# Climate change and global issues in allergy and immunology



Susan E. Pacheco, MD,<sup>a</sup> Guillermo Guidos-Fogelbach, MD, PhD,<sup>b</sup> Isabella Annesi-Maesano, MD, PhD, DSc,<sup>c</sup>
Ruby Pawankar, MD, PhD,<sup>d</sup> Gennaro D' Amato, MD,<sup>e,f</sup> Patricia Latour-Staffeld, MD,<sup>g,h</sup> Marylin Urrutia-Pereira, MD, PhD,<sup>i</sup>
Matthew J. Kesic, PhD, PA-C,<sup>j</sup> and Michelle L. Hernandez, MD,<sup>k</sup> on behalf of the American Academy of Allergy, Asthma & Immunology Environmental Exposures and Respiratory Health Committee

Houston, Tex; Mexico City, Mexico;

Montpellier, France; Tokyo, Japan; Naples, Italy: Santo Domingo, Dominican Republic; Bagé, Rio Grande do Sul, Brazil; and Buies Creek and Chapel Hill, NC

The steady increase in global temperatures, resulting from the combustion of fossil fuels and the accumulation of greenhouse gases (GHGs), continues to destabilize all ecosystems worldwide. Although annual emissions must be halved 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. To this effect, July 2021 was recently declared the hottest month ever recorded in 142 years. The ramifications of these changes for 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 effects of GHGs 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 disproportionally affect disadvantaged and vulnerable populations. This review article is an update for allergists

From <sup>8</sup>the University of Texas Health Science Center, McGovern Medical School, Houston; <sup>b</sup>E.N.M H/SEPI. Instituto Politecnico Nacional. Mexico City; <sup>c</sup>the Institute Desbrest of Epidemiology and Public Health. INSERM and Montpellier University, Montpellier; <sup>d</sup>the Division of Allergy. Department of Pediatrics, Nippon Medical School, Tokyo; <sup>e</sup>the Chairman Committee of World Allergy Organization on "Aerobiology. Climate Change. Biodiversity, and Allergy". Division of Respiratory Diseases and Allergy. High Specialty Hospital A. Cardarelli. Naples; <sup>f</sup>the School of Specialization in Respiratory Diseases, University of Naples. Federico II. Naples; <sup>g</sup>the Centro Avanzado De Alergia y Asma Santo Domingo; <sup>h</sup>the School of Medicine, Universidad Nacional Pedro Henriquez Ureña. Santo Domingo; <sup>t</sup>the Pediatrics Department, Federal University of Pampa, Bagé; <sup>t</sup>the Campbell University Physician Assistant Program College of Pharmacy and Health Sciences, Campbell University, Buies Creek; and <sup>k</sup>Clinical Research Unit. Children's Research Institute, University of North Carolina School of Medicine, Chapel Hill.

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication August 11, 2021; revised October 12, 2021; accepted for publication October 18, 2021.

Available online October 21, 2021.

Corresponding author: Susan E. Pacheco, MD, University of Texas Health Science Center at Houston, McGovern Medical School, Department of Pediatrics, Houston, TX 77030. E-mail: Susan.E.Pacheco@uth.tmc.edu.

The CrossMark symbol notifies online readers when updates have been made to the article such as errata or minor corrections

0091-6749/\$36.00

© 2021 Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology

https://doi.org/10.1016/j.jaci.2021.10.011

and immunologists about the health impacts of climate change that are already evident in our daily practices. It is also a call to action and advocacy, including to integrate climate change—related mitigation, education, and adaptation measures to protect our patients and avert further injury to our planet. (J Allergy Clin Immunol 2021;148:1366-77.)

**Key words:** Climate change, global warming, human health, allergy, asthma, vulnerable populations, air pollution, greenhouse gases, heat wayes, wildfires, dust storms, tropical storms, thunderstorms

We have seen an accelerated rise in global temperatures and ensuing global warming since the mid-19th century. These events are associated with increased production of greenhouse gases (GHGs) 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, vears, or decades. Anthropogenic activities such as burning of fossil fuels, deforestation, land use, livestock production, fertilization, and industrial processes have increased GHG emissions. Globally, carbon dioxide (CO<sub>2</sub>), methane (CH<sub>4</sub>), nitrous oxide (N<sub>2</sub>O), and halogenated gases are the main gases generated by human activities. This increase in GHGs 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."2

From the Industrial Revolution's inception to the present day, the concentration of  $CO_2$  in the atmosphere has increased from an average of 280 ppm to more than 415 ppm, a 48% change. This rise has led to an increased global average surface temperature of about 1°C ( $\sim$ 2°F) above preindustrial levels.³ Unfortunately, the rate of global warming has been faster in the past few decades, with 7 of the 10 warmest years occurring since 2014.⁴ To this effect, the Earth's global average temperature in 2020 tied it with 2016 as the warmest year on record.⁵ 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.⁶

Although a 1°C increase in global average surface temperatures appears to be relatively minor, the ramifications of these small

Abbreviations used

COPD: Chronic obstructive pulmonary disease

GHG: Greenhouse gases
HDM: House dust mite
O<sub>3</sub>: Ground-level ozone

 $PM_{2.5}$ : Particulate matter less than or equal to 2.5  $\mu m$  SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

WHO: World Health Organization

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 heat waves, 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. 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, including the following, will continue to increase because of climate change: 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.

This review article will address many of the changes and health conditions that affect the practice of allergy and immunology as well as the disproportional impact of climate change on vulnerable populations. However, it does not address many other environmental changes and adverse health outcomes associated with the climate crisis. These have been addressed comprehensively in other publications available to the reader. <sup>7-11</sup>

# 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 on 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 GHGs responsible for climate change and other byproducts that are major components of air pollution. Some of the resulting climate change-driven environmental changes may further contribute to the deterioration of air quality (Fig 1). Air pollution is a mixture of particles and gases emitted directly into the atmosphere or generated by chemical or photochemical reactions, such as tropospheric or ground-level ozone (O<sub>3</sub>). Natural, biologic, and anthropogenic sources of outdoor air pollution are shown in Table I. 12-15 weather and meteorologic variables affected by climate change (eg, temperature, changes in precipitation pattern, wind patterns) further affect the distribution of air pollutants. <sup>16</sup> Additionally, climate-driven changes (eg, wildfires, storms, O3-increased pollen, heat waves requiring higher demands for electricity) increase biologic and anthropogenic sources of air pollution, promoting a feed-forward loop of pollution and poor air quality resulting from climate change (Fig 2).

Exposure to air pollution, especially  $O_3$  and particulate matter smaller than or equal to 2.5 µm (PM<sub>2.5</sub>), has profound impacts on human health. 17 At least 90% of the world's population live in areas with low air quality, where the concentration of pollutants exceeds the guidelines established by the World Health Organization (WHO). 18 In the United States, more than 40% of the population (more than 135 million individuals) live in areas with poor air quality. <sup>19</sup> In 2015, PM<sub>2.5</sub> was responsible for 4.2 million premature deaths per year worldwide, 20 with more than 92% of pollution-related deaths occurring in low-income and middleincome countries.<sup>17</sup> 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<sub>2.5</sub>.<sup>20</sup>

Epidemiologic and experimental studies have also specifically highlighted the role of air pollution in the development of allergic disease (reviewed by Burbank et al<sup>21</sup>), as well as asthma development, <sup>22-25</sup> exacerbations, <sup>26</sup> and mortality. <sup>25,27</sup> Early-life exposure to air pollution is associated with an increased risk of aeroallergen sensitization <sup>28,29</sup> and food sensitization as early as age 1 year. <sup>30</sup>

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. 31-33 Air pollutants comprising volatile organic compounds, PM, traffic-related air pollution, and tobacco smoke have been demonstrated to adversely affect skin barrier integrity through the generation of reactive oxygen species and epigenetic modifications of the immune system. These mechanisms subsequently predispose infants to development of atopic dermatitis, increasing the risk of future allergic disease via the atopic march.<sup>34</sup> 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 and the important immunoregulatory genes Forkhead box P3 (FOXP3), IL4, IL10, and interferon gamma  $(INFG)^{35}$  through DNA methylation. <sup>36-38</sup> Clinically, increased methylation of FOXP3 secondary to air pollution exposure has been associated with increased risk of asthma diagnosis at age 7<sup>39</sup> and asthma severity.<sup>36</sup> Thus, beyond previously established relationships between various environmental factors and climate change and respiratory conditions such as rhinitis and asthma, <sup>18,19</sup> the feed-forward cycle of air 1368 PACHECO ET AL

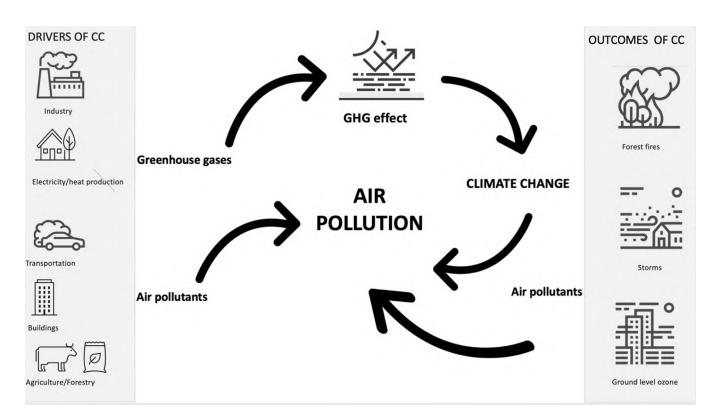


FIG 1. Relationship between the drivers of climate change (CC) and the outcomes of CC and air pollution.

TABLE I. Sources of air pollutants

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

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. Exposure to atmospheric pollutants has been associated with respiratory viral infections, such as influenza, measles, mumps, rhinovirus, and respiratory syncytial virus. Epidemiologic studies have also suggested that exposure to air pollution is associated with the increase in infection by SARS-CoV-2 and mortality associated with COVID-19. Exposure to atmospheric pollutants can predispose vulnerable and immunocompromised populations to development of a more intense inflammatory response and tissue damage by COVID-19. 43

# Increased pollen seasons and allergen exposure

J ALLERGY CLIN IMMUNOL DECEMBER 2021

The increase in global temperature and CO<sub>2</sub> 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.<sup>4</sup> 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. 46-49 Climate change has contributed to the increased production of various aeroallergens and changes in their geographic distribution.<sup>50</sup> Changes to the flowering season due to climate change will extend allergenic seasons,<sup>51</sup> 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 southward in the Southern Hemisphere. These changes in plant habitat may increase the risk of pollen allergy. 52,53 The European Union-funded Health Impacts of Airborne Allergen Information Network (HIALINE) project examined the effects of increasing temperature and CO<sub>2</sub> on pollen distribution, production, and dissemination. The HIA-LINE project found that daily pollen concentrations and daily allergen content, the "pollen potency" of grasses (Phleum pratense 5, which is one of the major allergens), olives (Olea europaea 1), and birches (Betula verrucosa 1) were independent of each other,<sup>54</sup> suggesting that climate change affects these 2 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 (Fig 3). 55.59 For example, particulate

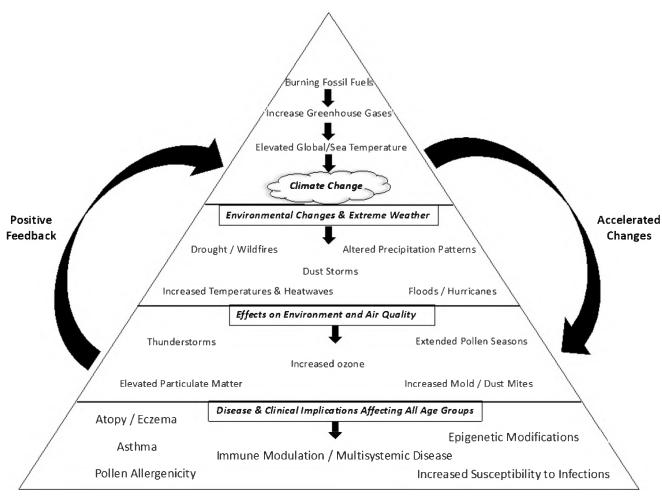


FIG 2. Disease and clinical implications caused by the ripple effect from climate change.

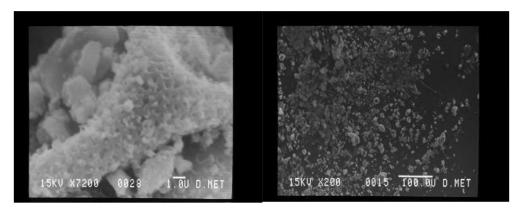


FIG 3. Electron microscopy images of particle matter in pollen exine. Courtesy of Guillermo Guidos-Fogelbach.

matter, diesel exhaust particles,  $O_3$ ,  $N_2O$ , and  $SO_2$  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. 45,57,60 Additionally, air pollutants interact with allergen-

carrying submicronic and paucimicronic particles derived from pollen 46,61 and can reach peripheral airways, inducing asthma in sensitized subjects. Collectively, biologic particulates (such as pollen) and nonbiologic particulates (carbon, silica, metals, ultrafine dust, and others) interact with each other in the atmosphere, with direct effects on the health of the population owing either to their direct irritant effect or to interactions among these

different kinds of particulate matter. The observed interactions among biologic and nonbiologic airborne particulates highlight the need for exposome characterization and modification in asthma and allergy through the use of novel research methods. 33,56

These changes in pollen seasons and allergen exposure have translated to notable health effects. A body of epidemiologic evidence suggests that the prevalence of pollen-related allergic respiratory diseases (eg, rhinitis and asthma) has increased in past decades. <sup>62</sup> High levels of vehicular emissions, urbanization, and Westernized lifestyles correlate with the increased frequency of pollen-induced respiratory allergies in urban areas compared with in rural areas. <sup>48</sup> Furthermore, many allergenic pollen species have been associated with seasonal asthma exacerbations in both children and adults. <sup>63,64</sup> Climate change will also increase the frequency and intensity of floods and cyclones and thus fungal spore production, <sup>52</sup> which is a powerful asthma and rhinitis trigger.

Increased pollen exposure may also influence susceptibility to viral infections. Patients with allergy who are exposed to airborne pollen have been noted to have greater vulnerability to viral infections, <sup>65-67</sup> including SARS-CoV-2. In addition, published evidence supports the idea that pollen exerts immunomodulatory effects that impair the antiviral response and may account for susceptibility to viral infections, including inhibition of the antivirals nuclear factor-κB, myeloid differentiation primary response protein 88 (MyD88), and interferon in the respiratory epithelium in addition to improving the release of IL-1 IL-1β, IL-18, IL-28A, and IL-33 family cytokines from epithelial cells *in vitro*. <sup>67</sup> Thus, it is possible that these changes affect the susceptibility to infections in patients with allergy.

#### **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 heat waves directly and indirectly affect human health.

**Temperature changes and heat waves.** Warming of the planet is not uniform and, in general, is higher over land than over the oceans. Overall, climate trends are moving toward hotter versus cold temperature extremes across the globe. These temperature changes are drivers of a rise in sea level, 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. <sup>68</sup>

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 heatrelated mortality burden during warm seasons, resulting from anthropogenic warming during the 1991-2018 period, was 37.0% (range 20.5%-76.3%). During the 2003 European summer heat wave, in excess of 70,000 people (mostly older) individuals died. Unlerable groups mainly include individuals older than 65 years who have chronic medical conditions such as diabetes and cardiovascular, lung, and kidney disease.

More recently, a heat wave in the Pacific Northwest of North America caused at least 1000 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 those of 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. Tompounded by the increased temperatures due to climate change, these heat islands are expected to amplify the morbidity and mortality of heat waves. According to the 2018 Revision of the United Nations World Urbanization Prospects, 55% of the world's population resided in urban areas in 2018. That number is projected to increase to 68% by 2050.

**Wildfires.** Increased drought conditions seen with climate change promote environments that encourage increased frequency and severity of wildland fires<sup>74</sup> such as the Dixie Fire, which has burned more than 960,000 acres (380,000 hectares) in California since July 2021, or the Siberia fires, which burned more than 40,000,000 acres in 2021—more than all the other worlds fires combined.<sup>75,76</sup> In addition to the civilian deaths associated with these events, wildfires are also associated with significant total damage and economic losses, surpassing \$10 billion in the 2018 California Camp Fire, \$12 billion in the 2020 California fires, and \$110 billion 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 United States, and they can cause abrupt increases in  $PM_{2.5}$ , with peak levels exceeding  $1000~\mu g/m^3.^{77}$  Exposure to wildfire smoke has been associated with asthmarelated emergency room visits,  $^{78,79}$  hospitalizations, and premature deaths.  $^{80}$  Children and those with chronic diseases are especially vulnerable to the effects of wildfire exposures.  $^{81-83}$ 

The health effects of wildfires affect both airway and systemic inflammation. Field studies of wildland firefighters and controlled chamber studies of experimental exposure to wood smoke particles have reported worsened lung function<sup>84</sup> and neutrophilic airway inflammation. 85,86 Epidemiologic studies have shown that wildfire smoke is associated with an increased risk of cardiovascular morbidity, including ischemic events, heart failure, and arrhythmias<sup>87,88</sup> that are thought to be attributable to systemic inflammatory effects of smoke-related PM exposure. 89 The effects of wildfires are not limited to local regions; because of the Jet Stream and cross-continental air currents, smoke from the 2021 Bootleg Blaze in Oregon (in the western United States) reached New York City in July 2021, pushing the Air Quality Index in northeastern US cities to 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. 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 United States), affecting weather conditions, agricultural production, ecosystems, and human health.

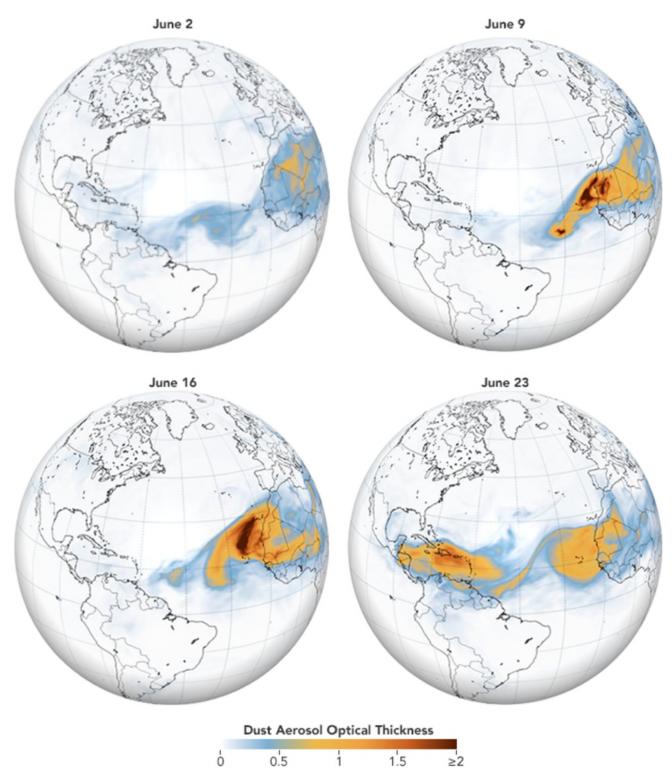


FIG 4. Saharan ("Godzilla") dust cloud across the Atlantic ocean. 93

The Sahara dust is a mixture of particulate matter smaller than 10 micrometers and  $PM_{2.5}$ ,  $^{91}$  composed of clay and silicates, minerals, quartz, silicon dioxide, iron oxides, aluminum, titanium, magnesium, sodium, and evaporated minerals. These dust storms also transport pollen, microbial agents (eg, fungi, viruses, bacteria), and anthropogenic pollutants. Saharan dust

storms can have levels of particulate matter smaller than 10  $\mu m$  and levels of  $PM_{2.5}$  exceeding the allowable thresholds deemed safe for human health  $^{92}$  that have been established by the WHO, the US Environmental Protection Agency, and the European Union. During the Sahara dust storm in June 2020, for example, levels of  $PM_{2.5}$  in Florida, Texas, and Georgia

reached "unhealthy levels" (151-200  $\mu$ g/m<sup>3</sup>) on the Air Quality Index (Fig 4).<sup>93</sup>

Several studies have reported significant associations between exposure to Saharan dust and hospital admissions due to asthma, COPD exacerbations, and cardiovascular and cerebrovascular conditions. <sup>94-96</sup> In addition, Saharan dust storms have been linked with mortality due to respiratory diseases and severe cardiovascular and ischemic events among vulnerable populations. <sup>91,94,96,97</sup> In West Africa, exposure to these dust storms has been associated with increased infant mortality. <sup>98</sup>

Hurricanes and cyclones. One of the consequences of climate change and global warming is the increasing frequency and intensity of floods and cyclones. 48 The increase in moisture and dampness associated with water intrusion during storms and floods affects indoor environments, leading to increased dampness and humidity and supporting the growth of house dust mites and molds. House dust mites (HDMs), which are 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. 99 Consequently, sensitization to HDMs has increased in subtropical and tropical areas. Furthermore, many urban pest species that are sources of allergens, such as cockroaches and rodents, may be affected by climate change that alters the natural environment as a result of flooding or drought and the urban environment as a result of changes in land use. 100 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 development of respiratory illnesses. The link of molds with asthma and rhinitis is well known and has been established through exposure to dampness and moisture in indoor environments as a proxy of microbial agents. <sup>101</sup> In addition, mold metabolites, such as microbial volatile organic compounds, have been involved in nonallergic asthma and chronic bronchitis, although rarely. <sup>102</sup>

Thunderstorms and asthma. Climate change is also associated with the increase in frequency and intensity of thunderstorms, <sup>103</sup> which can result in thunderstorm asthma, <sup>104-107</sup> an observed increase in acute bronchospasm cases following thunderstorms in the local vicinity. Thunderstorms occurring during the pollen season have induced severe asthma attacks and deaths in patients with pollen allergy. <sup>104,105</sup> Events from Europe, North America, the Middle East, and Australia have been reported. A thunderstorm in the pollen season increases the concentration of pollen grains and hydration and rupture of pollens by osmotic shock, with release of allergen-carrying paucimicronic particles of respirable size (such as starch granules and other cytoplasmic components) into the atmosphere.<sup>52</sup> The main allergen culprits are thought to be pollen grains, especially grasses and weeds and mold spores, particularly Alternaria and Cladosporium. 108 Besides the associated inflammatory and adjuvant effect in the allergic response, diesel exhaust particles can transport adsorbed aeroallergen molecules released from pollen grains deeper into the airways and increase retention of these antigenic molecules. 109,110

### **VULNERABLE POPULATIONS**

The vulnerability of individuals to climate change, driven by the degree and type of exposure, their sensitivity, and their adaptive capacity, is greatly affected by the social determinants of health (Fig 5<sup>111</sup>). 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 later), people with disabilities, and those with chronic medical conditions (including immunodeficiency) are at the highest risk. 112-114 Considering the fact that impoverished populations have a higher probability of chronic diseases, exposure to environmental pollution can affect individuals with underlying asthma, COPD, and pulmonary fibrosis 115 differentially, putting them at greater risk of hospitalization 116,117 and mortality, as demonstrated recently in European cities. 118

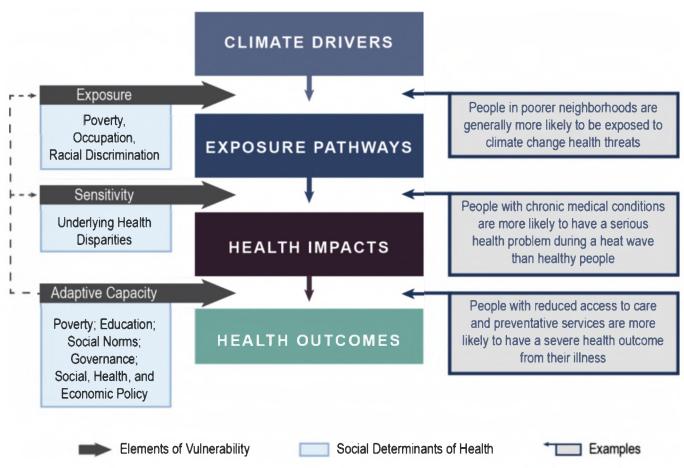
# **Elderly individuals**

Many variables make older adults more vulnerable to the environmental effects of climate change. This is a serious threat to consider in a world in which the aging population will continue to increase. It is expected that by 2050, 1 in 5 people in the world will be aged 60 years or older, with 80% of them living in developing countries and many already affected by climate change or with limited resources for adaptation. Their physiology, chronic medical conditions, psychological and socioeconomic status, living arrangements, access to care, and limited mobility and transportation increase their vulnerability to heat waves, air pollution, extreme weather events, and infections. Owing to their extent, exposure to heat and air pollution can be very impactful. Exposure to air pollution, in particular,  $PM_{2.5}$  and  $O_3$ , exacerbate underlying medical conditions, including asthma, <sup>120</sup> and increase the mortality of elderly individuals. For example, exposure to PM<sub>2.5</sub> 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. 121 Other conditions affected by PM<sub>2.5</sub> in older adults include respiratory conditions such as asthma and COPD, chronic kidney disease, diabetes, and dementia (including Alzheimer disease).

Heat-induced illness is among the major vulnerabilities for elderly individuals. Variables such as age-related physiologic 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 capacity to adapt to changes in temperature. In the United States, 40% of all heat-related deaths from 2004 to 2018 were in individuals age 65 years or older. During the 2003 European heat wave, 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 older in 2020, a number that is expected to increase to 1.5 billion in 2050. 122

# Pregnant women

The harmful effects of climate change begin before gestation or during the prenatal period. Exposure to air pollution compromises placental development and affects fetal programming, predisposing the fetus to congenital malformations, immunologic system alterations, allergic diseases, asthma, and respiratory



**FIG 5.** Intersection of social determinants of health and vulnerability. Used with permission from the US Global Change Research Program (Gamble JL, Balbus J, Berger M, Bouye K, Campbell V, Chief K, et al, 2016: Ch. 9: Populations of Concern. The Impacts of Climate Change on Human Health in the United States: A Scientific Assessment. US Global Change Research Program, Washington, DC, 247-286). 111

conditions.  $^{123,124}$  These effects can extend from infancy to adulthood and can have transgenerational effects, which is a plausible explanation for the development of chronic airway dysfunction, even in the absence of atopic predisposition.  $^{125,126}$  For example, exposure to traffic-related air pollution,  $PM_{2.5}$ , and  $O_3$  during the prenatal period has been associated with adverse birth outcomes such as prematurity and low birth weight,  $^{127-129}$  increased risk of wheezing in toddlers,  $^{130}$  reduced  $FEV_1$  in children,  $^{131}$  and asthma diagnosis at age 6 years.  $^{132}$  Other climate-related changes such as increased ambient temperature during pregnancy can lead to congenital heart disease (a problem that is projected to increase as temperatures increase)  $^{133}$  and an increase in preterm births.  $^{127}$ 

Stressful experiences during pregnancy can affect 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. <sup>134–136</sup>

# Children

Children are a particularly high-risk group on account of their developing organ systems, their higher level of exposure owing to their physiology, the nature of their daily activities, their

psychological immaturity, and their dependence on adults. 131 For these reasons, continued exposure to air pollution, extreme weather events (storms, floods, droughts, and heat waves), 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 by 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 this review article, we have highlighted a few examples of how climate change affects pediatric health. <sup>61,76-79,124,125,129</sup> Beyond respiratory health, exposure to air pollution has been associated with hematologic malignancies, <sup>132</sup> increased airway infections and mortality, <sup>133</sup> metabolic abnormalities observed in type 2 diabetes, <sup>134</sup> and hypertension. <sup>135</sup> Among the most alarming effects of air pollution in children growing in very polluted cities are the neuroinflammatory changes and brain histologic changes similar to those found in Parkinson disease and Alzheimer disease. 136,137 Placed in context, more than 90% of children in the world breathe polluted air. The WHO estimated that in 2016, about 600,000 children died of acute lower respiratory infections resulting from ambient and household air pollution. 133 In addition, from 1990 to 2000, climate change–related extreme weather events directly affected about 66.5 million children, with a mortality of about 600,000 every year. 138 Increasing

1374 PACHECO ET AL

J ALLERGY CLIN IMMUNOL

DECEMBER 2021

exposure will continue to affect the emotional well-being and mental health of children. <sup>137</sup>

### **CLIMATE CHANGE MITIGATION STRATEGIES**

Implementing mitigation strategies to reduce GHG emissions is critical to prevent further warming of the planet and protect public health. Although these necessary measures will take time to affect the Earth's temperature, a decrease in the use of fossil fuels has faster co-benefits for human health. Reduced reliance on fossil fuels can dramatically affect air quality and the prevention of stroke, pulmonary and cardiovascular diseases. 138 In the case of PM<sub>2.5</sub>, more than 50,000 deaths per year could be prevented in European cities by complying with the WHO air pollution guidelines for PM<sub>2.5</sub>. <sup>118</sup> On a larger scale, the WHO estimates that more than 80% of deaths related to PM<sub>2.5</sub> could be prevented by following the most recently updated guidelines for PM<sub>2.5</sub>. <sup>139</sup> Engagement in active travel activities (eg, biking and walking) can help reduce cardiovascular disease, dementia, malignancies, mental illness, and obesity (Lancet Commission 2015). The improved indoor air quality resulting from use of clean energy and energy efficiency can decrease respiratory conditions, infections, and malignancy. 140

### CONCLUSION

Humanity is living unprecedented times. The Earth's temperature has increased by 1.0°C compared with preindustrial levels. The Intergovernmental Panel for Climate Change has stated that to avert some of the more severe and potentially irreversible impacts of climate change, warming should not rise by more than 1.5°C.8 Despite this, CO<sub>2</sub> emissions have continued to increase —up to almost 419 ppm in June 2021, which was the fifth warmest June on record. An increase in global temperature by more than 1.5° C translates to increased damage to vulnerable populations, increased morbidity. and mortality due to heat waves and O<sub>3</sub> exposure, increases in some vector-borne diseases, and decreased food availability. As reviewed in this article, the 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 development or exacerbation of atopic disorders, respiratory health, and susceptibility to infection.

Although all humans are affected by climate change, the impact of the climate crisis affects different people in different ways. People of color, minorities, residents of developing countries, those living in island nations, indigenous people, and poor communities are examples of groups that have and will suffer the most. According to the WHO, more than 60,000 people die of natural disasters per year, mostly in developing countries. Outdoor air pollution causes 4.2 million deaths per year—most of them in low- and middle-income countries. In addition, developing countries and indigenous communities will be disproportionately affected 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 infrastructure, and poverty. 141,142 These sequelae of climate change have promoted increasing numbers of climate refugees, primarily from Africa, Asia, and Latin America. 143 Although a proactive approach, planned relocation or managed retreat of small islands and coastal communities in response 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. <sup>144</sup> The United Nations High Commissioner for Refugees reported that 21.5 million people had been displaced by climate change–related disasters since 2010. <sup>145</sup> The Institute for Economics and Peace estimates that the number of people at risk of relocation secondary to climate change could reach at least 1.2 billion by 2050. <sup>146</sup> Ironically, many of these groups have barely contributed to the emissions responsible for climate change but will be affected the most owing to their limited resources and adaptability. Between 1990 and 2015, more than half (52%) of the emissions released into the atmosphere were produced by the wealthiest 10% of people. <sup>147</sup>

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, <sup>148</sup> increasing the social divide, often along ethnic lines. For example, in the United States, communities with more Black and Hispanic individuals live in places with higher temperatures, <sup>19,149</sup> breathe more polluted air, and receive less support during government-led recovery efforts after natural disasters, <sup>150-153</sup> such as during Hurricane Harvey in Texas and Hurricane Maria in Puerto Rico. 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. <sup>154</sup>

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 2 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 those of us who are reading the *Journal of Allergy and Clinical Immunology* to step up, educate, create awareness, and advocate for the future of our patients and every person in the world. As health care providers, we have a unique opportunity to make a difference, as most people are not aware of the link between climate change and health. <sup>10</sup> 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. <sup>132</sup> Lifestyle changes, including changes in our diets and 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 affect every individual in the world and all future generations. We have the responsibility to advocate for our patients and the general public, and to educate our governments to decrease the impact of climate change on public health.

## REFERENCES

 Overview: weather, global warming and climate change. National Aeronautics and Space Administration Global Climate Change; 2021. Available at: https:// climate.nasa.gov/resources/global-warming-vs-climate-change/. Accessed June 21, 2021.

- United Nations Framework Convention on Climate Change. 1992. Available at: https://unfccc.int/files/essential\_background/background\_publications\_htmlpdf/application/pdf/conveng.pdf. Accessed June 6, 2021.
- Greenhouse gases. National Oceanic and Atmospheric Administration. Available at: https://www.ncdc.noaa.gov/monitoring-references/faq/greenhouse-gases.php. Accessed July 7, 2021.
- More near-record warm years are likely on horizon. National Oceanic and Atmospheric Administration National Centers for Environmental Information; 2021. Available at: https://www.ncei.noaa.gov/news/projected-ranks. Accessed July 7, 2021.
- 2020 tied for warmest year on record, NASA analysis shows. National Aeronautics and Space Administration; 2021. Available at: https://climate.nasa.gov/news/3061/2020-tied-for-warmest-year-on-record-nasa-analysis-shows/. Accessed July 7, 2021.
- Special report: global warming of 1.5 °C. Intergovernmental Panel on Climate Change; 2018. Available at: https://www.ipcc.ch/sr15/. Accessed June 6, 2021.
- Mental health and our changing climate: impacts, implications, and guidance. PsycEXTRA Dataset: American Psychological Association; 2017. Available at: https://www.apa.org/news/press/releases/2017/03/mental-health-climate.pdf. Accessed July 2, 2021.
- Ahdoot S, Pacheco SE. Global climate change and children's health. Pediatrics 2015;136:e1468-84.
- 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. In: U.S. Global Change Research Program; 2018; Available at: https://nca2018.globalchange. gov/chapter/14/. Accessed June 15, 2021.
- 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;397:129-70.
- Romanello M, McGushin A, Di Napoli C, Drummond P, Hughes N, Jamart L, et al. The 2021 report of the Lancet Countdown on health and climate change: code red for a healthy future. Lancet 2021; https://doi.org/10.1016/S0140-6736(21)01787-6.
- IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Outdoor Air pollution. Volume 109. Lyon, France: WHO: International Agency for Research on Cancer; 2016.
- 13. US Environmental Protection Agency. Greenhouse gases. What are the trends in greenhouse gas emissions and concentrations and their impacts on human health and the environment? Available at: https://www.epa.gov/report-environment/greenhouse-gases. Accessed June 28, 2021.
- US Environmental Protection Agency. Global Greenhouse Emissions Data. Available at: https://www.epa.gov/ghgemissions/global-greenhouse-gas-emissions-data. Accessed June 28, 2021.
- 15. IPCC, 2014: Climate Change 2014: Mitigation of Climate Change. Contribution of Working Group III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. In: Edenhofer O, R. Pichs-Madruga, Sokona Y, Farahani E, Kadner S, Seyboth K, editors. Cambridge University Press; 2015.
- Kinney PL. Interactions of climate change, air pollution, and human health. Curr Environ Health Rep 2018;5:179-86.
- Landrigan PJ, Fuller R, Acosta NJR, Adeyi O, Arnold R, Basu NN, et al. The Lancet Commission on Pollution and Health. Lancet 2018;391:462-512.
- World Health Organization. Air pollution. 2021. Available at: https://www.who.int/health-topics/air-pollution#tab=tab\_1. Accessed June 28, 2021.
- American Lung Association. State of the Air. 2021. Available at: https://www.lung.org/research/sota. Accessed July 15, 2021.
- 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;389:1907-18.
- Burbank AJ, Sood AK, Kesic MJ, Peden DB, Hernandez ML. Environmental determinants of allergy and asthma in early life. J Allergy Clin Immunol 2017;140:1-12.
- 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.
- 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;138:1703-6.e1.
- 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;16:751-9.
- Yang SI. Particulate matter and childhood allergic diseases. Korean J Pediatr 2019;62:22-9.
- 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: e0138146.

- 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;200:24-32.
- 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;136:295-303.e7.
- 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;114:126-33.
- 30. 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;123:902-8.
- Ahn K. The role of air pollutants in atopic dermatitis. J Allergy Clin Immunol 2014;134:993-9, [discussion 1000].
- 32. Nguyen GH, Andersen LK, Davis MDP. Climate change and atopic dermatitis: is there a link? Int J Dermatol 2019;58:279-82.
- Stefanovic N, Irvine AD, Flohr C. The role of the environment and exposome in atopic dermatitis. Curr Treat Options Allergy 2021;1-20.
- Paller AS, Spergel JM, Mina-Osorio P, Irvine AD. The atopic march and atopic multimorbidity: many trajectories, many pathways. J Allergy Clin Immunol 2019;143:46-55.
- 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;11:4067.
- 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;126:845-52.e10.
- Ho SM. Environmental epigenetics of asthma: an update. J Allergy Clin Immunol 2010;126:453-65.
- Gruzieva 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;125:104-10.
- 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;131:592-4.e1-3.
- Domingo JL, Rovira J. Effects of air pollutants on the transmission and severity of respiratory viral infections. Environ Res 2020;187:109650.
- Urrutia-Pereira M, Mello-da-Silva CA, Sole D. COVID-19 and air pollution: a dangerous association? Allergol Immunopathol (Madr) 2020;48:496-9.
- Kim H, Bell ML. Air pollution and COVID-19 mortality in New York City. Am J Respir Crit Care Med 2021;204:97-9.
- 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;1486:15-38
- Schiavoni G, D'Amato G, Afferni C. The dangerous liaison between pollens and pollution in respiratory allergy. Ann Allergy Asthma Immunol 2017;118.
- 45. 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).
- 46. 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;8:12.
- 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;20:2099-121.
- Takaro TK, Knowlton K, Balmes JR. Climate change and respiratory health: current evidence and knowledge gaps. Expert Rev Respir Med 2013;7:349-61.
- 49. 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. Lancet Planetary Health 2019;3:e124-31.
- 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:e0205677.
- 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;11:12816.
- 52. 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;8:25.
- D'Amato M, Cecchi L, Annesi-Maesano I, D'Amato G. News on climate change, air pollution, and allergic triggers of asthma. J Investig Allergol Clin Immunol 2018;28:91-7.
- 54. 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: 87-95 e6
- 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).
- Cecchi L, D'Amato G, Annesi-Maesano I. External exposome and allergic respiratory and skin diseases. J Allergy Clin Immunol 2018;141:846-57.
- 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.
- 58. 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;143:1702-10.
- Schmidt CW. Pollen overload: seasonal allergies in a changing climate. Environ Health Perspect 2016;124:A70-5.
- 60. 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;70:341-78.
- Filippidou EC, Koukouliata AJ. Ozone effects on the respiratory system. Prog Health Sci 2011;1:144-55.
- 62. Custovic A. To what extent is allergen exposure a risk factor for the development of allergic disease? Clin Exp Allergy 2015;45:54-62.
- 63. 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.
- 64. 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;19:254-9.
- 65. 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;13:100109.
- 66. 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).
- Gilles S, Blume C, Wimmer M, Damialis A, Meulenbroek L, Gokkaya M, et al. Pollen exposure weakens innate defense against respiratory viruses. Allergy 2020:75:576-87.
- 68. Knutson TR, Chung MV, Vecchi G, Sun J, Hsieh T-L, Smith A. Climate change is probably increasing the intensity of tropical cyclones. In: Critical Issues in Climate Change Science. ScienceBrief Review; 2021.
- 69. Vicedo-Cabrera A, Scovronick N, Sera F, Royé D, Schneider R, Tobias A, et al. The burden of heat-related mortality attributable to recent human-induced climate change. Nature Climate Change 2021;182.
- Robine J-M, Cheung K, Roy S, Oyen H, Griffiths C, Michel j-p, et al. Death toll
  exceeded 70,000 in Europe during the summer of 2003. Comptes rendus biologies
  2008;331:171-8.
- Lancet countdown on health and climate change: exposure of vulnerable populations to heatwaves.
   Health and Heat 2020. Available at: https://www.lancetcountdown.org/data-platform/climate-change-impacts-exposures-and-vulne rability/1-1-health-and-heat/1-1-3-exposure-of-vulnerable-populations-to-heatwaves. Accessed July 5, 2021.
- Manoli G, Fatichi S, Schläpfer M, Yu K, Crowther TW, Meili N, et al. Magnitude of urban heat islands largely explained by climate and population. Nature 2019;573:55-60.
- Potestio M. Estimate on number of suspected heat-related deaths rises to 808. The Toronto Star; 2021. Available at: https://www.thestar.com/news/canada/2021/07/ 21/estimate-on-number-of-suspected-heat-related-deaths-rises-to-808.html. Accessed November 9, 2021...
- Hurteau MD, Westerling AL, Wiedinmyer C, Bryant BP. Projected effects of climate and development on California wildfire emissions through 2100. Environ Sci Technol 2014;48:2298-304.
- Siberia's wildfires are bigger than all the world's other blazes combined. Washington Post; 2021. Available at: https://www.washingtonpost.com/world/2021/08/11/siberia-fires-russia-climate/. Accessed November 9, 2021.
- Group NWC. Dixie Fire. Available at: https://inciweb.nwcg.gov/incident/article/ 7690/67256/. Accessed October 8, 2021.
- National Emissions Inventory (NEI) data 2011. US Environmental Protection Agency. Available at: https://www.epa.gov/air-emissions-inventories/2011-national-emissions-inventory-nei-data. Accessed October 8, 2021.
- Aguilera R, Corringham T, Gershunov A, Leibel S, Benmarhnia T. Fine particles in wildfire smoke and pediatric respiratory health in California. Pediatrics 2021;147(4).
- Rice MB, Henderson SB, Lambert AA, Cromar KR, Hall JA, Cascio WE, et al. Respiratory impacts of wildland fire smoke: future challenges and policy opportunities. An official American Thoracic Society workshop report. Ann Am Thorac Soc 2021;18:921-30.

- Reid CE, Brauer M, Johnston FH, Jerrett M, Balmes JR, Elliott CT. Critical review of health impacts of wildfire smoke exposure. Environ Health Perspect 2016;124:1334-43.
- 81. Kodgule R, Salvi S. Exposure to biomass smoke as a cause for airway disease in women and children. Curr Opin Allergy Clin Immunol 2012;12:82-90.
- Po JY, FitzGerald JM, Carlsten C. Respiratory disease associated with solid biomass fuel exposure in rural women and children: systematic review and meta-analysis. Thorax 2011;66:232-9.
- Schei MA, Hessen JO, Smith KR, Bruce N, McCracken J, Lopez V. Childhood asthma and indoor woodsmoke from cooking in Guatemala. J Expo Anal Environ Epidemiol 2004;14(Suppl 1):S110-7.
- Liu D, Tager IB, Balmes JR, Harrison RJ. The effect of smoke inhalation on lung function and airway responsiveness in wildland fire fighters. Am Rev Respir Dis 1992;146:1469-73.
- 85. 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;143:2299-2302.e.
- 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;69:170-5.
- 87. 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 fire-fighters and the public. Inhal Toxicol 2016;28:95-139.
- Nelin TD, Joseph AM, Gorr MW, Wold LE. Direct and indirect effects of particulate matter on the cardiovascular system. Toxicol Lett 2012;208:293-9.
- 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.
- Sakhamuri S, Cummings S. Increasing trans-Atlantic intrusion of Sahara dust: a cause of concern? The Lancet Planetary Health 2019;3:e242-3.
- 91. 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;4:423-34.
- Monteil MA. Saharan dust clouds and human health in the English-speaking Caribbean: what we know and don't know. Environ Geochem Health 2008;30:339-43.
- Administration NASA. A dust plume to remember. Available at: https://earthobservatory.nasa.gov/images/146913/a-dust-plume-to-remember. Accessed July 24, 2021.
- 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.
- 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).
- Kotsyfakis M, Zarogiannis SG, Patelarou E. The health impact of Saharan dust exposure. Int J Occup Med Environ Health 2019;32:749-60.
- Zhang X, Zhao L, Tong DQ, Wu G, Dan M, Teng B. A systematic review of global desert dust and associated human health effects. Atmosphere 2016;7:158.
- Heft-Neal S, Burney J, Bendavid E, et al. Dust pollution from the Sahara and African infant mortality. Nat Sustain 2020;3:863-71.
- Acevedo N, Zakzuk J, Caraballo L. House dust mite allergy under changing environments. Allergy Asthma Immunol Res 2019;11:450-69.
- 100. IPCC. 2019. Climate Change and Land: an IPCC special report on climate change, desertification, land degradation, sustainable land management, food security, and greenhouse gas fluxes in terrestrial ecosystems. Available at: https:// www.ipcc.ch/srccl/. Accessed August 1, 2021.
- 101. 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;17:284-96.
- 102. 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;216:155-62.
- 103. Maupin CR, Roark EB, Thirumalai K, et al. Abrupt Southern Great Plains thunderstorm shifts linked to glacial climate variability. Nat Geosci 2021;14:396-401.
- 104. 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;8:391-5.
- 105. Davies JM. Pollen allergies. Encyclopedia of environmental health. 2nd ed. In: Nriagu J, editor. Encyclopedia of environmental health. 2nd ed. Amsterdam, The Netherlands: Elsevier; 2019, pp. 300-22.
- 106. World Health Organization Regional Office for Europe. Review of evidence on health aspects of air pollution – REVIHAAP Project: technical report. Copenhagen, Denmark: World Health Organization; 2013.

- 107. Thien F. Melbourne epidemic thunderstorm asthma event 2016: lessons learnt from the perfect storm. Respirology 2018;23:976-977.
- D'Amato G, Annesi Maesano I, Molino A, Vitale C, D'Amato M. Thunderstormrelated asthma attacks. J Allergy Clin Immunol 2017;139:1786-7.
- 109. D'Amato G. Effects of climatic changes and urban air pollution on the rising trends of respiratory allergy and asthma. Multidisciplinary Respiratory Medicine 2011;6:28.
- 110. 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;27:246-51.
- Populations of concern. GlobalChange.gov. Available at: https://health2016. globalchange.gov/populations-concern. Accessed July 7, 2021.
- 112. 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;12:15419-33.
- 113. 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;16:1478-87.
- 114. USGCRP, 2018: Impacts, Risks, and Adaptation in the United States: Fourth National Climate Assessment, Volume II. Available at: https://nca2018. globalchange.gov/. Accessed July 5, 2021.
- 115. 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).
- 116. 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.
- 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.
- 118. 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:e121-34.
- HelpAge International. Climate change in an ageing world. HelpAge position paper. 2015. Available at: https://reliefweb.int/sites/reliefweb.int/files/resources/ COP21\_HelpAge\_PositionPaper\_Final\_0.pdf. Accessed October 2, 2021.
- 120. 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;57:28-39.
- 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.
- United Nations Department of Economic and Social Affairs Population Division.
   World population ageing 2020 highlights: living arrangements of older persons.
   2020. (ST/ESA/SER.A/451). Accessed: October 1, 2021.
- 123. Korten I, Ramsey K, Latzin P. Air pollution during pregnancy and lung development in the child. Paediatr Respir Rev 2017;21:38-46.
- 124. World Health Organization. Air pollution and child health: prescribing clean air. Available at: https://www.who.int/publications/i/item/air-pollution-and-child-health. Accessed July 14, 2021.
- 125. 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).
- 126. Wooldridge G, Murthy S. Pediatric critical care and the climate emergency: our responsibilities and a call for change. Front Pediatr 2020;8:472.
- 127. 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:e208243.
- 128. 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.
- 129. 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;28:3296-306.
- 130. 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;133:713-22.e4.
- 131. 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;70:64-73.
- 132. 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: 1052-9.

- 133. 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: e010995.
- 134. 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.
- 135. 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;70:141-5.
- 136. Mallett LH, Etzel RA. Flooding: what is the impact on pregnancy and child health? Disasters 2018;42:432-58.
- Burke S, Sanson A, Hoorn J. The psychological effects of climate change on children. Curr Psychiatry Rep 2018;20.
- World Health Organization. Ambient (outdoor) air pollution. Available at: https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health. Accessed July 6, 2021.
- 139. World Health Organization. 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. Accessed October 5, 2021.
- 140. Data OWi. Energy poverty and indoor air pollution: a problem as old as humanity that we can end within our lifetime. Available at: https://ourworldindata.org/ energy-poverty-air-pollution. Accessed October 5, 2021.
- 141. 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:e20191375.
- 142. 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;39:2153-9.
- 143. Balsari S, Dresser C, Leaning J. Climate change, migration, and civil strife. Curr Environ Health Rep 2020;7:404-14.
- 144. 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.
- 145. Agency UR. Data reveals impacts of climate emergency on displacement. Available at: https://www.unhcr.org/en-us/news/stories/2021/4/60806d124/data-reveals-impacts-climate-emergency-displacement.html. Accessed October 6, 2021.
- 146. Institute for Economics and Peace. Over one billion people at threat of being displaced by 2050 due to environmental change, conflict and civil unrest. Available at: <a href="https://www.prnewswire.com/news-releases/iep-over-one-billion-people-at-threat-of-being-displaced-by-2050-due-to-environmental-change-conflict-and-civil-unrest-301125350.html. Accessed October 8, 2021.</a>
- 147. OXFAM International. Carbon emissions of richest 1 percent more than double the emissions of the poorest half of humanity. Available at: https://www. oxfam.org/en/press-releases/carbon-emissions-richest-1-percent-more-doubleemissions-poorest-half-humanity. Accessed October 8, 2021.
- 148. The Lancet Planetary Health. Strands of injustice. Lancet Planet Health 2020;4: e256.
- 149. Union of Concerned Scientists. Killer heat in the United States: climate choices and the future of dangerously hot days. 2019. Available at: https://www.ucsusa.org/sites/default/files/attach/2019/07/killer-heat-analysis-full-report.pdf. Accessed November 9, 2021.
- 150. 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.
- 151. 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:e001191.
- 152. Ramirez F. Harvey aid shortchanges Texas cities with minorities, study finds. Houston Chronicle; 2018. Available at: https://www.chron.com/news/houston-texas/texas/article/Harvey-recovery-funding-short-changed-minorities-13281543. php. Accessed July 17, 2021.
- 153. Vinik D. 'People just give up': low-income hurricane victims slam federal relief programs. Politico 2018Available at: https://www.politico.com/story/2018/05/29/ houston-hurricane-harvey-fema-597912. Accessed July 17, 2021.
- 154. Kingsley SL, Eliot MN, Carlson L, Finn J, MacIntosh DL, Suh HH, et al. Proximity of US schools to major roadways: a nationwide assessment. J Expo Sci Environ Epidemiol 2014;24:253-9.