atopica

FINAL report

4.1 FINAL Publishable summary

4.1.1 Executive summary

Current and future global and regional climate, land use and air quality change impact human health. The European region is expected to have an increase in the occurrence of extreme events, which may possibly cause migration of new invasive plant species and disease vectors. Changes in widespread urban sprawl, population and traffic increase and land degradation are additional factors. *Ambrosia artemisiifolia* L. (Asteraceae) called common ragweed is an example of an invasive plant species with significant impact on society, at many levels. It is an annual herbaceous, highly invasive plant that is spreading in Europe and produces allergenic pollen that causes hay fever (rhino-conjunctivitis), asthma and atopic dermatitis. It has a significant negative impact on the European economy through its affect on health, agriculture, biodiversity and even tourism. The rates of Ambrosia spread and consequent allergy are on the rise and will lead to increased European health care costs. The results of the Atopica project for the basis of an understanding of the complex interplay across these multiple stressors potentially exacerbating the overall effect of environmental change on human health in synergistic ways. Our integrated and cross-disciplinary approach to assess health risks consequent to severe environmental change could be used to assist in the design of suitable adaptation policies.

We used a highly interdisciplinary and integrated approach that included the evaluation and modeling of the influence of changes in climate, air quality, land use, subsequent distribution of invasive allergenic plant species and allergic pollen distribution on human health. We explored the combined pan-European impact of changes in climate, land use and air pollution on allergen pollen-induced diseases through a chain of quantitative physical and statistical models, studied vulnerable groups of allergic patients and search for predictive factors, established statistical models of disease response to pollen concentrations for assessing future trends and risk, and examined the effects of environmental change on pollen in laboratory experiments.

The main results of the project include:

- The identification of daily weather patterns and seasonal climate conditions most conducive for high pollen concentrations over different European regions (most noticeably the Southeast Europe pollen Hot-spot) and analysis of future changes in climate conditions most conducive to high Ambrosia pollen concentrations indicating an increase in pollen concentrations due to global warming.
- New targeted RegCM and WRF simulations for Ambrosia calculations

- Developement and validation of an ELPIS downscaling tool
- Production of downscaled data under future climate conditions for calculations of future Ambrosia distributions.
- A chain of models enabling the simulation of Ambrosia and birch pollen, including an Ambrosia invasion model, which were applied to the scenarios of seed spread, air quality and land use changes for two different future periods. Results on the 'Effects of climate change and seed dispersal on airborne ragweed pollen loads in Europe' can be found at Hamaoui-Laguel, L., Nature Climate Change (2015) doi:10.1038/nclimate2652.
- A targeted analysis over Croatia.
- Simulated an ensemble of emission scenarios for air quality under climate change.
- Determined that the highest ragweed sensitisation rate to Ambrosia is in an urban area with the lowest air quality and the *de novo* sensitisation to Ambrosia in children is estimated at a yearly rate of up to 3% depending on the exposure level; Sensitisation is associated with age, birth order, gender and atopic parents.
- Determined that in 60-89 year-old Europeans exposed to relatively low Ambrosia (20-40grains/m3/24h) since 2000), atopic diseases were frequent with 31% suffering from rhinoconjunctivitis. Atopic diseases decreased with age, but were still prevalent past age 80.
- Determined that the first manifestation of eczema, rhinoconjunctivitis and asthma occurred past age 60 in more than 10% of those affected and that the two clinically most relevant allergens in the elderly in the German study are house dust mite and birch pollen.
- Determined that epigenetic markers in the childhood populations were differentially methylated regions between allergic and non-allergic children, which clustered around genes involved in regulation of pathways related to atopy and Th2 cell differentiation, immune system response-regulating signaling, e.g., MAP kinases, Toll-like receptors and NGF signaling pathways.
- Established a dose-dependent robust model of pollen-induced allergic asthma in mice
- Determined that urban compared with rural pollen collected from plants in Austria induced more severe allergic asthma in mice and that the environment influences ragweed pollen allergenicity.

- Determined that the number of people sensitised to ragweed pollen in Europe is likely to more than double within the next 50 years and that control of ragweed has important public health benefits.
- Determined that Ambrosia sensitisation is positively associated with Ambrosia pollen levels and identified a number of socioeconomic, genetic factors and early life factors.
- Determined that rural residence was found to be protective against Ambrosia sensitization, however, the causal mechanisms remain unknown.
- Determined that short-term variations in Ambrosia pollen area positively associated with allergic symptoms in children, but that different symptoms (eyes, nose and lungs) respond to pollen levels on varying time lags.
- Determined that dissemination activities of the project results were successful (e.g., the Nature Climate Change (2015) doi:10.1038/nclimate2652 paper alone generated hundreds of newspaper articles and several television and radio reports)

The intention of Atopica was to provide input into plans for early detection and preventive management initiatives, along with sustainable strategies to control and reduce this invasive plant. Preventing future Ambrosia invasion and reducing the current invasion will incur heavy costs to farmers and governments in Europe. Thus, we present our results with the aim to assist in decisions and policy regarding these strategies based on cost-benefit ratios especially in the context of the effects on health and health care costs.

4.1.2 Summary of project context and objectives

With clear evidence for current and future global and regional climate, land use and air quality change, it is crucial to improve our understanding of how these environmental changes will impact human health. As assessed in the last report of the Intergovernmental Panel on Climate Change (IPCC), climate change foreseen for the next several decades of the 21st century over the European region is expected to increase the occurrence of extreme events and to possibly cause migration of new invasive plant species and disease vectors. In addition, these changes might occur in correspondence of widespread urban sprawl, population and traffic increase and land degradation. The complex interplay across these multiple stressors might exacerbate the overall effect of environmental change on human health in synergistic ways that are difficult to assess from a disciplinary perspective. Therefore, there is an urgent need to develop integrated and cross-disciplinary approaches to assess health risks consequent to severe environmental change and to design suitable adaptation policies.

Ambrosia artemisiifolia L. (Asteraceae) called common ragweed is an annual herbaceous plant with origins in North America. Although it was first observed in Europe in the mid 19th century, it began to spread in Europe after 1940, first in Hungary and then spread to Eastern European countries, South Eastern France and Northern Italy. It has continued to spread into many continental Europe countries. It is a highly invasive plant with allergenic pollen that causes hay fever (rhino-conjunctivitis), asthma and atopic dermatitis. *Ambrosia* has a significant negative impact on the European economy through its affect on health, agriculture, biodiversity and even tourism. The rates at which *Ambrosia* is spreading and the rates at which individuals are becoming allergic are on the rise. The relative rise in the prevalence of allergy related to the coming *Ambrosia* epidemic may add an enormous burden on European health care costs. Furthermore, it invades crops potentially reducing yields of commercial agriculture products and further reduces the economy by reducing tourism. It is, therefore, necessary to increase awareness of invasive plants along with early detection and preventive management initiatives, along with sustainable strategies to control and reduce this invasive plant. To prevent future invasion and reduce current invasion will incur heavy costs to farmers in Europe. Decisions and policy regarding these strategies need to be based on cost-benefit ratios especially in the context of the effects on health and health care costs.

Our objectives were:

- To explore the combined pan-European impact of changes in climate, land use and air pollution on allergen pollen-induced diseases through a chain of quantitative physical and statistical models
- To study vulnerable groups of atopic patients and search for predictive biomarkers
- To establish statistical models of disease response to pollen concentrations for assessing future trends and risk
- To examine the effects of environmental change in animal models for theoretical model assessment and validation
- To communicate with relevant stakeholders and provide recommendations for potential response strategies to policy makers
- To collect and analyse available observed datasets and climate model simulations over Europe for the recent past (1990-2010) from previous and ongoing projects
- To identify climate conditions conducive to pollen emission, spread and outbursts

- To collect and analyse available future climate projections (2010-2030; 2050-2070) over Europe from previous and on-going projects
- Completion of targeted experiments as needed by pollen and air quality simulations
- Post-processing and downscaling of climate model output and provision of tailored climate data for pollen and air quality simulations
- Provide gridded simulations of recent past airborne birch, Ambrosia pollen, O3, NO2 and particulate matter concentrations and evaluate model skill using observations (not addressed in this report)
- Provide projections of future Ambrosia, birch pollen, ozone and particulate matter concentrations and their uncertainties (not addressed in this report)
- To determine the prevalence and future incidence of allergy to Ambrosia in children from different exposure sites
- To determine morbidity and severity coming from different levels of exposure during three consecutive pollination seasons in children allergic to Ambrosia
- To study de novo sensitisation to Ambrosia in aged vs. adult patients in regions with increasing Ambrosia exposure epidemiologically
- To study the mechanism of de novo sensitisation during age vs. sensitisation during youth by intra-individual comparisons
- To determine the clinical relevance of Ambrosia sensitisation in elderly patients with new onset eczema in a region with new exposure to Ambrosia
- To determine the influence of air pollution and climate-modified allergenic pollen on allergic asthma
- To investigate the mechanism involved in increased in vivo climate-modified pollen and pollutants on allergenicity
- To quantify spatial and temporal dimensions of the association between pollen exposure and allergy (prevalence, severity) using regional case studies, which includes consideration of urbanisation effects
- To perform a European-wide spatial integrated assessment of allergic disease vulnerability to environmental (climate, pollen, air quality, land use) variability and change

- To assess risk of allergic disease vulnerability to climate driven change in pollen concentrations and quantification of uncertainty
- To promote an effective communication flow amongst multidisciplinary beneficiaries to find a 'common language for successful exchange of information and knowledge.
- To disseminate results to the scientific community, defined target groups and opinion leaders, industrial players, media and general audiences
- To identify, reach and involve end users of the project's results, e.g., representative of public environment and health institutions (national Ministries of Environment and Ministries of Health, etc.), health professional associations, parent groups, and media

Atopica teams achieved their objectives. We evaluated and modeled the influence of changes in climate, air quality, land use, subsequent distribution of invasive allergenic plant species and allergic pollen distribution on human health. We explored the combined pan-European impact of changes in climate, land use and air pollution on allergen pollen-induced diseases through a chain of quantitative physical and statistical models, studied vulnerable groups of allergic patients and search for predictive factors, established statistical models of disease response to pollen concentrations for assessing future trends and risk, examined the effects of environmental change on pollen in laboratory experiments, and communicated these results with relevant stakeholders.

4.1.3 Description of the main S&T results/foregrounds

Environmental results/foregrounds

- We completed: i) production of a metadata bank as an information portal to large datasets held in different sites; ii) production of a databank of small size Atopica datasets. The metadata and databank are held centrally at UEA and are linked to, and accessible from, the Atopica internal web pages. They will be maintained by UEA for two years beyond the end of the project. The metadata covered climate datasets, pollen and air quality data, and clinical data, data for the Croatian spatial and temporal case-study analyses and socio-economic data from the project for the European-wide assessment. The Atopica metadatabase will be made publically available after the end of the project.
- We focused on the role of meteorological and climatic conditions in determining pollen emissions and concentrations at time scales from daily to seasonal. Observed and simulated climatic variables and pollen concentrations were intercompared at stations in different

European countries (Croatia, Hungary, Italy, Switzerland and France). It was also investigated whether the WRF and RegCM models used in Atopica reproduce the weather and climate conditions favourable to high pollen concentrations.

- At the daily scale we studied the relations between weather types typical of the ambrosia pollen season and the pollen outbursts. Four weather types were identified for the summer season, Atlantic Low (AL), Atlantic Ridge (AR), Blocking (BL), and North Atlantic Oscillation (NAO) and each day was classified in one of the four clusters. Composites of daily pollen loads indicate higher concentrations for one specific regime, the AL, which is characterised by anticyclonic hot weather over western/central Europe with southwesterly flow. High AL pollen counts are found in most French, Italian, and Swiss sites. Over Croatia high loads are found for the BL regime over the coastal regions, while in Hungarian sites almost no regime differencing is obtained.

- At the seasonal scale, we investigated the seasonal temperature and precipitation conditions that are particularly conducive to high pollen concentrations, since they determine both the release of pollen and its wash-out by rain. We analysed pollen, temperature and precipitation data at 7 stations lying in the southeast Europe pollen hotspot: Gior and Debrecen in Hungary (data for the period 1999-2012) and Ivanic, Samobor, Velica, Split and Zagreb in Croatia (data for the period 2008-2012). We calculated correlations between pollen amounts during the peak season (August-September) and temperature and precipitation during either the same period or the preceding two months (pre pollen season). The dominant signal was found to be a positive (negative) correlation with August-September temperature (precipitation), and negative (positive) correlation with June-July temperature (precipitation). These correlations are indicative of the following process: wet/cool conditions prior to the growing season favor the growth of ragweed, and warm/dry conditions during the growing season favor pollen release and inhibit pollen removal, both processes leading to high pollen amounts (and vice versa for low pollen amount conditions). We also found that the RegCM model is capable of reproducing these observed correlations.

  We then devised the following seasonal scale temperature and precipitation indices describing the process above:

$$Temperature\ index: \overline{T(June - July)} - \overline{T(August - September)}$$

$Precipitaton\ index: \overline{P(June-July)} - \overline{P(August-September)}$

The correlations with seasonal pollen amounts were negative for the temperature index and positive for the precipitation index at all 7 stations, both when using observed and modeled climate variables, confirming the climate/pollen interaction identified above. It is also suggested that the indices designed here might be useful seasonal prediction tools for pollen amounts over this region.

- We analysed available climate change projections over Europe from global and regional climate models, both to place the results of the Atopica projections within a broader context and to investigate whether climate conditions conducive to high pollen concentrations might change in intensity and frequency in the future. These simulations are available from two major international programs, CMIP5 (Climate Model Intercomparison Project 5) and CORDEX (COordinated Regional Downscaling Experiment). We focused this task onthe southeastern Europe "hot-spot" using the indices identified in the project.

- We investigated changes in the indices above for a RegCM scenario simulation driven by the HadGEM model, i.e., the models used to produce projections of future pollen concentrations, a large ensemble of CMIP5 GCMs and an ensemble of 5 CORDEX simulations at high resolution (up to 12 km). All ensembles of projections suggest that future climate conditions under global warming scenarios are generally more conducive to higher pollen concentration seasons over the southeast Europe pollen hot-spot region, however with a relatively large uncertainty in the quantification of this result due to a relatively large inter-model spread. Through a comparison between projected climate and total pollen amounts with RegCM from the project, we also found a linear relationship between 20-year mean Europe-wide temperature and pollen change, which could in principle be used as a long-term pollen prediction tool. This however includes not only the contribution of climate to pollen concentrations but also that of changes in Ambrosia distribution as well as dispersion of Ambrosia.

- We completed new simulations with the WRF and RegCM4 models over a domain encompassing the entire European region at 50 km grid spacing for use in the pollen and air quality calculations within the project. Simulations were completed for three periods, present day (1990-2010), near future (2010-2030) and long term (2050-2070), under the RCP4.5 and RCP8.5 greenhouse gas concentration pathways using the RegCM model driven by the HadGEM (ICTP) and the WRF model driven by the IPSL GCM (CNRS). High-resolution

(12 km) simulations for the Croatia case study were also conducted with the WRF model for years where observations of pollen loads were available (2012 and 2013).

- We produced local-scale daily climate scenarios for modelling the distribution of Ambrosia using the Sirius 2010 plant model for the baseline, 1990-2010, near future, 2010-2030, and long-term, 2050-2070, climate scenarios (WP2). This was achieved using ELPIS, a repository of local-scale climate scenarios for Europe based on downscaled data with the LARS-WG weather generator, which was applied to three contrasting GCMs in the CMIP5 archive, "hot" HadGEM2-ES (used to drive the RegCM pollen simulations), "medium" EC-EARTH and "cool" GISS-E2-R-CC and two representative concentration pathways, RCP4.5 and RCP8.5. The CSI was also calculated for IPSL-CM5A-MR climate projections to provide the required input to WP2.

- Results on 'A Process-Based Approach to Predicting the Effect of Climate Change on the Distribution of an Invasive Allergenic Plant in Europe; by Jonathan Storkey, Pierre Stratonovitch, Daniel S. Chapman, Francesco Vidotto, and Mikhail A. Semenov are available at DOI: 10.1371/journal.pone.0088156.

- We examined the prevalence and future incidence of allergy to Ambrosia in children from different exposure sites and to try to determine the morbidity and disease/symptom severity from different levels of exposure during three consecutive ragweed (Ambrosia) pollination seasons. They also aimed at identifying patients with *de novo* sensitisation to Ambrosia during three consecutive pollination seasons.

- Three distinct geographical regions of Croatia, differing in geographical, microclimate and other features, including different airborne ragweed pollen concentrations, were chosen for analysis: Slavonia, Zagreb and Dalmatia. Slavonia - with high ragweed pollen concentration; Zagreb area - with medium (intermediate) ragweed pollen concentration; Dalmatia - with low ragweed pollen concentration.

Experimental animal model results/foregrounds

- A dose-dependent robust model of pollen-induced allergic asthma in mice was established. Urban compared with rural pollen collected from plants in Austria induced more severe allergic asthma in mice. The environment influences ragweed pollen allergenicity and require further study to understand the mechanisms underlying the affects.

Clinical studies results/foregrounds

- Children were recruited through kindergartens and primary schools, and inclusion criteria included age (2-13 years) and residence in the local area. Informed consent was obtained from the parents following the delivery of a presentation and written material regarding the study. The study protocol and informed consent, based on the International and local legislation on the matter (Declaration of Helsinki, Declaration on Human Rights), were approved by the Local (Hospital's) Ethics Committee. Sample children underwent skin prick tests with commercially available standard allergen extracts. In addition to ragweed pollen they were tested for a standard range of inhaled allergens. The wheal size was recorded according to the ISAAC (International Study of Asthma and Allergies in Childhood) standardised protocol. Parents were also asked to complete the ISAAC Phase II questionnaire providing information about disease symptoms and severity, along with data on environment, lifestyle and clinical management. Questions were also asked about demographic factors (e.g., age and gender), socioeconomic factors (e.g., parents' income and education), lifestyle factors (e.g., smoking in pregnancy, breastfeeding, and household conditions), family history (e.g., birth order, parental and familiar atopy) and medical history (e.g., use of antibiotics, sensitisation to other allergens). Blood samples were taken from ¼ of children.

- In total, 4106 children were recruited to the study between April 2012 and June 2014. We identified in a cross sectional way, the influence and the prevalence of allergic diseases at a certain sensitisation level and examined socio-economic factors, to detect how these together with exposure levels interfere in developing sensitisation and symptoms/disease expression in allergic patients. We obtained detailed spatio-temporal data (from pollen diaries) during three consecutive ragweed pollination seasons in a small subset of participants, along with environmental data, both outdoor and indoor pollen exposure, air quality (pollution) and meteorological data.

- Identification of *de novo* sensitisation/allergy played an important role in this research. We obtained data on *de novo* sensitisation for most participants during three consecutive ragweed pollination seasons; along with follow ups on the morbidity and disease/symptom severity and the health impact data in children from the primary population allergic to Ambrosia.

- The total number of children sensitised to one or more aeroallergens was 27.6% of the sample, so quite a high percentage. The highest ragweed sensitisation rate (wheal size ≥3 mm in a skin prick test) was observed in the Zagreb area (14.58%), followed by similar

sensitisation rate in Slavonia (14.26%). The lowest ragweed sensitisation rate was in Dalmatia (1.53%), in the region the he lowest airborne ragweed pollen concentrations measured. The analysis of sensitisation in two age groups (4-6 and 7-10 years) revealed higher prevalence of Ambrosia, birch and *D. pteronyssinus* sensitisation as well as double sensitisation (birch and Ambrosia) in the older age group for all 3 regions. Sensitisation to the above-mentioned allergens was more prevalent in male participants. Levels of air pollution differed significantly in the 3 regions: the highest concentrations of NO_2, O_3 and PM10 were measured in the urban area of Zagreb, while the levels of air pollutants were low in Slavonia and Dalmatia.

- The *de novo* sensitisation rate to ragweed was 3% in Zagreb and 4.78 % in Slavonia in 2014. It was also observed that *de novo* sensitisation was more prevalent in the older age group.
- During this research, it emerged that there is a higher sensitisation rate for Ambrosia than other allergens. Sensitisation to Ambrosia also increases the prevalence of other symptomatic conditions in patients, such as wheezing, dyspnea, asthma, rhinitis, rhino-conjunctivitis, rashes and eczema.
- The highest ragweed sensitisation rate was in an urban area with the lowest air quality (Zagreb area).
- Regional differences in sensitisation to Ambrosia in Croatian children are not associated solely to pollen concentration and influences of other environmental factors cannot be excluded.
- *de novo* sensitisation to Ambrosia in children was estimated at a yearly rate of up to 3% and was dependent on the exposure level.
- Additional sensitisation to Ambrosia makes a population sicker.
- Sensitised children can have life lasting chronic allergic disorders,
- Sensitisation is associated with demographic (age, birth order, gender) and genetic factors (atopic parent).
- Mono-sensitisation is associated with genetic factors (atopic parent) but not with demographic factors.
- To our knowledge this is the first project to examine the impact of climate change upon allergy associated with pollen that models the impact from the changing plant distribution to

altered pollen production and dispersal and through to consequences for people. It is therefore, methodologically unique and a guide for future research on climate change and pollen allergy.

- Using a unique dataset of simulated future pollen levels and a systematic review of previous studies relating pollen levels to human health responses, our best estimate is that across Europe the number of individuals with Ambrosia allergy is likely to increase from current levels of 30 million to over 50 million by the period 2020-2040 and to over 70 million by 2041-2060. These number are reduced by around a quarter when only those who are expected to experience symptoms are considered. Currently areas most affected by Ambrosia pollen are around Hungary and the Balkans. In the future this area is likely to expand northwards into Germany, the Netherlands, Belgium, the UK and northern and eastern France. Increases are also projected in Northern Italy, Eastern Bulgaria and Romania. The majority of the pollen increase and hence increase in allergy is climate related. However, the project also indicates that measures to control the spread of Ambrosia can have a large public health impact. Therefore, as well as the previously documented agricultural benefits of Ambrosia control, such control would also have important public health benefits.

- Within Croatia a large cohort of over 4000 children was tested for allergy sensitisation and additionally a host of information gathered on disease symptoms and severity. In addition, questions were asked about demographic factors, socioeconomic factors, lifestyle factors, family history and medical history. A unique element was added to these data through the use of a Geographical Information System to identify a further range of variables relating to the environment of the child's home. These data were analysed statistically to examine the factors that affect sensitisation to Ambrosia as well as the development of allergic disease in this cohort of children. Overall, the results indicate that sensitisation was positively associated with Ambrosia pollen levels but that sensitisation levels did not rise further as the mean total annual pollen level increased beyond levels of around 4000 grains m^3. A range of demographic, genetic, early life history and environmental factors were also found to be important. In terms of the development of allergy disease in children, a range of demographic, genetic and socioeconomic factors were again significant. Ambrosia sensitisation was associated with all allergy disease with the exception of wheeze. Allergy disease was also associated with sensitisation to host of other allergens, although the effect of allergen varied by disease.

- A subset of around 100 children from this cohort were recruited between 2012 and 2014 and kept daily pollen diaries detailing the presence and severity of allergy symptoms (nose, eye and lung). For each of these children daily pollen, air quality and weather data were obtained from nearby recording stations. This has generated one of the largest datasets to date with which to relate daily allergy symptoms to daily pollen, weather and air pollution data. We are aware of only one similar but smaller study conducted in France. These data were analysed using time-series regression techniques and demonstrated clear links between Ambrosia pollen levels and allergy symptoms although the precise relationships and lags between pollen and symptoms vary by symptom type. Finally by using modelled daily baseline and daily future pollen data we have uniquely been able to examine how climate change may affect the severity of allergy symptoms into the future.

- One important feature of the work conducted in Atopica is that we have been transparent about the assumptions underlying our analyses and the fact that all stages of the analyses undertaken are subject to uncertainties. Within this, we highlight the poor availability of pollen and plant observation data as being particularly notable. The research would also have benefitted from a greater number of climate and air quality simulation as well as more years of patient data. Despite these assumptions and uncertainties we are confident that our key messages are robust.

4.1.4 Potential impact

Atopica project results are expected to have significant socio-economic impact along with impact on the environment, invasive alien species, and on the health and wellbeing of Europeans. Along with new knowledge, we have established a meta-database and a data bank contain information on climate, pollen and air quality as well as clinical data that will be publically available.

Specific impacts are:

- The identification of weather patterns and seasonal temperature and precipitation conditions most suitable for Ambrosia pollen outbursts and high seasonal Ambrosia pollen concentrations over different European regions, most noticeably the southeast Europe pollen hot-spot, including Hungary, Croatia and surrounding regions. In conjunction with operational seasonal climate forecasts routinely conducted at different European institutions, the defined metrics, e.g., the seasonal temperature and precipitation - pollen indices, have the potential to be used in seasonal prediction of pollen levels, which may help relevant stakeholders and policy-makers to devise suitable response strategies for sensitive

populations and public/private health providers. Finally, the temperature change - pollen relationship identified may provide a simple but effective tool to produce first-order estimates of future changes in Europe-wide pollen burdens based on model projections of global warming, which will also provide information for the design of long-term response policies.

- In the Atopica paper, "A Process-Based Approach to Predicting the Effect of Climate Change on the Distribution of an Invasive Allergenic Plant in Europe by Jonathan Storkey, Pierre Stratonovitch, Daniel S. Chapman, Francesco Vidotto, and Mikhail A. Semenov (DOI: 10.1371/journal.pone.0088156), the model predicted a northward shift in the available climatic niche for populations to establish and persist, creating a risk of increased health problems in countries including the UK and Denmark. This was accompanied by an increase in relative pollen production at the northern edge of its range. The southern European limit for *A. artemisiifolia* was not expected to change; populations continued to be limited by drought stress in Spain and Southern Italy. The process-based approach to modelling the impact of climate change on plant populations captures interactions of climate, land use and plant competition at the local scale. This report highlights potential changes and spread of the plants which will impact significantly in areas not currently affected.

- In a more recent Atopica paper, 'Effects of climate change and seed dispersal on airborne ragweed pollen loads in Europe', Hamaoui-Laguel, L. et al. (doi:10.1038/nclimate2652), predictive models indicate that about a third of the airborne pollen increase is due to on-going seed dispersal, irrespective of climate change. The remaining two-thirds are related to climate and land-use changes that will extend ragweed habitat suitability in northern and eastern Europe and increase pollen production in established ragweed areas owing to increasing CO_2. Therefore, climate change and ragweed seed dispersal in current and future suitable areas will increase airborne pollen concentrations. These results would impact the incidence and prevalence of ragweed allergy leading to increased numbers of Europeans sensitized and suffering from Ambrosia allergy.

- Cross-sectional prevalence data collection in children at different sites of exposure to both pollen (especially ragweed) and air pollution, identification of spatial data (children`s mobility and place of residence) in relation to exposure to ragweed pollen and pollutants, identification of *de novo* allergy to ragweed, will impact on the determination of the prevalence and future incidence in allergy to Ambrosia in children from different exposure sites as to pollen concentrations and air pollution, help determine the association between

the ragweed sensitisation rate and outdoor exposure (as well as indoor) and air pollutants, and help to better understand and quantify the effect of environmental and anthropogenic factors on air pollution and pollen concentration, and induced allergic diseases in Europe. Integration of different types of data (genetic, epigenetic, demographic, lifestyle, environmental) with clinical data obtained through this study will provide an unprecedented assessment of the atopic and allergic phenotype in the paediatric European population.

- The societal implications are that due to the on-going Ambrosia invasion and climate change, associated allergic disease is likely to increase in the EU in the next 40 years. The problem is likely to expand from its current range around Hungary and the Balkans northwards into Germany, the Netherlands, Belgium, the UK and northern and eastern France. This will impact health and health services in these countries. The impacts may be greatest in the poorer regions of the EU that have less capacity to adapt to these changes. Control measures against Ambrosia can have large human health benefits. Ambrosia spread as an important public health issue, and mitigation against climate change have beneficial impacts.

- In terms of managing current and future allergy associated with Ambrosia, Atopica has demonstrated impact by highlighting key groups of people who are most vulnerable to Ambrosia pollen and who are priorities for intervention and adaptation. The results from the time-series analysis quantified the impact of medical intervention upon Ambrosia, demonstrating an impact that medication has on allergy symptom reduction. These results provide guides to possible adaptation measures.

- A publically available meta-database from the results will impact future studies as it will enable scientists to further utilize Atopica data.

- Dissemination of project results has the potential to increase awareness of Ambrosia, what it looks like, where to find it, what it is does to allergic individuals and how climate and environment may influence Europeans. Dissemination of the results may impact the individual, risk assessors, management/mitigation practices, government/policy-making decisions and risk managers.

- A main impact would be that airborne pollen are considered an air quality issue, as it is a particulate matter in the air that causes illness, similar to other $PM_{2.5}$ of PM_{10} particulates. When airborne Ambrosia pollen levels are measured and have thresholds associated with them, the impact would be considerable. For example, management and mitigation strategies would have to be implemented to maintain levels below thresholds. This would

have an impact on the concentration of pollen in the air and could reduce the number of individuals who will become sensitized to the pollen and reduce exacerbations in allergic patients. This would then reduce health-related costs, productivity (less loss of days work, less missed school days, etc.) and reduce increasing plant spread with the associated impact on agriculture and industry.

4.1.5 Address of the project public website and contact details

A project logo, diagrams and photographs illustrating and promoting the work of the project (including videos, etc.), as well as the list of all beneficiaries with the corresponding contact names can be submitted without any restriction.

The website is: www.atopica.eu.

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4.2 Use of dissemination of foreground

This part of the report is available on the Participant Portal

4.3 Report on societal implications

This part of the report is available on the Participant Portal