The impact of environmental injustice and social determinants of health on the role of air pollution in asthma and allergic disease in the United States

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Activity Objectives:

1. To understand the ways in which exposures to environmental air pollution are associated with asthma, atopic dermatitis, and allergies.
2. To understand how social determinants of health (SDOH) modify the effects of environmental exposures on atopic diseases resulting in continued racial disparities.
3. To recognize the association between racial residential segregation and increased pollutant exposures.

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There is clear evidence that exposure to environmental air pollution is associated with immune dysregulation, asthma, and other allergic diseases. However, the burden of air pollution exposure is not equally distributed across the United States. Many social and environmental factors place communities of color and people who are in poverty at increased risk of exposure to pollution and morbidity from asthma and allergies. Here, we review the evidence that supports the relationship between air pollution and asthma, while considering the social determinants of health that contribute to disparities in exposures and outcomes. (J Allergy Clin Immunol 2021;148:1089-101.)

Key words: *Atopy, systemic racism, health equity, air quality, health disparities*

It has become increasingly apparent that structural and social factors, rather than biological or genetic factors alone, contribute both to increases in exposure to air pollution and to disparities in allergic diseases including asthma.[1-4] The recently popularized term social determinants of health (SDOH) refers to social and environmental conditions that affect health and quality of life. The United States Healthy People 2030 commission defines SDOH in 5 broad domains (Box 1 and Fig 1): (1) neighborhood and built environment, (2) social and community context, (3)

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Abbreviations used
CO: Carbon monoxide
DEP: Diesel exhaust particle
ED: Emergency department
NO_x: Nitrogen oxides
NO_2: Nitrogen dioxide
OR: Odds ratio
O_3: Ozone
PM: Particulate matter
$PM_{2.5}$: PM <2.5 microns in diameter
PM_{10}: PM <10 microns in diameter
RR: Risk ratio
SDOH: Social determinants of health
SES: Socioeconomic status

economic stability, (4) education access and quality, and (5) health care access and quality.[5] In this review, we will use this framework to discuss relationships between social and environmental conditions that contribute to increased exposure to air pollution as well as increased risk for asthma and other allergic diseases, resulting in health disparities within the United States.

National air pollution levels in the United States have declined in recent decades, yet according to the Environmental Protection Agency, millions of people nationwide presently live in areas with pollutant concentrations above air quality standards, with marked disparities in air pollution exposure among people of color (ie, non-White individuals, Box 1).[2,6-8] Although the term environmental air pollution encompasses all solid particles or gases that are emitted into the air, including pollen and mold spores, we will focus our discussion on examples of specific gases and particles from anthropogenic sources (eg, industrial, domestic, transportation, and agricultural) that have been associated with the development and symptoms of asthma and allergic diseases. For example, ambient pollutants such as carbon monoxide (CO), sulfur dioxide (SO_2), and particulate matter (PM) are mostly derived through industrial combustion, coal and fossil fuel burning, and vehicle emissions. Secondary pollutants, such as ozone (O_3), are formed in the atmosphere as a product of nitrogen oxides (NO_x), volatile organic compounds, heat, and sunlight.[8] Because many pollutants are sourced from vehicle emissions including diesel exhaust particles (DEPs) and gases, concentrations are generally higher in areas with greater traffic volume and in closer proximity to roadways.

In this review, we will discuss the complex relationships between exposure to environmental air pollutants that are risk factors for asthma and allergic diseases (Fig 1). At the forefront of our discussion will be the SDOH that place communities of color and those in poverty at increased risk of both exposure to pollutants and outcomes of asthma and allergic disease. Our review of the literature on relationships between air pollution, immune response, and asthma and allergic diseases is meant to serve only as an introduction to allow us to discuss the interplay with SDOH, and is not a comprehensive review as has been conducted elsewhere.[9-12]

ENVIRONMENTAL RACISM, SDOH, AND AIR POLLUTION

The term "environmental racism" refers to the policies and practices that differentially disadvantage individuals, groups, or communities on the basis of their race[13,14] (Box 1). From the time that European colonizers settled into what is now known as the United States, and throughout the history of the country, housing, social, and economic inequalities have been systemically perpetuated throughout the nation, creating inequity. In the United States, where a person lives can determine the quality of air they breathe, the types of homes they live in, and their risk of development and morbidity from asthma and other allergic diseases. We now use the term "social determinants of health" to describe the many social and environmental factors that are rooted in systemic racism and place populations at increased risk for diseases including asthma and atopy.

Historical practices such as the 1930s Home Owners' Loan Corporation practice of redlining[15] have led to increased segregation and lack of financial investment in communities of color. These practices barred Black and Brown families from obtaining home mortgages, thus eliminating opportunities for generational wealth. Segregation by race and poverty in the United States was further exacerbated in the 1960s by "white flight" when many White families fled urban communities for the suburbs. Policies such as urban renewal, meant to improve the quality of impoverished housing in blighted communities, further displaced low-income families due to their inability to afford the new middle-income homes.[16] Thus, in the United States, gentrification has forced more families, predominantly families of color, into poverty, where they are at greater risk for exposure to environmental pollutants and occupational hazards, though the latter is beyond the scope of this review. The aforementioned institutionalized systems of inequity have led to concentrations of poverty that are often geographically colocated in communities of color. As highlighted by Tessum et al,[2] air pollution is often greatest in communities with larger proportions of minority individuals. Using air quality models of PM less than 2.5 microns in diameter ($PM_{2.5}$) that results from anthropogenic sources, the authors observed that about 75% of all $PM_{2.5}$ exposure in the United States disproportionately affects racial and ethnic minorities across all states, urban and rural areas, income levels, and exposure levels. Pollutant sources from industry, light-duty gasoline vehicles, construction, and heavy-duty diesel vehicles all had the highest disparity in exposure between non-White (eg, Black, Hispanic, and Asian) and White individuals.[2]

At the state level, in North Carolina, Gray et al[7] observed that neighborhoods with higher predicted annual average concentrations of $PM_{2.5}$ also had greater percentages of individuals who identified as Black or Hispanic, higher poverty, lower education, and greater neighborhood deprivation. Furthermore, Jones et al[17] noted that for adults who lived in census tracts within 6 US cities with more than 60% of the population identifying as Hispanic, $PM_{2.5}$ and NO_x concentrations were 8% and 31% higher, respectively, compared with those in tracts with less than 25% Hispanic residents.[17] A 2019 US study found that racial segregation within a community leads to greater disparities in exposure to air pollution than individual-level race or ethnicity alone.[18] Although Black and Hispanic individuals had greater exposure to PM less than 10 microns in diameter (PM_{10}), $PM_{2.5}$, and nitrogen dioxide (NO_2) than Whites, differences were more pronounced in segregated neighborhoods, measured by dissimilarity in the geographic distribution of Black, Hispanic, and Asian individuals, respectively, as compared with Whites.[18]

Box 1. Definitions of key terms

Term	Definition
Persons/communities of color	A person or community of people who are considered or identify as non-White. In the United States, this includes people who identify as Black, Hispanic/Latinx, Native American, Pacific Islander, Asian, or any other racial or ethnic group that has been historically marginalized
Environmental racism	Environmental policies and practices that differentially disadvantage individuals, groups, or communities on the basis of their race
SDOH*	Conditions in the places where people live, learn, work, and play that affect a wide range of health and quality-of-life risks and outcomes. The 5 broad categories of SDOH as outlined by Healthy People 2030 are described below
Neighborhood and built environment	The connection between where a person lives (eg, housing, neighborhood, and environment) and their health and well-being. Examples include quality of housing, access to transportation, availability of healthy foods, air and water quality, and neighborhood crime and violence
Social and community context	The connection between characteristics of the contexts within which people live, learn, work, and play and their health and well-being. Examples include cohesion within a community, civic participation, racism, discrimination, conditions in the workplace, and incarceration
Economic stability	The connection between the financial resources people have (eg, income, cost of living, and SES) and their health. Examples include poverty, food security, and housing stability
Education access and quality	The connection of education to health and well-being. Examples include graduating from high school, enrollment in higher education, educational attainment in general, language and literacy, and early childhood education and development
Health care access and quality	The connection between people's access to and understanding of health services and their own health (or the health of their children). Examples include access to health care, access to primary care, health insurance coverage, and health literacy

*Definitions for SDOH taken from the Centers for Diseases Control and Prevention and can be found at https://www.cdc.gov/socialdeterminants/about.html.

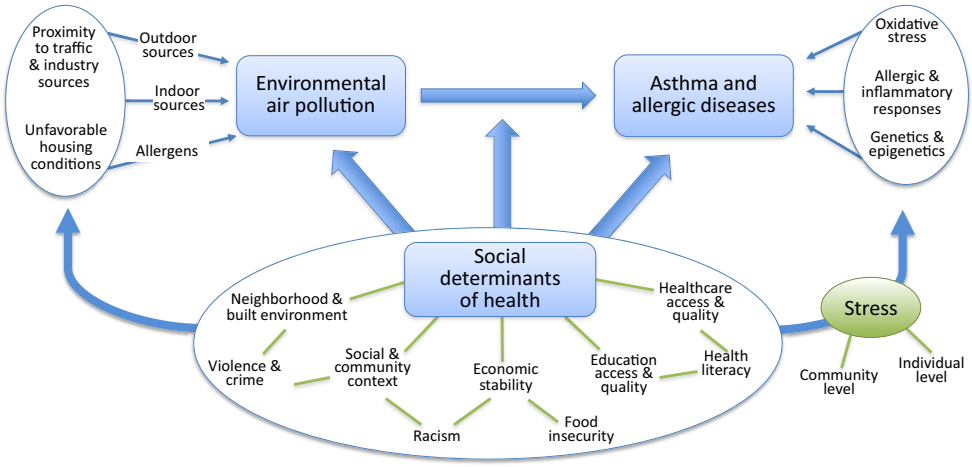

FIG 1. Conceptual diagram representing some of the complex relationships between Healthy People 2030 Social Determinants of Health and the influence on environmental air pollution exposure, asthma, and allergic diseases.

Policies such as exclusionary zoning laws, restricted covenants, and eminent domain dictate where low-income housing projects are built, and where high-pollutant sources such as toxic waste disposal sites, bus depots, and waste transfer stations are placed within a region. Fig 2 demonstrates an example from New York City where most solid waste transfer stations and bus depots, which are known sources of DEP, are concentrated in high-poverty communities and communities of color. Over the last 2 decades, New York City has transitioned much of its bus fleet from diesel to hybrid and electric fuel sources; however, this transition has not yet occurred for the garbage trucks that funnel through low-income and minority communities overburdened by environmental risk and harm[19] on a daily basis.

A number of guidelines and federal policies have been instituted in the last 60 years to improve environmental conditions and quality of health. These include the 1964 Surgeon General's Report, which led to drastic improvements in smoking rates, thus reducing environmental tobacco smoke exposure risk, and the Clean Air Act of 1970, which led to reductions in pollutant concentrations (eg, CO and O_3), thus improving air quality. Yet, despite these policy advancements, as Gaffney et al[20] discovered in their review of National Health and Nutrition Examination Survey data from 1959 to 2018, disparities in smoking, childhood asthma, and chronic obstructive pulmonary disease have all worsened during this same time period, specifically between poor and wealthy individuals. For example, childhood asthma rates have

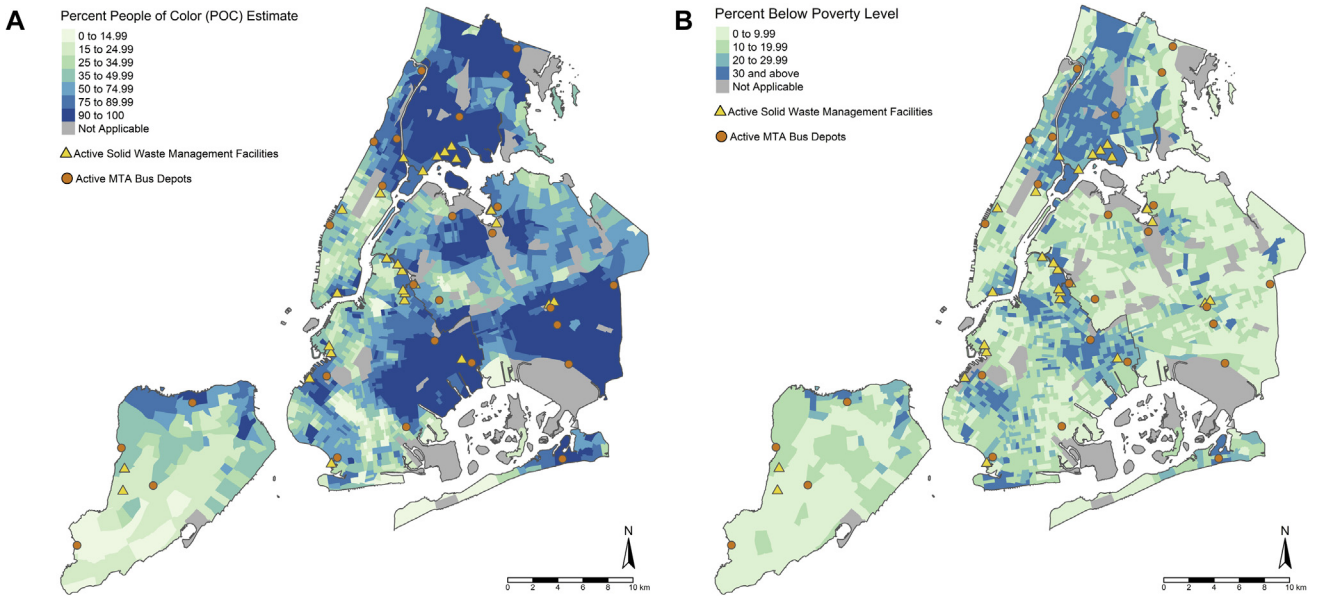

FIG 2. Locations of active solid waste management facilities (yellow triangles) and active metropolitan transit authority (MTA) bus depots (orange circles) throughout New York City compared with the estimated percentage of people of color (**A**) and percentage of people below the federal poverty level (**B**) based on American Community Survey data aggregated from 2015 to 2019. Data Sources: American Community Survey, US Census Bureau (5-year population demographic estimates, 2015-2019); Metropolitan Transportation Authority Bus Operations Depot Roster published by Calvin Huang & Tony Frazz, accessed June 2, 2021; Open Data, State of New York, data.ny.gov (Transfer Stations - Solid Waste Management Facilities Map); NYC Department of City Planning (NYC shapefile by 2010 census tracts, accessed June 7, 2021); NYC Open Data (NYC borough boundaries; accessed June 8, 2021).

increased across all populations over time; yet, there was no difference in prevalence between lowest and highest income families from 1976 to 1980, and from 2017 to 2018, there was a 4.9% greater prevalence in the poorest compared with the wealthiest families. Although this study did not specifically investigate changes in air quality across the same time periods, these findings, along with those above, suggest that not all communities have experienced improvements in air quality equally, contributing to continued or worsening disparities in respiratory outcomes.

THE INFLUENCE OF AIR POLLUTION ON IMMUNE RESPONSES, ASTHMA, AND ALLERGIC DISEASES

Air pollution and the immune response

Multiple clinical and animal studies have demonstrated strong associations between exposure to environmental air pollutants and disruption in the immune response that is linked to asthma and allergic diseases.[21-26] Fig 3 summarizes examples of well-characterized eosinophilic, neutrophilic, and epigenetic changes promoted by air pollution that have been established in mostly animal models. PM, including DEP, can function as adjuvant to the immune response by promoting T_H2 eosinophilic pathways.[21-25] For example, ovalbumin-sensitized mice exposed to ultrafine particles demonstrated enhanced expression of T_H2 cytokines (IL-5 and IL-13), eotaxin, and the Muc5ac gene.[22,23] Exposure to pollutants can also potentiate allergic sensitization, such as DEP co-exposure with house dust mite allergen and ragweed, which induced greater levels of sensitization to those allergens, and expression of IL-4, IL-5, and IL-13 in murine and animal studies.[25] Direct mast cell activation has been identified as another potential mechanism of pollution-induced immune responses. For example, in one study, murine mast cells were activated by tobacco smoke via α7 nicotinic acetylcholine receptors.[27]

Air pollution can also trigger airway inflammation via neutrophilic pathways, which can drive steroid-resistant asthma via mixed T_H2 and T_H17 pathways[28] (Fig 3). In a murine model, ambient PM exposure induced airway hyperresponsiveness in mice via increased production of T_H2- and T_H17-associated cytokines (IL-17A, IL-17F, IL-13, and IL-5).[29] Similarly, low-dose $PM_{2.5}$ exposure enhanced sensitization and airway hyperresponsiveness to dust mite in another murine model and increased expression of the IL-17A gene and related cytokines.[30]

Epigenetic studies also offer insight into the relationship between ambient pollutant exposure and the expression of genes that have downstream effects on respiratory health.[31] Methylation of the forkhead box p3 gene, a marker of regulatory T cells, can influence asthma outcomes via unregulated inflammatory pathways.[32,33] Elevated polycyclic aromatic hydrocarbon exposure contributed significantly to increased methylation of the forkhead box p3 gene locus and impaired regulatory T-cell response in atopic children.[32]

These and other studies[21-33] illustrate the direct links between exposure to specific environmental pollutants and altered immune responses through unique pathways that contribute to allergic diseases and are associated with asthma. Most of this body literature is from studies in animal models due to the challenges of studying discrete immune pathways in humans. As suggested by the multiple different mechanisms discussed (Fig 3), the impact of the environment can play an influential role in promoting eosinophilic and neutrophilic inflammation. This supports the common notion that development of atopy is multifactorial—a complex

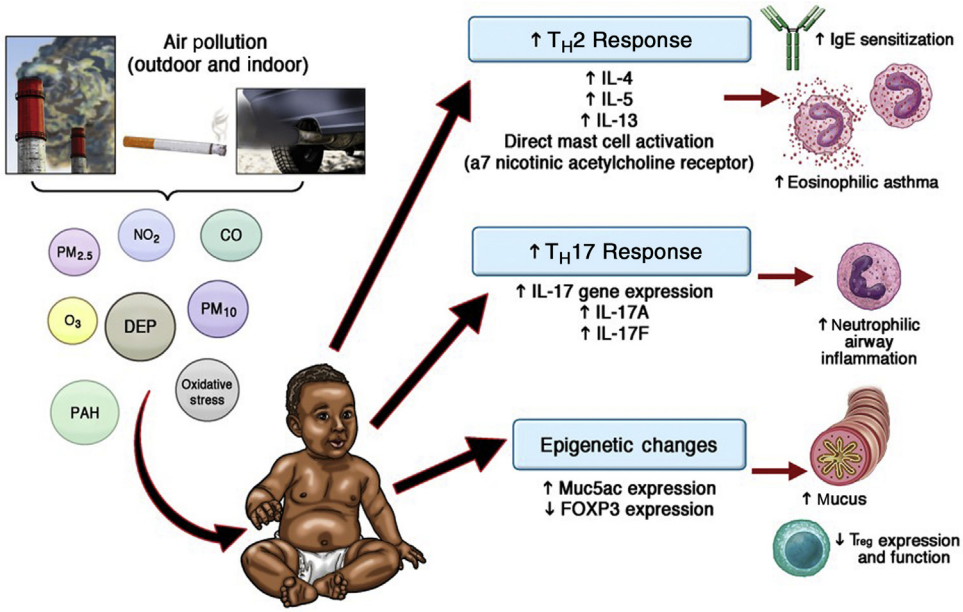

FIG 3. Summary figure of key eosinophilic, neutrophilic, and epigenetic pathways, mostly from animal models, that are implicated in the relationship between exposure to environmental air pollution and immune dysregulation that leads to asthma and other allergic diseases. *PAH,* Polycyclic aromatic hydrocarbon.

interaction between genetic susceptibility and environment leading to asthma and allergic sensitization.[34] Arguably, the effects of air pollution are not straightforward; however, the data presented suggest that air pollution, through various mechanisms, promotes sensitization and airway inflammation, which can influence clinical outcomes in vulnerable populations.[11,34,35]

Air pollution and asthma

Impaired immune responses triggered by air pollution as described above have been implicated in downstream clinical outcomes including the development of allergic asthma. Human studies that examine associations between pollutants and asthma are complex due to the mixture of pollution sources and components that are often highly correlated, making it difficult to distinguish the direct effects of individual pollutants.[36] In addition, exposure profiles vary across different populations. For example, O_3 tends to be higher in suburban communities, whereas traffic-related particulates are often more prevalent in urban communities. Yet, despite these limitations, several studies have identified links between specific pollutants or combinations of pollutants and asthma.

There is strong evidence to support links between air pollution exposure and the development of asthma in children.[37] For example, increased exposure to $PM_{2.5}$, NO_x, and CO during the first year of life is associated with increased risk of asthma diagnosis by age 5 years, whereas decreases in NO_2 and $PM_{2.5}$ are associated with reductions in childhood asthma incidence.[38,39] Reductions in NO_2, $PM_{2.5}$, and PM_{10} have also been associated with lung function growth during adolescence.[40] The evidence from these large cohorts of primarily urban populations suggests that exposure to air pollution, largely resulting from traffic sources, contributes to asthma development and affects respiratory function. Lung function impairment from pollutant exposure was further illustrated in a smaller study of 44 children with asthma in Cincinnati, Ohio. Authors identified that indoor $PM_{2.5}$ exposure was positively associated with decreased lung function, including FEV_1/forced vital capacity and forced expiratory flow at 25% to 75% of forced vital capacity, although outdoor $PM_{2.5}$ exposure was not.[41] Although demonstrated in a limited sample, these findings suggest that because a large proportion of time is spent indoors, indoor air pollution may have similar or larger effects than those observed for outdoor air pollution.

In addition to the development of lung function impairment and asthma, childhood exposure to air pollution is associated with increased asthma morbidity, including poor asthma symptom control and greater emergency department (ED) utilization.[42,43] Indoor exposure to NO_2, which is predominantly derived from gas stove cooking, has been linked to increases in asthma severity, nighttime symptoms, and rescue medication use.[44] Secondhand smoke is another indoor pollutant, with greater prevalence in communities of color[45,46] and is associated with more frequent asthma symptoms, exacerbations, greater medication utilization, and hospitalizations.[47,48] Although children may be more vulnerable to the hazardous respiratory effects of air pollution, particularly through its influence on impaired lung development,[49] similar associations have been observed among adults, with increased exposure to pollutants leading to worsening of asthma symptoms and severity.[42]

Air pollution and other allergic diseases

Although there is a dearth of studies that have investigated exposure to air pollution and allergic disease in US populations, multiple non-US studies have demonstrated that air pollution can influence atopy in children.[26,50-66] The outcomes of these studies may be generalizable to the US population; however, we must acknowledge the limitations of applying these data to different

TABLE I. The combined influence of social and environmental factors on asthma and allergic disease in the United States

Author (year)	Exposure; Effect modifier	Study population	Main findings	Key limitations
Asthma development				
Kravitz-Wirtz et al[102] (2018)	Annual average NO_2 and $PM_{2.5}$ by census block group; Neighborhood poverty level	A total of 5,897 children from 2 cohorts (1997 & 2014) of the Panel Study of Income Dynamics who responded to the Child Development Supplement (national study in the United States)	Interquartile range (IQR) increases in exposure to NO_2 (8.51 ppb) and $PM_{2.5}$ (4.43 $\mu g/m^3$), respectively, measured in the child's year of birth are associated with higher odds of subsequent childhood asthma diagnosis (NO_2 OR, 1.25; 95% CI, 1.10-1.41; $PM_{2.5}$ OR, 1.25; 95% CI, 1.06-1.46) and this association is strongest in neighborhoods with high poverty levels (ie, >20%; NO_2 OR, 1.31; 95% CI, 1.08-1.60; $PM_{2.5}$ OR, 1.35; 95% CI, 1.03-1.78)	Self-reported childhood asthma diagnosis; pollutant estimates reflect annual average for year of birth so imprecision in whether exposure was pre/postnatal; no consideration of other climatological factors
Lee et al[110] (2018)	Daily prenatal $PM_{2.5}$ concentrations; Prenatal maternal stress (ie, negative life events)	Participants in pregnancy cohort study (Asthma Coalition on Community, Environment and Social Stress; n = 736 mothers/children) in Boston, Mass	Prenatal $PM_{2.5}$ exposure was positively associated with the odds of childhood asthma diagnosis by age 6 y (OR, 1.17; 95% CI, 1.04-1.30 per 1.7 $\mu g/m^3$ [IQR] increase in $PM_{2.5}$). Stronger effects were observed for children whose mothers had high prenatal stress (3+ negative life events) as compared with those with low prenatal maternal stress, with a critical period of $PM_{2.5}$ and stress exposure identified at 19-23–wk gestation (OR, 1.15; 95% CI, 1.03-1.26)	Models not adjusted for indoor pollution exposure, except tobacco smoke exposure; study population limited to inner-city mothers, most of whom identified as either Hispanic or Black, potentially limiting generalizability
Asthma morbidity				
Gharibi et al[109] (2019)	Daily 8-h maximum ozone concentration; Race/ethnicity	A total of 1,101 ED visits for asthma attacks in San Joaquin Valley, Calif (June-September 2015)	Increases in O_3 exposure are associated with higher odds of asthma-related ED visits the following 1 and 3 d later (OR = 1.034; 95% CI, 1.011-1.062; OR, 1.066; 95% CI, 1.032-1.082 per 18.1 ppb [IQR] increase in O_3). The positive association between O_3 exposure and asthma-related ED visits was strongest for Black individuals (vs White & Hispanic). Specifically, among Black individuals, increases in O_3 were associated with higher odds of asthma ED visits 3 through 6 d after exposure, but only 3 d after exposure among Hispanic individuals	Considered exposed as those within 15 km of monitoring station; limited generalizability due to high ozone levels in San Joaquin Valley (ie, above state and national standards)
Sheffield et al[104] (2019)	Ozone; Violent crime and socioeconomic deprivation	A total of 11,719 children ages 5-18 y with an outpatient asthma ED visit in an NYC hospital between 2005 and 2011	O_3 exposure is associated with a higher risk of asthma-related ED visits for children (9.4% excess risk of ED visits 2 d after exposure; 95% CI, 6.3%-12.7% per 10 ppb increase in O_3). This association is stronger in areas with the greatest (vs least) socioeconomic deprivation and highest (vs lowest) levels of violent crime, respectively	Stress and deprivation assessed at community level rather than at individual level; urban setting of NYC may limit generalizability

(Continued)

TABLE I. *(Continued)*

Author (year)	Exposure; Effect modifier	Study population	Main findings	Key limitations
O'Lenick et al[105] (2017)	Air pollution (ie, NO_2, EC, O_3, $PM_{2.5}$); Neighborhood SES	A total of 128,758 outpatient asthma ED visits among children ages 5- 18 y in Atlanta hospitals between 2002 and 2008	$PM_{2.5}$, EC, and O_3 exposure, respectively, is positively associated with the odds of asthma-related ED visits among children (ie, moving average for day of exposure through 2 d after exposure; $PM_{2.5}$ OR, 1.027; 95% CI, 1.012-1.043 per IQR increase in $PM_{2.5}$, 10 $\mu g/m^3$; EC OR, 1.013; 95% CI, 1.005-1.022 per IQR increase in EC, 0.5 $\mu g/m^3$; O_3 OR, 1.073; 95% CI, 1.043-1.104 per IQR increase in O_3, 25 ppb). These associations are generally stronger in areas with greater deprivation (eg, ≥20% poverty) and lower SES but vary depending on the specific measure used to assess SES. When stratified by quartile of poverty, the association between $PM_{2.5}$ and asthma ED visits is stronger in both the highest and lowest poverty quartiles compared with the second and third quartiles	Spatial resolution for pollution estimates (ie, 12 km × 12 km grid cells); potential variability in baseline risk of asthma-related ED visits; setting of Atlanta may limit generalizability
Glad et al[108] (2012)	Air pollution (ie, daily mean $PM_{2.5}$ and daily 1-h maximum O_3); Race	A total of 6,979 individuals discharged with primary diagnosis of asthma from EDs in Allegheny County (Pittsburgh, Pa) from 2002 to 2005	Increases in $PM_{2.5}$ were associated with higher odds of ED visits the day after exposure (OR, 1.036; 95% CI, 1.001-1.073 per 10 $\mu g/m^3$). However, among African American individuals, increases in $PM_{2.5}$ exposure were associated with higher odds of ED visits for asthma 1 through 3 d later (OR, 1.055; 95% CI, 1.001-1.112; OR, 1.067; 95% CI, 1.015-1.122; OR, 1.053; 95% CI, 1.002-1.106). For the total sample, increases in O_3 were also associated with higher odds of ED visits 2 d later, even after adjustment for $PM_{2.5}$ (OR, 1.021; 95% CI, 1.001-1.042 per 10 ppb increase in O_3)	Main models presented are single-pollutant and racial differences not observed in models with both pollutants; few confounders considered; large metropolitan study area may limit generalizability
Nachman and Parker[107] (2012)	Annual average $PM_{2.5}$ concentrations; Race/ethnicity	A total of 109,485 National Health Interview Survey (2002-2005) respondents (ie, adults ages 18+ y in the United States)	Among all adults, exposure to $PM_{2.5}$ was positively associated with sinusitis (OR, 1.18; 95% CI, 1.08-1.30 per 10 $\mu g/m^3$ increase in $PM_{2.5}$) but not current asthma, recent (past year) asthma attacks, or chronic bronchitis. However, increased $PM_{2.5}$ exposure was associated with significantly higher odds of current asthma and recent asthma attacks among non-Hispanic Blacks (OR, 1.73; 95% CI, 1.17-2.56; OR, 1.76; 95% CI, 1.07-2.91) and of sinusitis among non-Hispanic Whites (OR, 1.31; 95% CI, 1.18-1.46)	Self-reported survey data; inability to assess potential variability among subgroups of those who identified as Hispanic; limited to respondents for whom geographic location data were available; lack of adjustment for stress exposure

(Continued)

TABLE I. *(Continued)*

Author (year)	Exposure; Effect modifier	Study population	Main findings	Key limitations
Atopy and allergic disease				
Lynch et al[103] (2014)	Indoor allergen and bacterial exposures in inner-city households; No effect modifier assessed but sample restricted to primarily racial and ethnic minority children living in neighborhoods with at least 20% of families below federal poverty level	A total of 560 children in an urban longitudinal birth cohort from Boston, Baltimore, NYC, and St Louis (URECA)	Early exposures to high levels of allergens and a bacteria-rich environment can be protective against atopy and wheezing in young children. Exposure to high levels of cockroach, mouse, and cat allergen during the first year of life was negatively associated with recurrent wheeze at age 3 y (OR, 0.6; 95% CI, 0.65-0.75). However, this association was not significant for exposures during the second or third year of life. In a nested case-control study of 104 households, house dust bacterial content during the first year of life and reduced exposure to *Firmicutes* and *Bacteriodetes* were associated with atopy and wheezing. In children without atopy or wheezing, exposure to high levels of bacteria and allergens appeared to be protective	Variation in household dust sample collection sites; most households not included in the microbial analysis

EC, Elemental carbon; *NYC*, New York City; *OR*, odds ratio; *URECA*, Urban Environment and Childhood Asthma.

groups of people. Specifically, there are differences in the prominent pollutants in different geographical regions due to differences in emission sources. For example, several lower income Asian and African nations have markedly higher $PM_{2.5}$ concentrations, compared with the United States, Canada, and several European countries that have comparable population-weighted annual average $PM_{2.5}$ concentrations, making these countries more commensurate when discussing the impact of air pollution on the development of asthma and atopy in the United States.[67] Equally important, there is variation between studies in the methods of comparing and reporting pollutants and differences in the evaluation of sensitization in the study populations. Although we acknowledge these differences, results from these international birth cohorts, as outlined in Table E1 in this article's Online Repository at www.jacionline.org, offer valuable insight regarding the impact of air pollution on the development of allergic diseases.

In a US study, the Cincinnati Childhood Allergy and Air Pollution birth cohort, exposure to DEP in the first year of life was positively associated with aeroallergen sensitization by ages 2 and 3 years.[51] In another large US cohort of more than 900 mother-child dyads, black carbon and $PM_{2.5}$ exposures were associated with increased risk of sensitization to food and aeroallergens.[54] Postnatal tobacco smoke exposure has also been identified as a risk factor for sensitization to food allergens during the first year of life[56-58,68] (Table E1). Air pollution also has an effect on the development of atopic dermatitis in children, which has been demonstrated in Asian and German studies.[59-63]

The development of atopy is multifactorial; however, as these studies suggest, chronic exposure to air pollution can influence and can sometimes accelerate sensitization to foods, inhalants, and the development of atopic dermatitis. Furthermore, this process can be amplified by additional social and structural factors, such as poverty, housing, and discrimination. As a foreground for understanding the combined effects of air pollution and SDOH on asthma and allergic diseases, it is important to review what is known about SDOH and their impact on asthma and atopy.

THE INFLUENCE OF SDOH ON ASTHMA AND ALLERGIC DISEASE

The 5 domains of SDOH as outlined by the US Healthy People 2030 commission[5] provide a framework for understanding the multifactorial social and environmental contributors to health within US populations (Fig 1). Although the categorization of race in the United States is a social construct that is often misused as a proxy for genetic ancestry, racial discrimination, as discussed in the second section, often places communities of color in high-poverty or low-socioeconomic circumstances. Thus, it is often difficult to disentangle the independent contributions of social and environmental conditions that are driven by racial segregation and racism, and their relationship with asthma and allergic outcomes.

SDOH and asthma

Socioeconomic factors are key predictors of health disparities in asthma, particularly socioeconomic status (SES), which encompasses economic factors, access to resources, employment, and educational opportunities. Specifically, low income and poverty are associated with higher asthma prevalence,[69] exacerbations,[70] and poor asthma control, which is also affected by low educational attainment.[71] An example of the interplay

between SES and educational attainment is illustrated in a cross-sectional analysis of 150 children with asthma in the greater Chicago metropolitan area. In this sample, higher parental education level, or prestige-based SES, was associated with better ratings of home environmental control and reduced tobacco smoke exposure, whereas resource-based SES, or access to family assets, was not.[72] Low health literacy and socioeconomic hardship can amplify racial disparities in asthma knowledge, asthma-related quality of life, and hospitalization outcomes.[73-75] Food insecurity is also associated with cost-related underuse of medication and prescription delay for many chronic health conditions, including asthma.[76,77] Greater asthma morbidity comes with considerable economic burden due to increased health care utilization and medication use. Increased health care costs and cost-related barriers associated with asthma often most heavily impact poor and non-White individuals, thus further contributing to disparities in asthma outcomes.[78-80] Relatedly, poverty can also have intergenerational effects on asthma outcomes. In one study, children with asthma whose parents grew up in lower SES households had lower asthma control test scores and higher production of proinflammatory and allergic cytokines independent of current family SES.[81] Although observational, these studies include both state and national data, which collectively suggest that socioeconomic factors can contribute to disparities in asthma outcomes among US populations.

Yet, Assari and Moghani Lankarani[82] demonstrated that the protective association of living above the federal poverty level and reduced odds of asthma was significant only for White children and not for Black children. In addition, Beck et al[1] found that although the risk of readmission for asthma among African American children was more than double that of White children, 80% of this disparity was explained by differences in financial and social hardship, caregiver educational attainment and marital status, and environmental factors such as traffic-related air pollution exposure, medication access, vehicle ownership, and salivary cotinine.[1] After adjusting for these variables, there was no significant difference in the hazard of readmission between African American and White children with asthma,[1] thus identifying these specific SDOH as potential targets for intervention to improve asthma-related outcomes at the individual level. Furthermore, although acculturation has been linked to increased asthma burden and decreased lung function among US Hispanic and Latino populations who also face disproportionate poverty levels, these relationships may also be affected by environmental factors (eg, prenatal tobacco smoke and pest exposure).[83,84]

Several studies have used measures of area deprivation as a way of assessing the complex interactions between neighborhood socioeconomic and social risk factors. For example, Nkoy et al[85] used the Area Deprivation Index as a predictor of asthma-related hospitalization outcomes and found that areas with higher deprivation had significantly longer length of stay, higher costs, and a greater number of readmissions for asthma within 6 months of discharge. If combined with measures of air pollution, these comprehensive indexes may be a promising way to capture and characterize the complex relationships between multiple environmental and social conditions that influence health and disease.

Regulation of asthma and allergy genes can also be affected by SES.[81,86,87] Miller et al[86] reported that upregulation of T_H2 skewed cytokines in children with lower SES and asthma. This has also been reported in other cohorts.[81,87] Although genetic susceptibility influences biological and immune response and affects racial and ethnic disparities in asthma and atopy, such disparities are largely affected by social and structural factors that serve as determinants of health.[1]

SDOH and other allergic diseases

Multiple studies have suggested that socioeconomic factors play a role in eczema and other allergic diseases, although further research is needed in this area. For example, an in-office survey at the University of North Carolina Medical Center identified multiple SDOH influencing eczema severity in African American children, namely lower parental income, parental educational attainment, and higher environmental tobacco smoke exposure.[88] Similarly, the economic impact of food allergy is not equal. Gupta et al[89] found that lower income households (ie, adjusted gross income <$50K/y) had lower direct medical costs associated with subspecialty care and allergen-free foods compared with higher income households (adjusted gross income >$100K/y). Yet, lower income families spent 2.5 times more in annual costs for ED visits and hospitalizations related to allergic reactions than higher income families.[89,90] These findings may help to explain some of the disparities in allergic disease outcomes observed across US populations. Although not the focus of this review, the impact of the SDOH on the diagnosis and management of allergic rhinitis, food allergy, and atopic dermatitis is an area of burgeoning interest and there is growing evidence that underserved patients experience significant disparities in care.[12]

The role of stress in immune response, allergy, and asthma

A growing body of work has described the impact of stress on health and human conditions, including the understanding of allostatic load or the cumulative impact of chronic stress that leads to impaired immune response and chronic disease such as asthma and allergies.[91] Structural factors such as systemic racism and discrimination can lead to both individual- and community-level stress and exacerbate disparities in asthma and allergic disease.[4,92-94] Stress can be a potent source of immune dysregulation, specifically affecting the immune response to aeroallergens, pulmonary inflammation, and responses to allergen-specific treatments and diagnostic tools.[93,94] Cortisol elevations can promote a T_H2 response, resulting in increased IgE production.[95,96] In allergic murine models, stress was found to promote resistant pulmonary inflammation to glucocorticoids.[97] Kiecolt-Glaser et al[98] demonstrated that exposure to a validated laboratory stressor to provoke anxiety substantially increased skin prick test size and late-phase IL-6 cytokine production. Oxidative stress can alter the methylation of T_H genes, which in some predisposed populations may result in a more T_H2 allergic response.[99,100]

Individual and neighborhood stress is also a result of and contributor to community violence. Concerns about neighborhood safety have been linked to reduced physical activity and may increase exposure to chronic stress, leading to greater inflammation and impaired immune response among individuals with asthma.[101] In addition, among African American youth, Thakur et al[4] demonstrated that the perceived experience of any discrimination increased the odds of asthma and poor asthma control, which suggests that addressing structural racism may offer a pathway through which to mitigate stress and its effects on asthma.

INTERACTIONS BETWEEN SOCIAL ENVIRONMENTAL FACTORS, AIR POLLUTION, ALLERGY, AND ASTHMA

Although numerous studies have investigated independent effects of air pollution and SDOH on asthma and allergy as briefly discussed above, few have explored combined effects that place environmental exposures and social conditions in the same context (Table I). Examining the combined influence of social and environmental factors is important because of the increased risk in certain groups for developing atopy and asthma compounded by living in neighborhoods where there is increased exposure to air pollution and unfavorable housing conditions.[2,3,6,7] For example, low-income and poor-quality housing in urban communities is often located near high traffic sources and is often associated with an abundance of indoor aeroallergens such as mold, cockroach, and mouse. These exposures have been linked to asthma morbidity and are often difficult to mitigate in the setting of poverty.[3]

Evidence suggests that the established association between prenatal and early postnatal exposure to $PM_{2.5}$ and NO_2 and subsequent asthma diagnosis varies by neighborhood poverty level, with the strongest associations observed in high-poverty areas and weaker to no effects observed in low- and moderate-poverty areas.[102] However, there is evidence that factors associated with poverty may have some protective effects toward preventing atopy and wheezing in young children. In the Urban Environment and Childhood Asthma birth cohort of 560 primarily ethnic minority children from neighborhoods with at least 20% of families living below the federal poverty level, high exposure to cockroach, mouse, and cat allergen was inversely associated with recurrent wheezing episodes.[103] Within the Urban Environment and Childhood Asthma cohort, in a smaller, nested case-control study of 104 children, household dust samplings were analyzed for bacterial content during the first year of life. Forty-one percent of the children with no wheezing or atopy lived in an environment with high levels of bacteria and indoor allergen exposure. More specifically, reduced exposure to the *Firmicutes* and *Bacteriodetes* phyla was associated with atopy and wheezing. On the basis of these data, the authors concluded that high allergen and bacterial household exposures may serve a protective role in preventing the development of atopy in susceptible populations, consistent with the hygiene hypothesis.[103]

In addition to the family and household, neighborhood and community factors may enhance the impact of air pollution on the development of atopy and wheezing. In children, high O_3 exposure has been demonstrated to increase the risk of ED visits for asthma. However, research suggests that these associations are stronger for children living in areas with higher levels of violent crime and socioeconomic deprivation,[104] with effect modification by socioeconomic deprivation also observed in relationships between exposure to NO_2, elemental carbon, and ED visits.[106] More specifically, O'Lenick et al[105] examined neighborhood-level SES according to 6 main criteria—education, income, poverty, unemployment, household type, and transportation—as well as by using the Neighborhood Deprivation Index and the Townsend Index. Generally, there were stronger associations between air pollution (ie, O_3, $PM_{2.5}$, NO_2, elemental carbon) and asthma ED visits among children ages 5 to 18 years in areas with higher deprivation or lower SES. However, these results differed depending on the criteria used to define SES. When examining the effects across quartiles, there were stronger associations between $PM_{2.5}$ and asthma ED visits in both the highest and lowest poverty levels. Thus, it is important to consider the many other social and structural factors that affect these relationships at both the individual and neighborhood levels. In the United States, higher levels of poverty or lower SES are generally located in closer proximity to industrial facilities and roadways, leading to greater pollution exposure, which may partially explain socioeconomic disparities in asthma outcomes[2] that may be in contrast to the structural and social environments of other countries.[106]

As discussed previously, disproportionate exposure to air pollution may partially explain racial and ethnic disparities in asthma and allergic diseases.[1,2,6,7,69,92,107-109] In a US study, Nachman and Parker[107] found that 10 $\mu g/m^3$ increases in $PM_{2.5}$ were not associated with either current asthma or recent asthma exacerbations overall in adults; however, among individuals who identified as non-Hispanic Black, increases in $PM_{2.5}$ were associated with significantly higher odds of current asthma and recent attacks. In another study in Pennsylvania, Glad et al[108] found that 10 $\mu g/m^3$ increases in $PM_{2.5}$ exposure were associated with higher odds of ED visits for asthma 1 through 3 days later only among African American individuals. Still another study conducted in California demonstrated similar findings in association with O_3 exposure.[109] Specifically, controlling for exposure to copollutants ($PM_{2.5}$, NO_2, CO) and temperature, 18.1 ppb increases in O_3 concentration 3 days before an asthma attack were associated with higher odds of asthma ED visits. This association was strongest among Black patients followed by Hispanics but was not significant among White patients. However, among White patients, there were significantly lower odds of asthma ED visits observed for O_3 exposure on the day of the ED visit and for the average exposure between the day of the ED visit and the day before.[109] These studies highlight that in addition to some communities of color experiencing higher concentrations of air pollutants, there may be a differential response to air pollution compared with White populations that is likely driven by a confluence of social and environmental factors that are colocated in communities of color. However, studies that offer subgroup analysis by racial groups should always be interpreted with caution, especially if the studies were not designed and powered to evaluate differences across social races.

Stress can also modify associations between air pollution and asthma and allergic diseases. For example, maternal $PM_{2.5}$ exposure during pregnancy and subsequent childhood asthma diagnosis may be modified by prenatal exposure to maternal negative life events. Specifically, Lee et al[110] found that the effect of $PM_{2.5}$ exposure on childhood asthma diagnosis was stronger among mothers with high stress exposure (ie, 3+ negative life events in the past 6 months), with a critical gestation period of exposure between 19 and 23 weeks, and no association between $PM_{2.5}$ and asthma observed among those with low maternal stress exposure. This study, along with evidence from non-US populations (see Table E2 in this article's Online Repository at www.jacionline.org),[92,111,112] suggests that greater exposure to stress exacerbates the relationship between air pollution exposure and the development and morbidity of asthma and allergic diseases in children. The mechanisms for these associations may be partially explained by a framework proposed by Clougherty and Kubzansky[113] who differentiate between the impact of chronic

and acute stress exposure on pollution-related respiratory susceptibility. The authors posit that acute stress increases ventilation and bronchodilation, opposite to the short-term effects of air pollution exposure, and chronic stress impairs immune function, increasing susceptibility to air pollution.

CONCLUSIONS

Exposure to environmental air pollution is associated with asthma and other atopic diseases. Although substantial efforts have been made to improve air quality in the United States, the cleaner air and health benefits of such interventions have not been experienced by all communities equally. Social and environmental factors such as neighborhood environment, social cohesion, economic stability, and access to quality education and health care all play a role in prevalence of disease among people of color and the poor. As a result, where and how one lives significantly influences individual and community risk for environmentally triggered diseases such as asthma, allergies, and eczema. To truly eliminate environmental injustice and disparities in atopic health outcomes, we must address the systemic policies and practices that are rooted in racism and inequality.

What do we know?

- **The development of and morbidity from asthma and allergic diseases is multifactorial.**
- **Studies in animal models suggest that air pollution may promote eosinophilic and neutrophilic inflammatory pathways driving the development of aeroallergen sensitization and asthma.**
- **Because of environmental racism, impoverished and racial and ethnic minority populations are disproportionately affected by air pollution.**
- **The deleterious effects of air pollution on asthma and allergic diseases may be influenced by SDOH (eg, social and structural factors at the individual and community level, such as poverty, neighborhood deprivation, and chronic stress).**

What is still unknown?

- **Limited studies have evaluated the combined impact of SDOH and exposure to environmental air pollution in how they affect the development of allergic diseases such as allergic rhinitis, food allergy, and atopic dermatitis.**
- **Further research is needed to explore the relationships between air pollution, asthma, and SDOH within the domains of education access and quality and health care access and quality.**
- **The growing field of implementation science can offer insight into how the implementation of policies and interventions that target SDOH influence environmental air pollution exposure and outcomes of asthma and other allergic diseases.**

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TABLE E1. US and international clinical studies demonstrating the impact of indoor and outdoor air pollution on the development of atopy in children

Disease	Reference	Population	Findings
Allergic rhinitis	Melen et al[E1] (2021)	Four European birth cohorts (n = 6,163 children) in the MeDALL consortium	Increased risk of sensitization to birch pollen per 10 μg/m^3 increase in NO_2 exposure (OR, 1.12; 95% CI, 1.01-1.25) Increased sensitization to grass (Phl p1) and cat (Fel d1) linked to high $PM_{2.5}$ exposure at birth
	Codispoti et al[E2] (2015)	US birth cohort with a family history of parental atopy (n = 634 children)	DEP exposure during the first year of life was positively associated with aeroallergen sensitization at 2 y (OR, 1.4; 95% CI, 0.97-2.0) and 3 y (OR, 1.35; 95% CI, 0.98-1.85)
	Deng et al[E3] (2016)	Chinese cohort (n = 2,598 preschool children)	Lifetime prevalence of allergic rhinitis significantly associated with TRAP exposure during the third trimester of pregnancy (OR, 1.4; 95% CI, 1.08-1.82) and during the first year of life for 11 μg/m^3 increase in NO_2 (OR, 1.36; 95% CI, 1.03-1.78)
	Gruzieva et al[E4] (2012)	BAMSE Swedish birth cohort (n = 2,545 children)	High NO and PM exposure during the first year of life was associated with higher odds of pollen sensitization at age 4 y (OR, 1.83; 95% CI, 1.02-3.28)
	Lannerö et al[E5] (2008)	BAMSE Swedish birth cohort (n = 2,614 children)	Dose-response effect found between ETS exposure during early infancy and IgE sensitization Increased risk of sensitization to indoor aeroallergens (OR, 1.96; 95% CI, 1.28-2.99) and food allergens (OR, 1.46; 95% CI, 1.11-1.93) among children exposed to ETS at age 2 mo
	Morgenstern et al[E6] (2008)	Two German birth cohorts (GINI and LISA) (n = 2,860 at 4 y, n = 3,061 at 6 y)	Strong positive distance- dependent association found between $PM_{2.5}$ exposure and hay fever (OR, 1.59; 95% CI, 1.11-2.27) and sensitization to pollen (OR, 1.40; 95% CI, 1.20-1.64)
	Oftedal et al[E7] (2007)	Norwegian cohort (n = 2,244 children)	No association between long-term exposure to TRAP and aeroallergen sensitization in 9-10-y-olds Lifetime air pollution exposure to NO_2 was positively associated with *D farinae* sensitization (OR, 1.88; 95% CI, 1.02-3.47)
	Kulig et al[E8] (1999)	German MAS birth cohort (n = 342 children)	No significant association between ETS exposure and sensitization to inhalants
Food allergy	Sordillo et al[E9] (2019)	Project Viva, US prebirth cohort (n = 996 mother-baby dyads)	Third-trimester BC and $PM_{2.5}$ exposure associated with ~30% increased risk of sensitization to aero- and food allergens (egg white, cow's milk, wheat, peanut, and soybean) by adolescence
	Thacher et al[E10] (2016)	BAMSE Swedish birth cohort (n = 3,316 children)	Secondhand smoke exposure during infancy (without prenatal exposure) associated with increased risk of food sensitization at age 4 y (OR, 1.47; 95% CI, 1.08-2.00) and persistent sensitization at 16 y (OR, 1.50; 95% CI, 1.00-2.24)
	Sbihi et al[E11] (2015)	CHILD Canadian birth cohort (n = 2,477 children)	NO_2 exposure after birth positively associated with the development of sensitization (positive skin prick test result) to multiple aero- and food allergens (cow's milk, egg white, soybean, and peanut) (OR, 1.17; 95% CI, 0.95-1.47)
	Gruzieva et al[E4] (2012)	BAMSE Swedish birth cohort (n = 2,545 children)	Air pollution exposure during the first year of life associated with increased risk of food sensitization, among children with no sensitization at age 4 y (OR, 2.3; 95% CI, 1.10-4.82)
	Lannerö et al[E5] (2008)	BAMSE Swedish birth cohort (n = 2,614 children)	Dose-response effect found between ETS exposure during early infancy and IgE sensitization Increased risk of sensitization to indoor aeroallergens (OR, 1.96; 95% CI, 1.28-2.99) and food allergens (OR, 1.46; 95% CI, 1.11-1.93) among children exposed to ETS at age 2 mo
	Kulig et al[E8] (1999)	German MAS birth cohort (n = 342 children)	Prenatal and postnatal ETS exposure associated with high risk of sensitization to food allergens in exposed 3-y-olds compared with the unexposed group (OR, 2.3; 95% CI, 1.1-4.6) No significant association between ETS exposure and sensitization to inhalants

(Continued)

TABLE E1. *(Continued)*

Disease	Reference	Population	Findings
Atopic dermatitis	Deng et al[E3] (2016)	Chinese cohort (n = 2,598 preschool children)	Significant association between NO_2 exposure during the first trimester of pregnancy and the development of eczema (OR, 1.54; 95% CI, 1.14-2.09)
	Lee et al[E12] (2008)	Taiwanese middle school students (n = 317, 926) living within 2 km of air monitoring stations	Flexural eczema positively associated with TRAP (NO_x and CO) exposure Recurrent eczema in girls positively associated with NO_x and CO exposure
	Morgenstern et al[E6] (2008)	Two German birth cohorts (GINI and LISA) (n = 2,860 at 4 y, n = 3,061 at 6 y)	NO_2 exposure per 6.4 $\mu g/m^3$ positively associated with physician eczema diagnosis (OR, 1.18; 95% CI, 1.00-1.39)

Sensitization defined as sIgE >0.35 kU/L by Immunocap or positive skin prick testing result (immediate skin hypersensitivity test wheal 3 mm larger than that with saline or glycerin control).

BAMSE, Children, Allergy, Milieu, Stockholm Epidemiological Survey (Barn Allergi Miljö Stockholm Epidemiologi); *BC*, black carbon; *CCAAPS*, Cincinnati Childhood Allergy and Air Pollution birth cohort; *CHILD*, Canadian Healthy Infant Longitudinal Development; *ETS*, environmental tobacco smoke; *GINA*, German Infant Nutritional Intervention study; *LISA*, Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children; *MAS*, Multicenter Allergy Study; *MeDALL*, Mechanisms of the Development of Allergy European cohorts; *TRAP*, traffic-related air pollution.

TABLE E2. International studies that describe the combined influence of air pollution and social/environmental factors on asthma and allergic disease

Author (year)	Exposure; Effect modifier	Study population	Main findings	Main limitations
Pierangeli et al[E13] (2020)	Air pollution (ie, NO_2, $PM_{2.5}$, BC); Social deprivation	Population in Barcelona (ie, Health Impact Assessment used to quantitatively estimate childhood asthma cases attributable to pollution estimates modeled under different scenarios based on asthma incidence in Spain, number of children in Barcelona, and land use regression modeled air pollution data)	If Barcelona achieved World Health Organization guidelines for air pollution, an estimated 18% (454; CI, 199-600) and 19% (478; CI, 173-735) of childhood asthma cases would be attributable to NO_2 and $PM_{2.5}$, respectively. If Barcelona achieved the minimum air pollution levels previously reported in a meta-analysis (ie, 1.5 $\mu g/m^3$ NO_2; 0.4 $\mu g/m^3$ $PM_{2.5}$; 0.4×10^{-5}/m BC), an estimated 48% (1230; CI, 602-1521), 39% (992; CI, 390-1417), and 31% (789; CI, 340-1186) of childhood asthma cases would be attributable to NO_2, $PM_{2.5}$, and BC, respectively. In this scenario, areas in the lowest quartile of social deprivation had a statistically significantly greater proportion of estimated childhood asthma cases attributable to BC exposure as compared with those in the highest quartile of social deprivation (216; CI, 94-322, vs 193, CI, 83-294)	Models were single-pollutant and did not estimate combined exposure effects; deprivation data from 2001 but pollution data from 2012; many assumptions in Health Impact Assessment analysis that do not reflect actual exposure or outcomes
Rancière et al[E14] (2017)	Traffic-related air pollution (ie, NO_x) exposure in first year of life; Stressful family events	A total of 2,015 children from the PARIS (Pollution and Asthma Risk: an Infant Study) birth cohort (Paris, France)	TRAP exposure in children's first year of life was positively associated with persistent wheeze (OR, 1.27; 95% CI, 1.09-1.47, per IQR increase in average NO_x, equivalent of 26 $\mu g/m^3$ NO_2), ever asthma (OR, 1.15; 95% CI, 1.01-1.31), and ever asthma with current respiratory symptoms (OR, 1.20; 95% CI, 1.02-1.41) at age 4 y. Yet, when stratified, TRAP exposure was associated with higher odds of these outcomes only among children also exposed to stressful family events (persistent wheeze OR, 1.46; 95% CI, 1.19-1.79; ever asthma OR, 1.25; 95% CI, 1.05-1.49; ever asthma with current respiratory symptoms OR, 1.34; 95% CI, 1.07-1.68). Among children exposed to stressful family events, TRAP exposure was also associated with higher odds of persistent dry night cough (OR, 1.29; 95% CI, 1.08-1.55) and persistent rhinitis symptoms (OR, 1.26; 95% CI, 1.06-1.49)	Exposure assessed during first year of life, but it is possible that acute or more recent exposure could influence associations observed; attrition in cohort/loss to follow-up; primarily high SES families limiting generalizability; parent self-report of stressful family events and children's symptoms; does not consider other pollutants

(Continued)

TABLE E2. *(Continued)*

Author (year)	Exposure; Effect modifier	Study population	Main findings	Main limitations
Rosa et al[E15] (2017)	Daily prenatal $PM_{2.5}$ concentrations; Prenatal maternal stress (ie, negative life events)	Pregnant women in Mexico City followed until children were aged 48 mo (n = 552 mother/child dyads)	Greater exposure to $PM_{2.5}$ during the first trimester of pregnancy was associated with a higher risk of current (past year) wheeze at age 48 mo only among those children who were also exposed to high prenatal stress (>3 negative life events; RR, 1.35; 95% CI, 1.00-1.83 per 3.8 $\mu g/m^3$ [IQR] increase in $PM_{2.5}$)	Wheeze reported by mothers and lung function not measured; physician diagnosis of asthma not assessed; other environmental exposures not mentioned (eg, pests and mold); spatial resolution for air monitoring of 1 km × 1 km
Astell-Burt et al[E16] (2013)	Annual average $PM_{2.5}$ and PM_{10} concentrations; Experience of racism	A total of 4,775 adolescents in the Determinants of Adolescent Social wellbeing and Health (DASH) study in the United Kingdom (ages 11-13 y in wave 1; 14-16 y in wave 2)	Neither pollution exposure nor racism was associated with lung function. However, asthma prevalence was observed to increase with the quartile of exposure to $PM_{2.5}$ and PM_{10}, respectively. Except at the lowest quartile of $PM_{2.5}$ or PM_{10} exposure, a higher prevalence of asthma was observed among those who had also experienced racism as compared with those who had not	Lung function only assessed in wave 1; single-pollutant models/other pollutants not considered; potential underreporting of experience of racism; spatial resolution of pollutant estimates is unclear

BC, Black carbon; *IQR*, interquartile range; *RR*, risk ratio.