



Perspective

Asthma in the melting pot



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Introduction

America is becoming more diverse, with minority groups increasing at higher rates than whites. The health implications are vast, impacting all medical conditions. However, because asthma remains a persistent public health problem where disease burden is higher in minorities and low income populations, the need to find solutions is crucial.¹ These disparities or differences have been documented and defined to a significant degree in the literature, but what is lacking are solutions to tackle these differences.

The approach we must consider taking to thwart asthma disparities is described by Thomas et al.² This generations framework allows one to easily follow the progression of investigation: description of differences, explanation of differences, and solutions for differences. Asthma disparities research has spanned across the generations; however, a clear need exists for greater efforts in second- and third-generation research.

In this perspective, we highlight research advances in the asthma health disparities research spectrum and make recommendations of innovative approaches to achieve equity and social justice.

Current Asthma Research and Risk Factors for Disparities

Complex interactions are seen among asthma risk factors influencing its development and trajectory, including but not

limited to environmental exposures, diet, obesity, race/ethnicity, socioeconomic status, and genetics.

Environmental Exposures

The indoor environment's role in asthma etiology and management has been of growing interest in the past few decades. Questions remain regarding environmental remediation in asthma management because of publication bias; however, the current literature has consistently demonstrated that multifaceted interventions are effective, and exposures in nonresidential areas (eg, mold and mouse allergen in school) can significantly impact asthma.³

Although cockroach and mouse are both recognized as major asthma triggers in some urban communities, mouse sensitization and exposure were associated with increased acute health care visits, higher fractional exhaled nitric oxide, decreased forced expiratory volume in 1 second/forced vital capacity, increased prevalence of bronchodilator reversibility, even when both mouse and cockroach were present in high concentrations in the home.⁴ Interestingly, the School Inner City Asthma Study found that mouse allergen had high rates of detections in homes, but rates were significantly higher in schools.⁵ Mouse allergen exposure, independent of sensitization and home allergen exposure, was significantly associated with more asthma symptom days and decreased forced expiratory volume in 1 second percentage predicted, suggesting the school environment's importance in urban asthma. An ongoing school-specific environmental intervention is being conducted, targeting school-specific exposures found to be important, including mouse, particulates, and pollutants: NCT02291302.

Growing evidence also suggests that ambient air pollution contributes to poor asthma outcomes and asthma development. The mechanisms underlying this association include DNA methylation, increased allergen release, pollutants (eg, diesel fuel) acting

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as adjuvants in IgE-mediated mechanisms, enhanced allergenicity, and activated respiratory reflexes. Asthma exacerbations are significantly associated with higher concentrations of NO₂, SO₂, particulate air pollutants, and traffic-related air pollution.⁶ Minority and low-income communities are particularly at risk because of their proximity to dense vehicular traffic, highways, and industrial facilities resulting from residential segregation and redlining. Pregnant women exposed to ambient air pollution are at increased risk of having term low-birth-weight infants; and maternal asthma alone increases the risk of term low-birth-weight.⁷ However, insufficient evidence exists to conclude whether maternal asthma is an effect modifier of this relationship.

Environmental remediation has always been an important part of asthma management despite the conflicting evidence regarding its efficacy. Criticism has largely been related to cost and practicality, and whether changes truly associate with improved outcomes. Growing interest has been expressed in single-component environmental remediation studies, because teasing out which component contributed to asthma outcomes is difficult. Several recently published, promising single-component studies are available, such as Mouse Allergen and Asthma Intervention Trial,⁸ which evaluated integrated pest management and education targeting mouse allergen, and NO-Roach,⁹ which evaluated cockroach insecticidal bait. However, more studies with pragmatic designs are needed to evaluate integration into real-world settings and health services research approaches to support payer coverage of remediation.

Diet

Dietary influence on asthma is complex. Conflicting studies exist regarding associations of vitamin D and asthma. Some have demonstrated that low vitamin D levels correlate with poor asthma control; however, in the landmark VIDA study, vitamin D supplementation in adults failed to improve asthma control.¹⁰ More recently, dietary sugar intake has been investigated as a potential asthma risk factor, because its intake influences the pathogenesis of inflammatory conditions such as diabetes and hepatosteatosis. In a pre-birth cohort of mother–child pairs, higher prenatal maternal intake of sugar-sweetened beverages, and early childhood intake of fructose were associated with greater odds of asthma diagnosis in mid-childhood.¹¹ However, dietary influence on asthma is not well understood, and it is likely influenced by a delicate balance between anti-inflammatory and inflammatory nutrients. Further investigation on this mechanism is needed, particularly as dietary sugar intake can be affected by income, education, and food security, therefore having implications for disparities.

Obesity

Obesity is accepted as a risk factor for incident asthma and asthma severity. Mechanisms include dysanapsis (incongruence between lung and airway growth), increased mechanical load, and metabolic inflammation.¹² However, questions remain: At what age does being obese matter regarding lung development and asthma pathogenesis? How does weight loss affect lung and immune function? Is there a critical “age” window when a child’s increased fat mass could negatively impact their asthma prognosis? A need also exists for predictive tools to assess risk of asthma in these already high-risk groups. African Americans and Latinos have higher rates of overweight and obesity compared with whites. Similar to diet, how do social determinants of health interact with the association between obesity and asthma?

Advances in Research in SES

Despite the advances in our understanding of complex interrelationships of multiple asthma risk factors associated with

asthma disparities, unmet needs exist. Whether the mechanisms through which these factors lead to health outcome differences is unclear; innovative study designs will allow further elucidation. A need also exists for medical scientists to consider historical and social context influences. Additionally, evaluating other factors that are increasingly being examined in the social sciences and discussed in our current political landscape despite being a long-standing issue—such as discrimination and structural racism—is needed. Black race was associated with significant differences in asthma care patterns amongst white and Black patients in the same Detroit-managed care plan by Zoratti et al.¹³ Black patients had more asthma emergency department visits, fewer inhaled steroid prescriptions, more oral steroid prescriptions, more asthma admissions, and fewer asthma specialist visits, despite having equal health care access, suggesting that other factors were contributing to the differences.

Study Design

Traditional randomized controlled trials may not always be the most appropriate approach to health disparities research interventions. Communities will not see the value of not receiving the intervention for the sake of science. An appropriate alternative is the stepped-wedge design in which all subjects get the intervention, but the order in which the intervention is executed is randomized.¹⁴

Additionally, because intervention trials are not always feasible, several alternative analytic approaches can be used instead. Mediation analysis describes a chain of causal influences.¹⁵ It can be used to explain why and how an intervention would work, determinants of disparities, understanding intervention effectiveness, and determining the differential effectiveness of multifaceted studies’ components. Modeling is also a great alternative when randomized controlled trials cannot be done ethically or practically for public health policy research. It can allow one to simulate different assumptions before policy implementation.¹⁶

Dissemination and implementation (D&I) research are emerging areas of scientific inquiry developed out of the need to reduce the discovery-to-improved health gap.¹⁷ Dissemination and implementation research is a much-needed addition to our repertoire of scientific inquiry to reduce asthma disparities by informing how we can translate research findings into real-world practice and community settings. The Center for Translation Research and Implementation Science, one of the National Heart, Lung, and Blood Institute scientific divisions, was established to support and identify critical findings in this area. Patient-Centered Outcomes Research Institute (PCORI) has also recently supported investigators with funding to conduct dissemination and implementation research of PCORI-funded projects to ensure that patient-centered results are accessible and used.

Another area in need of more development is the use of biomarkers to measure the social disadvantage impact in asthma outcomes. Social scientists are evaluating the association between social adversity and biomarkers such as DNA methylation and telomere length.¹⁸ Over time individuals may age faster if they have experienced poverty or social deprivation. Perhaps asthma cohort studies can include assessments of social deprivation and collection of biological samples to elucidate its impact on asthma onset and morbidity.

Inner-City Asthma in the Age of Gentrification

The term *inner city asthma* was widely used in the 1980s and 1990s to refer to asthma health disparities. More recently, we have adopted the term asthma in *disadvantaged populations*, because it is all encompassing and includes underrepresented minorities, low-income groups, or individuals from suburban or rural

communities; *asthma disparities* is not limited to the inner-city or urban areas.

Moreover, in the age of urban gentrification, we see a demographic shift in inner-city communities, which impact our asthma disparities characterization. In the past, most inner-city areas were plagued by economic and environmental deprivation (eg, dilapidated buildings, rodent exposure, pollution). More recently, an influx of higher-income earners into urban areas has occurred, leading to improved community resources; thus, *inner city* is not necessarily synonymous with poverty and its associated conditions. Keet and colleagues¹⁹ conducted a study of children enrolled in Medicaid and found urban residence was not associated with a higher asthma prevalence, but it was associated with higher asthma morbidity. Reexamining these paradigms of asthma risk factors and performing rigorous analyses to uncover complexities among associations of neighborhood and asthma are important. It is not solely one's neighborhood but the segregation within the neighborhood that contribute to disease and health disparities.²⁰ To move the field of asthma health disparities forward, we need to create novel study designs to further capture and disentangle the relationship between race, socioeconomic status, and neighborhood to determine effects on asthma.

Stress, Racism, and Discrimination

In addition to the physical environment contributing to asthma, an emerging body of literature suggests that being a member of a marginalized group is associated with chronic stress and racism leading to inflammation. Inflammation may contribute to immunological changes and airway hyperresponsiveness. In prospective analyses conducted in the Black Women's Health Study, participants in the highest quartile, compared with the lowest quartile of self-reported racism, had a higher incidence of adult-onset asthma.²¹ In a pediatric study, African American youth who reported any perceived discrimination had greater odds of asthma and worse asthma control.²²

Genetics

Growing interest has been expressed in finding genetic variants associated with asthma to allow improved classification, such as phenotypes and endotypes. Because Latinos and African Americans have worse outcomes, finding genetic markers to clarify the sources of these differences has been emphasized. One area recently emphasized in pharmacogenetics is whether a genetic association with bronchodilator response is present. Mak et al²³ attempted to identify a genetic variant but concluded that the lack of diverse data despite extensive collaborative efforts made it impossible to replicate their findings.²³ We believe it is unlikely that genetic variants in minority groups will explain the sole source of asthma disparities; it is more likely socioeconomic disadvantage causes biological changes (DNA methylation, inflammatory effects); however, a significant first step is that researchers must make intentional, tailored efforts to diversify their study populations for genetics research. This issue also highlights the tension between precision medicine and macro-level or public health approaches to disease. We must be cautious about the current direction of genomics research and acknowledge that it cannot be used in isolation, without factoring in other health determinants.²⁴

Conclusion: Future of Research

Moving the needle on disparities research requires a systematic approach and going beyond documenting the problem. The PCORI has funded several multicomponent interventions to improve patient-centered outcomes for minorities with uncontrolled asthma. These projects encompass improving adherence to evidence-based asthma guidelines and health worker home visits

to enhanced outpatient care. The National Institute of Allergy and Infectious Diseases—funded School Inner City Asthma Study has also taken the innovative approach of evaluating the association between asthma symptoms and urban school environment exposures. These efforts will shed light on solutions for real-world settings involving stakeholder engagement.

We also must consider the impact of our current sociopolitical environment on health. Efforts to increase coal power generation and funding reduction for air quality regulation enforcement will cripple our progress in producing clean and renewable forms of energy and will increase air pollution.²⁵ Recent dramatic societal events have been associated with increased racial animosity, stress in targeted racial/ethnic groups, mortality risk, worry, and rumination, particularly over concern regarding health care coverage reduction.²⁶ Examining current events' effects on health outcomes will allow improved recognition for the causes of differences, and hopefully identify more areas to change with policy.

The future direction of asthma research entails moving beyond detecting problems to evaluating the causes of the differences and creating solutions. This direction will require more collaborative efforts across research disciplines and sectors, to enrich a body of research to inform and activate policy reform.

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