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REVIEW

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Global change, climate change, and asthma in children: Direct and indirect effects - A WAO Pediatric Asthma Committee Report

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ABSTRACT

The twenty-first century has seen a fundamental shift in disease epidemiology with anthropogenic environmental change emerging as the likely dominant factor affecting the distribution and severity of current and future human disease. This is especially true of allergic diseases and asthma with their intimate relationship with the natural environment. Climate change-related variables including increased ambient temperature, heat waves, extreme weather events, air pollution, and rainfall distribution, all can directly affect asthma in children, but each of these variables also indirectly affects asthma via alterations in pollen production and release, outdoor allergen exposure or the microbiome. Air pollution, with its many and varied respiratory consequences, is likely to have the greatest effect, as it has increased globally due to rapid increases in fossil fuel combustion, global population, crowding, and megacities, as well as forest burning and trees succumbing to an increasingly hostile environment. Human activities have also caused substantial deterioration of the global microbiome with reductions in biodiversity for molds, bacteria, and viruses. Reduced microbiome diversity has, in turn, been associated with increases in Th2 allergic responses and allergic disease. The collective effect of these changes has already shifted allergy and asthma disease patterns. Given that changes in climate have been relatively small to date, the unavoidable, much greater shifts in climate in the future are concerning. Determining the relative scale of the direct versus indirect effects of climate change variables is needed if effective avoidance and adaptive measures are to be implemented. This would also require much more basic, epidemiological, and clinical research to understand the causal mechanisms, the most relevant climate factors involved, the regions most affected and, most importantly, effective and actionable adaptation measures. We suggest that allergy and respiratory health workers should follow current guidance to reduce present risks related to climate change and watch for new recommendations to reduce future risks. Since the respiratory system is the one most affected by climate change, they also need to call for more research in this area and show strong leadership in

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advocating for urgent action to protect children by reducing or reversing factors that have led to our deteriorating climate.

Keywords: Climate change, Environmental pollution, Global changes, Pediatric asthma, Direct effects, Indirect effects

INTRODUCTION

Humans have in a very short time caused major damage to the earth's ecosystems [1] and despite urgent calls for action, damage continues to accelerate.[2] The climate crisis, a phenomenon started over the past 5 decades, is a component of this damage and the World Health Organization (WHO) now states that it is the greatest threat to future human health.[3] Climate change has already caused major changes to environmental antigens and human exposure, leading to an increase in immunologic diseases, including allergic diseases.[4,5] And it is expected that by 2025 more than 50% of all Europeans will suffer from at least 1 type of allergy, with no age, social, or geographical distinction.[6] The prevalence of pediatric asthma has, in parallel, increased in recent decades, with growing evidence pointing to the role of climate change and air pollution as contributing factors that are not expected to reduce in the imminent future.[6,7]

Global changes implicate complex and overlapping anthropogenic phenomena including climate changes, landscape transformations, environmental pollution and the increased transport of organisms on a continental scale. The analysis of each driver of global change has many manifestations but the combination of them reflects the complexity of this global crisis.

Climate change includes changes in 4 major dimensions: Firstly, atmosphere changes, including increased levels of greenhouse gases, leading to increase of ambient temperature of the Earth's surface; secondly, land changes resulting from the increase of rainfall during wet seasons and raining less during dry seasons, as well as shifts in climate zones; thirdly, ice changes including the thawing of ice leading to huge quantities of water into the oceans; and lastly, the ocean which is warming faster than any other time, increasing sea levels and become more acidic.[8] Air pollution, particularly through use of fossil fuel, is a major inducer of climate change, and is further increased by it. Rapid increases in temperature have already affected physical and biological systems, regionally and globally.[9,10] These changes derive from the anthropogenic increase in concentrations of greenhouse gases and come in parallel to destruction of the natural environment, urbanization, industrialization, and Western lifestyle, all of which are strongly associated with the observed loss of biodiversity.[4]

Carbon emissions from all human sources, including agriculture and land use, were estimated at a massive 43 billion tons in 2019,[4] giving insight into why the insulating properties of carbon dioxide (CO2) have elevated surface temperature. Increases in global temperature have brought major changes to the distribution of antigens. Changes in rainfall patterns and humidity have produced widespread increases and decreases in forest distribution,[11] each of which will affect aeroallergens. Air pollution has intensified from increases in human activities and population density,[12] but also from increasing air stagnation in larger cities[12] and equatorial regions.[13] Collectively, these changes have produced major changes in global patterns of flora and fauna,[1] significant reductions in planetary biodiversity,[1] and widespread changes in antigen distribution[14] and asthma prevalence.

Air pollution is the most important climate change variable directly affecting respiratory disease. Almost the entire global human population breathes air that exceeds WHO air quality limits with immediate impact in early life and significant lifelong consequences.[15] Pollutants have physicochemical characteristics favoring the transport of antigens into the respiratory tract and facilitating their penetration into the airway epithelium, both of which could in part explain the increasing frequency of respiratory diseases, including asthma, in children.[16] WHO has called environmental pollution a "silent killer".

Recent studies have demonstrated the role of climate change in the development of asthma,[17,18,19] including the frequency of asthma-related exacerbations, and increases in emergency room presentations and hospital admissions.[20] In this report, the Pediatric Asthma Committee of the World Allergy Organization (WAO), aims to summarize and discuss the direct and indirect impacts of the climate crisis on pediatric asthma and the urgent need to activate the world society for mitigation and adaptation measures. The interrelationships between the direct climate change factors and the indirect effects on the environment specific to allergy and asthma are summarized in Fig. 1.

Air pollution and pediatric asthma

Primary pollutants (pollutants emitted from the original source) and secondary pollutants (pollutants that form when primary pollutants react in the atmosphere) are major components of climate change[21] and have direct effects on susceptibility to asthma.

Exposure to a large number and variety of air pollutants can damage the airway epithelium,[22] hamper mucociliary clearance, affect mucus production, and trigger airway hyper-reactivity.[23,24] Mechanistically, studies have described the role of air pollutants in inducing airway inflammation, oxygen free-radical production in the lungs, cytokine and chemokine release, production of white blood cells, the neutrophil influx, covalent modification of key cellular enzymes, and stimulation of irritant receptors.[25,26] Additionally, pollutants (ie, ozone [O3], particulate matter [PM2.5]) may act as adjuvants by skewing immune responses towards type-2, IgE production, and stimulation of Th17 responses.[27,28] Pro-inflammatory effects in the respiratory tract result from free radical generation by particulate components, with volatile organic compounds and gases (ie, nitrogen oxides, O3, sulfur dioxide [SO2]) contributing to the induction of oxidative stress.[27,29] The latest research implicates nitrogen dioxide as a cause of abnormal lung development,[30] lung inflammation,[31] and asthma.[32] Overall, air pollutants may interfere with immune responses, alter the microbiota, and act directly on respiratory epithelium, facilitating the penetration of allergens.[33] Environmental tobacco smoke is a major contributor to pediatric asthma development.[34]

The recent American Lung Association State of the Air 2023,[35] reporting on levels of air pollution from official monitoring sites during 2018–2020, found that 3 out of 8 Americans are exposed to unhealthy levels of O3 smog (Failing grade-F); in the years 2018-20 more than 122 million people lived in the 156 counties which earned an F for O3. Although this number is lower than those reported

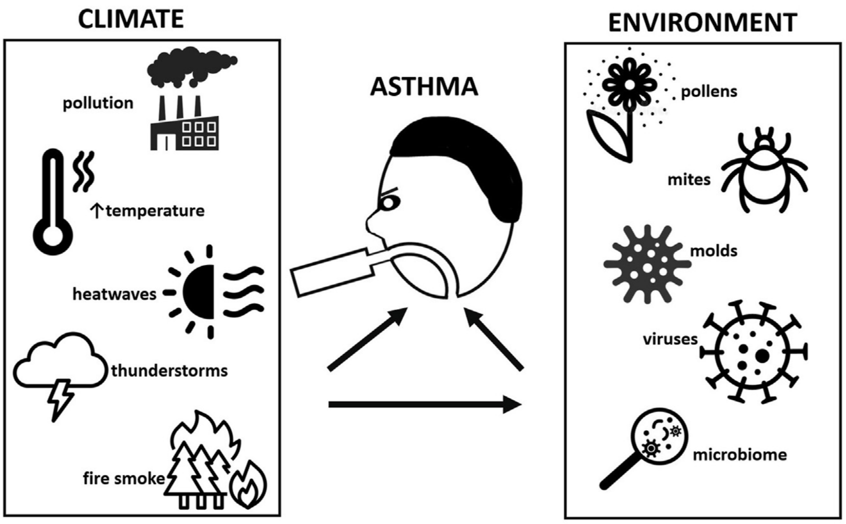

Fig. 1 Climatic and environmental factors that affect asthma. Climate change variables can have **direct** effects on the airway in asthmatic children as well as **indirect** effects through environmental factors that influence asthma.

in the past four reports and there have been trends toward improvement since the Clean Air Act of 1970, it is still worse than the 116 million of the 2017 report.

Air temperature and increasing levels of CO2

Globally, the Intergovernmental Panel on Climate Change (IPCC) reported in 2022 that average CO2 concentration has increased from 250 to 410 parts per million over the past 150 years[36] with the latest reports showing it has now reached 417 parts per million.[37] The IPCC 6th assessment also reported projections showing that mean air temperature would increase by nearly 5°C by 2100 if Shared Socioeconomic Pathway 5-8.5 is followed.[36] Such an increase in temperature would have catastrophic effects on the entire global ecosystem[38] and every aspect of human health including asthma.

A potentially serious but little-appreciated long-term concern regarding CO2 is that the very high levels predicted by current trajectories to 2100 may directly have an adverse effect on mammalian lung structure and function. This has been shown in offspring of pregnant mice exposed to 890 ppm of CO2,[39] a level within current 2100 projections. Whether this *in utero* toxicity will occur in humans and, if it does, how it will interact with the many other CO2 contributions to asthma is unknown but greatly concerning.

CO2 is not usually considered a pollutant, but increasing levels will affect many aspects of global ecology. CO2 is used by plants in photosynthesis and increasing CO2 levels increase this process,[40] but the scale of the effect on plant biomass is difficult to determine due to the many diverse effects of CO2.[41] Rising CO_2 levels may indirectly influence asthma by increasing the levels and allergenicity of pollen including ragweed[40] and oak.[42] How much CO2 influences pollen production cannot be determined easily due to the effects of other climate change variables including temperature and rainfall.[40]

Effects of extreme weather phenomena on asthma

Thunderstorms

"Thunderstorm asthma" is a phenomenon describing asthma exacerbations that occur due to environmental factors triggered by thunderstorms in individuals with grass pollen or mold allergy. Epidemics have been reported in many geographical regions, such as the United Kingdom or Italy, but are more commonly observed in south-east Australia during the grass pollen season.[43]

The epidemiology of asthma exacerbations recorded after thunderstorms is well established, but whether the effect is direct or indirect is unclear, as the pathophysiological mechanisms involved have yet to be determined. Most patients with thunderstorm asthma have seasonal allergic rhinitis. In normal conditions, large pollen grains do not reach the lower airways, because of their size (>10 μm diameter).[20] From different studies, it is proposed that during thunderstorms outflow cold air sweeps up pollen grains, ruptures them through osmotic shock, and then concentrate them in a shallow band of air at the ground level.[44] Under this phenomenon, smaller, paucimicronic allergenic particles are released from pollen grains or other allergenic plant species and in some cases also Alternaria species[45] and reach the lower respiratory tract triggering severe asthma exacerbation.[46]

The impact of fires on asthma

During a wildfire, a variety of pollutants are released because of their incomplete combustion, including suspended particulate matter, carbon monoxide, formaldehyde, nitrogen dioxide, and polycyclic aromatic hydrocarbons.[47] As a result, significant associations between wildfire smoke and emergency hospital admissions due to asthma exacerbations have been identified and are likely to be direct effects of the smoke on the respiratory system. In people with severe asthma, intense and prolonged PM2.5 exposure from bushfires has an enhanced effect allowing deposition into terminal alveoli and associated with acute and persistent symptoms.[48]

Smoke from wildfires may travel thousands of kilometers, depending on the concentrations of fire and smoke and the wind patterns, which may change daily and last several weeks. Exposure to PM2.5 particles stimulates dendritic cells and T cells to produce type-2 cytokines and activate pro-inflammatory genes in a process mediated by free radical and oxidative stress mechanisms, resulting in acute bronchospasm.[49]

The impact of floods on asthmatic children

Flooding from extreme precipitation caused by rain, snow or hail can be considered an indirect cause of asthma, as it leads to the accumulation of fungal species and that can become a prominent cause of physical illness. Studies of flood-ravaged homes report elevated number of several fungi species (*Cladosporium*, *Alternaria*, *and Penicillium* spp.) and bacteria.[50] A recent meta-analysis reported that exposure to several fungi species increases the frequency of asthma exacerbations, and exposure to mold as an infant increased the risk of asthma later in childhood.[51] Immunologically, fungal exposure may modify asthma morbidity by promoting Th17 immune responses, and bioaerosols act as pathogen-associated molecular patterns to trigger responses leading to upper and lower airway irritation and inflammation.[52] Additionally, children exposed to high levels of mold have elevated levels of IL-17A and have more frequent asthma-related symptoms[53]

Major allergens

Pollen

Climate change affects pollen production, distribution, and allergenicity.[54,55] In this way, climate change indirectly affects those with respiratory allergies, with asthmatic children being among the most susceptible populations.[56]

Plants respond to global warming in different ways, depending on their genotype and degree of phenotypic plasticity, which vary markedly with different climate change variables and effects.[4,40] Thus, the influence of pollution and climate change on pollen is multifaceted.[57]

Pollutants are one of the main plant stressors, causing indirect effects on asthma via their effects on pollen grains.[58] Additionally, pollutants can favor an increase in the concentration and biological activity of pollens' allergenic proteins,[59] probably as a result of a lower photosynthetic efficiency and a greater degree of oxidative stress.[60] In elevated humidity conditions, pollen burst and release cytoplasmic contents in a species-specific manner, triggering IgE responses in allergic individuals. During germination or tube burst in cases of osmotic shock, fine allergenic particles are released in the atmosphere.[61]

Additionally, increasing ambient temperature in many regions often correlates with increases in pollen concentrations and pollen season length on selected taxa.[62] Data from the last 2 decades identified an advance of 20 days in pollen seasons,[63] and a significant increase in daily pollen concentrations.[64] Considering the expected temperature changes at the end of this century, the estimated trends are that the pollen season will start up to 6 weeks earlier, last over 2 weeks longer, and the annual total pollen emission will increase up to 40%.[63,65] Longer seasons and increases in atmospheric pollen mass increase human exposure to allergens, leading to an increase in symptomatic sensitization from early in life.[66]

Climate change is influencing vegetation patterns and plant physiology through spatial and temporal changes in temperature and humidity that can lead to the disappearance of native species and the establishment of non-native species with the consequent greater risk of allergic sensitization.[59]

Pollution and temperature changes may also induce the release from pollen of enzymes and bioactive pollen-associated lipid mediators (PALMs) with pro-inflammatory and immunomodulatory actions that can also trigger and enhance allergies.[67] Diesel particles appear to prime cells to react more rapidly to pollen exposure, especially inflammation-related genes, a factor known to facilitate the development of allergic sensitization.[68]

Mites

Whereas most of the climate change and allergy studies have focused on outdoor aeroallergens, there are also significant impacts on indoor aeroallergens. For example, there are effects on house dust mite (HDM) antigens which are important sensitizers for respiratory allergic diseases including pediatric asthma.[69] HDM are sensitive to microenvironment modifications including those from climate change which could therefore modify the HDM life cycle.[70]

Outdoor temperature and indoor humidity are principal factors affecting growth and survival of HDM favoring their presence and proliferation.[70] HDM are composed of approximately 75% water by mass, requiring high air humidity to prevent excessive loss, with relative humidity below 50% being adverse for growth and replication.[71] A Mediterranean climate (living near the coast, with higher humidity) was associated with a higher prevalence of HDM sensitization in patients with allergic rhinitis and asthma, compared to a Continental climate in France and Italy.[72]

Global warming expands HDM habitats. The pattern of increased sensitization to HDM became evident in the last decades, particularly in tropical and developing regions. Global warming may influence the life cycle of mites, providing larger species diversity and a growing source of antigens to become sensitized.[70] Additionally, extreme meteorological effects like flooding, can result in a long-term increase in moisture which favors the growth HDM.[71]

Climate change may cause some areas where HDMs reside to expand exposing more people to HDM allergens, and other areas to contract reducing HDM exposure. An expected consequence of climate change is increased time indoors, increasing exposure to indoor allergens including HDM.[54]

As mentioned before, air pollutants such as diesel exhaust interact with aeroallergens including HDM, increasing the risk of sensitization. Two decades ago, a northern European epidemiological study reported a significant association between lifetime pollution exposure and sensitization to *Dermatofagoides farinae*.[56,73]

Environmental control measures specifically directed against HDM have not demonstrated a major benefit; however, in sensitized children, a significant reduction in asthma exacerbations requiring emergency department assistance has been reported.[69]

At present, there is no conclusive evidence that climate change increases the risk of allergic diseases related with HDM. However, the above evidence supports this concept.

Fungi

Climate is the major agriculture ecosystem factor influencing the life cycle stages of fungi and the observed environmental changes result in the imbalance between plant growth and the related health impacts on population.[74]

As in HDM, temperature and humidity are the major factors contributing to survival and replication of molds. Molds are fungi that grow in warm conditions; studies estimate a prevalence of 20% in humid conditions and 25% when the environment is warm. After extreme weather events, such as floods, stagnant water, water intrusion into homes and increased carbon dioxide, there are increased levels and subsequent exposure to these allergens both indoors and outdoors.[20,75] The slowly increasing atmospheric concentration of allergenic fungal spores (Cladosporium), together with an early seasonal onset and greater allergenicity, could lead to an increased risk for allergic diseases.[52,70]

Fungal spores are easily transmitted from outdoors to the domestic or work environment, where access to water or through transpiration, can promote their growth. Based on several studies, 20–50% of US houses are damp, varying according to the different geographical regions and climates. A 1.4–2.2 fold increased risk of respiratory conditions such as asthma/wheeze has been observed in infants, children and adults living in damp houses.[76] Furthermore, birth cohorts show that dampness is related closely to asthma symptoms in first 2 years of life.[76] However, conclusive evidence of an increase in asthma due to fungal spores from damp conditions is lacking.

Vulnerable populations are most commonly those living in old or poorly ventilated buildings and over-crowded houses with inappropriate heating, insulation, and ventilation. Additionally depending on the geographical area, communities living in flood-prone regions such as coasts/rivers have higher exposure to molds and subsequently suffer more asthma related symptoms.[20]

Other allergens

Climate changes augment pest-related diseases through alteration of the natural environment by flooding or drought and the urban environment by changes in land use. Urban pest species such as cockroaches and rodents are major sources of allergens. Dampness enhances colonization of the households by cockroaches. Children sensitized to cockroach allergens are at an increased risk of asthma morbidity and hospitalizations.[77,78] Mouse and rat allergens are found primarily in inner-city homes and are common global allergens.[79]

Flooding of indoor environments after massive storms potentially increases the exposure to mosquitos and use of repellents. "Mosquito-killing" spirals generate high concentrations of particulate matter. The same happens when burning incense indoors.[80] Habitats of stinging insects such as bees and wasps could be influenced by climate change, and these are also well-known allergens.[20] Increasing evidence suggests that bites from certain tick species can lead to alpha-gal syndrome (AGS). Climate change will likely facilitate the expansion of AGS in new regions secondary to the potential alteration in tick habitats.[81]

Allergenic helminths are more common in hot tropical areas including Africa; some helminth infestations such as ascaris may extend their habitat with global warming. *Ascaris lumbricoides* induces a Th2 response and specific IgE synthesis and is associated with allergy and asthma in school-aged children. In addition, tropomyosin from ascaris cross-reacts with mite tropomyosin [82,83]

Sensitization to furry animals including pets is detected in up to 15% of the population.[50] Sensitization to cat Fel d 1 and dog Can f 1 is prevalent amongst asthmatic children and associated with poor outcomes. Some outdoor fungal spores, such as Alternaria can be found indoors due to transfer via pets.[79] The synergistic effects between extreme heat and aeroallergens intensify the toxic effect of air pollutants, which in turn increases the allergenicity of aeroallergens.[84]

The penetration of outdoor pollutants further deteriorates the quality of indoor air. Children are exposed to allergenic and non-allergenic stimuli indoors. Indoor environments are a mixture of allergens and chemical pollutants such as paints, adhesives, flooring chemicals, cleaning products, asbestos, and combustion products from heaters and cooking, and above all, tobacco smoke. Burning candles is another source of particulate emission.[20,84,79] Asthmatic children may suffer within the context of the so-called sick building syndrome which is dominated by older buildings, multifamily dwellings, lack of ventilation, dampness, and living near heavy traffic, each of which can potentiate indoor pollution and aeroallergen effects.[78] Finally, the adoption of sedentary lifestyles significantly increases the probability of exposure to internal aerosols, especially in closed spaces with inadequate ventilation. The COVID-19 pandemic has increased the time spent indoors due to lockdowns/quarantine and hence the exposure to indoor aeroallergens and excessive use of household cleaning products and disinfectants with significant increase in volatile organic compound concentrations within the home.[20,84,79]

Climate change and the microbiome

Currently, biodiversity is declining faster than any time in human history. Climate change is a leading cause for the observed decline in macrodiversity with the accompanying decline in environmental and human microdiversity.[85] As the microbiome is a key factor in the development and maintenance of the immune system, the alteration of both environmental and host microbiota may account for the increase in Th2 responses[86] and the prevalence of asthma and allergies,[85] but probably many other chronic conditions as well. Furthermore, environmental changes impose dietary, and lifestyle shifts that increase the risk for food allergy and asthma through intestinal mucosal dysbiosis.

The lungs harbor diverse microorganisms, including microbiome, virome, and mycobiome (fungi), each of which may be influenced by inhaled irritants/toxicants. Exposure to pollutants disrupts the structure and function of the microbiome community, resulting in an imbalance of antioxidant and pro-inflammatory conditions with downstream consequences for human health.[87] Studies have identified lung microbiome alterations associated with specific asthma phenotypes and severity patterns.[88] Certain fungi may act as adjuvant factors that can increase Th2 immune responses. For example, gut mycobiome overgrowth is linked to increased child susceptibility to asthma development by school age.[89]

Climate change and viral infections

Clean air is an important contributor to the overall and respiratory health, while poor air quality

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confers a high risk for adverse health outcomes, especially in the vulnerable asthmatic population.[90] Epidemiological data from children demonstrate more severe viral-induced asthma symptoms and worse lung function outcomes in the presence of increased exposure to high concentrations of chemical air pollutants.[91] Pollen exposure increases the risk of rhinovirus (RVs) and Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[86,87] respiratory infections. Viruses and allergens have been shown to interact with pollutants such as O3 and fine particles (PM2.5), increasing their morbidity effects.[92]

Implicated mechanisms that increase susceptibility to viruses and harm from them in the presence of chemical air pollutants include impairment of the mucosal barrier function. Exposure to ambient particulate matters and diesel exhaust particles reduces barrier integrity, while nitrogen dioxide exposure increases epithelial expression of ICAM-1, the receptor for RV-A and RV-B.[93] Moreover, exposure to air pollutants contributes substantially to increased oxidative stress, favoring Type-2 responses, subsequently affecting pulmonary health.[94] Finally, *in-vitro* studies have documented that ambient particular matter can disrupt the balance between Th1 and cytotoxic T lymphocyte type-1 (Tc1) responses, potentially affecting the antiviral defense mechanisms.[93] Viral infections in turn, especially RVs, impair antibacterial innate immune responses,[95] thus affecting the overall microbiome homeostasis. Viruses, microbes, allergens, and chemical pollutants exhibit a complex interaction with the human immune system, depending upon several factors such as the age, predisposition and identity of the agent.[96] Viruses may be a driver of respiratory allergies in children[92] and affected by changes in viral epidemiology from anthropogenic influences.[97] Nevertheless, the overall effect may vary considerably, making it difficult to predict with accuracy the impact of pollutants on viral and microbial effects on health.

Vulnerable populations

The vulnerability of individuals to climate change is greatly influenced by social determinants. Low-income countries (LICs) are particularly vulnerable because of poverty, poor sanitation, high prevalence of malnutrition, infections, non-communicable diseases, poor quality housing, smoke exposure and weak non-resilient healthcare systems. People living in such conditions, indigenous groups, racial and ethnic minorities, vulnerable occupational groups, aged populations, pregnant women and children, people with disabilities, and those with chronic medical conditions will bear the brunt of climate change because of their high exposure and limited adaptive capacity.[98,99]

Climate change injustice for low- and middle-income countries (LMIC)

LMIC are less responsible for climate change but face its greatest challenges. The global health burden of ambient fine PM2.5 is increasing annually[100] despite progress in reducing exposure in some countries. However, PM2.5-attributable health risks are inequitably distributed across countries and cities, and its impact varies, influenced more by poverty and social factors than by contamination levels.[101] Globally, LMIC experience greater exposure to unhealthy levels of airborne particulates compared to the global average, but NO2 patterns show less variability. In high-income countries, studies reported that secondhand smoke, ambient pollution, and traffic emissions were the most important sources of personal exposures, while household cooking and heating with biomass and coal is more relevant in LMICs.[102,103]

Future prospects

Anthropogenic activities have inflicted major and lasting damage on every measurable aspect of the Earth's delicate ecosystems.[38] For many systems, this may now have reached a level where climate change "tipping points" have been reached, resulting in change accelerating and becoming unstoppable.[104] Despite calls for urgent action[36] and rapid increases renewable energy production, the rates of carbon dioxide and methane emissions continue to increase.[104] Clearly, immediate reduction of greenhouse gas emissions should be a primary objective for society to have any chance in slowing the emerging dangers wrought by an increasingly hostile climate.

One of the greatest impacts of climate change on health, but also a major reminder of its effects, is on childhood asthma.[17,19] Measures to reduce climate change impacts on health have been introduced in some countries and these include the design and construction of buildings, and use of air conditioning systems in homes to protect from temperature extremes and reduce condensation and humidity. To help protect children from climate change, patients and families can use tools, such as the US Environmental Protection Agency's (EPA) Air Quality Index,[105] which provides daily levels of ground-level O3, particle pollution (PM10 and PM2.5), carbon monoxide, nitrogen dioxide, and SO2, and allows the public to learn quickly when air quality levels are unhealthy and may exacerbate asthma symptoms. Accurate and affordable indoor air pollution monitors are also needed.

In more affected regions, after air quality alerts from local authorities such as the EPA,[105] asthmatic children should keep windows and doors closed and use high efficiency particulate air filters to remove fine particles of smoke in the air. Air filtering is an area that needs urgent support, to develop affordable, low-energy and effective devices for use worldwide. Children with asthma and their families, should be aware of the risks of exposure to high levels of pollutants, allergens and viruses[106] and the possible effect of thunderstorms, in order to avoid these exposures and minimize the risk of asthma attacks.

CONCLUSION

Climatic factors that have changed under the spectrum of "climate change" all have direct effects on childhood asthma, but these effects may be overshadowed by the indirect effects these factors have on environmental allergens and the microbiome. To fully determine the impact of climate change on asthma and respiratory allergies would require an understanding of the complexity of interactions of the direct effects on the airways, and the indirect effects of pollen and microbes on the immune system, and the microbiome and respiratory infections on the airway. These relationships are especially important in young children as early damage can have life-long consequences.[107] Climatic factors affect pollination and life cycles of aeroallergens and alter the distribution and severity of allergic disease. The seasonality and severity of allergy and asthma in children are influenced by the growth patterns of allergenic species which act synergistically with pollutants and can be enhanced by global warming. More intensely focused research on indoor and outdoor air pollutants and their effects on health is needed to identify the best targets for intervention, as well as adaptation measures. Future increases in ambient temperature and air pollution will have marked effects on all aspects of global public health. Global geospatial studies that use environmental climate and health data are needed determine regions where climate has most affected respiratory and allergic disease and the climatic variables involved.[108] Current evidence shows that the respiratory as well as the immune systems are the most affected system by climate.[15] In view of this, allergists, immunologists and respiratory physicians should do everything in their power to influence international agencies, governments, private businesses and the general public to take urgent action to reduce our carbon footprint and reverse the damage we have done to the natural environment. Even with such action, there is now concern that it may already be too late to stop catastrophic environmental decline.[38,109,104,110]

Abbreviations

WAO: World Allergy Organization; IPCC: Intergovernmental Panel on Climate Change; CO2: Carbon dioxide; PALMs: Pollen-associated lipid mediators; HDM: House Dust Mites; AGS: alpha-gal syndrome; PM: Particulate Matter; Tc1: T lymphocyte type-1; LICs: Low Income Countries; LMIC: Low- and Middle-Income Countries.

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All authors have given their consent for publication.

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Each author's potential conflicts of interest have been disclosed.

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REFERENCES

1. Bradshaw CJA, Ehrlich PR, Beattie A, et al. Underestimating the challenges of avoiding a ghastly future. *Frontiers in Conservation Science*. 2021;1(9).
2. Seibert MK, Rees WE. Through the eye of a needle: an eco-heterodox perspective on the renewable energy transition. *Energies*. 2021;14:4508.
3. WHO. *Climate Change and Health*. World Health Organization; 2021.
4. Ray C, Ming X. Climate change and human health: a review of allergies, autoimmunity and the microbiome. *Int J Environ Res Publ Health*. 2020;17(13).
5. Singh AB, Kumar P. Climate change and allergic diseases: an overview. *Front Allergy*. 2022;3:964987.
6. European Academy of Allergy and Clinical & Immunology. *Advocacy Manifesto Tackling the Allergy Crisis in Europe - Concerted Policy Action Needed*. 2015 (Brussels, Belgium).
7. Biagioni B, Cecchi L, D'Amato G, Annesi-Maesano I. Environmental influences on childhood asthma: climate change. *Pediatr Allergy Immunol*. 2023 May;34(5):e13961.
8. IPCC. In: Masson-Delmotte V, Zhai P, Pirani A, eds. *Climate Change 2021: The Physical Science Basis. Contribution of Working Group I to the Sixth Assessment Report of the Intergovernmental Panel on Climate*. Cambridge, United Kingdom and New York, NY, USA: 2021, Cambridge University Press; 2021. In press.
9. Rosenzweig C, Karoly D, Vicarelli M, et al. Attributing physical and biological impacts to anthropogenic climate change. *Nature*. 2008 May 15;453:7193.
10. Garcia RA, Cabeza M, Rahbek C, Araújo MB. Multiple dimensions of climate change and their implications for biodiversity. *Science*. 2014 May 2;344(6183):1247579.
11. Albrich K, Rammer W, Seidl R. Climate change causes critical transitions and irreversible alterations of mountain forests. *Global Change Biol*. 2020;26(7):4013–4027.
12. Lee D, Wang SY, Zhao L, Kim HC, Kim K, Yoon J-H. Long-term increase in atmospheric stagnant conditions over northeast Asia and the role of greenhouse gases-driven warming. *Atmos Environ*. 2020;241:117772.
13. Horton EH, Harshvardhan, Diffenbaugh NS. Response of air stagnation frequency to anthropogenically enhanced radiative forcing. *Environ Res Lett*. 2013;7(4).
14. Hanski I, von Hertzen L, Fyhrquist N, et al. Environmental biodiversity, human microbiota, and allergy are interrelated. *Proc Natl Acad Sci U S A*. 2012;109(21):8334–8339.
15. Landrigan PJ, Fuller R, Fisher S, et al. Pollution and children's health. *Sci Total Environ*. 2019 Feb 10;650(Pt 2):2389–2394.
16. Dondi A, Carbone C, Manieri E, et al. Outdoor air pollution and childhood respiratory disease: the role of oxidative stress. *Int J Mol Sci*. 2023;24(5).
17. Perera F, Nadeau K. Climate change, fossil-fuel pollution, and children's health. *N Engl J Med*. 2022;386(24):2303–2314.
18. Yadav A, Pacheco SE. Prebirth effects of climate change on children's respiratory health. *Curr Opin Pediatr*. 2023;35(3):344–349.
19. Kline O, Prunicki M. Climate change impacts on children's respiratory health. *Curr Opin Pediatr*. 2023;35(3):350–355.
20. D'Amato G, Holgate ST, Pawankar R, Ledford DK, Cecchi L, Al-Ahmad. Meteorological conditions, climate change, new emerging factors, and asthma and related allergic disorders. A statement of the World Allergy Organization. *The World Allergy Organization journal*. 2015;8(1):25.
21. García Martínez J. [Importance of environmental and preventive measures in the control of asthma in the child]. *Allergol Immunopathol*. 2000;28(3):158–162.
22. Celebi Sozener Z, Özbey Yücel Ü, Altiner S, et al. The external exposome and allergies: from the perspective of the epithelial barrier hypothesis. *Frontiers in allergy*. 2022;3:887672.

23. Spann K, Snape N, Baturcam E, Fantino E. The impact of early-life exposure to air-borne environmental insults on the function of the airway epithelium in asthma. *Ann Glob Health*. 2016;82(1):28–40.

24. Gasana J, Dillikar D, Mendy A, Forno E, Ramos Vieira E. Motor vehicle air pollution and asthma in children: a meta-analysis. *Environ Res*. 2012;117:36–45.

25. Clifford RL, Jones MJ, MacIsaac JL, et al. Inhalation of diesel exhaust and allergen alters human bronchial epithelium DNA methylation. *J Allergy Clin Immunol*. 2017;139(1):112–121.

26. Brandt EB, Biagini Myers JM, Acciani TH, et al. Exposure to allergen and diesel exhaust particles potentiates secondary allergen-specific memory responses, promoting asthma susceptibility. *J Allergy Clin Immunol*. 2015;136(2):295–303.

27. Atmosphere Nel A. Air pollution-related illness: effects of particles. *Science*. 2005;308(5723):804–806.

28. Orellano P, Quaranta N, Reynoso J, et al. Effect of outdoor air pollution on asthma exacerbations in children and adults: systematic review and multilevel meta-analysis. *PLoS One*. 2017;12(3).

29. Bernstein JA, Alexis N, Barnes C, et al. Health effects of air pollution. *J Allergy Clin Immunol*. 2004;114(5):1116–1123.

30. Yue H, Yang X, Wu X, et al. Maternal NO(2) exposure disturbs the long noncoding RNA expression profile in the lungs of offspring in time-series patterns. *Ecotoxicol Environ Saf*. 2022;246:114140.

31. Lu C, Wang F, Liu Q, Deng M, Yang X, Ma P. Effect of NO(2) exposure on airway inflammation and oxidative stress in asthmatic mice. *J Hazard Mater*. 2023;457:131787.

32. Shabnum J, Ahmad SS, Noor MJ. Spatial variance and estimation of nitrogen dioxide levels as a contributing factor to asthma epidemiology in Rawalpindi, Pakistan. *Environ Monit Assess*. 2023;195(10):1208.

33. Urrutia-Pereira M, Badellino H, Ansotegui IJ, Guidos G, Solé D. Climate change and allergic diseases in children and adolescents. *Allergol Immunopathol*. 2022;1:7–16, 50(S Pt.

34. Xepapadaki P, Manios Y, Liarigkovinos T, et al. Association of passive exposure of pregnant women to environmental tobacco smoke with asthma symptoms in children. *Pediatr Allergy Immunol*. 2009;20:5.

35. Association ALS. *American Lung Association State of the Air Report 2023*. American Lung and 2023; 2023.

36. IPCC. Climate change 2022: mitigation of climate change. Contribution of Working Group III to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change. 2022. ([P.R. Shukla, J. Skea, R. Slade, A. Al Khourdajie, R. van Diemen, D. McCollum). Cambridge University Press, Cambridge, UK and New York, NY, USA.

37. *Cape grim greenhouse gas data*; 2023 [cited 19 October 2023]. Available from: https://capegrim.csiro.au/.

38. Bradshaw CJA, Ehrlich PR, Beattie A, et al. Underestimating the challenges of avoiding a ghastly future. *Frontiers in Conservation Science*. 2021;1:9.

39. Larcombe AN, Papini MG, Chivers EK, Berry LJ, Lucas RM, Wyrwoll CS. Mouse lung structure and function after long-term exposure to an atmospheric carbon dioxide level predicted by climate change modeling. *Environ Health Perspect*. 2021;129(1):17001.

40. Ziska LH. Climate, carbon dioxide, and plant-based aero-allergens: a deeper botanical perspective. *Front Allergy*. 2021;2:714724.

41. Maschler J, Bialic-Murphy L, Wan J, et al. Links across ecological scales: plant biomass responses to elevated CO(2). *Global Change Biol*. 2022;28(21):6115–6134.

42. Kim KR, Oh JW, Woo SY, et al. Does the increase in ambient CO(2) concentration elevate allergy risks posed by oak pollen? *Int J Biometeorol*. 2018;62(9):1587–1594.

43. Silver JD, Sutherland MF, Johnston FH, et al. Seasonal asthma in Melbourne, Australia, and some observations on the occurrence of thunderstorm asthma and its predictability. *PLoS One*. 2018;13(4):e0194929.

44. D'Amato G, Vitale C, Lanza M, Molino A, D'Amato M. Climate change, air pollution, and allergic respiratory diseases: an update. *Curr Opin Allergy Clin Immunol*. 2016 Oct;16(5):434–440.

45. D'Amato G, Annesi Maesano I, Molino A, Vitale C, D'Amato M. Thunderstorm-related asthma attacks. *J Allergy Clin Immunol*. 2017 Jun;139(6):1786–1787.

46. Chatelier J, Chan S, Tan JA, Stewart AG, Douglass JA. Managing exacerbations in thunderstorm asthma: current insights. *J Inflamm Res*. 2021 Sep 8;14:4537–4550. και.

47. Vakalopoulos A, Dharmage SC, Dharmaratne S, Jayasinghe P, Lall O, Ambrose I, et al. Household air pollution from biomass fuel for cooking and adverse fetal growth outcomes in rural Sri Lanka. *Int J Environ Res Publ Health*. 2021;18(4):1878.

48. Beyene T, Harvey ES, Van Buskirk J, et al. 'Breathing fire': impact of prolonged bushfire smoke exposure in people with severe asthma. *Int J Environ Res Publ Health*. 2022;19(12).

49. Wang IJ, Karmaus WJ, Yang CC. Polycyclic aromatic hydrocarbons exposure, oxidative stress, and asthma in children. *Int Arch Occup Environ Health*. 2017;90(3):297–303.

50. Chew GL, Wilson J, Rabito FA, Grimsley F, Iqbal S, Reponen T, Muilenberg ML, Thorne PS, Dearborn DG, Morley RL. Mold and endotoxin levels in the aftermath of Hurricane Katrina: a pilot project of homes in New Orleans undergoing renovation. Environ Health. 2010 Oct 15;408(22):5489-98.

51. Murrison LB, Brandt EB, Myers JB, Hershey GKK. Environmental exposures and mechanisms in allergy and asthma development. *J Clin Invest*. 2019;129(4):1504–1515.

52. Hoppe KA, Metwali N, Perry SS, Hart T, Kostle PA, Thorne PS. Assessment of airborne exposures and health in flooded homes undergoing renovation. *Indoor Air*. 2012;22(6):446–456.

53. Zhang Z, Biagini Myers JM, Brandt EB, et al. β-Glucan exacerbates allergic asthma independent of fungal sensitization and promotes steroid-resistant TH2/TH17 responses. *J Allergy Clin Immunol*. 2017;139:54–65.

54. Eguiluz-Gracia I, Mathioudakis AG, Bartel S, et al. The need for clean air: the way air pollution and climate change affect allergic rhinitis and asthma. *Allergy*. 2020;75(9):2170–2184.

55. Menzel A, Ghasemifard H, Yuan Y, Estrella N. A first pre-season pollen transport climatology to bavaria, Germany. *Front. Allergy*. 2021;2.

56. D'Amato G, Bergmann KC, Cecchi L, Annesi-Maesano I, Sanduzzi. Climate change and air pollution: effects on pollen

allergy and other allergic respiratory diseases. *Allergo journal international*. 2014;23(1):17–23.

57. Gehrig R, Clot B. 50 Years of pollen monitoring in basel (Switzerland) demonstrate the influence of climate change on airborne pollen. *Front Allergy*. 2021;2:677159.
58. Sénéchal H, Visez N, Charpin D, et al. A review of the effects of major atmospheric pollutants on pollen grains, pollen content, and allergenicity. *Sci World J*. 2015;2015:940243.
59. Bartra J, Mullol J, del Cuvillo A, et al. Air pollution and allergens. *J Invest Allergol Clin Immunol*. 2007;17(Supplement 2):3–8.
60. Lucas JA, Gutierrez-Albanchez E, Alfaya T, Feo-Brito F, Gutiérrez-Mañero FJ. Oxidative stress in ryegrass growing under different air pollution levels and its likely effects on pollen allergenicity. *Plant Physiol Biochem*. Feb 2019;135: 331–340.
61. Grewling Ł, Ribeiro H, Antunes C, et al. Outdoor airborne allergens: characterization, behavior and monitoring in Europe. *Sci Total Environ*. Dec 20, 2023;905: 167042.
62. Nickovic WRL, Abatzoglou JT, Anderegg LDL, Bielory L, Kinney PL, Ziska L. Anthropogenic climate change is worsening North American pollen seasons. *Proc Natl Acad Sci USA*. 2021;118.
63. Zhang Y, Steiner AL. Projected climate-driven changes in pollen emission season length and magnitude over the continental United States. *Nat Commun*. 2022;13(1):1234.
64. Addison-Smith B, Milic A, Dwarakanath D, et al. Medium-term increases in ambient grass pollen between 1994-1999 and 2016-2020 in a subtropical climate zone. *Front Allergy*. 2021;2:705313.
65. Zhang Y, Bielory L, Mi Z, Cai T, Robock A, Georgopoulos P. Allergenic pollen season variations in the past two decades under changing climate in the United States. *Global Change Biol*. 2015;21(4):1581–1589.
66. Lee KS, Kim K, Choi YJ, et al. Increased sensitization rates to tree pollens in allergic children and adolescents and a change in the pollen season in the metropolitan area of Seoul, Korea. *Pediatr Allergy Immunol*. 2021;32(5):872–879.
67. Reinmuth-Selzle K, Kampf CJ, Lucas K, Lang-Yona N, Fröhlich-Nowoisky J. Air pollution and climate change effects on allergies in the anthropocene: abundance, interaction, and modification of allergens and adjuvants. *Environ Sci Technol*. 2017;51(8):4119–4141.
68. Candeias J, Zimmermann EJ, Bisig C, Gawlitta N, Oeder S, Gröger T. The priming effect of diesel exhaust on native pollen exposure at the air-liquid interface. *Environ Res*. 2022;211:112968.
69. Murray CS, Foden P, Sumner H, Shepley E, Custovic A, Simpson A. Preventing severe asthma exacerbations in children. A randomized trial of mite-impermeable bedcovers. *Am J Respir Crit Care Med*. 2017 Jul 15;196(2):150–158.
70. Acevedo N, Zakzuk J, Caraballo L. House dust mite allergy under changing environments. *Allergy Asthma Immunol Res*. Jul 2019;11(4):450–469.
71. Portnoy J, Miller JD, Williams PB, et al. Khan D,et al.,Joint taskforce on practice parameters and workgr. *Practice Parameter. Ann Allergy Asthma Immunol*. 2013 Dec;111(6): 465–507.
72. Charpin D, Ramadour M, Lavaud F, et al. Climate and allergic sensitization to airborne allergens in the general population: data from the French six cities study. *Int Arch Allergy Immunol*. 2017;172(4):236–241.
73. Oftedal B, Brunekreef B, Nystad W, Nafstad P. Residential outdoor air pollution and allergen sensitization in schoolchildren in Oslo, Norway. *Clin Exp Allergy : journal of the British Society for Allergy and Clinical Immunology*. 2007;37(11):1632–1640.
74. Zingales V, Taroncher M, Martino PA, Ruiz MJ, Caloni F. Climate change and effects on molds and mycotoxins. *Toxins*. June 30, 2022;14(7):445.
75. Takaro TK, Henderson SB. Climate change primer for respirologists. *Can Respir J J Can Thorac Soc*. 2015;22(1):52–54.
76. Mendell MJ, Mirer AG, Cheung K, Tong M, Douwes J. Respiratory and allergic health effects of dampness, mold, and dampness-related agents: a review of the epidemiologic evidence. *Environ Health Perspect*. 2011;119:748–756.
77. Katelaris CH, Beggs PJ. Climate change: allergens and allergic diseases. *Intern Med J*. 2018;48(2):129–134.
78. Ketema RM, Araki A, Ait Bamai Y, Saito T, Kishi R. Lifestyle behaviors and home and school environment in association with sick building syndrome among elementary school children: a cross-sectional study. *Environ Health Prev Med*. 2020;25(1):28.
79. Gray-Ffrench M, Fernandes RM, Sinha IP, Abrams EM. Allergen management in children with type 2-high asthma. *J Asthma Allergy*. 2022;15:381–394.
80. Poole JA, Barnes CS, Demain JG, et al. Impact of weather and climate change with indoor and outdoor air quality in asthma: a work group report of the aaaai environmental exposure and respiratory health committee. *J Allergy Clin Immunol*. 2019;143(5):1702–1710.
81. Young I, Prematunge C, Pussegoda K, Corrin T, Waddell L. Tick exposures and alpha-gal syndrome: a systematic review of the evidence. *Ticks and tick-borne diseases*. 2021;12(3): 101674.
82. Caraballo L, Zakzuk J, Lee BW, et al. Particularities of allergy in the tropics. *The World Allergy Organization journal*. 2016;9(20):20, 9.
83. El-Gamal YM, Hossny EM, El-Sayed ZA, Reda SM. Allergy and immunology in Africa: challenges and unmet needs. *J Allergy Clin Immunol*. 2017;140(5):1240–1243.
84. Urrutia-Pereira M, Badellino H, Ansotegui IJ, Guidos G, Solé D. Climate change and allergic diseases in children and adolescents. *Allergol Immunopathol*. 2022;50:7–16. S Pt 1.
85. Ray C, Ming X. Climate change and human health: a review of allergies, autoimmunity and the microbiome. *Int J Environ Res Publ Health*. Jul 2020;17(13):4814.
86. Marri PR, Stern DA, Wright AL, Billheimer D, Martinez FD. Asthma-associated differences in microbial composition of induced sputum. *J Allergy Clin Immunol*. 2013;131(2):346–352. e1-3.
87. Adar SD, Huffnagle GB, Curtis JL. The respiratory microbiome: an underappreciated player in the human

response to inhaled pollutants? *Ann Epidemiol*. May 2016;26(5):355–359.

88. Loverdos K, Bellos G, Kokolatou L, et al. Lung microbiome in asthma: current perspectives. *J Clin Med*. Nov 2019;8(11):1967.

89. Arrieta MC, Arevalo A, Stiemsma L, et al. Associations between infant fungal and bacterial dysbiosis and childhood atopic wheeze in a nonindustrialized setting. *J Allergy Clin Immunol*. 2018;142(2):424–434.

90. Sheehan WJ, Permaul P, Petty CR, et al. Association between allergen exposure in inner-city schools and asthma morbidity among students. *JAMA Pediatr*. 2017;171(1):31–38.

91. Chauhan AJ, Inskip HM, Linaker CH, et al. Personal exposure to nitrogen dioxide (NO2) and the severity of virus-induced asthma in children. *Lancet (London, England)*. 2003;361(9373):1939–1944, 2003.

92. Makrinioti H., Maggina P., Lakoumentas J., et al. Recurrent wheeze exacerbations following acute bronchiolitis—a machine learning approach. *Front Allergy*. 2021;2:728389.

93. Pfeffer PE, Mudway IS, Grigg J. Air pollution and asthma: mechanisms of harm and considerations for clinical interventions. *Chest*. 2021;159(4):1346–1355.

94. Quezada-Maldonado EM, Sanchez-Perez Y, Chirino YI, Garcia-Cuellar CM. Airborne particulate matter induces oxidative damage, DNA adduct formation and alterations in DNA repair pathways. *Environ Pollut*. 2021;287:117313.

95. Moskwa S, Piotrowski W, Marczak J. et al. Innate immune response to viral infections in primary bronchial epithelial cells is modified by the atopic status of asthmatic patients. *Allergy Asthma Immunol Res*. 2018;10:144–154.

96. Skevaki CL, Tsialta P, Trochoutsou AI, et al. Associations between viral and bacterial potential pathogens in the nasopharynx of children with and without respiratory symptoms. *Pediatr Infect Dis J*. 2015;34(12):1296–1301.

97. Papadopoulos NG, Mathioudakis AG, Custovic A, et al. Childhood asthma outcomes during the COVID-19 pandemic: findings from the PeARL multi-national cohort. *Allergy*. 2021;76(6):1765–1775.

98. Pacheco SE, Guidos-Fogelbach G, Annesi-Maesano I, et al. Climate change and global issues in allergy and immunology. *J Allergy Clin Immunol*. 2021;148(6):1366–1377.

99. Roos N, Kovats S, Haajat S, et al. CHAMNHA consortium. *Acta Obstet Gynecol Scand*. 2021;100:566–570.

100. Southerland V, Brauer M, Mohegh A, et al. Global urban temporal trends in fine particulate matter (PM2·5) and attributable health burdens: estimates from global datasets. *Lancet Planet Health*. 2022;6.

101. Castillo MD, Kinney PL, Southerland V, et al. Estimating intra-urban inequities in pm2.5-attributable health impacts: a case study for Washington, DC. *GeoHealth*. 2021;5(11): e2021GH000431.

102. Cortez-Ramirez J, Wilches-Vega J, Paris-Pineda O, Rod JE, Ayurzana L, Sly P. Environmental risk factors associated with respiratory diseases in children with socioeconomic disadvantage. *Heliyon*. 2022;7(4):e06820.

103. Lim S, Bassey E, Bos B, et al. Comparing human exposure to fine particulate matter in low and high-income countries: a systematic review of studies measuring personal PM2.5 exposure. *Sci Total Environ*. 2022:833.

104. Rees WE. Overshoot: cognitive obsolescence and the population conundrum. *Population and Sustainability and*. 2023;7(1).

105. *United States Environmental Protection Agency Air Quality Index*; 2023 [Internet]. (Available from:) https://www.epa.gov/air-quality.

106. Papadopoulos NG, Akdis C, Akdis M, et al. Addressing adverse synergies between chemical and biological pollutants at schools-The "SynAir-G" hypothesis. *Allergy*. 2024 Feb;79(2): 294–301.

107. Belgrave DCM, Granell R, Turner SW, Curtin JA, Buchan IE, Le Souef PN, et al. Lung Function Trajectories from Pre-school Age to Adulthood and Their Associations with Early Life Factors: A Retrospective Analysis of Three Population-Based Birth Cohort Studi. *Lancet Respir Med*. 2018;6(7):526–534.

108. Le Souëf PN, Saraswati CM, Judge M, Bradshaw CJ. Spatially explicit analyses of environmental and health data to determine past, emerging and future threats to child health. *J Paediatr Child Health*. 2021;57(11):1830–1834.

109. Seibert MK, Rees WE. Through the eye of a needle: an eco-heterodox perspective on the renewable energy transition. *Energies*. 2021;14:4508.

110. Kemp L, Xu C, Depledge J, et al. Climate Endgame: exploring catastrophic climate change scenarios. *Proc Natl Acad Sci USA*. 2022;119(34):e2108146119.