Health Climate Change impacts report card technical paper

4. Pollen and Human Health: impacts of anthropogenic climate change

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Key Messages

- Pollen plays a role in the health and well-being of individuals with symptoms appearing after acute exposure, as witnessed by the reactions of the immune system (especially via type I IgE-related hypersensitivity) leading to rhinitis, allergy, eczema and asthma. [**H**]
- The UK has a variety of plants (trees, grasses and weeds) that release pollen in different amounts at different times of year. Individuals can vary in the size and type of reaction that they may have to pollen, from mild itching, sneezing and redness through to anaphylactic shock and death. [**H**]
- Some thunderstorms have been associated with increased hospital admittances for asthma exacerbations. [**H**]
- Higher temperatures, presence of high concentrations of CO_2 and a different mix of other atmospheric gases, different patterns of rainfall and humidity, extended growing seasons, lack of frost to trigger end of pollination season and increased anthropogenic chemicals concentrations may lead to increased amounts and/or allergenicity of pollen [**L**]
- An increase in the ability of plants to grow more, pollinate longer, see the introduction of novel species into the UK, and changes in plant protein structures increasing the risk of recognition by human immune system as a harmful, rather than benign substance. [**L**]

Introduction and Scope

This paper will examine the relationship between pollen and health outcomes in the context of environmental change, with the major focus on asthma. It will predominantly focus on UK events (while accounting for European influences), but will also give global examples where UK data is not in existence. It will give examples of current effects of climate change on pollen and its relationship to human health, and propose some potential future effects. The main health outcome focussed on will be asthma exacerbation as this is where health incidents are routinely recorded, but not forgetting there are other related health issues such as rhinitis (where symptoms are routinely treated with over-the-counter medication).

In the UK, the pollen season consists of three overlapping parts: tree pollen, weed pollen and grass pollen. Dozens of different species contribute to overall allergenic and particulate respiratory load (as do other organisms such as fungal spores, as well as outdoor, indoor and occupational environments), which can also be influenced by long-range transport from continental Europe.[1, 2] Climatic factors are relevant in modulating both the start and intensity of the pollen season for individual species and during the pollen season with prevailing weather conditions having a strong effect on the health burden.

Examination of phenology during different years has enable researchers to see that changes in preseason temperature and rainfall are important predictors of the volume of tree and grass pollen produced.[3] Whether these inter-seasonal changes will turn lead to changes on the decadal time scale, or if plants “reset” their pollen production and protein conformation is a key question that remains unanswered in the area. A second potential avenue is via increased CO_2 which may see increased biomass production and allergenicity. Examinations of the relationship between pollen and asthma exacerbation have been made using differing analytic designs in the UK and other countries and we will describe the current state of knowledge here.

Evidence of Current Sensitivity of Pollen Exposures to Climate Factors - Environmental Change, Temperature, CO_2 and Humidity, Frost

The cause of asthma is unknown but it is known to involve both genes and environmental factors and may be classified as due to intrinsic (non-allergic) or extrinsic (allergic) origin. In an episode of asthma, environmental triggers such as allergens inflame the airways. In atopic asthma, patients have an immune system that is hypersensitive to certain triggers (via immediate IgE type 1 hypersensitivity). In response to the challenge by an allergen the bronchi spasm and contract, and inflammation proceeds which leads to further contraction and excessive mucus production leading to coughing and breathing difficulties.[4, 5] These reactions may resolve after 1-2 hours but secondary reactions do also occur in 50% of patients 3-12 hours after initial trigger.[6] Pollen is only one of a large number of environmental allergens found to induce asthmatic symptoms and other allergens include house dust mites, fungi (mould), cockroach particles and animal dander. Subjects with asthma and pollen exposure have been found to have reduced lung function and increased pulmonary inflammation.[7, 8] Individuals become allergic to specific proteins and so may be allergic to individual species of plant,[9] and not all pollens.

The concentration of aeroallergens at ground level is known to be closely related to meteorological phenomena.[10] The changing environment has been recorded as altering plant growth and this has the potential to alter pollen exposure in the population.

Different species react differently to environmental factors [11] and the relationship between flowering phenology and temperature is not straightforward. Trees belonging to the Betulaceae family (i.e. hazel, alder and birch) which blossom in early spring are greatly dependent on temperature and require chilling (vernalisation) before winter dormancy is terminated, followed by a period of heat before growth is resumed and flowering occurs,[12] and may have reached its limit.[13] A number of specific studies exist, often focussing on a small region. It is also common amongst trees that the flowering intensity varies from one year to the next ("masting"). Grasses are the most important group when examining the population health of exposure to pollen as not only do grasses have the highest incidence of sensitisation (i.e. recognition by the immune system) they also have the highest clinical relevance i.e. sensitisation and patients displaying symptoms on exposure.[5] For grasses, aggregated temperature and rainfall in the growing season can be used to forecast start and intensity of the pollen season,[14] and there are regional variations.

During the pollen season high temperatures can exacerbate pollen levels and allergic reactions[15] as such conditions are often associated with calm, high pressure weather systems. Westerly winds and/or rain can suppress release of pollen or dilute pollen concentrations (through wet deposition). Southerly winds may carry pollen from France to the UK and changing weather patterns may bring increased volumes and species of pollen to the UK.[2]

Changes in the frequency of weather events such as thunderstorms during pollen seasons may induce hydration of pollen grains and their fragmentation which generates atmospheric biological aerosols carrying allergens. As a consequence asthma outbreaks have been observed in pollinosis patients (allergic rhinitis caused by plant pollen, as opposed to hay fever which is only grass pollen).[16] Sferics (lightning), temperature and rainfall were increased at the time of epidemics compared to control times. Simultaneous presence of sferics and grass pollen only

increased the risk of asthma epidemic by 15% (with wide confidence intervals of 2-45%) and two thirds of asthma epidemics were not preceded by thunderstorms.[17] Some authors have asserted that the scale of thunderstorm asthma and the burden it places on health services supports the need for a public health strategy.[18] In four years in the UK there were only 3 events per year.[17] Similarly in Australia, where there is greater exposure to grass pollen, low numbers have been found.[19]

Effects of Pollen Exposure on Health and Wellbeing Outcomes (Asthma)

Exposure to pollen in humans is primarily via the pulmonary route. Pollen, due to its size (0.006 -100 μm), can lead to exposure from the lips and nasal passage through to the bronchioles. The rapid increase in asthma over the preceding two decades has suggested that environmental risk factors are involved.[20] Sensitisation and immediate type I reactions (via IgE antibodies) are strongly associated with exposure to proteins derived from pollens. The association between sensitisation to grass pollens and symptoms of hay fever occurring during the grass pollen season provides strong evidence for a causal role of grass pollen in this disease.[16] Pollen is known to trigger symptoms in asthma, but may also be involved in disease initiation via increased inflammation.[21]

It appears that exposure at different times of life may have differing effects including *in utero*, perinatal and infancy, puberty and older age. This has been highlighted by epidemiological studies that have examined the relationship, predominantly by comparing area of high and low pollen and or presence of allergenic species within geographic areas.[22] Other authors have speculated geographical differences in allergic disease prevalence may be due to chronic exposure to allergens such as pollen.[23] This has been further explored via the concept that birth at a particular time of year (exposure to high/lower pollen levels at different stages of development either in utero or in early life) may increase risk development of asthma and other atopic diseases.[24]

Distribution of Impacts by Age, Gender, Socio-economic Status

Increases in negative health outcomes due to pollen exposure in the context of environmental change are expected to have differential impact on subsections of the population. The variation is predominantly due to differences in susceptibility to asthma in the population due to age, sex and socioeconomic status. Differential exposures may also occur, as exemplified by differences in the built environment such as urban canyons.[25]

Asthma is a disease that is more prevalent among the young. Recent estimates by the ISAAC study reveal a prevalence in the UK of 20·9% of 6-7 year olds [26] where asthma prevalence is about 9.4% of adult population, making it one of the most prevalent diseases in the UK population.[27] Increased exposure and sensitisation to pollen has the potential to promote asthma in the paediatric population via the atopic march (children developing different allergic diseases in an order related to their age and development), and lead to persistent symptoms and adult onset allergies later in life affecting the aging population.[28]

In general prevalence of asthma is higher in boys and post puberty, higher in women. This trend has been found in a variety of atopic diseases [29] and IgE sensitisation as measured by skin prick test to a variety of pollens.[30] This trend of increased prevalence of asthma in boys may be due to greater exposure to risk factors for asthma in boys.[31]

Low socioeconomic status (SES) has been associated with asthma itself and risk factors for asthma such as obesity and tobacco smoking (although complicated by whether allergic or non-allergic asthma is examined), both in the UK [32] and other countries.[33] Evidence around the risk of asthma due to SES is limited, as is the evidence for the hypothesis of low income/SES and health status, including asthma, in later life.[34] The risk of increased asthma via increased pollen exposure may occur with concurrent risk factors for asthma found in the population with lower SES, with the increased suburbanisation of poverty and decline in rural economies and their associated higher exposure to pollen.

Some ethnicities within multi-ethnic populations found in many developed countries have the potential for increased risk of pollen-associated asthma. Some populations such as Afro-Americans and Afro-Caribbeans have increased risk of asthma but the role of pollen here is uncertain, as is the contribution of genes and other environmental factors.[35]

Regional Differences

Geographical regional differences have been found in the strength of the relationship between pollen and asthma, which are probably due to differences in exposure, but may also be due to differences in behaviour and genetic susceptibility for asthma and allergic disease in differing populations. The prevalence of sensitisation to Timothy grass was significantly higher than that of any other pollen species, and hence distribution of this grass and its pollen and has led to regional differences in the UK being noted.[36] Northern European and Mediterranean areas have different pollen species that appear to dominate and high prevalence of grass pollen sensitisation have been found in Northern as opposed to Southern Europe.[36] Birch and grass pollen exposures have been found to vary considerably across Europe, but as yet have not been linked to asthma or allergy incidence, or even allergic sensitisation.[37] Ragweed (genus Ambrosia, with 50 species) pollen has been found to be a common allergen and is found in South-Western US, and Eastern Europe (e.g. Hungary) and has been predicted to spread, with areas of the UK at risk.[38] The effect of urbanisation must also be considered (with 81% of Western European populations living in built up environments, 85% in UK). The potential for exposure to weed species in the future has an increased risk. For example ragweed has been found to grow faster, flowered earlier, and produced significantly greater above-ground biomass and ragweed pollen at urban locations than at rural locations.[39]

It has been known for over 15 years that grass pollen can attach to air pollutants such as diesel exhaust carbon particles and allow allergenic moieties become concentrated in polluted air and hence also has a heterogeneous distribution.[40] In addition diesel exhaust particles can act as adjuvants,[41] and this may be linked to the presence of metals and an range of other environmental pollutants such as PSP, polytetrafluoroethylene (Teflon), titanium dioxide (TiO_2) or amorphous silica particles have been shown to increase allergic sensitisation.[42] Hence concentrations of these will vary with population and industrial densities.

Importation of birch and cypress to urban gardens can increase the risk of exposure to more asthmatics in the population.[43] This is further compounded by the use of “male” plants by urban planners and city councils in “*botanical sexism*” in urban environments,[44] meaning more pollen bearing plants are present. Greater international travel also brings a larger volume of people into contact with species

that they may not have come into contact with in the past. Similarly, migration from one country to another involves exposure to a new set of pollutants and allergens as well as changes in housing conditions, diet and accessibility to medical services which may affect migrants' health,[16] and their children's. Further, trade in bird seeds and other garden products may see a much more rapid spread and colonisation of species such as ragweed, assisted by their weed traits. Some areas have particular species that have high allergenic potential that have a strong effect on the population with the Japanese Cedar as an example,[45] with one third of the population suffering sugi-pollinosis.

Review of Studies: - those with estimated current burden attributable to observed climate change (1970-2013)

The content of this review here will focus predominantly on how temperature and CO_2 affects the relationship between pollen and health outcomes. Few studies on health and pollen have been performed in the UK and so much of the discussion here is on data collected in other countries which should only be extrapolated back for the UK with caution, together with information on the observed climate change on pollen phenology.

Birch pollen season is getting earlier at the rate of 6 days per 10 years in the time 1970-1999 across Europe and 4 days per 10 years in London, increasing the risk of exposure in the population.[46] This may be countered by decreased risk of upper respiratory tract infections due to warmer winter temperatures in both adults [47] and children [48], although this has not been replicated in all studies, making predictions of increased asthma exacerbations in the population more complicated.

In the UK Spring has been occurring earlier over the last decades[49] and with wind-pollinated plants in particular,[50] and in the US between 1995 and 2009, the pollen season lengthened 13 to 27 days above 44 degrees North.[51] Across Europe the birch and olive pollen season is arriving earlier.[46, 52] There is some evidence that human health outcomes might benefit from a shortening of specific plant pollen seasons, despite it coming earlier in the year.[53]

A high rate of wheezing attacks during the high pollen seasons of spring and autumn has been revealed in a series of studies, which examined the relationship between allergic pollen and asthma exacerbations. Numerous epidemiological studies worldwide have provided evidence of an association between asthma or wheeze related visits to ED and raised daily pollen counts.[21, 54-56] Evidence is now mounting that even lower levels of pollen (at <20 grains/m^3), in the absence of thunderstorms, may play a role in increasing paediatric ED visits, as well as at the higher measures of pollen count (>50 grains/m^3) reported more extensively in the literature.[57] Not all studies have found associations between high pollen counts and hospital admissions, with Garty et al.,[48] reporting no increase in paediatric ED admissions for wheezing diagnosed as acute asthma attacks during periods of high pollen, although they did correlate with NO_x, SO_2, high barometric pressure, and maximum and minimum temperature. Temperature alone may also play a role in increasing asthma attack risk in children.[58] Although the potential impact of climate change has been know and reported for some time,[10] few models have been prepared that examine the current burden attributable to existing climate variance.

Increases in CO_2 have been proposed to increase the risk of asthma both by increased pollen biomass as well as increased allergenicity of the pollens produced.[59] It should be noted that these experiments were performed over short time periods and more evidence needs to be collected to reflect decadal length

changes in CO_2 concentrations. Greenhouse grown ragweed subjected to differing concentrations of CO_2 has revealed differently expressed sequence tags, including those encoding allergenic ragweed proteins (Amb a) increased under elevated CO_2 and drought stress, but this species is not yet endemic in the UK.[60] Assessment of important allergen producing grass species Timothy grass (*Phleum pratense*) grown in elevated levels of CO_2 (800 ppm) and O_3 (80 ppb) has been undertaken and higher CO_2 increased the amount of grass pollen produced by 50% per flower, regardless of O_3 levels.[61]

Review of Studies: - those with estimated future health impacts on human health from changes in pollen

The influence of climate change on asthma is difficult to measure as it has the potential to act via numerous mechanisms via complex pathways. Future predictions of the effects on pollen on human health will have included the effects of climate change which may result in earlier seasonal appearance of respiratory symptoms and longer duration of exposure to aeroallergens. This may be further compounded by the effects of climate change on plant distribution through range shifts and invasions. This can lead to changed exposure to pollen in the population from more plants, with different flowering seasons. Lastly, variations in the potency of allergen carriers (e.g. the amount of allergen per pollen grain) might make it difficult to correlate symptoms and effectiveness of treatment with pollen or fungal spore counts.[62-65]

Increases in exposure due to changes in allergenic moieties (amount and allergenicity of pollen), extended time pollen is produced by plants; hotter, drier, windier environments increasing risk of human exposure. In addition the potential exists for increased exposure to air pollution (chemical and particular components leading to inflammation) due to increased heat, wind, reduced rainfall and risk of fires causing individuals to be more sensitive to allergens. Projected climate changes will also see the population spending more time outside with clement weather and hence increased exposure to allergens.

Other secondary environmental changes may also be linked to increases in diseases related to pollen exposure. An increase in the levels of particulate matter and ozone which lower the bronchoconstrictive threshold to environmental allergens such as pollen, as well as increase the body's production of IgE and cytokines will increase incidence.[41, 66] Increases in CO_2 have been predicted to increase pollen biomass and allergenicity.[3] Extreme weather events involving high winds, heavy precipitation, and thunderstorms, which may increase in incidence of exposure over mid-latitudes due to climate change, may also contribute to large sudden bursts of allergen release.[17, 67]

Zhang et al. employed a Bayesian framework to model effects of climate change on birch and oak pollen. Their results suggest that annual productions and peak values from 2020 to 2100 under different scenarios will be 1.3 to 8.0 and 1.1 to 7.3 times higher respectively than the mean values for 2000.[68] In a related study, projections for Betula (birch) and Quercus (oak) pollen in the US were obtained for the 2050s.[69]

A regional study offers perhaps some insight in what should be possible in this research area utilising a trans-disciplinary approach.[70] Here a regional-scale pollen emission and transport modelling framework was developed that treats allergenic pollens as non-reactive tracers within the coupled Weather Research and Forecasting Community Multiscale Air Quality (WRF/CMAQ) modelling system.

Future predicted climatic conditions can be run in the model and have suggested the pollen season will commence 5-6 days earlier. Sensitivity studies suggest that the estimation of the pollen pool is a major source of uncertainty for simulated pollen concentrations.[71]

Potential for Impacts to be avoided by Adaptation Measures

Adaptation measures fall broadly into two categories:

1) managing the hazard (e.g. pollen/air pollution, planting); and
2) managing the vulnerability (i.e. people's exposure to pollen, e.g. via pollen forecasts, pollen samplers etc.).

1) Managing the hazard

Activities that can help mitigate the impact of additional climate change-induced respiratory disease include continued research into risk factors, physician and patient education, optimising production and distribution of information on high exposure times and places, and actively considering the budgetary impact of increased prevalence and severity of respiratory disease, providing economic evidence to increase and transfer knowledge in this area.

Selective planting of non-allergenic species may reduce the pollen load on a population. The high levels of Japanese cedars planted post-war may well have added to the asthma burden now being experience by Japan.[45] Regulation of planting of allergenic species may reduce the allergen load, particularly in areas of high density population (e.g. plane trees in London). Similarly the associated risk factor of air pollution may be another pathway to reduce effect of pollen exposure. A reduction in air pollution via regulation of $PM_{2.5}$ may also reduce the risk of asthma related to pollen indirectly. Impact of mechanisms of disease needs to progress and then risk of these calculated in models, e.g. increased air pollution impairing regulatory T cell function.[72]

3) Managing the vulnerability

Measurement of Pollen

The forecasting of pollen-levels, either species-specific or in terms of general categories, is still in its infancy. Some encouraging progress has been made for e.g. birch pollen, where the relevant functionality has been added to a Finnish atmospheric dispersion model.[73] Early modelling studies are encouraging and a widespread use of such functionality in numerical weather models, combined with a denser pollen monitoring network, could in future lead to detailed pollen forecasts.

Recent IT developments in IT may benefit forecasting for asthma/allergy sufferers. Developments have enabled significant progress in pollen monitoring and in alerting allergy sufferers. These methods have benefited particularly from the widespread availability of smartphones, i.e. devices which can communicate data between local devices and large-area connectivity. Such devices also allow for precise geo-coding of collected information.

Also developed recently with new technologies are individual pollen samplers. There is now a working prototype of an individual pollen sampler which is a wearable/portable device to be used in clinical trials, allergy anamnesis, academic research or individually, to assess an individual's exposure to aeroallergens in the daily life. It is labour intensive as it uses the same principle as the Burkard pollen

trap while at the same time recording the location and whether the wearer is in or outdoors (via UV level detector).

Under development are automated near-real-time pollen samplers to replace the technology of the Burkhard samplers. Optical properties of pollens are used to detect them in WIBS (Wide Issue Bioaerosol Sensor, Universities of Hertfordshire & Manchester).[74] It is an optical particle counter featuring a dual wavelength fluorescence spectrometer and detects pollen particles through a combination of scattered light and fluorescence of specific pollen proteins. Another approach used in Japan is the so-called "Pollen-bots" that automatically analyse air samples and submit data in hourly intervals to a central website.[75] The "Pollen-bots" network uses light scattering alone to detect two particular pollen types (Japanese cedar (sugi) & Japanese cypress (hinoki)) which cause widespread allergic reactions there.[76] More similar to the traditional Burkard pollen trap is another machine developed by German company Hund, their pollen monitor BAA500 is the first of a future line of fully-automated analytical devices for monitoring airborne particles or particles transported in liquids. It combines automated sampling, digital image processing and analysis, and archival storage of the sample carriers in an autonomous unit. The BAA500 has so far been employed only in a small number of locations, due to their high costs.

Assessment of Pollen Exposure

Several methods exist for monitoring and recording pollen health outcomes. "Propeller-Health" is a device that attaches to an asthma inhaler whose use is communicated usage via Bluetooth to a smartphone, which in turn geo-tags the usage data and uploads it to a central database. Researchers staff can examine asthma clusters, which can be either further investigated or assess for public health interventions.[77]

The Pollen-Diary is a sophisticated two-way communication tool, which is available throughout Europe. Allergy sufferers download a smartphone app which they can individualise, and which receives its data from a Europe-wide database (data is submitted by national pollen service providers; in the UK these data come from the Met Office). The app warns on specific species, and also invites sufferers to record their individual symptoms. Evaluations for specific countries have been carried out and have been published in the peer-reviewed literature.[78]

A range of novel treatments for allergic rhinitis is current in use and being refined. For example MK-3641 is a short ragweed sublingual therapy, currently under investigation for immunotherapy of ragweed pollen-induced allergic rhinitis. After the first dose was administered in a health care setting, self-administration was found to be well tolerated, with systemic reactions and use of adrenalin uncommon.[79] These treatment pathways may be of use in the future but it is unclear if a preventive strategy has more value, due to the cost of intense contact with health professionals and risk of anaphylaxis.

Conclusions / Evidence Gaps

We have learnt much over recent years on the meteorological and bio-aerosol component of environmental exposure and risk of asthma symptom exacerbations. While the linkage between exposure to pollen and attendance at ED has been firmed up in recent years, but many studies are still only providing ecological level evidence. To further explore risk factors of asthma exacerbations associated with pollen exposure a higher level of evidence needs to be collected, and will be facilitated by better measures of exposure data (e.g. pollen measures and/or modelling) and

health outcomes measures (e.g. greater detail of asthma diagnosis i.e. allergic versus non-atopic asthma) as well as confounders and other risk factors e.g. tobacco smoking status).

A potential public health pathway of prevention of asthma or lowering its incidence, especially in high risk populations, may be undertaken via limiting exposure to certain pollen species during critical time periods in immune system development. Only the first glimpses of the importance of this have been made but several groups are now reporting that residence in an area with high pollen load (quantity and allergenicity) increases the risk of asthma outcomes in later life. Several factors need to be explored around issues of sex, ethnicity and timing of exposure.

A major evidence gap exists on the importance of thunderstorm asthma currently as a phenomenon impacting public health. Evidence needs to be provided as to whether it is a scientific novelty where small numbers of people are affected (in comparison the other public health questions) or is it a threat to sustained ED provision that can be countered by preventative action utilising forecasts. Differential reports of frequency is made difficult by the variety of risk factors involved i.e. correct thunderstorm weather pattern in an area of high population density during a period of high airborne quantities of pollen that the immune system of the population recognises. Further epidemiological work needs to occur with sufficient sample size to ensure adequate confidence intervals can be attributed to the prevalence of this phenomena, and whether measures such as public health information or increased staffing levels in ED based on meteorological forecasts is appropriate.

Further evidence needs to be collected via modelling to better understand the existing relationship between pollen exposure and asthma, while also gaining understanding how pollen timing, quantity and quality may be changing with changing environments. These changing environments will also alter associated risk factors such as parallel respiratory exposures or human behaviours and these models will feed into forecasting models that will provide quantification of remediation or adaption measures required so that with changing environmental conditions we are well placed to choose appropriate routes of public health policy.

Examination of other disease types and its relationship to pollen (e.g. allergic rhinitis, food allergy and eosinophilic esophagitis,[80] cardiovascular[81], preterm births[82] or mental health[83]) needs further study. This would enable a holistic approach to be undertaken such that overall population health could be predicted, with potential for effects ameliorated, and improved rather than just focus on a single disease.

So far efforts in the reduction in the prevalence of asthma on the health system has relied on decreases in asthma exacerbations and attacks predominately by increasing patients ability to manage their condition via availability of appropriate medication and understanding of environmental and behavioural (e.g. exercise) triggers (and approximately 90% of asthmatics have relatively symptom free lives if managed appropriately).

But further wins may be possible by increasing the immune health of the population and decreasing inflammatory responses to triggers, but little progress has yet been made in this area, probably due to the complex nature of the disease involving interactions between environment and genes. Important findings around high exposure to pollen during infancy and increased risk of asthma in later life need to be explored, especially considering the risk of exposure to increased quantities and increased allergenicity of pollen in the future with a changing environment. This

may provide answers to reasons for increasing prevalence of asthma and other inflammatory related diseases over recent years.

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