.03.007
- Andrusaityte, S., Grazuleviciene, R., Kudzyte, J., Bernotiene, A., Dedele, A., Nieuwenhuijsen, M.J., (2016). “Associations between neighbourhood greenness and asthma in preschool children in Kaunas, Lithuania: A case-control study”. BMJ Open 6, e010341. https://doi.org/10.1136/bmjopen-2015-010341
- Asam, C., Hofer, H., Wolf, M., Aglas, L., Wallner, M., (2015). “Tree pollen allergens - An update from a molecular perspective”. Allergy Eur. J. Allergy Clin. Immunol. https://doi.org/10.1111/all.12696
- Banay, R. F., C. P. Bezold, P. James, J. E. Hart and F. Laden (2017). "Residential greenness: current perspectives on its impact on maternal health and pregnancy outcomes." Int J Womens Health 9: 133-144.
- Barker, D. and K. Thornburg (2013). "Placental programming of chronic diseases, cancer and lifespan: a review." Placenta 34 10: 841-845.
- Barker, D. J. (2004). "Developmental origins of adult health and disease." J Epidemiol Community Health 58(2): 114-115.
- Bartra, J., J. Belmonte, J. M. Torres-Rodriguez and A. Cistero-Bahima (2009). "Sensitization to Alternaria in patients with respiratory allergy." Front Biosci (Landmark Ed) 14: 3372-3379.

- Biedermann, T., Winther, L., Till, S.J., Panzner, P., Knulst, A., Valovirta, E., (2019). “Birch pollen allergy in Europe”. Allergy 74, all.13758. https://doi.org/10.1111/all.13758
- Bijnens, E. M., C. Derom, E. Thiery, S. Weyers and T. S. Nawrot (2020). "Residential green space and child intelligence and behavior across urban, suburban, and rural areas in Belgium: A longitudinal birth cohort study of twins." PLOS Medicine 17(8): e1003213.
- Blomme, K., Tomassen, P., Lapeere, H., Huvenne, W., Bonny, M., Acke, F., Bachert, C., Gevaert, P., (2013). “Prevalence of Allergic Sensitization versus Allergic Rhinitis Symptoms in an Unselected Population”. Int. Arch. Allergy Immunol. 160, 200–207. https://doi.org/10.1159/000339853
- Bogawski, P., Borycka, K., Grewling, Ł., Kasprzyk, I., (2019a). “Detecting distant sources of airborne pollen for Poland: Integrating back-trajectory and dispersion modelling with a satellite-based phenology”. Sci. Total Environ. 689, 109–125. https://doi.org/10.1016/j.scitotenv.2019.06.348
- Bogawski, P., Grewling, Ł., Dziób, K., Sobieraj, K., Dalc, M., Dylawerska, B., Pupkowski, D., Nalej, A., Nowak, M., Szymańska, A., Kostecki, Ł., Nowak, M.M., Jackowiak, B., (2019b). “Lidar-Derived Tree Crown Parameters: Are They New Variables Explaining Local Birch (Betula sp.) Pollen Concentrations?” Forests 10, 1154. https://doi.org/10.3390/f10121154
- Browning, M., Lee, K., (2017). “Within What Distance Does “Greenness” Best Predict Physical Health? A Systematic Review of Articles with GIS Buffer Analyses across the Lifespan”. Int. J. Environ. Res. Public Health 14, 675. https://doi.org/10.3390/ijerph14070675
- Calabrese, J.M., Certain, G., Kraan, C., Dormann, C.F., (2014). “Stacking species distribution models and adjusting bias by linking them to macroecological models”. Glob. Ecol. Biogeogr. 23, 99–112. https://doi.org/10.1111/geb.12102
- Cao, Y., DeWalt, R.E., Robinson, J.L., Tweddale, T., Hinz, L., Pessino, M., (2013). Using Maxent to model the historic distributions of stonefly species in Illinois streams: The effects of regularization and threshold selections. Ecol. Modell. 259, 30–39. https://doi.org/10.1016/J.ECOLMODEL.2013.03.012
- Cariñanos, Grilo, Pinho, Casares-Porcel, Branquinho, Acil, Andreucci, Anjos, Bianco, Brini, Calaza-Martínez, Calvo, Carrari, Castro, Chiesura, Correia, Gonçalves, Gonçalves, Mexia, Mirabile, Paoletti, Santos-Reis, Semenzato, Vilhar, 2019. Estimation of the Allergenic Potential of Urban Trees and Urban Parks: Towards the Healthy Design of Urban Green Spaces of the Future. Int. J. Environ. Res. Public Health 16, 1357. https://doi.org/10.3390/ijerph16081357
- Cariñanos, P., Adinolfi, C., Díaz de la Guardia, C., De Linares, C., Casares-Porcel, M., (2016). “Characterization of Allergen Emission Sources in Urban Areas”. J. Environ. Qual. 45, 244–252. https://doi.org/10.2134/jeq2015.02.0075
- Cariñanos, P., Casares-Porcel, M., Díaz de la Guardia, C., Aira, M.J., Belmonte, J., Boi, M., Elvira-Rendueles, B., De Linares, C., Fernández-Rodriguez, S., Maya-Manzano, J.M., Pérez-Badía, R., Rodriguez-de la Cruz, D., Rodríguez-Rajo, F.J., Rojo-Úbeda, J., Romero-Zarco, C., Sánchez-Reyes, E., Sánchez-Sánchez, J., Tormo-Molina, R., Vega Maray, A.M., (2017). “Assessing allergenicity in urban parks: A nature-based solution to reduce the impact on public health”. Environ. Res. 155, 219–227. https://doi.org/10.1016/j.envres.2017.02.015

- Cariñanos, P., Casares-Porcel, M., Quesada-Rubio, J.M., (2014). “Estimating the allergenic potential of urban green spaces: A case-study in Granada, Spain”. Landsc. Urban Plan. 123, 134–144. https://doi.org/10.1016/j.landurbplan.2013.12.009
- Chappuis, C., Tummon, F., Clot, B., Konzelmann, T., Calpini, B., Crouzy, B., (2020). “Automatic pollen monitoring: first insights from hourly data. Aerobiologia (Bologna)”. 36, 159–170. https://doi.org/10.1007/s10453-019-09619-6
- Cipriani, F., Calamelli, E., Ricci, G., (2017). “Allergen avoidance in allergic asthma.” Front. Pediatr. https://doi.org/10.3389/fped.2017.00103
- Clarke, K.R., (1993). “Non-parametric multivariate analyses of changes in community structure”. Aust. J. Ecol. 18, 117–143. https://doi.org/10.1111/j.1442-9993.1993.tb00438.x
- Cohen, D.A., Marsh, T., Williamson, S., Han, B., Derose, K.P., Golinelli, D., McKenzie, T.L., (2014). “The potential for pocket parks to increase physical activity”. Am. J. Heal. Promot. 28, S19–S26. https://doi.org/10.4278/ajhp.130430-QUAN-213
- Core Team R, (2017). “R: A language and environment for statistical computing.”
- Cornelis, J., Hermy, M., Roelandt, B., De Keersmaeker, L., Vandekerkhove Kris, (2009). (Bosplantengemeenschappen in Vlaanderen, een typologie van bossen gebasseerd op de kruidlaag”. INBO.M.2009.5. Agentschap voor Natuur en Bos en Intituut voor Natuur- en Bosonderzoek, Brussel.

- Dadvand, P., A. de Nazelle, F. Figueras, X. Basagaña, J. Su, E. Amoly, M. Jerrett, M. Vrijheid, J. Sunyer and M. J. Nieuwenhuijsen (2012). "Green space, health inequality and pregnancy." Environ Int 40: 110-115.
- Dadvand, P., I. Rivas, X. Basagaña, M. Alvarez-Pedrerol, J. Su, M. De Castro Pascual, F. Amato, M. Jerret, X. Querol, J. Sunyer and M. J. Nieuwenhuijsen (2015). "The association between greenness and traffic-related air pollution at schools." Science of The Total Environment 523: 59-63.
- Dadvand, P., C. Tischer, M. Estarlich, S. Llop, A. Dalmau-Bueno, M. López-Vicente, A. Valentín, C. de Keijzer, A. Fernández-Somoano, N. Lertxundi, C. Rodriguez-Dehli, M. Gascon, M. Guxens, D. Zugna, X. Basagaña, M. J. Nieuwenhuijsen, J. Ibarluzea, F. Ballester and J. Sunyer (2017). "Lifelong Residential Exposure to Green Space and Attention: A Population-based Prospective Study." Environ Health Perspect 125(9): 097016.
- Dadvand, P., C. M. Villanueva, L. Font-Ribera, D. Martinez, X. Basagaña, J. Belmonte, M. Vrijheid, R. Gražulevičienė, M. Kogevinas and M. J. Nieuwenhuijsen (2014). "Risks and benefits of green spaces for children: a cross-sectional study of associations with sedentary behavior, obesity, asthma, and allergy." Environ Health Perspect 122(12): 1329-1335.
- Dadvand, P., J. Wright, D. Martinez, X. Basagaña, R. R. McEachan, M. Cirach, C. J. Gidlow, K. de Hoogh, R. Gražulevičienė and M. J. Nieuwenhuijsen (2014). "Inequality, green spaces, and pregnant women: roles of ethnicity and individual and neighbourhood socioeconomic status." Environ Int 71: 101-108.

- D'Amato, G., Cecchi, L., Bonini, S., Nunes, C., Annesi-Maesano, I., Behrendt, H., Liccardi, G., Popov, T., van Cauwenberge, P., 2007. Allergenic pollen and pollen allergy in Europe. Allergy 62, 976–990. https://doi.org/10.1111/j.1398-9995.2007.01393.x
- D'Amato, M., Cecchi, L., Annesi-Maesano, I., D'Amato, G., (2018). "News on Climate Change, Air Pollution, and Allergic Triggers of Asthma". J Investig Allergol Clin Immunol 28, 91–97. https://doi.org/10.18176/jiaci.0228
- De Linares, C., J. Belmonte, M. Canela, C. Guardia, F. Alba-Sánchez, S. Ruiz and S. Alonso-Pérez (2010). "Dispersal patterns of Alternaria conidia in Spain." Agricultural and Forest Meteorology 150: 1491-1500.
- De Marco, P., Nóbrega, C.C., (2018). "Evaluating collinearity effects on species distribution models: An approach based on virtual species simulation". PLoS One 13, e0202403. https://doi.org/10.1371/journal.pone.0202403
- Dėdelė, A., Miškinytė, A., Gražulevičienė, R., (2019). "The impact of particulate matter on allergy risk among adults: integrated exposure assessment". Environ. Sci. Pollut. Res. 26, 10070–10082. https://doi.org/10.1007/s11356-019-04442-5
- Dejeux, E., H. El abdalaoui, I. G. Gut and J. Tost (2009). "Identification and quantification of differentially methylated loci by the pyrosequencing technology." Methods Mol Biol 507: 189-205.
- Delcloo, A. Hamdi, R. Deckmyn, A., De Backer, H., Forêt, G., Termonia, P. and Van Langenhove, H. (2014). "A One Year Evaluation of the CTM CHIMERE Using SURFEX/TEB Within the High Resolution NWP Models ALARO and ALADIN for Belgium, Air Pollution Modeling and its Application XXIII" NATO Science for Peace and Security Series C: Environmental Security 2014, 495-498, DOI: 10.1007/978-3-319-04379-1_81.
- Dellavalle, C., E. Triche, B. Leaderer and M. Bell (2011). "Effects of Ambient Pollen Concentrations on Frequency and Severity of Asthma Symptoms Among Asthmatic Children." Epidemiology (Cambridge, Mass.) 23: 55-63.
- Dharmage, S. C., J. L. Perret and A. Custovic (2019). "Epidemiology of Asthma in Children and Adults." Front Pediatr 7: 246.
- Doherty, S.T., Lemieux, C.J., Canally, C., (2014). "Tracking human activity and well-being in natural environments using wearable sensors and experience sampling". Soc. Sci. Med. 106, 83–92. https://doi.org/10.1016/J.SOCSCIMED.2014.01.048
- Dondeyne, S., Vanierschot, L., Langohr, R., Ranst, E. Van, Deckers, J., (2014). "The soil map of the Flemish region converted to the 3rd edition of the World Reference Base for soil resources".
- Donovan, G.H., Gatziolis, D., Longley, I., Douwes, J., (2018). "Vegetation diversity protects against childhood asthma: results from a large New Zealand birth cohort". Nat. Plants 1. https://doi.org/10.1038/s41477-018-0151-8
- Dons, E., Int Panis, L., Van Poppel, M., Theunis, J., Willems, H., Torfs, R., Wets, G., (2011). "Impact of time-activity patterns on personal exposure to black carbon". Atmos. Environ. 45, 3594–3602. https://doi.org/10.1016/j.atmosenv.2011.03.064

- Dons, E., Laeremans, M., Orjuela, J.P., Avila-Palencia, I., de Nazelle, A., Nieuwenhuijsen, M., Van Poppel, M., Carrasco-Turigas, G., Standaert, A., De Boever, P., Nawrot, T., Int Panis, L., (2019). “Transport most likely to cause air pollution peak exposures in everyday life: Evidence from over 2000 days of personal monitoring.” Atmos. Environ. 213, 424–432. https://doi.org/10.1016/j.atmosenv.2019.06.035
- Dujardin, S., Linard, C. & Dendoncker, N. (2017). “Research note on mapping allergenic tree species in Belgium”. BR/154/A1/RespirIT, Belgian research action through interdisciplinary networks.
- Dzhambov, A., D. Dimitrova and E. Dimitrakova (2014). "Association between residential greenness and birth weight: Systematic review and meta-analysis." Urban Forestry & Urban Greening 13: 621-629.
- ECOPLAN, 2014. ECOPLAN Monitor [WWW Document]. URL http://www.ecosysteemdiensten.be/cms/
- Eisenman, T.S., Jariwala, S.P., Lovasi, G.S., (2019). “Urban trees and asthma: a call for epidemiological research”. Lancet Respir. Med. https://doi.org/10.1016/S2213-2600(19)30193-6
- Elith, J., H. Graham, C., P. Anderson, R., Dudík, M., Ferrier, S., Guisan, A., J. Hijmans, R., Huettmann, F., R. Leathwick, J., Lehmann, A., Li, J., G. Lohmann, L., A. Loiselle, B., Manion, G., Moritz, C., Nakamura, M., Nakazawa, Y., McC. M. Overton, J., Townsend Peterson, A., J. Phillips, S., Richardson, K., Scachetti-Pereira, R., E. Schapire, R., Soberón, J., Williams, S., S. Wisz, M., E. Zimmermann, N., (2006). “Novel methods improve prediction of species’ distributions from occurrence data”. Ecography (Cop.). 29, 129–151. https://doi.org/10.1111/j.2006.0906-7590.04596.x
- Elith, J., Phillips, S.J., Hastie, T., Dudík, M., Chee, Y.E., Yates, C.J., (2011). “A statistical explanation of MaxEnt for ecologists”. Divers. Distrib. 17, 43–57. https://doi.org/10.1111/j.1472-4642.2010.00725.x
- Engemann, K., C. B. Pedersen, L. Arge, C. Tsirogiannis, P. B. Mortensen and J.-C. Svenning (2019). "Residential green space in childhood is associated with lower risk of psychiatric disorders from adolescence into adulthood." Proceedings of the National Academy of Sciences 116(11): 5188-5193.
- ESRI, 2011. ArcGIS Desktop: Release 10.
- Feng, X. and T. Astell-Burt (2017). "The Relationship between Neighbourhood Green Space and Child Mental Wellbeing Depends upon Whom You Ask: Multilevel Evidence from 3083 Children Aged 12-13 Years." Int J Environ Res Public Health 14(3).
- Fernández-Fuego, D., Bertrand, A., González, A., (2017). “Metal accumulation and detoxification mechanisms in mycorrhizal Betula pubescens”. Environ. Pollut. 231, 1153–1162. https://doi.org/10.1016/j.envpol.2017.07.072
- Ficetola, G.F., Thuiller, W., Padoa-Schioppa, E., (2009). “From introduction to the establishment of alien species: bioclimatic differences between presence and reproduction localities in the slider turtle”. Divers. Distrib. 15, 108–116. https://doi.org/10.1111/j.1472-4642.2008.00516.x
- Frisk, V., R. Amsel and H. E. Whyte (2002). "The importance of head growth patterns in predicting the cognitive abilities and literacy skills of small-for-gestational-age children." Dev Neuropsychol 22(3): 565-593.
- Fuertes, E., I. Markevych, G. Bowatte, O. Gruzieva, U. Gehring, A. Becker, D. Berdel, A. von Berg, A. Bergström, M. Brauer, B. Brunekreef, I. Brüske, C. Carlsten, M. Chan-Yeung, S. C. Dharmage, B. Hoffmann, C. Klümper, G. H. Koppelman, A. Kozyrskyj, M. Korek, I. Kull, C. Lodge, A. Lowe, E. MacIntyre,

G. Pershagen, M. Standl, D. Sugiri, A. Wijga and J. Heinrich (2016). "Residential greenness is differentially associated with childhood allergic rhinitis and aeroallergen sensitization in seven birth cohorts." Allergy 71(10): 1461-1471.

- Fuhlbrigge, A., B. Jackson and R. Wright (2002). "Gender and asthma." Immunology and Allergy Clinics of North America - IMMUNOL ALLERGY CLIN N AMER 22: 753-789.
- Galán, C., Smith, M., Thibaudon, M., Frenguelli, G., Oteros, J., Gehrig, R., Berger, U., Clot, B., Brandao, R., Group, E.Q.W., (2014). “Pollen monitoring: minimum requirements and reproducibility of analysis. Aerobiologia (Bologna)”. 30, 385–395. https://doi.org/10.1007/s10453-014-9335-5
- Gaspar, P., O. Cases and L. Maroteaux (2003). "The developmental role of serotonin: news from mouse molecular genetics." Nat Rev Neurosci 4(12): 1002-1012.
- Gavish, Y., Marsh, C.J., Kuemmerlen, M., Stoll, S., Haase, P., Kunin, W.E., (2017). “Accounting for biotic interactions through alpha-diversity constraints in stacked species distribution models”. Methods Ecol. Evol. 8, 1092–1102. https://doi.org/10.1111/2041-210X.12731
- Gehrig, R., (2019). “Representativeness of pollen traps: a review of the national pollen network of Switzerland. Aerobiologia (Bologna)”. 35, 577–581. https://doi.org/10.1007/s10453-019-09593-z
- Grandjean, P. and P. J. Landrigan (2014). "Neurobehavioural effects of developmental toxicity." Lancet Neurol 13(3): 330-338.
- Groenkaart Vlaanderen (2012). Groenkaart Vlaanderen. V. G. e. B. Vlaanderen. Vlaanderen 0. Groenkaart en Boswijzer Vlaanderen, Vlaanderen 0. Groenkaart en Boswijzer Vlaanderen.
- Grote, R., Samson, R., Alonso, R., Amorim, J.H., Cariñanos, P., Churkina, G., Fares, S., Thiec, D. Le, Niinemets, Ü., Mikkelsen, T.N., Paoletti, E., Tiwary, A., Calfapietra, C., (2016). “Functional traits of urban trees: air pollution mitigation potential”. Front. Ecol. Environ. https://doi.org/10.1002/fee.1426
- Guan, H., Wei, H., He, X., Ren, Z., An, B., (2017). “The tree-species-specific effect of forest bathing on perceived anxiety alleviation of young-adults in urban forests”. Ann. For. Res. 60, 327–341. https://doi.org/10.15287/afr.2017.897
- Guisan, A., Rahbek, C., (2011). “SESAM - a new framework integrating macroecological and species distribution models for predicting spatio-temporal patterns of species assemblages.” J. Biogeogr. 38, 1433–1444. https://doi.org/10.1111/j.1365-2699.2011.02550.x
- Hadden, C., T. Fahmi, A. Cooper, A. V. Savenka, V. V. Lupashin, D. J. Roberts, L. Maroteaux, S. Hauguel-de Mouzon and F. Kilic (2017). "Serotonin transporter protects the placental cells against apoptosis in caspase 3-independent pathway." J Cell Physiol 232(12): 3520-3529.
- Hajat, S., Haines, A., Atkinson, R.W., Bremner, S.A., Anderson, H.R., Emberlin, J., (2001). “Association between air pollution and daily consultations with general practitioners for allergic rhinitis in London, United Kingdom”. Am. J. Epidemiol. 153, 704–714. https://doi.org/10.1093/aje/153.7.704
- Hamdi, R., O. Giot, R. De Troch, A. Deckmyn, P. Termonia. Future climate of Brussels and Paris for the 2050s under the A1B scenario. Urban Climate, 10.1016/j.uclim.2015.03.003, 04/2015; 12:160-182.
- Hanski, I., L. von Hertzen, N. Fyhrquist, K. Koskinen, K. Torppa, T. Laatikainen, P. Karisola, P. Auvinen, L. Paulin, M. J. Mäkelä, E. Vartiainen, T. U. Kosunen, H. Alenius and T. Haahtela (2012). "Environmental

biodiversity, human microbiota, and allergy are interrelated." Proc Natl Acad Sci U S A 109(21): 8334-8339.

- Hazlehurst, M.F., Spalt, E.W., Curl, C.L., Davey, M.E., Vedal, S., Burke, G.L., Kaufman, J.D., (2017). “Integrating data from multiple time-location measurement methods for use in exposure assessment: the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air)”. J. Expo. Sci. Environ. Epidemiol. 27, 569–574. https://doi.org/10.1038/jes.2016.84
- Hemery, G.E., Savill, P.S. & Pryor, S.N. (2005). “Applications of the crown diameter–stem diameter relationship for different species of broadleaved trees”. Forest Ecology and Management, 215, 285–294.
- Janssen, B. G., N. Madhloum, W. Gyselaers, E. Bijnens, D. B. Clemente, B. Cox, J. Hogervorst, L. Luyten, D. S. Martens, M. Peusens, M. Plusquin, E. B. Provost, H. A. Roels, N. D. Saenen, M. Tsamou, A. Vriens, E. Winckelmans, K. Vrijens and T. S. Nawrot (2017). "Cohort Profile: The ENVIRonmental influence ON early AGEing (ENVIRONAGE): a birth cohort study." Int J Epidemiol 46(5): 1386-1387m.
- Hijmans, R., 2020. raster package | R Documentation.
- Hjort, J., Hugg, T.T., Antikainen, H., Rusanen, J., Sofiev, M., Kukkonen, J., Jaakkola, M.S., Jaakkola, J.J.K., (2016). “Fine-Scale Exposure to Allergenic Pollen in the Urban Environment: Evaluation of Land Use Regression Approach”. Environ. Health Perspect. 124, 619–26. https://doi.org/10.1289/ehp.1509761
- Hoebeke, L., Bruffaerts, N., Verstraeten, C., Delcloo, A., De Smedt, T., Packeu, A., Detandt, M., Hendrickx, M., (2018). “Thirty-four years of pollen monitoring: an evaluation of the temporal variation of pollen seasons in Belgium”. Aerobiologia (Bologna). 34, 139–155. https://doi.org/10.1007/s10453-017-9503-5
- Hunter, R.F., Cleland, C., Cleary, A., Droomers, M., Wheeler, B.W., Sinnett, D., Nieuwenhuijsen, M.J., Braubach, M., (2019). “Environmental, health, wellbeing, social and equity effects of urban green space interventions: A meta-narrative evidence synthesis”. Environ. Int. 130, 104923. https://doi.org/10.1016/j.envint.2019.104923
- Jaakkola, J.J.K., (2003). “Case-crossover design in air pollution epidemiology”, in: European Respiratory Journal, Supplement. European Respiratory Society, pp. 81–85. https://doi.org/10.1183/09031936.03.00402703
- Janssen, S., G. Dumont, F. Fierens and C. Mensink (2008). "Spatial interpolation of air pollution measurements using CORINE land cover data." Atmospheric Environment 42(20): 4884-4903.
- Jochner-Oette, S., Stitz, T., Jetschni, J., Cariñanos, P., (2018). “The Influence of Individual-Specific Plant Parameters and Species Composition on the Allergenic Potential of Urban Green Spaces”. Forests 9, 284. https://doi.org/10.3390/f9060284
- Kahn, P. (1997). "Developmental Psychology and the Biophilia Hypothesis: Children's Affiliation with Nature." Developmental Review 17: 1-61.
- Kalogiros, L.A., Lagouvardos, K., Nikoletseas, S., Papadopoulos, N., Tzamalis, P., (2018). “Allergymap: A Hybrid mHealth Mobile Crowdsensing System for Allergic Diseases Epidemiology : multidisciplinary case study” IEEE International Conference on Pervasive Computing and Communications Workshops,

PerCom Workshops 2018. Institute of Electrical and Electronics Engineers Inc., pp. 597–602. https://doi.org/10.1109/PERCOMW.2018.8480280

- Kellert, S. R. (2002). “Experiencing nature: Affective, cognitive, and evaluative development in children. Children and nature: Psychological, sociocultural, and evolutionary investigations.” Cambridge, MA, US, MIT Press: 117-151.
- Kenkel, N.C., Orloci, L., (1986). “Applying Metric and Nonmetric Multidimensional Scaling to Ecological Studies: Some New Results”. Ecology 67, 919–928. https://doi.org/10.2307/1939814
- Kim, Hyun Jin, Min, J.Y., Kim, Hye Jin, Min, K.B., (2020). “Association between green areas and allergic disease in Korean adults: A cross-sectional study”. Ann. Occup. Environ. Med. 32. https://doi.org/10.35371/aoem.2020.32.e5
- Korpilo, S., Virtanen, T., Lehvävirta, S., (2017). “Smartphone GPS tracking—Inexpensive and efficient data collection on recreational movement”. Landsc. Urban Plan. 157, 608–617. https://doi.org/10.1016/j.landurbplan.2016.08.005
- Kouznetsov, R., Sofiev, M. (2012). “A methodology for evaluation of vertical dispersion and dry deposition of atmospheric aerosols.” Journal of Geophysical Research, 117, doi: 10.1029/2011JD016366.
- Kuo, F. E. and A. F. Taylor (2004). "A potential natural treatment for attention-deficit/hyperactivity disorder: evidence from a national study." Am J Public Health 94(9): 1580-1586.
- Kwon, M.Y., Lee, J.S., Park, S., (2019). “The effect of outdoor air pollutants and greenness on allergic rhinitis incidence rates: a cross-sectional study in Seoul, Korea”. Int. J. Sustain. Dev. World Ecol. 26, 258–267. https://doi.org/10.1080/13504509.2019.1570982
- Labib, S.M., Lindley, S., Huck, J.J., (2020). “Spatial dimensions of the influence of urban green-blue spaces on human health: A systematic review.” Environ. Res. https://doi.org/10.1016/j.envres.2019.108869
- Lake, I.R., Jones, N.R., Agnew, M., Goodess, C.M., Giorgi, F., Hamaoui-Laguel, L., Semenov, M.A., Solomon, F., Storkey, J., Vautard, R., Epstein, M.M., (2017). “Climate change and future pollen allergy in Europe”. Environ. Health Perspect. https://doi.org/10.1289/EHP173
- Lambert, K. A., G. Bowatte, R. Tham, C. Lodge, L. Prendergast, J. Heinrich, M. J. Abramson, S. C. Dharmage and B. Erbas (2017). "Residential greenness and allergic respiratory diseases in children and adolescents - A systematic review and meta-analysis." Environ Res 159: 212-221.
- Lambert, K., Bowatte, G., Tham, R., Lodge, C., Prendergast, L., Heinrich, J., Abramson, M., Dharmage, S., Erbas, B., (2018). “Greenspace and Atopic Sensitization in Children and Adolescents—A Systematic Review” Int. J. Environ. Res. Public Health 15, 2539. https://doi.org/10.3390/ijerph15112539
- Landsgebruikskaart Vlaanderen (2012). Landsgebruikskaart Vlaanderen. V. O.-D. O.-A. V. P. v. Omgeving, Vlaamse Overheid - Departement Omgeving - Afdeling Vlaams Planbureau voor Omgeving.
- Leather, S.R., (2018). “Ecological Armageddon” – more evidence for the drastic decline in insect numbers. Ann. Appl. Biol. https://doi.org/10.1111/aab.12410

- Liddicoat, C., Bi, P., Waycott, M., Glover, J., Lowe, A.J., Weinstein, P., (2018). “Landscape biodiversity correlates with respiratory health in Australia”. J. Environ. Manage. 206, 113–122. https://doi.org/10.1016/j.jenvman.2017.10.007
- Linkosalo, T., Ranta, H., Oksanen, A., Siljamo, P., Luomajoki, A., Kukkonen, J., Sofiev, M. (2010). “A double-threshold temperature sum model for predicting the flowering duration and relative intensity of Betula pendula and B. pubescens”. Agricultural and Forest Meteorology, 150, 6–11. doi:10.1016/j.agrformet.2010.08.007.
- Lovasi, G. S., J. W. Quinn, K. M. Neckerman, M. S. Perzanowski and A. Rundle (2008). "Children living in areas with more street trees have lower prevalence of asthma." J Epidemiol Community Health 62(7): 647-649.
- Lovasi, G.S., O’Neil-Dunne, J.P.M., Lu, J.W.T., Sheehan, D., Perzanowski, M.S., MacFaden, S.W., King, K.L., Matte, T., Miller, R.L., Hoepner, L.A., Perera, F.P., Rundle, A., (2013). “Urban Tree Canopy and Asthma, Wheeze, Rhinitis, and Allergic Sensitization to Tree Pollen in a New York City Birth Cohort”. Environ. Health Perspect. 121, 494–500. https://doi.org/10.1289/ehp.1205513
- MacKerron, G., Mourato, S., (2013). “Happiness is greater in natural environments”. Glob. Environ. Chang. 23, 992–1000. https://doi.org/10.1016/J.GLOENVCHA.2013.03.010
- Markevych, I., C. M. Tiesler, E. Fuertes, M. Romanos, P. Dadvand, M. J. Nieuwenhuijsen, D. Berdel, S. Koletzko and J. Heinrich (2014). "Access to urban green spaces and behavioural problems in children: Results from the GINIplus and LISAplus studies." Environ Int 71: 29-35.
- Matricardi, P.M., Dramburg, S., Alvarez-Perea, A., Antolín-Amérigo, D., Apfelbacher, C., Atanaskovic-Markovic, M., Berger, U., Blaiss, M.S., Blank, S., Boni, E., Bonini, M., Bousquet, J., Brockow, K., Buters, J., Cardona, V., Caubet, J., Cavkaytar, Ö., Elliott, T., Esteban-Gorgojo, I., Fonseca, J.A., Gardner, J., Gevaert, P., Ghiordanescu, I., Hellings, P., Hoffmann-Sommergruber, K., Fusun Kalpaklioglu, A., Marmouz, F., Meijide Calderón, Á., Mösges, R., Nakonechna, A., Ollert, M., Oteros, J., Pajno, G., Panaitescu, C., Perez-Formigo, D., Pfaar, O., Pitsios, C., Rudenko, M., Ryan, D., Sánchez-García, S., Shih, J., Tripodi, S., Van der Poel, L., Os-Medendorp, H., Varricchi, G., Wittmann, J., Worm, M., Agache, I., (2020). “The role of mobile health technologies in allergy care: An EAACI position paper”. Allergy 75, 259–272. https://doi.org/10.1111/all.13953
- McInnes, R.N., Hemming, D., Burgess, P., Lyndsay, D., Osborne, N.J., Skjøth, C.A., Thomas, S., Vardoulakis, S., (2017). “Mapping allergenic pollen vegetation in UK to study environmental exposure and human health.” Sci. Total Environ. 599–600, 483–499. https://doi.org/10.1016/J.SCITOTENV.2017.04.136
- McKay, R. (2011). "Remarkable role for the placenta." Nature 472(7343): 298-299.
- Merow, C., Smith, M.J., Silander, J.A., (2013). “A practical guide to MaxEnt for modeling species’ distributions: what it does, and why inputs and settings matter.” Ecography (Cop.). 36, 1058–1069. https://doi.org/10.1111/j.1600-0587.2013.07872.x

- Müller-Rompa, S. E. K., I. Markevych, A. J. Hose, G. Loss, I. M. Wouters, J. Genuneit, C. Braun-Fahrländer, E. Horak, A. Boznanski, D. Heederik, E. von Mutius, J. Heinrich and M. J. Ege (2018). "An approach to the asthma-protective farm effect by geocoding: Good farms and better farms." Pediatr Allergy Immunol 29(3): 275-282.
- Neumann, J.E., Anenberg, S.C., Weinberger, K.R., Amend, M., Gulati, S., Crimmins, A., Roman, H., Fann, N., Kinney, P.L., (2019). "Estimates of Present and Future Asthma Emergency Department Visits Associated With Exposure to Oak, Birch, and Grass Pollen in the United States". GeoHealth 3, 11–27. https://doi.org/10.1029/2018GH000153
- Nieuwenhuijsen, M. J., P. Dadvand, J. Grellier, D. Martinez and M. Vrijheid (2013). "Environmental risk factors of pregnancy outcomes: a summary of recent meta-analyses of epidemiological studies." Environ Health 12: 6.
- Nordbø, E.C.A., Nordh, H., Raanaas, R.K., Aamodt, G., (2018). "GIS-derived measures of the built environment determinants of mental health and activity participation in childhood and adolescence: A systematic review". Landsc. Urban Plan. https://doi.org/10.1016/j.landurbplan.2018.04.009
- Ogren, T.L., (2000). "Allergy-Free Gardening: The Revolutionary Guide to Healthy Landscaping". Ten Speed Press. https://doi.org/10.5070/g311310411
- Oksanen, J., Blanchet, F.G., Friendly, M., Kindt, R., Legendre, P., Mcglinn, D., Minchin, P.R., O'hara, R.B., Simpson, G.L., Solymos, P., Henry, M., Stevens, H., Szoecs, E., Maintainer, H.W., (2019). Package "vegan", Community Ecology Package Version 2.5-6.
- Orlanski, I., (1975). "A Rational Subdivision of Scales for Atmospheric Processes." Bull. Am. Meteorol. Soc. 56, 527–530.
- Oteros, J., Pusch, G., Weichenmeier, I., Heimann, U., Möller, R., Röseler, S., Traidl-Hoffmann, C., Schmidt-Weber, C., Buters, J.T.M., (2015). "Automatic and Online Pollen Monitoring". Int. Arch. Allergy Immunol. 167, 158–166. https://doi.org/10.1159/000436968
- Oteros, J., Sofiev, M., Smith, M., Clot, B., Damialis, A., Prank, M., Werchan, M., Wachter, R., Weber, A., Kutzora, S., Heinze, S., Herr, C.E.W., Menzel, A., Bergmann, K.-C., Traidl-Hoffmann, C., Schmidt-Weber, C.B., Buters, J.T.M., (2019). "Building an automatic pollen monitoring network (ePIN): Selection of optimal sites by clustering pollen stations". Sci. Total Environ. 688, 1263–1274. https://doi.org/10.1016/J.SCITOTENV.2019.06.131
- Oufkir, T. and C. Vaillancourt (2011). "Phosphorylation of JAK2 by serotonin 5-HT (2A) receptor activates both STAT3 and ERK1/2 pathways and increases growth of JEG-3 human placental choriocarcinoma cell." Placenta 32(12): 1033-1040.
- Parmes, E., Pesce, G., Sabel, C.E., Baldacci, S., Bono, R., Brescianini, S., D'Ippolito, C., Hanke, W., Horvat, M., Liedes, H., Maio, S., Marchetti, P., Marcon, A., Medda, E., Molinier, M., Panunzi, S., Pärkkä, J., Polańska, K., Prud'homme, J., Ricci, P., Snoj Tratnik, J., Squillacioti, G., Stazi, M.A., Maesano, C.N., Annesi-Maesano, I., (2020). "Influence of residential land cover on childhood allergic and respiratory symptoms and diseases: Evidence from 9 European cohorts". Environ. Res. 183, 108953. https://doi.org/10.1016/j.envres.2019.108953

- Pearson, R.G., Raxworthy, C.J., Nakamura, M., Townsend Peterson, A., (2006). “Predicting species distributions from small numbers of occurrence records: a test case using cryptic geckos in Madagascar”. J. Biogeogr. 34, 102–117. https://doi.org/10.1111/j.1365-2699.2006.01594.x
- Peel, R.G., Hertel, O., Smith, M., Kennedy, R., (2013). “Personal exposure to grass pollen: relating inhaled dose to background concentration”. Ann. Allergy, Asthma Immunol. 111, 548–554. https://doi.org/10.1016/J.ANAI.2013.09.002
- Perera, F. P., W. Jedrychowski, V. Rauh and R. M. Whyatt (1999). "Molecular epidemiologic research on the effects of environmental pollutants on the fetus." Environ Health Perspect 107 Suppl 3(Suppl 3): 451-460.
- Phillips, S.J., Anderson, R.P., Schapire, R.E., (2006). “Maximum entropy modeling of species geographic distributions”. Ecol. Modell. 190, 231–259. https://doi.org/10.1016/j.ecolmodel.2005.03.026
- Pilat, M., A. McFarland, A. Snelgrove, K. Collins, T. Waliczek and J. Zajicek (2012). "The Effect of Tree Cover and Vegetation on Incidence of Childhood Asthma in Metropolitan Statistical Areas of Texas." HortTechnology 22: 631-637.
- R Development Core Team (2019). R : A langugage and environment for statistical computing. Vienna, Austria, R Foundation for Statistical Computing.
- Rega-Brodsky, C.C., Nilon, C.H., Warren, P.S., (2018). “Balancing urban biodiversity needs and resident preferences for vacant lot management”. Sustain. 10, 1–21. https://doi.org/10.3390/su10051679
- Ring, J., (2012). “Davos Declaration: Allergy as a global problem”. Allergy 67, 141–143. https://doi.org/10.1111/j.1398-9995.2011.02770.x
- Rojo, J., Oteros, J., Pérez-Badia, R., Cervigón, P., Ferencova, Z., Gutiérrez-Bustillo, A.M., Bergmann, K.-C., Oliver, G., Thibaudon, M., Albertini, R., Rodríguez-De la Cruz, D., Sánchez-Reyes, E., Sánchez-Sánchez, J., Pessi, A.-M., Reiniharju, J., Saarto, A., Calderón, M.C., Guerrero, C., Berra, D., Bonini, M., Chiodini, E., Fernández-González, D., García, J., Trigo, M.M., Myszkowska, D., Fernández-Rodríguez, S., Tormo-Molina, R., Damialis, A., Kolek, F., Traidl-Hoffmann, C., Severova, E., Caeiro, E., Ribeiro, H., Magyar, D., Makra, L., Udvardy, O., Alcázar, P., Galán, C., Borycka, K., Kasprzyk, I., Newbigin, E., Adams-Groom, B., Apangu, G.P., Frisk, C.A., Skjøth, C.A., Radišić, P., Šikoparija, B., Celenk, S., Schmidt-Weber, C.B., Buters, J., (2019). “Near-ground effect of height on pollen exposure”. Environ. Res. 174, 160–169. https://doi.org/10.1016/J.ENVRES.2019.04.027
- Rojo, J., Pérez-Badia, R., (2015). “Spatiotemporal analysis of olive flowering using geostatistical techniques”. Sci. Total Environ. 505, 860–869. https://doi.org/10.1016/j.scitotenv.2014.10.022
- Romero-Morte, J., Rojo, J., Rivero, R., Fernández-González, F., Pérez-Badia, R., (2018). “Standardised index for measuring atmospheric grass-pollen emission”. Sci. Total Environ. 612, 180–191. https://doi.org/10.1016/j.scitotenv.2017.08.139
- Rufo, J.C., Paciência, I., Ribeiro, A.I., (2019). “Green Environments and Allergic Diseases in Children: a Scoping Review”. Curr. Epidemiol. Reports 6, 442–448. https://doi.org/10.1007/s40471-019-00218-0

- Samson, R., Grote, R., Calfapietra, C., Cariñanos, P., Fares, S., Paoletti, E., Tiwary, A., (2017). “Urban Trees and Their Relation to Air Pollution” Future City. Springer International Publishing AG, pp. 21–30. https://doi.org/10.1007/978-3-319-50280-9_3
- Sánchez-Robles, J.M., García-Castaño, J.L., Balao, F., Terrab, A., Navarro-Sampedro, L., Tremetsberger, K., Talavera, S., (2014). “Effects of tree architecture on pollen dispersal and mating patterns in Abies pinsapo Boiss. (Pinaceae)”. Mol. Ecol. 23, 6165–6178. https://doi.org/10.1111/mec.12983
- Schutte, A. R., J. C. Torquati and H. L. Beattie (2017). "Impact of Urban Nature on Executive Functioning in Early and Middle Childhood." Environment and Behavior 49(1): 3-30.
- Schwarz, N., Moretti, M., Bugalho, M.N., Davies, Z.G., Haase, D., Hack, J., Hof, A., Melero, Y., Pett, T.J., Knapp, S., (2017). “Understanding biodiversity-ecosystem service relationships in urban areas: A comprehensive literature review”. Ecosyst. Serv. https://doi.org/10.1016/j.ecoser.2017.08.014
- Shen, L., Stopher, P.R., (2013). “Should we change the rules for trip identification for GPS travel records?”, Australasian Transport Research Forum.
- Sjöman, H., Morgenroth, J., Sjöman, J.D., Sæbø, A., Kowarik, I., (2016). “Diversification of the urban forest—Can we afford to exclude exotic tree species?” Urban For. Urban Green. 18, 237–241. https://doi.org/10.1016/j.ufug.2016.06.011
- Skounti, M., A. Philalithis and E. Galanakis (2007). "Variations in prevalence of attention deficit hyperactivity disorder worldwide." Eur J Pediatr 166(2): 117-123.
- Skowronek, S., Ewald, M., Isermann, M., Van De Kerchove, R., Lenoir, J., Aerts, R., Warrie, J., Hattab, T., Honnay, O., Schmidtlein, S., Rocchini, D., Somers, B., Feilhauer, H., (2017). “Mapping an invasive bryophyte species using hyperspectral remote sensing data.” Biol. Invasions 19, 239–254. https://doi.org/10.1007/s10530-016-1276-1
- Sofiev, M., Siljamo, P., Ranta, H. & Rantio-Lehtimäki, A. (2006). “Towards numerical forecasting of long-range air transport of birch pollen: theoretical considerations and a feasibility study”. International Journal of Biometeorology, 50: 392–402 DOI 10.1007/s00484-006-0027-x.
- Sofiev, M., Siljamo, P., Ranta, H., Linkosalo, T., Jaeger, S., Rasmussen, A., Rantio-Lehtimaki, A., Severova, E., Kukkonen, J. (2013). “A numerical model of birch pollen emission and dispersion in the atmosphere. Description of the emission module”. International Journal of Biometeorology, 57, 45–58, DOI
- Sofiev, M., Bergmann, K.-C., (2013). “Allergenic Pollen: A Review of the Production, Release, Distribution and Health Impacts”. Springer Science+Business Media, Dordrecht. https://doi.org/10.1007/978-94-007-4881-1
- South, E.C., Kondo, M.C., Cheney, R.A., Branas, C.C., (2015). “Neighborhood blight, stress, and health: A walking trial of urban greening and ambulatory heart rate”. Am. J. Public Health 105, 909–913. https://doi.org/10.2105/AJPH.2014.302526
- Spellerberg, I.F., Eriksson, N.E., Crump, V.S.A., (2006). “Silver birch (Betula pendula) pollen and human health: Problems for an exotic tree in New Zealand. Arboric”. Urban For. 32, 133–137.
- Stiemsma, L. T., L. A. Reynolds, S. E. Turvey and B. B. Finlay (2015). "The hygiene hypothesis: current perspectives and future therapies." Immunotargets Ther 4: 143-157.

- Steinle, S., Reis, S., Sabel, C.E., Semple, S., Twigg, M.M., Braban, C.F., Leeson, S.R., Heal, M.R., Harrison, D., Lin, C., Wu, H., (2015). “Personal exposure monitoring of PM2.5 in indoor and outdoor microenvironments”. Sci. Total Environ. 508, 383–394. https://doi.org/10.1016/j.scitotenv.2014.12.003
- Sunyer, J. and P. Dadvand (2019). "Pre-natal brain development as a target for urban air pollution." Basic Clin Pharmacol Toxicol 125 Suppl 3: 81-88.
- Tartakovsky, L., Baibikov, V., Czerwinski, J., Gutman, M., Kasper, M., Popescu, D., Veinblat, M., Zvirin, Y., (2013). “In-vehicle particle air pollution and its mitigation”. Atmos. Environ. 64, 320–328. https://doi.org/10.1016/j.atmosenv.2012.10.003
- Taylor, A. F. and F. E. Kuo (2009). "Children with attention deficits concentrate better after walk in the park." J Atten Disord 12(5): 402-409.
- Taylor, A. F., F. E. Kuo and W. C. Sullivan (2001). "Coping with add:The Surprising Connection to Green Play Settings." Environment and Behavior 33(1): 54-77.
- Tischer, C., P. Dadvand, X. Basagana, E. Fuertes, A. Bergström, O. Gruzieva, E. Melen, D. Berdel, J. Heinrich, S. Koletzko, I. Markevych, M. Standl, D. Sugiri, L. Cirugeda, M. Estarlich, A. Fernández-Somoano, A. Ferrero, J. Ibarlueza, A. Lertxundi, A. Tardón, J. Sunyer and J. M. Anto (2018). "Urban upbringing and childhood respiratory and allergic conditions: A multi-country holistic study." Environ Res 161: 276-283.
- Tischer, C., M. Gascon, A. Fernández-Somoano, A. Tardón, A. Lertxundi Materola, J. Ibarluzea, A. Ferrero, M. Estarlich, M. Cirach, M. Vrijheid, E. Fuertes, A. Dalmau-Bueno, M. J. Nieuwenhuijsen, J. M. Antó, J. Sunyer and P. Dadvand (2017). "Urban green and grey space in relation to respiratory health in children." Eur Respir J 49(6).
- Tischer, C., F. Weikl, A. J. Probst, M. Standl, J. Heinrich and K. Pritsch (2016). "Urban Dust Microbiome: Impact on Later Atopy and Wheezing." Environ Health Perspect 124(12): 1919-1923.
- Tost, J. and I. G. Gut (2007). "Analysis of gene-specific DNA methylation patterns by pyrosequencing technology." Methods Mol Biol 373: 89-102.
- Trotta-Moreu, N., Lobo, J.M., (2010). “Deriving the Species Richness Distribution of Geotrupinae (Coleoptera: Scarabaeoidea) in Mexico From the Overlap of Individual Model Predictions”. Environ. Entomol. 39, 42–49. https://doi.org/10.1603/EN08179
- Underner, M., J. Perriot, G. Peiffer and J. C. Meurice (2015). "[Influence of tobacco smoking on the risk of developing asthma]." Rev Mal Respir 32(2): 110-137.
- van den Berg, A. E. and C. G. van den Berg (2011). "A comparison of children with ADHD in a natural and built setting." Child: Care, Health and Development 37(3): 430-439.
- Van Gerven, L., Boeckxstaens, G., Hellings, P., (2012). “Up-date on neuro-immune mechanisms involved in allergic and non-allergic rhinitis”. Rhinol. J. 50, 227–235. https://doi.org/10.4193/rhin11.152
- van Heezik, Y., Brymer, E., (2018). “Nature as a Commodity: What’s Good for Human Health Might Not Be Good for Ecosystem Health”. Front. Psychol. 9, 1673. https://doi.org/10.3389/fpsyg.2018.01673

- Van Landuyt, W., Vanhecke, L., Brosens, D., (2012). “Florabank1: a grid-based database on vascular plant distribution in the northern part of Belgium (Flanders and the Brussels Capital region)”. PhytoKeys 12, 59–67. https://doi.org/10.3897/phytokeys.12.2849
- Vautard R., M. Beekmann, J. Roux, D. Gombert (2001) “Validation of a deterministic forecasting system for the ozone concentrations over the Paris area” Atmospheric Environment 35 2449-2461.
- Veena, S. R., G. V. Krishnaveni, A. K. Wills, A. V. Kurpad, S. Muthayya, J. C. Hill, S. C. Karat, K. K. Nagarajaiah, C. H. D. Fall and K. Srinivasan (2010). "Association of Birthweight and Head Circumference at Birth to Cognitive Performance in 9- to 10-Year-Old Children in South India: Prospective Birth Cohort Study." Pediatric Research 67(4): 424-429.
- Velasco-Jiménez, M.J., Alcázar, P., Cariñanos, P., Galán, C., (2020). “Allergenicity of the urban green areas in the city of Córdoba (Spain)”. Urban For. Urban Green. 49, 126600. https://doi.org/10.1016/j.ufug.2020.126600
- Verstraeten, W.W., Dujardin, S., Hoebeke, L., Bruffaerts, N., Kouznetsov, R., Dendoncker, N., Hamdi, R., Linard, C., Hendrickx, M., Sofiev, M. & Delcloo, A.W. (2019). “Spatio-temporal monitoring and modelling of birch pollen levels in Belgium.” Aerobiologia. 35(4), 703-717. https://doi.org/10.1007/s10453-019-09607-w.
- Vieira, S. E. (2015). "The health burden of pollution: the impact of prenatal exposure to air pollutants." Int J Chron Obstruct Pulmon Dis 10: 1111-1121.
- Visschedijk, A.J.H., Zandveld, P.Y.J., and Denier van der Gon, H.A.C.A.,High resolution gridded European database for the EU Integrate Project GEMS, TNO-report 2007-A-R0233/B.
- Vriens, L., De Knijf, G., De Saeger, S., Guelinckx, R., Oosterlynck, P., Van Hove, M., Paelinckx, D., (2011). “De Biologische Waarderingskaart. Biotopen en hun verspreiding in Vlaanderen en het Brussels Hoofdstedelijk Gewest.” Mededelingen van Het Instituut Voor Natuur- En Bosonderzoek. INBO.M.2011.1, Brussels, p. 416.
- Wallen, M.P., Gomersall, S.R., Keating, S.E., Wisløff, U., Coombes, J.S., (2016). “Accuracy of Heart Rate Watches: Implications for Weight Management”. PLoS One 11, e0154420. https://doi.org/10.1371/journal.pone.0154420
- Weikl, F., C. Tischer, A. Probst, I. Markevych, S. Jochner and K. Pritsch (2016). "Fungal and Bacterial Communities in Indoor Dust Follow Different Environmental Determinants." PloS one 11: e0154131.
- Werchan, B., Werchan, M., Mücke, H.G., Gauger, U., Simoleit, A., Zuberbier, T., Bergmann, K.C., 2017. Spatial distribution of allergenic pollen through a large metropolitan area. Environ. Monit. Assess. 189. https://doi.org/10.1007/s10661-017-5876-8
- Westra, T., Verschelde, P., Van Calster, H., Els, L., Onkelinx, T., Quataert, P., Govaere, L., Waterinckx, M., (2015). “Opmaak van een analysestramien voor de gegevens van de Vlaamse Bosinventarisatie”. Brussels. https://doi.org/INBO.R.2015.903482
- White, M.P., Alcock, I., Wheeler, B.W., Depledge, M.H., (2013). “Would You Be Happier Living in a Greener Urban Area? A Fixed-Effects Analysis of Panel Data”. Psychol. Sci. 24, 920–928. https://doi.org/10.1177/0956797612464659

- Wolch, J.R., Byrne, J., Newell, J.P., (2014). “Urban green space, public health, and environmental justice: The challenge of making cities ‘just green enough.’” Landsc. Urban Plan. 125, 234–244. https://doi.org/10.1016/J.LANDURBPLAN.2014.01.017
- Wong, C. T., J. Wais and D. A. Crawford (2015). "Prenatal exposure to common environmental factors affects brain lipids and increases risk of developing autism spectrum disorders." European Journal of Neuroscience 42(10): 2742-2760.
- Yang, M., C. Chu, M. Bloom, S. Li, G. Chen, I. Markevych, L. Knibbs, G. Bowatte, S. Dharmage, M. Shigematsu, A. Leskinen, M.-R. Hirvonen, M. Roponen, P. Jalava, S.-Q. Wang, S. Lin, X.-W. Zeng, L.-W. Hu and G.-H. Dong (2018). "Is smaller worse? New insights about associations of PM1 and respiratory health in children and adolescents." Environment international 120: 516-524.
- Younan, D., C. Tuvblad, L. Li, J. Wu, F. Lurmann, M. Franklin, K. Berhane, R. McConnell, A. H. Wu, L. A. Baker and J. C. Chen (2016). "Environmental Determinants of Aggression in Adolescents: Role of Urban Neighborhood Greenspace." J Am Acad Child Adolesc Psychiatry 55(7): 591-601.
- Young, C., Hofmann, M., Frey, D., Moretti, M., Bauer, N., (2020). “Psychological restoration in urban gardens related to garden type, biodiversity and garden-related stress.” Landsc. Urban Plan. 198, 103777. https://doi.org/10.1016/j.landurbplan.2020.103777
- Zach, A., N. Meyer, L. Hendrowarsito, S. Kolb, G. Bolte, U. Nennstiel-Ratzel, N. I. Stilianakis and C. Herr (2016). "Association of sociodemographic and environmental factors with the mental health status among preschool children-Results from a cross-sectional study in Bavaria, Germany." Int J Hyg Environ Health 219(4-5): 458-467.
- Zeltser, L. M. and R. L. Leibel (2011). "Roles of the placenta in fetal brain development." Proc Natl Acad Sci U S A 108(38): 15667-15668.
- Zinsstag, J., Schelling, E., Crump, L., Whittaker, M., Tanner, M., Stephen, C., (2020). “One Health: The Theory and Practice of Integrated Health Approaches”.

ANNEXES

Annex 1 – full text of Stas M., Aerts R., Hendrickx M., Bruffaerts N., Dendoncker N., Hoebeke L., Linard C., Nawrot T., Van Nieuwenhuyse A., Aerts J.-M., Van Orshoven J., & Somers B. (2021) Association between local airborne tree pollen composition and surrounding land cover across different spatial scales in northern Belgium. Urban Forestry & Urban Greening. https://doi.org/10.1016/j.ufug.2021.127082

Annex 2 – full text of Stas, M., Aerts, R., Hendrickx, M., Dendoncker, N., Dujardin, S., Linard, C., Nawrot, T., Van Nieuwenhuyse, A., Aerts, J.-M., Van Orshoven, J., & Somers, B. Residential green space types, allergy symptoms and mental health in a cohort of tree pollen allergy patients. Landscape and Urban Planning, 210, https://doi.org/10.1016/j.landurbplan.2021.104070

Annex 3 - Stas, M., Aerts, R., Hendrickx, M., Delcloo, A. Dendoncker, N., Dujardin, S., Linard, C., Nawrot, T., Van Nieuwenhuyse, A., Aerts, J.-M., Van Orshoven, J., & Somers, B. Dynamic exposure to green space and tree pollen allergy symptom severity: a case-crossover study in Belgium Science of the Total Environment (under review)