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Climate change, aeroallergens, and the aeroexposome

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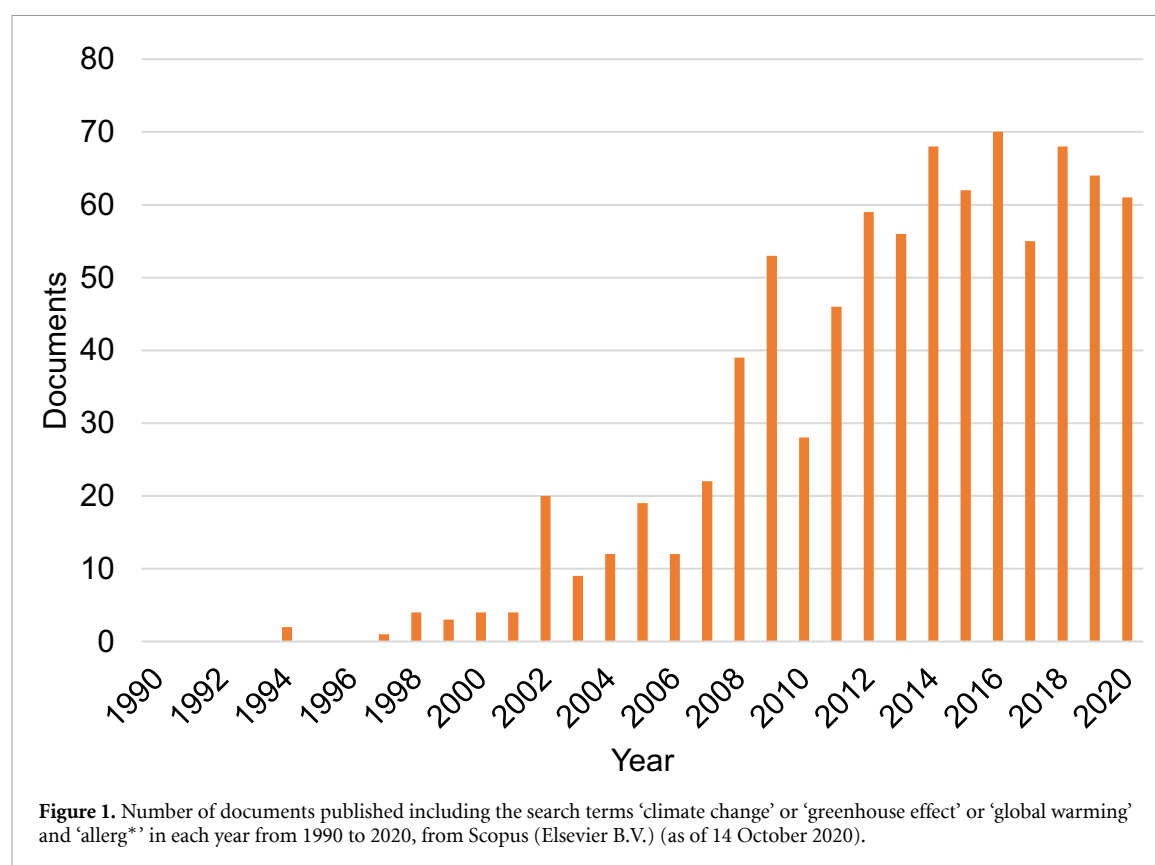
Abstract

Allergic diseases are a major public health problem globally and are increasing. The impacts of climate change on aeroallergens such as pollen and fungal spores and allergic respiratory diseases such as allergic asthma and allergic rhinitis have been considered since the early years of climate change and human health research, and exploration of this topic has accelerated over the past decade or so. This review examines the impacts of climate change on aeroallergens, including interactions with air pollutants, and the resulting impacts on allergic respiratory diseases. It discusses mitigation and adaptation in this context. It does this with a focus on advances over the last 2 years (2019 and 2020) to highlight research at the frontier of this field. It also explores the growing recognition of the need for a more holistic and integrated approach to environmental monitoring and exposure and presents the concept of the aeroexposome as a frame through which these impacts of climate change and responses to them could be viewed moving forward. As the evidence of impacts of climate change on aeroallergen production and atmospheric concentration, seasonality, distribution, and allergenicity mounts, crucial research demonstrating the resulting impacts on health outcomes such as aeroallergen sensitisation prevalence, asthma emergency department visits, and asthma hospitalisations is now emerging. It is vital that the momentum of the last decade continue with research to fill the many gaps that remain in our knowledge of this complex topic—refining analytical techniques, broadening the geographical coverage (to include, for example, the Southern Hemisphere), and more explicitly exploring the impacts of climate change on indoor aeroallergens.

1. Introduction

Climate change has been described as the biggest global health threat of the 21st century (Costello *et al* 2009). While much attention has been paid to the impact of climate change on heat-related diseases, water- and vector-borne diseases, and the impacts of weather-related natural disasters, there has been less of a focus on the consequences of climate change on air quality and the resulting disease burden. This applies to changes in chemical air pollutants but also to changes in airborne allergens such as pollen and fungal spores. However, the impacts of climate change on these aeroallergens and allergic respiratory diseases such as allergic asthma and allergic rhinitis have been considered since the early years of climate change and human health research (e.g. Longstreth 1991), and exploration of this topic has accelerated over the past decade or so (figure 1).

Allergic diseases are a major public health problem globally and are on the rise (Asher *et al* 2020). More than 339 million people are living with asthma and it is the most common chronic disease among children worldwide (World Health Organization 2020). The prevalence of allergic rhinitis is even higher, conservatively estimated to occur in approximately 500 million people worldwide (Ozdoganoglu and Songu 2012). Similarly, the prevalence of sensitisation to environmental aeroallergens is high globally, with one international study reporting prevalence ranging from 17% to over 50% in adults aged 20–44 years across 35 centres in 15 developed countries (Bousquet *et al* 2007). The prevalence of sensitisation to environmental aeroallergens is even higher in atopic patients (Damialis *et al* 2019). For example, in some locations, sensitisation to grass pollen can exceed 80% (Frei *et al* 1995, Subiza *et al* 1995, Belder *et al* 2007).



This review examines the impacts of climate change on aeroallergens, including interactions with air pollutants, and the resulting impacts on allergic diseases. It does this with a focus on advances over the last few years since the publication of the book on this topic titled *Impacts of Climate Change on Allergens and Allergic Diseases* (Beggs 2016) and especially the last 2 years (2019 and 2020) to highlight research at the frontier of this field. Web of Science (Clarivate Analytics) and Scopus (Elsevier B.V.) were searched using the topic search terms ‘climate change’ and ‘*allerg*’ (where quotation marks search for an exact phrase, and the asterisk (*) wildcard represents any group of characters, including no character, and would therefore include terms such as allergen, allergens, allergy, allergies, allergic, allergenic, allergenicity, aeroallergen, etc). Only English language documents were considered. This review also explores the growing recognition of the need for a more holistic and integrated approach to environmental monitoring and exposure and presents the concept of the aeroexposome as a frame through which these impacts of climate change and responses to them could be viewed moving forward.

2. Climate change and aeroallergens

The observed and projected impacts of climate change on aeroallergens include changes in their production and atmospheric concentration, changes in the timing and duration of the pollen season,

changes in pollen and fungal spore allergenicity, and changes in the geographical and spatial distribution of aeroallergens and the organisms that produce them (such as plants).

Many studies have examined long-term trends in the timing and duration of the pollen season and associated these with changes in temperature. For example, Velasco-Jiménez *et al* (2020) have recently reported the findings of their study of the trends in pollen seasons of winter flowering trees in Andalusia, Spain, over the years 1994–2017, showing that flowering has been delayed over recent years, particularly for trees that bloom closer to spring (i.e. poplar and elm). Other studies have found advances in the start of the pollen season. García-Mozo *et al* (2014), for example, studied a 30 year (1982–2011) olive pollen record from Spain and found trends towards earlier pollen season start and peak date and delayed pollen season end (García-Mozo *et al* 2014).

Location-specific studies of long-term trends in aeroallergen concentrations continue, adding to the body of literature in this area. Fernández-González *et al* (2020) studied airborne pollen concentration trends of oak (*Quercus*) in Ourense (the North-Western Iberian Peninsula) during the 27 year period 1993–2019. They found significant increasing trends in the annual pollen integral of 7.9% pollen grains per year, and the pollen peak concentration of 7.5% pollen grains per year. They also detected a trend to a delay of the oak main pollen season onset of 0.47 d yr⁻¹ (Fernández-González *et al* 2020).

Olsen *et al* (2020) studied airborne *Cladosporium* and *Alternaria* spore concentrations over a 26 year period (1990–2015) in Copenhagen, Denmark. They found a decreasing trend in the *Alternaria* seasonal spore integral and *Alternaria* and *Cladosporium* annual peak concentrations. While temperature has increased at this location over this period, they explained the decreasing spore trend by growing urbanisation around Copenhagen and by changes in agricultural practices (Olsen *et al* 2020).

The last decade or so has seen the appearance of major synthesis studies which have examined trends in the pollen of multiple species from multiple sites regionally and hemispherically. Ziello *et al* (2012) analysed a data set consisting of 1221 pollen time series at 97 locations in 13 European countries from 23 pollen taxa. The time series length ranged from 10 to 28 years in the period 1977–2009. They found an increasing trend in the yearly amount of airborne pollen for many taxa, which was more pronounced in urban than semi-rural/rural areas, and suggested that the anthropogenic increase in atmospheric carbon dioxide (CO₂) concentrations may be influential. More recently, Ziska *et al* (2019) analysed multiple pollen (aeroallergen) taxa from 17 locations across three continents in the Northern Hemisphere with long-term (~26 years on average) records. They found that 12 of the 17 locations had significant increases in seasonal cumulative pollen or annual pollen load, and 11 of the 17 locations had a significant increase in pollen season duration over time, increasing on average by 0.9 d yr⁻¹ (Ziska *et al* 2019). These were associated with increases in temperature at the respective locations.

It is important to note that most, if not all, of the research on observed changes in aeroallergen concentrations and seasonality is from the Northern Hemisphere, and the results of such studies in the Southern Hemisphere are urgently needed to provide a much fuller picture of these impacts globally (Davies *et al* 2021). Similarly, Jochner-Oette *et al* (2019) have recently suggested that linear models, which are usually used to analyse long-term changes in pollen concentrations, may not be fully suitable for describing these changes in recent decades. They analysed several pollen taxa from six locations in Switzerland using both Bayesian statistics that describe discontinuities (i.e. change points) and linear models, finding that trends of linear regressions differed considerably in magnitude or even differed in sign compared to the Bayesian results (Jochner-Oette *et al* 2019).

Experimental research has been conducted to examine the impacts of increasing temperature and elevated CO₂ on ragweed pollen allergenicity. For example, El Kelish *et al* (2014) examined ragweed pollen allergenicity under elevated CO₂ and drought stress. They found a strong up-regulation of allergenic ragweed protein (Amb a) transcripts under

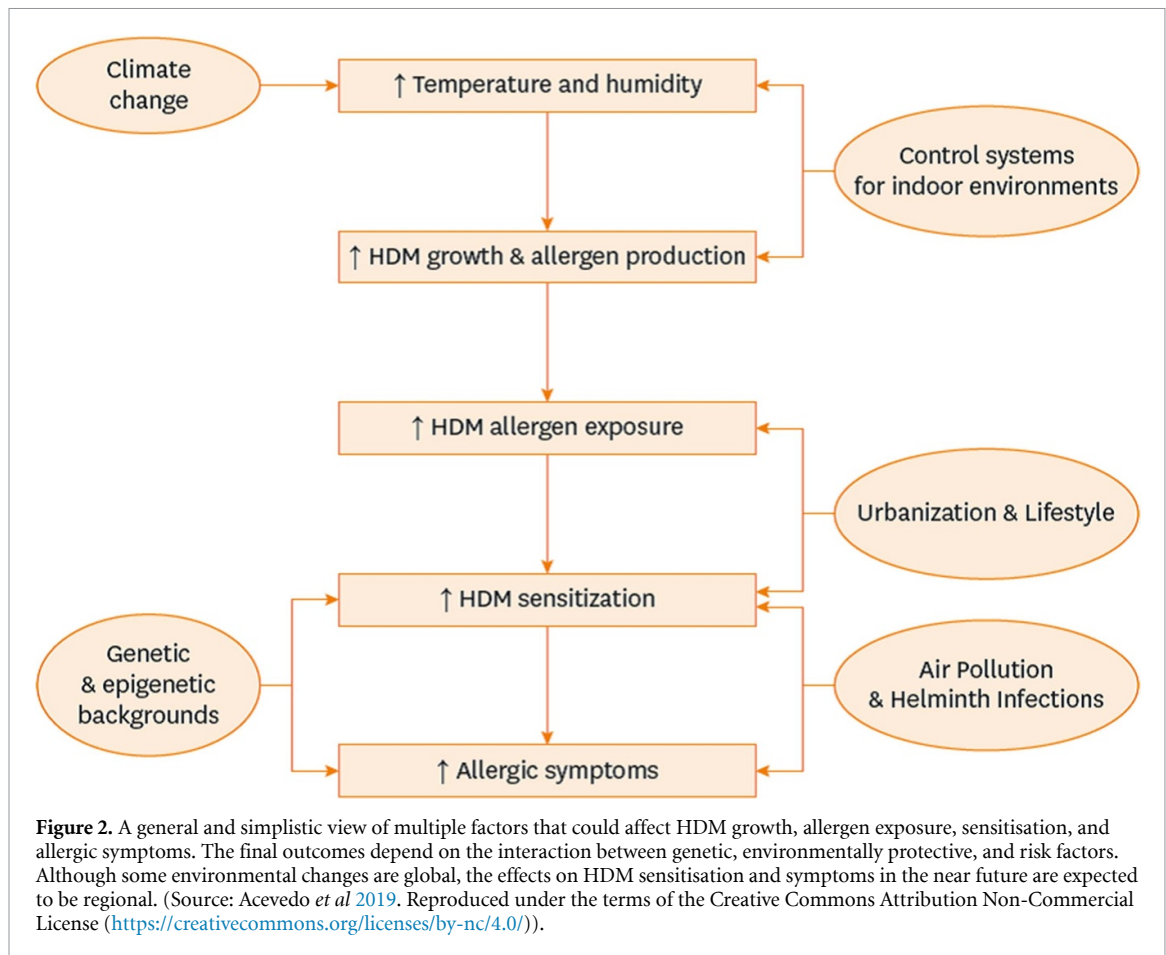
elevated CO₂, drought stress and elevated CO₂ plus drought stress conditions and concluded that under expected global change conditions, the allergenicity of ragweed pollen may increase, thereby affecting human health (El Kelish *et al* 2014). A significant advance in this field is the study by Rauer *et al* (2020) who demonstrated that pollen from ragweed plants grown experimentally under elevated CO₂ elicits a stronger allergic response *in vivo* and *in vitro*. Also recently, Gentili *et al* (2019) examined experimentally the response of ragweed to increasing temperature. They found that the number of male inflorescence and pollen allergenicity were temperature-responsive traits, with pollen allergenicity increasing with temperature (Gentili *et al* 2019).

These experimental studies build on earlier research starting in 2000 that examined the impacts of elevated CO₂ on a range of allergenic pollen and fungal spores. This includes Ziska and Caulfield (2000) and Wayne *et al* (2002) who studied ragweed pollen production, Singer *et al* (2005) who studied ragweed pollen allergen content, and Wolf *et al* (2010) who investigated *Alternaria* and *Cladosporium* fungal spore production.

While the vast majority of research on the impacts of climate change on aeroallergens has focussed on outdoor aeroallergens such as pollen and fungal spores, there are also important impacts on indoor aeroallergens such as those produced by the house dust mite (HDM) and indoor fungi and moulds (Mudarri 2010, Chew and Saha 2016, Poole *et al* 2019). Acevedo *et al* (2019) have recently conducted a comprehensive review of the impacts of climate change on the HDM, its allergen and associated allergic disease, suggesting that global or regional changes in temperature, humidity, air pollution or other environmental conditions could modify natural HDM growth, allergen production, and survival (figure 2).

3. Interactions between climate change, aeroallergens and air pollutants

Consideration of the impacts of climate change on allergic respiratory diseases requires recognition that there are important interactions between aeroallergens and air pollutants, and that climate change impacts not only aeroallergens but also air pollutants. Air pollution can interact with pollen-producing plants and pollen in the atmosphere. It can also act in a synergistic manner with allergens such as pollen to enhance the development of allergic disease (Kinney *et al* 2016). Ozone (O₃), nitrogen oxides, and combustion- or traffic-related airborne particulate matter can increase the abundance and induce chemical modifications of allergens, increase oxidative stress in the human body, and slant the immune system toward allergic reactions (Reinmuth-Selzle *et al* 2017).



In particular, air pollutants can act as adjuvants and change the immunogenicity of allergenic proteins.

Albertine *et al* (2014) experimentally studied the impacts of elevated atmospheric CO₂ and O₃ concentrations that may occur in the future on Timothy grass pollen and allergen production. Elevated CO₂ concentration significantly increased the quantity of grass pollen produced, even when levels of O₃ (a plant growth and reproduction suppressor) were also elevated (Albertine *et al* 2014). However, elevated O₃ significantly decreased the Timothy grass allergen protein concentration of the pollen, but the net effect when both this and increasing pollen production were considered indicated increased allergen exposure under elevated levels of both these gases (Albertine *et al* 2014).

Recently, Lucas *et al* (2019) studied ryegrass pollen allergenicity of plants growing under different air pollution levels, and found that the pollen from plants growing in higher nitrogen dioxide (NO₂) and sulphur dioxide (SO₂) levels had significantly higher nicotinamide adenine dinucleotide phosphate (reduced) oxidase activity and hydrogen peroxide (H₂O₂) levels, suggesting a likely higher allergenic capacity of this pollen.

4. Climate change impacts on allergic respiratory diseases

Building on the solid foundation of research on the impacts of climate change on aeroallergens, studies of the observed and projected impacts of climate change on allergic respiratory diseases themselves have emerged in the last few years.

Sapkota *et al* (2019) examined changes in the timing of the start of the spring tree green-up season and changes in hay fever prevalence in adults in the US for the years 2001–2013. They found that people living in counties with a very early start of season (relative to its long-term average) had a 14% higher odds of hay fever compared to those living in counties where start of spring was within the normal range. Interestingly, they also found that people living in counties with very late start of season had an 18% higher odds of hay fever compared to those living in counties where start of spring was within the normal range (Sapkota *et al* 2019). They suggested that these findings arose because ‘early onset of spring increases the duration of exposure to tree pollen, while very late onset of spring increases the propensity of exposure because of simultaneous blooming’ (Sapkota *et al* 2019).

Sapkota *et al* (2020) applied similar methods to examine the association between changes in

timing of spring onset and asthma hospitalisation in Maryland, US. After adjusting for extreme heat events and concentrations of particulate matter with an aerodynamic diameter less than $2.5\ \mu\text{m}$ ($\text{PM}_{2.5}$), their modelling revealed that very early onset of spring was associated with increased risk of asthma hospitalisation.

Several studies focussed on projected future impacts of climate change on allergic respiratory diseases have also emerged in recent years. Building on their earlier work (Storkey *et al* 2014, Hamaoui-Laguel *et al* 2015), Lake *et al* (2017, 2018) produced quantitative estimates of the potential impact of climate change on common ragweed (*Ambrosia artemisiifolia*) pollen allergy in Europe using a process-based model to estimate the change in ragweed's range and a second model to simulate current and future ragweed pollen concentrations. They found that allergic sensitisation to ragweed will more than double in Europe, from 33 to 77 million people, by 2041–2060 (Lake *et al* 2017, 2018). They also suggested that higher ragweed pollen concentrations and a longer ragweed pollen season may also increase the severity of allergy symptoms.

Anenberg *et al* (2017a, 2017b) estimated impacts of climate change on oak pollen season length and the resulting asthma emergency department visits in the US. They examined moderate and severe climate change scenarios at two points in the future: 2050 and 2090. They found that severe climate change could increase oak pollen season length and associated asthma emergency department visits by 5% and 10% on average in 2050 and 2090, and that the increases under moderate climate change were only half these values (Anenberg *et al* 2017a, 2017b). Neumann *et al* (2019) used additional monitor data and epidemiologic functions to extend these analyses, and broadened the pollen taxa to include oak, birch, and grass. The study found a 14% increase in pollen-related asthma emergency department visits in 2090 under a higher greenhouse gas emissions scenario, but only an 8% increase under a moderate emissions scenario, reflecting projected increases in pollen season length (Neumann *et al* 2019).

5. Policy responses

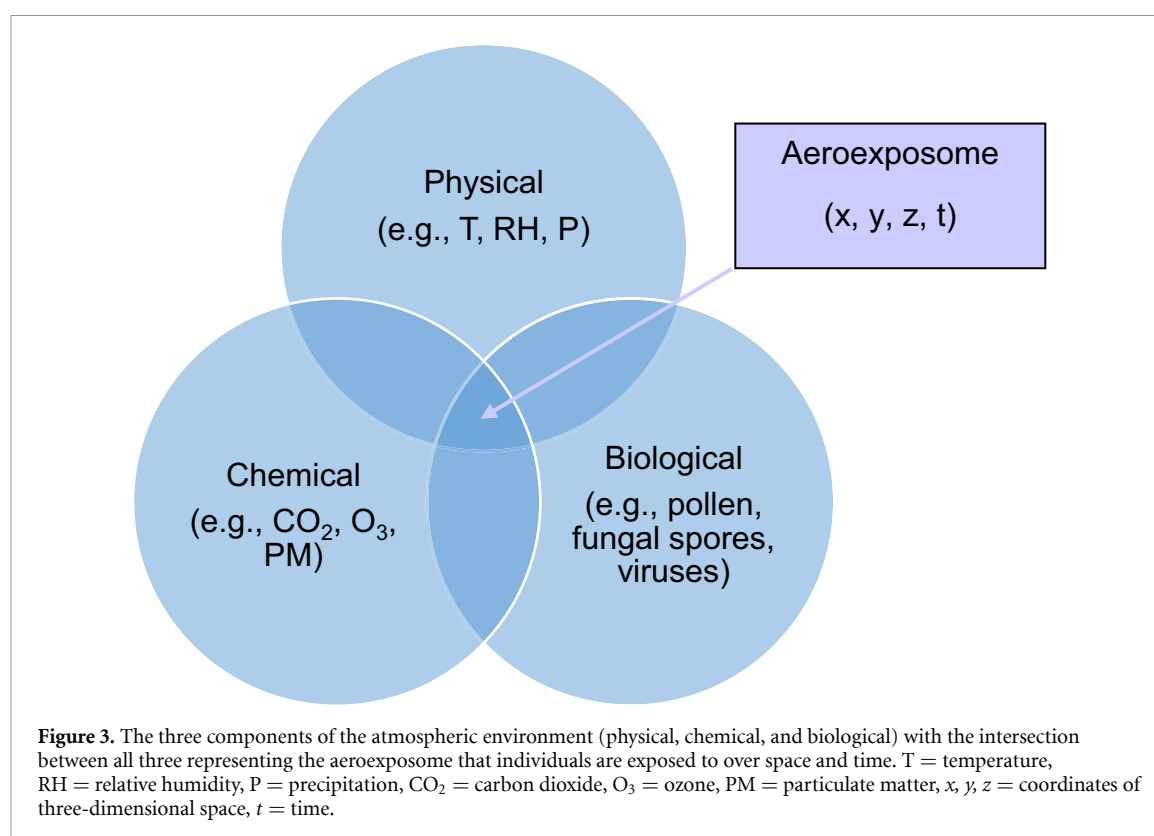
As the preceding sections have shown, the impacts of climate change on aeroallergens and allergic respiratory diseases increase with increasing climate change scenarios. Mitigation of climate change is therefore the first line of defence against such high end projections. Interestingly, and importantly, just as the impacts of climate change on aeroallergens and allergic respiratory diseases are a function of both increases in temperature and increases in CO_2 , mitigation of climate change will have a double benefit in this context—limiting both the extent of temperature increase and CO_2 increase. At the same time, it

is broadly recognised that adaptation is an essential complement to mitigation. Health professionals are increasingly being called upon to advocate for effective mitigation and adaptation strategies to minimise climate change's respiratory health effects (Deng *et al* 2020). While a range of adaptation options have been described (e.g. Beggs 2010), there is limited in-depth research that has explored these options. This section describes some of the research that is emerging in this area.

A couple of recent studies serve to illustrate several adaptation measures, these being management of allergenic plants, planting practices and policies, and urban/settlement planning. Schaffner *et al* (2020) examined the public health effects of ragweed (*A. artemisiifolia*) in Europe and the potential impact of the accidentally introduced leaf beetle (*Ophraella communa*) on the number of ragweed allergy patients and healthcare costs. They demonstrated that the very high disease burden and associated healthcare costs could be significantly reduced through biological control of invasive alien species such as ragweed.

Salmond *et al* (2016) conducted an in-depth review using an urban ecosystems services framework to evaluate the direct, and locally generated, ecosystems services and disservices provided by street trees. Their focus was on the services of major importance to human health and well-being including climate regulation, air quality regulation, and aesthetics and cultural services (Salmond *et al* 2016). They explored in detail, amongst other things, the trade-off between street tree-related increased deposition and removal processes which act to reduce air pollution concentrations, against reduced horizontal and vertical dispersion and increased biogenic emissions and pollen. Importantly, they argued that current scientific understanding is limited due to methodological problems with past research in this area, and suggest that a holistic approach is required to evaluate the services and disservices provided by street trees at different scales (Salmond *et al* 2016).

Aeroallergen monitoring has long been recognised as a key environmental health indicator for climate change (e.g. English *et al* 2009). More recently, in recognition of the interactions of the physical, chemical, and biological aspects of the atmospheric environment, there have been calls for an integrated approach to not only monitoring and assessment but also forecasting and communication of air quality (e.g. Klein *et al* 2012). Technological advances are now starting to make at least components of this a reality, such as the use of smartphone technology that provides real-time access to integrated systems that track exposure to air pollutants, aeroallergens, and weather (Johnston *et al* 2018). The next section presents the concept of the aeroexposome as a development needed in future monitoring and impact assessment studies.



6. Aeroexposome

It is now clear that a holistic and integrated framework around environmental exposures relevant to allergic respiratory diseases is required. This has very recently prompted consideration of the exposome in this context, including in relation to climate change (Cecchi *et al* 2018, 2020). The concept of an exposome was first put forward by Wild (2005), encompassing life-course environmental exposures (including lifestyle factors), from the prenatal period onwards. In this context, environment is defined in the broad sense of ‘non-genetic’ (Wild 2012).

As a development of the exposome concept and how it applies to allergic respiratory diseases, the aeroexposome, introduced here for the first time, can be defined as the complete physical, chemical, and biological atmospheric exposure from the prenatal period onwards (figure 3). This recognises the importance of weather and climate and climate change, air pollutants, and of course aeroallergens, and importantly the interactions among them. For allergic respiratory diseases, it is not only the lifetime exposure that is likely important. We know that exposures at specific life stages are important in disease development (e.g. Lu *et al* 2020), and acute exposures will contribute to exacerbations (the triggering of symptoms) in those with these diseases (e.g. Thien *et al* 2018). We also know that the biological component of the aeroexposome must include all respirable airborne biological particles. This includes sub-pollen sized allergenic particles and molecules. It also includes

viruses which can be involved in the development of asthma (Budden *et al* 2019, Mikhail and Grayson 2019), and for which pollen exposure can heighten the risk of infection (van Cleemput *et al* 2019, Gilles *et al* 2020). This raises important questions regarding COVID-19, the disease caused by severe acute respiratory syndrome coronavirus 2, such as what interactions or associations are there between it and pollen exposure, and how might climate change influence such interactions. The aeroexposome concept can be applied to environmental monitoring, exposure assessment, epidemiological analysis, and so on.

The aeroexposome includes components of what Wild (2012) described as the general external and specific external domains of the exposome. These include climate, environmental pollutants (i.e. air pollutants), infectious agents (e.g. airborne viruses), and of course other components of the atmospheric environment such as airborne pollen and fungal spores. Conversely, there are many exposures that would be excluded from consideration of the aeroexposome. These include diet, lifestyle factors such as alcohol, education, financial status, psychological and mental stress, and so on.

While a focus on the aeroexposome may seem at odds with the comprehensive nature of the exposome concept, it may be that such a focus enhances the utility of what might otherwise be a currently unfathomable challenge, and in doing so makes comprehensive atmospheric environmental exposure assessment of direct relevance to allergic respiratory diseases a reality. The exposome, and aeroexposome,

as it relates to allergic respiratory diseases will best be achieved through a coordinated and international effort (Vermeulen *et al* 2020), and for this an inter-governmental partnership with direct and explicit involvement of, for example, relevant United Nations bodies such as the World Meteorological Organization, World Health Organization, and United Nations Environment Programme would perhaps ensure the coverage and sustainability that would be called for.

7. Conclusion

Evidence of impacts of climate change on aeroallergen production and atmospheric concentration, seasonality, distribution, and allergenicity continues to mount, and crucial research demonstrating the resulting impacts on health outcomes such as aeroallergen sensitisation prevalence, asthma emergency department visits, and asthma hospitalisations is now emerging. It is vital that the momentum of the last decade continue with research to fill the many gaps that remain in our knowledge of this complex topic—refining analytical techniques, broadening the geographical coverage (to include, for example, the Southern Hemisphere), and more explicitly exploring the impacts of climate change on indoor aeroallergens. Similarly, in recognition of the roles and interactions of the physical, chemical, and biological components of the atmospheric environment, a more complete and integrated approach to monitoring, assessment, forecasting, and communication of air quality is now required, and the aeroexposome provides a conceptual frame through which to view this.

Data availability statement

No new data were created or analysed in this study.

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