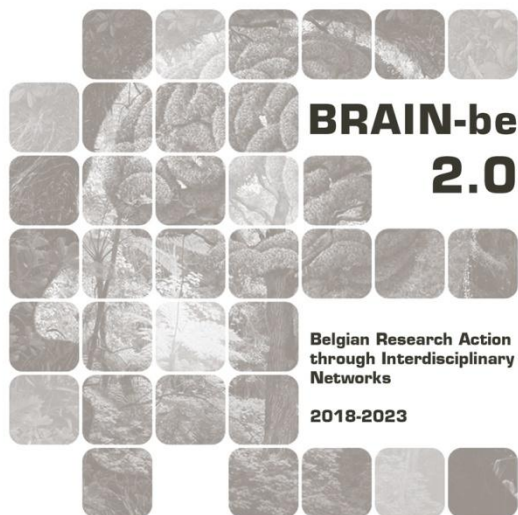


## **RETROPOLLEN**

**Reconstructing four decades of spatio-temporal airborne pollen levels for Belgium to assess the health impact**

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Pillar 2: Heritage science



## NETWORK PROJECT

### RETROPOLLEN

**Reconstructing four decades of spatio-temporal airborne pollen levels for Belgium to assess the health impact**

**Contract - B2/191/P2**

### FINAL REPORT

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## **ABSTRACT**

### **Context**

Worldwide the burden of allergic respiratory diseases increases, enhanced by large-scale air pollution and climate change. In Europe, a quarter of the population suffers from pollinosis. While medical management of allergic rhinitis and asthma is feasible, aeroallergen avoidance is usually the most effective approach to reduce symptoms and pollinosis morbidity. Avoidance can be achieved only if the allergenic pollen exposure can be forecasted and if the effects on public health are well understood.

### **Objectives**

The overall objective of RETROPOLLEN is to assess public health effects of airborne birch and grass pollen in relation to surface air pollution, weather and climate change using up to four decades of historical observations. This will be accomplished by

(i) reconstructing the spatio-temporal distributions of airborne pollen levels of birches and grasses near the surface in Belgium using the operational pollen transport model SILAM at RMI, meteorological datasets and four decades of land-use and land-use change data combined with long time series of vegetation indices from satellite remote sensing platforms.

(ii) compiling and making available historical datasets on airborne pollen observations (from 1982 on, Sciensano), medical data on patients suffering from cardiovascular and respiratory diseases including rhinitis and asthma (from Erasme-ULB hospital & Zeepreventorium), mortality rates (STATBEL), surface air pollution data (IRCEL-CELINE) and meteorological data.

(iii) evaluating the impact of (co-)exposure to pollen with air pollutants and meteorological processes on the public health based on statistical health and epidemiology models (UHasselt).

Ultimately, a robust forecast model for pollen levels and new insights for prevention measures against pollinosis in Belgium was aimed at, potentially leading to the development of a pollen app for Belgium including new insights in the critical allergy threshold of pollen levels in combination with unfavourable conditions of air pollution and meteorology.

### **Conclusions**

RETROPOLLEN has collected almost four decades of historical observations to assess the impact of airborne pollen levels of birches and grasses in relation to surface air pollution and climate change on the public health in Belgium. We show that high levels of birch pollen and surface ozone are associated with a decrease in lung function in patients with asthma and cystic fibrosis. High grass pollen amounts also had a clear negative impact on sensitized patients. Additionally, adverse effects on the lung function of patients with asthma and cystic fibrosis were found for NO<sub>2</sub> and peak surface ozone levels. The odds of mortality due to cardiovascular and respiratory diseases increased substantially in conditions with high air pollution, higher temperature and high airborne birch and grass pollen concentrations. A forecasting system for birch and grass pollen levels was developed and the info is now continuously disseminated to the public at large using the RMI website and RMI weather app, and via the AirAllergy app and website of Sciensano.

**Keywords**

Airborne birch and grass pollen levels, air pollution, meteorology, climate, forecasts, public health



## 1. INTRODUCTION

Allergic respiratory diseases are increasing globally, with pollinosis affecting about a quarter of European adults and a third of children, but in some parts the prevalence is over 40% (D'Amato et al., 2007). In Belgium, allergies have recently become the most common chronic disease (Van der Heyden et al., 2025). Anthropogenic emissions and climate change amplify immune responses and biogenic pollen emissions, affecting patients with asthma or cystic fibrosis (CF) badly. Globally, air pollution has caused 4.2 million premature deaths in 2019 (WHO), while allergic respiratory conditions are rising across Europe exacerbated by immune reactions to biogenic aerosol (pollen among others) emissions.

Timely spatially distributed information on current and forthcoming allergenic pollen exposure episodes may help sensitized people to take preventive measures and adapt the doses of antihistaminic medication they usually take. These warnings must be based on a quantitative pollen forecasting system that requires a modelling approach. Moreover, assessing the impact of co-exposure to air pollution and airborne allergenic pollen on the public health must be based on detailed information on the spatiotemporal distribution of allergenic pollen over a sufficiently long period. Stated otherwise, for every day and every location in Belgium we need to know the pollen levels, the meteorology and air pollution data for analysing the effect on health. Until the start of this project, the only information on allergenic pollen in Belgium is provided by the Belgian aerobiological surveillance network. Sciensano has a longstanding history of observing various types of pollen in the outdoor air since 1982 at daily basis at the Brussels station which is one of the oldest and most stable in Europe (Ziello et al., 2012). Retrospective observations, however, do not permit planning of future outdoor exposure. In contrast, Chemical Transport Models (CTMs) are able to estimate and forecast airborne levels 3 to 5 days ahead both in a consistent spatial as well as temporal way by dealing with pollen as large biogenic aerosols emitted by vegetation and subjected to transport and deposition under various meteorological conditions (Sofiev et al., 2015).

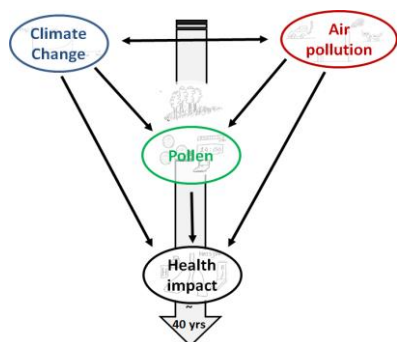
## 2. STATE OF THE ART AND OBJECTIVES

At the Royal Meteorological Institute of Belgium, the CTM SILAM (System for Integrated modelling of Atmospheric coMposition) has been successfully used to model time series of airborne pollen of birches and grasses based for the Belgian territory (Delcloo et al., 2019; Verstraeten et al., 2019). Combining this CTM with observations of airborne allergenic pollen by the Belgian Aerobiological Surveillance Network, created an opportunity to reconstruct the spatio-temporal distributions of airborne pollen levels near the surface for the time period 1982-2019 and to investigate interactions between pollen concentrations, meteorology and climate change, air pollution and public health.

The overall objective of the RETROPOLLEN project was to assess the impact of airborne birch and grass pollen levels in relation to surface air pollution and climate change on the public health in Belgium using up to four decades of historical observations. This required the (i) reconstruction of the spatio-temporal distributions of airborne pollen levels near the surface using the CTM SILAM ingesting ECMWF's (European Centre for Medium-Range Weather Forecasts) reanalysed meteorological datasets and four decades of land-use and land-use change data estimated from the heritage of long time series of vegetation indices derived from various satellite remote sensing platforms such as NOAA-AVHRR and its successors. Furthermore, it required (ii) the compilation of historical datasets on airborne pollen observations (from 1982 on, from Sciensano), medical data on patients suffering from



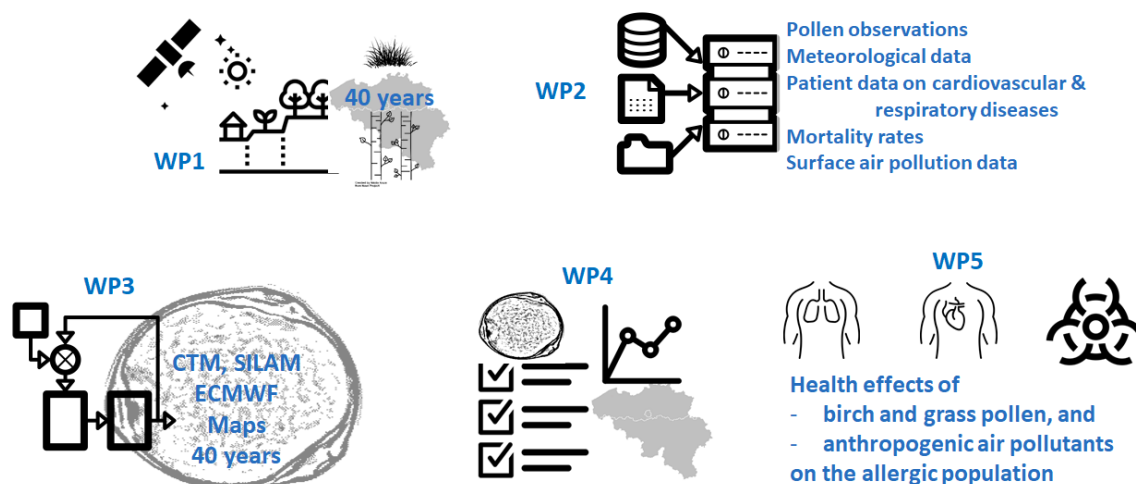
cardiovascular and respiratory diseases including rhinitis and asthma (Erasme Hospital-ULB from 1998 on; Ziepreventorium from late 1980s on), mortality rates (from 1987 on, STATBEL), surface air pollution data (from the 1990s on, IRCEL-CELINE) interpolated from regional network measurements, and ECMWF and in-house meteorological data. (iii) It needs the evaluation and understanding of the impact of co-exposure to these biogenic particles with air pollutants on the population health based on statistical health and epidemiology models. Ultimately, a robust forecast model for pollen levels and new insights for measures of prevention against pollinosis in Belgium were aimed for, which then could lead to the development of a Belgian pollen app including new insights in the critical allergy threshold of pollen levels. These objectives are illustrated in a schematic way below (Figure 1).



**Figure 1. Schematic representation of the project objectives:** assessing public health effects of birch and grass airborne pollen levels in relation to anthropogenic air pollution and climate change for Belgium using up to four decades of historical observations. This project focuses on the explicit connections of climate change, air pollution and pollen to health outcomes. The interactions between climate change and air pollution are implicit; the Interaction between climate change and pollen will be estimated using specific meteorological data from climate scenarios in the applied pollen transport model SILAM.

### 3. METHODOLOGY

For assessing public health effects of allergenic airborne pollen from birch trees and grasses in relation to air pollution and climate change for Belgium we aim at using up to four decades of historical observations. Consequently, data acquisition is a major task within the project. The scheme below illustrates the five Work Packages (WP) required for meeting the project objectives (Figure 2).



**Figure 2. RETROPOLLEN consists of five main Work Packages (WP) required for meeting the project objectives.**

In WP1, the spatio-temporal distribution of birches and grasses in Belgium back to 1982 are reconstructed using remotely sensed data. In WP2, ready-to-use historical observational datasets are

compiled including patient data, mortality rates and surface air pollution. In WP3, the pollen releases, levels and transport of birch and grass pollen for all seasons back to 1982 are modelled and evaluated with observations from the aerobiological surveillance network in WP4. Based on all the collected data including the reconstructed spatio-temporal distributions of birch and grass pollen levels we aim in WP 5 at quantifying the public health impact of pollen exposure, air pollution and climate change in Belgium. Below a brief overview of the content and the principal investigator of the WP's are listed including the different project tasks.

#### **WP1. Reconstructing the spatio-temporal distribution of birches and grasses in Belgium back to 1982 using remotely sensed data (RMI)**

The pollen transport model SILAM can reconstruct airborne birch and grass pollen levels near the surface in Belgium back to 1982 only if appropriate meteorological data and the location of the emitting sources of pollen are available. Stated otherwise, the spatial distributions of birches (Task 1.1) and grasslands (Task 1.2) are required, as well as their inter-seasonal variation or change over time. By combining a forest inventory based areal birch fraction map (Verstraeten et al., 2019) with four decades of spaceborne Normalized Difference Vegetation Index (NDVI) from the NOAA-AVHRR sensor (AVHRR-GIMMS3g NDVI, Pinzon & Tucker, 2014) in a Random Forest statistical framework we have introduced seasonal variations in the birch and grass pollen emission source maps. For grass pollen emission maps we have combined these NDVI data with grass maps from CORINE landcover maps (Verstraeten et al., 2021). Consequently, spatio-temporal variations in birch fractions and grass pollen sources for the period 1982-2019 has been reconstructed on the native 0.1 by 0.1° gridcells for birch and 0.05 by 0.05° gridcells for grass maps (Task 1.3) (more details in Verstraeten et al., 2022, 2023) which can then be used in WP3 for running the pollen transport SILAM.

#### **WP2. Compiling ready-to-use historical observational datasets (Sciensano, IRCEL-CELINE, Erasme Hospital-ULB, Zeepreventorium)**

Observations of daily airborne pollen data (amount of grains/m<sup>3</sup>/day) for grasses and birches (and other species) (Bruffaerts et al., 2018; Hoebeke et al., 2018) has been made available by Sciensano based on the Hirst method (Hirst, 1952) in its Belgian Aerobiological Surveillance Network operational since 1982 for Brussels and since 1984 for De Haan (Task 2.1). In total, 15 pollen taxa in 144 yearly time-series have been collected between 1982 and 2019 in 13 distinct locations in Belgium. To date, five stations are operational (Brussels, De Haan, Genk, Marche-en-Famenne, Tournai => Baudour, see also Table 1).

Surface observations of anthropogenic air pollution across Belgium has been obtained from IRCEL-CELINE (Task 2.2). To provide more accurate data at the patients' locations, interpolated concentrations of NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, PM<sub>2.5</sub>, and black carbon (BC) were used. Calculations were performed using the RIO interpolation model (Janssen et al 2008) at a 4 x 4 km spatial resolution, and subsequently aggregated by municipality (NIS-codes) based on overlapping areas and the corresponding population densities. Daily mean values were calculated for all pollutants; for ozone (O<sub>3</sub>), the daily maximum 8-hour running average was also included. These observations were made available since 1995 for ozone

and NO<sub>2</sub>, since 2000 for PM<sub>10</sub>, since 2008 for PM<sub>2.5</sub>, and since 2011 for black carbon - corresponding to the start dates of their respective measurements.

Daily mortality counts (Task 2.3) on the municipality level has been obtained from Statistical Bureau - STATBEL (<https://statbel.fgov.be/nl>). Deaths from all causes other than accidents or violence are considered (ICD-9, 800) from 1987 on. Separately, we also have considered all respiratory diseases (ICD-9, 460–519) and all cardiovascular diseases (ICD-9, 390–459).

Hospital admissions for asthma crisis events and respiratory troubles, associated with residence location (Task 2.4) have been compiled by the Erasme Hospital (ULB). This data base includes symptomatic diagnosis and functional data (associated with age, gender, pollen-specific cutaneous or blood test results and asthmatic background): seasonal rhinitis symptoms, asthma exacerbation events, lung function tests and exhaled nitric oxide levels. Detailed analysis of anthropometric parameters, asthma control questionnaires, lung function tests and allergy work up, were gathered in a database of ~500 patient files from 1998 on. Zeepreventorium collected lung function tests, serological RAST tests, skin tests, eosinophilic test, and clinical data including treatment dating back to ~1989 covering ~750 patient files (Task 2.5). Also patients with cystic fibrosis were included in the acquired dataset.

### **WP3. Modelling the releases, levels and transport of airborne birch and grass pollen near the surface for all seasons back to 1982 (RMI, Sciensano)**

The pollen levels in the air close to the surface were simulated using the pollen transport model SILAM (System for Integrated modeLLing of Atmospheric composition, Sofiev et al., 2015) over the Belgian territory. SILAM is a large-scale dispersion model developed for atmospheric composition and air quality. The main processes involved in pollen transport are advection with wind, mixing due to turbulence, gravitational settling or dry deposition, and scavenging with precipitation (wet deposition). The timing of flowering in SILAM is approached using accumulated ambient temperature during a certain time period (cfr. degree day methodology) which can be refined with phenology data retrieved from remote sensing. A first step (Task 3.1) has been installing, compiling and pre-running the pollen model for birch and grass pollen at RMI. It also includes the model initializations and collections of meteorological data (ECMWF, REANALYSIS data). Model runs has been performed using 0.25° x 0.25° spatial meteorological ECMWF data and 0.1° x 0.1° emissions source maps for birches and 0.05° x 0.05° for grasses (from WP 1., Tasks 1.1-1.3) and daily pollen level output has been delivered on a 0.1° x 0.1° grid as best spatial resolution for now. Annual birch and grassland maps were converted into SILAM friendly input files from 2019 back to 1982 covering almost four decades (Task 3.2). Next, 1982-2019 multi-annual simulations of daily birch and grass pollen distributions over Belgium has been provided (Task 3.3) using the reconstructed vegetation maps and the ECMWF REANALYSIS meteorological data from Task 1.1, Task 1.2, Task 3.1, Task 3.2 as input for SILAM. Finally, based on the model performance analysis of the simulations, a prototype warning system has been set up using a short-term forecast of birch and grass pollen concentrations as demonstration (Task 3.4)

#### **WP4. Evaluation of the spatio-temporal modelling of airborne pollen levels (RMI, Sciensano)**

Based on the multi-site validation methodology the simulated airborne grass and birch pollen levels has been evaluated using observations from the Belgian aerobiological surveillance network taking into account the nature of pollen emissions (Task 4.1). Pollen series represent strongly non-stationary and non-ergodic processes limiting the usual model–measurement comparison statistics to the main season (Sofiev et al., 2015). Among other metrics, correlation coefficients and Odd Ratio will be used for validation. Next step is filling-in the gaps in the pollen database (Task 4.2) combining observations with modelled data to complete time series of pollen levels at locations with interrupted measurements as a resource for further studies. The spatio-temporal distribution of birch and grass pollen emission sources ingested by SILAM will allow to conduct the mapping of a fictive pollen network considering optimal amount and location of monitoring stations (Task 4.3). The “footprint” map generated by SILAM could delineate the area where the sources would influence the station observations, as it was recently performed for the new pollen network in Bavaria (Oteros et al., 2019). This method could identify potential redundancy of old and current monitoring stations of the Belgian network, and could highlight potential locations for building additional stations.

#### **WP5. Quantifying the public health impact of pollen exposure, anthropogenic air pollution and climate change in Belgium (UHasselt, Sciensano, Erasme Hospital-ULB, Zeepreventorium, IRCEL-CELINE, RMI)**

##### **WP5.1. Daily mortality connected to birch and grass pollen exposure, air pollution, and climate change on public health in Belgium**

The association between pollen exposure and mortality using death counts from all causes other than accidents or violence, all respiratory diseases only, and all cardiovascular diseases on the municipality level (STATBEL data) are assessed in a case-crossover design (Task 5.1). This technique, developed by Maclure (Maclure & Mittleman 2000), combines features of the crossover design and the matched case–control design. Similar to a crossover study, each subject serves as his or her own control, and, as in matched case–control studies, the inference is based on a comparison of exposure distribution rather than the risk of disease (Jaakkola 2003). The case-crossover design is now widely used for analysing short-term health effects and avoids confounding of personal (not time varying variables) such as socio-economic background, gender, smoking etc. The hazard period, which is the brief time period when a subject is at risk, is defined as the day of death (event day). We select control days based on three criteria. First, we will select control days from the same calendar month and year as the event days, both before and after the event. We chose this bidirectional time-stratified design above other selection strategies to avoid issues of bias (Janes et al., 2005; Mittleman, 2005). Second, control days and event days have to be at least 3 days apart from each other to avoid short-term autocorrelation (Levy et al., 2021). Based on this strategy, each case day was matched with 3-4 control days. To address potential confounding, we will adjust the conditional logistic regression models for daily mean temperature and relative humidity using lag0–lag2 moving averages, modelled with natural cubic splines with 3 degrees of freedom (df).

To study the independent effect of pollen from air pollution, daily residential air pollution levels from IRCEL-CELINE has been included in the models (Task 5.2). Also the effect of modification of air pollution

and pollen levels on mortality has been studied (Task 5.3). The impact of climate change scenarios on short-term mortality is assessed by considering the CORDEX.BE dataset (Termonia et al., 2018) available at RMI (Task 5.4). We investigate the impact of climate change scenarios on short-term mortality by modelling the rolling means of lag0 - lag2 of temperature and precipitation with natural cubic splines with 3 degrees of freedom as in the main exposure, and we analyse their effect on all-cause-mortality for either temperature and precipitation alone and additionally while adjusting for the other. The effect of specific climate change induced meteorology on the grass and birch pollen levels near the surface can easily be quantified using SILAM by comparing the pollen outputs with reference conditions. Additional model runs with specific meteorological conditions will be compared with the reference run. By differentiating with the reference run, the effect of the specific meteorology can be assessed directly (Task 5.5).

## **WP5.2. The effect of pollen, air pollution and climate change on allergy risk**

Distributed Lag Linear (DLM) and Non-linear Models (DLNM) (Gasparrini 2011) and Case time series (CTS) models (Gasparrini 2021) were applied in order to model time-trends in a longitudinal design (Task 5.6). The required patient data are made available by the Erasme Hospital and Zeepreventorium and has been converted to clinical scores. We first evaluate the data in a DL(N)Ms accounting for the repeated measurements by including the IDs as a random effect's variable, applying a mixed model design. Therefore, we constructed cross-bases for pollen levels, daily temperature, and precipitation. In detail, we investigated the associations between pollen exposure with %FEV1 and FeNO in linear Gaussian models over a lag period of 0-2 days. Because including non-linear relationships did not significantly improve the model fit the analyses with birch pollen were performed with linear terms. For the models with grass pollen a non-linear fit with knots at 50 and 100 grains/m<sup>3</sup> was used. Additionally, an unconstrained distributed lag model was added to adjust for precipitation and a bi-dimensional spline to account for the average temperature. Furthermore, we have adjusted for shared long-term and seasonal trends by including natural cubic splines of time (6 degrees of freedom/year for the models including all patients, 2 degrees of freedom/year in the models including only sensitized patients). In the models for air pollution exposures, we adjusted for the average temperature. Secondly, we applied the newly developed CTS design, taking into account lagging effects. This novel self-matched method was designed to analyse transient changes in the risk of acute outcomes associated with time-varying exposures. Compared with other techniques to model aggregated time series, it allows individual-level analysis, typical of self-matched methods such as the case-crossover design (Gasparrini 2021). This method is very suited for analysing longitudinal data resources. In brief, we build personalized daily time series for each participant between their first and last lung function measurements. In contrast to the DL(N)M models with the subjects added as random effects variables, we used subject/year strata intercepts. Therefore, the subjects in the analysis served as their own controls by comparing their in- and out-of-season symptoms. Sensitized individuals of the cohort are their own controls by comparing in- and out-of-season symptoms. Covariate effects of medication, air pollution, meteorological conditions and the stage of the pollen season on lung function has been investigated (Task 5.7). The changes in allergy symptoms estimated by the non-linear dose-response curves generated in Task 5.6 were taken into account the medication used by patients for prevention or on the day of symptoms (by using rhinitis and asthma-related medication scores). Taking medication

on the previous day is associated with a lower likelihood of eye symptoms in children (Jones et al., 2019).

Also weather conditions and air pollution influence allergic symptoms, independently from its impact on pollen concentration (Arnedo-Pena et al., 2013), hence it has been investigated how temperature and rainfall specifically drive allergic symptoms as covariates under natural pollen exposure (Task 5.8). Interpolated air pollutant concentrations (NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, PM<sub>2.5</sub>, black carbon) have been included as covariates in the association models (Task 5.9). Finally, the critical thresholds of pollen concentration (“medium” or “high”) to alert the allergic population will be reviewed (Task 5.10) by determining breaking points for rhinitis and asthma symptom apparition/worsening from the inflexion points observed on all the non-linear dose-response curves generated in Task 5.6. The number of selected thresholds will depend on the clinical relevance for use as population warning.

#### **WP6. Dissemination & outreach (All partners)**

For the scientific audience the technical contents, the science questions, the data requirements and related uncertainty of the modelled birch and grass pollen levels of this project proposal were presented on workshops, colloquia, congresses and in scientific journals (Task 6.1). To ensure outreach for the end-user and public at large and to ensure stakeholder engagement, the network AirAllergy and communication platforms such as websites, apps, Twitter were further developed and used (Task 6.2). This proposal aimed ultimately at providing real-time spatial explicit information on expected pollen levels with a 3-day forecast formatted for social media (e.g. Twitter, Facebook), blogs, websites, and a possible integration in the RMI/Sciensano smartphone apps, using plain text and infographics (Task 6.3).

#### 4. SCIENTIFIC RESULTS AND RECOMMENDATIONS

The scientific results are given for each Task of each Work Package (WP) as was foreseen in the project proposal (see also section 3 of this report). For the sake of synthesis, we describe some results of tasks in a combined way.

##### WP1. Assessing the spatial distribution of birch and grass pollen emissions sources in Belgium over time, converted into the pollen transport model SILAM (Task 1.1+1.2+1.3)

For the period 1982-2019 we have compiled maps of birch fraction distributions and grass pollen emission sources for Belgium for every season. 38 years of birch pollen emission sources for Belgium were created based on a birch fraction map derived from forest inventory data combined with 38 years of AVHRR-GIMMS3g NDVI data (1982-2015) extended with NDVI data from METOP-AVHRR after 2015 in a Random Forest statistical approach. Similarly, 38 years of grass pollen emission source maps were generated.

These maps were then converted into SILAM friendly input formats for running SILAM in a bottom-up approach. Illustrations of the spatio-temporal variations of birch fractions and grass pollen sources for the period 1982-2019 are given below (Figure. 3) (based on Verstraeten et al., 2022, 2023).

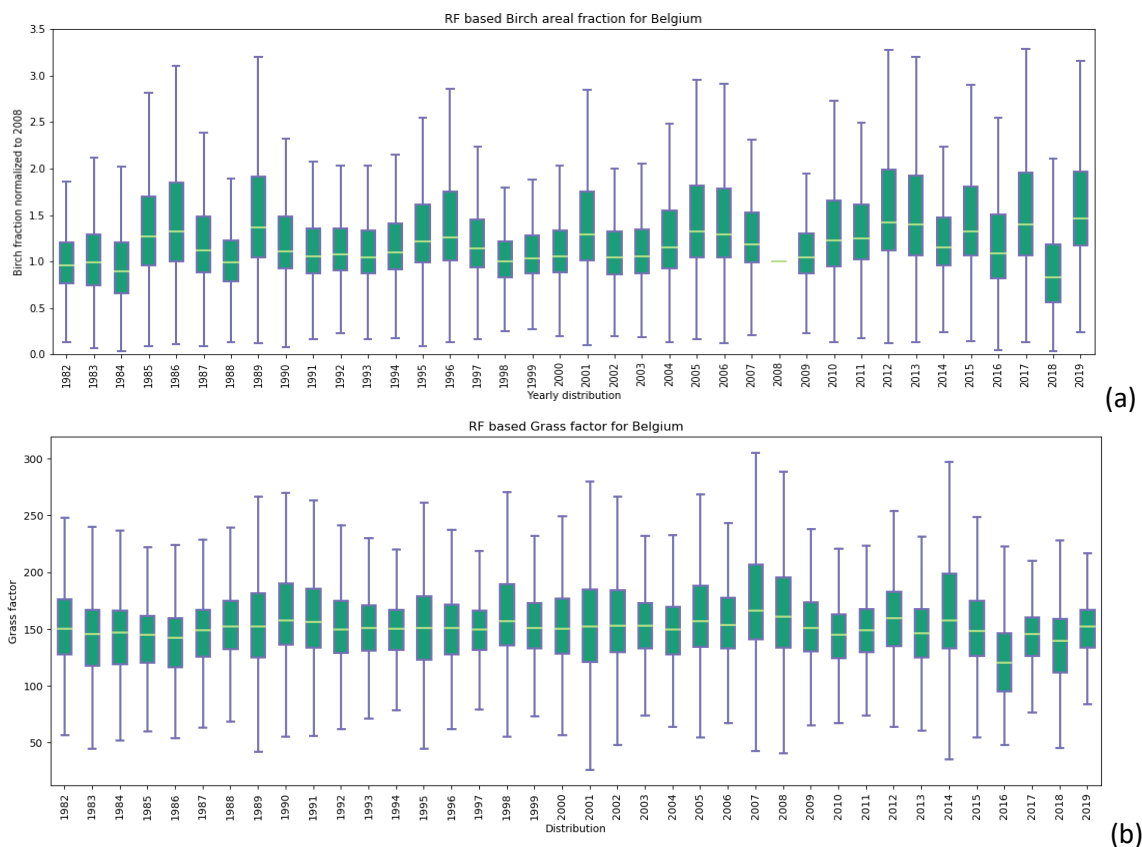


Figure 3 (a). The relative variations in the birch fraction distributions in Belgium for the period 1982-2019 with respect to 2008 (set to one) using the Random Forest statistical approach on the GIMMS/METOP NDVI time series and a reference areal birch fraction map. (b) The same for grass pollen emissions sources.

### **Deliverable: Areal fraction maps of birches and grasses for Belgium back to 1982**

Below, for illustrative purposes of the 38 birch and grass pollen emission source maps that were reconstructed for the period 1982-2019 (Verstraeten et al., 2022, 2023), we show the areal birch fraction maps for four different years, one for every decade (Figure 4).

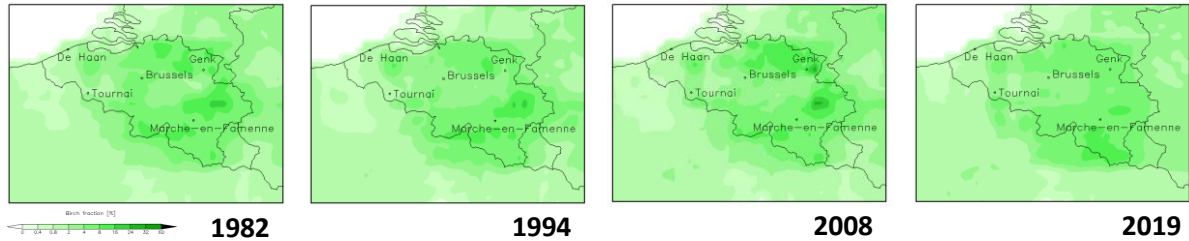


Figure 4. Four birch areal fraction maps used for running the pollen transport model SILAM as illustration of 38 constructed pollen emission source maps.



## WP2. Observations of allergenic pollen of birches and grass, air pollution, and mortality rates on cardiovascular and respiratory diseases (Tasks 2.1+2.2+2.3)

Daily mean airborne pollen concentration data (grains/m<sup>3</sup> air) for grasses and birches were provided by Sciensano. These pollen data include not only recent measurements from the five currently operational stations of the AirAllergy network, but also historical data from former monitoring sites that are no longer active (e.g., Hasselt, Antwerp, Namur, Liège, etc.). The latter were digitized through a manual encoding process from archived paper records originating from the former Scientific Institute of Public Health (WIV-ISP) and the Institute of Hygiene and Epidemiology (IPH). As a result, the project enabled the creation of a comprehensive digital database spanning four decades of pollen observations. This dataset is of high scientific value, not only for the specific objectives of the project, but also as a valuable resource for future studies, including those related to climate change. Furthermore, the database has been made accessible through a newly developed API, facilitating data sharing both within the consortium and with Sciensano's current and future scientific partners (Figure 5).

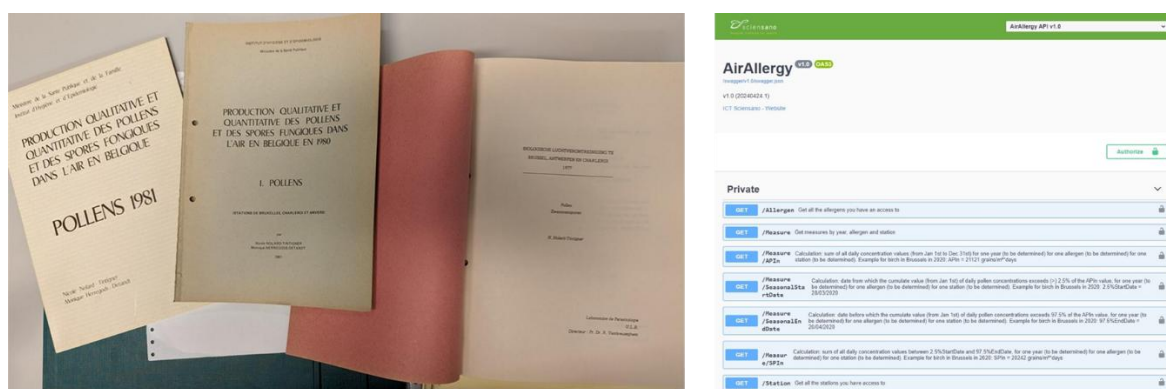


Figure 5. Digitization of historical pollen records and development of an API for scientific data sharing.

The interpolated surface data on air pollution across Belgium were provided by IRCEL-CELINE, and ECMWF meteorological data via the RMI. Below, in Figure 6, the time-series periods with available data on birch and grass pollen, air pollutants, weather (temperature and precipitation), and patient data are shown starting from 1987 on (with the earliest clinical data collected during the project) and ending in 2022. Seasonal patterns of the data are recognizable for most of the exposures.

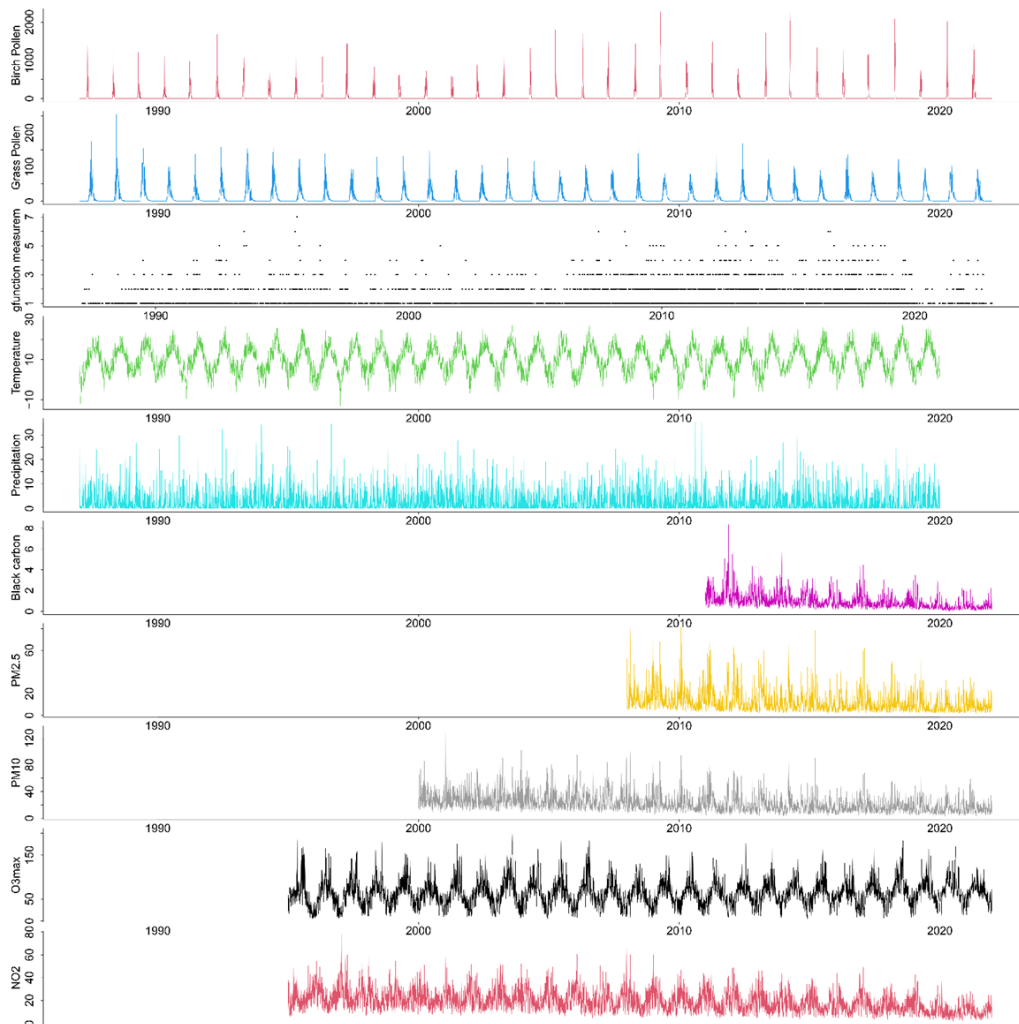


Figure 6. Overview of the periods with available data for the different exposures (birch and grass pollen, air pollution) and patient observations.

Spatio-temporal mortality rates on cardiovascular and respiratory diseases at the different NIS codes were obtained from STATBEL and linked with the exposure data at UHasselt for further analysis in WP5.1. based on the flowchart shown below (Figure 7).

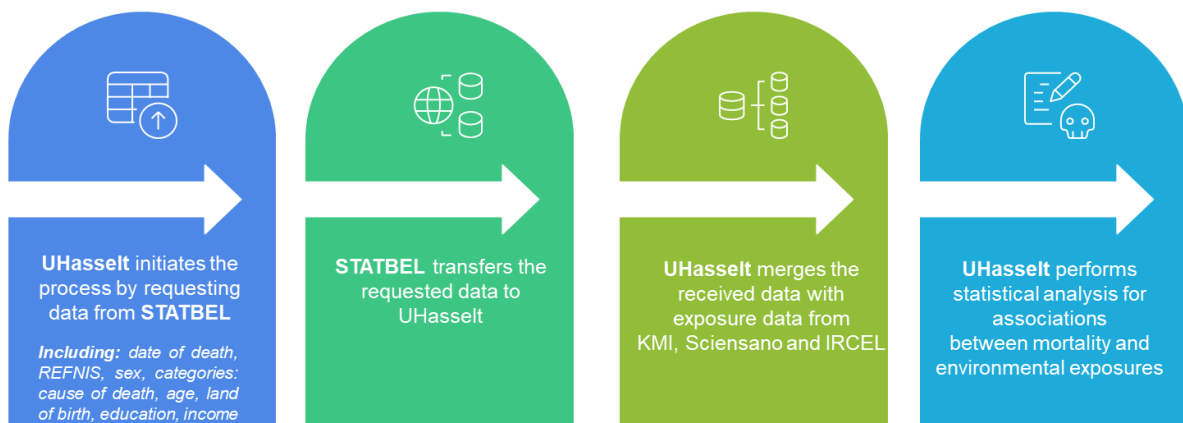


Figure 7. Data processing work-flow for WP5.1.

## WP2. Clinical data collection on patients with respiratory diseases (Tasks 2.4+2.5)

Hospital admissions for asthma crisis events and respiratory troubles, associated with age, gender and residence location were compiled by the Erasme Hospital (ULB) and the Zeepreventorium. A schematic overview of the patient selection is shown in Figure 8.

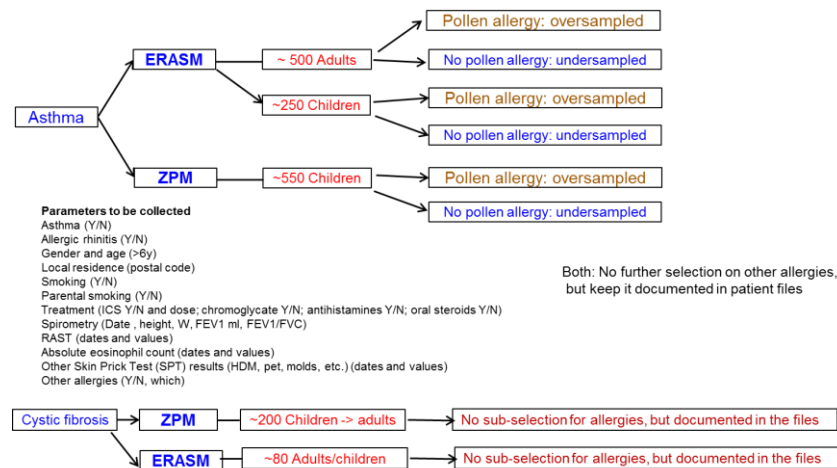


Figure 8. Two sets of historical data were collected, one focusing on asthma and one on cystic fibrosis (CF) going back to the early 1990s.

Finally, five different clinical datasets were obtained spanning different periods between 1983 and 2022 as illustrated in Figure 9.: Historical data from adults with asthma (Erasme Hospital) as well as from children with asthma (Erasme Hospital Pediatric Department, and Zeepreventorium) as well as from patients with cystic fibrosis from both institutions.

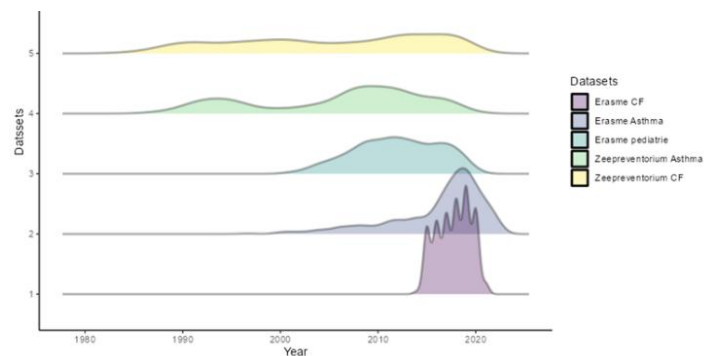


Figure 9. Density plots showing the temporal distribution of the five patient cohorts from 1983 until 2022.

## Deliverable: Data pool of historical observational datasets

The clinical data from Erasme and Ziepreventorium were collected using a uniform codebook template as shown below (Figure 10). These data (and the STATBEL data) were anonymized before they were transferred to UHasselt for further statistical analysis in combination with environmental data including air pollution, pollen levels, temperature, precipitation, wind, etc.

RETROPOLLEN Codebook				
variable name	information source	description	variable type	unit/coding
ID	/	Person's complete identification number	char	/
<b>Geographic location</b>				
Resid	Patient file	Postal code of residence	num	/
<b>Demographic characteristics</b>				
Age	Patient file	Age of the participant	num	years
Gender	Patient file	Gender of participant	num	0=woman; 1=man
Ethn	Patient file	Country of birth	num	/
<b>Lifestyle characteristics</b>				
Smoke	Patient file	Does participant smoke?	num	0 = no; 1 = yes
Par_smoke for children	Patient file	Do parents of participant smoke?	num	0 = no; 1 = yes
<b>Medical history</b>				
Asthma/CysticFibrosis	Patient file	Participant has DR confirmed asthma/cystic fibrosis	num	0 = no; 1 = yes
Allerg_rhin	Patient file		num	0 = no; 1 = yes
Allerg_rhin_GRASS_pol	Patient file	GRASS	num	0 = no; 1 = yes
Allerg_rhin_BIRCH_pol	Patient file	BIRCH	num	0 = no; 1 = yes
Allerg_rhin_mixed_tree_pol	Patient file	Mixed tree, not specific known for birch	num	0 = no; 1 = yes
Allerg_rhin_other_pol	Patient file	Other pollen	num	0 = no; 1 = yes
Allerg_rhin_for_other_body	Patient file	Other allergies	num	0 = no; 1 = yes
Oth_allerg	Patient file		num	0 = no; 1 = yes
Descr_oth_allerg	Patient file	Description of other allergies	char	
<b>Treatment</b>				
ICS_1	Patient file	descriptive variable	ICS1...	
ICS_dose 1	Patient file	dose		
ICS_2				
ICS_dose 2				
and so one				
Chromoglyc	Patient file			
Antihista	Patient file			
steroids	Patient file			
<b>Measurements</b>				

Figure 10. The codebook as applied into RETROPOLLEN for collecting the clinical data in a structured way.

### WP3. Installing, compiling, testing and running the pollen transport SILAM using the collected meteo data and birch and grass pollen emission sources for the multi-annual simulation of airborne birch and grass pollen levels near the surface (Task 3.1+3.2+3.3)

Here we have reconstructed almost four decades (1982-2019) of daily spatially distributed airborne birch and grass pollen levels in Belgium by ingesting seasonal dynamic areal birch fraction maps and grass pollen emission sources of WP1 into the pollen transport model SILAM in a bottom-up approach. A 1982-2019 time series of airborne birch pollen levels, both observations as well as model runs are shown below (Figure 11) (Verstraeten et al., 2022, 2023) which was extended in a later phase of the project to 2022 to match the patient data time span.

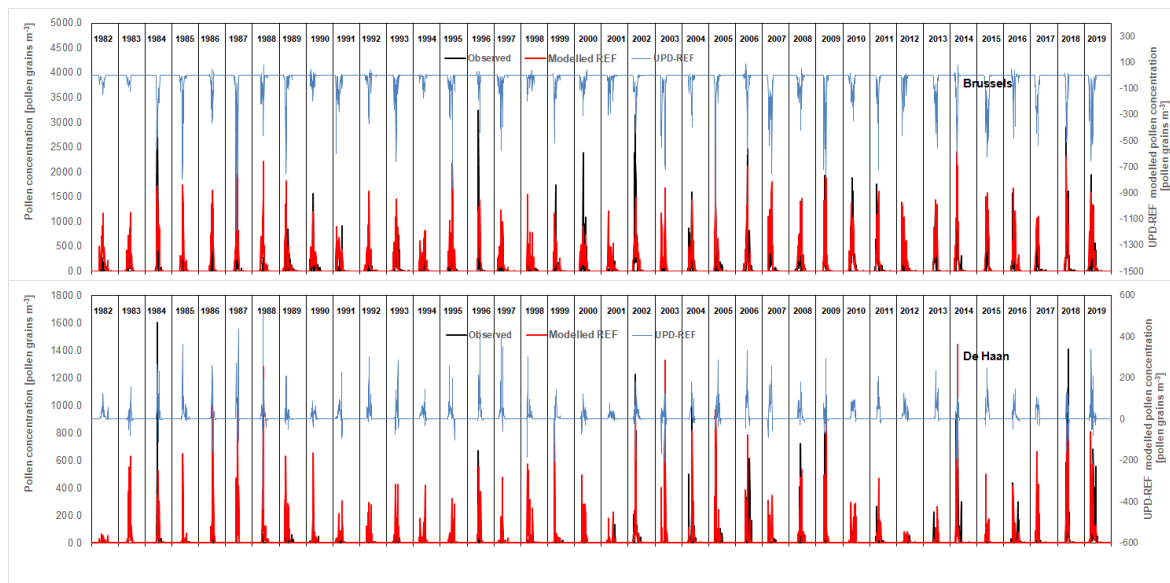


Figure 11. The observed (black) and modelled (reference run in red) 1982-2019 daily airborne birch pollen level time series near the surface (pollen grains  $\text{m}^{-3}$ ) at the monitoring stations of Brussels (upper panel) and De Haan (lower panel). In blue the contribution of the variable birch pollen emission sources to the airborne pollen.

### WP3. Set-up of a framework of prototype warning system for allergenic pollen (Task 3.4)

A prototype warning system for airborne birch and grass pollen levels was tested and evaluated. An online forecasting system for the 2022 birch and grass pollen seasons (from March 1<sup>st</sup> 2022 on) was set-up using ECMWF forecast data four days-ahead in order to predict the amount of birch pollen in the air near the surface. These forecasts were online on a website of the RMI with restricted access for users. Since March 2023, the RMI in collaboration with Sciensano provides a 4-day period of warnings for airborne birch pollen risks for the public at large (<https://www.meteo.be/en/weather/forecasts/pollen-allergy-and-hay-fever>). On the RMI website and in the RMI app everybody can consult the expected allergy risks for birch pollen (and later in the season for grass pollen from May on) for their specific location. This information is also provided at the AirAllergy website of Sciensano (<https://airallergy.sciensano.be/>), and has been incorporated in the new AirAllergy app of Sciensano released on 2024. A screenshot of the RMI website and the app is given below in Figure 12 for 18-21 April 18<sup>th</sup> – 21<sup>th</sup> 2023. Forecasting alder pollen was also added in 2025.

Birch

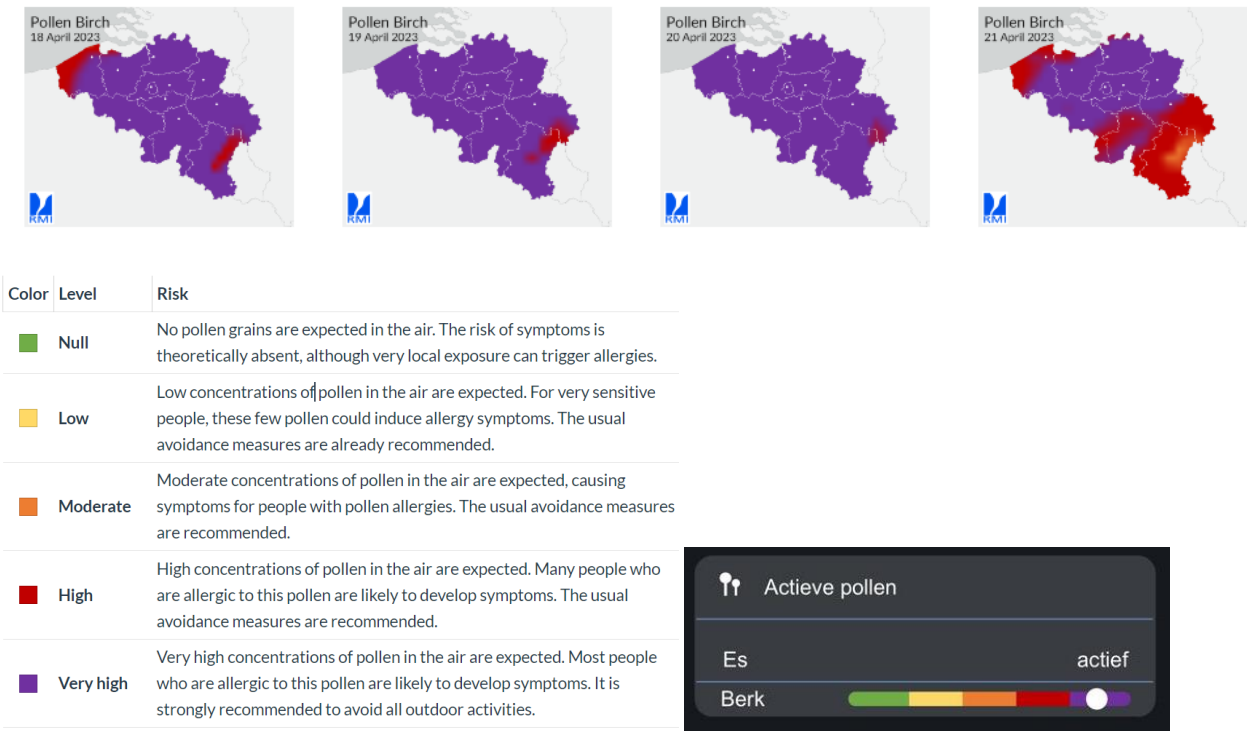


Figure 12. The forecast of the birch pollen allergy risk in the air near the surface for the period April 18<sup>th</sup> to 21<sup>th</sup> 2023, and at the bottom a screenshot of the information shown in the RMI app for the location selected by the user. For other pollen types (here ash), the app also provides qualitative information based on Sciensano’s measurements from Brussels station, indicating whether the pollination season is currently active or not.

Deliverable: Four decades of birch & grass pollen levels for Belgium, and the 4-day allergenic pollen forecasting

The spatio-temporal distributions of airborne birch and grass pollen levels near the surface for Belgium for the period 1982-2022 is available at the RMI. At the website and in the RMI app, the forecasts for pollen from alder, birch and grasses are provided (see also Figure 12 as example). (<https://www.meteo.be/en/weather/forecasts/pollen-allergy-and-hay-fever>). The same and additional information is also available on the Sciensano AirAllergy website (<https://airallergy.sciensano.be/>) and in the AirAllergy App (see screenshot below, Figure 13).

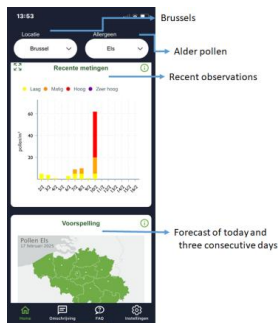
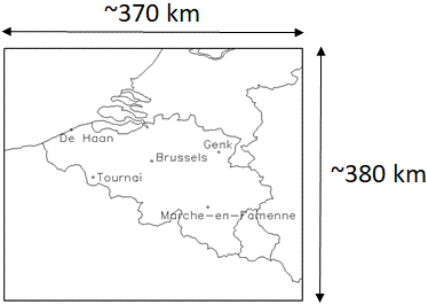


Figure 13. The Sciensano AirAllergy app containing observations on different pollen types for different location and the forecast maps of RMI when available.

**WP4. Evaluating the modelling performance of birch and grass pollen simulations using a multi-site validation (Task 4.1)**

As illustrated in Figure 11, almost four decades of spatial distributed airborne birch and grass pollen levels near the surface has been produced using the CTM model SILAM. In order to evaluate the performance of the pollen transport model, we have compared the modelled time series with observed data from the pollen monitoring network of Sciensano at the five current stations as given in Table 1 including their specific location.

Table 1. The locations of the Belgian aerobiological surveillance network used in this research. Belgium covers 30,689 km<sup>2</sup> and counts 11,763,650 inhabitants (on 01.01.2024) (Statbel, 2024).

Pollen monitoring locations	Latitude / Longitude	
De Haan (DH)	51.274 N / 3.022 E	
Tournai (TO)	50.614 N / 3.387 E	
Brussels (BR)	50.825 N / 4.383 E	
Marche-en-Famenne (MF)	50.200 N / 5.312 E	
Genk (GE)	50.965 N / 5.495 E	

(Verstraeten et al., 2025).

Below we illustrate the model performance for airborne birch pollen levels for Brussels, De Haan and Genk (Figure 14). This is based on Taylor diagrams showing the determination coefficient ( $R^2$ ) and the slopes between the daily SILAM modelled and observed birch pollen concentrations for each pollen season from 1982 to 2019 (Verstraeten et al., 2022). The mean  $R^2$  values of individual pollen seasons between daily observed and SILAM modelled birch pollen levels range between 0.35 and 0.63. Table A1 (see Annex) shows evaluation statistics for modelled grass pollen levels for Belgium. For the purpose of illustration, the seasonal time series of observed and SILAM modelled daily mean airborne grass pollen concentration (pollen grains/m<sup>3</sup>) near the surface for the worst and best model simulation for each monitoring stations of the Belgian aerobiological surveillance network extracted is shown in Figure A1 (see Annex) (Verstraeten et al., 2021).

Another way of evaluating the model performance is by computing the change rate in the seasonal cycles of daily birch pollen levels between 1982 and 2019 as observed at the monitoring station of Brussels (in black line), and as modelled by SILAM using the 38 maps of birch pollen emission sources based on NDVI and RF (Verstraeten et al., 2022) as illustrated in Figure A2 (see Annex). Computing the Sen slopes over 38 years for each day of the pollen season is very appropriate for the analysis of local changes in pollen levels and it has the advantage that it can illustrate changes that occur within the pollen season including shifts in the start and end of the season. As an indicator for overall trend, the Area Under the Curve (AUC) was calculated (numbers given in the Figure A2).

The AUC values are in the same order of magnitude for the observations (794) and the UPD model run (1054), indicating comparable temporal behaviour of the birch seasons over four decades. For the REF run, however, the AUC is substantially higher (1432). Apart from similarities, also differences in the



seasonal cycle between observations and model runs can be derived from Figure 6. Between the end of March and mid-April, the curves are more comparable. The model values show negative trends for the 3rd week of April on, while the trends in the observations lag behind by 4 days. The slopes in the early and late period of the birch pollen season are much steeper (increasing and decreasing, respectively) for the models compared with the slopes computed from the observations. The slopes of the UPD run and observations are more similar in the middle part of the birch pollen season. More complicated is that the AUC value computed from the daily slopes based on the difference of the UPD and REF SILAM runs (AUC = -195) is not just the difference of the AUC values separately computed from the UPD and REF SILAM runs (AUC = -378). By taking the difference between the UPD and REF SILAM runs (UPD-REF), we can isolate the contribution of the changing birch pollen emission sources over 1982-2019 to the changing amount of pollen in the air driven by meteorology. The difference in the daily slopes of the birch pollen season computed for the UPD and REF runs separately deviates strongly from the daily slopes directly computed from the difference of the UPD and REF runs.

This methodology is also used for each gridcell of Belgium and the AUC values are plotted to evaluate the trends in daily pollen over time and to quantify the impact of meteorological factors (see also WP5.1 for further details).

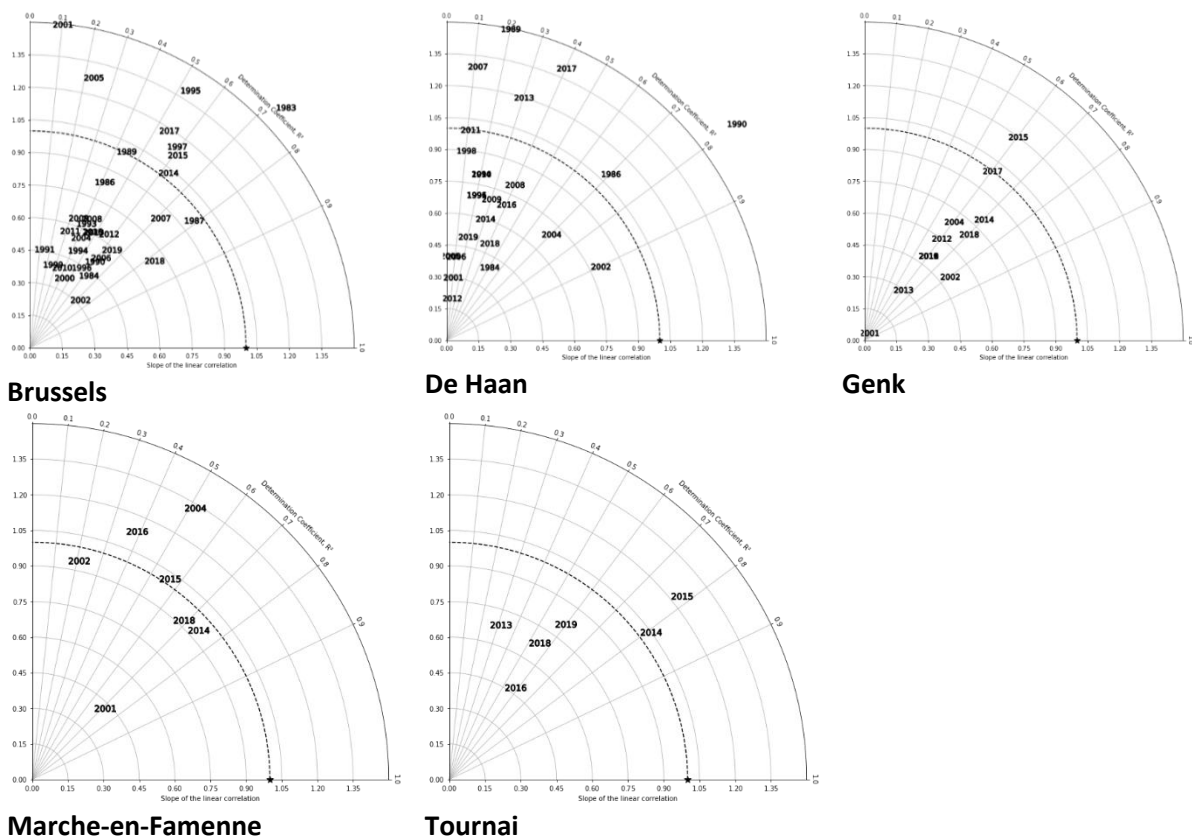


Figure 14. Taylor diagrams including the determination coefficient ( $R^2$ ) and the slopes between the daily SILAM modelled and observed birch pollen concentrations for each pollen season from 1982 to 2019 collected at the pollen monitoring stations of Brussels, De Haan, Genk, Marche-en-Famenne, Tournai.



When evaluating the model performance, the question may arise which uncertainty in modelling and forecasting airborne pollen levels can be expected. In order to assess the uncertainty in modelling airborne birch pollen levels near the surface using SILAM we have applied a Monte-Carlo error approach summarized by the relative Coefficient of Variation (CV%) as descriptive statistic for the season of 2018 in Belgium. For the major inputs that drive the birch pollen model - the amount and location of birch trees ( $0.1^\circ \times 0.1^\circ$  map), the start and end of the birch pollen season ( $1^\circ \times 1^\circ$  map), and the ripening temperature of birch catkins - sets of 100 randomly sampled data layers were prepared for running SILAM 100 times. For each set of model input, 100 spatio-temporal maps of airborne birch pollen levels were produced and its spread was quantified by the CV% (Verstraeten et al., 2024). In Figure A3 (see Annex), we show the 2018 time series of modelled airborne birch pollen levels near the surface for Brussels based on 100 simulations from SILAM. The black line is the mean time series, while the grey zone represents the total range of the simulations (minimum, maximum). From top till bottom panels: time series based on 100 SILAM runs only using 100 different birch pollen emission maps; 100 runs using only 100 different heatsum maps indicating the start of the birch pollen season; 100 runs using only 100 different heatsum maps indicating the end (Diff) of the birch pollen season; 100 runs combining 100 different emission maps, 100 different heatsum maps for start and 100 heatsum maps for the end (Diff); 100 runs combining 100 different emission maps, 100 different heatsum maps for start, 100 heatsum maps indicating the end (Diff), and 100 different threshold temperatures for heat accumulation. The percentiles 5 and 95 are illustrated. This is for the gridcell covering Brussels. In Figure A4 (see Annex) we show the maps with the averaged CV% for each gridcell of Belgium for the same five error scenarios. In short, the spatial uncertainty of pollen emissions sources in SILAM is substantially high, but the uncertainties of the parameters determining the start and end of the season are at least equally important. By accumulating the effects of all investigated model input uncertainties including the impact of the catkins-ripening temperature, CV% values of 50% and more are obtained when quantifying the variation of the modelled airborne birch pollen levels. These errors are in line with reported values from the current reference method for monitoring airborne birch pollen grains near the surface. More details and error maps can be found in Verstraeten et al. (2024).

#### WP4. Filling-in the gaps in the pollen database and evaluating the optimal location for pollen stations (Tasks 4.2+4.3)

We have analysed the Belgian aerobiological surveillance network design that consists of five pollen monitoring stations (see Table 1, Verstraeten et al., 2025) in order to evaluate the spatio-temporal quality and the spatial coverage ability of observing pollen from most emission sources in Belgium.

Firstly, we have focused on the network quality, evaluating how well the interpolated daily observed concentration fields reproduce the spatio-temporal reference data quantified by the Root-Mean-Square-Error (RMSE), from the 2013 to 2021 birch and grass pollen seasons for evaluating if we can fill-in spatial gaps. The reference dataset was derived from the pollen transport model SILAM (System for Integrated modeLLing of Atmospheric coMposition) using ECMWF ERA5 meteorology and pollen emission sources specific for Belgium. The surveillance network performs well with respect to the spatio-temporal reference dataset for airborne birch and grass pollen near the surface. The quality threshold is met in 79% of the birch pollen days and 80% of the grass pollen days over the nine pollen seasons. For the 2015 birch pollen season 100% is reached, for 2020 only 46%. For grass pollen the values range between 63% and 98% for 2021 and 2017 respectively.

Secondly, for evaluating the network coverage representativeness, we perform a footprint-based analysis by running SILAM in the backward mode for the same seasons, which indicates the areas contributing to the concentrations observed in each station. This shows that on average the coverage of the monitoring stations for birch pollen is quite good with typical large inter-seasonal differences. For grass pollen, the average coverage is larger, and the inter-seasonal variation is much lower. Out of five stations three crucial monitoring sites for birch and grass pollen observations were identified: De Haan, Brussels and Marche-en-Famenne. Figure 15 shows the coverage of the network using the integrated individual footprints at each site for every day of the pollen season. The average footprints of each monitoring site over 10 seasons were summed for all the five locations resulting in the maps of Figure 15 (footprints left for birch pollen, right for grass pollen). The station footprints of the 2013-2018 individual birch and grass pollen seasons are shown in Figure A5 (see Annex).

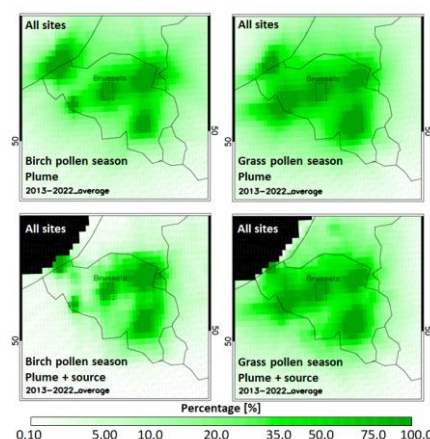


Figure 15. The average sum of all (five) station footprints of the Belgian aerobiological surveillance network over the pollen seasons 2013 to 2022. Left panels for birch pollen seasons, right panels for grass pollen seasons. Top panels show footprints based on the modelled plumes weighted with the observed Seasonal Pollen Integral (SPIn), the bottom panels illustrate the scaled plumes by considering the pollen emissions sources (grasses, birch trees) and the observed SPIn. The greenish colour of a gridcell indicates that the surface gridcell contributes to the pollen observed at the stations. The greener, the larger the contribution.

## Deliverable: Validation statistics of the modelled pollen, homogenized database on allergenic pollen for Belgium, locations suitable for representative pollen stations

The tables below show the overall evaluation statistics for the modelled airborne birch (Table 2) and grass pollen levels (Table 3) near the surface compared with the pollen observation network.

Table 2. Slope, intercept and the determination coefficient ( $R^2$ ) between the daily observed and SILAM modelled birch pollen levels at five pollen monitoring stations in Belgium (107 seasons) covering the period 1982-2019 (Verstraeten et al., 2022).

Daily Values		De Haan	Brussels	Genk	Marche-Famenne	Tournai
UPDATE NDVI RF	Slope	0.70	0.61	0.75	1.12	0.78
	Intercept	22.32	47.74	52.22	73.84	21.76
	$R^2$	0.27	0.36	0.53	0.46	0.56

Table 3. The same as in Table 2 but for grass pollen.

1982-2019 period	De Haan	Brussels	Genk	Marche-en-F	Tournai
slope	0.74	0.48	0.33	0.40	0.25
intercept	12.67	10.97	10.70	15.68	10.78
$R^2$	0.24	0.34	0.36	0.40	0.36

Below, in Figure 16, we can derive that the three selected locations (De Haan, Brussels, Marche-en-Famenne) for birch and grass pollen monitoring is necessary for covering the largest parts of the Belgian territory.

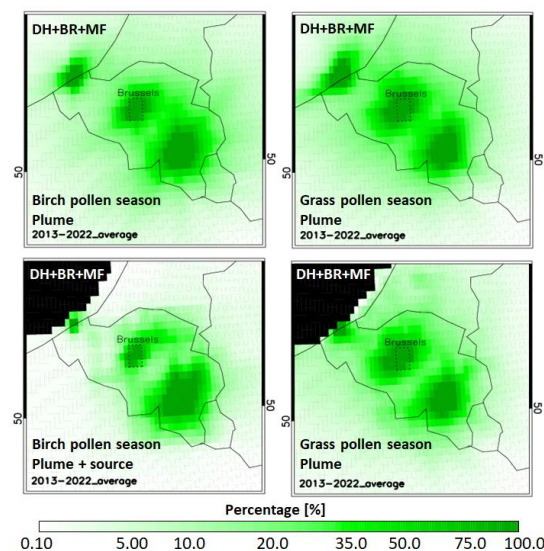


Figure 16. The average sum of three selected station footprints (DH, BR, MF) of the Belgian aerobiological surveillance network over the pollen seasons 2013 to 2022. See also caption Figure 15.

## **WP5. Daily mortality linked to birch and grass pollen exposure, air pollution, weather and climate change in Belgium (Tasks 5.1+5.2+5.3+5.4+5.5)**

The study area includes all Belgian municipalities with a population of 11,697,557 inhabitants on January 1<sup>st</sup>, 2023. People were included in the analysis if they were residing in the study area at the time of their death and died from natural causes between January 1<sup>st</sup>, 1992 and December 31<sup>st</sup>, 2022. The International Classification of Diseases (10<sup>th</sup> revision, version 2019) was used to characterize the cases of natural mortality (A00-R99) into cause-specific mortality from cardiovascular diseases (I00 - I99), respiratory diseases (J00-J99) and other causes. The classification of cause of death was available for data between 2000 -2021. The date of death, sex, age, (age groups 0-24; 25-44; 45-64; 65-69; 70-74; 75-79; 80-84; 85-89, 90+), and cause of death (were provided by STATBEL, the Belgian statistical office. Information about the nationality was classified as being Belgian, being from neighboring countries, being from other EU countries or from countries outside the EU, and available from the year 2000 onwards.

Equivalent net taxable household income was categorized in quartiles and educational attainment was classified as low, medium or high according to the International Standard Classification of Education (ISCED), <https://uis.unesco.org/en/topic/international-standard-classification-education-isced>. The data was derived from IPCAL and CENSUS registries and available from 2006 and 2001 on respectively. Environmental exposures were assessed for the REFNIS code of the residence at the time of death. Daily mean concentrations (in  $\mu\text{g}/\text{m}^3$ ) of air pollutants [ $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{NO}_2$ ,  $\text{O}_3$ 8-hour-maximum ( $\text{O}_3\text{max}$ ) and black carbon (BC)] were provided by IRCEL-CELINE and estimated by the RIO interpolation model ( $\text{PM}_{2.5}$ : 2008-2021,  $\text{PM}_{10}$ : 2000-2021,  $\text{O}_3\text{max}$ : 1995-2021,  $\text{NO}_2$ : 1995 – 2021, BC: 2011-2021). Information on daily mean temperature and daily mean precipitation were provided by the RMI covering the whole study period.

### **Statistical analyses**

A space-time-stratified case-crossover design was used to assess the association between mortality and birch- and grass pollen and each air pollutant, separately (Task 5.1). This design was proposed by Maclure et al. to assess the effect of a transient exposure on acute health outcomes (Maclure and Mittleman 2000). This design has the advantage of controlling for variables which do not vary on a short time (sex, age or socioeconomic status for instance). One way to perform the analysis is by conditional logistic regression which is analogous to analysing matched case-control studies. It requires the dataset to be converted from a time-series format into an individual matched case-control format (Janes et al. 2005). For every case on a given day, that day is designated as the "case," while other days within the same stratum (e.g., same day of the week, month, year, and location) serve as "controls." In this model, variables representing long-term trends and seasonality are not necessary. If individual-level exposure data are available, the individual-time-stratified case-crossover design using conditional logistic regression is recommended. Aggregating individuals into daily counts and averaging their exposure at the community level may introduce exposure bias (Wu et al. 2021).

Because the pollen seasons when pollen concentrations were recorded (for grass between May 1<sup>st</sup> – September 30<sup>th</sup> for birch from March 1<sup>st</sup> until July 1<sup>st</sup> (from 2020 on until June 1<sup>st</sup>)) did not cover the

whole years missing values outside these periods were replaced with zero, assuming that no pollen was present outside the seasons.

To identify the optimal lag time between exposure and outcome for each exposure, we evaluated a range of single and cumulative lag days, extending up to 7 days, using the Akaike Information Criterion (AIC) of distributed lag linear models (DLM) as described by Gasparrini et al. (Gasparrini 2014). To address potential confounding, we adjusted the conditional logistic regression models for daily mean temperature and relative humidity using lag0–lag2 moving averages, modelled with natural cubic splines with 3 degrees of freedom (df). For ease of interpretation, the odds ratios from the logistic regressions were converted into percentage changes. The packages *survival*, *dlm* splines and *rSPARCS* of the R software (R Foundation for Statistical Computing, Vienna, Austria) were used to preprocess the data and perform the analyses. Especially, the functionality of the “*rSPARCS*” package (Zhang et al. 2018) to expand the data set of cases (deaths) to include the corresponding control days was applied.

To disentangle the effect of the primary exposure on the outcome, independent of the group status, stratified analyses were carried out for individual characteristics (sex, age, household income, education, ethnicity, cause of death). Furthermore, to investigate the effect of birch and grass pollen independent of air pollution we included the rolling mean of lag0-lag2 for each air pollutant separately as covariate in the main model, modelled with natural cubic splines with 3 degrees of freedom (Task 5.2). To detect potential effect modification, stratified analyses were carried out and for the effect of air pollutants (below or above median) in the association between pollen exposure and all-cause-mortality (Task 5.3). Effect modification was evaluated by the p-value for the interaction term's coefficient (threshold 5%). The main analysis was then repeated for the stratified groups with low and high exposure values. Additionally, we constructed a heatmap showing the Pearson correlation coefficient for the pollen and air pollutant data as well as the climate variables in order to elucidate underlying mechanisms explaining subgroup differences and potential confounding. In order to calculate the correlations, first the mean exposure values of each day across all REFNIS codes were calculated for all exposures, and subsequently the merged data was limited to the period for which all exposure values were available (January 1<sup>st</sup> 2011 – December 31<sup>st</sup> 2021). For Task 5.4 we investigated the impact of climate change scenarios on short-term mortality by modelling the rolling means of lag0 - lag2 of temperature and precipitation with natural cubic splines with 3 degrees of freedom as in the main exposure, and analysed their effect on all-cause-mortality for either temperature and precipitation alone and additionally while adjusting for the other. The result was evaluated for the three df and assessed for the presence of a trend. Finally, in order to assess changes in the relationship between the pollen-mortality association for different climate scenarios like very warm and very dry, very warm and very wet, very cold and very dry and very cold and very wet (Task 5.5) we selected different combinations of temperature and precipitation based on the distribution of the values in the data. For the very warm climate we selected cases with a temperature above the third quartile of observations and for the cold climate cases those below the first quartile of temperature observations. Likewise, we performed the selection concerning the precipitation and then combined the different climate scenarios accordingly. We then performed the analysis stratified for the 4 different climate scenarios. To evaluate the subgroup-specific effects we formally tested their difference with the main analysis of all deaths as reference by applying Z-tests and compared the resulting Z to the standard normal distribution to retrieve a p-value (Altman and Bland 2003).

## Results

Of the 3,310,753 natural deaths registered in Belgium between 1992 and 2022 deaths from cardiovascular and respiratory causes represented 29.6% and 10.5% of the cases, respectively (Table 4).

Table 4. Descriptive data of the study population representing natural deaths in Belgium between 1992-2022.

Population	N (%)
<b>All</b>	<b>3310753 (100)</b>
<b>Sex</b>	<b>3310753 (100)</b>
Women	1668592 (49.6)
Men	1642161 (50.4)
<b>Age</b>	<b>3310753 (100)</b>
0-44 years	137813 (4.2)
45-64 years	451341 (13.6)
65-74 years	589206 (17.8)
75-84 years	1011375 (30.5)
85+	1121018 (33.9)
<b>Taxable household income in quartiles<sup>a</sup></b>	<b>1791877 (54.1)</b>
1 <sup>st</sup>	544214 (30.4)
2 <sup>nd</sup>	745697 (41.6)
3 <sup>rd</sup>	315559 (17.6)
4 <sup>th</sup>	186407 (10.4)
<b>Education<sup>b</sup></b>	<b>1665662 (50.3)</b>
Low	1184174 (71.1)
Middle	290903 (17.5)
High	190585 (11.4)
<b>Nationality<sup>c</sup></b>	<b>2474402 (74.7)</b>
Belgium	2220682 (89.7)
Neighboring countries <sup>d</sup>	80665 (3.3)
Other EU countries	96038 (3.9)
Other	77017 (3.1)
<b>Cause of death<sup>e</sup></b>	<b>2358025 (71.2)</b>
Cardiovascular	697451 (29.6)
Respiratory	248168 (10.5)
Other	1412406 (59.9)
<b>Season<sup>f</sup></b>	<b>3310753 (100)</b>
Cold	2033311
Warm	1277916

<sup>a</sup> available from 2006 on

<sup>b</sup> according to the International Standard Classification of Education (ISCED), available from 2001 on

<sup>c</sup> available from 2000 on

<sup>d</sup> including the following countries Germany; France; Luxembourg; the Netherlands; the United Kingdom;

<sup>e</sup> according to The International Classification of Diseases (10<sup>th</sup> revision, version 2019), available from 2000 on

<sup>f</sup> warm season = May -September, cold season = October - April

For the grass pollen season which spans the period between May 1<sup>st</sup> – September 30<sup>th</sup> the daily average pollen concentration between 1992-2022 was 21.78 grains/m<sup>3</sup> (IQR 1 grains/m<sup>3</sup> - 32 grains/m<sup>3</sup>, range 0 grains/m<sup>3</sup> - 712 grains/m<sup>3</sup>). For birch pollen the season spanned the period from March 1<sup>st</sup> until July 1<sup>st</sup> (from 2020 on until June 1<sup>st</sup>) 30<sup>th</sup> the daily average pollen concentration between 1992-2022 was 99.18 grains/m<sup>3</sup> (IQR 0 grains/m<sup>3</sup> - 7 grains/m<sup>3</sup>, range 0 grains/m<sup>3</sup> - 9984 grains/m<sup>3</sup>).

The daily mean temperature between 1992-2022 was 10.9 °C (IQR 5.25°C - 15.11 °C, range -18.50°C - 32.46°C, and the daily mean precipitation was 2.53 mm (IQR 0.04 mm- 3.43 mm, range 0 mm - 88.88 mm).

The average daily concentrations for PM<sub>2.5</sub>, PM<sub>10</sub>, O<sub>3</sub>max and NO<sub>2</sub> and BC were: PM<sub>2.5</sub>: 12.58 µg/m<sup>3</sup> (SD 10.63 µg/m<sup>3</sup>, IQR 5.6 µg/m<sup>3</sup> – 16.3 µg/m<sup>3</sup>, range 1 µg/m<sup>3</sup> – 130.5 µg/m<sup>3</sup>); PM<sub>10</sub>: 25.83 µg/m<sup>3</sup> (SD 14.83 µg/m<sup>3</sup>, IQR 15.8 µg/m<sup>3</sup> – 32.3 µg/m<sup>3</sup>, range 1 µg /m<sup>3</sup> – 223.5 µg/m<sup>3</sup>); O<sub>3</sub>max: 63.2 µg/m<sup>3</sup> (SD 29.27 µg/m<sup>3</sup>, IQR 44.8 µg/m<sup>3</sup> – 78.8 µg /m<sup>3</sup>, range 1 µg/m<sup>3</sup> – 246.6 µg/m<sup>3</sup>); NO<sub>2</sub>: 19.36 µg /m<sup>3</sup> (SD 11.19 µg/m<sup>3</sup>, IQR 11 – 25.6 µg/m<sup>3</sup>, range 1 µg/m<sup>3</sup> – 166.8 µg/m<sup>3</sup>) BC: 0.96 µg/m<sup>3</sup> (SD 0.80 µg/m<sup>3</sup>, IQR 0.4 µg/m<sup>3</sup> – 1.2 µg/m<sup>3</sup>, range 0 µg/m<sup>3</sup> – 16.8 µg/m<sup>3</sup>) respectively.

In this section we report the results on the effect of pollen, air pollution and meteorology on mortality (Task 5.1). The minimum AICs were obtained for birch pollen, grass pollen and O<sub>3</sub>max at lag0 and for the other air pollutants at lag7. The respective percentage changes for all-causes mortality associated with 10 µg or grains/m<sup>3</sup> increase in pollutants (birch pollen 100 grains/m<sup>3</sup> and BC 1 µg/m<sup>3</sup>) were 0.22% (95% CI: 0.14%, 0.3%) for birch pollen, -0.1% (95% CI: -1%, 0.081%) for grass pollen, 0.79% (95% CI: 0.6%, 0.98%) for PM<sub>2.5</sub>, 0.32% (95% CI: 0.2%, 0.44%) for PM<sub>10</sub>, 0.40% [0.32%, 0.48%] for O<sub>3</sub>max, 0.65% (95% CI: 0.49%, 0.81%) for NO<sub>2</sub> and 0.57% (95% CI: 0.27%, 0.86%) for BC (Table 5). Furthermore, for particulate matter, the effect was increasing for each increase in age-category, with the highest odds of all-cause -mortality in the age-group of very old (85+) individuals (Table 5).

For the cause-specific mortality in the category of CVD, most risk increases were lower except for grass pollen exposure where the odds percentage reached a statistically significant increase of 0.25% (95% CI: 0.018%, 0.48%) for each 10 grains/m<sup>3</sup> and for NO<sub>2</sub> (0.71% instead of 0.65% for a 10 µg/m<sup>3</sup> increase). For the group of respiratory deaths all percentage increases were smaller and all, except of PM<sub>2.5</sub> were not statistically significant (the confidence intervals for the percent change crossed zero) (Table 5). When visualizing the association between pollen, temperature and odds of all-cause-mortality (Figure 17A-C) as well as air pollutants, temperature and odds of all-cause-mortality (Figure 18A-H) the associations remained comparable to those including precipitation except that the effect of NO<sub>2</sub> decreased (Figure 18E/F) and the effect of O<sub>3</sub> max increased (Figure 18G/H).

Table 5. Percentage changes for all deaths and subgroup-specific mortality. Percentage changes were assessed on different lag days: lag 0 for birch pollen, grass pollen and O<sub>3</sub>max, and lag7 for PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub> and black carbon.

	Birch pollen <sup>a</sup>	Grass pollen <sup>b</sup>	PM <sub>2.5</sub> <sup>b</sup>	PM <sub>10</sub> <sup>b</sup>	O <sub>3</sub> max <sup>b</sup>	NO <sub>2</sub> <sup>b</sup>	Black carbon <sup>c</sup>
<b>All</b>	<b>0.22 [0.14, 0.3]*</b>	<b>-0.1 [-1, 0.081]</b>	<b>0.79 [0.6, 0.98]*</b>	<b>0.32 [0.2, 0.44]*</b>	<b>0.4 [0.32, 0.48]*</b>	<b>0.65 [0.49, 0.81]*</b>	<b>0.57 [0.27, 0.86]*</b>
Sex							
Women	0.25 [0.14, 0.36]*	-0.07 [-0.3, 0.069]	0.79 [0.53, 1.1]*	0.39 [0.23, 0.56]*	0.36 [0.25, 0.47]*	0.61 [0.39, 0.84]*	0.55 [0.14, 0.96]*
Men	0.18 [0.00, 0.30]*	0.035 [-1, 0.17]	0.78 [0.51, 1.1]*	0.25 [0.08, 0.42]*	0.44 [0.33, 0.55]*	0.69 [0.47, 0.92]*	0.59 [0.17, 1]*
Age							
0-44 years	-0.022 [-0.43, 0.39]	-0.61 [-1.1, -0.14]*	-0.13 [-1.2, 0.96]	0.0025[-0.61, 0.62]*	0.28 [-0.098, 0.65]	-0.29 [-1.1, 0.5]	-0.47 [-2.1, 1.2]
45-64 years	0.13 [-0.08, 0.35]	0.15 [-0.1, 0.41]	0.53 [-0.1, 1.1]	0.41 [0.081, 0.74]*	0.45 [0.24, 0.66]*	0.8 [0.37, 1.2]*	0.15 [-0.67, 0.98]
65-74 years	0.12 [-0.07, 0.31]	0.10 [-0.13, 0.33]	0.8 [0.31, 1.3]*	0.1 [-0.19, 0.4]	0.42 [0.24, 0.61]*	0.3 [-0.081, 0.68]	0.31 [-0.45, 1.1]
75-84 years	0.29 [0.15, 0.43]*	-0.067 [-0.25, 0.11]	0.75 [0.4, 1.1]*	0.15 [-0.062, 0.36]	0.4 [0.26, 0.54]*	0.43 [0.14, 0.71]*	0.48 [-0.066, 1]
85+	0.26 [0.12, 0.39]*	-0.031 [-0.21, 0.14]	0.97 [0.66, 1.3]*	0.59 [0.39, 0.79]*	0.39 [0.26, 0.53]*	1.1 [0.81, 1.4]*	0.94 [0.48, 1.4]*
Household income							
1st	0.2 [0.03, 0.37]*	-0.16 [-0.39, 0.092]	0.92 [0.57, 1.3]*	0.51 [0.25, 0.78]*	0.46 [0.27, 0.65]*	1.1 [0.66, 1.5]*	1.1 [0.53, 1.6]*
2nd	0.25 [0.1, 0.39]*	0.11 [-0.11, 0.32]	0.6 [0.3, 0.9]*	0.37 [0.13, 0.6]*	0.41 [0.24, 0.57]*	0.47 [0.13, 0.82]*	0.17 [-0.29, 0.62]
3rd	0.21 [-1, 0.44]	0.033 [-0.29, 0.35]	0.83 [0.36, 1.3]*	0.42 [0.061, 0.78]*	0.52 [0.27, 0.77]*	0.82 [0.29, 1.3]*	0.8 [0.095, 1.5]*
4th	-0.06 [-0.35, 0.24]	-0.24 [-0.65, 0.18]	1.2 [0.58, 1.8]*	0.65 [0.19, 1.1]*	0.064 [-0.26, 0.39]	0.92 [0.24, 1.6]*	0.34 [-0.58, 1.3]
Education <sup>b</sup>							
Low	0.22 [0.11, 0.34]*	0.026 [-0.2, 0.2]	0.7 [0.45, 0.95]*	0.27 [0.1, 0.44]*	0.54 [0.42, 0.66]*	0.62 [0.36, 0.88]*	0.5 [0.12, 0.89]*
Middle	0.039 [-0.2, 0.27]*	0.063 [-0.29, 0.41]	0.78 [0.29, 1.3]*	0.16 [-0.2, 0.51]	0.44 [0.19, 0.68]*	0.21 [-0.3, 0.73]	0.36 [-0.38, 1.1]
High	0.21 [-0.09, 0.5]	0.19 [-0.24, 0.63]	0.83 [0.21, 1.5]*	0.24 [-0.2, 0.67]	0.19 [-0.12, 0.49]	0.21 [-0.42, 0.84]	0.14 [-0.79, 1.1]
Nationality							
Belgium	0.22 [0.13, 0.31]*	0.07 [-0.06, 0.19]	0.81 [0.61, 1]*	0.34 [0.21, 0.46]*	0.39 [0.3, 0.48]*	0.66 [0.47, 0.85]*	0.52 [0.21, 0.84]*
Other	0.14 [-0.12, 0.39]*	-0.27 [-0.62, 0.1]	0.57 [-0.041, 1.2]	0.16 [-0.22, 0.56]	0.71 [0.43, 0.99]*	0.26 [-0.29, 0.83]	0.9 [0.013, 1.8]*
Cause of death <sup>c</sup>							
CVD	0.028 [-0.2, 0.19]	0.25 [0.018, 0.48]*	0.74 [0.39, 1.1]*	0.25 [0.035, 0.46]*	0.41 [0.25, 0.57]*	0.71 [0.38, 1]*	0.55 [-0.007, 1.1]
Respiratory	0.038 [-0.3, 0.3]	0.014 [-0.4, 0.42]	0.6 [0.037, 1.2]*	0.2 [-0.15, 0.56]	0.19 [-0.075, 0.46]	0.31 [-0.22, 0.85]	0.44 [-0.5, 1.3]
Other	0.3 [0.19, 0.41]*	-0.02 [-0.18, 0.14]	0.84 [0.59, 1.1]*	0.38 [0.23, 0.54]*	0.47 [0.35, 0.58]*	0.63 [0.39, 0.87]*	0.59 [0.22, 0.97]*
Season							
Cold	0.17 [0.09, 0.25]*	/	0.85 [0.64, 1.1]*	0.4 [0.27, 0.54]*	0.37 [0.26, 0.49]*	0.74 [0.56, 0.92]*	0.62 [0.31, 0.93]*
Warm	0.88 [0.5, 1.3]*	0.0027 [-0.1, 0.1]	0.5 [0.014, 0.98]*	0.015 [-0.26, 0.28]	0.41 [0.3, 0.53]*	0.32 [-0.038, 0.68]	0.21 [-0.69, 1.1]

<sup>a</sup> percent change for an increase of 100 grains /m<sup>3</sup>

<sup>b</sup> percent change for an increase of 10 grains or µg/m<sup>3</sup>

<sup>c</sup> percent change for an increase of 1 µg/m<sup>3</sup>

An asterisk denotes statistical significance at a 95% level



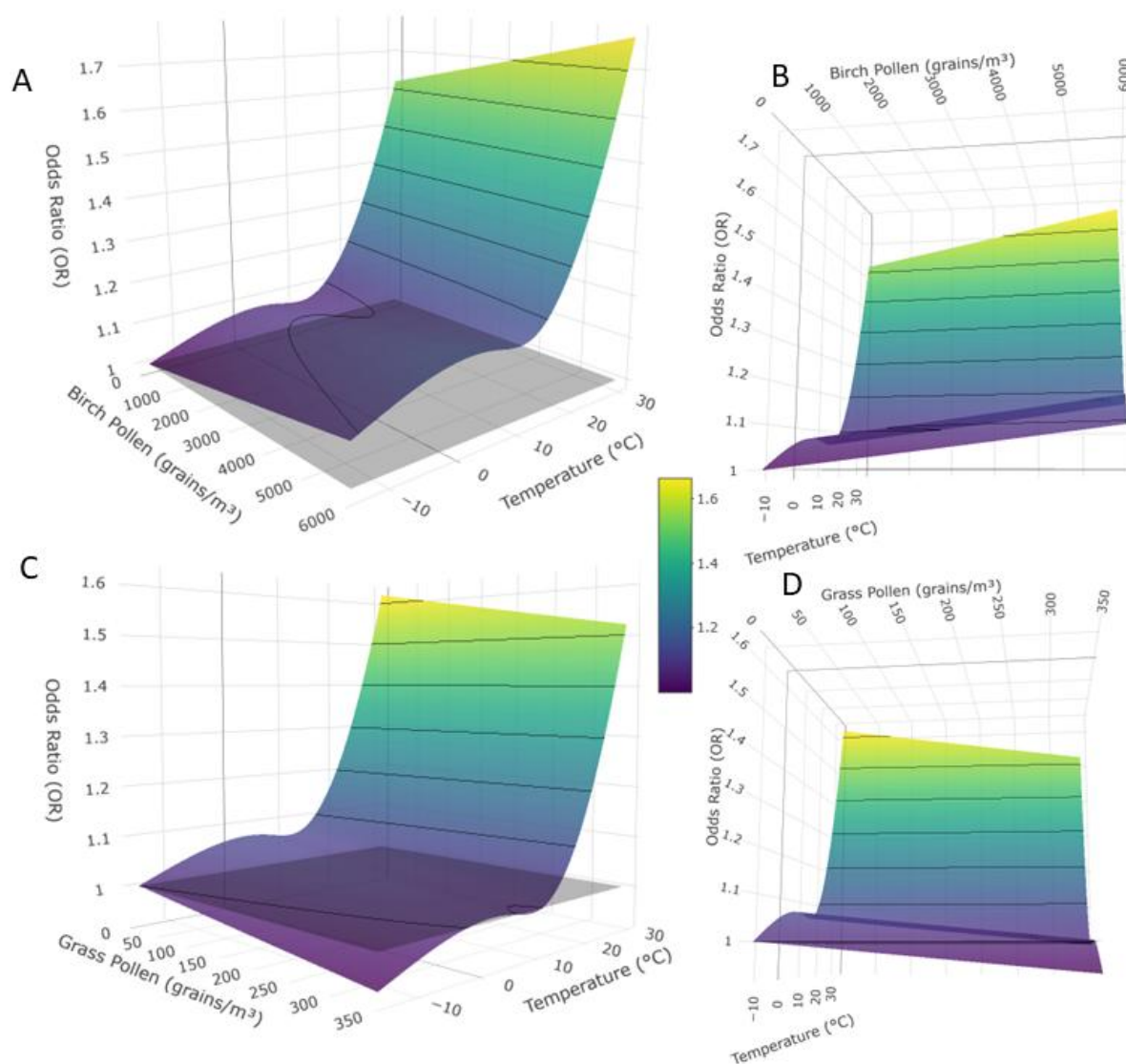


Figure 17. Surface plots of the association between odds of all-cause-mortality, temperature and birch pollen concentrations (A/B), and odds of all-cause-mortality, temperature and grass pollen concentrations (C/D).

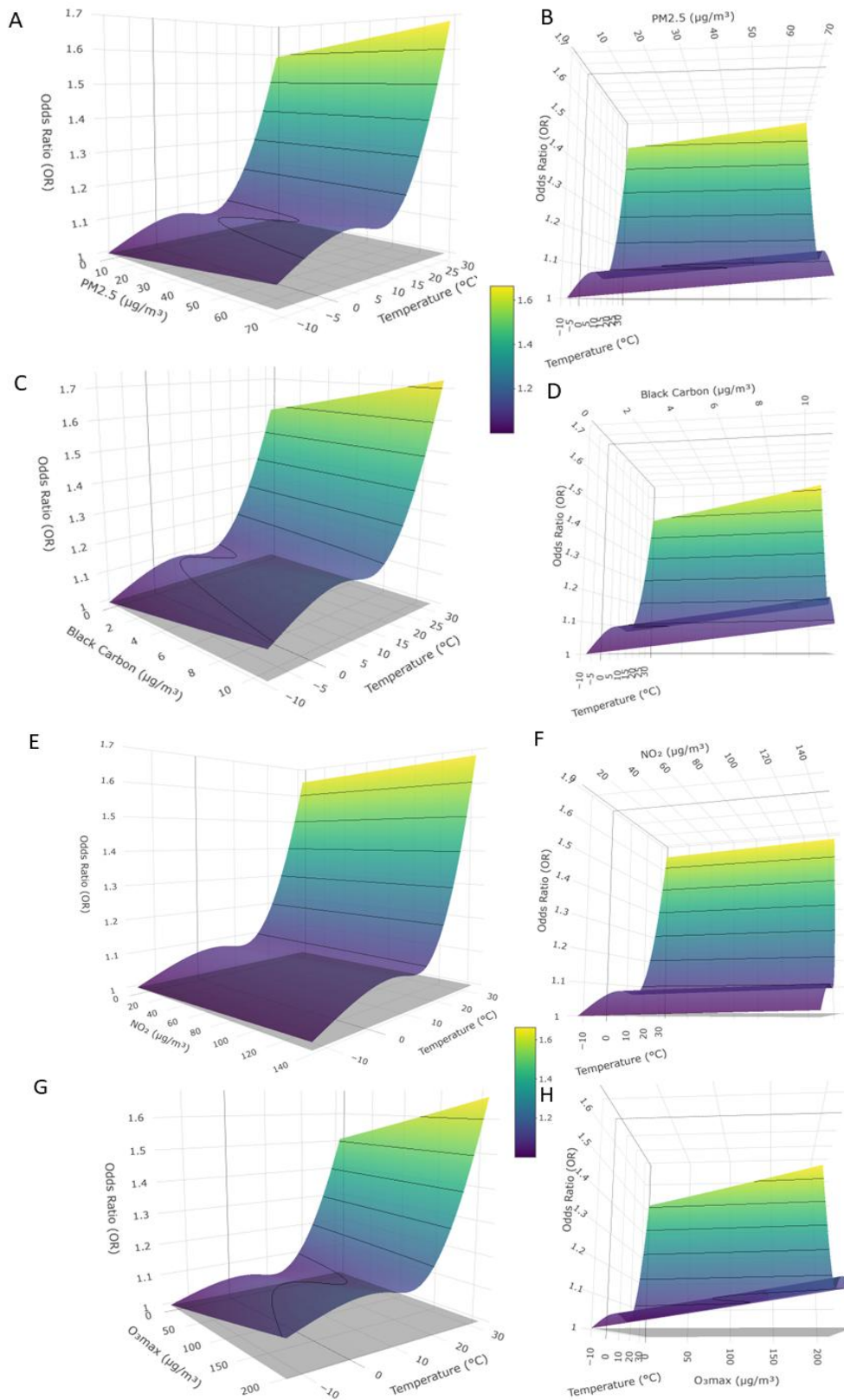


Figure 18. Surface plots of the association between odds of all-cause mortality temperature and PM<sub>2.5</sub> (A/B), black carbon (C/D), NO<sub>2</sub> (E/ F), and O<sub>3</sub>max (G and H).

In order to assess the independent effect of pollen from air pollution on mortality (Task 5.3), an adjustment for air pollutants in the analysis of all-cause mortality the estimate did not show significantly change for birch pollen exposure. In the adjusted analyses for grass pollen exposure the effect remained statistically non-significant for all models (Table 6).

Table 6. Percentage changes for all deaths associated with birch and grass pollen in models additionally adjusted for air pollutant exposure averaged over the day of death and the two preceding days.

Model	PM <sub>2.5</sub>	PM <sub>10</sub>	O <sub>3</sub> max	NO <sub>2</sub>	Black carbon
Birch pollen <sup>a</sup>	0.18 [0.080, 0.028] *	0.20 [0.11, 0.29] *	0.19 [0.11, 0.27] *	0.19 [0.11, 0.28] *	0.24 [0.12, 0.35] *
Grass pollen <sup>b</sup>	-0.069 [-0.21, 0.10]	0.063 [-0.060, 0.19]	0.027 [-0.091, 0.14]	0.035 [-0.080, 0.15]	-0.081 [-0.25, 0.093]

<sup>a</sup> percent change for an increase of 100 grains /m<sup>3</sup>

<sup>b</sup> percent change for an increase of 10 grains /m<sup>3</sup>

The effect of modification of air pollution and pollen levels on mortality is estimated here (Task 5.3). The interaction terms for grass pollen and all air pollutants except PM<sub>2.5</sub> were statistically significant (Table 7). For birch pollen, they were significant for PM<sub>2.5</sub>, O<sub>3</sub>max and black carbon. Except for NO<sub>2</sub> the effect of birch pollen concentrations on the risk of all-cause-mortality were higher in the group of low air pollutant exposure compared to high (above median) air pollutant concentrations (Table 8). For grass pollen this was the case for NO<sub>2</sub>, which showed the only statistically significant association (Table 8). This might reflect the only partial overlap between pollen season and periods of stronger air pollution. Especially in the case of the grass pollen season spanning the period between May 1<sup>st</sup> – September 30<sup>th</sup> there was a negative correlation with all air pollutants except O<sub>3</sub>max (Figure 19). Therefore, it is unlikely that there are many measurements of pollen in the groups with above median air pollution values which are situated mostly in the winter period (negative correlation with temperature in Figure 19).

Table 7. P-values for the interaction between pollen and air pollutants.

	PM <sub>2.5</sub>	PM <sub>10</sub>	O <sub>3</sub> max	NO <sub>2</sub>	Black carbon
Birch pollen	0.00053*	0.065	0.00017*	0.079	0.0027*
Grass pollen	0.27	0.00082*	0.00031*	0.000025*	0.0027*

Table 8. Percentage changes for all deaths associated with birch and grass pollen in subgroups stratified for high (above or equal median) air pollutant exposure and low (below median) air pollutant values averaged over the day of death and the two preceding days.

Model	PM <sub>2.5</sub> <sup>b</sup>	PM <sub>10</sub> <sup>b</sup>	O <sub>3</sub> max <sup>b</sup>	NO <sub>2</sub> <sup>b</sup>	Black carbon <sup>c</sup>
Birch <sup>a</sup> (LAP)	0.32 [0.07, 0.58]*	0.29 [0.06, 0.52]*	0.41 [0.28, 0.54]*	-0.13 [-0.61, 0.35]	0.57 [0.38, 0.76]*
Grass <sup>b</sup> (LAP)	0.01 [-0.23, 0.24]	0.06 [-0.13, 0.26]	0.09 [-0.06, 0.23]	0.55 [0.10, 0.83]*	-0.10 [-0.34, 0.13]
Birch <sup>a</sup> (HAP)	0.17 [0.04, 0.29]*	0.24 [0.13, 0.35]*	0.05 [-0.07, 0.17]	0.21 [0.13, 0.3]*	0.02 [-0.15, 0.19]
Grass <sup>b</sup> (HAP)	-0.18 [-0.44, 0.08]	0.08 [-0.13, 0.29]	-0.06 [-0.28, 0.17]	0.02 [-0.1, 0.15]	0.06 [-0.26, 0.37]

<sup>a</sup> percent change for an increase of 100 grains /m<sup>3</sup>

<sup>b</sup> percent change for an increase of 10 grains /m<sup>3</sup>

LAP: Low air pollution; HAP: High air pollution

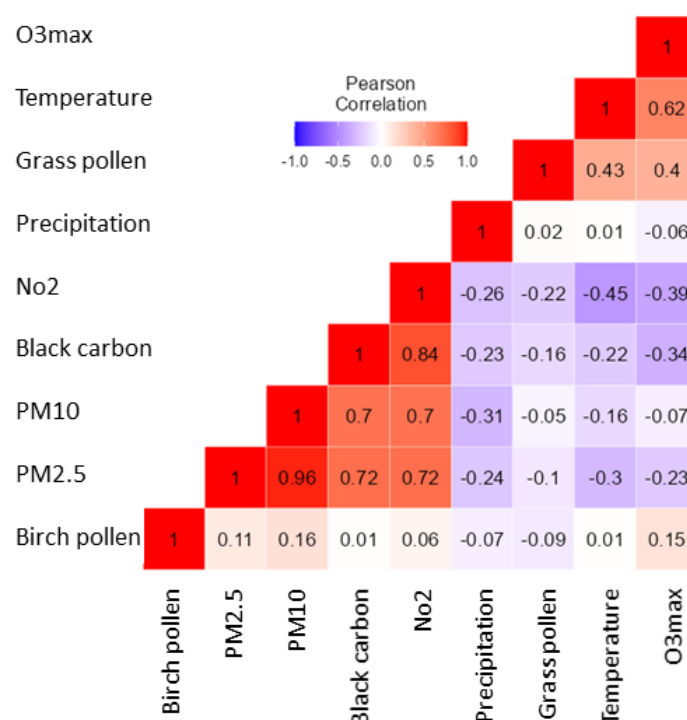


Figure 19. Pearson Correlation heatmap of the different exposures.

We assessed the effect of meteorology and climate change on short term mortality (Tasks 5.2 and 5.4) by analysing the effect of temperature and precipitation on mortality with a conditional logistic regression model with averaged temperature and precipitation at the day of death and the two preceding modelled with a natural cubic spline with 3 degrees of freedom (df). The percent changes of the odds of mortality for each of the 3 degrees of freedom are shown in Table 9. The knots of the natural cubic spline for temperature were placed at 6.44°C and 13.16°C and those for precipitation at 0.603 mm and 2.95 mm. When considering each base function of the df from Figure 20 A, the interpretation of the ORs for the different temperature ranges was as follows:

**For temperatures below 6.44°C** the second basis (red) dominated, so the model's odds ratios for this range primarily reflected the coefficient of the second basis function. Therefore, a percent change of 44.43% [37.45%,51.76%] reflects the effect of temperature below 6.44°C.

**For temperatures between 6.44°C to 13.16°C**, the first basis (black) plays a stronger role in the middle range, with contributions tapering off as temperature increases further. Therefore, a percent change of -1.19% [-2.52%, 0.15%] reflects the effect in the range between 6.44°C to 13.16°C:

**For temperatures above 13.16°C** the third basis (green) becomes the dominant contributor, reflecting its larger values at higher temperatures. Therefore, a percent change of 53.88% [50.64%, 57.20%] reflects the effect above 13.16°C.

For precipitation the contribution of each base function of the df from Figure 20B together with the ORs for the different precipitation ranges was as follows:

For the **precipitation below 0.603 mm** the second basis (red line) dominated this range. The effect of precipitation here is represented by the odds ratio for df 2, with a small, statistically not significant, increase in odds of 5.91% [-0.56%, 12.80%].

For **precipitation between 0.603 mm and 2.94 mm** Basis 1 (black line) and Basis 2 are most influential. The effect of precipitation in this range is represented by the slightly negative but statistically non-significant odds ratio for df 1 (-0.14% [-2.01%, 1.77%]) and the slightly positive but also statistically non-significant odds ratio of df2, which indicate only negligible effects of precipitation in this middle range.

For **precipitation above 2.94 mm** Basis 3 (green line) dominates for higher precipitation values. The odds ratio for df 3 reflects a stronger increase in odds for higher precipitation of about 11.29% [-2.49%,27.01%].

Table 9. Percentage changes for the odds of all-cause death associated with temperature and precipitation averaged over the day of death and the two preceding days and modelled with a natural cubic spline with 3 degrees of freedom. The change is calculated for a 1-unit increase (°C or mm) in temperature or precipitation.

Exposure, (degree of freedom/basis)	Percent change [95% CI]
Temperature, (1)	-1.19% [-2.52%,0.15%]
Temperature, (2)	44.43% [37.45%,51.76%]
Temperature, (3)	53.88% [50.64%,57.20%]
Precipitation, (1)	-0.14% [-2.01%,1.77%]
Precipitation, (2)	5.91% [-0.56%,12.80%]
Precipitation, (3)	11.29% [-2.49%,27.01%]

The %change is statistical significant if the signs in the CI is the same as the change sign (Temp, (2) and (3))

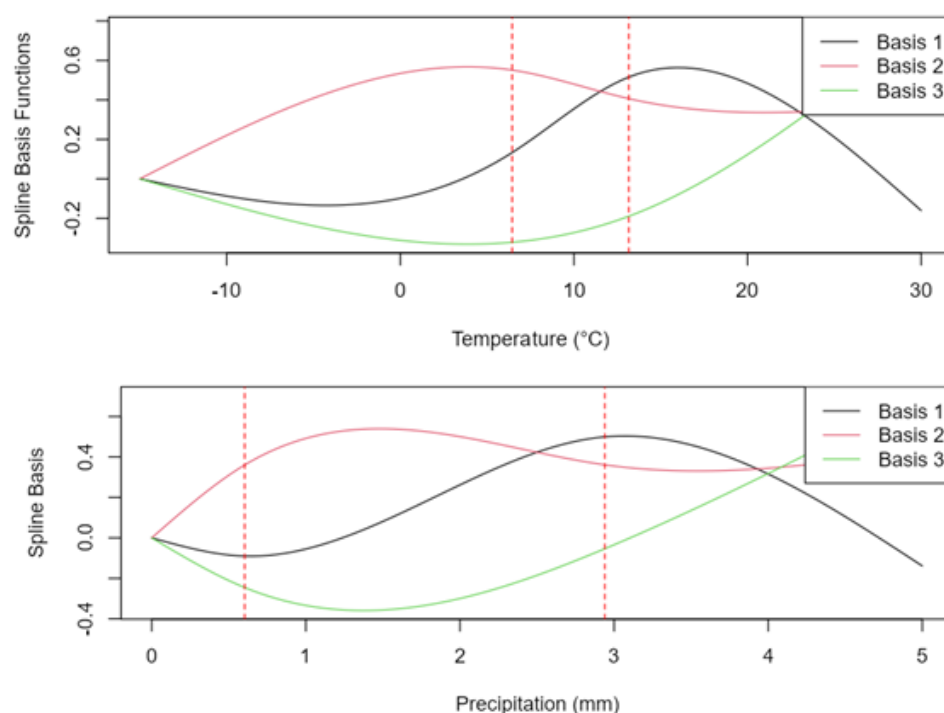


Figure 20. Flow of the spline bases with indication of knot placement for A temperature and B precipitation. The vertical dashed lines indicate the placement of the knots.

The surface plot of the association between temperature, precipitation and odds of all-cause-mortality (Figure 21A-D) shows that the lowest odds of mortality are at dry colder temperatures with a further decrease around 13 degrees and the highest odds are for wet and very warm weather.

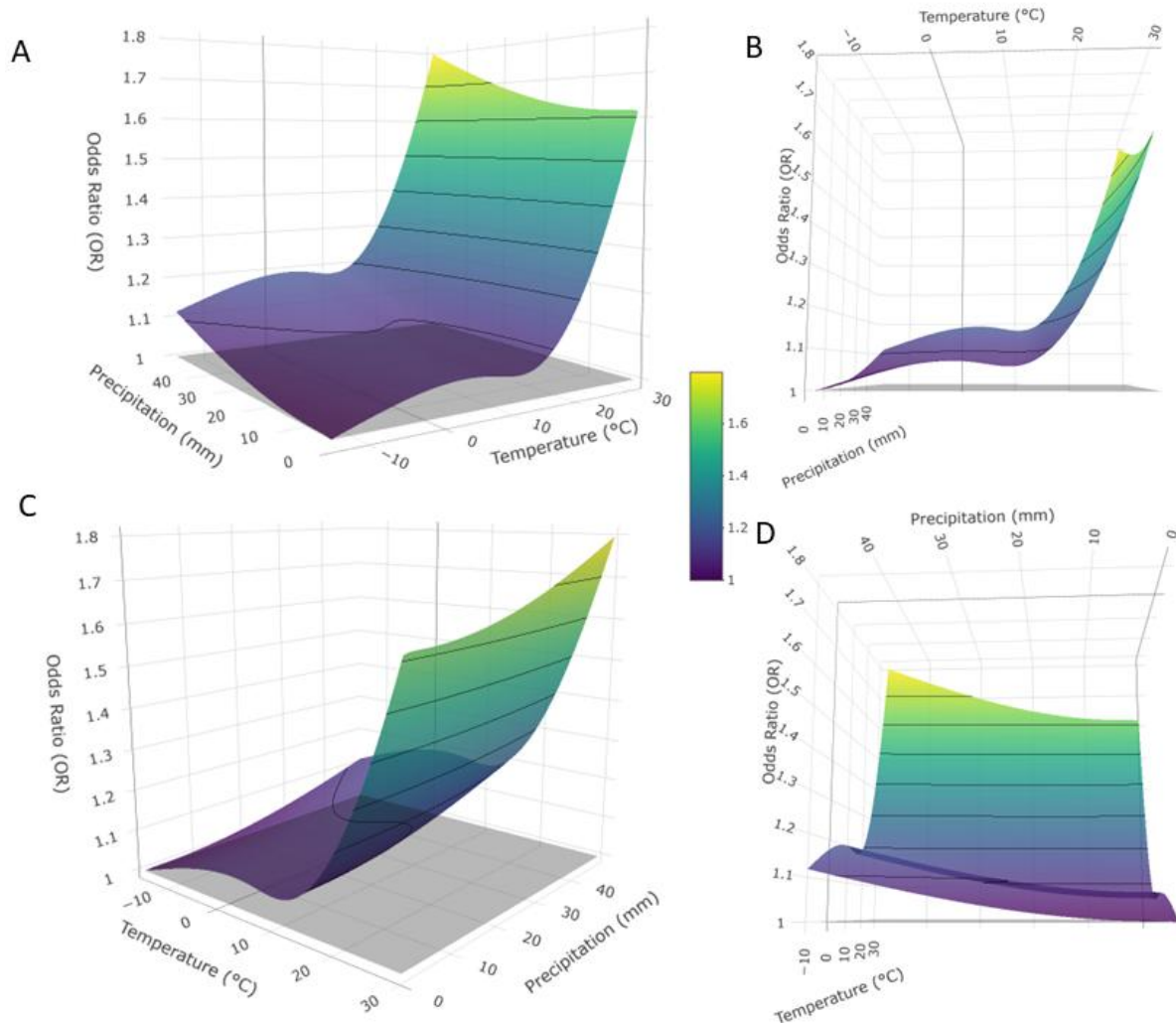


Figure 21. Association between temperature, precipitation and odds of mortality in a surface plot with different perspectives A, B, C and D.

To further investigate how climate change affects the association between pollen concentrations on odds of all-cause-mortality (Task 5.4), we stratified the data to represent different climate scenarios, namely very hot and dry (i), very hot and wet (ii), very cold and wet (iii), and very cold and dry (iv) (Table 10). For very cold weather scenarios representing temperatures below the first quartile no observations of grass pollen measurements were available which is plausible given the positive correlation between grass pollen and temperature (Figure 19) and explained by the seasonal distribution of the grass pollen season (May-September). In comparison with the main analysis of all deaths none of the subgroup analyses in different climate scenarios was significantly different as indicated by p-values above the 5% threshold (Table 10). Furthermore, all associations had wide 95% CIs, crossing 1. Especially the association of birch pollen with odds of all-cause-mortality for very warm wet weather had an inflated CI indicating an unstable model probably because of almost entirely zero values of birch pollen under these conditions.

Table 10. Percentage changes for all deaths associated with birch and grass pollen in models stratified for combinations of exposure to temperature and precipitation below the 1<sup>st</sup> or above the 3<sup>rd</sup> exposure quartile respectively. The p- value indicates subgroup specific differences in comparison to all deaths/climate conditions in the main analysis as reference assessed with a Z-test.

climate	N	birch pollen <sup>a</sup>	p-value Z-test	grass pollen <sup>b</sup>	p-value Z-test
cold dry	1049101	-4.80 [-10.18, 0.92]	0.08	/	/
cold wet	698879	-4.30 [-8.56, 0.17]	0.05	/	/
warm dry	1078855	0.56 [-0.11, 1.23]	0.32	0.16 [-0.37, 0.68]	0.51
warm wet	777483	15506.90 [-94.76, >100]	0.22	0.12 [-0.33, 0.58]	0.54

<sup>a</sup> percent change for an increase of 100 grains /m<sup>3</sup>

<sup>b</sup> percent change for an increase of 10 grains /m<sup>3</sup>

## Summary and Conclusions:

In Task 5.1 we found that all pollutants except the grass pollen were associated with increased odds of all-course-mortality. Grass pollen and NO<sub>2</sub> exposure showed increased odds of CVD -related -mortality compared to all-cause-mortality but for respiratory deaths all percentage increases were lower and mostly not statistically significant which could also be due to the smaller sample sizes. The findings of air pollutants and mortality confirm earlier reports of consistent associations between mostly man-made air pollutants for Belgium (Demoury et al. 2024) and other countries (Bateson and Schwartz 2004; Kan and Chen 2003). For pollen exposure, a previous study in the Helsinki Metropolitan Area, Finland, in 1994–2014 also found a statistically significant association between birch, but not between grass-pollen and mortality (Jaakkola et al. 2021). In contrast, another study, investigating the association between airborne pollen concentrations and daily all-cause and cause-specific mortality in the Netherlands between 1986–1994, found significant dose-response related associations predominantly for grass pollen (Brunekreef et al. 2000). Taking into account the observations from our analysis, which included data spanning 30 years with exposure peaks of nearly 10,000 grains/m<sup>3</sup> for birch pollen, this corresponds to an increase of 4.5% in the odds of all-cause-mortality on a day with a birch pollen concentration of 2,000 grains/m<sup>3</sup>—a rise with a significant health-political impact.

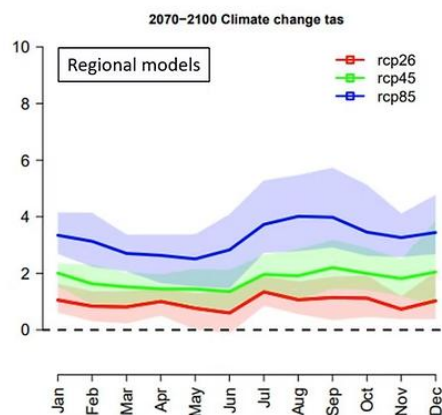
Even though the interaction term p-values for pollen and air pollution exposure were mostly statistically significant (Task 5.1), indicating effect modification, we did not find major differences in the odds of all-cause-mortality when adding the different air-pollutants to the main models of pollen exposure (Task 5.3) which is in line with the findings of a previous systematic review which only found limited evidence for synergistic effects from simultaneous exposure to air pollution and pollen (Anenberg et al. 2020). In the stratified analysis for birch pollen exposure with low and high air pollutant exposure we further found that the odds for all-cause-mortality seem to be higher in the group of low air pollutant exposure. This may be due to the fact that the particulate air pollutants were negatively correlated with temperature. As temperature itself had a very strong influence on mortality (Task 5.2), even though the models were adjusted for temperature, we cannot exclude the presence of residual confounding.

Regarding the impact of climate change scenarios on short-term mortality (Tasks 5.2 and 5.4) we could observe by visual inspection of the surface plots (Figure 21) and assessment of the ranges represented by the splines in the conditional logistic models, that temperatures below and above the temperature optimum increased the odds of all-cause-mortality. Furthered, the highest odds were associated with very warm and wet climate which is in line with previous reports (Anderson and Bell 2011; Ho et al.



2025), and also raises questions about the potential roles of heat waves and thunderstorm-asthma conditions, which are increasingly reported in the literature. Elsewhere also a higher impact of cold vs. high temperatures has been reported (Gasparrini et al. 2015), which might be due to the different assessment in time-series models with more emphasis on the effect of moderate deviations from non-optimum ambient temperature instead of the effects of extreme temperature events. For the assessment of specific meteorological conditions in the relationship between pollen exposure and all-cause-mortality, we applied a stratified analysis for different extreme weather conditions. None of the outcomes was statistically significant, probably also due to small sample sizes which resulted in underpowered and unstable estimations. The non-significant trends for the association between birch pollen and all-cause mortality in cold-dry and cold-wet weather were both negative in contrast to the also non-significant positive association for very warm dry weather, also suggesting a potential synergistic effect between temperature and birch pollen exposure on mortality odds, which could exacerbate the issue of pollen-related mortality in the context of future climate change.

From the CORDEX analysis (Task 5.4) for Belgium ([https://www.belspo.be/belspo/brain-be/projects/FinalReports/CORDEXbe\\_FinRep\\_AD.pdf](https://www.belspo.be/belspo/brain-be/projects/FinalReports/CORDEXbe_FinRep_AD.pdf)), a tendency in increasing temperatures and precipitation is derived for the RCP8.5 scenario. Annual temperature is projected to increase with 2.6 to 3.5K on average for Belgium (see also panel below) with climate changes close to the North Sea lower than the ones present in the South-East of Belgium. For urban areas the temperature increase will even be stronger. The CORDEX-report shows a relative increase in winter precipitation of 20% on average everywhere in Belgium, and extreme precipitation (defined as 99<sup>th</sup> percentile of daily precipitation) is positive everywhere and on average 12%.



[https://www.belspo.be/belspo/brain-be/projects/FinalReports/CORDEXbe\\_FinRep\\_AD.pdf](https://www.belspo.be/belspo/brain-be/projects/FinalReports/CORDEXbe_FinRep_AD.pdf)

Long-term (1991-2020) average spring temperatures (T) for Central Belgium (see website RMI on meteo.be) are situated around the 10-11°C, while summer temperatures are in the range of 18 to 20°C. Spring precipitation (P) is 166 mm (1.82 mm/d) and for the summertime 234 mm (2.56 mm/d). Daily values can vary substantially. If one combines the results of the CORDEX analysis with long-term averaged spring and summer temperatures and precipitation, the contribution of basis 2 and 3 (Figure 20) of these weather variables in the statistical analysis affecting the odds of mortality are the largest. From CORDEX we know that the average temperature and precipitation will increase shifting more and more to basis 3. That is why we focus on basis 2 and 3 in this analysis. From these numbers, and from Figure 20, Figure 21 and Table 9 we observe a strong increase in the odds for higher mortality due to these weather variables. If both weather variables increase more (for instance more extreme



precipitation), the contribution of basis 3 becomes more dominant, the odds are higher. From Figure 21, a merged increase in the odds can be visually derived of at least 20%, especially with extreme precipitation. For current to the RCP8.5 summertime (T,P) combination, the OR for mortality increases with 7%, while if extreme precipitation would occur (30 mm/d or more), the OR is 12.3% higher. For the springtime (T,P) combination an increase in OR is 1.9%, and 7.6% with the occurrence of extreme precipitation.

The effect of meteorology/climate on the airborne pollen levels in Belgium (Task 5.5) was addressed in Verstraeten et al. (2023) using the Area Under the Curve (AUC) and associations with meteorological variables. This is illustrated below in Figure 22, Figure 23 and Figure 24 for birch pollen. Our findings show that during the period 1982–2019 a strong increase in birch pollen concentrations is associated with increasing radiation, decreasing precipitation and decreasing horizontal wind speed near the surface. A strong decrease of grass pollen concentrations over time is driven by a decreasing trend in grass pollen sources, and it is also associated with decreasing precipitation. The magnitude of the associations between meteorology and airborne birch pollen concentrations are almost twice the association between meteorology and grass pollen, and the spatial variations are substantial even on the scales of small countries. The specific contribution of birch tree and pollen production dynamics to the concentrations of birch pollen in the air over time is highly associated with wind speed and precipitation. Introducing the inter-seasonal variation in birch pollen production during the period 1982–2019 intensifies the climate induced increase of airborne birch pollen concentrations with ~6%. In contrast, the grass pollen production dynamics resulted into ~10 times less grass pollen over the studied period compared to climate change effects (less production of pollen by grasses, or less sources for grass pollen as suggested in Figure 25). For the grass pollen concentrations, a decline in the pollen amounts was also reported for the Benelux between 1982 and 2020 (de Weger et al., 2021), which corresponds to the decreasing trend observed at Brussels for the period 1982 - 2015 (Bruffaerts et al., 2018).

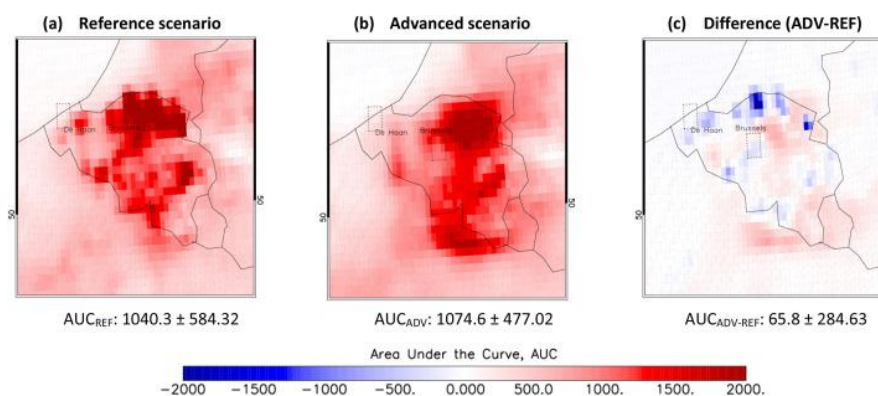


Figure 22. Spatial distribution of the Area Under the Curve (AUC) values of airborne birch pollen concentrations for Belgium based on the reference scenario of SILAM for the period 1982–2019. (b) Same as for (a) but using the advanced scenario of SILAM. (c) Same as for (a), but the AUC is computed from the time series of the difference between the advanced (ADV) and reference (REF) SILAM. The locations with the longest time series of observed pollen concentration are indicated as rectangles (Brussels at 50.825 N/4.383 E; De Haan at 51.274 N/3.022 E). The spatially averaged AUC values ( $\pm$  dev) for Belgium are also provided (Verstraeten et al., 2023).

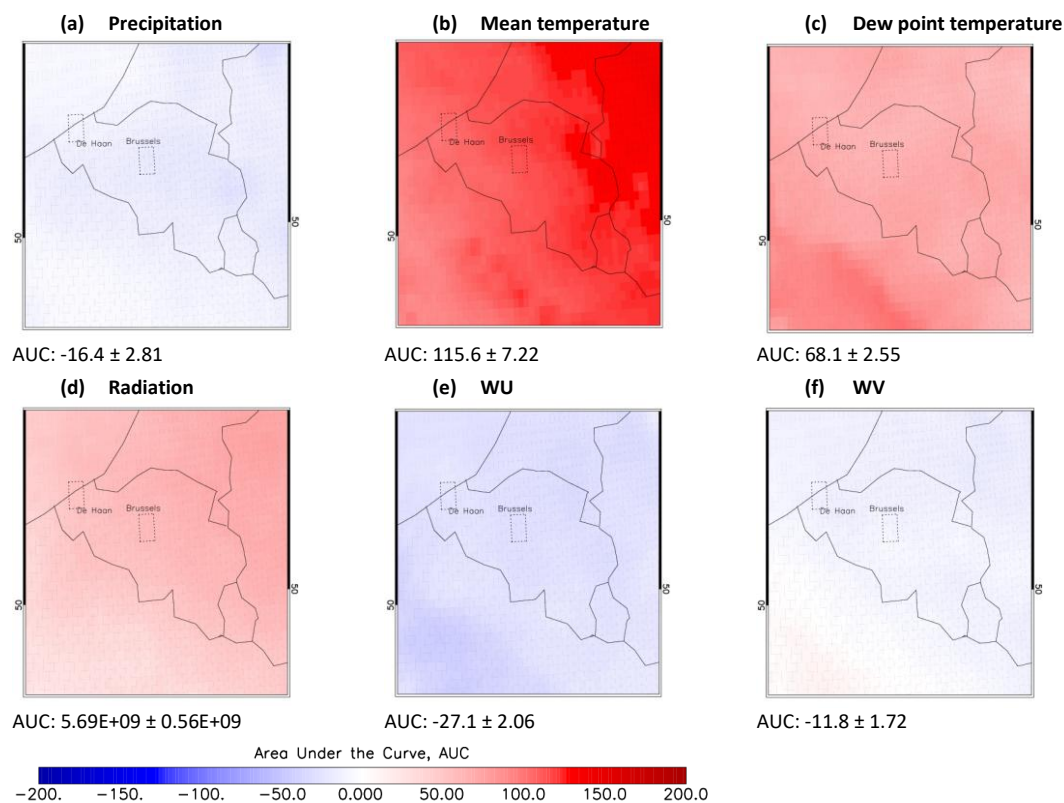


Figure 23. Spatial distribution of the Area Under the Curve (AUC) of a selection of ERA5 meteorology during the birch pollen season (March-June) for the period 1982-2019 in Belgium. (a) Daily precipitation, (b) mean air temperature, (c) mean dew point temperature, (d) radiation, (e) the horizontal wind speed WU, and WV (f). Radiation is scaled with 1E-08. The spatially averaged AUC values ( $\pm$  stdev) of each map are also provided (Verstraeten et al., 2023).

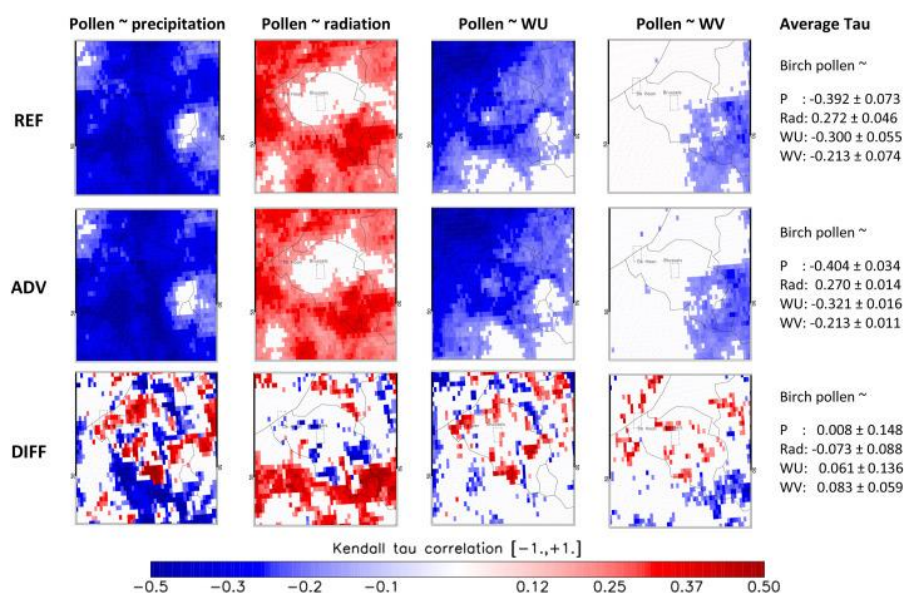


Figure. 24. Spatial distribution of the Kendall tau correlation for on one hand the birch pollen concentrations derived from the reference and advanced SILAM scenarios, and from the difference time series, and on the other hand the meteorological variables precipitation, radiation and horizontal wind speed components. Only

significant correlations (P-value <0.05) are shown, based on Mann-Kendall non-parametric procedure. The spatially averaged correlation (tau) and the stdev for each map are also given (right column) (Verstraeten et al., 2023).

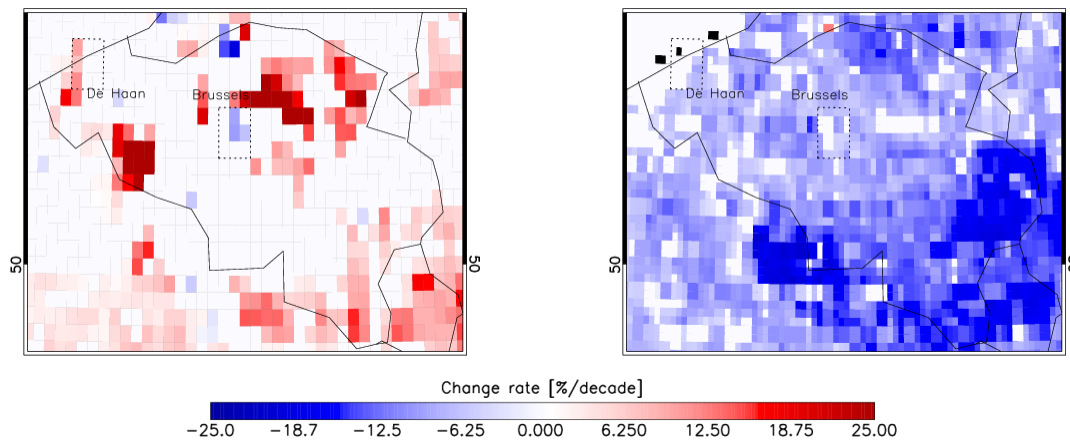


Figure 25. Decadal change rate in Theil-Sen slopes of birch pollen emission sources (left panel, reprocessed from Verstraeten et al., 2022) and grass pollen emission sources (right panel) between 1982 and 2019 based on the Random Forest methodology and the NDVI time series (Verstraeten et al., 2023).

#### WP5. The effect of pollen, air pollution and climate change on allergy risk (Tasks 5.6+5.7+5.8+5.9+5.10)

The patient selection procedure was set-up and a codebook was development for obtaining the appropriate data set (see the before mentioned illustration of the codebook). A request for getting retrospective clinical patient data was submitted and approved by the ethical commission of the Erasme Hospital of the Université Libre de Bruxelles (ULB).

The spatial distribution of the patients' residential addresses across Belgium (absolute values not corrected for population density) is shown in Figure 26A, indicating that the NIS-code regions of Gent, Antwerp and Brussels contributed the highest number of patients. Within Brussels, most of the patients came from the NIS-code region of Anderlecht, where the Erasme Hospital is situated (Figure 26B). When assigning the corresponding NIS codes to the postal codes of the patient's home address, patients' hospital stays before lung function measurements were taken into account. For patients with CF of the Erasme Hospital, the NIS code of the hospital (21001 for Anderlecht) was used when the variable "hospit = 1" indicated that the data was obtained during hospitalization. In the case of the Zeepreventorium, patients often stayed at the Zeepreventorium for extended periods. The NIS code of the Zeepreventorium was used after visual evaluation of the data if the patient was at home, or the Zeepreventorium directly before spirometry using the following guidelines: (i) The home NIS code was used for the first date in a row because it was assumed that the spirometry was performed on the day of admission; (ii) When the stay spanned the Christmas period, it was assumed that the patients went home for Christmas. The first date in January was therefore linked with the exposure at home address (NIS code).

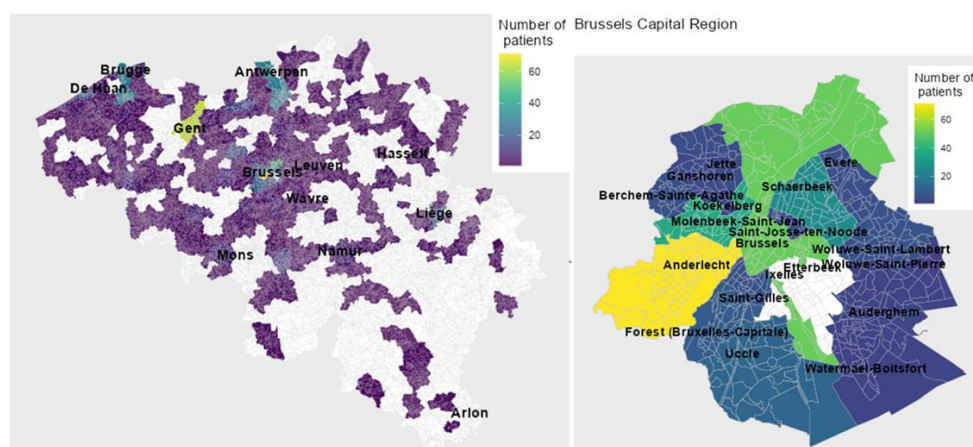


Figure 26. Spatial distribution of the patients' residential addresses across **A** whole of Belgium, and **B** in detail for Brussels. Darker colors indicate a higher number of addresses per NIS code.

From the total of 1171 individuals with 8873 observations, 283 individuals (1905 observations) were sensitized to birch pollen, and 456 individuals (2942 observations) were sensitized to grass pollen (Figure 27).

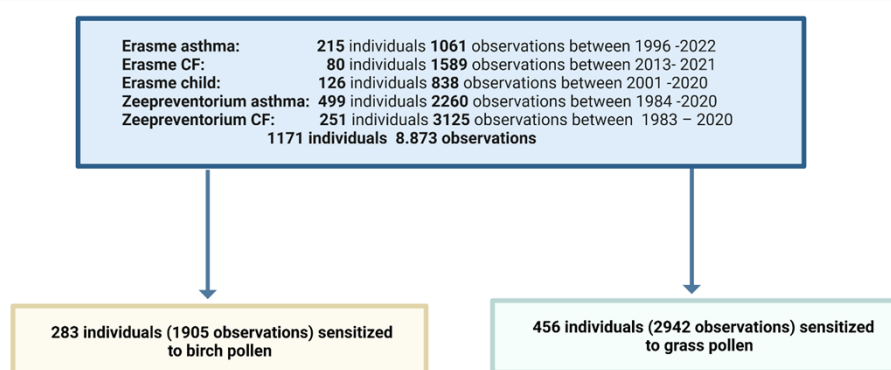


Figure 27. Flow chart indicating the number of patients and observations per cohort and how many patients are sensitized to birch and grass pollen.

For the different patient cohorts, the percentage of patients sensitized to pollen differed (Figure 28). While about 10% of the general population in Belgium is allergic to pollen from trees of the birch family, about 18% has an allergy to grass pollen (<https://www.sciensano.be/nl/gezondheidsonderwerpen/stuifmeelallergie/cijfers#pollenallergie-in-belgi->). In all patient populations, the percentage of individuals sensitized to birch pollen was higher than that for grass pollen. Generally, the percentage of sensitized individuals was much larger in the patients with asthma than in the patients with CF. Children had the highest rate of pollen sensitization, with about 97.6% of them allergic to at least one type of pollen (Figure 28).

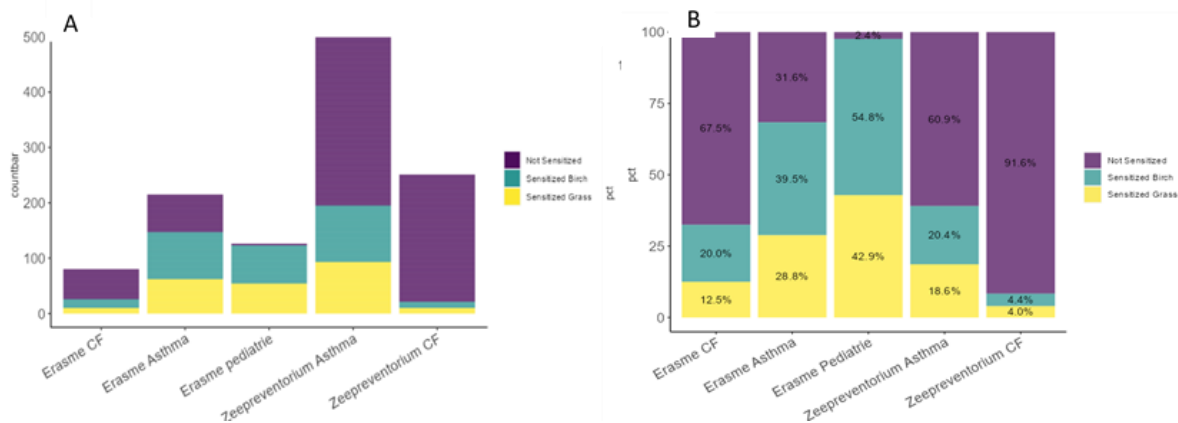


Figure 28. Bar plots of A: the total number of patients and B the percentages of patients per dataset/hospital sensitized to birch pollen, grass pollen, or not sensitized.

In the longitudinal dataset with repeated patient visits, the dose-response associations were investigated between observed airborne pollen concentration of birch and grass species and lung function measurements as well as Fractional Exhaled Nitric Oxide (FeNO) as a noninvasive marker of inflammation. The patient group from Erasme Asthma had 815 FeNO measurements (30%), the group from Erasme pediatrie 492 (18%), Zeepreventorium Asthma 456 (17%), and Zeepreventorium CF 954 measurements (35%). In the FeNO analyses, no measurements from Erasme CF were present. Because FeNO values in CF patients can be decreased due to the disease symptoms and therefore not reflect the inflammation status correctly we performed a sensitivity analysis for the CTS design, excluding CF patients.

We converted the absolute spirometry measurement of forced expiratory volume 1 second (FEV1) provided in liters to percent predicted (%) according to gender, age, and height of the individual at the time-point of measurement with the R package “rspro”, (NHANES3 (National Health and Nutrition Examination Survey; Hankinson et al. 1999) to provide comparability of the results,

In the analysis of the associations between pollen concentrations and %FEV1 and FeNO, we first evaluated the data in a Distributed Log Non-linear Model (DLNM) accounting for the repeated measurements by including the IDs as a random effect’s variable, applying a mixed model design. Therefore, we constructed cross-bases for pollen levels, daily temperature, and precipitation. In detail, we investigated the associations between pollen exposure with %FEV1 and FeNO in linear Gaussian models over a lag period of 0-2 days. Because including non-linear relationships did not significantly improve the model fit, the analyses with birch pollen were performed with linear terms. For the models with grass pollen a non-linear fit with knots at 50 and 100 grains/m<sup>3</sup> was used. Additionally, an unconstrained distributed lag model was added to adjust for precipitation and a bi-dimensional spline to account for the average temperature. Furthermore, we have adjusted for shared long-term and seasonal trends by including natural cubic splines of time (6 degrees of freedom/year for the models including all patients, 2 degrees of freedom/year in the models including only sensitized patients). In the models for air pollution exposures, we adjusted for the average temperature. Secondly, we applied the newly developed case time series design, taking into account lagging effects. This novel self-matched method was designed to analyze transient changes in the risk of acute outcomes associated with time-varying exposures. Compared with other techniques to model



aggregated time series, it allows individual-level analysis, typical of self-matched methods such as the case-crossover design. This method is very suited for analyzing longitudinal data resources.

In brief, applying the case-time-series design, we build personalized daily time series for each participant between their first and last lung function measurements. In contrast to the DLNM models with the subjects added as random effects variables, we used subject/year strata intercepts. Therefore, the subjects in the analysis served as their own controls by comparing their in- and out-of-season symptoms.

## Results

The results of the DLNM model with the repeated measures accounted for by adjusting on the subject level as random effects, show a significant inverse link between cumulative exposure over lag 0-2 for black carbon ( $\beta = -0.55$ , 95% CI: -1.02, - 0.08) (Table 11 and Figure29 G No evidence was found for associations between birch or grass pollen concentrations with %FEV1 in the DLNM model (Table 11 and Figure29A/B).

Table 11. Associations between **pollen and air pollutants** with predicted FEV1 % and FeNO in the DLNM model with random effects variable for the patients.

	%FEV1		FeNO	
	$\beta$	95% CI	$\beta$	95% CI
Birch pollen	-0.11	-0.28, 0.067	0.76	-0.36 - 1.88
Grass pollen	-0.41	-0.85, 0.035	0.71	-0.57- 2.00
Black carbon	<b>-0.55</b>	<b>-1.02, -0.08</b>	1.09	-0.18- 2.36
PM10	-0.051	-0.30, 0.20	-0.20	-0.98 - 0.59
PM2.5	-0.056	-0.38, 0.27	-0.30	-1.55 - 0.94
NO2	-0.16	-0.50 - 0.18	0.095	-0.87- 1.06
O3max	-0.15	-0.31, 0.010	-0.11	-0.66- 0.43

Estimates are for increases of 10 units except for birch pollen (100 units) and black carbon (1 unit)

In the case time series design, there was evidence for an inverse cumulative (lag 0-2) dose-response association between birch pollen levels and %FEV1 (Task 5.6). When evaluating the data up to 2020 (before the COVID-19 pandemic and up to and including 2022, the strength of association was comparable ( $\beta = -0.28$ , 95% CI: -0.47, -0.091 and  $\beta = -0.29$ , 95% CI: -0.47 - -0.10) (Table 12, Figure30A). Furthermore, concerning the impact of air pollution on the patients, O<sub>3</sub>max showed a significant inverse association with %FEV1 in the model with data until the COVID-19 pandemic ( $\beta = -0.17$ , 95% CI: -0.33 - -7.3e-04) (Table 12) (Task 5.9). In the group of patients sensitized to birch or grass pollen, the cumulative association between grass pollen concentrations and %FEV1 was significant in the case time series design ( $\beta = -0.92$ , 95% CI: -1.63, -0.21) (Table 13, Figure31B). Additionally, there was a significant association between birch pollen exposure and FeNO in patients sensitized to birch pollen ( $\beta = 1.20$ , 95% CI: 0.062, 2.34) (Table 13, Figure31A). In the sensitivity analysis excluding CF patients the effect was more pronounced ( $\beta = 1.83$ , 95% CI: 0.72, 2.94).

When performing the analysis for patients with CF and asthma separately, birch and grass pollen exposure were significantly associated with FEV1 ( $\beta = -0.22$ , 95% CI: -0.34, -0.018 and  $\beta = -0.76$ , 95% CI: -1.45, -0.066 respectively) only in patients with CF (Table 14, Figure31C/D). For children separately (<18 years) (n=806) combined birch pollen exposure over lag0-lag2 was significantly associated with decreased %FEV1 ( $\beta = -0.37$ , 95% CI: -0.70, -0.029).

When investigating potential influence of other air pollutants in the association between pollen exposure and lung function (Task 5.9) we found a significantly stronger association of birch pollen on FEV<sub>1</sub> at above median PM<sub>10</sub> levels ( $p = 0.05$ ) (Figure 32).

Table 12. Associations between **pollen and air pollutants** with predicted FEV1 % and FeNO in the case-time-series model stratified for the individual patients. To account for potential changes in air pollutant concentrations during the COVID-19 pandemic the results are shown for the years before 2020 and up to and including 2022.

	< <b>2020</b>				≤ <b>2022</b>			
	%FEV1		FENO		% FEV1		FENO	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Birch pollen	<b>-0.28</b>	<b>-0.47, -0.091</b>	0.27	-3.28, 3.81	<b>-0.29</b>	<b>-0.47, -0.10</b>	0.45	-0.21, 1.11
Grass pollen	-0.48	-1.13, 0.17	-0.063	-1.63, 1.74	-0.54	-1.17, 0.10	0.50	-0.88, 1.89
Black carbon	-0.044	-0.55, 0.47	0.79	-0.55, 2.12	-0.060	-0.56, 0.44	-0.013	-0.18, 2.36
PM10	-0.026	-0.29, 0.24	-0.30	-1.16, 0.55	-0.035	-0.30, 0.23	-0.40	-1.45, 0.65
PM2.5	0.11	-0.23, 0.45	-0.30	-1.55, 0.94	0.093	-0.24, 0.43	0.093	-0.24, 0.43
NO2	-0.20	-0.52, 0.12	-0.27	-1.34, 0.80	-0.18	-0.49, 0.13	0.048	-0.94, 1.0
O3max	<b>-0.17</b>	<b>-0.33, -7.3e-04</b>	-0.15	-0.61, 0.30	-0.15	-0.30, 0.011	-0.25	-0.70, 0.19

Estimates are for increases of 10 units except for birch pollen (100 units) and black carbon (1 unit)

Table 13. Associations between pollen concentrations with predicted %FEV1 and FeNO for patients sensitized to birch and grass pollen respectively in the case time series design stratified for the individual patients.

	<b>Birch</b>				<b>Grass</b>			
	%FEV1		FENO		% FEV1		FENO	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Birch pollen	-0.22	-0.56, 0.14	<b>1.20</b>	<b>0.062, 2.34</b>	-	-	-	-
Grass pollen	-	-	-	-	<b>-0.92</b>	<b>-1.63, -0.21</b>	-0.035	-2.73, 2.66
Black carbon	-0.55	-1.43, 0.53	1.61	-2.60, 5.83	0.75	-0.80, 0.95	-1.28	-5.02, 2.45
PM10	-0.39	-0.85, 0.18	0.19	-2.05, 2.42	-0.21	-0.67, 0.24	-0.72	-2.75, 1.32
PM2.5	-0.39	-1.02, 0.26	0.48	-2.08, 3.04	-0.15	-0.72, 0.42	-0.72	-3.07, 1.62
NO2	-0.22	-0.82, 0.38	0.23	-2.21, 2.68	-0.15	-0.65, 0.43	1.16	-0.70, 3.02
O3max	-0.014	-0.27, 0.025	-0.38	-1.42, 0.67	-0.0042	-0.23, 0.22	-0.19	-1.08, 0.71

Estimates are for increases of 10 units except for birch pollen (100 units) and black carbon (1 unit)

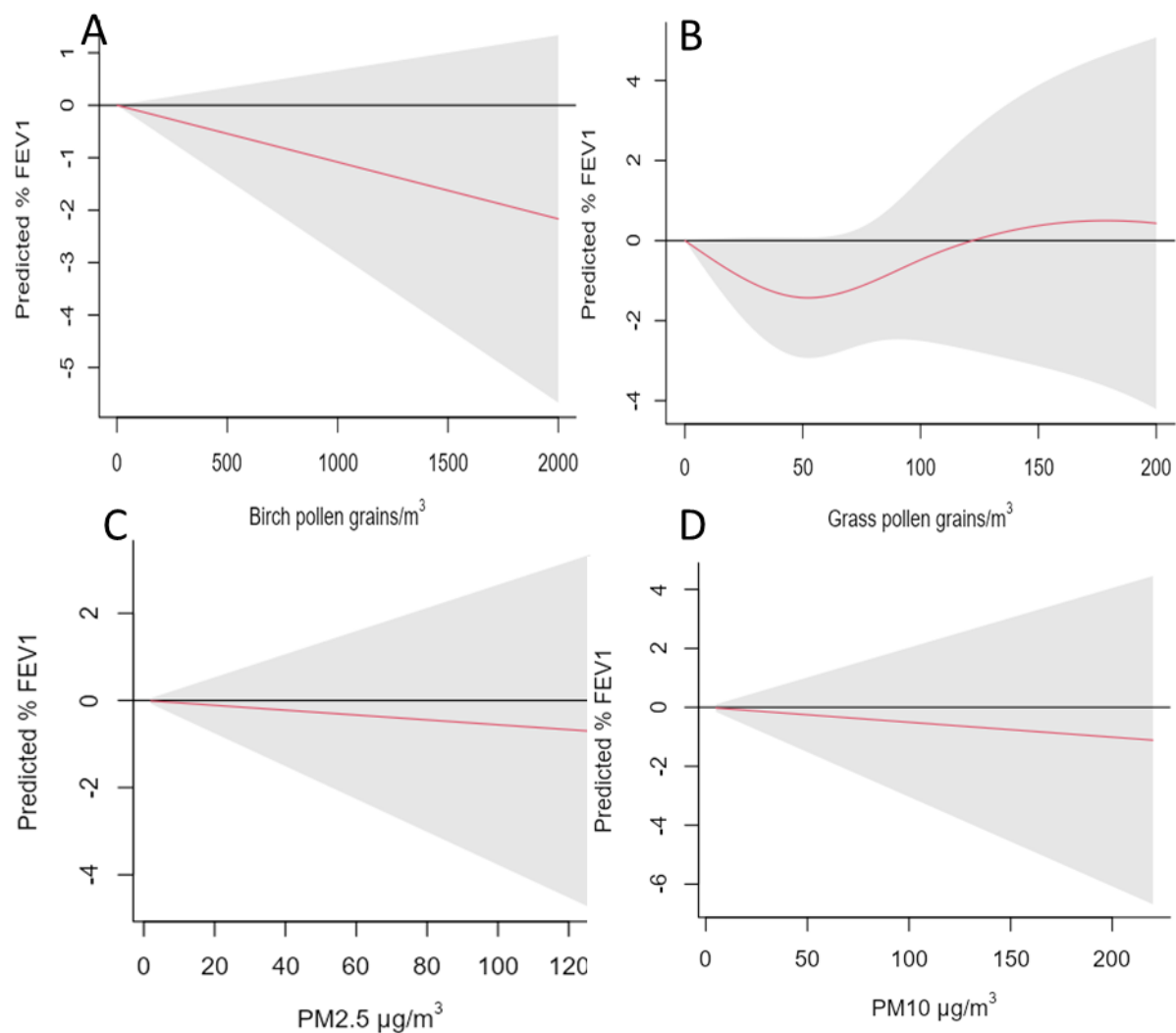
Table 14. Associations between pollen concentrations with predicted %FEV1 for CF and asthma patients separately evaluated in in case time series models.

	CF patients		Asthma patients	
	β	95% CI	β	95% CI
Birch pollen	<b>-0.22</b>	<b>-0.34, -0.018</b>	-0.35	-0.79, 0.088
Grass pollen	<b>-0.76</b>	<b>-1.45, -0.066</b>	-0.66	-2.38, 1.51
Black carbon	0.35	-0.21, 0.91	-0.42	-1.69, 0.84
PM10	-0.047	-0.36, 0.26	-0.12	-0.63, 0.39
PM2.5	0.059	-0.31, 0.50	0.055	-0.58, 0.69
NO2	-0.30	-0.72, 0.12	0.14	-0.39, 0.66
O3max	-0.12	-0.32, 0.077	-0.067	-0.35, 0.21

Estimates are for increases of 10 units except for birch pollen (100 units) and black carbon (1 unit)

By applying different statistical models, we found evidence for adverse effects on the lung function of patients with asthma and CF. With the new case time series design we found evidence that a

cumulative increase of 100 grains/m<sup>3</sup> birch pollen (dose relationship, Task 5.10) on the day of examination and the two previous days was associated with a decrease of 0.29% predicted FEV1 in a group of patients with asthma and CF. For an exposure of 2000 grains/m<sup>3</sup>, which is not uncommon during the birch pollen season, this translates to a decrease of about 5.8% predicted FEV1 patients with asthma (Figure 30). In patients CF with the decrease is 4.4% and for grass pollen even 7.6%. In a patient population with an already lowered lung function due to asthma or CF this means a significant decline in health and quality of life. Furthermore, in the group of patients sensitized to grass pollen a cumulative increase of 10 grains/m<sup>3</sup> on the day of examination and the two previous days was associated with a decrease of 0.92% predicted FEV1. The cumulative effect was strongest for a pollen concentration around 45 grains/m<sup>3</sup> (Figure 31) (dose relationship, Task 5.10). Additionally, adverse effects on the lung function of patients with asthma and CF could be demonstrated for O<sub>3</sub>max (Task 5.9).





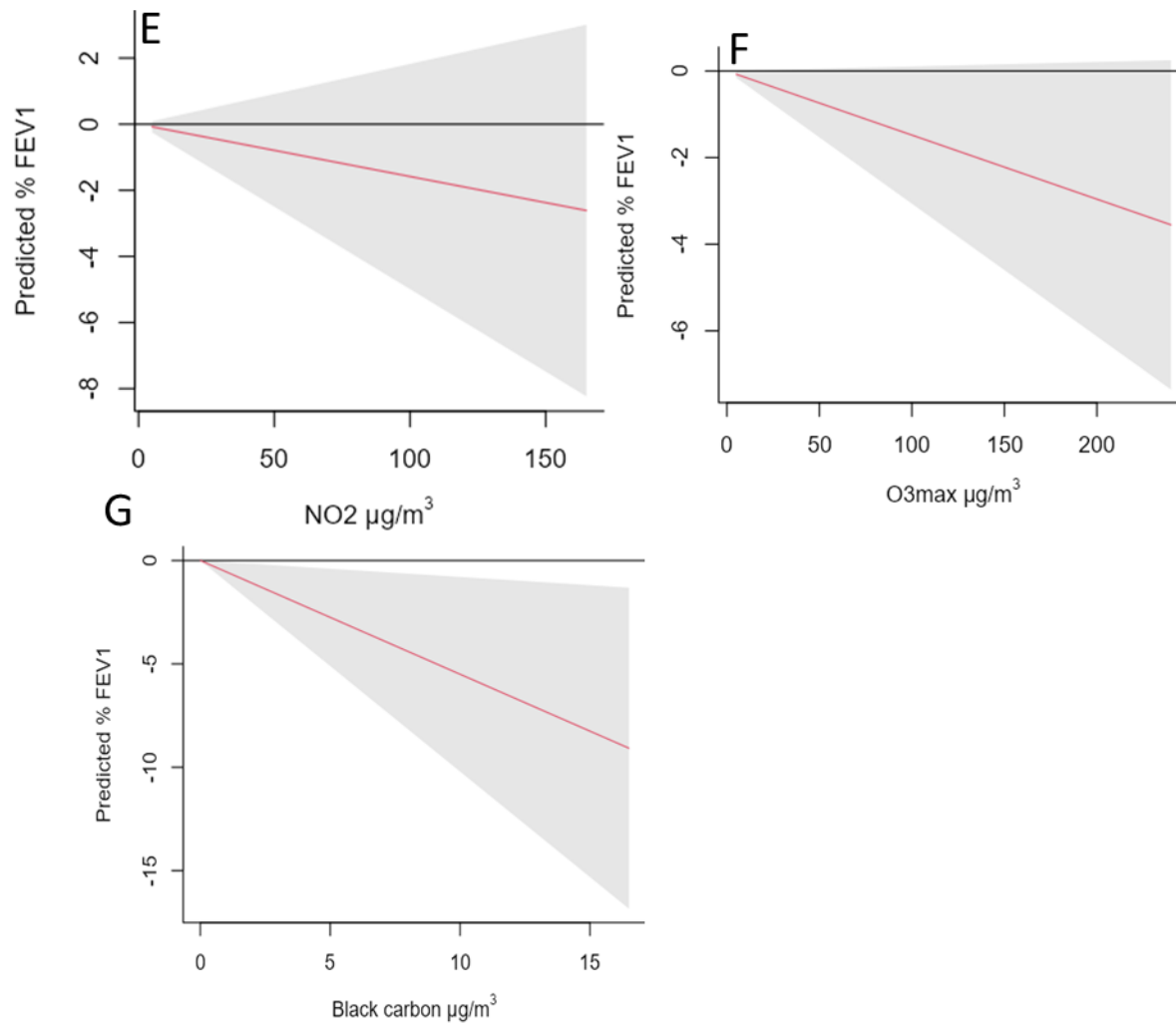


Figure 29. Distributed lag (non-)linear model (DLNM) with the cumulative (lag 0-2) dose-response associations between **A** birch pollen and **B** grass pollen concentrations, **C** PM<sub>2.5</sub>, **D** PM<sub>10</sub>, **E** NO<sub>2</sub>, **F** maximum 8h mean ozone, **G** black carbon and percent predicted FEV1 (%FEV1). Associations are presented as the change in %FEV1 with shading showing the 95% confidence interval for a 100 grain/m<sup>3</sup> and 10 grain/m<sup>3</sup> increase in birch and grass pollen, respectively.

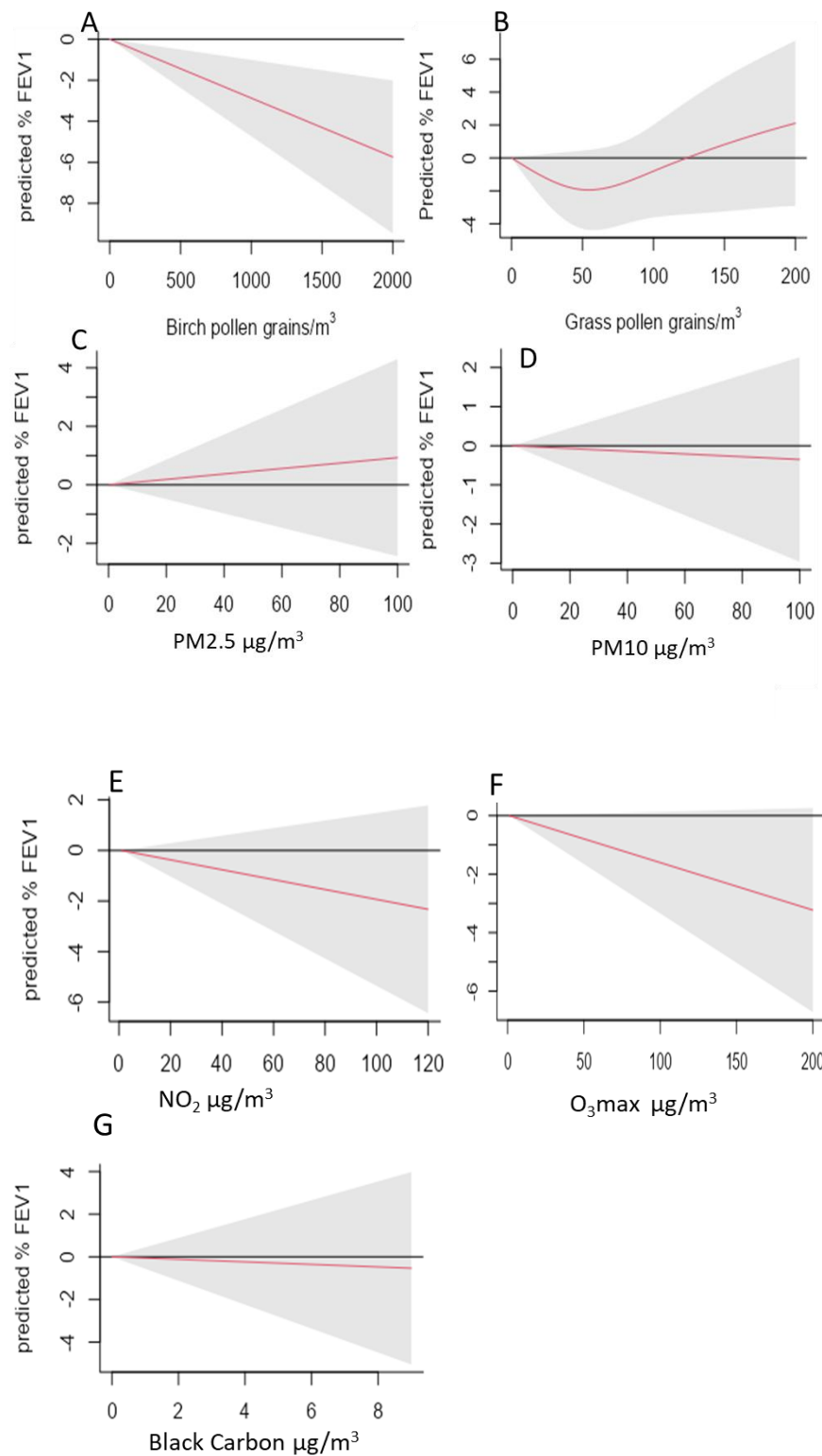


Figure 30. Case time series (CTS) model with the cumulative (lag 0-2) dose-response associations between **A** birch pollen and **B** grass pollen concentrations **C** PM<sub>2.5</sub>, **D** PM<sub>10</sub>, **E** NO<sub>2</sub>, **F** maximum 8h mean ozone, **G** black carbon and percent predicted FEV<sub>1</sub> (%FEV<sub>1</sub>). Associations are presented as the change in %FEV<sub>1</sub> with shading showing the 95% confidence interval.

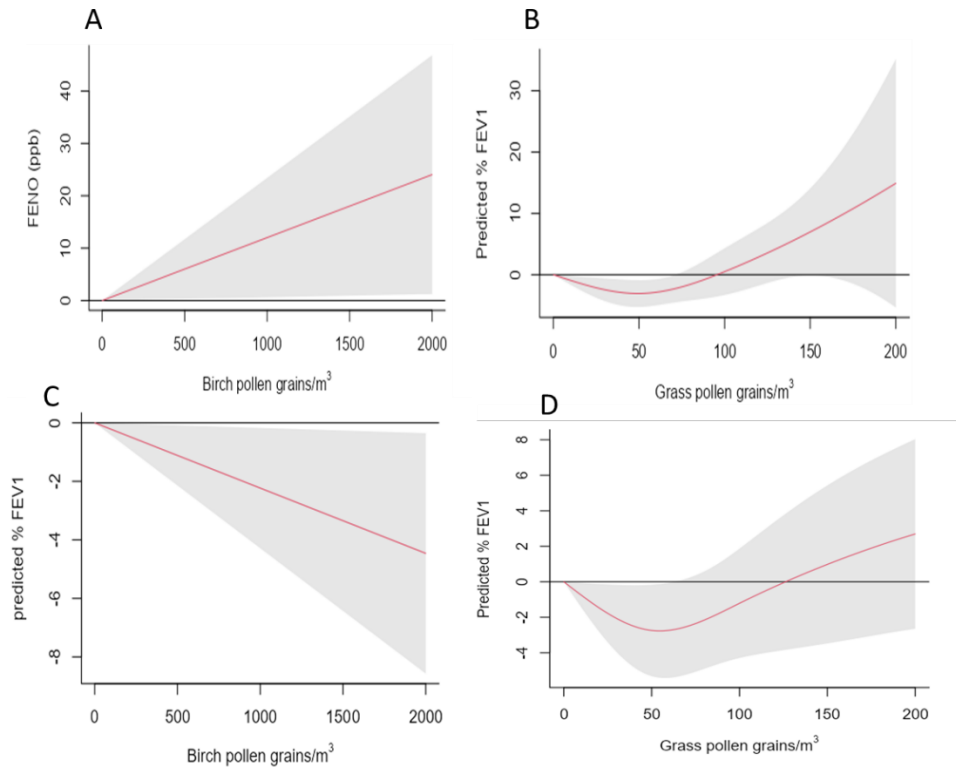


Figure 31. Case time series (CTS) model with in **A** the cumulative effect of lag 0-2 between birch pollen and FENO in sensitized patients, **B** the cumulative effect of lag 0-2 for grass pollen and percent predicted FEV<sub>1</sub> (%FEV<sub>1</sub>) in sensitized patients, **C** the cumulative effect of lag 0-2 for birch pollen and FEV<sub>1</sub> in CF patients and **D**, the cumulative effect of lag 0-2 for grass pollen and %FEV<sub>1</sub> in CF patients. Association between grass pollen concentrations and %FEV<sub>1</sub> for patients sensitized to grass pollen.

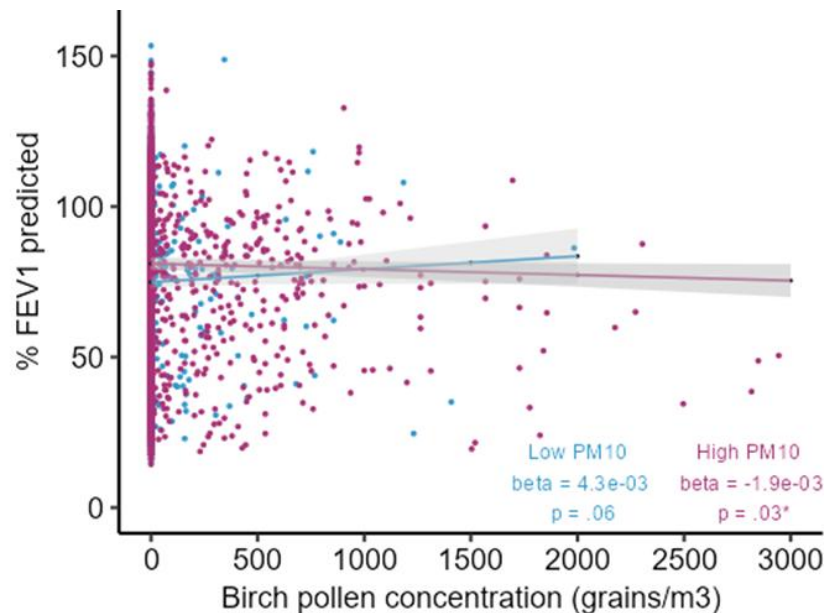


Figure 32. Case time series (CTS) model stratified for the cumulative effect of birch pollen exposure (lag0-lag2) on percent predicted FEV<sub>1</sub> (%FEV<sub>1</sub>) under below median (blue) and above median (purple) exposure levels of PM<sub>10</sub>. The grey bands show the 95% confidence interval.

To analyze the covariate effects of medication, air pollution, and the stage of the pollen season, the historical clinical data set - although considerable- was insufficient to perform a meaningful statistical analysis (Task 5.7). Therefore, we are unable to report results for this. Temperature and precipitation were adjusted for in all models investigating the effect of pollen and air pollutant exposure on lung function and allergy symptoms.

The effect of temperature and rainfall on the lung function (Task 5.8) was also analyzed. Below, Figure 33A shows a linear association between precipitation and percent predicted FEV<sub>1</sub> (%FEV<sub>1</sub>), although statistical not significant. For temperature, the association is more complex showing a decreasing trend with %FEV<sub>1</sub> below 15°C and above 20°C and a very small positive trend between 15 and 20°C (Figure 33B), although also not statistical significant.

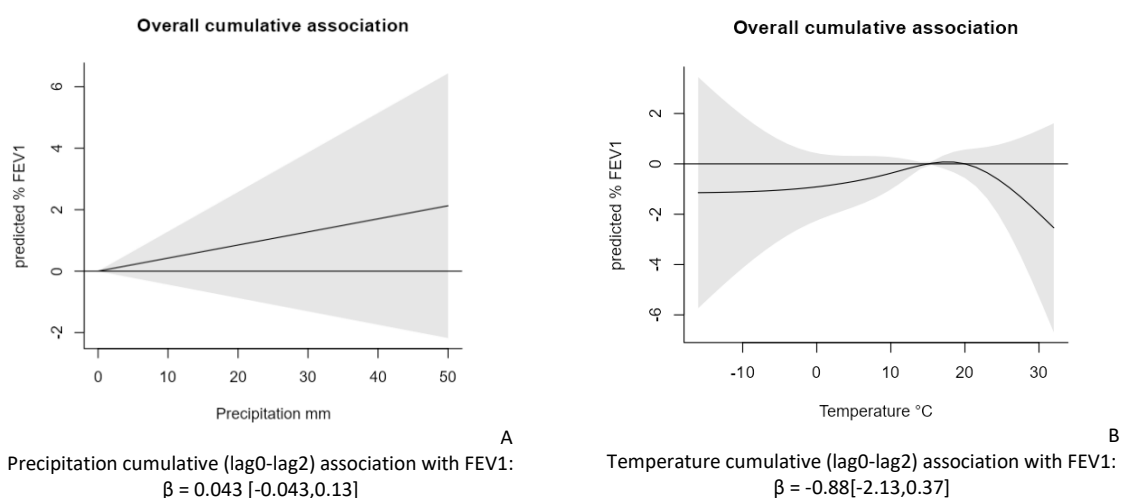


Figure 32. Overall cumulative association between percent predicted FEV<sub>1</sub> (%FEV<sub>1</sub>) and precipitation (A) and with temperature (B).

Deliverable: Thresholds of pollen amounts for allergy alert are in the order of magnitude of the existing ones for grass pollen (45 grains/m<sup>3</sup>); Identification and impact of the various contributors to allergy/mortality; Effect of climate change on pollen release; Allergy Risk Indicator combining weather, pollen, and air pollution.

## 5. DISSEMINATION AND VALORISATION

### WP 6 with Tasks 6.1+6.2+6.3

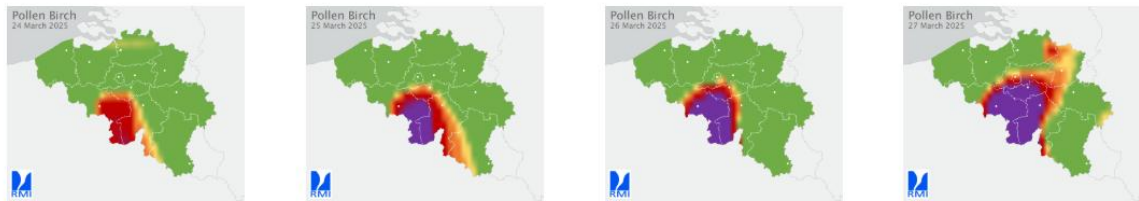
Throughout participations and presentations on workshops, colloquia, congresses (e.g. AGU, EGU, European and World Symposium on Aerobiology) and by collaborations (data exchanges, multilateral meetings) and publishing in peer-reviewed scientific journals, we have been reaching multidisciplinary research communities (Task 6.1) which is also illustrated by the list of publications.

Reaching out to stakeholders and the public at large is also essential since it creates a sustained engagement and thus enlarges the impact of the project output. Since March 2023, the RMI in collaboration with Sciensano provides 4-day warnings for airborne birch pollen risks and since May 2023 for grass pollen. Lately, we also have added warnings for alder pollen, not included in the original RETROPOLLEN proposal. On the RMI website and in the RMI app the public at large can consult the expected allergy risks for alder, birch and grass. This information is also provided at the AirAllergy website from Sciensano and the AirAllergy app (see also Deliverables of WP4). This is a huge step forward, since now patients suffering from alder/birch/grass pollen induced allergies can consult the expected allergy risks for their location (Task 6.3) four days ahead. The press releases on this pollen forecast system were picked up by newspapers, radio and TV and every start of the pollen season references is made by the press to the observations of Sciensano and the forecasts made by RMI (Task 6.2) (e.g. <https://www.hln.be/weer-wetenschap/golf-van-stuifmeel-op-komst-mensen-met-hooikoorts-in-deze-3-provincies-nemen-best-hun-voorzorgen~a6d0169e/>; <https://www.vrt.be/vrtnws/nl/2025/02/21/weerbericht-21-februari-kmi-warm-zonnig/>, among others).

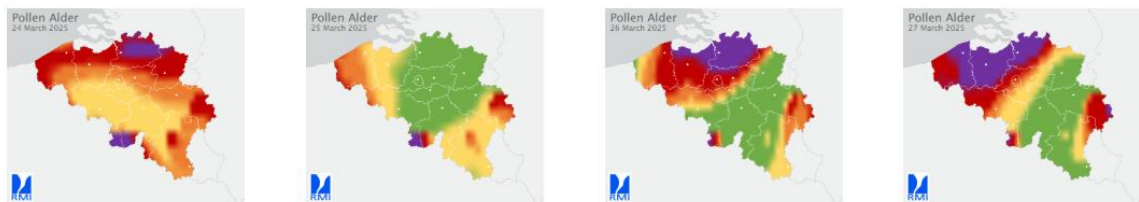
**Deliverables:** Presentations & publications, websites with pollen forecasts of RMI and Sciensano, twitter, apps with pollen info of RMI and Sciensano.

The infographics below illustrate the capability of the consortium to provide information on various allergenic pollen as shown for alder and birch.

## Birch



## Alder



Color	Level	Risk
Green	Null	No pollen grains are expected in the air. The risk of symptoms is theoretically absent, although very local exposure can trigger allergies.
Yellow	Low	Low concentrations of pollen in the air are expected. For very sensitive people, these few pollen could induce allergy symptoms. The usual avoidance measures are already recommended.
Orange	Moderate	Moderate concentrations of pollen in the air are expected, causing symptoms for people with pollen allergies. The usual avoidance measures are recommended.
Red	High	High concentrations of pollen in the air are expected. Many people who are allergic to this pollen are likely to develop symptoms. The usual avoidance measures are recommended.
Purple	Very high	Very high concentrations of pollen in the air are expected. Most people who are allergic to this pollen are likely to develop symptoms. It is strongly recommended to avoid all outdoor activities.



Website RMI and RMI app for Ukkel, March 24<sup>th</sup> 2025



AirAllergy App from Sciensano (left February 2<sup>nd</sup> 2025, right March 24<sup>th</sup> 2025)

## 6. GENERAL CONCLUSIONS, RECOMMENDATIONS AND FEEDBACKS

Allergic respiratory diseases are increasing globally, with pollinosis affecting about a quarter of European adults and a third of children. Anthropogenic emissions and climate change amplify immune responses and biogenic pollen emissions, affecting patients with asthma or cystic fibrosis (CF) badly. Globally, air pollution has caused 4.2 million premature deaths in 2019 (WHO), while allergic respiratory conditions are rising across Europe exacerbated by immune reactions to biogenic aerosol (pollen among others) emissions.

The RETROPOLLEN project reconstructed four decades of airborne birch and grass pollen levels near the surface in Belgium to assess public health impacts. Here we analysed dose-response associations between environmental exposures and historical clinical data of vulnerable patients, exploring the influence of air pollution and climate on pollen-related health effects. Historical data of all kinds from Zeepreventorium in De Haan (patient health data), the Erasme ULB Hospital in Brussels (patient health data), Sciensano (pollen observations in Belgium), STATBEL (data on economical, societal and health from inhabitants of Belgium) and the RMI (meteorological data and allergenic pollen modelling) have been gathered, compiled and analysed by the consortium. Finally, UHasselt linked the datasets and has performed the statistical data analysis.

We report that for 2,000 birch pollen/m<sup>3</sup> and 100 grass pollen/m<sup>3</sup>, the lung function decreased by 4.4% and 7.6% in patients with CF, and 5.8% in patients with asthma for birch pollen, posing significant health impacts. Stronger birch pollen effects with particulate matter emphasize the need for public health measures to protect vulnerable groups from ambient pollutants.

This study further analysed natural mortality in all Belgian municipalities, encompassing a population of 11,697,557 inhabitants (2023). Individuals residing in Belgium at the time of their death between 1992 and 2022, were included. Birch pollen exposure increased the odds of all-cause mortality with 4.5% at a concentration of 2,000 grains/m<sup>3</sup>. Synergistic effects under extreme weather and with higher surface ozone concentrations were found, emphasizing significant health impacts of pollen in the context of climate change and air quality.

Finally, during the RETROPOLLEN project a robust forecast model for grass and birch pollen levels near the surface was developed. It provides a 4-day forecast that is now continuously disseminated to the public at large using the RMI website and weather app, and via the AirAllergy app and website of Sciensano. During the final course of the project also alder pollen forecasts were made available and the forecast of mugwort pollen is scheduled for operations from July 2025 on.

Patients with respiratory diseases may benefit from more research considering additional allergenic pollen types, and pollen forecasts at more detailed spatial resolutions, i.e. at the scale of citizens. This requires the development and integration of very detailed pollen emission source maps with very detailed meteorological data fields. What is more, also complex processes that might affect the variability in the allergenic power of pollen due to various environmental factors must be investigated and unravelled further (Daelemans et al., 2025). Integrating these allergenic power of pollen with pollen amounts and air pollution data into the pollen forecasting model might inform patients with respiratory diseases about the allergy impact on a timely manner for the location they live.

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**Delcloo A., Verstraeten, W.W., Kouznetsov, R., Bruffaerts, N., Dujardin, S., Hendrickx, M., Sofiev, M.** (2021). Spatio-Temporal Modeling of Grass and Birch Pollen in Belgium. In: Mensink C., Matthias V. (eds) Air Pollution Modeling and its Application XXVII. ITM 2019. Springer Proceedings in Complexity. Springer, Berlin, Heidelberg, [https://doi.org/10.1007/978-3-662-63760-9\\_17](https://doi.org/10.1007/978-3-662-63760-9_17).

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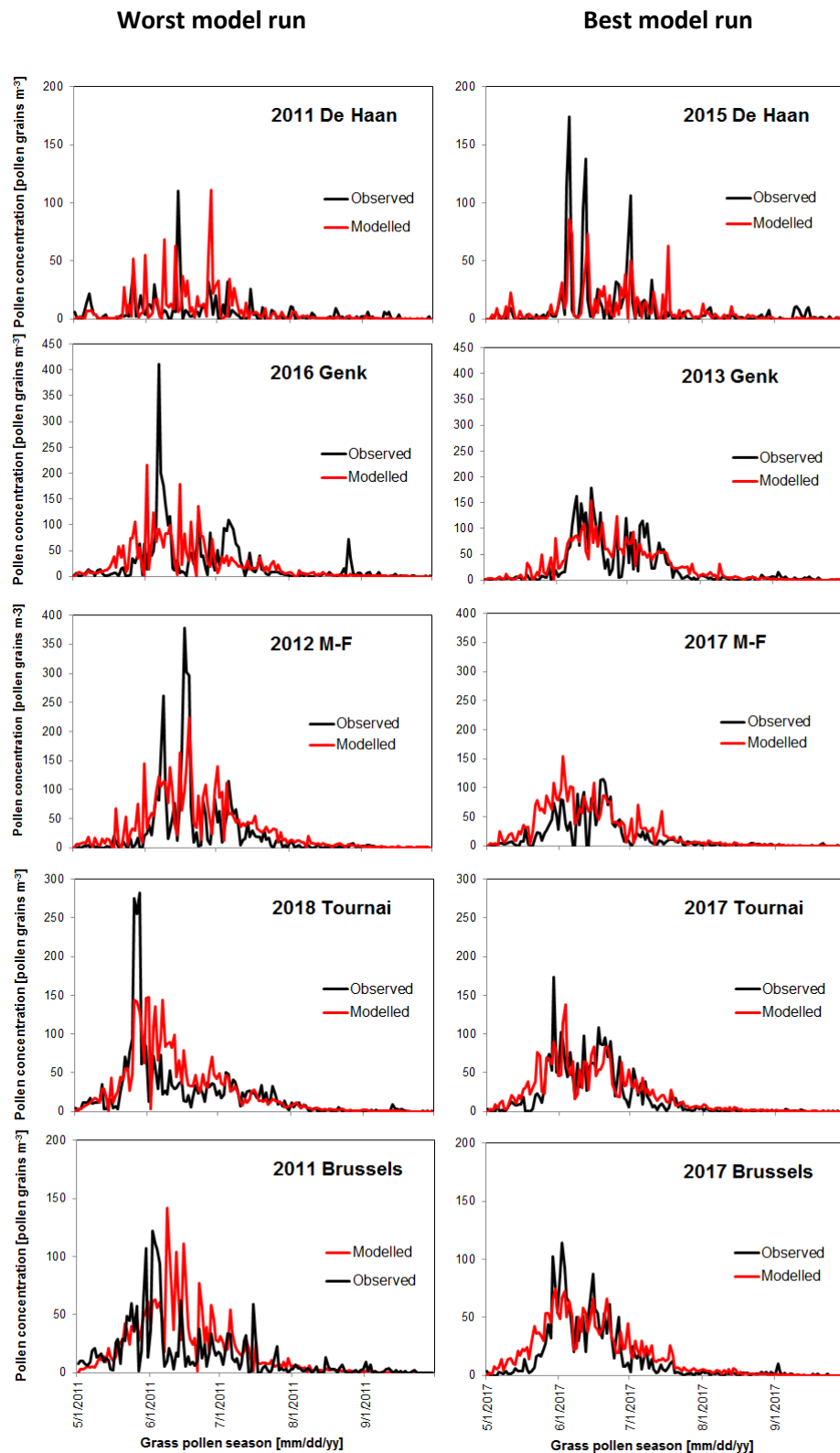
## 8. ACKNOWLEDGEMENTS

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## ANNEXES

**Table A1.** Airborne grass pollen concentration for each individual grass pollen season from 2008 to 2018 simulated with the SILAM model using the temporally scaled and updated grass pollen emission sources and varying start and end of the pollen season compared to observations collected at the five pollen monitoring stations in Belgium. Slope, intercept and the determination coefficient ( $R^2$ ) between modelled and observed grass pollen concentrations are given for each grass pollen season (Verstraeten et al., 2021).

	Brussel	De Haan	Genk	M-F	Tournai
2008 slope	0.97	0.32			
Intc	3.80	5.35			
$R^2$	0.69	0.07			
2009 slope	0.54	0.34			
Intc	9.12	5.71			
$R^2$	0.54	0.06			
2010 slope	0.73	0.63			
Intc	9.34	4.60			
$R^2$	0.51	0.10			
2011 slope	0.57	0.31	0.46		
Intc	10.66	5.68	11.90		
$R^2$	0.25	0.05	0.29		
2012 slope	0.59	0.30	0.35	0.88	
Intc	9.83	6.48	14.42	10.15	
$R^2$	0.40	0.17	0.25	0.43	
2013 slope	0.68	0.30	0.66	0.51	0.56
Intc	7.30	4.29	10.41	18.88	9.96
$R^2$	0.70	0.15	0.67	0.47	0.59
2014 slope	0.66	0.29	0.53	0.51	0.68
Intc	6.70	3.06	9.41	14.85	5.67
$R^2$	0.56	0.31	0.49	0.54	0.57
2015 slope	0.52	0.34	0.41	0.32	0.46
Intc	10.26	4.80	13.05	24.87	15.11
$R^2$	0.57	0.32	0.44	0.44	0.55
2016 slope	0.46	0.30	0.32	0.72	0.45
Intc	13.02	3.97	15.68	9.62	11.72
$R^2$	0.34	0.19	0.18	0.44	0.57
2017 slope	0.73	0.55	0.66	0.96	0.70
Intc	6.53	4.57	8.13	8.90	7.91
$R^2$	0.74	0.25	0.59	0.62	0.61
2018 slope	0.63	0.20	0.57	0.67	0.60
Intc	12.43	5.33	14.08	13.90	13.36
$R^2$	0.40	0.07	0.32	0.54	0.47



**Figure A1.** Seasonal time series of observed (black) and SILAM modelled (red) daily mean airborne grass pollen concentration (pollen grains/m<sup>3</sup>) near the surface for the worst and best model simulation for each monitoring stations of the Belgian aerobiological surveillance network. The statistics for each individual grass pollen season are given in Table A1 (Verstraeten et al., 2021).

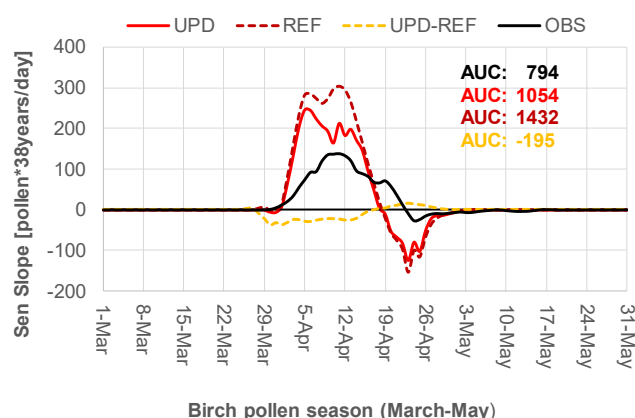


Figure A2. Change rate in the seasonal cycles of daily birch pollen levels between 1982 and 2019 as observed at the monitoring station of Brussels (in black line), and as modelled by SILAM using the 38 maps of birch pollen emission sources based on NDVI and RF (UPS in red line), as using only one reference map for the period 1982-2019 (REF, dashed brown), and the difference (see dashed yellow). The area under the curve (AUC) is included (Verstraeten et al., 2022).

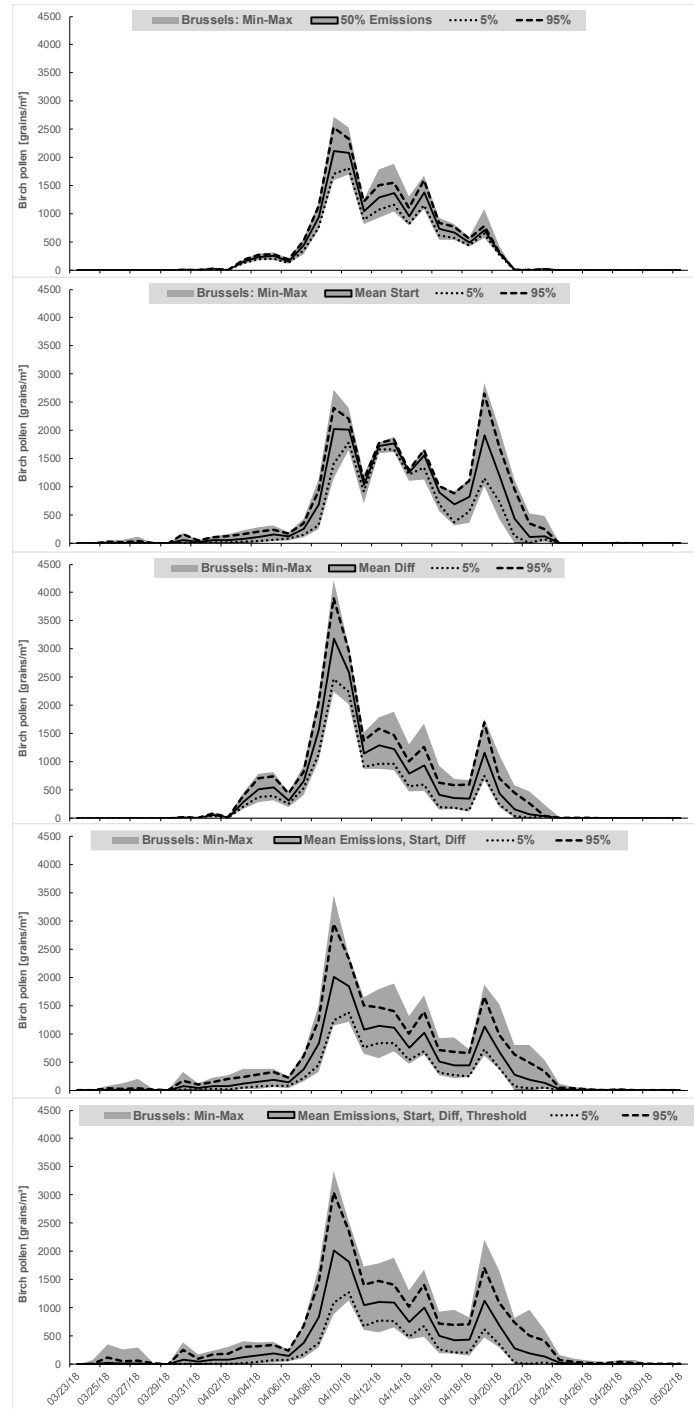
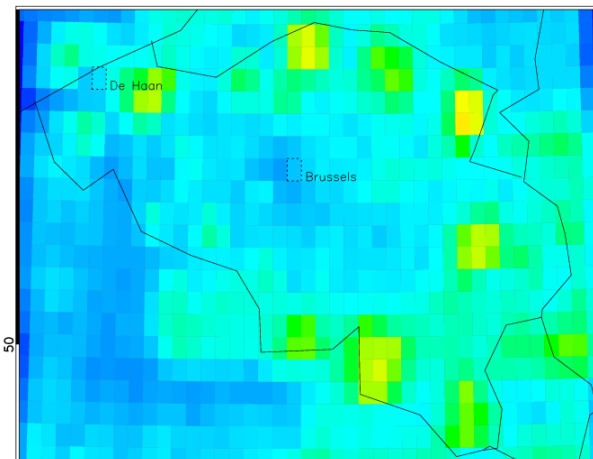


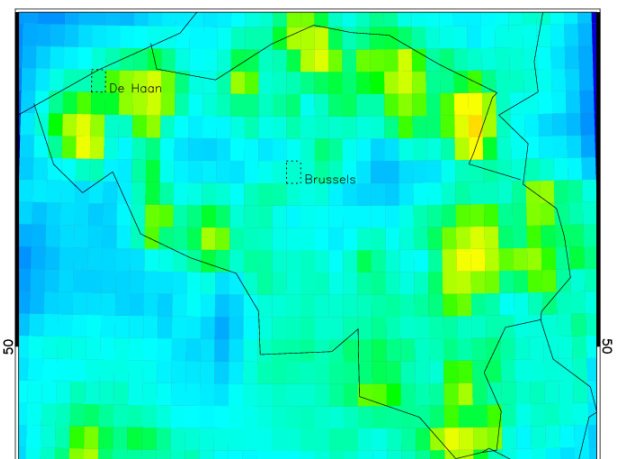
Figure A3. The 2018 time series of modelled airborne birch pollen levels near the surface for Brussels based on 100 simulations from SILAM. The black line is the mean time series, while the grey zone represents the total range of the simulations (minimum, maximum). From top till bottom panels: time series based on 100 SILAM runs only using 100 different birch pollen emission maps; 100 runs using only 100 different heatsum maps indicating the start of the birch pollen season; 100 runs using only 100 different heatsum maps indicating the end (Diff) of the birch pollen season; 100 runs combining 100 different emission maps, 100 different heatsum maps for start and 100 heatsum maps for the end (Diff); 100 runs combining 100 different emission maps, 100 different heatsum maps for start, 100 heatsum maps indicating the end (Diff), and 100 different threshold temperatures for heat accumulation. The percentiles 5 and 95 are illustrated (Verstraeten et al., 2024).



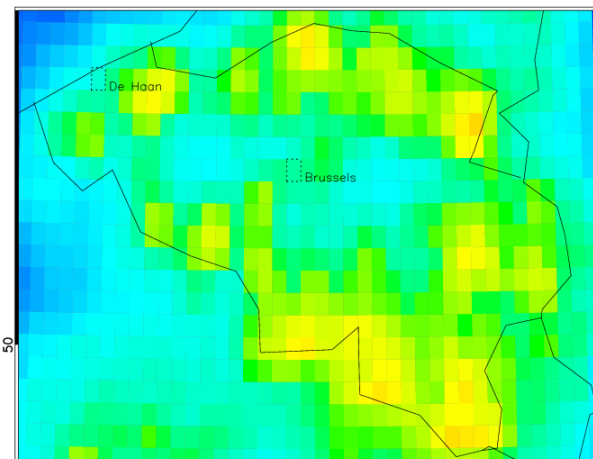
**Scenario 1: Emissions**



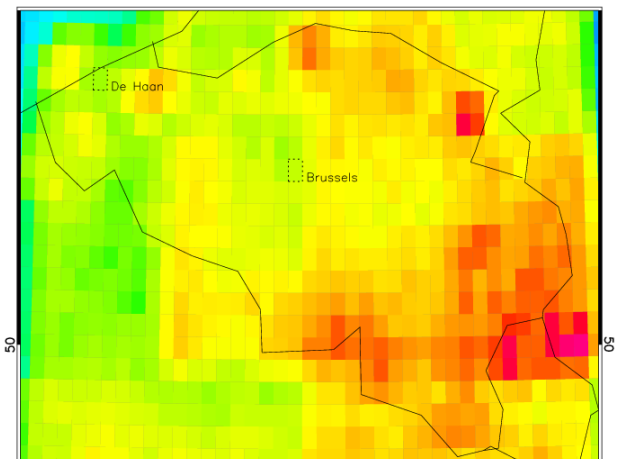
**Scenario 2: Heatsum Start**



**Scenario 3: Heatsum End (Diff)**



**Scenario 4: Emissions + Start + End (Diff)**



**Scenario 5: Emissions + Start + End + Threshold temperature**

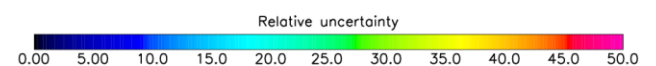
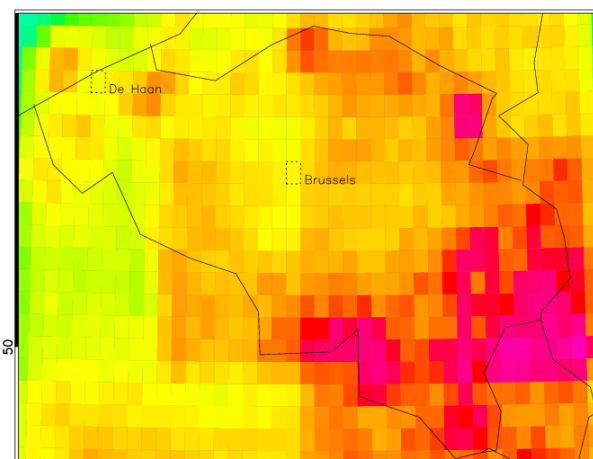


Figure A4. The spatial distribution of the relative Coefficient of Variation when modelling airborne birch pollen levels near the surface for the 2018 season derived from 100 SILAM runs for different input scenarios (only emissions, only heatsum start, only heatsum end (diff), the combination of all three, and finally the combination with varying threshold temperatures) (Verstraeten et al., 2024).

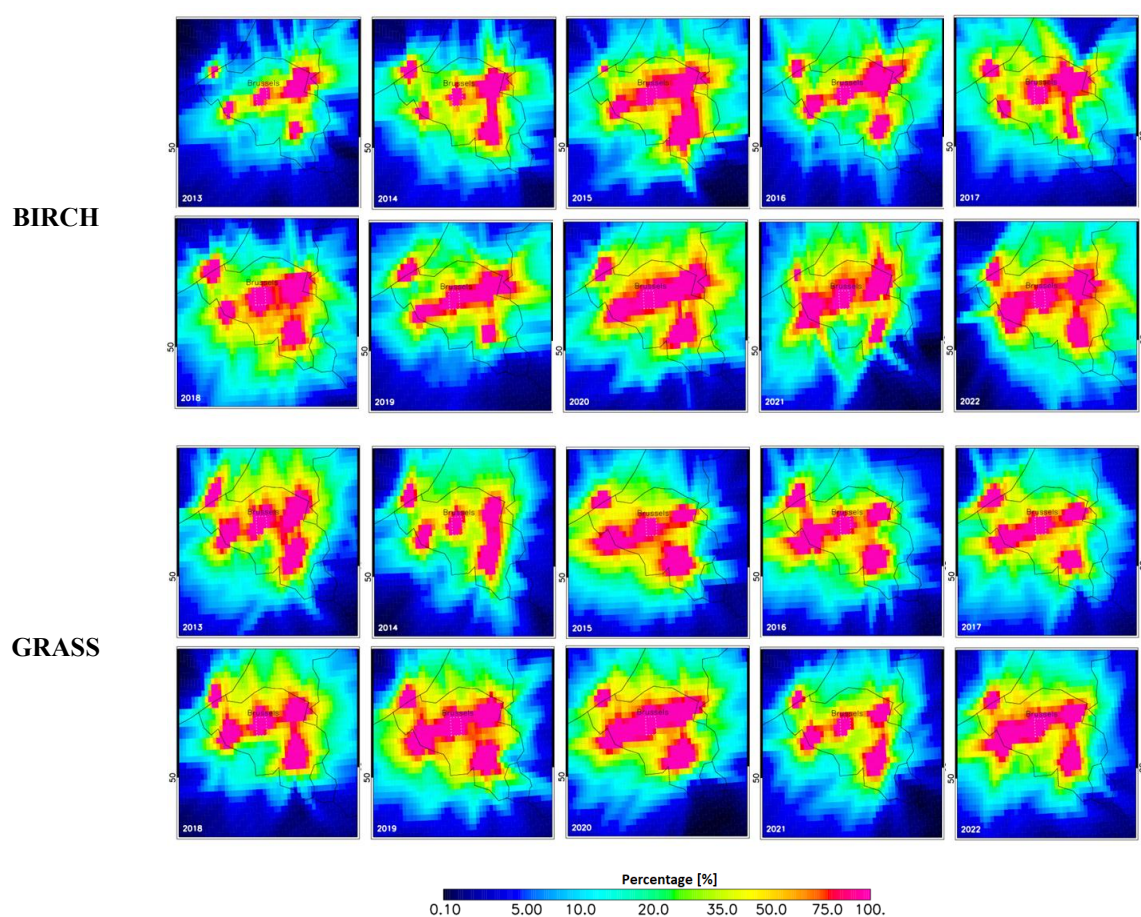


Figure A5. The sum of all station footprints of the Belgian aerobiological surveillance network over the individual birch pollen seasons (March-April) (upper panels) and over the individual grass pollen seasons (May-July) (lower panels) from 2013 to 2022 (Verstraeten et al., 2025).