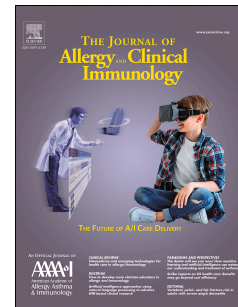


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Climate Change and Global Issues in Allergy and Immunology

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Greenhouse gases

Heatwaves

Wildfires

Dust storms

Tropical storms

Thunderstorms

Abbreviations

- 102 GHG - Greenhouse gasses
- 103 SARS-CoV-2 - Severe acute respiratory syndrome coronavirus 2
- 104 O₃ - Ground-level ozone
- 105 PM_{2.5} - Particulate Matter 2.5
- 106 PM₁₀ – Particulate Matter 10
- 107 CO₂ - Carbon dioxide
- 108 COPD - Chronic obstructive pulmonary disease
- 109 AD - Atopic Dermatitis
- 110 WHO - World Health Organization
- 111 UN - United Nations
- 112 CH₄ - Methane
- 113 N₂O - Nitrous oxide
- 114 HDM - House dust Mites

ABSTRACT

The steady increase in global temperatures, resulting from the combustion of fossil fuels and the accumulation of greenhouse gases (GHG), continues to destabilize all ecosystems worldwide. Although annual emissions must halve by 2030 and reach net-zero by 2050 to limit some of the most catastrophic impacts associated with a warming planet, the world's efforts to curb GHG emissions fall short of the commitments made in the 2015 Paris Agreement (1). To this effect, July 2021 was recently declared the hottest month ever recorded in 142 years (2). The ramifications of these changes on global temperatures are complex and further promote outdoor air pollution, pollen exposure, and extreme weather events. Besides worsening respiratory health, air pollution, promotes atopy and susceptibility to infections. The GHG effects on pollen affect the frequency and severity of asthma and allergic rhinitis. Changes in temperature, air pollution, and extreme weather events exert adverse multisystemic health effects and disproportionately affect disadvantaged and vulnerable populations. This article is an update for allergists and immunologists about the health impacts of climate change, already evident in our daily practices. It is also a call to action and advocacy, including integrating climate change-related mitigation, education, and adaptation measures to protect our patients and avert further injury to our planet.

INTRODUCTION

We have seen an accelerated rise in global temperatures and ensuing global warming since the mid-nineteenth century; these events are associated with increased production of GHG stemming from the Industrial Revolution. The term “climate” refers to the long-term regional or global average of temperature, humidity, and rainfall patterns over seasons, years, or decades (3). Anthropogenic activities such as burning fossil fuels, deforestation, land use, livestock production, fertilization, and industrial processes have increased GHG emissions. Globally, carbon dioxide (CO₂), methane (CH₄), nitrous oxide (N₂O), and halogenated gases are the main gases generated by human activities. This increase in GHG has led to climate change, defined by the United Nations Framework Convention on Climate Change as “a change of climate which is attributed directly or indirectly to human activity that alters the composition of the global atmosphere and which is in addition to natural climate variability observed over comparable periods” (4).

From the Industrial Revolution’s inception to the present day, the concentration of CO₂ in the atmosphere increased from an average of 280 parts per million (ppm) to over 415 ppm, a 48% change. This rise has led to an increased global average surface temperature of about 1 °C (about 2 °F) above pre-industrial levels (5). Unfortunately, the rate of global warming has been faster in the last few decades, with seven of the ten warmest years occurring since 2014 (6). To this effect, the Earth’s global average temperature in 2020 tied with 2016 as the warmest year on record (7). At the current rate, warming will likely reach 1.5°C between 2030 and 2052 (high confidence) and will continue to increase if we do not implement aggressive mitigation measures (8).

Although a 1 °C increase in global average surface temperatures appears to be relatively minor, the ramifications of these small temperature changes are significant. Increasing temperatures have destabilized all ecosystems globally, causing disruption of societal structures, the environment, and all aspects of human health. Climate change has led to higher global temperatures and heatwaves, rising sea levels, altered precipitation patterns, altered plant growth seasons, increased frequency or intensity of extreme weather events, droughts, and changes in the distribution of infectious vectors (3). Vulnerable individuals will disproportionately bear the brunt of climate change. These changes will magnify existing disparities, challenging ongoing efforts for social and environmental justice. Compounding this challenge are the social determinants of health inherent to individuals and communities, added to overlapping crises, such as the ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic.

The health impacts of climate change are pervasive and multisystemic, affecting most, if not all, organ systems. Chronic medical disorders will continue to increase because of climate change, including cardiovascular, cerebrovascular, renal, and respiratory diseases; neurodegenerative conditions, and mental disease; atopic and infectious diseases; metabolic disorders, and malignancy. The damage can begin in the prenatal period, leading to adverse birth outcomes, neurodevelopmental disorders, and congenital heart disease. The insidious nature of the damage undermines awareness and action, as the changes may go unnoticed before symptoms arise. Humans are affected at all stages of life, from the prenatal period to advanced age.

179

180 This article will address many of the changes and health conditions that affect the practice
181 of allergy and immunology, and the disproportional impact of climate change on
182 vulnerable populations. However, it does not address many other environmental changes
183 and adverse health outcomes associated with the climate crisis. These have been
184 addressed comprehensively in other publications available to the reader (9-13).

DRIVERS AND OUTCOMES OF CLIMATE CHANGE: ASSOCIATED HEALTH IMPACTS

The following discussion, although not comprehensive, reviews the impact of climate change and the use of fossil fuels in outdoor air pollution and highlights climate-associated changes with widespread impact on human health, many of them affecting the practice of allergy and immunology.

Outdoor air pollution

Human activities and reliance on fossil fuels have led to increased concentrations of anthropogenic GHG, responsible for climate change and other by-products, major components of air pollution. Some of the resulting climate change-driven environmental changes may further contribute to the deterioration of air quality (**Figure 1**). Air pollution is a mixture of particles and gases directly emitted to the atmosphere or generated by chemical or photochemical reactions, such as tropospheric or ground-level ozone (O₃). Natural, biological, and anthropogenic sources of outdoor air pollution are shown in **Table I** (14-17). Local weather and meteorological variables affected by climate change (e.g., temperature, changes in precipitation pattern, wind patterns) further affect the distribution of air pollutants (18). Additionally, climate-driven changes (e.g., wildfires, storms, O₃ increased pollen, heatwaves requiring higher demands for electricity) increase biological, and anthropogenic sources of air pollution, promoting a feed-forward loop of pollution and poor air quality resulting from climate change (**Figure 2**).

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Exposure to air pollution, especially O₃ and Particulate Matter less than or equal to 2.5 µm (PM_{2.5}), has profound impacts on human health (19). At least 90% of the world's population live in areas of low air quality, where the concentration of pollutants exceeds guidelines established by the World Health Organization (WHO) (20). In the US, over 40% of the population, more than 135 million individuals, live in areas with poor air quality (21). In 2015, PM_{2.5} was responsible for 4.2 million premature deaths per year worldwide (22), with over 92% of pollution-related deaths occurring in low-income and middle-income countries (19). Chronic obstructive pulmonary disease (COPD), lung cancer, and cardiovascular events are the most significant morbidities associated with air pollution. COPD is the leading cause of death attributable to all air pollution, and ischemic heart disease is the leading cause of death attributable to PM_{2.5} (22).

Epidemiological and experimental studies have also specifically highlighted the role of air pollution on the development of allergic disease [reviewed by (23)], as well as asthma development (24-27), exacerbations (28), and mortality (27, 29). Early-life exposure to air pollution is associated with an increased risk of aeroallergen sensitization (30, 31) and food sensitization as early as age 1 (32).

Alongside climate change-related factors (increased GHG emissions, rising global temperatures, humidity, and atmospheric UV radiation levels), air pollution has been specifically associated with increased prevalence of atopic dermatitis (AD) (33-35). Air pollutants comprising volatile organic compounds, PM, Traffic-Related Air Pollution, and tobacco smoke have been demonstrated to impact adversely on skin barrier integrity

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through the generation of reactive oxygen species and epigenetic modifications of the immune system. These mechanisms subsequently predispose infants to AD development, increasing the risk of future allergic disease via the atopic march (36). In addition, the oxidative stress response triggered by air pollution can promote epigenetic modifications that regulate gene expression of immune cells, including modification of regulatory T-cells (Tregs) and the important immunoregulatory genes *FOXP3*, *IL-4*, *IL-10*, and *INF-γ* (37) through DNA methylation (38-40). Clinically, increased methylation of *FOXP3* secondary to air pollution exposure was associated with increased risk of asthma diagnosis at age 7 (41) and asthma severity (38). Thus, beyond previously established relationships between various environmental factors and climate change on respiratory conditions such as rhinitis and asthma (20, 21) the feed-forward cycle of air pollution and climate change establish prime conditions for increased incidence and prevalence of all atopic diseases.

Air pollution has also been linked with increased susceptibility to respiratory viral infections through various mechanisms, including increased epithelial cell permeability, changes in expression of epithelial cell-bound viral receptors, and impaired antiviral immunity (42). Exposure to atmospheric pollutants was associated with respiratory viral infections, such as influenza, measles, mumps, rhinovirus, and respiratory syncytial virus. Epidemiological studies also suggested that exposure to air pollution is associated with the increase in infection by SARS-CoV-2 and mortality associated with COVID-19 (43, 44). Exposure to atmospheric pollutants can predispose vulnerable and

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immunocompromised populations to develop a more intense inflammatory response and tissue damage by COVID-19 (45).

Increased pollen seasons and allergen exposure

The increase in global temperature and CO₂ concentration associated with climate change has modified the duration of pollen seasons, times of pollen release, amount of pollen produced, and in some cases, pollen composition and allergenicity(46, 47). Changes in rainfall and rainfall patterns, hurricanes, and stronger winds could expand the reach of pollen species in the atmosphere carrying nonnative pollen species to different regions, potentially sensitizing susceptible populations in remote areas (48-51). Climate change has contributed to the increased production of various aeroallergens and changes in their geographical distribution (52). Changes to the flowering season due to climate change will extend allergenic seasons (53), with subsequent increases in human exposure. Long-term changes in warming will modify patterns of plant habitat and species density, with gradual movement northward in the Northern Hemisphere and further south in the Southern Hemisphere. These changes in plant habitat may increase the risk of pollen allergy (54, 55). The European Union-funded Health Impacts of Airborne Allergen Information Network (HIALINE) project examined the effects of increasing temperature and CO₂ on pollen distribution, production, and dissemination. The HIALINE project found that daily pollen concentrations and daily allergen content, the "pollen potency" of grasses (one of the major allergens Phl p 5), olives (Ole e 1), and birches (Bet v 1) were independent of each other (56), suggesting that climate change impacts these two distinct components dictating human responses to pollen exposure.

Air pollutants also interact with airborne allergens and enhance the risk of allergic sensitization and exacerbation of symptoms in sensitized individuals (**Figure 3**)(57-61). For example, particulate matter, diesel exhaust particles, O₃, N₂O, and SO₂ have all been shown to have an inflammatory effect on the airways of susceptible subjects, causing increased permeability, easier penetration of allergens into the mucus membranes, and interaction with cells of the immune system.

Air pollution has been shown to increase pollen allergenicity (47, 59, 62). Additionally, air pollutants interact with allergen-carrying submicronic and paucimicronic particles derived from pollen (48, 63), and can reach peripheral airways inducing asthma in sensitized subjects. Collectively, biological (such as pollen) and non-biological particulates (carbon, silica, metals, ultrafine dust, and others) interact with each other in the atmosphere with direct effects on the health of the population, either due to their direct irritant effect or due to interactions among these different kinds of particulate matter. The observed interactions among biological and non-biological airborne particulates highlight the need for exposome characterization and modification in asthma and allergy using novel research methods (35, 58).

These changes in pollen seasons and allergen exposure have translated to notable health effects. A body of epidemiological evidence suggests that the prevalence of pollen-related allergic respiratory diseases, e.g., rhinitis and asthma, has increased in past decades (64). High levels of vehicular emissions, urbanization, and westernized lifestyles

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correlate with the increased frequency of pollen-induced respiratory allergies in urban areas compared to rural areas (50). Furthermore, many allergenic pollen species were associated with seasonal asthma exacerbations in both children and adults (65, 66). Climate change will also increase the frequency and intensity of floods and cyclones and thus fungal spore production (54), powerful asthma and rhinitis trigger.

Increased pollen exposure may also influence susceptibility to viral infections. Allergic patients exposed to airborne pollen have been noted to have greater vulnerability to viral infections (67-69), including SARS-CoV-2. In addition, published evidence supports that pollen exerts immunomodulatory effects that impair the antiviral response and may account for susceptibility to viral infections, including the inhibition of the antivirals NF- κ B, MyD88, and IFN in the respiratory epithelium in addition to improving the release of IL-1 IL-1 β , IL-18, IL-28A and IL-33 family cytokines from epithelial cells in vitro (69). Thus, it is possible that these changes affect the susceptibility to infections in allergic patients.

Extreme weather events

Extreme weather events are hallmarks of climate change, and their frequency will continue to increase. Tropical storms, thunderstorms, dust storms, droughts and floods, wildfires, and heatwaves directly and indirectly impact human health.

Temperature changes and heatwaves

Warming of the planet is not uniform and, in general, is higher over land compared to the oceans. Overall, climate trends are moving towards hotter vs. cold temperature extremes

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across the globe. These temperature changes are drivers of sea-level rise, melting of the polar ice caps, change in precipitation patterns, and droughts. In addition, ocean warming is thought to be a driver of the increase in the intensification rate observed in tropical storms(70).

Besides global and environmental impacts, increasing temperatures have a direct toll on human health. The frequency, duration, and magnitude of extreme heat continue to increase with climate change. A study involving 43 countries estimated that the heat-related mortality burden during warm seasons, from anthropogenic warming during the 1991-2018 period, was 37.0% (range 20.5–76.3%)(71). During the 2003 European summer heatwave, an excess of 70,000 people died, mostly older individuals(72). Vulnerable groups mainly include individuals over age 65 with chronic medical conditions such as diabetes, cardiovascular, lung, and kidney disease (73).

More recently, a heatwave in the Pacific Northwest of North America caused at least a thousand deaths. Complicating the impact of the increasing temperatures and heat waves are “urban heat islands.” Urban heat islands result from the urbanization process that replaces natural land cover, such as trees and vegetation, with concrete, buildings, and pavement. These alterations result in a temperature gradient, with temperatures in urban areas several degrees higher than surrounding rural areas. Although initially thought to be mainly the result of limited green cover and heat absorption by urban structures, recent models suggest that differences in convection efficiency and evapotranspiration have a more critical role in the temperature gradients observed (74). Compounded by the

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increased temperatures from climate change, these heat islands are expected to amplify the morbidity and mortality of heatwaves. According to the 2018 Revision of the United Nations World Urbanization Prospects, 55% of the world's population resided in urban areas in 2018. This number is projected to increase to 68% by 2050 (75).

Wildfires

Increased drought conditions seen with climate change promote environments that encourage increased frequency and severity of wildland fires (76) such as the Dixie Fire that has burned over 960,000 acres (380,000 hectares) in California since July 2021, or the Siberia fires, that have burned over 40,000,000 acres in 2021, more than all the other worlds fires combined (77, 78). In addition to the civilian deaths associated with these events, wildfires are also associated with significant total damage and economic losses, surpassing 10 billion US dollars in the 2018 California Camp Fire, 12 billion US dollars in the California 2020 fires, and 110 billion dollars in the 2019-2020 Australian fires.

Wildfires are a major health concern to wildland firefighters and members of the public for whom avoidance of wood smoke is not always possible. Wildland fires are an important source of ambient air PM_{2.5} in the U.S. and can cause abrupt increases in PM_{2.5} with peak levels exceeding >1000 µg/m³ (79). Wildfire smoke exposure has been associated with asthma-related emergency room visits (80, 81), hospitalizations, and premature deaths (82). Children and those with chronic diseases are especially vulnerable to the effects of wildfire exposures (83-85).

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The health effects of wildfires impact both airway and systemic inflammation. Field studies of wildland firefighters and controlled chamber studies of experimental wood smoke particle exposure have reported worsened lung function (86) and neutrophilic airway inflammation (87, 88). Epidemiological studies have shown that wildfire smoke is associated with an increased risk of cardiovascular morbidity, including ischemic events, heart failure, and arrhythmias (89, 90) thought to be attributable to systemic inflammatory effects of smoke-related PM exposure (91). The effects of wildfires are not limited to local regions; due to the Jet Stream and cross-continental air currents, smoke from the 2021 Bootleg Blaze in Oregon (Western US) reached New York City in July 2021, pushing the Air Quality Index in Northeastern US cities into unhealthy levels alongside reports of clinically significant respiratory irritant effects. Global strategies to reduce the frequency and severity of wildfires are urgently needed to mitigate the financial and health-related costs of these catastrophic events.

Saharan dust storms

Saharan dust storms travel thousands of miles across the globe, peaking during the months of June through August. The increased surface temperature and decreasing wintertime cold air surge activity of the Sahara Desert are the likely causes of the increased Sahara dust intrusion pattern (92). These dust storms have reached areas of southern Europe through the Mediterranean Sea, Asia, and the Americas (Mexico, Central and South America, the Caribbean, and the southern US), affecting weather conditions, agricultural production, ecosystems and human health (92).

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The Sahara dust is a mixture of particulate matter smaller than 10 micrometers (PM₁₀) and PM_{2.5}, (93), composed of clay and silicates, minerals, quartz, silicon dioxide, iron oxides, aluminum, titanium, magnesium, sodium, and evaporated minerals. They also transport pollen, microbial agents (e.g., fungi, viruses, bacteria), and anthropogenic pollutants. Saharan dust storms can have PM₁₀ and PM_{2.5} levels exceeding the allowable thresholds deemed safe for human health (94) established by the WHO, the Environmental Protection Agency (EPA), and the European Union (EU). For example, during the Sahara dust storm in June 2020, levels of PM_{2.5} in Florida, Texas, and Georgia reached “unhealthy levels” (between 151-200 µg/m³) on the air quality index (Figure 4)(95).

Several studies have reported significant associations between exposure to Saharan dust and hospital admissions due to asthma, COPD exacerbations, cardiovascular and cerebrovascular conditions (96-98). In addition, Saharan dust storms have been linked with mortality from respiratory diseases and severe cardiovascular and ischemic events among vulnerable populations (93, 96, 98, 99). In West Africa, exposure to these dust storms has been associated with increased infant mortality (100).

Hurricanes and Cyclones

One of the consequences of climate change and global warming is the increasing frequency and intensity of floods and cyclones (50). The increase in moisture and dampness associated with water intrusion during storms and floods affect indoor

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environments leading to increased dampness and humidity, supporting the growth of house dust mites and molds. House dust mites (HDMs), important sources of allergens inducing asthma and rhinitis, are very sensitive to microenvironment modifications. Therefore, global or regional changes in temperature, humidity, air pollution, or other environmental conditions could modify natural HDM growth, survival, and allergen production (101). Consequently, sensitization to HDMs has increased in subtropical and tropical areas. Furthermore, many urban pest species that are sources of allergens like cockroaches and rodents may be affected by climate change, which alters the natural environment because of flooding or drought and the urban environment as a result of changes in land use (102). These factors will affect the risk of pest-related diseases, including asthma and allergy.

Flooding of residential areas secondary to climate change also supports mold growth, increasing the risk of developing respiratory illnesses. The link between molds with asthma and rhinitis is well-known and has been established through exposure to dampness and moisture in indoor environments as proxy of microbial agents (103). In addition, mold metabolites, such as microbial volatile organic compounds, have been involved in nonallergic asthma and chronic bronchitis, although rarely (104).

Thunderstorms and asthma

Climate change is also associated with the increase in frequency and intensity of thunderstorms (105). This can result in thunderstorm asthma (106-109), an observed increase in acute bronchospasm cases following thunderstorms in the local vicinity. Thunderstorms occurring during the pollen season have induced severe asthma attacks

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434 and deaths in pollen-allergic patients (106, 107). Events have been reported from Europe,
435 North America, the Middle East, and Australia. The thunderstorm in the pollen season
436 increases the concentration of pollen grains, hydration, and rupture of pollens by osmotic
437 shock with release of allergen-carrying paucimicronic particles of respirable size such as
438 starch granules and other cytoplasmic components into the atmosphere (54). The main
439 allergen culprits are thought to be pollen grains, especially grasses and weeds, and mold
440 spores, particularly *Alternaria* and *Cladosporium* (110). Besides the associated
441 inflammatory and adjuvant effect in the allergic response, diesel exhaust particles can
442 transport adsorbed aeroallergen molecules released from pollen grains deeper in the
443 airways and increase retention of these antigenic molecules (111, 112).

VULNERABLE POPULATIONS

The vulnerability of individuals to climate change, driven by the degree and type of exposure, their sensitivity, and adaptive capacity, is greatly affected by the social determinants of health (**Figure 5**). People living in poverty or developing countries, communities of color, indigenous groups, racial and ethnic minorities, vulnerable occupational groups, and migrants will bear the brunt of climate change because of their exposure and limited adaptive capacity. Age, life stage, and health status affect the sensitivity to different climate change-related exposures. Elderly individuals, pregnant women and children (discussed below), people with disabilities, and those with chronic medical conditions, including immunodeficiency, are at the highest risk (113-115). Considering that impoverished populations have a higher probability of having chronic diseases, exposure to environmental pollution can affect individuals with underlying asthma, COPD, and pulmonary fibrosis (116) differentially, putting them at greater risk of hospitalization (117, 118), and mortality, as demonstrated recently in European cities (119).

Elderly individuals

Many variables make older adults more vulnerable to the environmental effects of climate change. This is a serious threat to consider in a world where the aging population is will continue to increase. By 2050 it is expected that 1 in 5 people in the world will be 60 years or more, with 80% of them living in developing countries, many already affected by climate change or with limited resources for adaptation(120). Their physiology, chronic medical conditions, psychological and socioeconomic status, living arrangements, access

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to care, limited mobility and transportation increase their vulnerability to heat waves, air pollution, extreme weather events, and infections. Due to their extent, exposure to heat and air pollution can be very impactful. Exposure to air pollution, in particular, PM_{2.5} and O₃, exacerbate underlying medical conditions, including asthma (121) and increase the mortality of elderly individuals. For example, exposure to PM_{2.5} has been associated with increased mortality in older or elderly populations, even at levels below those established by the US National Ambient Air Quality Standard (122). Other conditions affected by PM_{2.5} in older adults include respiratory conditions such as asthma and COPD, chronic kidney disease, diabetes, and dementia, including Alzheimer's disease.

Heat-induced illness is one of the major vulnerabilities for elderly individuals. Variables such as age-related physiological changes, chronic medical conditions, medications that affect sweating or alertness, disease-related fluid restrictions or limited intake, social isolation, and poverty are among the most common causes of decreased adaptive capacity to changes in temperature. In the US, 40% of all heat-related deaths from 2004-2018 were in individuals 65 or older. During the 2003 European heatwave, mortality was higher in elderly individuals with underlying respiratory conditions. To put the impact of climate-related changes in perspective, there were 727 million persons aged 65 years or over in 2020, a number that is expected to increase to 1.5 billion in 2050 (123).

Pregnancy

The harmful effects of climate change begin (before gestation) or during the prenatal period. Exposure to air pollution compromises placental development and affects fetal

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programming, predisposing to congenital malformations, immunological system alterations, allergic diseases, asthma, and respiratory conditions (124, 125). These effects can extend from infancy to adulthood and can have transgenerational effects, a plausible explanation for the development of chronic airway dysfunction, even in the absence of atopic predisposition (126, 127). For example, exposure to traffic-related air pollution, PM_{2.5}, and O₃ during the prenatal period has been associated with adverse birth outcomes such as prematurity and low birth weight (128-130), increased risk of wheezing in toddlers (131), reduced FEV₁ in children (132), and asthma diagnosis at age 6 (133). Other climate-related changes such as increased ambient temperature during pregnancy can lead to congenital heart disease, a problem projected to increase as temperatures increase (134), and increase in preterm birth (128).

Stressful experiences during pregnancy can impact birth outcomes and child development. For example, pregnancy during natural disasters such as the Quebec ice storm, the 2008 Iowa storm, floods, and hurricanes have been associated with adverse birth outcomes such as prematurity and low birth weight, increased adiposity in children, mood and neurodevelopmental disorders, and schizophrenia (135-137).

Children

Children are a particularly high-risk group due to their developing organ systems, their higher level of exposure due to their physiology, the nature of their daily activities, psychological immaturity, and dependence on adults (132). For these reasons, continued exposure to air pollution, extreme weather events (storms, floods, and droughts,

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heatwaves), shifting patterns of infectious vectors, and the change in the nutritional value of crops, impose a heavier burden on children, whose ability to adapt is affected by their mental and physiologic immaturity as well as the social determinants of health. Thus, the cumulative effects of these exposures make the threat of climate change a more urgent problem for humanity. In our review article, we have highlighted a few examples of how climate change affects pediatric health (63, 78-81, 125,126,130). Beyond respiratory health, exposure to air pollution has been associated with hematologic malignancies (133), increased airway infections and mortality (134), metabolic abnormalities observed in type 2 diabetes (135), and hypertension (136). One of the most alarming effects of air pollution in children growing in very polluted cities is the neuroinflammatory changes and brain histological changes similar to those found in Parkinson's and Alzheimer's disease (137, 138). Placed in context, over 90% of children in the world breathe polluted air. The WHO estimated that about 600,000 children died in 2016 from acute lower respiratory infections resulting from ambient and household air pollution (134). In addition, from 1990 – 2000, climate change-related extreme weather events directly affected about 66.5 million children, with a mortality of about 600,000 every year (139). Increasing exposure will continue to affect the emotional well-being and mental health of children (138).

CLIMATE CHANGE MITIGATION STRATEGIES

Implementing mitigation strategies to reduce GHG emissions is critical to prevent further warming of the planet and protect public health. While these necessary measures will take time to affect the Earth's temperature, the decrease in the use of fossil fuels has faster co-benefits for human health. Reduced reliance on fossil fuels can dramatically

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536 impact air quality and the prevention of stroke, pulmonary and cardiovascular
537 diseases(139). In the case of PM_{2.5}, over 50,000 deaths per year could be prevented in
538 European cities by complying with WHO air pollution guidelines for PM_{2.5} (119). At a
539 larger scale, the WHO estimates that over 80% of deaths related to PM_{2.5} could be
540 prevented by following the most updated guidelines for PM_{2.5} (140) Engagement in
541 active travel activities (e.g., biking and walking) can help reduce cardiovascular disease,
542 dementia, malignancies, mental illness, and obesity (Lancet commission 2015).
543 Improving energy efficiency and access to clean energy to poor communities by
544 improving indoor air quality can decrease respiratory conditions, infections, and
545 malignancy(141).

CONCLUSION

Humanity is living unprecedented times. The Earth's temperature has increased by 1.0°C since pre-industrial levels. The Intergovernmental Panel for Climate Change has stated that warming should not rise above 1.5°C to avert some of the more severe and potentially irreversible impacts of climate change (8). Despite this, CO₂ emissions continue to increase, up to almost 419 ppm in June 2021, the fifth warmest June on record. An increase in global temperature above 1.5 C translates to increased damage to vulnerable populations, increased morbidity, and mortality from heat waves and O₃ exposure, increased in some vector-borne diseases, and decreased food availability. As reviewed in this article, sequelae of the climate crisis contribute to rising levels of outdoor air pollution, pollen exposure, and extreme weather events, events that collectively increase the risk of developing or exacerbating atopic disorders, respiratory health, and infection susceptibility.

Although all humans are affected by climate change, the impact of the climate crisis affects people in different ways. People of color, minorities, developing countries, island nations, indigenous and poor communities are examples of groups that have and will suffer the most. According to the WHO, over 60,000 people a year die in natural disasters, mostly in developing countries. Outdoor air pollution causes 4.2 million deaths a year, most of them in low and middle-income countries. In addition, developing countries and indigenous communities will be disproportionately impacted by climate-related changes in crop yield and nutritional value, climate-sensitive infections such as malaria and dengue fever, deforestation and isolation, limited access to care, crumbling

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infrastructure, and poverty (142, 143). These sequelae of climate change have promoted increasing numbers of climate refugees, primarily from Africa, Asia, and Latin America(144). Although a proactive approach, planned relocation or managed retreat of small islands and coastal communities due to sea-level rise is a complex process requiring careful planning and consideration of physical and social determinants of health. Vulnerable populations, such as indigenous communities with limited financial resources and poor health status, will be disproportionately affected(145). The United Nations High Commissioner for Refugees reported that 21.5 million people had been displaced by climate change-related disasters since 2010(146). The Institute for Economics and Peace estimates that the number of people at risk for relocation secondary to climate change could reach at least 1.2 billion by the year 2050(147). Ironically, many of these groups have barely contributed to the emissions responsible for climate change but will be affected the most due to their limited resources and adaptability. Between 1990 and 2015, over half (52%) of the emissions released to the atmosphere were produced by the wealthiest 10%(148).

The inherent structural racism in the world perpetuates and magnifies the environmental impact of climate change. Variables such as political power, employment, access to education, and health care magnify these differences (149),increasing the social divide, oftenalong ethnic lines. For example, in the US, communities with more Blacks and Hispanics live in places with higher temperatures (21, 150), breathe more polluted air, and receive less support during government-led recovery efforts after natural disasters (151-154), such as during Hurricane Harvey in Texas and Hurricane Maria in Puerto Rico.

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In addition, a 2014 survey found that schools serving minority and underprivileged children were more likely to be located close to a major roadway, exposing them to the damaging effects of air pollution(155).

While the world continues to argue about controlling emissions to decrease further warming of the Earth, the innocent and the disadvantaged continue to suffer and die. The cataclysmic heat waves experienced in the summer of 2021 in Western North America and the massive floods in Western Europe are just two examples of the future awaiting us.

We must take a moment and reflect on our role during this unique moment in the history of humanity. It is up to us reading this journal to step up, educate, create awareness, and advocate for the future of our patients and every person in the world. As healthcare providers, we have a unique opportunity to make a difference as most people are not aware of the link between climate change and health (12). The medical profession is a trusted source of knowledge and can promote equitable climate solutions and health policies.

Even at the personal level, our daily choices can make a difference: the carbon footprint of private household activities accounts for about two-thirds of global emissions (133). Lifestyle changes, including changes in our diets, transportation habits, and the use of renewable energy, can help decrease global emissions. The decisions that we make today, inclusive of our individual and collective action and inaction, will impact every

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615 individual in the world and *all* future generations. We have the responsibility to advocate
616 for and educate governments, the public, and our patients to reduce the risk that climate
617 change has posed on deteriorating public health. This is our opportunity to change the
618 history of humanity.

REFERENCES

1. (NASA) NASA. Overview: Weather, Global Warming and Climate Change 2021 [Available from: <https://climate.nasa.gov/resources/global-warming-vs-climate-change/>].
2. Administration NOAA. It's official: July was Earth's hottest month on record 2021 [updated August 13, 2021. Available from: <https://www.noaa.gov/news/its-official-july-2021-was-earths-hottest-month-on-record>].
3. (NASA) NAASA. Overview: Weather, Global Warming and Climate Change 2021 [Available from: <https://climate.nasa.gov/resources/global-warming-vs-climate-change/>].
4. Nations U. United Nations Framework Convention on Climate Change. 1992.
5. Administration NOaA. Greenhouse Gases [Available from: <https://www.ncdc.noaa.gov/monitoring-references/faq/greenhouse-gases.php>].
6. More Near-Record Warm Years Are Likely On Horizon. 2021.
7. Administration NAS. 2020 Tied for Warmest Year on Record, NASA Analysis Shows 2021 [Available from: <https://climate.nasa.gov/news/3061/2020-tied-for-warmest-year-on-record-nasa-analysis-shows/>].
8. (IPCC) IPoCC. Special Report: Global Warming of 1.5 °C. 2018.
9. Mental Health and Our Changing Climate: Impacts, Implications, and Guidance. PsycEXTRA Dataset: American Psychological Association (APA); 2017.
10. Ahdoot S, Pacheco SE. Global Climate Change and Children's Health. *Pediatrics*. 2015;136(5):e1468-84.
11. Ebi KL, Balbus J, Luber G, Bole A, Crimmins AR, Glass GE, et al. Chapter 14 : Human Health. Impacts, Risks, and Adaptation in the United States: The Fourth National Climate Assessment, Volume II. U.S. Global Change Research Program; 2018.
12. Watts N, Amann M, Arnell N, Ayeb-Karlsson S, Beagley J, Belesova K, et al. The 2020 report of The Lancet Countdown on health and climate change: responding to converging crises. *Lancet*. 2021;397(10269):129-70.
13. Lancet Countdown on Health and Climate Change: Tracking the connections between public health and climate change. 2020.
14. IARC, editor. Outdoor air pollution. 2016.
15. EPA. Greenhouse Gases. What are the trends in greenhouse gas emissions and concentrations and their impacts on human health and the environment?
16. EPA. Global Greenhouse Emissions Data.
17. Change IPoCC. Climate change 2014: mitigation of climate change : working group III contribution to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change: Cambridge University Press; 2015.
18. Kinney PL. Interactions of Climate Change, Air Pollution, and Human Health. *Curr Environ Health Rep*. 2018;5(1):179-86.

19. Landrigan PJ, Fuller R, Acosta NJR, Adeyi O, Arnold R, Basu NN, et al. The Lancet Commission on pollution and health. *Lancet*. 2018;391(10119):462-512.
20. Organization WH. Air Pollution 2021 [Available from: https://www.who.int/health-topics/air-pollution#tab=tab_1].
21. Association AL. State of the Air. 2021.
22. Cohen AJ, Brauer M, Burnett R, Anderson HR, Frostad J, Estep K, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet*. 2017;389(10082):1907-18.
23. Burbank AJ, Sood AK, Kesic MJ, Peden DB, Hernandez ML. Environmental determinants of allergy and asthma in early life. *J Allergy Clin Immunol*. 2017;140(1):1-12.
24. Gilliland FD. Outdoor air pollution, genetic susceptibility, and asthma management: opportunities for intervention to reduce the burden of asthma. *Pediatrics*. 2009;123 Suppl 3:S168-73.
25. Nishimura KK, Iwanaga K, Oh SS, Pino-Yanes M, Eng C, Keswani A, et al. Early-life ozone exposure associated with asthma without sensitization in Latino children. *J Allergy Clin Immunol*. 2016;138(6):1703-6 e1.
26. Tager IB, Balmes J, Lurmann F, Ngo L, Alcorn S, Kunzli N. Chronic exposure to ambient ozone and lung function in young adults. *Epidemiology*. 2005;16(6):751-9.
27. Yang SI. Particulate matter and childhood allergic diseases. *Korean J Pediatr*. 2019;62(1):22-9.
28. Zheng XY, Ding H, Jiang LN, Chen SW, Zheng JP, Qiu M, et al. Association between Air Pollutants and Asthma Emergency Room Visits and Hospital Admissions in Time Series Studies: A Systematic Review and Meta-Analysis. *PLoS One*. 2015;10(9):e0138146.
29. Liu Y, Pan J, Zhang H, Shi C, Li G, Peng Z, et al. Short-Term Exposure to Ambient Air Pollution and Asthma Mortality. *Am J Respir Crit Care Med*. 2019;200(1):24-32.
30. Brandt EB, Biagini Myers JM, Acciani TH, Ryan PH, Sivaprasad U, Ruff B, 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 e7.
31. Codispoti CD, LeMasters GK, Levin L, Reponen T, Ryan PH, Biagini Myers JM, et al. Traffic pollution is associated with early childhood aeroallergen sensitization. *Ann Allergy Asthma Immunol*. 2015;114(2):126-33.
32. Sbihi H, Allen RW, Becker A, Brook JR, Mandhane P, Scott JA, et al. Perinatal Exposure to Traffic-Related Air Pollution and Atopy at 1 Year of Age in a Multi-Center Canadian Birth Cohort Study. *Environ Health Perspect*. 2015;123(9):902-8.
33. Ahn K. The role of air pollutants in atopic dermatitis. *J Allergy Clin Immunol*. 2014;134(5):993-9; discussion 1000.
34. Nguyen GH, Andersen LK, Davis MDP. Climate change and atopic dermatitis: is there a link? *Int J Dermatol*. 2019;58(3):279-82.
35. Stefanovic N, Irvine AD, Flohr C. The Role of the Environment and Exposome in Atopic Dermatitis. *Curr Treat Options Allergy*. 2021:1-20.
36. Paller AS, Spergel JM, Mina-Osorio P, Irvine AD. The atopic march and atopic multimorbidity: Many trajectories, many pathways. *J Allergy Clin Immunol*. 2019;143(1):46-55.

37. Prunicki M, Cauwenberghs N, Lee J, Zhou X, Movassagh H, Noth E, et al. Air pollution exposure is linked with methylation of immunoregulatory genes, altered immune cell profiles, and increased blood pressure in children. *Sci Rep*. 2021;11(1):4067.
38. Nadeau K, McDonald-Hyman C, Noth EM, Pratt B, Hammond SK, Balmes J, et al. Ambient air pollution impairs regulatory T-cell function in asthma. *J Allergy Clin Immunol*. 2010;126(4):845-52 e10.
39. Ho SM. Environmental epigenetics of asthma: an update. *J Allergy Clin Immunol*. 2010;126(3):453-65.
40. Gruziova O, Xu CJ, Breton CV, Annesi-Maesano I, Anto JM, Auffray C, et al. Epigenome-Wide Meta-Analysis of Methylation in Children Related to Prenatal NO₂ Air Pollution Exposure. *Environ Health Perspect*. 2017;125(1):104-10.
41. Brunst KJ, Leung YK, Ryan PH, Khurana Hershey GK, Levin L, Ji H, et al. Forkhead box protein 3 (FOXP3) hypermethylation is associated with diesel exhaust exposure and risk for childhood asthma. *J Allergy Clin Immunol*. 2013;131(2):592-4 e1-3.
42. Domingo JL, Rovira J. Effects of air pollutants on the transmission and severity of respiratory viral infections. *Environ Res*. 2020;187:109650.
43. Urrutia-Pereira M, Mello-da-Silva CA, Sole D. COVID-19 and air pollution: A dangerous association? *Allergol Immunopathol (Madr)*. 2020;48(5):496-9.
44. Kim H, Bell ML. Air Pollution and COVID-19 Mortality in New York City. *Am J Respir Crit Care Med*. 2021;204(1):97-9.
45. Woodby B, Arnold MM, Valacchi G. SARS-CoV-2 infection, COVID-19 pathogenesis, and exposure to air pollution: What is the connection? *Ann N Y Acad Sci*. 2021;1486(1):15-38.
46. Schiavoni G, D'Amato G, Afferni C. The dangerous liaison between pollens and pollution in respiratory allergy. *Annals of Allergy, Asthma & Immunology*. 2017;118.
47. Kurganskiy A, Creer S, de Vere N, Griffith GW, Osborne NJ, Wheeler BW, et al. Predicting the severity of the grass pollen season and the effect of climate change in Northwest Europe. *Sci Adv*. 2021;7(13).
48. D'Amato G, Baena-Cagnani CE, Cecchi L, Annesi-Maesano I, Nunes C, Ansotegui I, et al. Climate change, air pollution and extreme events leading to increasing prevalence of allergic respiratory diseases. *Multidiscip Respir Med*. 2013;8(1):12.
49. Kurganskiy A, Skjøth CA, Baklanov A, Sofiev M, Saarto A, Severova E, et al. Incorporation of pollen data in source maps is vital for pollen dispersion models. *Atmos Chem Phys*. 2020;20(4):2099-121.
50. Takaro TK, Knowlton K, Balmes JR. Climate change and respiratory health: current evidence and knowledge gaps. *Expert Rev Respir Med*. 2013;7(4):349-61.
51. Ziska LH, Makra L, Harry SK, Bruffaerts N, Hendrickx M, Coates F, et al. Temperature-related changes in airborne allergenic pollen abundance and seasonality across the northern hemisphere: a retrospective data analysis. *The Lancet Planetary Health*. 2019;3(3):e124-e31.
52. Case MJ, Stinson KA. Climate change impacts on the distribution of the allergenic plant, common ragweed (*Ambrosia artemisiifolia*) in the eastern United States. *PLoS One*. 2018;13(10):e0205677.
53. Paudel B, Chu T, Chen M, Sampath V, Prunicki M, Nadeau KC. Increased duration of pollen and mold exposure are linked to climate change. *Sci Rep*. 2021;11(1):12816.

54. D'Amato G, Holgate ST, Pawankar R, Ledford DK, Cecchi L, Al-Ahmad M, et al. Meteorological conditions, climate change, new emerging factors, and asthma and related allergic disorders. A statement of the World Allergy Organization. *World Allergy Organ J*. 2015;8(1):25.
55. M DA, Cecchi L, Annesi-Maesano I, G DA. News on Climate Change, Air Pollution, and Allergic Triggers of Asthma. *J Investig Allergol Clin Immunol*. 2018;28(2):91-7.
56. Buters J, Prank M, Sofiev M, Pusch G, Albertini R, Annesi-Maesano I, et al. Variation of the group 5 grass pollen allergen content of airborne pollen in relation to geographic location and time in season. *J Allergy Clin Immunol*. 2015;136(1):87-95 e6.
57. Anderegg WRL, Abatzoglou JT, Anderegg LDL, Bielory L, Kinney PL, Ziska L. Anthropogenic climate change is worsening North American pollen seasons. *Proc Natl Acad Sci U S A*. 2021;118(7).
58. Cecchi L, D'Amato G, Annesi-Maesano I. External exposome and allergic respiratory and skin diseases. *J Allergy Clin Immunol*. 2018;141(3):846-57.
59. Glick S, Gehrig R, Eeftens M. Multi-decade changes in pollen season onset, duration, and intensity: A concern for public health? *Sci Total Environ*. 2021;781:146382.
60. Poole JA, Barnes CS, Demain JG, Bernstein JA, Padukudru MA, Sheehan WJ, 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):1702-10.
61. Schmidt CW. Pollen Overload: Seasonal Allergies in a Changing Climate. *Environ Health Perspect*. 2016;124(4):A70-5.
62. Robichaud A. An overview of selected emerging outdoor airborne pollutants and air quality issues: The need to reduce uncertainty about environmental and human impacts. *J Air Waste Manag Assoc*. 2020;70(4):341-78.
63. Filippidou E, Koukoulia AJPiHS. Ozone effects on the respiratory system. 2011;1:144-55.
64. Custovic A. To what extent is allergen exposure a risk factor for the development of allergic disease? *Clin Exp Allergy*. 2015;45(1):54-62.
65. De Roos AJ, Kenyon CC, Zhao Y, Moore K, Melly S, Hubbard RA, et al. Ambient daily pollen levels in association with asthma exacerbation among children in Philadelphia, Pennsylvania. *Environ Int*. 2020;145:106138.
66. Huynh BT, Tual S, Turbelin C, Pelat C, Cecchi L, D'Amato G, et al. Short-term effects of airborne pollens on asthma attacks as seen by general practitioners in the Greater Paris area, 2003-2007. *Prim Care Respir J*. 2010;19(3):254-9.
67. Bergougnan C, Dittlein DC, Hummer E, Riepl R, Eisenbart S, Bock D, et al. Physical and immunological barrier of human primary nasal epithelial cells from non-allergic and allergic donors. *World Allergy Organ J*. 2020;13(3):100109.
68. Damialis A, Gilles S, Sofiev M, Sofieva V, Kolek F, Bayr D, et al. Higher airborne pollen concentrations correlated with increased SARS-CoV-2 infection rates, as evidenced from 31 countries across the globe. *Proc Natl Acad Sci U S A*. 2021;118(12).
69. Gilles S, Blume C, Wimmer M, Damialis A, Meulenbroek L, Gokkaya M, et al. Pollen exposure weakens innate defense against respiratory viruses. *Allergy*. 2020;75(3):576-87.

- 787 70. Knutson TR, Chung MV, Vecchi G, Sun J, Hsieh T-L, Smith A. Climate change is probably
788 increasing the intensity
789 of tropical cyclones. In: Critical Issues in
790 Climate Change Science. Corinne Le Quéré, Forste PLP, editors 2021.
- 791 71. Vicedo-Cabrera A, Scovronick N, Sera F, Royé D, Schneider R, Tobias A, et al. The burden
792 of heat-related mortality attributable to recent human-induced climate change. *Nature Climate*
793 *Change*. 2021;182.
- 794 72. Robine J-M, Cheung K, Roy S, Oyen H, Griffiths C, Michel j-p, et al. Death toll exceeded
795 70,000 in Europe during the summer of 2003. *Comptes rendus biologies*. 2008;331:171-8.
- 796 73. Lancet Countdown on Health and Climate Change: Exposure of Vulnerable populations
797 to Heatwaves. 1.1 Health and Heat. 2020.
- 798 74. Manoli G, Fatichi S, Schlöpfer M, Yu K, Crowther TW, Meili N, et al. Magnitude of urban
799 heat islands largely explained by climate and population. *Nature*. 2019;573(7772):55-60.
- 800 75. Potetsio M. Estimate on number of suspected heat-related deaths rises to 808. *The*
801 *Toronto Star*. 2021.
- 802 76. Hurteau MD, Westerling AL, Wiedinmyer C, Bryant BP. Projected effects of climate and
803 development on California wildfire emissions through 2100. *Environ Sci Technol*.
804 2014;48(4):2298-304.
- 805 77. Siberia's wildfires are bigger than all the world's other blazes combined. *Washington*
806 *Post*. 2021.
- 807 78. Group NWC. Dixie Fire 2021 [Available from:
808 <https://inciweb.nwcg.gov/incident/article/7690/67256/>].
- 809 79. Agency USEP. National Emissions Inventory (NEI) Data 2011 [Available from:
810 <https://www.epa.gov/air-emissions-inventories/2011-national-emissions-inventory-nei-data>].
- 811 80. Aguilera R, Corringham T, Gershunov A, Leibel S, Benmarhnia T. Fine Particles in Wildfire
812 Smoke and Pediatric Respiratory Health in California. *Pediatrics*. 2021;147(4).
- 813 81. Rice MB, Henderson SB, Lambert AA, Cromar KR, Hall JA, Cascio WE, et al. Respiratory
814 Impacts of Wildland Fire Smoke: Future Challenges and Policy Opportunities. An Official
815 American Thoracic Society Workshop Report. *Ann Am Thorac Soc*. 2021;18(6):921-30.
- 816 82. Reid CE, Brauer M, Johnston FH, Jerrett M, Balmes JR, Elliott CT. Critical Review of
817 Health Impacts of Wildfire Smoke Exposure. *Environ Health Perspect*. 2016;124(9):1334-43.
- 818 83. Kodgule R, Salvi S. Exposure to biomass smoke as a cause for airway disease in women
819 and children. *Curr Opin Allergy Clin Immunol*. 2012;12(1):82-90.
- 820 84. Po JY, FitzGerald JM, Carlsten C. Respiratory disease associated with solid biomass fuel
821 exposure in rural women and children: systematic review and meta-analysis. *Thorax*.
822 2011;66(3):232-9.
- 823 85. Schei MA, Hessen JO, Smith KR, Bruce N, McCracken J, Lopez V. Childhood asthma and
824 indoor woodsmoke from cooking in Guatemala. *J Expo Anal Environ Epidemiol*. 2004;14 Suppl
825 1:S110-7.
- 826 86. Liu D, Tager IB, Balmes JR, Harrison RJ. The effect of smoke inhalation on lung function
827 and airway responsiveness in wildland fire fighters. *Am Rev Respir Dis*. 1992;146(6):1469-73.

Pacheco

87. Burbank AJ, Vadlamudi A, Mills KH, Alt EM, Wells H, Zhou H, et al. The glutathione-S-transferase mu-1 null genotype increases wood smoke-induced airway inflammation. *J Allergy Clin Immunol*. 2019.
88. Ghio AJ, Soukup JM, Case M, Dailey LA, Richards J, Berntsen J, et al. Exposure to wood smoke particles produces inflammation in healthy volunteers. *Occup Environ Med*. 2012;69(3):170-5.
89. Adetona O, Reinhardt TE, Domitrovich J, Broyles G, Adetona AM, Kleinman MT, et al. Review of the health effects of wildland fire smoke on wildland firefighters and the public. *Inhal Toxicol*. 2016;28(3):95-139.
90. Nelin TD, Joseph AM, Gorr MW, Wold LE. Direct and indirect effects of particulate matter on the cardiovascular system. *Toxicol Lett*. 2012;208(3):293-9.
91. Croft DP, Cameron SJ, Morrell CN, Lowenstein CJ, Ling F, Zareba W, et al. Associations between ambient wood smoke and other particulate pollutants and biomarkers of systemic inflammation, coagulation and thrombosis in cardiac patients. *Environ Res*. 2017;154:352-61.
92. Sakhamuri S, Cummings S. Increasing trans-Atlantic intrusion of Sahara dust: a cause of concern? *The Lancet Planetary Health*. 2019;3(6):e242-e3.
93. Fogelbach GD, Staffeld PL, Sarabia AMC, López C, Duarte PA, Calderón OM, et al. Contaminación atmosférica en América Latina: impacto en la salud Y regulación actual - reporte del grupo del Comité de Aerobiología de la Sociedad Latinoamericana de Asma, Alergia e Inmunología. *BJAI*. 2020;4(4):423-34.
94. Monteil MA. Saharan dust clouds and human health in the English-speaking Caribbean: what we know and don't know. *Environ Geochem Health*. 2008;30(4):339-43.
95. Administration NAaS. A Dust Plume to Remember 2020 [Available from: <https://earthobservatory.nasa.gov/images/146913/a-dust-plume-to-remember>].
96. Aghababaeian H, Ostadtaghizadeh A, Ardalan A, Asgary A, Akbary M, Yekaninejad MS, et al. Global Health Impacts of Dust Storms: A Systematic Review. *Environ Health Insights*. 2021;15:11786302211018390.
97. Gutierrez MP, Zuidema P, Mirsaeidi M, Campos M, Kumar N. Association between African Dust Transport and Acute Exacerbations of COPD in Miami. *J Clin Med*. 2020;9(8).
98. Kotsyfakis M, Zarogiannis SG, Patelarou E. The health impact of Saharan dust exposure. 2019;32(6):749-60.
99. Zhang X, Zhao L, Tong DQ, Wu G, Dan M, Teng B. A Systematic Review of Global Desert Dust and Associated Human Health Effects. 2016;7(12):158.
100. Heft-Neal S, Burney, J., Bendavid, E. et al. . Dust pollution from the Sahara and African infant mortality. . *Nat Sustain*. 2020;3:863-71.
101. Acevedo N, Zakzuk J, Caraballo L. House Dust Mite Allergy Under Changing Environments. *Allergy Asthma Immunol Res*. 2019;11(4):450-69.
102. (IPCC) IPoCC. Special Report: Climate Change and Land. 2019.
103. Fisk WJ, Lei-Gomez Q, Mendell MJ. Meta-analyses of the associations of respiratory health effects with dampness and mold in homes. *Indoor Air*. 2007;17(4):284-96.
104. Hulin M, Moularat S, Kirchner S, Robine E, Mandin C, Annesi-Maesano I. Positive associations between respiratory outcomes and fungal index in rural inhabitants of a representative sample of French dwellings. *Int J Hyg Environ Health*. 2013;216(2):155-62.

105. Maupin CR, Roark, E.B., Thirumalai, K. et al. . Abrupt Southern Great Plains thunderstorm shifts linked to glacial climate variability. . *Nat Geosci* 2021;14:396–401
106. D'Amato G, Pawankar R, Vitale C, Lanza M, Molino A, Stanziola A, et al. Climate Change and Air Pollution: Effects on Respiratory Allergy. *Allergy Asthma Immunol Res.* 2016;8(5):391-5.
107. Davies JM. Encyclopedia of Environmental Health [Second Edition]. In: Nriagu J, editor. *Encyclopedia of Environmental Health [Second Edition]*. Netherlands: Elsevier; 2019.
108. Europe WHOROf. Review of evidence on health aspects of air pollution – REVIHAAP Project: Technical Report. Copenhagen: WHO Regional Office for Europe © World Health Organization 2013.; 2013.
109. Thien F. Melbourne epidemic thunderstorm asthma event 2016: Lessons learnt from the perfect storm. 2018;23(11):976-7.
110. D'Amato G, Annesi Maesano I, Molino A, Vitale C, D'Amato M. Thunderstorm-related asthma attacks. *J Allergy Clin Immunol.* 2017;139(6):1786-7.
111. D'Amato G. Effects of climatic changes and urban air pollution on the rising trends of respiratory allergy and asthma. *Multidisciplinary Respiratory Medicine.* 2011;6(1):28.
112. Knox RB, Suphioglu C, Taylor P, Desai R, Watson HC, Peng JL, et al. Major grass pollen allergen Lol p 1 binds to diesel exhaust particles: implications for asthma and air pollution. *Clin Exp Allergy.* 1997;27(3):246-51.
113. Akerlof KL, Delamater PL, Boules CR, Upperman CR, Mitchell CS. Vulnerable Populations Perceive Their Health as at Risk from Climate Change. *Int J Environ Res Public Health.* 2015;12(12):15419-33.
114. Schraufnagel DE, Balmes JR, De Matteis S, Hoffman B, Kim WJ, Perez-Padilla R, et al. Health Benefits of Air Pollution Reduction. *Ann Am Thorac Soc.* 2019;16(12):1478-87.
115. Program USGCR. The Fourth National Climate Assessment (NCA4) 2018.
116. Annesi-Maesano I, Forastiere F, Balmes J, Garcia E, Harkema J, Holgate S, et al. The clear and persistent impact of air pollution on chronic respiratory diseases: a call for interventions. *Eur Respir J.* 2021;57(3).
117. Du W, Zhang W, Hu H, Zhang M, He Y, Li Z. Associations between ambient air pollution and hospitalizations for acute exacerbation of chronic obstructive pulmonary disease in Jinhua, 2019. *Chemosphere.* 2021;267:128905.
118. Shin HH, Parajuli RP, Gogna P, Maquiling A, Dehghani P. Pollutant-sex specific differences in respiratory hospitalization and mortality risk attributable to short-term exposure to ambient air pollution. *Sci Total Environ.* 2021;755(Pt 2):143135.
119. Khomenko S, Cirach M, Pereira-Barboza E, Mueller N, Barrera-Gomez J, Rojas-Rueda D, et al. Premature mortality due to air pollution in European cities: a health impact assessment. *Lancet Planet Health.* 2021;5(3):e121-e34.
120. International H. Climate change in an ageing world. 2015.
121. Arnetz BB, Arnetz J, Harkema JR, Morishita M, Slonager K, Sudan S, et al. Neighborhood air pollution and household environmental health as it relates to respiratory health and healthcare utilization among elderly persons with asthma. *J Asthma.* 2020;57(1):28-39.
122. Bowe B, Xie Y, Yan Y, Al-Aly Z. Burden of Cause-Specific Mortality Associated With PM 2.5 Air Pollution in the United States. *JAMA Network Open.* 2019;2:e1915834.

Pacheco

123. United Nations Department of Economic and Social Affairs PD. World Population Ageing
2020 Highlights: Living arrangements of older persons 2020.
124. Korten I, Ramsey K, Latzin P. Air pollution during pregnancy and lung development in the
child. *Paediatr Respir Rev*. 2017;21:38-46.
125. (WHO) WHO. Air pollution and child health: prescribing clean air 2018 [Available from:
<https://www.who.int/publications/i/item/air-pollution-and-child-health>.
126. Mathiarasan S, Huls A. Impact of Environmental Injustice on Children's Health-
Interaction between Air Pollution and Socioeconomic Status. *Int J Environ Res Public Health*.
2021;18(2).
127. Wooldridge G, Murthy S. Pediatric Critical Care and the Climate Emergency: Our
Responsibilities and a Call for Change. *Front Pediatr*. 2020;8:472.
128. Bekkar B, Pacheco S, Basu R, DeNicola N. Association of Air Pollution and Heat Exposure
With Preterm Birth, Low Birth Weight, and Stillbirth in the US: A Systematic Review. *JAMA Netw
Open*. 2020;3(6):e208243.
129. Chen J, Fang J, Zhang Y, Xu Z, Byun HM, Li PH, et al. Associations of adverse pregnancy
outcomes with high ambient air pollution exposure: Results from the Project ELEFANT. *Sci Total
Environ*. 2021;761:143218.
130. Shang L, Huang L, Yang L, Leng L, Qi C, Xie G, et al. Impact of air pollution exposure
during various periods of pregnancy on term birth weight: a large-sample, retrospective
population-based cohort study. *Environ Sci Pollut Res Int*. 2021;28(3):3296-306.
131. Chiu YH, Coull BA, Sternthal MJ, Kloog I, Schwartz J, Cohen S, et al. Effects of prenatal
community violence and ambient air pollution on childhood wheeze in an urban population. *J
Allergy Clin Immunol*. 2014;133(3):713-22 e4.
132. Morales E, Garcia-Esteban R, de la Cruz OA, Basterrechea M, Lertxundi A, de Dicastillo
MD, et al. Intrauterine and early postnatal exposure to outdoor air pollution and lung function
at preschool age. *Thorax*. 2015;70(1):64-73.
133. Hsu HH, Chiu YH, Coull BA, Kloog I, Schwartz J, Lee A, et al. Prenatal Particulate Air
Pollution and Asthma Onset in Urban Children. Identifying Sensitive Windows and Sex
Differences. *Am J Respir Crit Care Med*. 2015;192(9):1052-9.
134. Zhang W, Spero TL, Nolte CG, Garcia VC, Lin Z, Romitti PA, et al. Projected Changes in
Maternal Heat Exposure During Early Pregnancy and the Associated Congenital Heart Defect
Burden in the United States. *J Am Heart Assoc*. 2019;8(3):e010995.
135. Liu GT, Dancause KN, Elgbeili G, Laplante DP, King S. Disaster-related prenatal maternal
stress explains increasing amounts of variance in body composition through childhood and
adolescence: Project Ice Storm. *Environ Res*. 2016;150:1-7.
136. Roseboom TJ, Painter RC, van Abeelen AF, Veenendaal MV, de Rooij SR. Hungry in the
womb: what are the consequences? Lessons from the Dutch famine. *Maturitas*.
2011;70(2):141-5.
137. Mallett LH ER. Flooding: what is the impact on pregnancy and child health? *Disasters*.
2018;42:432-58. .
138. Burke S, Sanson A, Hoorn J. The Psychological Effects of Climate Change on Children.
Current Psychiatry Reports. 2018;20.

139. Organization WH. Ambient (outdoor) air pollution 2021 [Available from: [https://www.who.int/news-room/fact-sheets/detail/ambient-\(outdoor\)-air-quality-and-health](https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health).]
140. Organization WH. New WHO Global Air Quality Guidelines aim to save millions of lives from air pollution 2021 [updated September 22,2021. Available from: <https://www.who.int/news/item/22-09-2021-new-who-global-air-quality-guidelines-aim-to-save-millions-of-lives-from-air-pollution>.]
141. Data OWi. Energy poverty and indoor air pollution: a problem as old as humanity that we can end within our lifetime 2021 [Available from: <https://ourworldindata.org/energy-poverty-air-pollution>.]
142. Ellwanger JH, Kulmann-Leal B, Kaminski VL, Valverde-Villegas JM, Veiga A, Spilki FR, et al. Beyond diversity loss and climate change: Impacts of Amazon deforestation on infectious diseases and public health. *An Acad Bras Cienc.* 2020;92(1):e20191375.
143. Schramm PJ, Al Janabi AL, Campbell LW, Donatuto JL, Gaughen SC. How Indigenous Communities Are Adapting To Climate Change: Insights From The Climate-Ready Tribes Initiative. *Health Aff (Millwood).* 2020;39(12):2153-9.
144. Balsari S, Dresser C, Leaning J. Climate Change, Migration, and Civil Strife. *Curr Environ Health Rep.* 2020;7(4):404-14.
145. Dannenberg A, Frumkin H, Hess J, Ebi K. Managed retreat as a strategy for climate change adaptation in small communities: public health implications. *Climatic Change.* 2019;153.
146. Agency UR. Data reveals impacts of climate emergency on displacement 2021 [Available from: <https://www.unhcr.org/en-us/news/stories/2021/4/60806d124/data-reveals-impacts-climate-emergency-displacement.html>.]
147. Peace IfEa. Over one billion people at threat of being displaced by 2050 due to environmental change, conflict and civil unrest 2021 [Available from: <https://www.economicsandpeace.org/wp-content/uploads/2020/09/Ecological-Threat-Register-Press-Release-27.08-FINAL.pdf>.]
148. International O. Carbon emissions of richest 1 percent more than double the emissions of the poorest half of humanity 2020 [Available from: <https://www.oxfam.org/en/press-releases/carbon-emissions-richest-1-percent-more-double-emissions-poorest-half-humanity>.]
149. The Lancet Planetary H. Strands of injustice. *Lancet Planet Health.* 2020;4(7):e256.
150. Scientists UoC. Killer Heat in the United States: Climate Choices and the Future of Dangerously Hot Days. 2019.
151. Collins TW, Grineski SE, Chakraborty J, Flores AB. Environmental injustice and Hurricane Harvey: A household-level study of socially disparate flood exposures in Greater Houston, Texas, USA. *Environ Res.* 2019;179(Pt A):108772.
152. Willison CE, Singer PM, Creary MS, Greer SL. Quantifying inequities in US federal response to hurricane disaster in Texas and Florida compared with Puerto Rico. *BMJ Glob Health.* 2019;4(1):e001191.
153. Ramirez F. Harvey aid shortchanges Texas cities with minorities, study finds. *Houston Chronicle.* 2018.
154. Vinik D. 'People just give up': Low-income hurricane victims slam federal relief programs. *Politico.* 2018.

Pacheco

155. Kingsley SL, Eliot MN, Carlson L, Finn J, MacIntosh DL, Suh HH, et al. Proximity of US schools to major roadways: a nationwide assessment. *Journal of exposure science & environmental epidemiology*. 2014;24(3):253-9.

Figure Legends:

Figure 1. Relationship between the drivers of climate change and the outcomes of climate change and air pollution.

Figure 2. Disease and Clinical Implications Caused by Ripple Effect from Climate Change.

Figure 3. Particle matter in pollen exine (Electron microscopy, permission use granted by G. Guidos.)

Figure 4. Saharan (“Godzilla”) dust cloud across the Atlantic ocean (<https://earthobservatory.nasa.gov/images/146913/a-dust-plume-to-remember>)

Figure 5. Intersection of Social Determinants of Health and Vulnerability (National Climate Assessment, <https://health2016.globalchange.gov/populations-concern>)

Table I. Sources of air pollutants

Natural sources	Anthropogenic sources
Volcanoes Wildfires Bioaerosols (molds, spores, viruses, bacteria, endotoxin, proteins, DNA) Volatile organic compounds from plants.	Electricity and heat production (burning of coal, natural gas, oil) Industry Agriculture, forestry, and other land use (cultivation, livestock, deforestation) Transportation (road, rail, air, marine) Buildings (heating, cooking in homes) Other: Halocarbons (industry, commercial, domestic sources)

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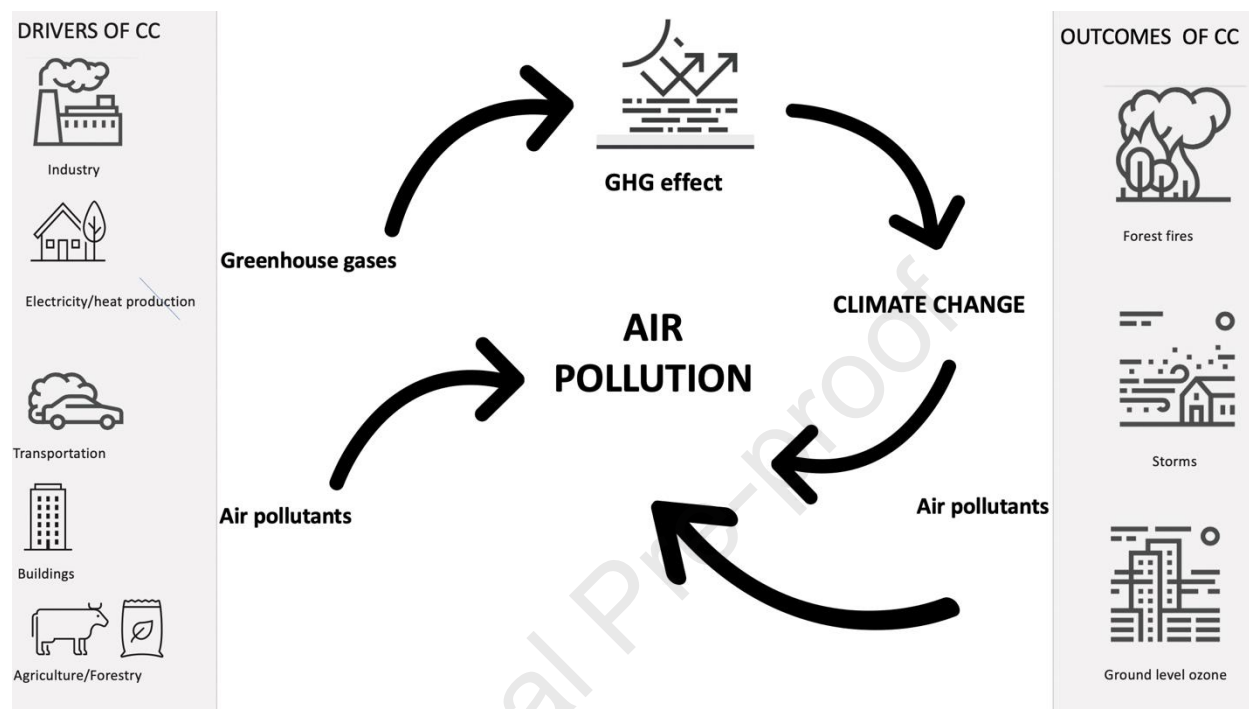


Figure 2. Disease and Clinical Implications Caused by Ripple Effect from Climate Change

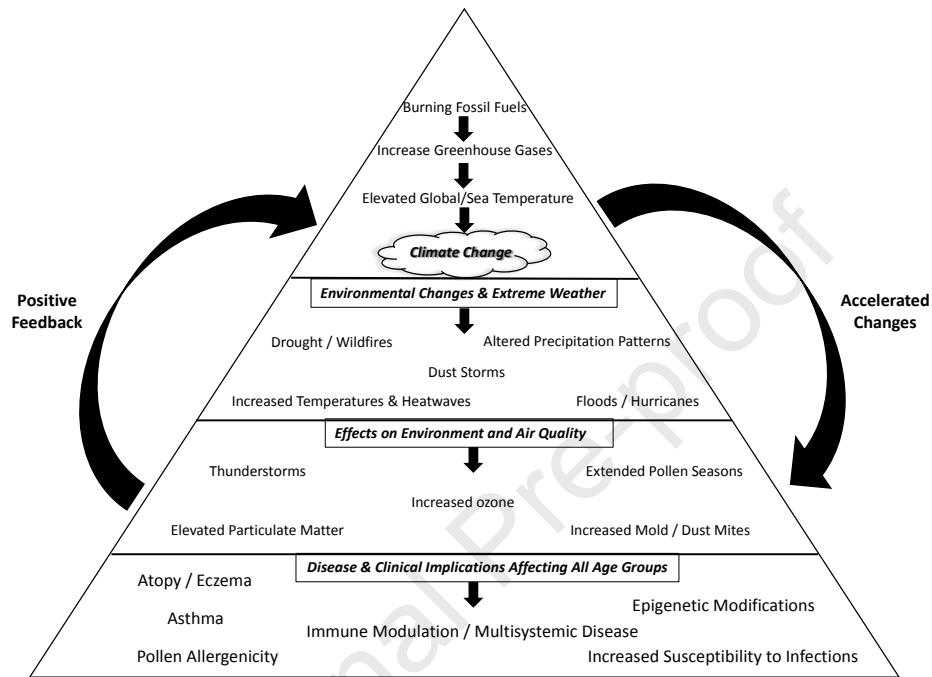


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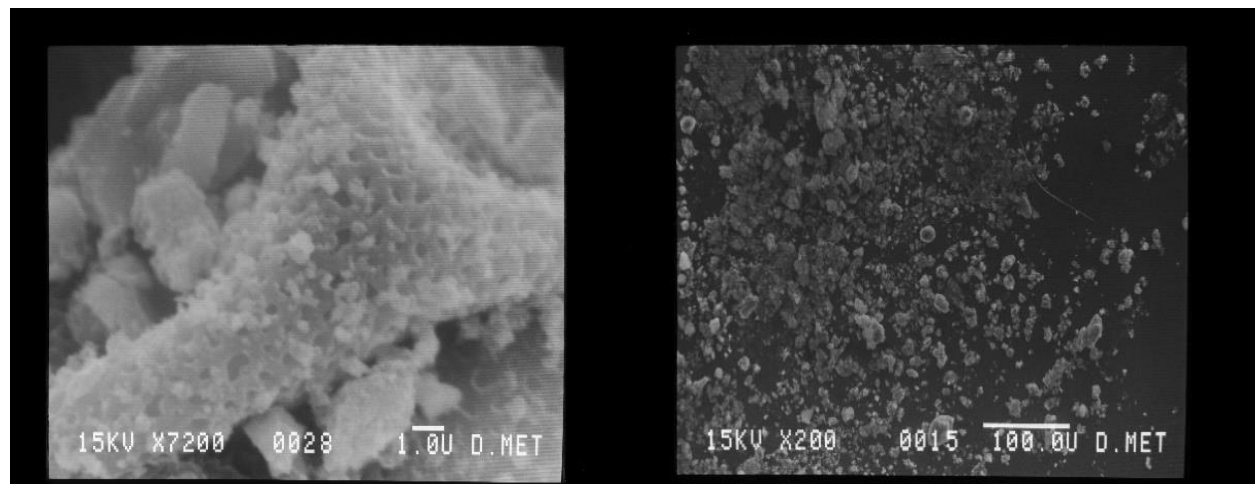


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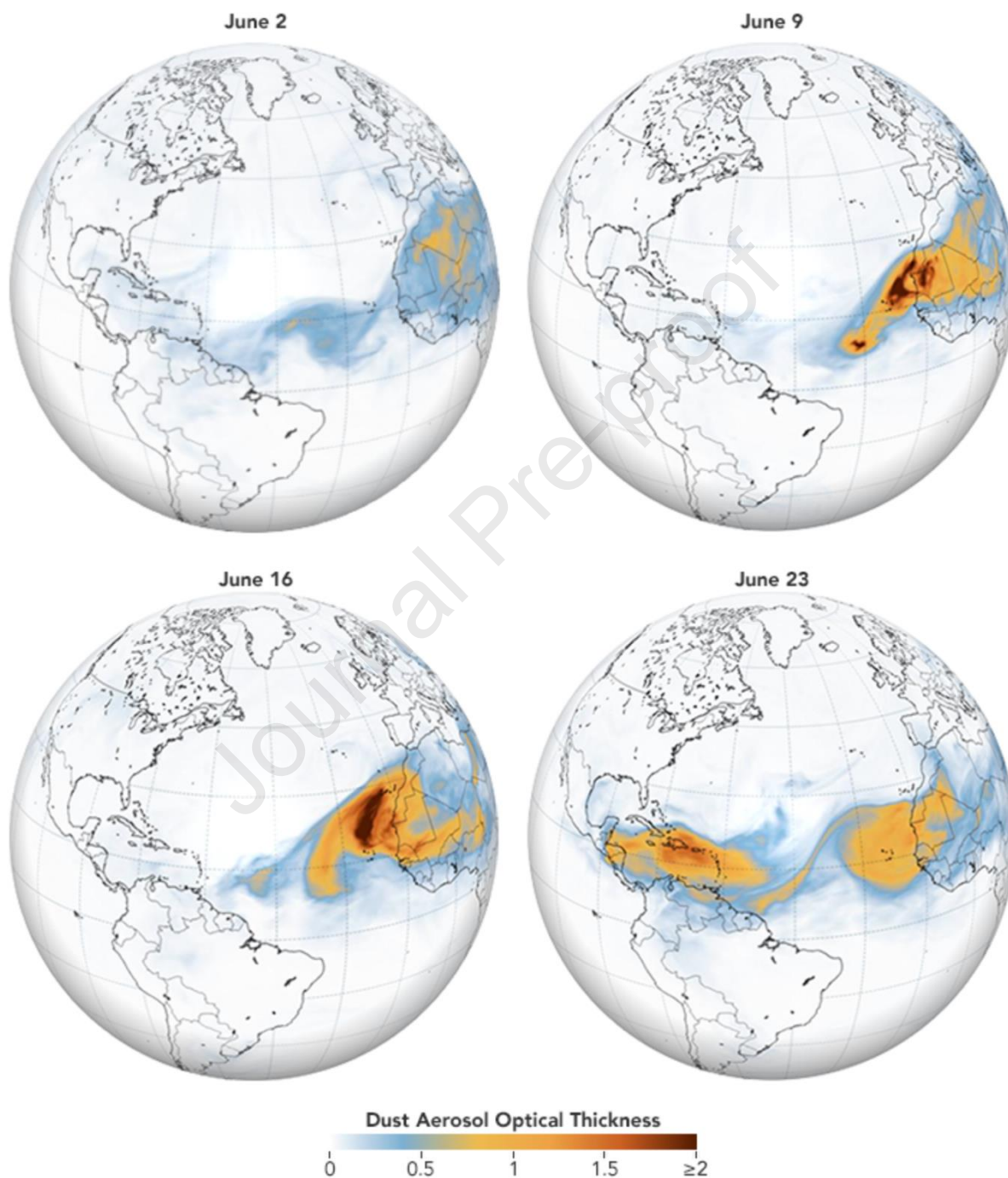


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