The Director General

Maisons-Alfort, 20 October 2020

OPINION
of the French Agency for Food, Environmental and Occupational Health & Safety

on the health impact and related costs of common ragweed in France

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ANSES undertakes independent and pluralistic scientific expert assessments.

ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.

It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with all necessary information concerning these risks as well as the requisite expertise and scientific and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).

Its opinions are published on its website. This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated 12 October 2020 shall prevail.

On 5 April 2018, ANSES received a formal request from the Directorate General for Health (DGS) to undertake the following expert appraisal: "state of knowledge on the health impact, and the related economic impact, of common ragweed in France and prediction of their changes".

1. Background and purpose of the request

As underlined in a previous ANSES publication (ANSES 2014), common ragweed[1] releases a highly allergenic pollen that can easily travel long distances and is thus a major public health challenge. Widespread in Hungary and in northern Italy, ragweed is also found in the Rhône Valley in France. Recent maps have shown wider spread of the plant in France over the past few years.

[1] The word "ragweed" will be used in the rest of the document in reference to common ragweed, the species of interest in this expert appraisal.

The health impact of ragweed is regularly assessed in Auvergne-Rhône-Alpes, the most affected region of France, by the Regional Health Agency (ARS) and the Regional Health Observatory (ORS). According to a telephone survey of the general public, the prevalence of ragweed allergy was estimated at 12.5% to 14.1% in this region and has been increasing since 2004 (Anzivino, Marant-Micallef, and Sonko 2014). High spatial disparities have been observed. Expenditure associated with this allergy (including use of medication, consultations and sick leave) was estimated at €8.9 to €13.2 million in 2014 in the Rhône-Alpes region (Gelas 2015). However, the health and economic impact of ragweed still needs to be assessed in the rest of France (outside of Auvergne-Rhône-Alpes).

The Third National Environmental Health Action Plan (2015-2019) provides for measures for the monitoring and assessment of ragweed in France, but with no legal framework. Decree no. 2017-645 of 26 April 2017 defines measures intended to prevent the appearance of ragweed or limit its spread; their implementation is placed under the responsibility of prefects after opinions issued by the ARS and the Departmental Council for the Environment and Health and Technological Risks (CODERST).

In this context, the Directorate General for Health submitted a formal request to ANSES on 5 April 2018 to:

- Document the prevalence of common ragweed allergy and its changes in recent years in France and abroad based on the level of exposure to ragweed pollen and the level of infestation.
- Identify potential mechanisms and factors associated with differentiated changes in this prevalence. These may include intrinsic factors related to the plant (local spread) and extrinsic factors related to human activity and climate change possibly favouring the spread of ragweed.
- Estimate the prevalence of ragweed allergy across France and how it may develop based on proposed scenarios of changes in the state of infestation. A distribution by *département* will be investigated.
- Assess the cost of ragweed allergy across France and how it may change taking the same change scenarios into account. A distribution of these costs by *département* will be investigated.

The impacts of ragweed vary in nature. In light of the objectives set, this appraisal focused on the health impact and ultimately the costs associated with this impact. However, data are also given for informational purposes to drive reflections concerning the agri-environmental impacts.

2. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with French standard NF X 50-110 "Quality in Expert Appraisals – General requirements of Competence for Expert Appraisals (May 2003)".

The expert appraisal falls within the sphere of competence of the Expert Committees (CES) on "Assessment of the risks related to air environments" (the lead CES) and "Biological risks for plant health". ANSES entrusted the expert appraisal to an *ad hoc* working group (WG), appointed after a public call for applications[2]. The methodological and scientific aspects of the work were presented to the Expert Committees between 5 July 2018 and 6 July 2020. The work was ultimately adopted by the CES on "Assessment of the risks related to air environments" on 6 July 2020.

[2] The "Ragweed" Working Group met 14 times between 18 January 2019 and 6 May 2020.

The expert appraisal work drew on a summary and critical analysis of the data published in the literature (scientific articles and institutional reports). Data were also collected during hearings with stakeholders involved in the control of ragweed or having produced scientific documentation of interest (Ragweed Observatory – FREDON France, Auvergne-Rhône-Alpes ARS, and Auvergne-Rhône-Alpes ORS). This data collection continued through a national questionnaire-based survey of healthcare professionals aiming to determine their knowledge of the health issues associated with ragweed as well as their practices. An international consultation was also held to gather information about the (health and environmental) impact of ragweed and the management methods potentially adopted abroad. Lastly, data required to assess the health impact of ragweed were obtained with the assistance of:

- Atmo Auvergne-Rhône-Alpes[3];
- the Auvergne-Rhône-Alpes ARS;
- the National Aerobiological Surveillance Network (RNSA);
- the Finnish Meteorological Institute.

ANSES analyses interests declared by experts before they are appointed and throughout their work in order to prevent risks of conflicts of interest in relation to the points addressed in expert appraisals. The experts' declarations of interests are published on the ANSES website (www.anses.fr).

3. ANALYSIS AND CONCLUSIONS OF THE CES AND WG

The CES on "Assessment of the risks related to air environments" adopted the collective appraisal work of the WG and its conclusions and recommendations, which are covered in this Opinion, at its meetings of 9 June 2020, 25 June 2020 and 6 July 2020 and informed the ANSES General Directorate accordingly.

3.1. Summary of results

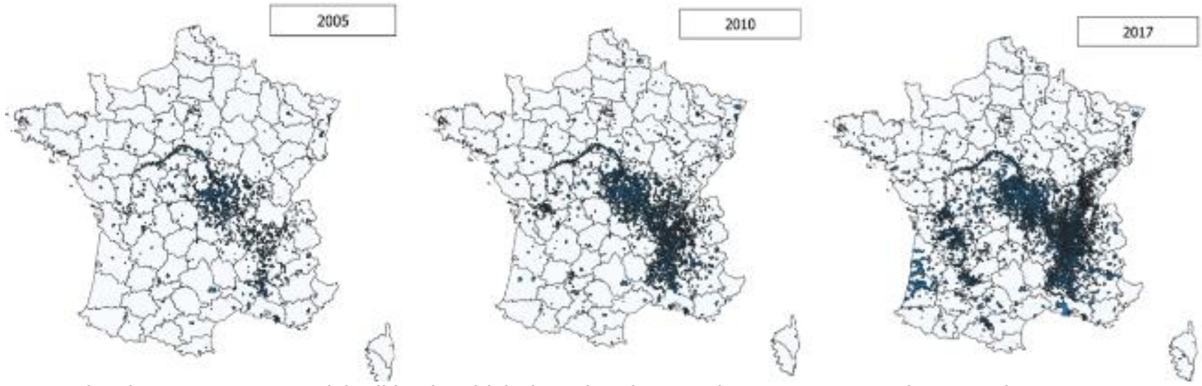
Description of common ragweed

Taxonomy, origin and current range

Common ragweed (*Ambrosia artemisiifolia* L., syn. *A. elatior* L.) is part of the Asteraceae family (tribe: *Heliantheae*; subtribe: *Ambrosiinae*). It was first identified in Europe in the late 18th century. It is currently found in a high percentage of European countries, mainly between latitudes 42° and 52° N. It is particularly abundant in the south of Eastern and Central Europe (primarily in Hungary, Croatia and Serbia).

In France, the main ragweed infestation areas are currently the Rhône Valley, the Loire Valley and the Centre-Val de Loire region. Since 2005, ragweed populations have been rapidly spreading and increasing in density in France (Figure 1). They were recently introduced into Poitou-Charentes, Midi-Pyrénées, Bourgogne-Franche-Comté, and Auvergne. Ragweed has also been reported in Martinique and Guadeloupe.

[3] Air quality monitoring associations for the Auvergne-Rhône-Alpes region



The dots represent municipalities in which there has been at least one report of ragweed. Source: Ragweed Observatory, FREDON France. Maps are based on the data from the network of national botanical and partner conservatories and on the validated AtlaSanté data of the reporting platform.

Figure 1. Maps showing the distribution of ragweed in France from 2005 to 2017

<u>Seed dispersal modes and vectors for spread</u>

There are multiple dispersal modes for ragweed seeds and vectors for the spread of the plant. Natural dispersal of the seeds occurs over short (barochory, a few metres) to long (hydrochory, several kilometres) distances but is considered minor. There are more anthropogenic vectors for the spread of ragweed: agricultural seeds, animal feed, bird seeds, agricultural machinery, contaminated soil, etc. These play a major role, showing an upward trend over the years; the propagation distances are generally long and large quantities of seeds are usually dispersed.

<u>Flowering and pollen</u>

Ragweed begins to flower when the days start getting shorter, after the summer solstice, when there is less than 14 hours of daylight. The phenological growth and flowering of the ragweed introduced in Europe are strongly correlated with latitude. Ragweed from northern latitudes in Germany flowers and disperses its pollen and seeds up to five weeks earlier than ragweed from southern France, for example. This high phenological variability may facilitate its future expansion. There also appears to be a longitudinal gradient in flowering phenology, where pollen grains are released earlier in Eastern than in Western Europe.

On the scale of a day, the release of pollen grains by ragweed, dependent on an increase in temperatures and low relative humidity, generally occurs after sunrise. It peaks from morning to mid-day (complete release of the grains within six hours). Ragweed pollen grains (17-29 µm) are spheroidal and have three furrows and three pores. They are easily dispersed in the atmosphere due to their low density and low settling velocity. Ragweed pollen grains can travel distances of up to a few hundred kilometres depending on the weather conditions. A single plant can produce 100 million to 3 billion pollen grains depending on its size.

In connection with climate change, by 2060, the annual quantity of ragweed pollen in the atmosphere is expected to increase and the area affected by this pollen is predicted to expand. The increase in CO_2 concentrations in the atmosphere is promoting the production of ragweed pollen.

<u>Ecology of ragweed</u>

Ragweed is a heliophilous pioneer plant that currently colonises all types of open disturbed habitats whether in its area of introduction, in France, or in its area of origin. It is also a ruderal species that grows on roadsides, in urban and suburban wastelands, on active construction sites and in abandoned quarries. It colonises certain disturbed semi-natural habitats such as riverbanks. In the agricultural sector, ragweed is considered a weed that infests spring crops (sunflower, peas, soya, maize, etc.), intercrops, set-aside land and uncultivated agricultural lands. In cultivated environments, it is highly competitive and can cause major yield losses, especially in row crops.

Ragweed has a broad ecological amplitude. It grows in a wide variety of soils with sandy or silty and even clayey-silty textures. The optimum soil pH for its development appears to be between 6 and 7 but the plant is also found in France on acidic and alkaline soils. Ragweed has a high capacity to resist water stress as well as salt and pollutants on roadsides.

- **Species management: strategy, regulations, control methods**

The primary objective of ragweed management is to limit pollen production in order to reduce related allergies. The secondary objective is to limit its undesirable effects on agricultural production. To achieve these objectives, Bullock *et al.* (2013) propose a management strategy based on the following four components: prevention, control (with mechanical, chemical or biological methods), information campaigns aimed at stakeholders and the general public, and monitoring.

The prevention and control of ragweed in France are largely organised by the public authorities. They rely on a legislative and regulatory framework, based primarily on the French Public Health Code (CSP). At the departmental level, the ragweed control strategy can be structured around an order issued by the prefecture in agreement with the Director General of the ARS and the Departmental Council for the Environment and Health and Technological Risks (CODERST) when at least one ragweed species has been reported or is likely to be present (Article R. 1338-4 of the CSP). In December 2019, 43 prefectoral orders and 25 control plans were identified. It is important to stress that many areas infested with ragweed in mainland France lack a prefectoral order.

Efforts have been undertaken to identify the main existing control methods (physical, chemical and biological). These methods aim to reduce, either temporarily or in the long term, the release of pollen and/or the spread of the seeds. Mechanical and chemical control has to be implemented for several years to bring about a long-term reduction in ragweed populations; all such methods must be carried out at specific stages of the plant's development and most have to be repeated at least twice a year. Techniques using agricultural machinery, although effective, are liable to be a new source of spreading ragweed seeds.

- **System for the metrological monitoring of pollen**

In France, the National Aerobiological Surveillance Network (RNSA) operates the main system for monitoring pollen. In 2019, it managed 73 all-pollen measurement sites equipped with sensors spread out across France (including in Cayenne, French Guiana); 10 additional sites are specifically dedicated to the monitoring of ragweed pollen. The distribution of the sensors throughout metropolitan France has been optimised to reduce inter-regional differences and the network has been adjusted based on population sizes concerned by pollen information. The pollen counts provided by the RNSA (in number of pollen grains per m^3 of air) are considered approximations of the exposure of the population.

The RNSA developed the theoretical allergy risk indicator ($RAth$) representing the clinical relevance of a pollen for an allergic individual in a specific area. It is on a scale of 0 (zero risk) to 5 (very high risk) and depends on the allergenic potential of the pollen, the duration of the pollen season, the weather conditions, pollen counts[4], and the geographic situation, i.e. infestation of the area by the species. The RNSA then developed the concept of allergy risk associated with exposure to pollen (RAEP) providing forecasts of the risk of allergy for the days to come. The RAEP is a score with values from 0 (zero risk) to 5 (very high risk). It takes several types of data into account: $RAth$, clinical observations (from doctors of the RNSA's sentinel network), weekly

[4] Pollen count: number of pollen grains in the air for a taxon.

phenological observations, and weather forecasts for the coming days (temperatures, precipitation, wind). An RAEP≥3 is considered clinically relevant, i.e. it indicates that people with allergies are very likely to develop symptoms. A correspondence between the RAEP and pollen counts was also established by the RNSA. For ragweed, an RAEP≥3 in an infested area corresponds to ≥6 ragweed pollen grains[5] per m^3 of air over the course of a day; this is the concentration from which allergic symptoms can appear in individuals with ragweed pollen allergy.

- **Modelling the spatial distribution of ragweed and its pollen**

Modelling is a particularly relevant tool for simulating or predicting the spatial distribution of ragweed and its pollen. These predictions are based on a series of numerical models characterising the weather conditions in the geographic area of interest, pollen emissions simulated using a detailed map of the plant's distribution, and pollen dispersal in the air.

Spatial distribution of ragweed

In the literature, three approaches have been used to develop detailed maps of ragweed's spatial distribution. The first approach is based on a presence and absence inventory. It is considered a bottom-up approach since the distribution is based on field observations and reports. The second approach uses the pollen counts obtained in measurement sites combined with land use data. It is considered a top-down approach since the pollen counts are used as inputs to obtain a map of the emitting source. Three publications outline methodological changes in the top-down approach, leading to the creation of a European ragweed inventory. The third approach is based on the use of ecological modelling of ragweed's presence and proliferation. These mathematical approaches are particularly relevant for the development of proliferation scenarios in connection with long-term climate change or the introduction of control or management policies.

The top-down approach combining pollen counts and land use data shows the best predictive performance whereas maps from ecological modelling very clearly produce the weakest results. Therefore, it seems that for the continuous modelling of pollen levels, the top-down approach should be favoured; it is simple and has promising potential for improvement.

Pollen emissions

The parameterisation of pollen emissions aims to represent the total amount of pollen emitted by the plant as well as the timing of these emissions. Emission processing modules are included in the current reference models such as COSMO-ART, SILAM, CHIMERE, and regCM[6]. Atmo Auvergne-Rhône-Alpes has adopted an empirical approach, based on pollen counts measured since 2002, to characterise ragweed pollen emissions in its region.

Pollen dispersal

Pollen dispersal modelling is the final link in the modelling chain and is used to map atmospheric levels of pollen once it has been released by the plant. The models initially developed for common atmospheric pollutants have been adapted for pollen. For ragweed pollen, the COSMO-ART and SILAM systems were assessed.

The COSMO-ART dispersal model considers weather forecasts and dispersal in the same simulation. This approach is able to model interactions between weather and air quality, for

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[5] For information, the corresponding value for grass pollen is ≥10 grains per m^3 of air.

[6] **COSMO-ART:** implemented by MeteoSwiss, it is an extension of the COSMO weather forecast model. **SILAM**: System for Integrated Modelling of Atmospheric Composition, developed by the Finnish Meteorological Institute. **CHIMERE**: chemistry-transport model developed by Institut P.S. Laplace CNRS and INERIS. **RegCM**: The Regional Climate Model System, developed by the National Center for Atmospheric Research. All initially developed to model common atmospheric pollutants, they have been adapted for the modelling of certain types of pollen.

example interactions between aerosols and clouds. The literature shows that the COSMO-ART system has good predictive performance, both in terms of representing the distribution of ragweed and representing the processes leading to the emission of pollen grains.

The SILAM chemistry-transport model, developed by the Finnish Meteorological Institute, is used to model concentrations of pollutants in ambient air, including ragweed pollen, throughout Europe. After calibration of the model's outputs, atmospheric pollen levels are considered well modelled in Europe.

Changes in spatial distribution according to various future scenarios

Modelling ragweed spread and pollen dispersal is a way to predict, among other things, changes in this spread and in pollen concentrations according to various future scenarios in connection with climate change, changes in land use (urbanisation, agricultural policies), or proliferation control (public policy).

The climate change and land use scenarios examined by Bullock *et al.* (2013) all predict a shift in infested areas towards Northern Europe by 2050, due to an increase in the climatic quality of the environment for ragweed. A similar shift in ragweed pollen clouds is also predicted, reflecting the shift in the species' distribution.

The results of the ATOPICA project[7] show that by 2060, there will be longer pollen seasons and higher pollen concentrations across Europe, including in areas that are not currently infested. Seed dispersal will be responsible for a 29% to 44% increase in atmospheric pollen concentrations, whereas the impact of climate change is much lower, evaluated at 13% to 17%.

These long-term models have several limitations related to the use of unsound ecological models and the lack of processes for calibrating or validating the models' outputs due to a lack of measured data. There are therefore multiple uncertainties associated with the results, making them less relevant for (future) health impact assessments.

- **State of knowledge on ragweed allergy and its characteristics**

Principle

Allergy is due to a hypersensitivity mechanism initiated by a specific immune response to a foreign substance, i.e. an allergen. It includes a first sensitisation stage, with no clinical expression, where the allergen is brought into contact with the mucous membranes, leading to an immune reaction characterised by the production of specific immunoglobulin E antibodies. A second stage is characterised by the onset of symptoms when the allergen comes into contact with the mucous membranes. However, progression to this second stage is not systematic. The timing leading up to allergic sensitisation and symptoms is poorly understood. This sequence of events, called the allergic march, generally occurs in an early stage of life and may last many years or else spontaneously disappear with age. Several environmental and individual risk factors, as well as their potential interactions, come into play in the development and onset of allergy. In the majority of cases, the clinical symptoms of allergy occur before the age of 20, around which the highest level of prevalence is observed.

➯ Ragweed pollen allergy has some specific characteristics. Several European studies underline that most adults who are newly allergic to ragweed did not have a genetic predisposition. In Europe, the average age of allergy onset is higher for ragweed pollen (>30 years) than for other pollens. Nonetheless, in the United States, where ragweed is native, allergic sensitisation is

[7] The ATOPICA project received funding from the European Union's Seventh Framework Programme: FP7/2007-2013 no. 282687.

observed from a very early age. Similarly, in areas with historical ragweed infestation in Europe, such as France and Hungary, allergic sensitisation to ragweed pollen is observed in very young children.

Allergic rhinitis

Allergic rhinitis refers to all of the functional nasal manifestations caused by the development of inflammation occurring when the mucous membranes are exposed to an airborne allergen. The typical symptoms are runny nose, sneezing, nasal congestion and nasal itching. There can be inflammation outside of the nasal sphere, affecting the tear ducts and conjunctiva. The symptoms then include conjunctivitis, itching, redness, watery eyes and swollen eyelids.

➪ Ragweed-induced allergic rhinitis or pollinosis is associated with the aforementioned typical symptoms but has some specific characteristics. In France, this form of allergic rhinitis usually occurs from mid-August to mid-September, when ragweed pollen is generally expected to reach peak levels, setting it apart from other pollens recognised as being highly allergenic, such as those of birch, cypress, and grasses. Due to its high allergenic potential, it is assumed that ragweed pollen causes symptoms in individuals with allergy whenever there are six or more grains per m^3 of air. This very low threshold makes the symptoms difficult to anticipate and control. It is very likely that higher levels cause symptoms that are proportionally more severe or more difficult to control.

Diagnosis

The clinical diagnosis of allergy or allergic rhinitis is based on the occurrence of typical symptoms, determination of the allergic nature of these symptoms, and identification of the responsible allergen; this primarily involves determining whether or not there is a seasonal pattern or a triggering factor. A skin test generally corroborates the diagnostic hypothesis by indicating whether there has been allergic sensitisation. If skin testing is inconclusive or needs to be validated, biological testing is performed using *in vitro* immunochemical techniques conducted in serum. These skin or blood tests only indicate whether there has been allergic sensitisation; the allergen in question is not necessarily responsible for the observed symptoms.

➪ The diagnosis of ragweed allergy goes through the same steps. The seasonality of the symptoms is fairly different from that of other pollens, thus enabling ragweed pollen to be identified as the triggering factor. The geographic locations and travel of patients should also be taken into account in the diagnosis. To be allergic to ragweed, a patient with symptoms in summer must have been in contact with ragweed pollen in the past, unless there is a potential cross-allergy.

Management and treatment

The management of allergic rhinitis involves the initiation of medical treatment to relieve the patient's symptoms, the control or avoidance of the factors triggering the symptoms, and patient education with regard to allergy in general and its treatment in order to improve compliance. Despite the harshness of the symptoms, allergic rhinitis is often underdiagnosed and undertreated, as it is considered as commonplace. The aim of first-line medical treatments is to provide patients with relief by reducing the intensity of their symptoms. The treatments are the same regardless of the allergen triggering the allergic rhinitis. Two complementary therapeutic classes are mainly used: antihistamines and corticosteroids in the form of nasal sprays. Combined therapy seems to be a relevant choice according to the latest international guidelines. In the most severe or disabling cases, desensitisation or specific immunotherapy is considered. Its aim is to induce tolerance in the body to an allergen of interest.

➪ The management and treatment of allergic rhinitis induced by ragweed pollen follow the general stages described above. Guidelines aiming to reduce exposure to pollen are essential in areas infested by the plant and in frontline areas.

Comorbidities

Allergic rhinitis is associated with multiple comorbidities, of which asthma is undoubtedly the most common. Although they both involve the same inflammatory cells and mediators, asthma affects the lower airways whereas respiratory allergy affects the upper spheres (eyes, nose, and throat). Asthma is a chronic inflammatory disease of the airways that typically manifests as reversible (spontaneously or with treatment) airflow obstruction, bronchial hyperreactivity and/or recurrent episodes of respiratory symptoms such as shortage of breath, wheezing, and coughing. The symptoms are episodic and can occur after exercise or after contact with a triggering factor. Allergy is a major risk factor for asthma, which means that it often precedes it. Up to 85% of asthmatic individuals have allergic rhinitis and 40% of individuals with allergic rhinitis experience asthma.

↳ Ragweed allergy seems to accompany asthma more frequently than other pollen allergies, as reported by several healthcare professionals consulted as part of this expert appraisal. However, there are very few data on this issue in the scientific literature.

Loss of quality of life

Allergic rhinitis heavily impacts quality of life. It can have negative consequences in terms of social and professional life, both in adults and in younger populations. Increased school absenteeism and reduced academic performance have been described.

↳ Ragweed allergy is no exception. According to the feedback from the survey of healthcare professionals conducted as part of this expert appraisal, it appears to be particularly disabling compared to other pollen allergies. However, in the literature, there are no studies comparing the impact of ragweed allergy on quality of life to the impact of grass allergy on quality of life.

Epidemiological tools

Several questionnaires dealing with allergy have been proposed and validated by the scientific community. They may include questions focusing on the typical symptoms (eyes, nose and throat) or the diagnosis itself (allergy, rhinitis and hay fever). The most informative question for identifying individuals with rhinitis mentions the occurrence of symptoms ("sneezing or a blocked or runny nose") without any respiratory infection ("when you did not have a cold or the flu"). Some recent questionnaires ask the respondents to list what triggered their symptoms (animals, dust, pollen, other) and/or include questions about the timing of their symptoms over the past year (frequency by season or by month). Clinical data, on allergic sensitisation for example, can be collected in a sub-sample of the study population in order to combine this information with that from the questionnaires.

↳ There is no standardised questionnaire specific to ragweed allergy. Identifying individuals allergic to ragweed thus requires the combined use of questions mentioning the symptoms or diagnosis and/or questions specifying the trigger or timing of the symptoms. Allergic sensitisation measurement can also be used if available.

Medical-administrative databases are emerging tools enabling the large-scale identification of sick individuals based on their reimbursements for or consumption of medical care. However, the use of these databases is only relevant when the expression of a disease is intrinsically and specifically related to the recorded procedures; otherwise, a classification bias can be introduced. The medications currently considered in the literature to identify allergic individuals from medical-administrative databases are those used as first-line treatments to reduce the symptoms.

↳ There is no specific, validated definition of allergic rhinitis induced by ragweed pollen based on medical-administrative data. Identifying individuals allergic to ragweed with such data would require the use of one or more definitions available in the literature, combined with a time period indicator such as the month or pollen season.

- **Prevalence of ragweed pollen allergy**

An estimated one-third of adults are allergic to pollen (all types) in France; this prevalence appears to be lower in children and adolescents, ranging from 7% to 20%. However, an exact estimate in the population is difficult to obtain due to the heterogeneity of the available data (methods and study populations). There are also sharp geographic variations, depending on the types of pollen observed in the air and their respective quantities. In France in 2006, the prevalence of allergic rhinitis ranged from 26% in the Southwest region to 37% near the Mediterranean. Lastly, the trivialisation of allergic rhinitis has made it a disease generally under-reported by the participants in these studies.

↳ Estimating the prevalence of ragweed allergy faces the same limitations. Major European studies now include the measurement of allergic sensitisation to ragweed in their panels of skin prick tests, thus enabling the prevalence of this sensitisation to be estimated on a large scale. Local studies have also been undertaken, very often in ragweed-infested areas. They have mainly focused on the quantification or estimation of the health impact of ragweed on their territories, considering allergic sensitisation (measured in patients undergoing allergy testing, for example) or the presence of symptoms (with detailed questionnaires on seasonality and triggers).

<u>In France</u>

In 1999, a telephone survey conducted by CAREPS[8] estimated that 8.5% of the population in the Rhône-Alpes region was allergic to ragweed. In 2004 and 2014, this figure was updated through studies financed by the Rhône-Alpes ARS, enabling changes in this prevalence to be assessed over time, in association with the presence of the plant (Anzivino, Marant-Micallef, and Sonko 2014). A methodology similar to that used in 1999 estimated the prevalence of ragweed allergy at 9.2% in 2004 and 13.3% in 2014. This increase was largely due to the rise in the number of cases in areas considered as highly exposed to pollen (from 10.6% to 21.0%). An increase in prevalence over time is expected and likely given the spread of the plant, the increase in atmospheric pollen levels, and the natural course of allergies (from allergic sensitisation to clinical expression). However, the magnitude of this increase is uncertain due to methodological differences noted between the 2004 and 2014 surveys.

French national health insurance data on reimbursements for medical care have been used since 2009 in Rhône-Alpes to quantify the health impact of ragweed allergy. Individuals with ragweed allergy were identified by matching reimbursements for medications ("tracers" of allergy) with the pollen season (from July to October) for 2012, 2013, 2014, and 2017. In 2012, the prevalence of ragweed allergy was thus estimated at 4.2% to 5.3%, even reaching 8.6% at the cantonal level (Gelas 2013). In 2013 and 2014, the corresponding figures were very similar (from 3.9% to 5.1% and from 3.5% to 4.7%, respectively) (Gelas 2015). In 2017, for the new Auvergne-Rhône-Alpes region, the figure was estimated at 10.1%, reaching 37.3% in certain municipalities (Auvergne-Rhône-Alpes ORS and ARS 2018). It is difficult to compare the figures from 2017 with those of previous years, due to the use of different methodologies: the region was larger, the database was more complete, and the list of "tracer" medications included anti-asthma medications for the first time in 2017.

<u>In Europe</u>

As part of the ATOPICA project, the current and future health impact of ragweed was estimated in Europe by Lake *et al.* (2017). A relationship expressing the proportion of the population with allergic sensitisation to ragweed according to (annual) pollen levels in the air was established based on the data in the literature. This relationship was then applied to maps of annual ragweed

[8] Rhône-Alpes Centre for Epidemiology and Preventive Health.

pollen levels specifically modelled as part of the project. This indicates that there are currently 23 to 34 million individuals sensitised to ragweed in the 28 EU Member States. This range is expected to reach 62 to 79 million by 2060 due to the spread of the plant to areas currently spared and the expected increase in atmospheric pollen levels, partly related to climate change. There are multiple uncertainties associated with these health impact assessments, in particular due to the choice of allergic sensitisation as the outcome of interest (with no systematic clinical relevance), the applied relationship (unreliable at low concentrations, similar for all areas, and having a wide confidence interval), and the modelling of current and future pollen levels.

■ Possible approaches for estimating the costs associated with ragweed

The nature of the costs and the method used to evaluate them can be significantly influenced by the point of view considered in the economic analysis[9,10]. In order to take a broad economic view, the experts of the working group chose to express the costs regardless of the type of stakeholder.

Table 1. Types of impacts, costs and potential monetisation approaches

<table>
<tr><th></th><th></th><th>Cost considered</th><th>Economic approach</th><th>Financial approach</th></tr>
<tr><td rowspan="10">Impacts of ragweed</td><td rowspan="6">Human health</td><td>Medical care</td><td>✓</td><td>✓</td></tr>
<tr><td>Production losses</td><td>✓</td><td>✓</td></tr>
<tr><td>Quality of life</td><td>✓</td><td>✗</td></tr>
<tr><td>Choice of residence</td><td>✓</td><td>✗</td></tr>
<tr><td>Patients’ families – empathy</td><td>✓</td><td>✗</td></tr>
<tr><td>Non-allergic exposed population – risk value</td><td>✓</td><td>✗</td></tr>
<tr><td rowspan="3">Agriculture*</td><td>Yield losses</td><td colspan="2">✓</td></tr>
<tr><td>Management cost</td><td colspan="2">✓</td></tr>
<tr><td>Suboptimal crop choices</td><td colspan="2">✓</td></tr>
<tr><td>Wild fauna and flora</td><td>Ecosystem service losses</td><td>✓</td><td>✗</td></tr>
</table>

** The dichotomy between the financial approach and the economic approach is no longer relevant due to the evaluation of ragweed’s impact on a production activity, visible through market values.*

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[9] Depending on the point of view adopted, the scope of the costs can vary. The senatorial report by Husson and Aïchi (2015) dealing with atmospheric pollution affirmed that merely measuring the health impact of atmospheric pollution in terms of gross domestic product [=expenditure] would be a restrictive approach that would only take one aspect of cost (the cost for public finance) into account and would thus exclude a large part of the cost borne by society.

[10] HAS. 2012. A Methodological guide – Choices in methods for economic evaluation. Guideline 2 : the perspective

The cost of the impacts of ragweed can be estimated using various methodologies, reflecting different realities (Table 1). From an accounting standpoint, it is possible to only consider costs in relation to their market valuation, when this exists. This "financial" approach can be overtaken by an economic vision through opportunity cost. The major drawback of the economic approach is the lack of data (mainly relating to willingness to pay). It should be noted that ragweed is also costly to society through the monitoring and management schemes needed.

Cost of medical care

Regarding ragweed allergy, the most complete approach for the evaluation of the cost of medical care in France is set out in a series of reports produced by the ARS for the ORS in the Auvergne-Rhône-Alpes region. For the entire region, the overall cost of medical care consumption[11] in association with ragweed allergy (including sick leave) was estimated at more than €40.6 million in 2017 (Auvergne-Rhône-Alpes ORS and ARS 2018). Within a narrow vision excluding the cost of sick leave paid for by France's health insurance scheme, the annual average cost per allergic individual was estimated at €53.

As part of a financial approach, the estimate of the Auvergne-Rhône-Alpes ARS and ORS appears as the most robust and the best suited for nationwide use in France. However, this approach should be considered as a partial view of the cost that only takes into consideration part of the economic value assigned to treatments. It thus constitutes a low-end estimate of the financial costs.

There is no willingness to pay[12] (WTP) for any of the therapeutic strategies dealing with the health consequences of ragweed.

Cost of production losses

A worker who is sick due to a ragweed allergy can generate two types of economic losses through their productive activity, which will vary depending on the consequences of the disease: i) the worker can be absent from their job, which can result in a loss of production, and ii) the worker can be present at their job, but with a reduced production capacity due to their state of health; this decrease in productivity ultimately leads to a loss of production.

It may be considered that the cost of ragweed on the job market can be measured in terms of the associated French national health insurance expenses for employees. The Auvergne-Rhône-Alpes ARS-ORS report is thus a good indicator in this regard. The annual average cost of sick leave was estimated at €8.60 per allergic individual receiving medical care. The accounting for production losses for non-employees is much more complex and relies on specific surveys on WTP.

Cost of lost quality of life

Poor health corresponds to loss of well-being. Several methods have been created to characterise a state of health, relying on standardised questionnaires, whether generic or specific to a disease. This state of health can then be translated into individual preference. Broadly speaking, utility measures of quality of life range from 0 (corresponding to death) to 1 (equal to perfect health). This reasoning can be applied in contexts of mortality and morbidity. The combination of these situations can lead to the determination of a health impact indicator, which can be assigned an economic value.

[11] For all of these costs, the valuation corresponds to the total cost/overall expenditure, including the share reimbursed by France's health insurance scheme as well as the share not reimbursed that is to be paid by the patient.

[12] Willingness to pay: maximum amount that an individual would be willing to pay to obtain a product.

As indicated by the College of Healthcare Economists in its Guideline no. 17, the value of a statistical (human) life can be measured in two ways: using the human capital approach, by calculating the discounted *per capita* lifetime income of the French population, and using the theory of well-being approach, where life-years gained are estimated by individuals.

In France, reference values (in particular the value of a life-year/value of a statistical life) were established following the publication of the report by the Quinet commission (Quinet 2013). These are consensus values and not statistical estimates in the traditional sense; they are not associated with confidence intervals. They are based on an interpretative compilation of the international literature that takes certain positions including, among other things, the discount rate to be used and the fact that the value is presented unconditionally (with no reference to age or other sociodemographic factors). The reference figure used in this case is the value of a year of life lived in good health, set at €115,000 in 2010.

Other types of costs

Other costs, which are difficult to quantify, can be mentioned in connection with the health impact of ragweed:

- Risk value: if there was an insurance market for protection against the risk of allergy, the expenses would need to be stated in the ORS-ARS report. The market is merely one form of risk monetisation (partial because the market does not capture WTP in its entirety).
- Value of the harm suffered by the relatives of an allergic individual.
- Restrictions related to the choice of a place of residence or profession that can result in loss of well-being for the affected individuals.

Estimation of agri-environmental costs

An in-depth assessment of the agri-environmental impacts of ragweed was undertaken by Bullock *et al.* (2013). The authors sought to assess the impacts of ragweed on animal health, biodiversity, agriculture and wild environments. The most significant economic impacts were observed in the agricultural sector.

The agricultural impacts of ragweed primarily involve crops[13] and can be broken down into two types: direct impacts related to productive activity and indirect or hidden impacts due to operators' choices. The dichotomy between the financial approach and the economic approach is no longer relevant here due to the evaluation of a production activity through market values. The literature shows that multiple crops are impacted by the presence of ragweed; these mainly include spring crops such as sunflower, sorghum, maize, soya and peas, and winter wheat/barley. Less frequently, even anecdotally, other crops – such as sugar beets, tobacco, pumpkins, kidney beans, grapevines, potatoes, and carrots – are affected. Three types of costs can be mentioned: yield losses, costs of ragweed management, and costs related to suboptimal crop choices.

■ Assessment of the health impact of ragweed and the related costs

Studies assessing the health impact of ragweed have been published in the European scientific literature (Schaffner *et al.* 2020, Lake *et al.* 2017). They considered allergic sensitisation to ragweed pollen as the health impact indicator. Nonetheless, as part of this formal request, ragweed allergy with symptom expression was chosen as the indicator of interest as it reflects clinical relevance.

[13] Animals can be allergic to ragweed pollen but this impact is likely minor.

The current prevalence of ragweed allergy was thus estimated at the level of public establishments for intermunicipal cooperation (EPCIs) in metropolitan France. This health impact was expressed in monetary terms. The French data available in the Auvergne-Rhône-Alpes region were used.

<u>Health impact assessment</u>

Four exposure-risk relationships[14] have been developed using medical-administrative data produced within the Auvergne-Rhône-Alpes region in 2017 (Auvergne-Rhône-Alpes ORS and ARS 2018). The prevalence (as a % of the population aged seven to 74) of ragweed allergy at municipal level was compared with the exposure data modelled by Atmo Auvergne-Rhône-Alpes for the same year in the region. Two exposure indicators were derived: the total annual number of pollen grains and the number of days with ≥6 grains/m^3 (corresponding to the number of days with an RAEP≥3) during the year. These data were aggregated at EPCI level *via* a population-weighted average. This level was used because it enables the production of detailed but intelligible graphic displays and is also relevant in terms of local management. The relationship between risk (prevalence) and exposure (total annual number of grains and number of days with ≥6 grains/m^3) was expressed by a log model and by a log-log model thus generating four exposure-risk relationships:

- Relationship 1): prevalence in % = log(total annual number of grains);
- Relationship 2): log(prevalence in %) = log(total annual number of grains);
- Relationship 3): prevalence in % = log(number of days with ≥6 grains/m^3);
- Relationship 4): log(prevalence in %) = log(number of days with ≥6 grains/m^3).

To estimate the prevalence of allergy throughout the metropolitan territory, these four exposure-risk relationships were applied to exposure data modelled by the SILAM modelling system for metropolitan France over the 2005-2011 period.

A map showing the health impact of ragweed, in terms of allergy prevalence associated with each of the four exposure-risk relationships, is available in Figure 2. Quantitative estimates by metropolitan *département* are available in the annex of this document. The highest prevalence is observed in the Auvergne-Rhône-Alpes region; between 540,000 and 764,000 people are considered to be allergic to ragweed depending on the relationship used. High spatial disparities are observed between the EPCIs (high prevalence in the Rhône Valley and low prevalence in Alpine areas). High prevalence levels are also observed in some EPCIs in the Bourgogne-Franche-Comté, Provence-Alpes-Côte d'Azur and Centre-Val de Loire regions.

<u>Health impact monetisation</u>

In light of the available data, three cost items were estimated:

- The cost of medical care (as part of a financial approach);
- The cost of production losses (as part of a financial approach);
- The cost of lost quality of life (as part of an economic approach).

The cost of medical care and cost of production losses are, by construction, proportional to the estimated prevalence levels. The cost of lost quality of life does not show the same spatial distribution as the previous costs as it includes disease duration and takes into account the burden borne by sick populations. At national level, depending on the relationship considered:

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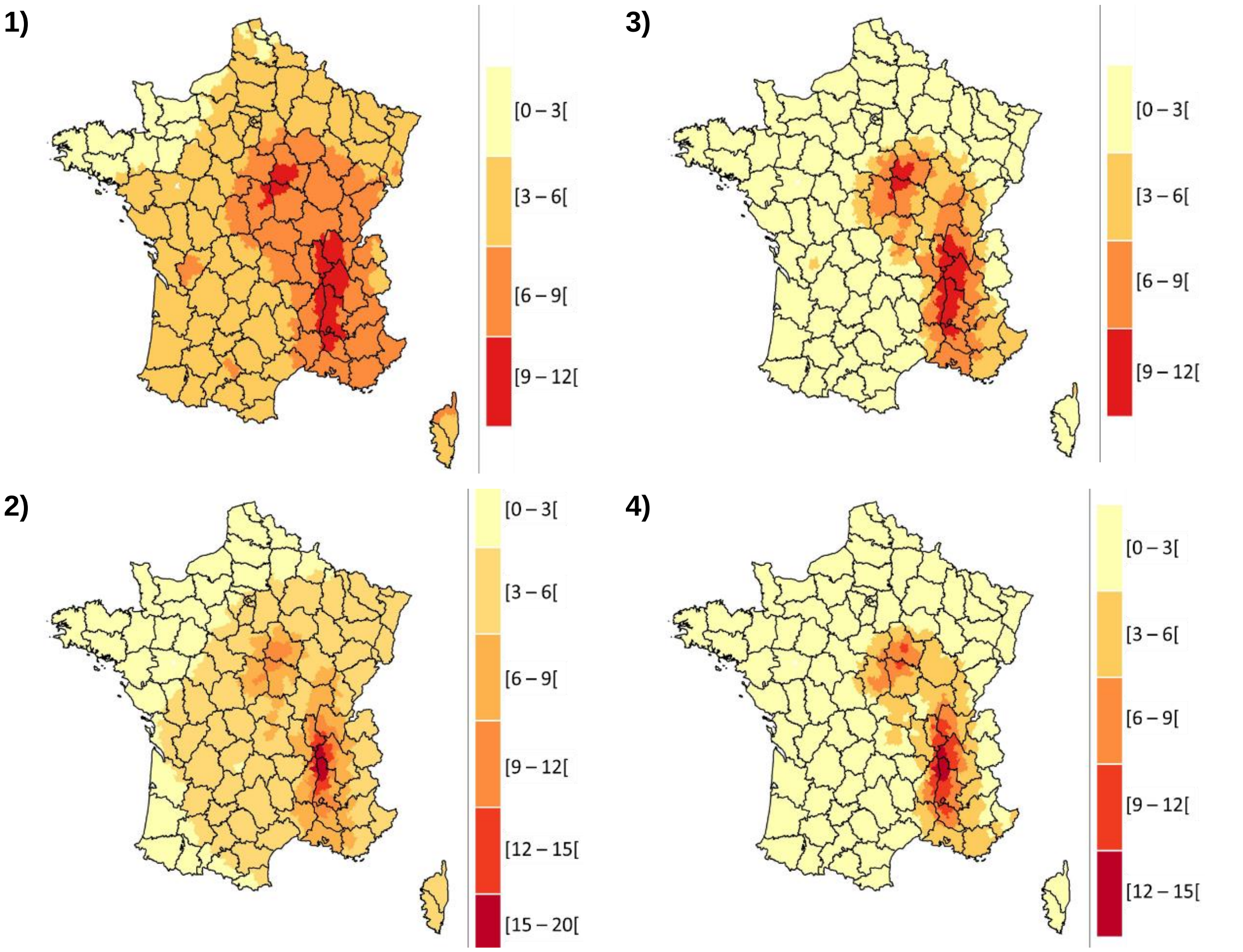
[14] An exposure-risk relationship mathematically describes the association between an exposure dose and an observed response (occurrence of a health effect or presence of a risk) over a given time period. In this case, a concentration (pollen grains per m^3 of air) and a prevalence (proportion of individuals with allergy in the population) are used as proxies for exposure and risk, respectively. For simplification purposes, and consistent with the standard terminology of health impact assessments, the term "exposure-risk" has been kept.



Central estimates of prevalence in metropolitan public establishments for intermunicipal cooperation (EPCIs). Values obtained when applying the four exposure-risk relationships to the average data modelled by SILAM for the 2005-2011 period. In black: the departmental borders.

Figure 2. Estimated prevalence of ragweed allergy (in %) in France for the various generated exposure-risk relationships (1 to 4) using French data

- The annual cost of medical care is estimated at €59 million to €186 million;
- The annual cost of production losses is estimated at €10 million to €30 million;
- The annual cost of lost quality of life is estimated at €346 million to €438 million.

Discussion

This expert appraisal is the first attempt to assess the health impact of ragweed in metropolitan France by estimating the prevalence of ragweed allergy. Use of this indicator, which reflects clinical relevance, improves the European studies already published in the literature. The assessment of the costs associated with this health impact benefits greatly from this improvement. However, the results should be interpreted with caution considering:

- The limitations inherent in the construction of exposure-risk relationships, relating in particular to the shape of the curve and the definition of the indicators used, such as potential classification biases;
- The fact that no individual or environmental parameters were taken into account in the construction of the exposure-risk relationships. Moreover, the proposed relationships do not represent individual risk;

- The non-specificity of certain economic data concerning the issue of ragweed. For example, no willingness to pay providing protection against the risk of ragweed allergy is mentioned in the economic literature.

However, this work has several strengths that support all of the results obtained. The analysis is based on the use of high-quality French data, for both the assessment and monetisation of the health impact. These data are mobilised using a standard methodology applied uniformly for the entire country, thus enabling areas with different levels of infestation to be compared. These estimates are clinically relevant, thanks to the definition of indicators, and reflect various aspects of the health impact of ragweed. The uncertainties associated with the data and methodology have been clarified throughout the analysis and have been partially quantified in the calculation of the orders of magnitude.

In the future, if ragweed continues to spread to areas that currently have little or no infestation, the related health impact will increase, even though this increase cannot currently be quantified.

4. CES CONCLUSIONS AND RECOMMENDATIONS

4.1. Conclusions of the CES

■ Knowledge of ragweed

Common ragweed has been present and spreading in France since the beginning of the 20th century. There are currently three types of infestation areas: areas with heavy infestation/establishment (for example: Rhône, Isère, Drôme, Nièvre, Cher), frontline areas (Charentes, Côte-d'Or, Gard), and areas that are still affected very little and/or are isolated from the two previous types of areas. The spread of common ragweed has accelerated since the 1960s.

Several vectors can foster this spread, in particular anthropogenic vectors, such as agricultural and/or mowing machinery and the transport of contaminated soil or seeds. It should be noted that the extent of the spread is not the same depending on the vector and the biology of the species (seed or vegetative reproduction, size and number of agricultural seeds, etc.).

It seems possible to curb the spread of the plant in frontline areas, in isolated areas and in areas with very little infestation. However, certain frontline areas still do not have any specific regulations.

Several control methods (chemical, physical, biological) exist depending on the infestation level, the surface area and the environment affected. Chemical control efforts come up against resistance phenomena. Not all methods are available or used in France. In particular, biological control is not implemented even though it has shown to be relevant and effective in China, Australia and Italy[15].

Ragweed management is still confronted with certain regulatory obstacles, such as the limited enforcement power of local mayors, particularly on private land, the coordination of control at European level, and current discrepancies between the French Rural and Maritime Fishing Code and the French Public Health Code.

From a health and agri-environmental standpoint, all ragweed species should be considered, especially with a view to control.

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[15] *Ophraella communa* was not voluntarily introduced in Italy as part of a control plan.

- **Available modelling approaches (spread of the plant and pollen dispersal) and associated relevance**

Monitoring of the plant and pollen relies on an observation and reporting (FREDON-Ragweed Observatory, FCBN) and pollen measurement (RNSA) system. There are innovative monitoring approaches whose large-scale feasibility needs to be confirmed (satellites or drones for the observation and automatic counting of pollen). These observations are essential to feed, calibrate and validate ragweed spread and pollen dispersal models.

Modelling provides short-term forecasts of pollen levels and long-term scenarios for the spread of the plant and the dispersal of its pollen. Modelling is also relevant for the *a priori* assessment of the effectiveness of control methods.

Several models are currently used to estimate the release and dispersal of ragweed pollen. The SILAM and COSMO-Art modelling systems are the most mature at European level. In France, the modelling system of Atmo Auvergne-Rhône-Alpes, which uses input data of excellent quality, is able to accurately represent daily pollen levels and related levels of allergy risk at regional level.

The long-term modelling of the distribution of ragweed and the dispersal of its pollen remains complex. The current methods have several limitations and the results are uncertain. However, the prediction of the plant's spread to Northern Europe, as compared to its current locations, due to climate change in particular, appears robust.

- **Current knowledge of the health impact of ragweed**

In general, allergic rhinitis induced by ragweed pollen, like that induced by other pollens, remains a trivialised, underdiagnosed, and undertreated chronic disease despite the observed major impact on quality of life.

Allergy associated with ragweed pollen has certain specific characteristics compared with allergy to other pollens; in particular, it has a later age of onset in France/Europe. This feature of the allergic march may be related to the "recent" introduction of ragweed in our regions as opposed to grasses, which are native plants. Moreover, ragweed pollen has high allergenic potential and a few grains are sufficient to cause symptoms in allergic individuals.

Several tools are currently used on a large scale to identify allergic individuals. These include skin tests, specific IgE blood tests, standardised questionnaires, medical-administrative databases concerning reimbursements for medical care, and sometimes a combination of the above. There is currently no standardised questionnaire or validated medical-administrative definition for ragweed allergy. However, the scientific literature often relies on highly detailed questionnaires (on seasonality and symptom triggers), which can be used to supplement information about allergic sensitisation.

The work undertaken by the ORS and ARS in Auvergne-Rhône-Alpes, the most infested region of France, provides local estimates of the health impact of ragweed pollen and constitutes a valuable and necessary tool to raise awareness and to implement fieldactions. Up to 13% of the regional population[16] is believed to be allergic to ragweed, although high geographic variability is observed. The methods and data used (telephone surveys and analysis of reimbursement data with multiple case definitions) are varied, are relevant in clinical and epidemiological terms, provide indications of uncertainty, and have many prospects for improvement.

Two health impact analyses of common ragweed in Europe were recently conducted on the basis of allergic sensitisation – one by Lake *et al.* as part of the ATOPICA project and the other by

[16] 284,604 cases considering the regional population in 2014.

Schaffner *et al.* as part of the COST-SMARTER project[17]. The estimated impacts were different: there were 32.6 million people sensitised to ragweed according to Lake *et al.* (2017) and 23.2 million according to Schaffner *et al.* (2020). However, such estimates have no systematic clinical relevance.

The prevalence of ragweed allergy has been estimated locally and on a larger scale in Europe. Today, depending on the infested area, 4.5% to 40.0% of the population may be allergic to ragweed (and up to 60% may be sensitised). The estimates, although uncertain, predict a 2.5-fold increase in the number of cases by 2060 in connection with the spread of the plant to currently non-infested areas, thereby exposing new populations to this pollen. Future changes in the allergenicity of ragweed pollen and/or in pollen production by the plant (both related to atmospheric pollution and weather conditions) may also play a role in this increased prevalence.

- **State of the art on the economic aspects of the impacts of common ragweed**

Estimating the cost of the impacts of ragweed draws from various methodological approaches – financial (based on market price) and economic (based on willingness to pay) – and on various points of view (sick individuals, patients' families, France's health insurance scheme, farmers, etc.).

Although several institutional reports have sought to estimate the health cost of ragweed using various approaches, all of those implemented can still be improved. The main challenge lies in the lack of robust data on the quantification and monetisation of the impacts, that could be used as inputs for these estimation models.

To estimate the cost of the impacts, the CES has taken an intentionally broad societal view, as recommended by the College of Healthcare Economists and the Senate. From a methodological standpoint, this "economic" approach is intended to be based on willingness to pay instead of on market prices to estimate the cost of the impacts of ragweed.

Concerning the monetisation of the health impacts, the Auvergne-Rhône-Alpes ORS has developed the most complete financial approach. According to the most recent estimate, the overall cost of medical care consumption in association with ragweed allergy came to over €40.6 million in the region in 2017. However, this view remains restrictive and only takes part of the economic costs into account.

Ragweed also has economic consequences in the agricultural sector. With no possibility of robustly quantifying the costs, it should be noted that the presence of ragweed leads to a decrease in yields, an increase in management costs, and suboptimal crop choices.

- **Quantification and monetisation of the health impact of common ragweed in France**

This expert appraisal is the first attempt to analyse the health impact of common ragweed throughout metropolitan France. The indicator used is based on allergy to ragweed pollen. This work shows the feasibility of such an analysis.

The main challenges lie in the availability of the data needed to develop the exposure-risk relationship, its application throughout metropolitan France, and the resulting economic calculation.

In light of the uncertainties, the prevalence of ragweed allergy at national level was estimated at 1.7% to 5.4% of the French population (1,115,000 to 3,504,000 allergic individuals). The cost of (medical) care was estimated at €59 million to €186 million, the cost of sick leave at €10 million to €30 million, and the cost of lost quality of life at €346 to €438 million.

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[17] SMARTER (Sustainable management of Ambrosia *artemisiifolia* in Europe): European Commission COST (Cooperation in Science and Technology) Action FA1203.

4.2. Recommendations of the CES

As a preamble, the CES agrees that the recommendations from ANSES's previous expert appraisals (ANSES 2014, 2017a, b) relating to ragweed still remain relevant. Through this expert appraisal and the conclusions set out above, the CES is issuing all of the following recommendations.

■ **For the preventive and active management of ragweed**

Ragweed management relies on stakeholder awareness, monitoring of the plant and its pollen, and control measures (mechanical, chemical, biological). Only a combination of these various actions at the local level may limit the health, environmental, and therefore economic impacts of ragweed. Although several management systems are already in place, it appears necessary to strengthen certain aspects of them.

In terms of prevention, the CES recommends:

- Continuing efforts to inform stakeholders and the general public about the plant and its management. For the time being, this information is relayed by the public authorities, in particular through the ARSs and their departmental delegations, as well as by monitoring organisations (FREDON - Ragweed Observatory, RNSA) and air quality monitoring associations, such as Atmo Auvergne-Rhône-Alpes within this region. It appears necessary to develop information campaigns in frontline areas *via* these organisations or their local offices.
- Developing the appointment of local coordinators (municipality, public establishment for intermunicipal cooperation (EPCI)). The EPCI level seems more appropriate for undertaking awareness-raising, information, and control actions. It is essential for such actions to be coordinated at local level to support these coordinators. This model, which is widespread in areas (such as the Auvergne-Rhône-Alpes region) that are heavily affected by ragweed, should be promoted at national level.
- Regarding the management of anthropogenic vectors, the current recommendations need to become requirements, especially those relating to the cleaning of agricultural equipment and the management of contaminated soil.
- Aiming for the absence of ragweed seeds in agricultural seed.

In terms of control, the CES recommends:

- Assessing the effectiveness of the various methods for controlling ragweed depending on the geographic area and its infestation level.
- Analysing Chinese and Italian feedback regarding the use of *Ophraella communa* for the biological control of ragweed.
- More closely monitoring anthropogenic activities, involving as many stakeholders as possible in control efforts, including the building and public works sector and the agricultural sector. Strong involvement of the agricultural sector is essential, to protect the health of the general population and agricultural workers likely to be highly exposed to ragweed pollen. This involvement would also help limit economic losses associated with the presence of ragweed in this industry sector (yield losses and/or suboptimal crop choices).
- Improving farmers' knowledge of good ragweed management practices by using all relevant information channels, in particular technical institutes and chambers of agriculture.
- Limiting the amount of bare land, with the exception of usable agricultural land, by establishing appropriate plant cover. In this case, it is important to favour species that are the least harmful to health.

- In heavily infested areas, continuing the actions currently being undertaken with the aim of stabilising and containing ragweed populations.
- Encouraging, in frontline areas, the introduction of specific regulations *via* prefectoral orders.

For more effective monitoring and modelling tools

Monitoring and modelling are ways of informing populations about the issue of ragweed. They also play a major role in species management.

Concerning operational monitoring, the CES recommends:

- Expanding and intensifying monitoring of the plant and its pollen in mainland France. It is therefore necessary to maintain the current observatories through the widespread involvement of the public authorities.
- Modernising the system for monitoring ragweed pollen by combining it with a system for modelling pollen dispersal in metropolitan France, following the example of what has been done in the Auvergne-Rhône-Alpes region.
- Regularly updating observations and reports at national level, as these are essential input and validation data for any modelling system. Moreover, it appears important to document the density of infestation beyond simple presence indicators.

Concerning models dealing with ragweed and its pollen, with the aim of improving useful knowledge for public action, the CES recommends:

- Testing, on a large scale, innovative methods such as systems for the automatic recognition and counting of pollen for monitoring and the use of satellites/drones for the observation of the plant’s distribution.
- Improving knowledge on the plant's phenology[18] and phenotypic plasticity[19] to be able to provide the best input for ecological ragweed spread models and pollen emission modules.
- Confirming the impact of climate change scenarios on the spread of ragweed and the release of its pollen, by initiating for example retrospective analyses using measurements and models from the past.

Concerning the centralisation, dissemination and mobilisation of information, the CES recommends:

- Regularly centralising and harmonising, at national and then European level, locally produced data on the presence of ragweed.
- Increasing the dissemination of monitoring and modelling information to the public authorities, healthcare professionals, the general population, and allergic individuals and making sure it is intelligible. This information should therefore be easy to understand, including for non-specialists[20]. These actions should be carried out nationally and regionally as well as on smaller levels (municipalities, healthcare areas).

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[18] Phenology: science of climatic influences on the seasonal development of plants.

[19] Ability to produce different phenotypes in response to changes in an environment.

[20] HCSP (2016). Opinion concerning the information and recommendations to be issued with a view to preventing health risks associated with allergenic pollen.

- **For the acquisition of new knowledge on the prevalence of allergy in the population and on changes in the allergenicity of pollen**

Research and expert appraisal efforts are necessary to better understand the health impact of ragweed. The CES therefore recommends:

- Monitoring the development of ragweed allergy, particularly in infested areas and frontline areas, by undertaking epidemiological studies analysing:
    - data from questionnaires having high informative power with regard to ragweed allergy;
    - data from medical care reimbursement databases to identify individuals with ragweed allergy;
    - results of skin tests or biological assays specific to ragweed sensitisation.
- Developing the joint use of the various tools mentioned above.
- Conducting studies to assess the impact of ragweed management systems on the health of populations.
- Assessing the health impact of ragweed in French overseas territories.
- Conducting studies on the allergenicity of ragweed pollen associated with the grains, fragments, and inflammatory components, and on possible cross-allergies.
- Conducting studies on the allergenicity of ragweed pollen depending on the effects of certain cofactors of interest, in particular the main gaseous and particulate atmospheric pollutants and climate change.

- **For better awareness of the issue of ragweed allergy**

Healthcare professionals play a key role in supporting individuals with allergies, whose symptoms are too often trivialised. The CES therefore recommends:

- Raising the awareness of healthcare professionals and of allergic or potentially allergic individuals in areas where ragweed is present and especially in areas where it is likely to develop (frontline areas).
- Fostering the development of networks of healthcare professionals and sentinel patients dedicated to allergy issues. These networks can facilitate information exchanges within health territories.
- The implementation, by the competent authorities, of a study on the means and maintenance of access to allergy treatment for as many people as possible.

- **For more accurate economic estimates**

The economic challenges associated with the impacts of ragweed appear significant and varied depending on the stakeholder, in particular. To improve the economic estimates made up to now, the CES recommends:

- Adopting the approach based on willingness to pay, which appears as the most relevant theoretically because it is able to fully estimate the economic impact on society.
- Undertaking research to determine the willingness to pay of the economic actors involved.
- Making up for the lack of data by assessing the burden of allergic rhinitis associated with ragweed, as well as willingness to pay to avoid allergy for allergic and non-allergic individuals and for third parties.

- Conducting a survey of farmers to assess the costs associated with the impacts in the agricultural sector (yields, management costs, land reallocation) and to find out about crop substitution practices.
- Continuing and improving the approach of the Auvergne-Rhône-Alpes ORS, in particular by broadening the scope of the costs considered and integrating a sensitivity analysis.

5. AGENCY CONCLUSIONS AND RECOMMENDATIONS

The French Agency for Food, Environmental and Occupational Health & Safety endorses the conclusions and recommendations of the CES on “Assessment of risk related to air environments” presented above.

This expert appraisal assessed a health impact, and certain associated costs, generated by common ragweed in metropolitan France. These findings designate ragweed as a national public health issue, whether in areas with heavy infestation, in newly affected areas or in those still with little infestation. The impact of ragweed on the health and well-being of populations should not be trivialised.

The economic considerations described in this expert appraisal are matters of society, of interest for public service managers. Regarding the two main types of approaches (financial, economic) examined by the experts, the economic approach has been favoured here. In practice, a wide range of approaches can be used depending on the cost items included in the analysis. ANSES stresses the importance of making an informed decision regarding the scope of the cost categories to be taken into account, in light of the issue raised on the one hand and based on the available data on the other. In addition, the possibility of comparing the results with analyses for other regions or other health issues is also a point that should be taken into consideration when defining the scope of analysis, but this is not always feasible.

ANSES underlines the importance of controlling the spread of ragweed. Sustained efforts in regions where the plant is present should be continued in order to contain populations. Actions should also be developed in frontline areas to curb the plant’s expansion. These areas therefore constitute a major challenge for those involved in controlling the plant. In this respect, ANSES supports the experts' recommendation aiming to make up for the lack of prefectural orders in these frontline areas, which is to promote local inter-departmental coordination.

This expert appraisal supplements the Agency’s work on the health impacts of pollen in ambient air, mould in buildings, and mould in ambient air – in metropolitan France and in the French Overseas *Départements* and Regions (DROMs) – by focusing specifically on data relating to ragweed.

All these different expert appraisals conducted by ANSES highlight the importance of improving the representativeness of the monitoring network for pollen and mould in ambient air in metropolitan France and in the DROMs for public health purposes. Such progress in terms of monitoring would improve the characterisation of exposure in the general population and would benefit the entire modelling chain aiming to predict levels of these pollutants in ambient air.

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KEYWORDS

Allergie, ambroisie, cartographie, coûts, coût social, impact économique, impact sanitaire, lutte, modélisation, pollinose, prévention, rhinite allergique.

Allergy, ragweed, maps, costs, social cost, economic impact, health impact, control, management, modelling, pollinosis, prevention, allergic rhinitis.

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ANNEX – ESTIMATED PREVALENCE OF RAGWEED ALLERGY (IN %) BY METROPOLITAN *DÉPARTEMENT*

This table gives average, high, and low estimates of the prevalence of ragweed allergy for all of the metropolitan *départements*, based on the estimates derived at the level of the EPCIs comprising them (*via* an average weighted for the number of inhabitants). To maintain the clarity of the results, the four exposure-risk relationships were considered together. Prevalence is expressed as a % of the population.

		Estimated prevalence of ragweed allergy (in %) Average central estimate [lowest estimate – highest estimate]
1	Ain	8.23 [7.19 - 9.40]
2	Aisne	1.82 [0 - 4.43]
3	Allier	5.39 [3.6 - 7.43]
4	Alpes-de-Haute-Provence	5.97 [4.17 - 7.88]
5	Hautes-Alpes	5.12 [3.31 - 7.24]
6	Alpes-Maritimes	5.03 [2.98 - 7.30]
7	Ardèche	9.26 [8.44 - 11.57]
8	Ardennes	1.69 [0 - 4.24]
9	Ariège	2.10 [0 - 5.29]
10	Aube	4.60 [2.66 - 6.99]
11	Aude	2.16 [0 - 5.39]
12	Aveyron	2.04 [0 - 5.07]
13	Bouches-du-Rhône	6.22 [4.47 - 8.05]
14	Calvados	0.95 [0 - 2.23]
15	Cantal	2.08 [0 - 5.04]
16	Charente	3.71 [1.74 - 6.61]
17	Charente-Maritime	1.97 [0 - 4.85]
18	Cher	7.10 [5.6 - 8.66]
19	Corrèze	1.96 [0 - 4.90]
21	Côte-d’Or	5.98 [4.32 - 7.80]
22	Côtes-d’Armor	0.78 [0 - 1.73]
23	Creuse	3.33 [1.60 - 6.01]
24	Dordogne	2.05 [0 - 5.11]
25	Doubs	3.73 [1.84 - 6.50]
26	Drôme	11.75 [10.27 - 15.39]
27	Eure	1.38 [0 - 3.43]
28	Eure-et-Loir	1.83 [0 - 4.55]
29	Finistère	0.85 [0 - 1.94]

		Estimated prevalence of ragweed allergy (in %) Average central estimate [lowest estimate – highest estimate]
2A	Corse-du-Sud	3.11 [1.23 - 6.01]
2B	Haute-Corse	3.58 [1.73 - 6.27]
30	Gard	6.02 [4.27 - 7.97]
31	Haute-Garonne	2.50 [0 - 6.08]
32	Gers	2.07 [0 - 5.20]
33	Gironde	1.79 [0 - 4.49]
34	Hérault	3.05 [1.04 - 6.14]
35	Ille-et-Vilaine	1.06 [0 - 2.54]
36	Indre	4.30 [2.36 - 6.81]
37	Indre-et-Loire	2.14 [0 - 5.24]
38	Isère	9.13 [8.26 - 10.96]
39	Jura	5.59 [3.81 - 7.56]
40	Landes	1.64 [0 - 4.12]
41	Loir-et-Cher	3.05 [1.33 - 5.85]
42	Loire	6.52 [4.80 - 8.43]
43	Haute-Loire	4.13 [2.26 - 6.78]
44	Loire-Atlantique	1.48 [0 - 3.70]
45	Loiret	4.24 [2.41 - 6.84]
46	Batch	2.03 [0 - 5.08]
47	Lot-et-Garonne	2.24 [0 - 5.57]
48	Lozère	2.59 [0.26 - 5.69]
49	Maine-et-Loire	1.51 [0 - 3.8]
50	Manche	0.77 [0 - 1.69]
51	Marne	2.20 [0.18 - 5.23]
52	Haute-Marne	3.69 [1.88 - 6.27]
53	Mayenne	1.13 [0 - 2.75]
54	Meurthe-et-Moselle	2.19 [0 - 5.32]
55	Meuse	2.34 [0 - 5.41]
56	Morbihan	1.12 [0 - 2.72]
57	Moselle	2.13 [0 - 5.27]
58	Nièvre	7.52 [6.43 - 8.76]
59	Nord	1.30 [0 - 3.21]
60	Oise	1.68 [0 - 4.21]
61	Orne	1.18 [0 - 2.89]
62	Pas-de-Calais	1.25 [0 - 3.06]
63	Puy-de-Dôme	5.28 [3.41 - 7.63]

		Estimated prevalence of ragweed allergy (in %) Average central estimate [lowest estimate – highest estimate]
64	Pyrénées-Atlantiques	1.66 [0 - 4.14]
65	Hautes-Pyrénées	1.63 [0 - 4.07]
66	Pyrénées-Orientales	1.97 [0 - 4.91]
67	Bas-Rhin	2.25 [0 - 5.54]
68	Haut-Rhin	2.66 [0 - 6.17]
69	Rhône	10.74 [9.75 - 13.43]
70	Haute-Saône	3.51 [1.65 - 6.41]
71	Saône-et-Loire	6.28 [4.68 - 8.03]
72	Sarthe	1.44 [0 - 3.64]
73	Savoie	5.45 [3.92 - 7.49]
74	Haute-Savoie	4.25 [2.31 - 6.9]
75, 92, 93, 94	Paris, Hauts-de-Seine, Seine-Saint-Denis, Val-de-Marne	2.34 [0 - 5.2]
76	Seine-Maritime	1.26 [0 - 3.09]
77	Seine-et-Marne	2.84 [0.81 - 5.73]
78	Yvelines	1.90 [0 - 4.68]
79	Deux-Sèvres	2.17 [0 - 4.99]
80	Somme	1.36 [0 - 3.37]
81	Tarn	2.29 [0 - 5.68]
82	Tarn-et-Garonne	2.43 [0 - 5.93]
83	Var	5.34 [3.3 - 7.54]
84	Vaucluse	8.75 [7.96 - 9.78]
85	Vendée	1.74 [0 - 4.34]
86	Vienne	2.50 [0 - 5.59]
87	Haute-Vienne	2.46 [0 - 5.55]
88	Vosges	2.48 [0.06 - 5.7]
89	Yonne	7.65 [6.39 - 9.05]
90	Territoire-de-Belfort	2.79 [0 - 6.16]
91	Essonne	2.46 [0.03 - 5.46]
95	Val-D'oise	1.96 [0 - 4.74]