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Chapter 5

Asthma in the Disadvantaged: A Phenotype in Need of a Personalized, Multidisciplinary Approach to Therapy

Drew A. Harris, Caitlin Welch, Morgan Soper and Yun Michael Shim

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Abstract

Most patients with asthma can be managed with standardized, traditional therapies; however, 5–10% of patients suffer from disease that is difficult to control. Uncontrolled asthma disproportionally affects low income and racial minority patients. The disadvantaged asthma phenotype is defined by the presence of overlapping social, economic and environmental factors. These factors, such as environmental exposures in substandard housing or suboptimal adherence to controller therapy due to impaired health literacy are challenging to address in the clinic or inpatient setting. Personalized management of the disadvantaged asthma phenotype must target these interconnected factors through a multidisciplinary approach that includes longitudinal collaboration with community-based organizations, social workers and legal aid.

Keywords: asthma phenotypes, vulnerable populations, asthma disparities, health equity, social determinants of health

1. Introduction

1.1. Health disparities in asthma

Asthma is a heterogeneous clinical syndrome centered on symptoms of dyspnea, cough, wheezing or chest tightness, along with reversible expiratory airway obstruction or bronchial hyperresponsiveness. Although asthma affects 5–10% of the world's population, asthma disproportionally impacts communities of color and the socioeconomically disadvantaged.

In adults, asthma is more common in non-Hispanic blacks (8.7%) and Puerto Ricans (13.3%) than in whites (7.6%), and asthma-specific mortality is significantly higher in non-Hispanic blacks (25.4 per million, annually) compared to whites (8.8 per million, annually) [1]. In children, the prevalence of asthma is much higher in Puerto Rican Hispanics (19.2%) and non-Hispanic blacks (12.7%) than in whites (8%) or Mexican Americans (6.4%) [2]. Asthma-specific mortality in children is nearly eight times higher in non-Hispanic blacks than in whites [3]. In addition to racial disparities, socioeconomic disparities in asthma outcomes are widespread, with socioeconomically disadvantaged asthmatics less likely to utilize preventative care for asthma and more likely to rely on urgent and emergent health care for asthma [4]. Asthma outcomes are substantially worse for racial minorities with lower socioeconomic status [5].

1.2. The disadvantaged asthma phenotype

The term "asthma" envelops multiple phenotypes of disease. A phenotype is defined by the observable properties produced by the interactions of a genotype and the environment. In recent years, multiple asthma phenotypes have been defined by natural history, clinical and physiological features, biology and biomarkers and response to therapy [6]. Specific asthma phenotypes are important to consider in order to identify a targeted, personalized approach to asthma therapies.

1.3. Social and environmental factors relevant in the disadvantaged asthma phenotype

Numerous social and environmental factors can influence the underlying immunologic and inflammatory processes that define an asthma phenotype. In this chapter, we introduce the disadvantaged asthma patient phenotype, defined by specific genetic, socioeconomic and environmental factors commonly experienced by the disadvantaged asthma patient.

Although genetics play an important role in the susceptibility of African American and Puerto Ricans to poor asthma outcomes [7, 8], race and ethnicity are complex social concepts that are informed by genetic, cultural and historical factors [9]. As such, it is challenging to separate genetic factors from social, cultural and environmental factors driving asthma disparities. Racial and ethnic disparities in asthma are likely due to a combination of genetic factors as well as socioeconomic and environmental determinants of health (see **Figure 1**).

These socioeconomic and environmental factors, such as environmental exposures in substandard housing or suboptimal adherence to controller therapy due to impaired health literacy are challenging to address in the clinic or inpatient setting. Personalized management of the disadvantaged asthma phenotype must target these interconnected factors through a multidisciplinary approach that includes longitudinal collaboration with community-based organizations, social workers and legal aid. This chapter will start with a description of specific socioeconomic and environmental challenges most relevant to identify in the disadvantaged asthma phenotype. Following this, recommendations for a multidisciplinary approach to address modifiable factors and improve asthma outcomes in the disadvantaged asthma patient will be presented.

1.4. Indoor allergens in the disadvantaged patient's home

Racial disparities in allergic sensitization are an important contributor to racial disparities in asthma outcomes. Given the epidemic of allergy that has emerged over the last few decades,

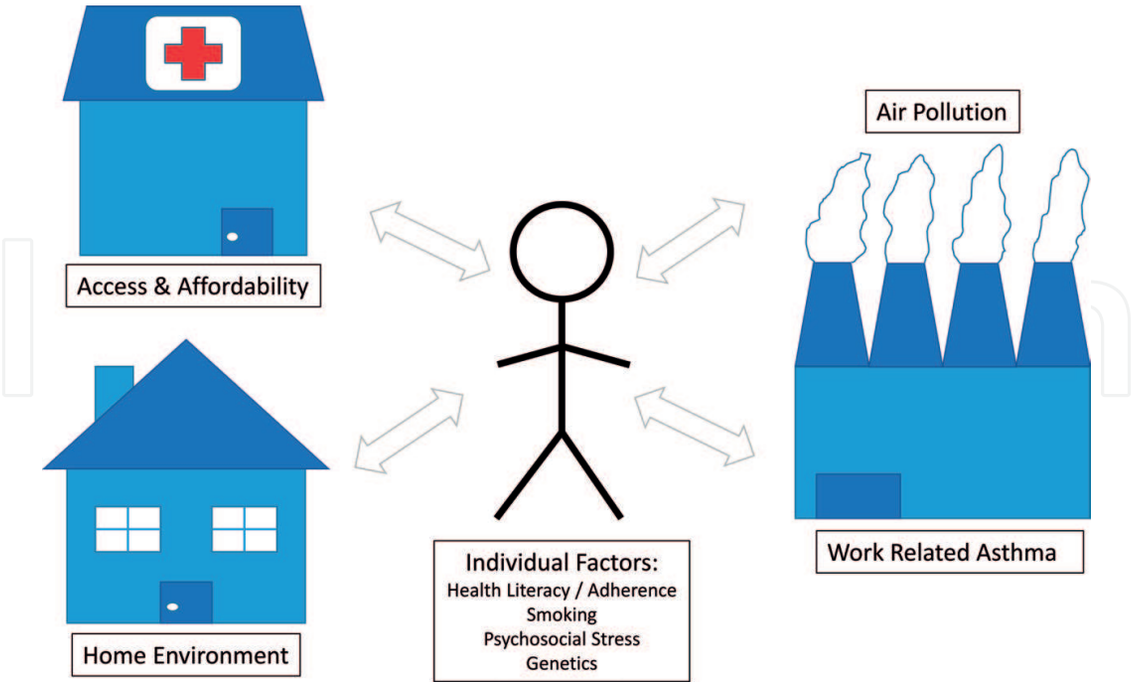

Figure 1. Multiple interconnected factors relevant to the disadvantaged asthma phenotype.

disparities in allergic sensitization are unlikely entirely explained by genetics alone. A combination of environmental exposures and host-susceptibility, such as epigenetic changes and gene-environment interactions, are important mechanisms to consider [10]. Within this context, the home environment is important to consider.

In the US, Black and Hispanic households are more than twice as likely as White households to live in substandard housing [11]. Living in substandard housing leads to increased exposure to indoor allergic asthma triggers such as cockroaches and mice. The increased exposures that racial minorities experience in substandard housing likely contributes to disparities in sensitization [12]. This has been demonstrated in multiple studies including: (1) The National Health and Nutrition Examination Surveys (NHANES) III study of 10,508 individuals, in which non-Hispanic black individuals were more likely than non-Hispanic white individuals to be atopic (62% versus 51.3%, OR = 1.6 95% confidence interval 1.2–1.8) [13]; (2) The Boston Epidemiology of Home Allergens and Asthma study, in which black women were 2.5 times more likely than white women to be sensitized to more than 3 allergens, including dust mite, dog, cat, cockroach, alternaria and aspergillus species [14]; and (3) A study in Hartford Connecticut in which Puerto Rican children with asthma were more likely than white children to be sensitized to indoor allergens such as cockroaches (OR 3.3 95%CI (1.7–6.4) and dust mites (OR 1.7 CI 1.2–2.4) [15].

Sensitization to indoor allergens such as cockroaches [15–17], dust mites [18], animals and the number of positive skin tests to allergens [19] has been associated with increased asthma morbidity and severity. Thus although the interplay between individual genetics and susceptibility to home environmental exposures is not yet fully understood, it is important to consider the exposure to high levels of indoor allergens as well as indoor allergy sensitization in identifying a treatment strategy for patients with a disadvantaged asthma phenotype.

1.5. Considerations for the disadvantaged patient living in a rural environment

Although asthma disparities have traditionally been associated with urban environments, there is increasing recognition that in the US, rural residents suffer from greater poverty and have less medical insurance than those living in urban areas [20]. Rural asthma patients are more likely to have to travel greater distances to travel to health care, which leads to increased asthma morbidity and mortality [21]. Within a month after an emergency room visit for asthma, rural adults are less likely than urban adults to have a follow up office visit for asthma [22]. Given the interconnectedness between poverty, access to care and many of the social and environmental factors discussed in this chapter, it is not surprising that recent evidence suggests that poverty and race, rather than residence in an urban location, are the major risk factors for prevalent asthma [9].

1.6. Work related asthma in the disadvantaged patient

In addition to indoor allergen exposures at home, exposures at work are an important but largely unappreciated determinant of asthma within disadvantaged populations [23]. Work-related asthma occurs in 20–50% of employed asthmatics due to exposures to dusts, fumes, cleaning products, mold, construction debris and temperature extremes [24]. Those who experience work-related asthma are more likely to become unemployed and have lost work time. In the disadvantaged asthma patient, work related asthma can have devastating financial consequences: job insecurity from work-related asthma can lead to worsened asthma measures [25], loss of insurance and healthcare access, and subsequent widened inequities [26]. The economic stress due to the cessation of work or reduced work hours due to asthma symptoms, and subsequent lower incomes can further worsen asthma outcomes [27–31]. Despite the prevalence and importance of work related asthma in disadvantaged populations, work related asthma is often unrecognized by both patients and providers [32].

1.7. Smoking and environmental tobacco smoke in the disadvantaged

Although overall smoking rates of declined in US adults from 20.9% in 2005 to 16.8% in 2014, there remains significant racial and socioeconomic disparities in smoke exposure. Individuals living below poverty (26.3%) smoke more often than those above poverty (15.2%). Households in poverty (36%) are more likely than households above poverty (22%) to have an in-home smoker. African Americans (21.5%), Hispanics (16.2%) and mixed race individuals (24.8%) are much more likely to smoke than Asians (13.3%) or Whites (12.9%) [33].

Cigarette smoking is associated with increased asthma incidence, increased asthma severity, worse asthma related quality of life, and increased risk of asthma hospitalizations [34]. Cigarette smoking may also reduce the responsiveness to inhaled corticosteroids, the cornerstone of controller therapy for asthma [35]. Cigarette smoke can cause divergent inflammatory responses depending on host-factors. Although racial and ethnic differences in susceptibility to tobacco smoke is controversial, African Americans have been shown in several studies to have increased susceptibility to cigarette smoke with worsened lung function [36] and more rapidly progressing lung disease [37] compared to Caucasians.

Environmental tobacco smoke increases risk for new onset asthma, especially in those with a genetic predisposition [38]. Maternal environmental tobacco smoke exposure during pregnancy is associated with childhood asthma, even if the mother does not smoke actively during pregnancy [39]. When exposed in childhood, environmental tobacco smoke is associated with increased asthma symptoms, missed school days, and worsened lung function [40]. Environmental tobacco smoke is further known to increase asthma exacerbations and hospitalizations in both children and adults [41, 42].

1.8. Outdoor air pollution disparities

In numerous studies around the world, lower socioeconomic individuals live in areas with increased air pollution [43–45]. Lower socioeconomic individuals are more susceptible to poor health effects from air pollution; high socioeconomic individuals have access to more resources to protect themselves from exposure to air pollution such as private transportation (versus relying on public transit), indoor versus outdoor work environments, access to climate control, including filtration for indoor environments [45]. In addition, there are racial disparities to outdoor air pollution exposure: even after controlling for urban area size and socioeconomic status, racial minorities are more exposed to outdoor air pollution than whites [46].

Air pollutants, including particulate matter, gases (ozone, nitrogen dioxide and sulfur dioxide) and mixed traffic air pollution cause oxidative injury to airways that leads to inflammation and remodeling which can lead to incident asthma. Air pollution may also increase the risk of sensitization and subsequent inflammatory responses to inhaled outdoor allergens [47]. Asthma is widely accepted to be aggravated by air pollution [48] and more recent evidence suggests air pollution may also contribute to new onset asthma in children [49]. In a study of 10 European cities, 14% of the cases of incident asthma and 15% of all asthma exacerbations were attributed to air pollution near roadways [50].

Given the disparate exposure and susceptibility to outdoor air pollution within the poor and racial minorities, and given the known impact of this exposure on incident asthma and asthma morbidity, air pollution is an important factor to consider in the disadvantaged asthma patient.

1.9. Psychosocial stress: increased in the disadvantaged patient

In the US, racial minorities and the SES disadvantaged experience higher amounts of psychosocial stress [51]. Poor neighborhoods have less shops, banks, health care services and transportation. Residents in these communities must then spend expend a greater amount of time and effort to address basic tasks of living [52]. Lower SES communities have higher community violence and crime rates [53], and greater crowding and exposure to noise [54]. In disadvantaged neighborhoods, smaller social networks [54], and decreased "social capital" (which describes a community's investment in public goods and community services), leads to increased community stress, such as violence [55], and decreased community resilience to stress. Low SES neighborhoods are also less likely to foster facilities for stress outlets such as regular exercise, which may lead to health compromising efforts to cope with stress such as smoking and substance abuse [52].

Although psychosocial stress is commonly associated with disorders that cause significant respiratory distress, such as vocal cord dysfunction [56], stress can also affect individual biology, disease progression and management of asthma [57]. Stress has been linked to increased asthma expression [58]. An acute stress may increase the risk of asthma exacerbations through an enhanced Th2 immune response [59]. Chronic stress potentiates airway reactivity and inflammatory response to asthma triggers, such as allergens and infections [58, 60]. Increased inflammatory cytokines (IL4, IL5, IFN-Gamma) and increased asthma symptoms have been linked to acute stressful events in children who also have chronic stress [61]. Chronic stress increases susceptibility to environmental pollutants on incident asthma [62, 63]. Stress reduces expression of the B2-adrenergic receptor, and in turn reduces response to bronchodilators, a cornerstone of asthma management [64].

In some studies, stress has been an even stronger risk factor than environmental exposures for asthma morbidity [65]. Multiple sources of stress, commonplace in the disadvantaged asthma patient, have been associated with increased asthma morbidity.

Although housing stress can lead to increased environmental exposures, an often-overlooked health effect of living in substandard housing is the deprivation, disadvantage, and emotional toll experienced by asthmatics and their households [66].

Housing stressors, including housing insecurity, inability to pay rent, living without heat or electricity, or trouble with a landlord has been shown to worsen asthma morbidity [67, 68]. Stress related to immigration and acculturation factors has also shown to worsen asthma morbidity and increase emergency room utilization for asthma [69]. Intimate partner violence has been shown to increase asthma incidence in affected families [70]. Individuals who experience higher severity of food insecurity develop worse asthma symptoms [71]. Stress related to perceived discrimination has also been shown to affect asthma morbidity in racial and ethnic minorities [72].

1.10. Suboptimal adherence and medication use

Inhaled corticosteroids improve long-term outcomes in asthma patients, and current guidelines recommend inhaled corticosteroids as the backbone of inhaled regimens for those with persistent asthma [73]. Despite this recommendation, in a nationally representative population study in the US, less than 1/3 of those who meet guideline based recommendations for treatment with an inhaled steroid are using them [74]. This unfortunate reality of practice is further magnified in disadvantaged asthma patients. In a study of 1485 children, black and Hispanic children with persistent asthma had significantly decreased odds of using inhaled corticosteroids compared to white children. These undertreated minority children had more than twice the odds of being hospitalized for asthma in the past year compared to white children [75]. In another study of 190 African American or Hispanic adults recently hospitalized with asthma and the majority of which living in poverty, less than half were utilizing inhaled corticosteroids [76].

2. A multidisciplinary approach to personalize asthma therapy within the disadvantaged asthma phenotype

Phenotypic categorization of asthma patients is essential to individualize and optimize asthma therapy. Patients with a disadvantaged asthma phenotype are no exception. The social and

environmental factors described above are essential to identify in order to individualize a treatment strategy that addresses the relevant social and environmental factors (**Table 1**).

With this in mind, how do we first identify these important factors in our disadvantaged asthma patients? Although there is an increasing trend in understanding social determinants of health in medical education [77], most medical providers are not trained or provided with sufficient resources to identify and address the social and environmental challenges faced by the disadvantaged asthma patient. Previous studies have suggested that many providers recognize the importance of social and environmental factors, but do not routinely screen for or identify them in their practice [78]. Time constraints and the perception that most social and environmental needs cannot be remedied are often cited by clinicians as reasons for not diagnosing social and environmental needs in their patients [79]. However, given the importance that these factors play in asthma control in the disadvantaged asthma patient, identifying these factors should be considered a cornerstone of the medical history in these patients.

Emerging evidence suggests screening for social needs and connecting patients to existing community organizations or services can significantly improve health outcomes [80]. There are many publically available tools accessible to providers to help identify social needs in clinical practice [81], including some that easily integrate into electronic health record systems [82]. These screening tools will help providers to identify patients with exposures in substandard housing, as well the presence of other social determinants of health known to impact asthma outcomes in the disadvantaged such as inadequate health literacy, the presence of interpersonal and community violence, housing, energy and food insecurity. Although work related asthma is not a focus of current social needs screening tools, a three-question survey tool has recently been endorsed by the American Thoracic Society and the National Institute of Occupational Safety and Health and should be considered in disadvantaged adults with new onset or newly worsening asthma [83].

A number of nonconventional interventions can be considered to address other factors discussed above that are known to exacerbate the burden and severity of asthma in patients with a disadvantaged asthma phenotype. A multidisciplinary team with unique expertise to personalize delivery of care and address the individual social, environmental, economic and medical care should be considered.

Management strategy summary for the disadvantaged asthma phenotype
Screen for modifiable social and environmental factors
Utilize a multidisciplinary approach to address identified social and environmental factors, including partnerships with social workers, legal aid and community resources
Ensure adherence to a guideline-based asthma medication regimen, including attention to access to care, cultural beliefs, inadequate health literacy, and disparities in prescribing patterns
Recognize work related asthma, assist patients with reducing workplace exposures and accessing benefits when unable to work due to asthma
Counsel and assist patients regarding smoking cessation

Table 1. Management summary.

First, many providers will recognize that social workers are often at the forefront of helping to ameliorate the social and environmental conditions that impact asthma. Social workers are indeed often able to connect patients to community, hospital or government resources to address the needs of disadvantaged patients. However, although social workers are vital in the care of many disadvantaged asthmatics, the complex factors described in this chapter will require active engagement by medical providers as well as collaboration with professionals outside of the traditional medical team.

As described above, ensuring adherence to a guideline-based asthma medication regimen, most often centered on an inhaled corticosteroid, is an additional critical component to treatment of the disadvantaged asthma patient. There are multiple explanations to the underuse of controller medications in disadvantaged asthma patients including limited access to care, cultural beliefs, inadequate health literacy, and disparities in prescribing patterns leading to suboptimal quality of care [75]. Despite these barriers, using a culturally sensitive approach through asthma education programs targeting disadvantaged asthma patients, multiple pediatric programs have successfully improved adherence to preventive therapies and improved asthma outcomes [84]. Identifying reasons for suboptimal adherence, such as fear of adverse effects, fear of addiction, cost, inconvenience or complexity of treatment regimens can lead to an individualized conversation, education and medication regimen changes that can improve adherence in the disadvantaged asthma patient [85].

In this context, ensuring access and affordability of prescribed asthma medication is essential. In the US, disadvantaged patients are challenged by the lack of currently available generic inhaled corticosteroids and bronchodilators. Although inhaled corticosteroids and bronchodilators have been the mainstay of asthma therapy for over five decades, most of these medications remain under active patents for specific device delivery mechanisms, as well as chemical formulations. For the uninsured patient, the cost of an inhaled corticosteroid and or any bronchodilators can be upwards of $4000 annually. Even for those with commercial insurance, the out of pocket deductible can approach $500 per year [86]. High cost of inhalers in general is due to at least two major historical events. First, when the Montreal Protocol entered into force in 1989 [87], chlorofluorocarbons (CFC) was phased out with fear that CFC in inhalers could contribute to destruction of the ozone layer. Even though the contribution from the CFC in inhaler was infinitesimal, the urgency based on an assumption that the ozone layer would repair itself within 50 years led to complete ban of CFC including CFC in inhalers. Subsequent development of hydrofluoroalkane (HFA) led to reformulated inhalers and disappearance of generic inhalers. Second, producing generic inhalers is a complex process unlike generic pills. Each inhaler carries multiple patents consisted of specific chemical formulation (including HFA) and the delivery system (protected under the FDA as an investigational device). Such challenge is highlighted by the recent difficulty in bringing out generic Advair to the U.S. by two pharmaceutical companies (Mylan and Hikma). Mylan and Hikma Pharmaceuticals were prepared to bring generic Advair to US marker in spring of 2017. However, the FDA extended complete response letters to both companies, in early 2017 which effectively put the possibility of generic Advair well into 2018. The details of why these companies failed to obtain FDA approval are still unclear.

Inadequate access and affordability of asthma treatments is not unique to the US. In a study of 24 countries, the median cost of an inhaled corticosteroid was 20% of average local monthly per

capita income [88]. Inhaled steroids are not even available to be purchased in some developing countries. One example is in India, where low-income patients with asthma do not have access to any inhaled corticosteroid through the public health care sector [89].

Second, collaboration with lawyers is an unconventional approach that holds promise to address multiple social and environmental factors that drive asthma morbidity within the disadvantaged asthma patient [90]. Although there is evidence to support home environmental interventions such as carpet removal, air cleaners, allergen impermeable covering for bedding and pest control to improve asthma outcomes [91, 92], in many instances, these interventions are insufficient in the disadvantaged asthma patient. For example, patients living with leaky pipes, mold, pests, inadequate heat, or wrongful evictions are more challenging environmental problems to address using conventional environmental interventions. Lawyers can advocate through legal recourse including tenant-landlord law, housing code enforcement, eviction and utility shutoff prevention programs to improve factors known to exacerbate asthma in the disadvantaged patient. Often funded in part by Legal Services Corporation (an independent nonprofit established by Congress in 1974 to provide support for civil legal aid to low-income Americans), there are over 133 independent non-profit legal aid programs, at least one in every state [24]. Despite this funding, there remains a substantial gap between low-income Americans' civil legal needs and available resources to address them [93]. Increasingly health systems are recognizing the importance of legal solutions to many social and environmental problems [94] and future research is needed to study the effectiveness of legal interventions and partnerships to improve health outcomes, such as in asthma.

Third, work-exacerbated asthma, as described above, is often unrecognized by patients, clinicians and providers and contributes to worse clinical and socioeconomic outcomes in the disadvantaged asthma patient [24, 95]. Clinicians must assume an active role to connect workplace exposures to asthma symptoms. Recognizing the challenges disadvantaged asthmatic workers face provides opportunities to help. Work related asthma can frequently be managed by reducing workplace exposures and/or providing work accommodations. If unable to work to due to work related asthma, clinicians can help the disadvantaged asthma patient access available benefits.

Fourth, given the known socioeconomic and racial differences in smoking and environmental smoke exposure and given the effects of smoke exposure on asthma outcomes, smoking cessation is an important goal in the disadvantaged asthma patient. Smoking cessation is associated with improvements in lung function and reduction in asthma symptoms [96]. However, Black and Hispanic smokers are less likely to make successful quit attempts than whites [97], which is in part, because black and Hispanics are less likely than white smokers to have been screened for tobacco use and advised to quit by health care professionals [98]. With this in mind, it is essential to ensure smoking cessation counseling and resources are integrated into the management of the disadvantaged asthma patient who smokes. Smoking cessation programs that target disadvantaged smokers and include referrals to community resources that address the socio-contextual mediators of tobacco use (including referrals to community resources to help with job counseling, educational opportunities and physical activity) is highly effective at improving smoking cessation rates compared to a more traditional approach [99].

3. Conclusions

Most patients with asthma can be managed with standardized, traditional therapies; however, 5–10% of patients suffer from disease that is difficult to control. Uncontrolled asthma disproportionally affects low income and racial minority patients. The disadvantaged asthma phenotype is defined by the presence of overlapping social, economic and environmental factors. These factors, such as environmental exposures in substandard housing or suboptimal adherence to controller therapy due to impaired health literacy are challenging to address in the clinic or inpatient setting. Personalized management of the disadvantaged asthma phenotype must target these interconnected factors through a multidisciplinary approach that includes longitudinal collaboration with community-based organizations, social workers and legal aid.

Conflict of interest

All authors have no conflicts of interest pertaining to the entirety of the above chapter.

Author details

Drew A. Harris*, Caitlin Welch, Morgan Soper and Yun Michael Shim

*Address all correspondence to: drew.harris@virginia.edu

Department of Medicine, Division of Pulmonary and Critical Care, Complex Airways Diseases Program, University of Virginia, Charlottesville, Virginia, USA

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