



## Exposure to green space and pollen allergy symptom severity: A case-crossover study in Belgium



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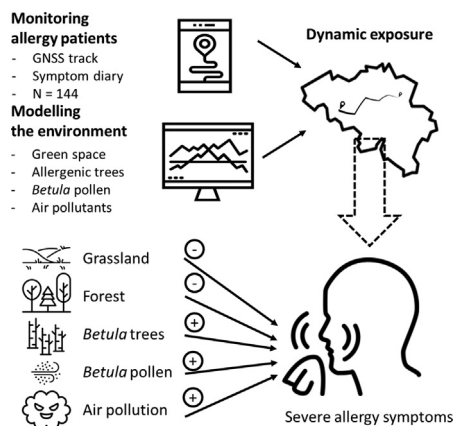
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### HIGHLIGHTS

- Spatio-temporal tracking allows for a realistic exposure assessment.
- Exposure to green space is inversely associated with severe allergy symptoms.
- Exposure to birch trees is associated with severe allergy symptoms.
- Exposure to pollen and air pollutants is associated with severe allergy symptoms.

### GRAPHICAL ABSTRACT



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### ABSTRACT

**Background:** The prevalence of pollen allergy has increased due to urbanization, climate change and air pollution. The effects of green space and air pollution on respiratory health of pollen allergy patients are complex and best studied in spatio-temporal detail.

**Methods:** We tracked 144 adults sensitized to Betulaceae pollen during the tree pollen season (January–May) of 2017 and 2018 and assessed their spatio-temporal exposure to green space, allergenic trees, air pollutants and

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birch pollen. Participants reported daily symptom severity scores. We extracted 404 case days with high symptom severity scores and matched these to 404 control days. The data were analyzed using conditional logistic regression with a 1:1 case-crossover design.

**Results:** Case days were associated with exposure to birch pollen concentration ( $100 \text{ grains/m}^3$ ) [adjusted odds ratio 1.045 and 95% confidence interval (1.014–1.078)],  $\text{O}_3$  concentration ( $10 \text{ }\mu\text{g/m}^3$ ) [1.504 (1.281–1.766)] and  $\text{PM}_{10}$  concentration ( $10 \text{ }\mu\text{g/m}^3$ ) [1.255 (1.007–1.565)] on the day of the severe allergy event and with the cumulative exposure of one and two days before. Exposure to grass cover (10% area fraction) [0.655 (0.446–0.960)], forest cover (10% area fraction) [0.543 (0.303–0.973)] and density of *Alnus* (10%) [0.622 (0.411–0.942)] were protective for severe allergy, but only on the day of the severe allergy event. Increased densities of *Betula* trees (10%) were a risk factor [unadjusted OR: 2.014 (1.162–3.490)].

**Conclusion:** Exposure to green space may mitigate tree pollen allergy symptom severity but only when the density of allergenic trees is low. Air pollutants contribute to more severe allergy symptoms. Spatio-temporal tracking allows for a more realistic exposure assessment.

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**1. Introduction**

The prevalence of allergic rhinitis in the human population is estimated to be 15–25% worldwide and is most commonly caused by aeroallergens such as plant pollen (Passali et al., 2018). Over the past decades, the prevalence of pollen allergy has increased and this trend is expected to continue due to urbanization, air pollution and climate change (D'Amato et al., 2016; Lake et al., 2017). Increased urbanization goes along with reduced exposure to natural environments. The Karelia Allergy Study monitored a rural and a more urbanized population and found an allergy gap due to a higher prevalence of birch pollen allergy in the urbanized population (Haahtela et al., 2015). Urbanization and air pollutants were found to induce alterations to the chemical composition of hazel pollen, intensifying their allergenic potential (Depciuch et al., 2017). In addition, birch catkins exposed to higher levels of ozone produce pollen with enhanced allergenicity (Beck et al., 2013). Oak trees have been found to produce more pollen and more allergenic proteins under elevated levels of  $\text{CO}_2$  expected under climate change (Kim et al., 2018). Furthermore, models from Zhang et al. (2013) found that higher levels of  $\text{CO}_2$  and temperature increases due to climate change would result in higher peak values in birch pollen counts and an earlier onset of the birch pollen season.

To mitigate effects of climate change and air pollutants in urban areas and improve quality of life, the creation and expansion of green spaces and urban forests is promoted (Livesley et al., 2016). Evapotranspiration of individual urban trees contributes to a cooling of the urban heat island (Ballinas and Barradas, 2016). In addition, urban forests remove air pollutants from the city's atmosphere (Bottalico et al., 2017) and take up carbon (Trlica et al., 2020). Access and exposure to urban green spaces has been associated with mental and physical health benefits (Kondo et al., 2018). Taking into account the 'biodiversity hypothesis', intertwining the built environment of the city with more natural environments can be beneficial to decrease allergies (Haahtela, 2019). However, the allergenic tree species in these urban green spaces emit pollen that may trigger allergies and asthma (Carlsten and Rider, 2017; Eisenman et al., 2019).

The effects of green spaces on the development of asthma and allergic rhinitis in children has been studied by many, but the results are heterogeneous (Ferrante et al., 2020; Lambert et al., 2017). Residential proximity to green space and residential greenness has been associated with a reduced risk of bronchitis and wheezing (Tischer et al., 2017), as well as lower odds of allergic nasal symptoms in children (Cilluffo et al., 2018). Other studies, however, find that children living with more green space around the residence suffer more from wheezing and have an increased risk of allergic rhinitis (Parmes et al., 2020) and asthma (Andrusaityte et al., 2016). Studies on adults are less common. A previous study in Northern Belgium found that adults sensitized to tree pollen experienced mental health benefits from residential exposure to green, despite their tree pollen allergy (Aerts et al., 2020). Two Korean

studies found contrasting results regarding the protective effects of green space on the prevalence of allergy symptoms in adults (Kim et al., 2020; Kwon et al., 2019). Several studies on adults report that tree cover, gardens and public parks mitigate poor asthma outcomes (Alcock et al., 2017; Douglas et al., 2019; Ulmer et al., 2016). Another study found more allergy symptoms and a higher asthma prevalence in Iranian palm tree garden workers as opposed to office employees (Amin et al., 2017).

The literature shows that green space can impact the respiratory health of allergy-sufferers significantly. The available studies are limited to either residential exposure (Aerts et al., 2020) or exposure at the administrative region level (Kim et al., 2020). A study of Jones et al. (2019) found no association between neighborhood natural environment and asthma exacerbation at the level of administrative regions and suggested that future research should assess exposure with more spatial and temporal detail. Indeed, exposure is highly dynamic (Dédélé et al., 2019) and to assess exposure risks it is needed to measure exposure beyond residential exposure (Steinle et al., 2015). Nowadays, the use of Global Navigation Satellite Systems (GNSS) is integrated in mobile phones allowing geo-locating and tracking of personal exposure at high spatio-temporal resolution during activities outside the residence (Dédélé et al., 2019; Steinle et al., 2015). Health benefits of nature are assumed to be dose-dependent (Shanahan et al., 2016a), GNSS tracking allows for a better approximation of the true nature dose. Green spaces promote physical activity (Calogiuri and Chroni, 2014; Nawrath et al., 2019) which is an important mechanism for health benefits (Aerts et al., 2018; Dadvand et al., 2016; Richardson et al., 2013). An active lifestyle and exposure to green have health benefits for the individual that are hypothesized to work synergistically (Shanahan et al., 2016b). Therefore, it is of interest to extract physical activity from spatio-temporal data to observe behavior-specific effects in detail. Additionally, extracting transport-behavior is of importance when studying exposure to air pollutants. Although transport makes up only 6% of daily activity time, it is the largest contributor to personal exposure to air pollution (Dons et al., 2011), because individuals might be exposed to peak concentrations during transport (Dons et al., 2019).

The aim of this study was to quantify the exposure of adults sensitized to tree pollen using a mobile health application. By using location services the mobile health application registered the whereabouts and exposure beyond the residence. By spatially overlaying GNSS tracks with environmental data we calculated dynamic exposure to three green space type covers (garden, grassland and forest), to density of three allergenic tree species (hazel, alder and birch), to birch pollen concentration, and to concentration of four air pollutants (black carbon, nitrogen dioxide, ozone and particulate matter smaller than  $10 \text{ }\mu\text{m}$ ). We hypothesized that green space types would have a protective effect, while density of allergenic trees would be a risk factor for severe allergy events with and without adjustment for exposure to birch pollen and air pollutants. We also hypothesized that using GNSS data to quantify

dynamic exposure for the whole day and for behavioral subsamples allows for a more realistic exposure calculation than when limited to residential exposure.

## 2. Materials and methods

### 2.1. Study design and population

The RespirIT study on respiratory health effects from exposure to green was approved by the Ethical Commission of the KU Leuven University Hospital (Belgian registration number B322201629692). In 2016 and 2017, adults with tree pollen allergy were recruited from the general population of Belgium. To participate in the study, participants needed to (1) be adults over 20 years old, (2) live in Belgium, (3) be sensitized to pollen of common hazel (*Corylus avellana*), alder (*Alnus* spp.) and/or birch (*Betula* spp.), and (4) be willing to use a mobile application to track their whereabouts. Of the 225 persons interested in participating, 189 (84%) met these criteria and were included in the RespirIT study (Fig. 1). Ultimately, due to restrictions of the statistical analyses (explained in Section 2.6) data of 45 participants were omitted, resulting in a dataset of 144 patients. Given that 189 people were eligible to participate, we had a response rate of 76%.

### 2.2. Mobile health application

After giving informed consent, the participants installed the RespirIT mobile health application on their personal smartphone to be used during the tree pollen season (January–May) of 2017 and/or 2018. The application recorded GNSS coordinates and activity levels from the gyroscopes of the smartphone at a 1 s frequency. At the end of each day, a questionnaire in the mobile health application allowed participants to log and score the severity of their allergy symptoms during the day. The 189 participants logged data for 8423 person-days (Fig. 1).

### 2.3. Definition of the outcome variable

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 flu, 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

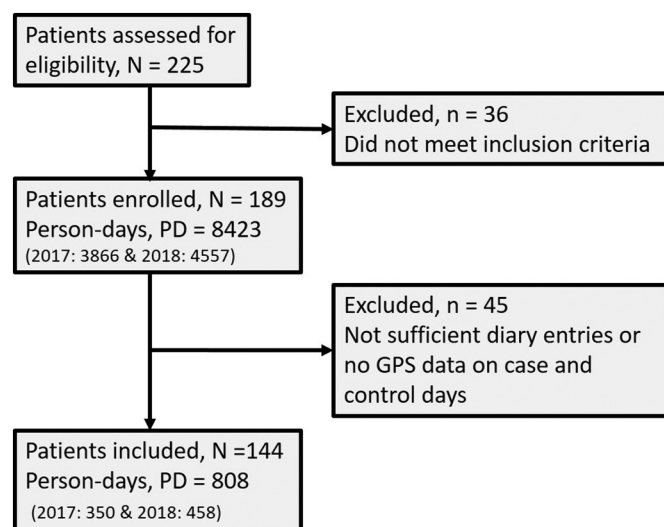


Fig. 1. Flow diagram of the selection process for the tree pollen allergy patients and data suitable for the case-cross-over analysis.

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). 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.

### 2.4. Definition of potential predictors

#### 2.4.1. Green space types

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 (m<sup>2</sup>) 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 1 km buffer around each 100 × 100 m reference grid cell. We used a 1 km buffer because associations between green space and health are often more relevant at larger scales beyond the direct surroundings (Browning and Lee, 2017; Stas et al., 2021).

#### 2.4.2. Allergenic tree density

The allergenic tree taxa of interest in this study are birch (*Betula* spp.), alder (*Alnus* spp.) and hazel (*Corylus avellana*), because these are the pollen taxa our participants are sensitized to. Predicted tree density for the three taxa was obtained per 100 m × 100 m grid cell through two modelling steps similar to those in the method of Hill et al. (2017). First, a species distribution model combined observational data from regional forest inventories (Alderweireld et al., 2015; Westra et al., 2015) and observations.org with environmental covariates to predict habitat suitability at a 100 m resolution. Second, abundance data from the forest inventory, the predicted habitat suitability and covariates of greenness (natural difference vegetation index, NDVI) were combined in a random forest model, resulting in a 100 m resolution model of predicted density of *Alnus*, *Betula*, and *Corylus*. Then, similarly to the green space cover, average density for each taxa was determined within a 1 km buffer around each 100 × 100 m raster cell.

#### 2.4.3. Birch pollen levels

Birch pollen levels are monitored at five measurement sites in Belgium by the Belgian aerobiological surveillance network (Sciensano, www.airallergy.be). These pollen counts were used to validate the birch pollen levels determined by the SILAM model as described by Verstraeten et al. (2019). SILAM provides daily birch pollen levels as grains/m<sup>3</sup> at a spatial resolution of 10 km. Ultimately daily pollen counts were converted to 100 grains/m<sup>3</sup> approximating the critical threshold above which the majority of sensitized patients experience allergy symptoms (80 grains/m<sup>3</sup>) as used by the Belgian aerobiological surveillance agency (Hoebeke et al., 2018; Sofiev and Bergmann, 2013).

#### 2.4.4. Air pollutants

In Belgium, pollutants such as black carbon (BC), nitrogen dioxide (NO<sub>2</sub>), ozone (O<sub>3</sub>) and particulate matter smaller than 10 μm (PM<sub>10</sub>)

are measured by a monitoring network set up by the Belgian Interregional Environment Agency (<https://www.irceline.be/en>). Based on this monitoring network hourly concentrations of air pollutants could be interpolated at a 4 km resolution using the RIO model (Janssen et al., 2008). Ultimately, daily average concentrations for BC, NO<sub>2</sub>, O<sub>3</sub> and PM<sub>10</sub> were calculated at a spatial resolution of 4 km.

## 2.5. Dynamic exposure

### 2.5.1. Extraction of behavior

We calculated dynamic exposure to the environmental features using GNSS tracks sampled at 1 s intervals. For annotation of the track with distinct behaviors, we down-sampled to 5 s intervals, which has shown to be a more suitable sampling frequency to successfully distinguish behaviors (Shen and Stopher, 2013). We defined three distinct behaviors: (1) stationary, when a person is sitting or standing; (2) active movement such as walking or bicycling; and (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 behavior, 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 s, a point with stationary or active transport behavior would be set to motorized transport behavior when motorized transport was detected within 30 s before and after the behavior of that point (Hazlehurst et al., 2017).

### 2.5.2. Exposure calculation

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 GNSS point corresponds to a 5 s 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 behavior subsample, the active transport subsample, and the motorized transport subsample.

## 2.6. Statistical analyses

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<sub>2</sub>, O<sub>3</sub> and PM<sub>10</sub>) on the one hand with the occurrence of severe allergy symptoms on the other hand. Case days were defined as those days with severe allergy, corresponding to the 25% highest symptom severity scores experienced per patient. Each patient served as its own control, thus 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, and (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 (Fig. 1).

Given the 1:1 case-crossover design, we used conditional logistic regression to estimate odds ratios with 95% confidence intervals. We assessed multicollinearity by calculating the inverse correlation matrix for the explanatory variables (Table S1). The diagonal of the inverse correlation matrix shows the variance inflation factor (VIF). All the VIF values are below 10, the commonly used threshold indicating that the levels of multicollinearity are acceptable to include the variables in a model together (O'Brien, 2007).

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. A first stratification was based on sex (men and women), a second stratification based on age (20–40 years old and 41–65 years old), and a third stratification based on the region (Brussels Capital Region, Flanders and Wallonia). For the stratification by region tracks that crossed region boundaries were omitted and case days were matched to control days spent in the same region. 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 report of this study follows the STROBE statement of items that should be included in reports of case-control studies (von Elm et al., 2008).

## 3. Results

### 3.1. Population characteristics

Table 1 shows that the cohort comprises more women (59.3%) than men (40.7%) with an average age of 40.4 (standard deviation of 9.9). Other population characteristics (BMI, smoking behavior, medication use, respiratory disease, education level) have been included in Table S2. There is no distinct difference in the total tracked time on case days ( $7.8 \pm 4.6$  h) and control days ( $7.6 \pm 4.8$  h). In addition, the time spent in the three behavior 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 in Table 1 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/m<sup>3</sup> (3.1–648.0) compared to control days 43.1 grains/m<sup>3</sup> (0–240.0). Finally, case days are characterized by higher levels of air pollutants as shown in Table 1.

### 3.2. Predictors of severe allergy

#### 3.2.1. Overall analysis

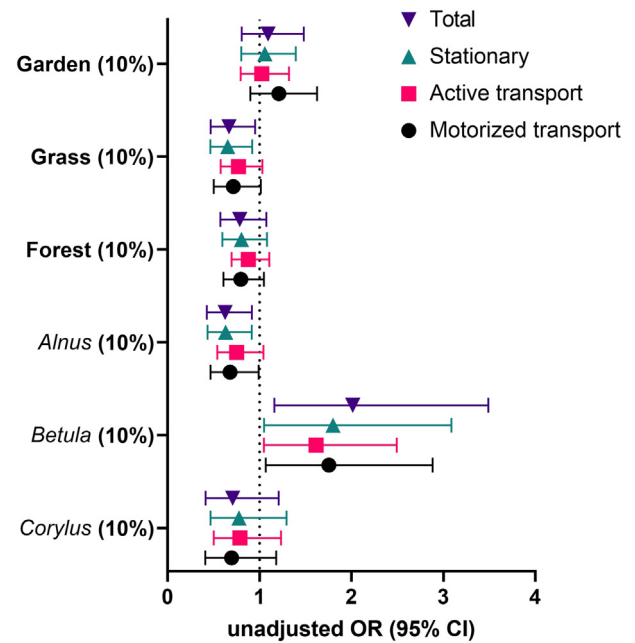
We found an inverse association between the magnitude of dynamic exposure to grass cover and severity of tree pollen allergy for the total track [unadjusted odds ratio (uOR): 0.668 and 95% confidence interval (CI): 0.469–0.952] and the stationary subsample [uOR: 0.654 with 95% CI: 0.465–0.921] as shown in Fig. 2 and Table S3. Dynamic exposure to grass cover was not significantly associated with severe allergy when patients were in transport, both for active [uOR: 0.771 with 95% CI: 0.577–1.031] as well as motorized transport [uOR: 0.714 with 95% CI:

**Table 1**  
Study population, potential predictors and symptom severity score (n = 144) for case and control days (808 person days).

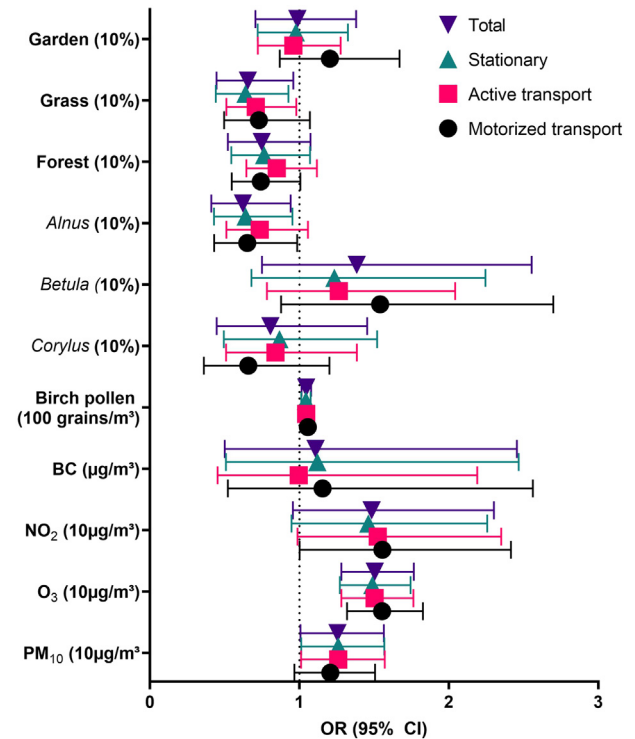
	n (%), or mean (SD), and median (25th–75th percentiles)	
	Case days	Control days
Sex		
Female	86 (59.7%)	86 (59.7%)
Male	58 (40.3%)	58 (40.3%)
Age (years)	40.4 (9.9)	40.4 (9.9)
Hours tracked	39.5 (32.0–48.3)	39.5 (32.0–48.3)
Stationary (h)	7.8 (4.6)	7.6 (4.8)
Active transport (h)	7.5 (4.3–10.7)	7.1 (4.0–10.4)
Motorized transport (h)	6.4 (4.4)	6.3 (4.4)
Motorized transport (h)	5.9 (2.9–8.9)	5.7 (2.7–9.0)
Motorized transport (h)	0.6 (0.6)	0.6 (0.7)
Motorized transport (h)	0.4 (0.2–0.8)	0.4 (0.2–0.8)
Motorized transport (h)	0.8 (0.8)	0.7 (0.7)
Motorized transport (h)	0.6 (0.2–1.4)	0.5 (0.2–1.0)
Exposure		
Garden cover in 1 km (%)	23.8 (9.2)	23.2 (9.0)
Grassland cover in 1 km (%)	23.2 (18.4–29.4)	22.8 (17.6–28.2)
Forest cover in 1 km (%)	13.3 (8.4)	14.5 (9.3)
Density of <i>Alnus</i> in 1 km (%)	11.8 (7.3–17.5)	12.5 (8.0–19.0)
Density of <i>Betula</i> in 1 km (%)	9.8 (9.4)	10.7 (11.0)
Density of <i>Corylus</i> in 1 km (%)	6.4 (2.9–14.0)	7.0 (3.0–14.8)
Density of <i>Alnus</i> in 1 km (%)	16.5 (7.8)	17.0 (8.1)
Density of <i>Betula</i> in 1 km (%)	14.8 (11.1–20.8)	15.6 (10.8–22.2)
Density of <i>Corylus</i> in 1 km (%)	36.1 (9.4)	35.0 (10.2)
Birch pollen (grains/m <sup>3</sup> )	38.9 (33.5–42.7)	38.4 (31.3–42.4)
Birch pollen (grains/m <sup>3</sup> )	19.4 (8.9)	18.6 (9.1)
Birch pollen (grains/m <sup>3</sup> )	18.4 (12.0–28.3)	17.4 (11.1–28.0)
BC (µg/m <sup>3</sup> )	551.8 (891.4)	283.9 (746.7)
NO <sub>2</sub> (µg/m <sup>3</sup> )	193.9 (3.1–648.0)	43.1 (0–240.0)
O <sub>3</sub> (µg/m <sup>3</sup> )	1.1 (0.5)	0.9 (0.5)
PM <sub>10</sub> (µg/m <sup>3</sup> )	1.0 (0.7–1.4)	0.8 (0.5–1.2)
PM <sub>10</sub> (µg/m <sup>3</sup> )	23.4 (9.8)	20.7 (10.3)
PM <sub>10</sub> (µg/m <sup>3</sup> )	22.5 (16.2–29.5)	18.7 (13.0–27.4)
PM <sub>10</sub> (µg/m <sup>3</sup> )	52.5 (16.2)	50.2 (16.0)
PM <sub>10</sub> (µg/m <sup>3</sup> )	54.1 (42.1–62.6)	52.1 (38.5–62.7)
PM <sub>10</sub> (µg/m <sup>3</sup> )	25.1 (13.3)	20.0 (11.1)
PM <sub>10</sub> (µg/m <sup>3</sup> )	21.6 (16.3–30.1)	17.4 (12.5–24.8)
Respiratory health endpoint		
Symptom severity score	12.3 (6.4)	1.1 (1.9)
Symptom severity score	11 (8–16)	0 (0–2)

0.502–1.014]. Density of *Alnus* trees was inversely associated with severe allergy for the total track [0.625 (0.427–0.917)], the stationary subsample [0.631 (0.435–0.915)] and the motorized transport subsample [0.679 (0.466–0.990)], but not the active transport subsample [0.751 (0.540–1.043)]. We found that *Betula* density was associated with severe allergy for the total track [2.014 (1.162–3.490)], the stationary subsample [1.800 (1.049–3.088)], the active transport subsample [1.616 (1.048–2.493)] and the motorized transport subsample [1.755 (1.068–2.884)].

In the model adjusted for birch pollen and air pollutant concentrations, shown in Fig. 3 and Table S4, *Betula* density is no longer significantly associated to severe allergy. Grass cover remained inversely associated to severe allergy for the total track [adjusted OR: 0.655 (0.446–0.960)], the stationary subsample [adjusted OR: 0.639 (0.441–0.927)] and the active transport subsample [adjusted OR: 0.708 (0.511–0.980)]. Also *Alnus* density remained inversely associated for the total track [0.622 (0.411–0.942)], the stationary subsample [0.640 (0.429–0.954)] and the motorized transport subsample [0.651 (0.430–0.986)]. Dynamic exposure to birch pollen was associated with severe allergy for the total track [1.045 (1.014–1.078)], the stationary subsample [1.043 (1.012–1.075)], the active transport subsample [1.045 (1.013–1.077)] and the motorized transport subsample [1.056 (1.023–1.091)]. Dynamic exposure to O<sub>3</sub> was associated with severe allergy for the total track [1.504 (1.281–1.766)], the stationary subsample [1.489 (1.271–1.744)], the active transport subsample [1.503 (1.281–1.763)] and the motorized transport subsample [1.553



**Fig. 2.** Associations (unadjusted odds ratio (uOR) 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. The dynamic exposure was calculated for the total GNSS track and the stationary, active transport and motorized transport subsamples of the track.



**Fig. 3.** Associations (adjusted odds ratio (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 are adjusted for dynamic exposure to birch pollen and to air pollutants: black carbon (BC), nitrogen dioxide (NO<sub>2</sub>), ozone (O<sub>3</sub>) and particulate matter <10 µm (PM<sub>10</sub>). The dynamic exposure was calculated for the total GNSS track and the stationary, active transport and motorized transport subsamples of the track.

(1.319–1.827)]. Dynamic exposure to PM<sub>10</sub> was associated to severe allergy for the total track [1.255 (1.007–1.565)], the stationary subsample [1.260 (1.012–1.568)] and the active transport subsample [1.260 (1.011–1.571)]. We found that exposure to nitrogen dioxide (NO<sub>2</sub>) during motorized transport was associated to severe allergy [1.555 (1.001–2.416)]. No significant associations were found between allergy severity and exposure to garden cover, forest cover, *Corylus* density and black carbon concentration.

### 3.2.2. Stratified analyses

For the stratified analysis of men (n = 58) and women (n = 86), there were respectively 338 and 470 person-days. For men we found that dynamic exposure to forest cover was inversely associated with severe allergy [uOR: 0.585 (0.348–0.985)] (Fig. S1 and Table S5). This inverse association remained when adjusted for birch pollen and air pollutants [aOR: 0.543 (0.303–0.973)] (Fig. S1 and Table S6). For women an inverse association with severe allergy was found for dynamic exposure to *Corylus* density [0.370 (0.145–0.943)] (Fig. S1 and Table S5). For the female participants we found an association between severe allergy and *Betula* density [2.522 (1.244–5.111)]. These associations found for women disappeared in the model adjusted for birch pollen and air pollutants (Fig. S1 and Table S6). For both men and women, we found an association between O<sub>3</sub> and severe allergy [men: 1.449 (1.130–1.859); women: 1.543 (1.231–1.935)]. In addition, there was an association between severe allergy and birch pollen [1.089 (1.034–1.147)] as well as PM<sub>10</sub> [1.375 (1.008–1.876)] for the female participants (Fig. S1 and Table S6).

In the stratified analysis by age group we found no significant associations with green space for the group aged 20–40. For the older group aged 41–65, dynamic exposure to grassland [0.495 (0.281–0.872)] and *Alnus* density [0.506 (0.285–0.897)] was inversely associated to severe allergy, *Betula* density [3.280 (1.377–7.809)] was associated to severe allergy (Fig. S2 and Table S7). These associations found for the age group 41–65 remained in the model adjusted for birch pollen and air pollutants (Fig. S2 and Table S8). In the adjusted models for both age groups birch pollen and O<sub>3</sub> were associated to severe allergy.

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 inverse associations between severe allergy and green space (Fig. S3 and Table S9). In Flanders, forest cover [0.504 (0.267–0.952)] and *Corylus* density [0.217 (0.059–0.802)] were inversely associated to severe allergy. The inverse association between forest cover and severe allergy [0.487 (0.238–0.997)] remained significant in the adjusted model (Fig. S3 and Table S10). In Brussels and Wallonia birch pollen levels were associated to severe allergy, [1.187 (1.031–1.367)] and [1.242 (1.030–1.497)] respectively. In Wallonia grassland cover was inversely associated to severe allergy in the adjusted model [0.047 (0.003–0.664)]. In both Flanders and Wallonia, we found an association between ozone (O<sub>3</sub>) and severe allergy, [1.572 (1.248–1.980)] and [2.771 (1.199–6.405)] respectively.

### 3.2.3. Sensitivity lag 0–1 and lag 0–2

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 (Fig. S4 and Table S11). For the adjusted model we found the same significant associations for lag 0–1 and lag 0–2 (Fig. S4 and Table S12). Birch pollen was associated to severe allergy at lag 0–1 [1.050 (1.008–1.094)] and lag 0–2 [1.044 (1.001–1.090)]. Dynamic exposure to O<sub>3</sub> and PM<sub>10</sub> were associated with severe allergy at lag 0–1 [O<sub>3</sub>: 1.788 (1.408–2.270); PM<sub>10</sub>: 1.449 (1.022–2.056)] and lag 0–2 [O<sub>3</sub>: 1.907 (1.388–2.620); PM<sub>10</sub>: 1.689 (1.059–2.696)].

## 4. Discussion

### 4.1. Key findings

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. These protective health effects were also observed for the older stratum of the participants. However, exposure to *Betula* trees was a risk factor for severe pollen allergy symptoms. For the male stratum and the region of Flanders we found a protective effect of forest cover. Protective effects of green space were only significant on the case day and not at lag 0–1 or lag 0–2.

Birch pollen and air pollutants (O<sub>3</sub> and PM<sub>10</sub>) were found to be risk factors for severe allergy. We found that NO<sub>2</sub> was a risk factor for severe allergy during the motorized transport subsample of the track. The risk effect of O<sub>3</sub> was found in the male and female subpopulation, while the associations with birch pollen and PM<sub>10</sub> were only significant for the female subpopulation. The risk effect of O<sub>3</sub> was found for Flanders and Wallonia, not in Brussels. In addition, birch pollen, O<sub>3</sub> and PM<sub>10</sub> were identified as risk factors at lag 0–1 and lag 0–2.

### 4.2. Comparisons with other studies

We found that our population of adults sensitized to tree pollen experienced a protective health effect of grassland cover during the tree pollen season of 2017 and 2018. The fact that grasslands are not a source of tree pollen might explain this association. It is possible that this protective effect might disappear during the grass pollen season, due to poly-sensitization (i.e. sensitization to both tree and grass pollen) or cross-reactivity (i.e. allergy symptoms caused due to molecular similarity of tree and grass pollen) (Canis et al., 2011; Panzner et al., 2014; Wölbing et al., 2017). However, in the stratified analysis by sex and by region we found a protective health effect of forest cover, indicating that allergy sufferers can experience health benefits from exposure to green spaces with trees during the tree pollen season. A recent cross-sectional study with 219,298 Korean adults found less reports of allergic rhinitis by patients living in greener administrative regions as derived from data managed by the Korean Statistical Information Service (Kim et al., 2020). Nonetheless, a contrasting result was found in an earlier Korean study, where greenness was based on satellite derived greenness (NDVI) at district level (Kwon et al., 2019). Another study found that more green space within a 1 km buffer around the residence was associated with a lower prevalence of respiratory disease, including asthma (Maas et al., 2009). Fuertes et al. (2020) found that growing up in a more vegetated area or in closer proximity to parks had positive effects on lung function measurable at an age of 24. While studies on adults are limited, the literature has several studies focused on children that reported heterogeneous results on the association of early-life exposure to green with asthma and allergy development (Lambert et al., 2018; Rufo et al., 2019). The protective pathway of childhood and lifetime exposure as defined in previous studies probably differs from the protective pathway of short-term dynamic exposure to green space as observed in this study. The health benefit of childhood exposure is mostly rooted in the biodiversity hypothesis stating that early-life exposure to natural environments and diverse microbiota is important for a normal development of immune responses (Ruokolainen et al., 2017). We, however, only found a protective effect of green space on the day of the severe allergy event and not on the previous days (lag0–1 and lag0–2). This short-term effect might indicate that green space is beneficial for respiratory health through the pathway of better air quality.

Although we found that green space can provide health benefits for allergy sufferers, we also found that the density of *Betula* trees in these green spaces was associated with severe allergy. *Betula* trees are the source of birch pollen, which was also associated with severe allergy. The patients in our cohort are sensitized to birch pollen and thus experience more severe allergy symptoms when exposed to higher densities

of *Betula* trees. The meta-analysis of Kitinoja et al. (2020) confirmed that short term exposure to pollen was associated to an increase in allergic and asthmatic symptoms. On the other hand, we found that *Alnus* density was inversely associated with severe allergy. In the female subpopulation, *Corylus* density was inversely associated with severe allergy. Although the majority of the included participants self-reported to be sensitized to pollen of these two allergenic trees, we unexpectedly found protective effects for *Alnus* and *Corylus* density. These taxa are, however, associated with distinct landscapes: alder trees (*Alnus* spp.) occur in wet landscapes (blue spaces) and hazel trees (*Corylus avellana*) are often found in species-rich small landscape elements (Cormont et al., 2016; Van Den Berge et al., 2018). Blue spaces have been frequently linked to mental health benefits and more and more to physical health benefits (Britton et al., 2020; Garrett et al., 2019; Kabisch et al., 2017). Small landscape elements are perceived to have a restorative health effect (Deng et al., 2020). Possibly, the density of these taxa is a proxy for the availability of blue spaces and small landscape elements that provide health benefits.

We found that high concentrations of air pollutants, especially O<sub>3</sub> and PM<sub>10</sub>, were associated with severe allergy events, which corresponds to results from previous research. A times-series analysis study in Changchun (China) found that the prevalence of allergic rhinitis was associated with PM<sub>10</sub> and NO<sub>2</sub> (Teng et al., 2017). For Taiwan, Chen et al. (2016) found that ambient levels of PM<sub>10</sub>, NO<sub>2</sub>, and O<sub>3</sub> were associated with an increase in the daily number of clinical visits related to allergic rhinitis. The recent study of Wang et al. (2020) included 14,965 allergic rhinitis outpatient records during the period of 2015–2018 in Xinxiang (China) and found that the number of outpatients was associated with high concentrations of air pollutants NO<sub>2</sub>, O<sub>3</sub> and PM<sub>10</sub> on the day of the clinical visit. Although children are often found to be more vulnerable to O<sub>3</sub> (Sacks et al., 2014), Wang et al. (2020) found a statistically stronger association between allergic rhinitis outpatients with O<sub>3</sub> for adults and not children. The European MASK-POLAR study collected pollen allergy symptoms through a mobile application from February 2017 until October 2018. Based on 36,440 symptom scores reported by 3323 geo-located individuals they found an association between O<sub>3</sub> and uncontrolled rhinitis during the grass pollen season but not during the birch pollen season (Bédard et al., 2020). We found, however, an association between O<sub>3</sub> and severe allergy during the tree pollen season, possibly because we used more detailed exposure data. Kwon et al. (2019) also found that associations between air pollutants and the prevalence of allergic rhinitis became weak when the spatial resolution of the exposure data was coarse. Dons et al. (2011) found that the exposure to black carbon can differ up to 30% between individuals who live at the same location. A Lithuanian mobile health study with 125 participants found that allergy risk increased with increasing personal exposure to PM<sub>10</sub> (Dédélé et al., 2019). However, in their approach, Dédélé et al. (2019) did not take into account the temporal variation in PM<sub>10</sub>. In our dynamic exposure approach air pollution data were available at hourly and daily resolution.

Co-exposure to pollen and air pollutants can result in more severe symptoms because pollutants interact with pollen creating smaller subpollen particles that can penetrate the respiratory system deeper than entire pollen grains (Fucheng et al., 2019; Sénéchal et al., 2015). Exposure to NO<sub>2</sub>, PM<sub>10</sub> and O<sub>3</sub> can also prime the airways making them more vulnerable for allergens (Naclerio et al., 2020; Schiavoni et al., 2017). Ultimately, birch pollen that were exposed to more O<sub>3</sub> have heightened allergenicity, producing a more severe reaction in skin prick tests (Beck et al., 2013).

For the most part, we found the same associations for the total track as for the tracks subsampled for specific behavior (i.e. stationary, active transport and motorized transport). During active transport no protective effect of green space was found. Outdoor activities, such as walking and cycling, increase breathing rate, resulting in higher inhaled levels of allergenic pollen (Mitakakis et al., 2008). The only time we found that NO<sub>2</sub> was associated with severe allergy was during motorized transport.

Traffic emissions are one of the main sources of NO<sub>2</sub> (Paraschiv and Paraschiv, 2019) and our dynamic exposure approach seems to be able to register peaks in personal NO<sub>2</sub> exposures during motorized transport as observed by Dons et al. (2019).

The stratified analysis for men and women resulted in differing significant associations. Birch pollen were only significantly associated with severe allergy in women. Pollen allergy has been found to affect men and women differently. The literature has described a sex-related shift in the prevalence of allergic rhinitis and asthma, which is more prevalent in boys during childhood but more predominant in women after puberty (Fröhlich et al., 2017; Pinart et al., 2017).

a protective effect of green was found for men (forest cover) and women (*Corylus* density), as well as a risk effect of O<sub>3</sub> (men and women) and PM<sub>10</sub> (women). Differences in green space effects could be due to behavioral effects. For women, perceived safety is a barrier to use green spaces (Wright Wendel et al., 2012). Women have been found to avoid areas with a high density of trees, lawns with trees (small landscape elements containing *Corylus*) might be preferred because they are perceived as safer (Jansson et al., 2013). Since women possibly avoid exposure to forests, this might explain why forest cover was not associated with women's allergy symptom severity. Exposure to safer small landscape elements, containing *Corylus*, contributed to less severe allergy symptoms in women.

Recruitment was most successful in Flanders, for this region the largest dataset was available. For Wallonia and Brussels only small datasets were available resulting in large 95% confidence intervals as a result of large standard errors (Nemes et al., 2009). We found regional effects of green space exposure: forest cover and *Corylus* density was protective for participants in Flanders, and grassland cover was protective for participants in Wallonia. Although Wallonia has more forest cover than Flanders, no significant effect of forest cover was found in this region. Possibly most participants in Wallonia had a high baseline exposure to forest cover, while exposure to forest cover varied more in Flanders. The protective effect of forests cover found in our cohort was larger in the less forested region of Flanders.

We found that birch pollen, O<sub>3</sub> and PM<sub>10</sub> were associated with severe allergy on the day of the event as well as the two days before the event (lag 0–1 and lag 0–2). Other studies confirm these short-term lag effects of pollen and pollutants on respiratory health outcomes. A British case-crossover study with 209 patients found that short term (lag 0–3) exposure to PM<sub>10</sub> was related to increased admission rates of people with asthma (Canova et al., 2012). Sacks et al. (2014) found that short term (lag 0–2) exposure to O<sub>3</sub> was associated with asthma-related visits to emergency departments of up to 5 (Kiotseridis et al., 2013) and 6 days (Hajat et al., 2001) have been observed. The associations found for lag 0–1 and lag 0–2 can be expected for longer lag periods. These were not included in the study because of the limited availability of person days with GNSS tracks of sufficient quality for more than three consecutive days.

#### 4.3. Strengths and limitations

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.

There are also limitations to this study, such as the rather limited number of participants and person-days available for the analysis.

First of all, the recruitment success of the study was limited, especially in the southern part of Belgium (Wallonia). First, the overall limited recruitment success is possibly due to the high effort required from the participants. Second, the effort required for using the mobile health application daily also caused a big drop-out, reflected in high numbers of person-days with GNSS tracks of poor quality that were not suitable for dynamic exposure calculations. Third, due to the careful matching of case-control pairs the dataset was further reduced for people who had only a limited number of diary entries. However, the carefully matched case-crossover pairs reduced the impact of the subjectivity inherent to the self-reported symptom severity scores. The spatial resolution of the birch pollen model (10 km) and the air pollutants model (4 km) limit the full potential of the dynamic exposure approach. Finally, due to the non-invasive nature of the study we had to rely on self-reported allergy status. We were unable to verify sensitivity to Betulaceae pollen through a skin-prick test.

## 5. Conclusion

We calculated dynamic exposure on 808 person-days obtained from a cohort of 144 adults residing in Belgium and sensitized to tree pollen. We found that severe allergy was associated with birch pollen levels, O<sub>3</sub> and PM<sub>10</sub> 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.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2021.146682>.

## Data statement

The research data is confidential. The land cover data that were used to quantify residential green space (Top10Vector, identifier BE.NGI-IGN/5F4130E6-DF5C-41E6-A956-BB9F04088D11) are copyrighted (©Institut Géographique National) and were used under federal use license 2016\_F014 granted by the Nationaal Geografisch Instituut (NGI-IGN) to the Belgian Science Policy Office (BELSPO).

## CRedit authorship contribution statement

**Michiel Stas:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Writing – original draft, Visualization. **Raf Aerts:** Conceptualization, Writing – review & editing, Visualization. **Marijke Hendrickx:** Conceptualization, Writing – review & editing, Funding acquisition. **Andy Delcloo:** Writing – review & editing, Funding acquisition. **Nicolas Dendoncker:** Writing – review & editing, Funding acquisition. **Sebastien Dujardin:** Methodology, Investigation, Writing – review & editing. **Catherine Linard:** Writing – review & editing, Funding acquisition. **Tim Nawrot:** Funding acquisition. **An Van Nieuwenhuysse:** Writing – review & editing, Funding acquisition. **Jean-Marie Aerts:** Writing – review & editing, Supervision, Funding acquisition. **Jos Van Orshoven:** Writing – review & editing, Supervision, Funding acquisition. **Ben Somers:** Writing – review & editing, Supervision, Project administration, Funding acquisition.

## Declaration of competing interest

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

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