Clinical Reviews in Allergy & Immunology (2019) 57:391–402
https://doi.org/10.1007/s12016-019-08727-y

The Role of Environmental Controls in Managing Asthma in Lower-Income Urban Communities

Laura Conrad[1] · Matthew S. Perzanowski[2]

Published online: 22 March 2019

Abstract

Children living in lower-income urban communities are at much greater risk of developing asthma, going to the emergency department for an asthma attack and being hospitalized for asthma than children living in upper- and middle-income communities. For many asthmatic children living in urban communities, especially those with greater morbidity, the allergic pathway is important in the etiology of the disease. The stages of developing allergic disease can be divided into the onset of allergic sensitization, development of allergic disease and subsequent exacerbations, and it is useful to consider the relevance of interventions at each of these stages. Indoor allergens and environmental exposures are a major contributor to allergic disease, particularly among lower socioeconomic status, urban, minority communities. These exposures include allergens, environmental tobacco smoke, combustion by-products, and mold, all of which can play an important role in asthma progression as well as morbidity. These exposures are often not found in isolation and thus these concomitant exposures need to be considered when conducting environmental interventions. There have been numerous studies looking at both primary and tertiary prevention strategies and the impact on allergic sensitization and asthma with varied results. While the outcomes of these studies have been mixed, what has emerged is the need for tertiary interventions to be targeted to the individual and to reduce all relevant exposures to which an asthmatic child is exposed and sensitized. In addition, effective intervention strategies must also consider other social determinants of asthma morbidity impacting low socioeconomic, urban communities.

Keywords Interventions · Allergens · Environmental tobacco smoke · Mold · Combustion by-products

Introduction

Urban communities in the USA have a higher asthma prevalence than suburban and rural communities [1]. Even more striking, asthma prevalence and morbidity vary within many cities. Throughout this review, we will use New York City (NYC) to illustrate how certain communities bear greater burdens of asthma morbidity and the exposures that can cause and exacerbate asthma as a mechanism for us to examine the complexities of reducing asthma morbidity through individual and community level environmental interventions. In NYC, emergency department visits and hospitalizations for asthma vary by an order of magnitude among neighborhoods (Fig. 1) [2]. This variability correlates not only with indexes of poverty, but also with environmental and non-environmental determinants of asthma morbidity. The urban environment is complex and can be defined beyond just its physical built environment (e.g., housing structure, buildings, streets, open spaces, and infrastructure) and higher population density. Features of the urban community that can also affect health include multiple environmental and social exposures as well as access to health care and the segregation of poor communities. Differences in socioeconomic status and access to health care in urban communities clearly contribute to asthma morbidity.

Children living in lower-income communities are at much greater risk of developing asthma, going to the emergency department (ED) for an asthma attack and being hospitalized for asthma than children living in upper- and middle-income

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s12016-019-08727-y) contains supplementary material, which is available to authorized users.

✉ Matthew S. Perzanowski
mp2217@cumc.columbia.edu

[1] Division of Pulmonology, Department of Pediatrics, Columbia University College of Physicians and Surgeons, New York, NY, USA

[2] Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, 722 West 168th Street, 11th floor, New York, NY 10032, USA

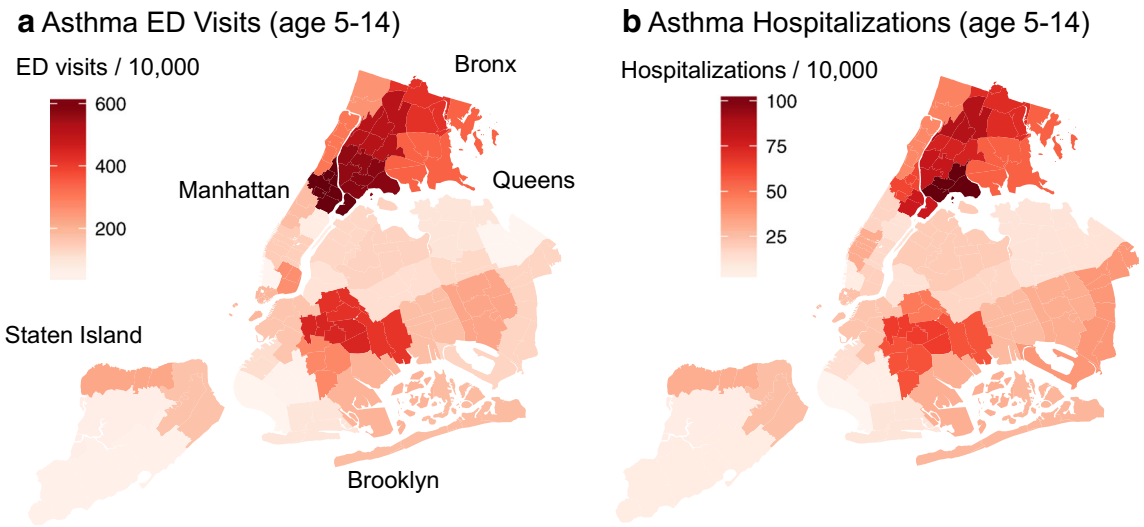

Fig. 1 Neighborhood rates of asthma **a** ED visits and b hospitalizations among 5–15 year-old children in New York City. Rates per 10,000 residents-based data reported by NYC Department of Health and Mental Hygiene reported for 2014 [2]

communities [3]. For many asthmatic children living in urban communities, especially those with greater morbidity, the allergic pathway appears to be important in the etiology of the disease [1]. The development of allergic disease can be conceptualized through what has been described as the "atopic march." With this paradigm, the steps to developing allergic disease are divided into the onset of allergic sensitization, the development of allergic disease and exacerbation of that disease, with the relevance of exposures evaluated separately for each step (Fig. 2). It is important to consider unscheduled medical visits (e.g., ED visits) and hospitalizations in this pathway, with environmental exposures involved in the steps that lead to the asthma attacks and health care access and utilization as modifying risk for these consequences.

Indoor allergens and other environmental exposures are a major contributor to asthma development and morbidity, particularly in individuals of minority groups in lower socioeconomic status living in inner-city homes. These exposures include allergens, environmental tobacco smoke, combustion by-products, and mold. There have been numerous studies looking at both primary and tertiary interventions and impact on allergic sensitization and asthma.

Allergens

Dust mite exposure has been associated with dust mite sensitization, which is a risk factor for the development of asthma [4]. Two major house dust mite allergenic proteins are Der p1 and Der f 1, from the species *Dermatophagoides pteronyssinus* and *Dematophagoides farinae*, respectively. There have been numerous studies looking at domestic exposure to these dust mite allergens and subsequent sensitization [5]. Wang et al. demonstrated in inner-city asthmatic children in the USA that having specific IgE antibodies to dust mites was associated with increased risk of asthma morbidity, which was defined as unscheduled visits, hospitalizations, and medication use, and that asthma morbidity increased in a linear manner with specific IgE levels [6]. Previous review articles have described that impermeable dust mite covers may help to reduce exposure levels to dust mites, although they have not been proven to be effective in preventing allergic disease. A systematic review in 2008 looked at the effects of multiple dust mite control measures on asthma outcomes and found successful mite exposure reduction with both physical and chemical interventions. However, these control measures did not reduce asthma

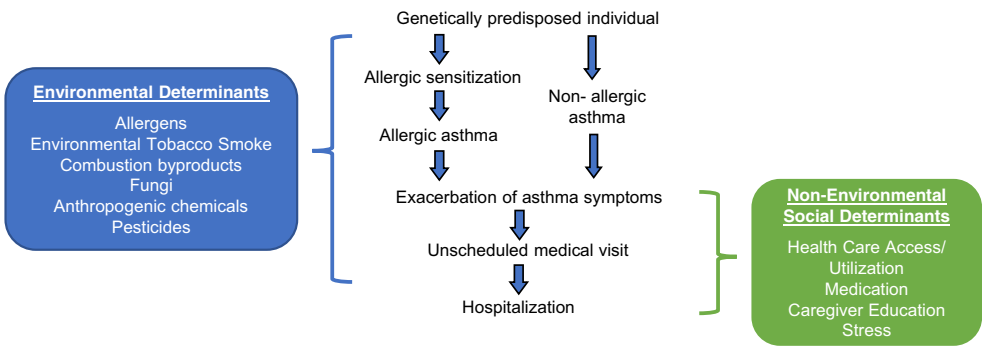

Fig. 2 Environmental and non-environmental determinants of the development exacerbation and consequences of urban asthma

morbidity, demonstrated with the most commonly used outcome of morning peak flow as a measure of asthma severity, which did not suggest any meaningful effect of interventions [7]. Additionally, a meta-analysis looking at impermeable dust mite covers and their primary and tertiary prevention of allergic disease concluded that the use of dust mite covers alone was not effective in preventing allergic disease or in decreasing allergic disease symptoms [8].

Cockroach infestations are associated with urban environments and cockroach allergy has been associated with increased asthma morbidity in inner-city children. German and American cockroaches are common and sensitization to allergens from both species is observed. A study looking at public housing residents in New York City found that 77% of residents had evidence of cockroaches, suggesting building level characteristics can affect high pest exposure [9]. In NYC, we found that cockroach sensitization, which is a strong risk factor for asthma, occurred more frequently among residents living in neighborhoods with a higher asthma prevalence compared with those living in neighborhoods with a lower asthma prevalence [10]. Figure 3 a illustrates domestic cockroach sightings in NYC, which highlights the large variability in frequency of cockroach sightings among NYC neighborhoods. In comparing the map in Fig. 3 a to those in Fig. 1, there is clearly a correlation between neighborhoods that have a higher asthma burden also having a higher burden of cockroaches in their homes. With respect to asthma morbidity, exposure to cockroach allergen has been found to be strongly associated with increased hospitalizations in children with asthma [9]. In an important study published in 1997, Rosenstreich et al. found that asthmatic children with both a positive skin test to cockroach allergen and a higher level of cockroach allergen in bedroom dust had the highest levels of asthma morbidity [11].

Integrated pest management (IPM), based on prevention, monitoring, and control as opposed to conventional chemical-based control, has been shown to be an effective approach to cockroach abatement. However, this can be costly and difficult to implement. One small randomized control trial in New Orleans showed that strategic placement of insecticidal bait significantly reduced cockroaches in homes and lead to improved asthma outcomes with decreased symptoms and health care utilization and improved lung function [12]. The findings from this study need to be replicated in other communities, but they suggest that less expensive interventions on cockroach allergen could be effective in reducing asthma symptoms.

Mice also contribute important allergens to the domestic environment. A national survey found detectable mouse allergen in over 80% of homes in the USA. However, the concentrations and detection frequencies in inner-city homes are often substantially higher than those found in suburban homes [13–15]. In addition to being important for pediatric asthma, rodent allergy is a well-known cause of occupational diseases. One study of employees at a mouse handling facility found that as many as half of non-mouse handling workers had significant levels of mouse allergen exposure [16]. Additionally, adults who work in these settings have been shown to transfer allergens from work environments to their homes. For example, the mattresses of laboratory animal workers have been found to contain significantly higher amounts of rodent allergen compared to controls who were not occupationally exposed [17]. Rat allergen has been studied less than mouse allergen. One multi-center study found rat allergen was detectable in only one third of dust samples from inner-city homes, which suggests it affects far fewer children than mouse allergen does [18]. These differences between mouse and rat allergen exposure can likely be explained by the behavior and nesting habits of the rodents, as rats tend to dwell outdoors.

In NYC, just as with cockroach, report of domestic rodent sightings is more common in neighborhoods where asthma morbidity is worse (Fig. 3b). Minority children living in lower-income urban environments exposed and sensitized to mouse have been shown to be at an increased risk of asthma severity [19]. Fishbein et al. found that among mouse sensitized children of Latino ethnicity, there were high health care utilization rates and increased asthma morbidity [20]. It has been shown that there is a linear dose-response relationship between domestic mouse allergen exposure and asthma morbidity among mouse-sensitized asthmatics [21]. This implies that environmental interventions to reduce significant exposure to mouse allergens would therefore be associated with a decrease in asthma morbidity. In a small study of 18 inner-city homes of asthmatic children, Phipatanakul et al. showed a significant reduction in mouse allergen levels using IPM, including vacuuming, pesticides, traps, and sealing of holes [22]. While they did not show improvement in lung function or asthma symptoms, this relatively small study was likely underpowered to show clinically relevant differences. Another study in inner-city school-aged asthmatics showed that rodent-specific environmental interventions reduced mouse allergen levels and improved asthma-related sleep and activity disturbances; however, there was no reduction in wheeze or health care utilization [23]. In a year-long randomized control trial, it was found that professionally delivered IPM plus pest management education intervention targeted at mouse allergen was not more effective than education alone in reducing asthma symptoms in mouse-sensitized and exposed children and adolescents with persistent asthma [24]. However, in this study, mouse allergen decreased in both the IPM and education group and decreases in mouse allergen exposure were associated with improvement in asthma morbidity, suggesting that mouse allergen reduction could be beneficial in reducing asthma morbidity.

In addition to exposure of allergens themselves, the timing of exposure to allergens and other exposures appears to play an important role in the pathogenesis of asthma. The age of onset of sensitization seems to play a significant role, with aeroallergen sensitization at a younger

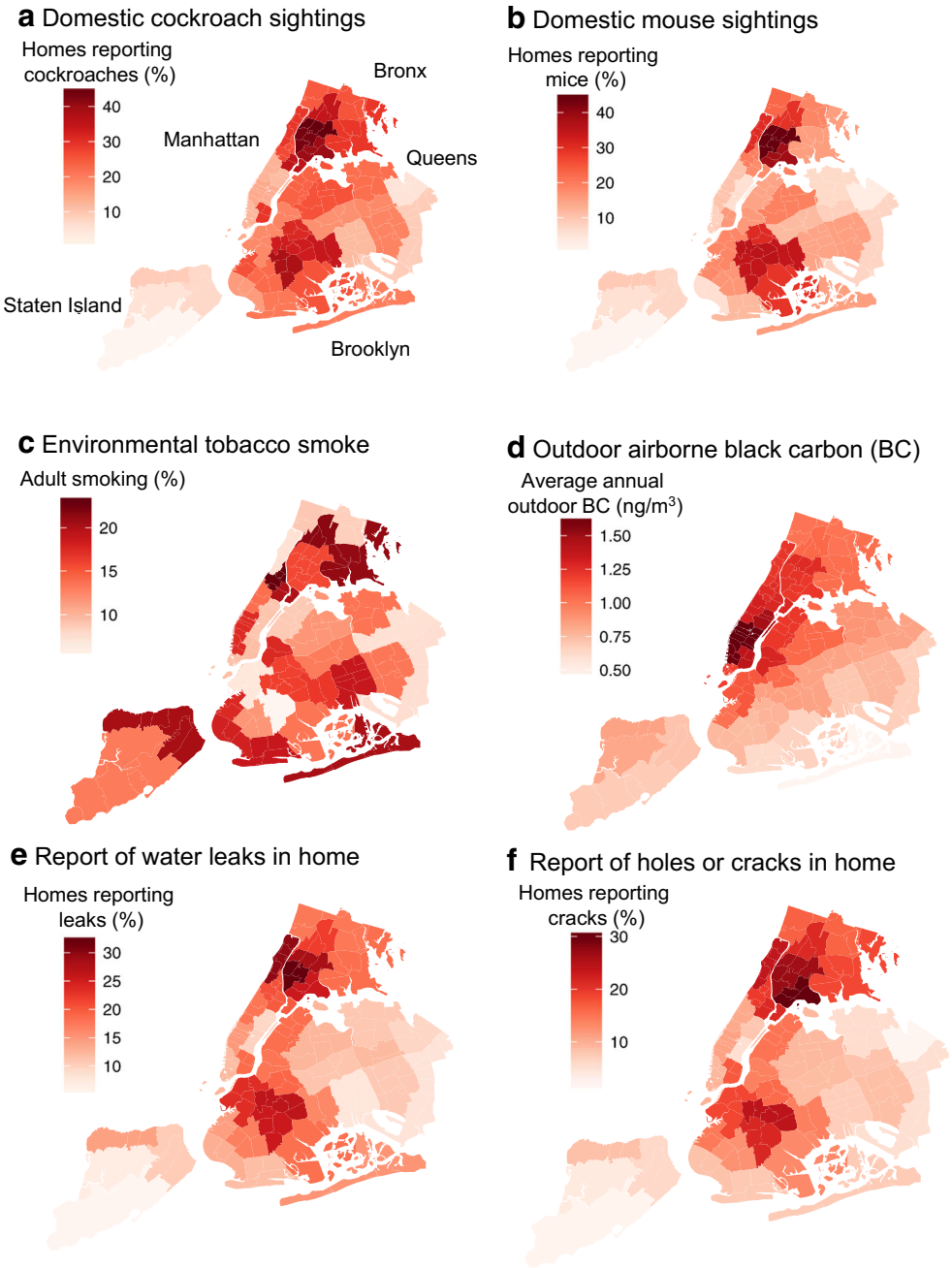

Fig. 3 **a**–**f** Distribution of environmental exposures related to asthma by neighborhood in NYC. Data for 2012–2014 reported by NYC Department of Health on their Environment and Health Data Portal [2]. Greater detail on survey methods available in supplementary online material

age being associated with increased risk of childhood asthma [25]. In a study based in lower-income, urban communities, exposure to cockroach, mouse, and cat allergens during infancy was associated with lower risk of asthma at age 7 years [26]. In contrast, among a cohort of NYC children, we observed that early life exposure to cockroach allergen was associated with increased risk of developing sensitization to cockroach by school age, an association significantly enhanced by co-exposure to the combustion by-products, polycyclic aromatic hydrocarbons [27]. Also, a pooled analysis from the European birth cohorts found no association between the presence of cats in the home during infancy and asthma at school age [28]. Another early life exposure study found that children exposed to high levels of dust mite allergen at age 2 to 3 months had a threefold increase in the odds of asthma by age 7 compared to those exposed to low levels [28]. There has also been some evidence to suggest that early life exposure to allergen and bacteria can have a protective effect on wheeze. For example, Lynch et al. found that in an inner-city environment, children with high levels of exposure to allergens such as cockroach and mouse as well as bacteria during the first year of life were less likely to develop recurrent wheeze and allergic sensitization [29].

Environmental Tobacco Smoke

Environmental tobacco smoke (ETS) is known to increase the prevalence of both upper and lower respiratory tract illnesses [30]. A systematic review and meta-analysis showed that exposure to passive smoking, especially pre- or postnatal maternal smoking, increases the risk of wheeze and the incidence of asthma at age 5 to 18 years [31]. A pooled analyses from 15 European birth cohorts found that children of mothers with passive smoke exposure during pregnancy were more likely to wheeze at age 2 years [32]. In Fig. 3 c, we show that NYC neighborhoods with higher asthma prevalence, such as Harlem and the South Bronx, also have increased frequency of adults smoking, which likely indicates that asthmatic children in these communities are at increased risk for ETS exposure.

Although it is clearly evident that ETS is a major risk factor for asthma, studies have shown that it is difficult to effectively reduce ETS. A Cochrane review of smoking control programs for reducing children's exposure to ETS showed that parental education and counseling programs have not been effective [33]. Similarly, a minimal intervention study to reduce secondhand smoke exposure among children with asthma from low-income minority families was shown to be ineffective [34]. One randomized control trial looked at use of air cleaners and a health coach to reduce particulate matter and found that air cleaners in homes of children with asthma lead to a significant reduction in indoor fine particulate matter (PM 2.5) concentrations and increased symptom free days; however, there was not a decrease in air nicotine or urinary cotinine [35]. Similarly, Lamphear et al. showed that HEPA air cleaners led to significant reductions in unscheduled asthma visits and levels of fine airborne pollutants, but did not decrease asthma symptoms, cotinine levels, or exhaled nitric-oxide levels [36].

There have also been larger scale public health campaigns in recent years to help reduce ETS exposure. A Cochrane review of institutional smoking bans showed that there has been a reduction in secondhand smoke exposure [37]. Recently, the US Department of Housing and Urban Development has mandated that public housing authorities prohibit smoking in residential apartments to reduce secondhand smoke exposure. Although implementation has been controversial, there is great potential for improvement in health outcomes. A study looking at the initiation of this policy and public housing in Philadelphia showed reduced secondhand smoke exposure. [38]

Community level interventions may be one solution to reducing ETS. Overall, in the USA, the prevalence of cigarette smoking among adults has been found to be highest among those living in rural and urban areas and lowest among individuals living in small and large metropolitan areas [39]. A recent study looking at trends in rural and urban cigarette smoking in the USA found that rural areas have a higher smoking prevalence than urban areas and moreover that the trend in cigarette use is declining more quickly among urban populations than in rural population [40]. The authors speculated that these trends may in part be explained by the ability to implement tobacco control and regulatory policies better in more densely populated areas [40]. In a study of ten US states, urban areas and areas with high per capita income were more likely to have strong smoke-free laws [41].

In addition to traditional tobacco smoke, electronic cigarettes (EC), also known as "e-cigarettes" or "nicotine delivery systems", have recently become popular; however, their safety, and the health effects from passive exposure has not been well studied [42]. ECs are battery-operated devices which use a heating mechanism to vaporize a liquid into an aerosol that is then inhaled. The inhaled aerosol typically contains nicotine, propylene glycol, and other chemicals. The safety profile of the inhaled aerosol has not been well established, although several studies have demonstrated that EC vapors contain not only nicotine, but other potentially toxic substances such as small amounts of heavy metals, known carcinogens, and ultra-fine particles [43]. A systematic review found that although risks of passive exposure to EC vapor is likely less than ETS exposure, the pollutants from EC vapors are at concentrations that are associated with potential adverse health effects [42].

Although there has been a decline in rates of cigarette smoking in youth over the last decade, there has been a dramatic increase in the use of EC among young people in the last 5 years and the use of e-cigarettes is now higher among high school students than adults [44]. One recent study found that among current high school cigarette smokers, those in urban schools were nearly twice as likely as rural students to also use e-cigarettes [45].

The long-term public health effects of ECs are not known and the regulation of EC use varies across the USA. The use of ECs in otherwise "smoke free" environments is not universally controlled. One study looking at indoor air quality at a 2-day EC event held in a large hotel room found that PM 2.5 concentrations were higher than in previously reported measures in hookah cafes and bars that allow cigarette smoking [46]. As of 2017, 12 US states had prohibited the use of ECs in venues in which conventional cigarette smoking was prohibited. [47]

Combustion By-products from Fossil Fuel

There is substantial evidence that exposure to the main components of combustion-related air pollution including, nitrogen dioxide, fine particulate matter, black carbon, and sulfur dioxide, is correlated with subsequent childhood asthma development [48]. A study in Southern California showed that exposure to air pollution (specifically nitrogen dioxide, acid

vapor, and elemental carbon) was associated with subsequent deficits in lung function among children ages 10 to 18 years [49]. Another study in Mexico City showed that long-term exposure to particulate matter less than 10 μm, nitrogen dioxide, and ozone was associated with lung function deficits over a 3-year follow-up period among school-aged children [50]. Nitrogen dioxide (NO_2) is a pollutant gas by-product of combustion from outdoor sources such as traffic and indoor sources such as gas stoves, heaters, and poorly ventilated furnaces and fireplaces. It has been shown to affect both allergic and non-allergic children with asthma [51]. A randomized intervention study focusing on gas stoves as the primary target of remediation of indoor NO_2 concentrations found reduction of up to 50% in indoor NO_2 concentrations when a gas stove was replaced with an electric stove [52]. They also demonstrated a 27% decrease in median kitchen NO_2 with placement of air purifiers with HEPA and carbon filters in the home [52]. An intervention study in New Zealand showed homes receiving more efficient heating devices in place of unflued gas heaters had lower NO2 concentrations than control homes [53]. Additionally, a randomized control trial of installing non-polluting, more effective home heating in households of children with asthma in New Zealand found no significant change in lung function, but a reduction in asthma symptoms including sleep disturbed by wheeze and nighttime cough [54].

Other major gaseous pollutants include ozone and sulfur dioxide. Sulfur dioxide (SO_2) is emitted from burning of sulfur-containing fossil fuels. Exposure to SO_2 has been shown to cause bronchoconstriction and associated with increases in respiratory morbidity [55]. Ozone is a potent oxidizing agent that is formed by a photochemical reaction between sunlight and pollutant precursors, particularly in warmer temperatures. Ozone exposure has long been shown to result in airway inflammation and hyper-responsiveness. One study demonstrated that chronic higher exposure levels of ozone in US metropolitan counties were associated with the prevalence of current asthma diagnosis and asthma exacerbations in the previous year [56]. Another study showed that ozone levels in Southern California contribute to an increase in the risk of hospitalization for children with asthma [57].

Black carbon is a major component of fine particulate matter (PM 2.5) in urban communities, which comes from incomplete combustion of fossil fuels. Its sources are primarily outdoors, such as truck traffic, but can also come from the burning of oil in residential boilers. It has been shown that children living in urban areas, such as the South Bronx, have higher exposure to traffic emissions, which is related to the built environment and highway truck traffic [58]. The burning of residual oil in boilers has also been a major source of ambient black carbon. In NYC, ambient black carbon is higher in neighborhoods with higher asthma prevalence and indoor black carbon has been associated with increased fractional exhaled nitric oxide in children, a biomarker of airway inflammation [59]. A prospective birth cohort of children in NYC showed a positive association between residential indoor levels of PM 2.5 and the development of new wheeze among children 5 to 7 years old [60].

Polycyclic aromatic hydrocarbons (PAHs) result from incomplete combustion of organic matter, such as coal, petroleum, and gasoline, and are another air pollutant that has been linked with asthma. One study found that obese young children were more likely to develop asthma in association with greater exposer to traffic-related air pollutants, including PAHs, from combustion sources compared with non-obese counterparts [61]. It has also been reported that young children in NYC who are repeatedly exposed to high PAH during prenatal and early childhood periods may be at greater risk of having asthma [62]. Another recent study highlighted that small-scale spatial variations related to the urban built environment may influence personal exposure to PAHs by demonstrating that ambient PAHs are significantly higher when measured from a window adjacent to a street compared to a window adjacent to an alley [63].

Overall, the major sources of these pollutants are from motor vehicles, power plants, and burning oil for heat. The built environment of cities, therefore, can contribute to exposure to these combustion by-products. One study found that closer residential proximity to a major roadway was associated with poorer asthma control in school-age children, with asthma control being defined as wheezing episodes requiring short-acting bronchodilator use that occurred more than twice weekly [64]. In addition, the distribution of local combustion by-product sources is not evenly distributed in the urban environment. In NYC, many neighborhoods with a higher asthma burden also have higher airborne black carbon (Fig. 3d), although the correlation between this environmental exposure and asthma morbidity on an ecological level are not as striking as for cockroaches and mice. A study from Atlanta, Georgia, found that neighborhood-level socioeconomic status (SES) is also a factor contributing vulnerability to air pollution-related pediatric asthma morbidity. They demonstrated a stronger association between neighborhood-level air pollution and ED visits for asthma among children living in communities with extremely low neighborhood SES compared to higher SES neighborhoods [65]. Although environmental regulation has helped to reduce emissions of pollutants, it is evident that additional large-scale policy initiatives to develop alternative power sources are still needed [66].

Mold

Another indoor environmental exposure that is an important risk factor for childhood asthma development and exacerbation is mold (i.e., fungi). Report of home dampness and presence of mold have been associated with asthma [67]. Again,

on an ecological level in NYC, we see that many of the neighborhood reporting higher rates of ED visits and hospitalizations for asthma also have a higher report of water leaks in their homes (Fig. 3e). In a birth cohort study, infants exposed to high concentrations of mold species common among water-damaged buildings were more likely to have asthma when they reached school age [68]. In addition, a case-control study that investigated objective measurements of indoor mold from both bedroom mattresses and play area floors found a significant association between mold exposure and current asthma in school-age children [69]. A recent meta-analysis showed that increased levels of certain molds pose a respiratory health risk in susceptible patients, with evidence of increased levels of the most common fungal allergens (*Penicillium*, *Aspergillus*, *Cladosporium*, and *Alternaria* species) being associated with increased exacerbation of current asthma symptoms in children and adults [70].

Interestingly, although exposure to indoor molds has been thought to influence the development of future asthma, there has been some recent evidence to suggest that the increased diversity of mold exposure may be protective. One study looking at the urban dust microbiome found that exposure to greater fungal diversity shortly after birth was associated with lower risk of development of wheezing and aeroallergen sensitization in later childhood [71]. Another study looking at indoor fungal diversity in schools found that exposure to higher fungal diversity was inversely associated with allergic sensitization; however, they did not observe the same association with asthma [72].

Indoor environmental factors that influence the presence of dampness and the concentration of molds within homes include modifiable risk factors such as residential characteristics, the built environment, and behavior, which, when altered, can in turn lower allergy burden [73]. In a small trial, Kercsmar et al. found that construction remediation targeting the root causes of indoor home moisture and mold (e.g., reduction in water infiltration, removal of water-damaged materials, and ventilation/heating/air-conditioning alternations) resulted in a reduction in asthma symptom days and health care utilization among inner-city asthmatic children with indoor mold exposure [74]. Another study showed that a comprehensive program including community health care worker in-home education in combination with weatherization (defined as home air tightness measurements, combustion safety testing, heating system assessment, and assessment of moisture-related problems) and healthy home interventions to reduce asthma triggers lead to a statistically significant reduction in visible mold and improved asthma control and caregiver quality of life [75].

In recent years, there has been some controversy regarding fungal allergy relating to a condition popularly termed "toxic mold syndrome" or "mycotoxicosis." Much of this debate has centered on exposure to *Stachybotrys chartarum*, sometimes referred to as "toxic mold" or "black mold." *Stachybotrys* tends to grow in water-damaged environments and is a marker for damp environment as it thrives on long-term moisture [76]. *Stachybotrys* was first reported to cause toxic reactions in farm animals in the 1930s and farm workers in the 1940s. In the 1990s, there was a rise in concern about indoor exposure in humans after a report linked exposure to pulmonary hemosiderosis in infants, which presumed myotoxins from *Stachybotrys* to be the cause of symptoms. However, additional analysis later showed that exposure to ETS and *S. chartarum* had equally significant associations indicating that although *S. chartarum* could not be excluded as the cause for the cases of pulmonary hemosiderosis, it was also not the proven cause [76]. The term "toxic mold" became popularized in recent decades after fungus-related legal actions were taken regarding building contamination and presumed health effects of "black mold." Mold-related symptoms are most likely to occur as a result of allergic sensitization, transient irritation, or infection; however, there has not been any scientific medical evidence to support building-related mycotoxicosis [77].

Other anthropogenic chemicals found in the urban environment have been linked to asthma outcomes in observational studies, including the phthalates and bisphenol A [78–80]. It may be important to consider some of these exposures in future interventions to reduce asthma development, although avoidance measures can be difficult with these ubiquitous chemicals.

Implementation of Interventions

Thorough implementation of environmental interventions to help manage asthma has been demonstrated in both home-based studies as well as through community health workers. A home-based environmental intervention study among inner-city children with atopic asthma found that individualized, home-based, comprehensive environmental intervention decreased exposure to indoor allergens resulting in reduced asthma-associated morbidity; however, it is important to note that in this study, both the intervention and control group had reduction in levels of cockroach and dust mite allergens in the bedroom [81]. Takaro et al. suggested in a pilot study that asthma-friendly home construction reduces exposure to indoor asthma triggers and improved asthma morbidity. These "breathe-easy" homes included optimized exterior moisture-proofing, flooring, and finishes that minimized dust accumulation and off gassing, and energy efficient ventilation with filtration. They demonstrated significant reduction in exposure to mold, rodents, and moisture; nonetheless, compared to the asthma control intervention who received in-home asthma education alone, there was only statistically significant improvement in nighttime symptoms and not other asthma outcomes [82]. Another recent study by Winn et al. evaluated

the use of commercially available in-home test kits by parents to quantify dust mite allergen levels in homes of mite allergic children. They concluded that in-home test kits and education may positively influence behaviors and attitudes towards dust mite reduction strategies and help reduce residential dust mite allergen levels. Interestingly, in the intervention homes, where test kits were used in addition to education, dust mite allergen concentrations in the child's bedroom and living room floors were reduced over time compared to control homes, which only received education; although, this finding was not seen for concentrations in the child's bed [83].

Another means of implementation of environmental interventions has been through community health workers. Krieger et al. demonstrated community health care workers reduced asthma symptom days, urgent visits, and simultaneously improved caregiver quality of life [84]. In a multicenter prospective study, home visits by trained counselors, Medical Indoor Environment Counselor (MIEC), had positive effects on compliance with advised mite reduction as well as reduction in mite allergen exposure levels on mattresses and carpets [85].

Although the rationale behind allergen avoidance interventions is logical, the data regarding efficacy of these interventions on allergic sensitization and asthma has not been consistent. For example, it has been shown that inner-city adults and children exposed and sensitized to household allergens on optimal asthma guideline therapy that had targeted allergen avoidance measures implemented showed decreased levels of household allergens, but did not demonstrate a reduction in need for asthma control pharmacologic therapy [86]. Furthermore, an intervention study looking at avoidance of dust mite and cockroach allergens in urban asthmatics showed that although there was a decrease in allergen concentrations and acute visits among the active allergen avoidance group, these findings were also observed in the placebo avoidance group [87]. Still, in both of these studies, as well as the randomized control trial of mouse allergen described earlier (where intervention and education control had decreases in mouse allergen), it is important to understand that reduction in allergen exposure in the control groups could have led to improvements in symptoms in both intervention and control groups. While this may have led to an overall null effect of the study intervention versus the control in improvement in asthma symptoms, it does not disprove the connection between domestic allergen reduction and improvement in asthma morbidity. However, it does complicate the clinical and public health recommendations.

O'Connor puts forth multiple justifications for the ineffectiveness of specific allergen avoidance interventions [88]. First, there may be failure to sufficiently reduce an exposure. For example, Brunekreef et al. noted in a birth cohort study looking at the relationship between atopic family history and exposure of newborn to dust mite allergen that baseline mite allergen levels on mattresses of newborns and parents were very low, which was possibly attributed to the unusual cold and dry weather the years of study initiation [89]. Additionally, if the individual is not sensitized or exposed to the targeted allergen of the intervention, there will not be a significant improvement. Location is another consideration, as reducing exposure in one location, but not all, will likely be ineffective. This can be seen on a larger scale with evidence to suggest that the home environments are not the only important site for allergen exposures. One study found that there were substantial levels of mouse allergen levels in urban schools and that concentrations of allergen in schools were higher when compared with concentrations in homes [90]. Hauptman et al. reviewed literature assessing the health effects of environmental exposures outside of the home on pediatric asthma morbidity and concluded that the school environment is a significant reservoir for allergens and pollutants [91]. On a smaller scale, impermeable dust mite covers for mattresses and pillows may not adequately reducing dust mite exposure in the home, as there are other common sites, such as carpets and furniture, that may contribute to high levels of dust mites. Finally, if the intervention only reduces one allergen, there may still be significant exposure to additional allergens or environmental factors.

As demonstration of the potential effectiveness of considering these multiple factors in designing an environmental intervention, a multi-center study enrolled 937 atopic children living in seven US cities [50]. The children were randomized to intervention and control groups. The intervention group received environmental interventions targeted only to those allergens that the child was sensitized and exposed to. In addition, environmental tobacco smoke was targeted. This individualized approach led to significant, sustained reduction in allergen (beyond the 1-year study period) and improvement in asthma symptoms.

It is also important to consider that there are multiple exposures within a given urban community. As illustrated in Fig. 3, it is apparent that these multiple exposures are common within urban communities, specifically within certain neighborhoods. In addition, report of holes or cracks in the walls of homes was also more common in these neighborhoods (Fig. 3e). Holes and cracks can contribute to cockroach and mouse infestation, but also suggest structural issues that may be difficult to intervene on in individual patients. Given these concomitant exposures and other sociodemographic-related risk factors, environmental interventions targeted within an individual's home may not be adequate to reduce exposure and sensitization given that a child may spend significant time in other settings within that community, such as a school. In addition, recognizing the non-environmental determinants for intervention is also essential, which may include access to health care, caregiver education, and psychosocial stress.

Future Directions

It is clear that the results of environmental interventions have been varied. However, there is evidence to suggest that identification of specific allergic sensitization in an individual coupled with targeted interventions to reduce allergens has been helpful and may be important in clinical management of these patients. It is not only essential to target specific allergens based on patient's sensitization, but also interventions need to have substantial allergen reduction to lead to a clinical effect. Most successful interventions to reduce allergen exposure and subsequently reduce asthma morbidity have been multifaceted, which can be difficult to translate into clinical application. It is apparent that future research is necessary to help determine which components of environmental interventions can be implemented efficaciously in clinical practice.

There is also a need to examine cost-effective interventions and their translation into public health policies to have an impact on asthma morbidity. There have been some advances with policies helping to reduce air pollution emissions in recent years. For example, NYC has implemented policies to phase out the use of residual heating oils that have historically contributed greatly to airborne combustion related by-products in NYC. Additionally, the Department of Housing and Urban Development has instituted smoke-free policies in public housing, which has shown success in reducing second-hand smoke exposure. Public health policies for integrated pest management and large-scale mold remediation are additional areas of interest to explore how best to implement at a policy level.

It is evident that future research is still needed to identify effective environmental interventions that reduce allergen exposure and asthma morbidity and that can be successfully translated into clinical practice. Large-scale environmental interventions also need to be evaluated on a community and population level to better understand how these interventions can be effectively translated into public health policy and asthma outcomes.

Compliance with Ethical Standards

Dr. Conrad reports no conflict of interest. In 2017, Dr. Perzanowski received an honorarium for speaking at a training symposium sponsored by Indoor Biotechnologies. No primary research was conducted for this review article and thus did not involve human participants or informed consent.

References

1. Togias A, Fenton MJ, Gergen PJ, Rotrosen D, Fauci AS (2010) Asthma in the inner city: the perspective of the National Institute of Allergy and Infectious Diseases. J Allergy Clin Immunol 125(3): 540–544
2. Environment and Health Data Portal: NYC Department of Health and Mental Hygiene (2018) http://a816-dohbesp.nyc.gov/IndicatorPublic/publictracking.aspx Accessed on 25 Nov 2018
3. Garg R, Karpati A, Leighton J, Perrin M, Shah M (2003) Asthma facts, Second edn. Department of Health and Mental Hygiene, New York City
4. Arshad SH (2005) Primary prevention of asthma and allergy. J Allergy Clin Immunol 116(1):3–14 quiz 5
5. Simpson A, Custovic A (2009) Prevention of allergic sensitization by environmental control. Curr Allergy Asthma Rep 9(5):363–369
6. Wang J, Visness C, Calatroni A, Gergen P, Mitchell H, Sampson H (2009) Effect of environmental allergen sensitization on asthma morbidity in inner city asthmatic children. Clin Exp Allergy 39: 1381–1389
7. Gotzsche PC, Johansen HK, Schmidt LM, Burr ML (2004) House dust mite control measures for asthma. Cochrane Database Syst Rev 4:CD001187
8. Arroyave WD, Rabito FA, Carlson JC, Friedman EE, Stinebaugh SJ (2014) Impermeable dust mite covers in the primary and tertiary prevention of allergic disease: a meta-analysis. Ann Allergy Asthma Immunol 112(3):237–248
9. Rabito FA, Carlson J, Holt EW, Iqbal S, James MA (2011) Cockroach exposure independent of sensitization status and association with hospitalizations for asthma in inner-city children. Ann Allergy Asthma Immunol 106(2):103–109
10. Olmedo O, Goldstein IF, Acosta L, Divjan A, Rundle AG, Chew GL, Mellins RB, Hoepner L, Andrews H, Lopez-Pintado S, Quinn JW, Perera FP, Miller RL, Jacobson JS, Perzanowski MS (2011) Neighborhood differences in exposure and sensitization to cockroach, mouse, dust mite, cat, and dog allergens in New York City. J Allergy Clin Immunol 128(2):284–292 **e7**
11. Rosenstreich DL, Eggleston P, Kattan M, Baker D, Slavin RG, Gergen P, Mitchell H, McNiff-Mortimer K, Lynn H, Ownby D, Malveaux F (1997) The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. N Engl J Med 336(19):1356–1363
12. Rabito FA, Carlson JC, He H, Werthmann D, Schal C (2017) A single intervention for cockroach control reduces cockroach exposure and asthma morbidity in children. J Allergy Clin Immunol 140(2):565–570
13. Cohn RD, Arbes SJ, Yin M, Jaramillo R, Zeldin DC (2004) National prevalence and exposure risk for mouse allergen in US households. J Allergy Clin Immunol 113(6):1167–1171
14. Phipatanakul W, Eggleston PA, Wright EC, Wood RA (2000) Mouse allergen. I. The prevalence of mouse allergen in inner-city homes. The National Cooperative Inner-City Asthma Study. J Allergy Clin Immunol 106(6):1070–1074
15. Matsui EC (2013) Management of rodent exposure and allergy in the pediatric population. Curr Allergy Asthma Rep 13(6):681–686
16. Curtin-Brosnan J, Paigen B, Hagberg KA, Langley S, O'Neil EA, Krevans M, Eggleston PA, Matsui EC (2010) Occupational mouse allergen exposure among non-mouse handlers. J Occup Environ Hyg 7(12):726–734
17. Krop EJ, Doekes G, Stone MJ, Aalberse RC, van der Zee JS (2007) Spreading of occupational allergens: laboratory animal allergens on hair-covering caps and in mattress dust of laboratory animal workers. Occup Environ Med 64(4):267–272
18. Perry T, Matsui E, Merriman B, Duong T, Eggleston P (2003) The prevalence of rat allergen in inner-city homes and its relationship to sensitization and asthma morbidity. J Allergy Clin Immunol 112(2): 346–352
19. Grant T, Aloe C, Perzanowski M, Phipatanakul W, Bollinger ME, Miller R, Matsui EC (2017) Mouse sensitization and exposure are associated with asthma severity in urban children. J Allergy Clin Immunol Pract 5(4):1008–1014 e1

20. Fishbein AB, Lee TA, Cai M, Oh SS, Eng C, Hu D, Huntsman S, Farber HJ, Serebrisky D, Silverberg J, Williams LK, Seibold MA, Sen S, Borrell LN, Avila P, Rodriguez-Cintron W, Rodriguez-Santana JR, Burchard EG, Kumar R (2016) Sensitization to mouse and cockroach allergens and asthma morbidity in urban minority youth: Genes-environments and Admixture in Latino American (GALA-II) and Study of African-Americans, Asthma, Genes, and Environments (SAGE-II). Ann Allergy Asthma Immunol 117(1): 43–49 e1
21. Torjusen EN, Diette GB, Breysse PN, Curtin-Brosnan J, Aloe C, Matsui EC (2013) Dose-response relationships between mouse allergen exposure and asthma morbidity among urban children and adolescents. Indoor Air 23(4):268–274
22. Phipatanakul W, Cronin B, Wood RA, Eggleston PA, Shih MC, Song L, Tachdjian R, Oettgen HC (2004) Effect of environmental intervention on mouse allergen levels in homes of inner-city Boston children with asthma. Ann Allergy Asthma Immunol 92(4):420–425
23. Pongracic JA, Visness CM, Gruchalla RS, Evans R 3rd, Mitchell HE (2008) Effect of mouse allergen and rodent environmental intervention on asthma in inner-city children. Ann Allergy Asthma Immunol 101(1):35–41
24. Matsui EC, Perzanowski M, Peng RD, Wise RA, Balcer-Whaley S, Newman M, Cunningham A, Divjan A, Bollinger ME, Zhai S, Chew G, Miller RL, Phipatanakul W (2017) Effect of an integrated pest management intervention on asthma symptoms among mouse-sensitized children and adolescents with asthma: a randomized clinical trial. JAMA 317(10):1027–1036
25. Rubner FJ, Jackson DJ, Evans MD, Gangnon RE, Tisler CJ, Pappas TE, Gern JE, Lemanske RF Jr (2017) Early life rhinovirus wheezing, allergic sensitization, and asthma risk at adolescence. J Allergy Clin Immunol 139(2):501–507
26. O'Connor GT, Lynch SV, Bloomberg GR, Kattan M, Wood RA, Gergen PJ, Jaffee KF, Calatroni A, Bacharier LB, Beigelman A, Sandel MT, Johnson CC, Faruqi A, Santee C, Fujimura KE, Fadrosh D, Boushey H, Visness CM, Gern JE (2018) Early-life home environment and risk of asthma among inner-city children. J Allergy Clin Immunol 141:1468–1475
27. Perzanowski MS, Chew GL, Divjan A, Jung KH, Ridder R, Tang D, Diaz D, Goldstein IF, Kinney PL, Rundle AG, Camann DE, Perera FP, Miller RL (2013) Early-life cockroach allergen and polycyclic aromatic hydrocarbon exposures predict cockroach sensitization among inner-city children. J Allergy Clin Immunol 131(3): 886–893
28. Celedon JC, Milton DK, Ramsey CD, Litonjua AA, Ryan L, Platts-Mills TA et al (2007) Exposure to dust mite allergen and endotoxin in early life and asthma and atopy in childhood. J Allergy Clin Immunol 120(1):144–149
29. Lynch SV, Wood RA, Boushey H, Bacharier LB, Bloomberg GR, Kattan M, O'Connor GT, Sandel MT, Calatroni A, Matsui E, Johnson CC, Lynn H, Visness CM, Jaffee KF, Gergen PJ, Gold DR, Wright RJ, Fujimura K, Rauch M, Busse WW, Gern JE (2014) Effects of early-life exposure to allergens and bacteria on recurrent wheeze and atopy in urban children. J Allergy Clin Immunol 134(3):593–601 e12
30. DiFranza JR, Lew RA (1996) Morbidity and mortality in children associated with the use of tobacco products by other people. Pediatrics 97(4):560–568
31. Burke H, Leonardi-Bee J, Hashim A, Pine-Abata H, Chen Y, Cook DG, Britton JR, McKeever TM (2012) Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. Pediatrics 129(4):735–744
32. Vardavas CI, Hohmann C, Patelarou E, Martinez D, Henderson AJ, Granell R, Sunyer J, Torrent M, Fantini MP, Gori D, Annesi-Maesano I, Slama R, Duijts L, de Jongste JC, Aurrekoetxea JJ, Basterrechea M, Morales E, Ballester F, Murcia M, Thijs C, Mommers M, Kuehni CE, Gaillard EA, Tischer C, Heinrich J, Pizzi C, Zugna D, Gehring U, Wijga A, Chatzi L, Vassilaki M, Bergström A, Eller E, Lau S, Keil T, Nieuwenhuijsen M, Kogevinas M (2016) The independent role of prenatal and postnatal exposure to active and passive smoking on the development of early wheeze in children. Eur Respir J 48(1):115–124
33. Baxi R, Sharma M, Roseby R, Polnay A, Priest N, Waters E et al (2014) Family and carer smoking control programmes for reducing children's exposure to environmental tobacco smoke. Cochrane Database Syst Rev 3:CD001746
34. Streja L, Crespi CM, Bastani R, Wong GC, Jones CA, Bernert JT, Tashkin D, Hammond SK, Berman BA (2014) Can a minimal intervention reduce secondhand smoke exposure among children with asthma from low income minority families? Results of a randomized trial. J Immigr Minor Health 16(2):256–264
35. Butz AM, Matsui EC, Breysse P, Curtin-Brosnan J, Eggleston P, Diette G et al (2011) A randomized trial of air cleaners and a health coach to improve indoor air quality for inner-city children with asthma and secondhand smoke exposure. Arch Pediatr Adolesc Med 165(8):741–748
36. Lanphear BP, Hornung RW, Khoury J, Yolton K, Lierl M, Kalkbrenner A (2011) Effects of HEPA air cleaners on unscheduled asthma visits and asthma symptoms for children exposed to secondhand tobacco smoke. Pediatrics 127(1):93–101
37. Frazer K, McHugh J, Callinan JE, Kelleher C (2016) Impact of institutional smoking bans on reducing harms and secondhand smoke exposure. Cochrane Database Syst Rev 5:CD011856
38. Klassen AC, Lee NL, Pankiewicz A, Ward R, Shuster M, Ogbenna BT et al (2017) Secondhand smoke exposure and smoke-free policy in Philadelphia public housing. Tob Regul Sci 3(2):192–203
39. Results from the 2016 National Survey on Drug Use and Health: Detailed Tables (2018) https://www.samhsa.gov/data/report/results-2016-national-survey-drug-use-and-health-detailed-tables Accessed on 30 Nov 2018
40. Doogan NJ, Roberts ME, Wewers ME, Stanton CA, Keith DR, Gaalema DE, Kurti AN, Redner R, Cepeda-Benito A, Bunn JY, Lopez AA, Higgins ST (2017) A growing geographic disparity: rural and urban cigarette smoking trends in the United States. Prev Med 104:79–85
41. Huang J, King BA, Babb SD, Xu X, Hallett C, Hopkins M (2015) Sociodemographic disparities in local smoke-free law coverage in 10 states. Am J Public Health 105(9):1806–1813
42. Hess IM, Lachireddy K, Capon A (2016) A systematic review of the health risks from passive exposure to electronic cigarette vapour. Public Health Res Pract 26(2). https://doi.org/10.17061/phrp2621617
43. Kaisar MA, Prasad S, Liles T, Cucullo L (2016) A decade of e-cigarettes: limited research & unresolved safety concerns. Toxicology 365:67–75
44. U.S. Department of Health and Human Services (2016) E-cigarette use among youth and young adults: a report of the surgeon general. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta
45. Noland M, Rayens MK, Wiggins AT, Huntington-Moskos L, Rayens EA, Howard T, Hahn EJ (2018) Current use of E-cigarettes and conventional cigarettes among US high school students in urban and rural locations: 2014 National Youth Tobacco Survey. Am J Health Promot 32(5):1239–1247
46. Soule EK, Maloney SF, Spindle TR, Rudy AK, Hiler MM, Cobb CO (2017) Electronic cigarette use and indoor air quality in a natural setting. Tob Control 26(1):109–112
47. Glantz SA, Bareham DW (2018) E-cigarettes: use, effects on smoking, risks, and policy implications. Annu Rev Public Health 39:215–235

48. Khreis H, Kelly C, Tate J, Parslow R, Lucas K, Nieuwenhuijsen M (2017) Exposure to traffic-related air pollution and risk of development of childhood asthma: a systematic review and meta-analysis. Environ Int 100:1–31
49. Gauderman WJ, Avol E, Gilliland F, Vora H, Thomas D, Berhane K, McConnell R, Kuenzli N, Lurmann F, Rappaport E, Margolis H, Bates D, Peters J (2004) The effect of air pollution on lung development from 10 to 18 years of age. N Engl J Med 351(11):1057–1067
50. Rojas-Martinez R, Perez-Padilla R, Olaiz-Fernandez G, Mendoza-Alvarado L, Moreno-Macias H, Fortoul T, McDonnell W, Loomis D, Romieu I (2007) Lung function growth in children with long-term exposure to air pollutants in Mexico City. Am J Respir Crit Care Med 176(4):377–384
51. Kattan M, Gergen PJ, Eggleston P, Visness CM, Mitchell HE (2007) Health effects of indoor nitrogen dioxide and passive smoking on urban asthmatic children. J Allergy Clin Immunol 120(3):618–624
52. Paulin LM, Diette GB, Scott M, McCormack MC, Matsui EC, Curtin-Brosnan J et al (2014) Home interventions are effective at decreasing indoor nitrogen dioxide concentrations. Indoor Air 24(4):416–424
53. Gillespie-Bennett J, Pierse N, Wickens K, Crane J, Nicholls S, Shields D, Boulic M, Viggers H, Baker M, Woodward A, Howden-Chapman P, The Housing, Heating, and Health Team* (2008) Sources of nitrogen dioxide (NO2) in New Zealand homes: findings from a community randomized controlled trial of heater substitutions. Indoor Air 18(6):521–528
54. Howden-Chapman P, Pierse N, Nicholls S, Gillespie-Bennett J, Viggers H, Cunningham M, Phipps R, Boulic M, Fjallstrom P, Free S, Chapman R, Lloyd B, Wickens K, Shields D, Baker M, Cunningham C, Woodward A, Bullen C, Crane J (2008) Effects of improved home heating on asthma in community dwelling children: randomised controlled trial. BMJ 337:a1411
55. Johns DO, Linn WS (2011) A review of controlled human SO(2) exposure studies contributing to the US EPA integrated science assessment for sulfur oxides. Inhal Toxicol 23(1):33–43
56. Akinbami LJ, Lynch CD, Parker JD, Woodruff TJ (2010) The association between childhood asthma prevalence and monitored air pollutants in metropolitan areas, United States, 2001-2004. Environ Res 110(3):294–301
57. Moore K, Neugebauer R, Lurmann F, Hall J, Brajer V, Alcorn S, Tager I (2008) Ambient ozone concentrations cause increased hospitalizations for asthma in children: an 18-year study in Southern California. Environ Health Perspect 116(8):1063–1070
58. Spira-Cohen A, Chen LC, Kendall M, Sheesley R, Thurston GD (2010) Personal exposures to traffic-related particle pollution among children with asthma in the South Bronx, NY. J Expo Sci Environ Epidemiol 20(5):446–456
59. Cornell AG, Chillrud SN, Mellins RB, Acosta LM, Miller RL, Quinn JW, Yan B, Divjan A, Olmedo OE, Lopez-Pintado S, Kinney PL, Perera FP, Jacobson JS, Goldstein IF, Rundle AG, Perzanowski MS (2012) Domestic airborne black carbon and exhaled nitric oxide in children in NYC. J Expo Sci Environ Epidemiol 22(3):258–266
60. Jung KH, Hsu SI, Yan B, Moors K, Chillrud SN, Ross J, Wang S, Perzanowski MS, Kinney PL, Whyatt RM, Perera FP, Miller RL (2012) Childhood exposure to fine particulate matter and black carbon and the development of new wheeze between ages 5 and 7 in an urban prospective cohort. Environ Int 45:44–50
61. Jung KH, Perzanowski M, Rundle A, Moors K, Yan B, Chillrud SN, Whyatt R, Camann D, Perera FP, Miller RL (2014) Polycyclic aromatic hydrocarbon exposure, obesity and childhood asthma in an urban cohort. Environ Res 128:35–41
62. Jung KH, Yan B, Hsu S, Moors K, Chillrud SN, Whyatt RM et al (2012) Repeated exposure to polycyclic aromatic hydrocarbons and asthma: effect of seroatopy. Ann Allergy Asthma Immunol 109: 249–254
63. Lovinsky-Desir S, Miller RL, Bautista J, Gil EN, Chillrud SN, Yan B et al (2016) Differences in ambient polycyclic aromatic hydrocarbon concentrations between streets and alleys in New York City: open space vs. semi-closed space. Int J Environ Res Public Health 13(1). https://doi.org/10.3390/ijerph13010127
64. Brown MS, Sarnat SE, DeMuth KA, Brown LA, Whitlock DR, Brown SW et al (2012) Residential proximity to a major roadway is associated with features of asthma control in children. PLoS One 7(5):e37044
65. O'Lenick CR, Winquist A, Mulholland JA, Friberg MD, Chang HH, Kramer MR, Darrow LA, Sarnat SE (2017) Assessment of neighbourhood-level socioeconomic status as a modifier of air pollution-asthma associations among children in Atlanta. J Epidemiol Community Health 71(2):129–136
66. Guarnieri M, Balmes JR (2014) Outdoor air pollution and asthma. Lancet 383(9928):1581–1592
67. IOM (2004) In: Medicine Io (ed) Damp Spaces and Health. National Academy Press, Washington, DC
68. Reponen T, Lockey J, Bernstein DI, Vesper SJ, Levin L, Khurana Hershey GK, Zheng S, Ryan P, Grinshpun SA, Villareal M, LeMasters G (2012) Infant origins of childhood asthma associated with specific molds. J Allergy Clin Immunol 130(3):639–644 e5
69. Oluwole O, Kirychuk SP, Lawson JA, Karunanayake C, Cockcroft DW, Willson PJ, Senthilselvan A, Rennie DC (2017) Indoor mold levels and current asthma among school-aged children in Saskatchewan, Canada. Indoor Air 27(2):311–319
70. Sharpe RA, Bearman N, Thornton CR, Husk K, Osborne NJ (2015) Indoor fungal diversity and asthma: a meta-analysis and systematic review of risk factors. J Allergy Clin Immunol 135(1):110–122
71. Tischer C, Weikl F, Probst AJ, Standl M, Heinrich J, Pritsch K (2016) Urban dust microbiome: impact on later atopy and wheezing. Environ Health Perspect 124(12):1919–1923
72. Cavaleiro Rufo J, Madureira J, Paciencia I, Aguiar L, Pereira C, Silva D et al (2017) Indoor fungal diversity in primary schools may differently influence allergic sensitization and asthma in children. Pediatr Allergy Immunol 28(4):332–339
73. Sharpe R, Thornton CR, Osborne NJ (2014) Modifiable factors governing indoor fungal diversity and risk of asthma. Clin Exp Allergy 44(5):631–641
74. Vesper SJ, McKinstry C, Yang C, Haugland RA, Kercsmar CM, Yike I, Schluchter MD, Kirchner HL, Sobolewski J, Allan TM, Dearborn DG (2006) Specific molds associated with asthma in water-damaged homes. J Occup Environ Med 48(8):852–858
75. Breysse J, Dixon S, Gregory J, Philby M, Jacobs DE, Krieger J (2014) Effect of weatherization combined with community health worker in-home education on asthma control. Am J Public Health 104(1):e57–e64
76. Rudert A, Portnoy J (2017) Mold allergy: is it real and what do we do about it? Expert Rev Clin Immunol 13(8):823–835
77. Chapman JA, Terr AI, Jacobs RL, Charlesworth EN, Bardana EJ Jr (2003) Toxic mold: phantom risk vs science. Ann Allergy Asthma Immunol 91(3):222–232
78. Whyatt RM, Rundle AG, Perzanowski MS, Just AC, Donohue KM, Calafat AM, Hoepner L, Perera FP, Miller RL (2014) Prenatal phthalate and early childhood bisphenol A exposures increase asthma risk in inner-city children. J Allergy Clin Immunol 134(5):1195–1197 e2
79. Whyatt RM, Perzanowski MS, Just AC, Rundle AG, Donohue KM, Calafat AM, Hoepner LA, Perera FP, Miller RL (2014) Asthma in inner-city children at 5-11 years of age and prenatal exposure to phthalates: the Columbia Center for Children's Environmental Health Cohort. Environ Health Perspect 122(10): 1141–1146

80. Just AC, Whyatt RM, Miller RL, Rundle AG, Chen Q, Calafat AM, Divjan A, Rosa MJ, Zhang H, Perera FP, Goldstein IF, Perzanowski MS (2012) Children's urinary phthalate metabolites and fractional exhaled nitric oxide in an urban cohort. Am J Respir Crit Care Med 186(9):830–837
81. Morgan WJ, Crain EF, Gruchalla RS, O'Connor GT, Kattan M, Evans R 3rd et al (2004) Results of a home-based environmental intervention among urban children with asthma. N Engl J Med 351(11):1068–1080
82. Takaro TK, Krieger J, Song L, Sharify D, Beaudet N (2011) The breathe-easy home: the impact of asthma-friendly home construction on clinical outcomes and trigger exposure. Am J Public Health 101(1):55–62
83. Winn AK, Salo PM, Klein C, Sever ML, Harris SF, Johndrow D, Crockett PW, Cohn RD, Zeldin DC (2016) Efficacy of an in-home test kit in reducing dust mite allergen levels: results of a randomized controlled pilot study. J Asthma 53(2):133–138
84. Krieger JW, Takaro TK, Song L, Weaver M (2005) The Seattle-King County Healthy Homes Project: a randomized, controlled trial of a community health worker intervention to decrease exposure to indoor asthma triggers. Am J Public Health 95(4):652–659
85. de Blay F, Fourgaut G, Hedelin G, Vervloet D, Michel FB, Godard P, Charpin D, Pauli G, the Scientific Committee of the MIEC study (2003) Medical Indoor Environment Counselor (MIEC): role in compliance with advice on mite allergen avoidance and on mite allergen exposure. Allergy 58(1):27–33
86. DiMango E, Serebrisky D, Narula S, Shim C, Keating C, Sheares B, Perzanowski M, Miller R, DiMango A, Andrews H, Merle D, Liu X, Calatroni A, Kattan M (2016) Individualized household allergen intervention lowers allergen level but not asthma medication use: a randomized controlled trial. J Allergy Clin Immunol Pract 4(4):671–679 e4
87. Carter MC, Perzanowski MS, Raymond A, Platts-Mills TA (2001) Home intervention in the treatment of asthma among inner-city children. J Allergy Clin Immunol 108(5):732–737
88. O'Connor GT (2005) Allergen avoidance in asthma: what do we do now? J Allergy Clin Immunol 116(1):26–30
89. Brunekreef B, van Strien R, Pronk A, Oldenwening M, de Jongste JC, Wijga A, Kerkhof M, Aalberse RC (2005) La mano de DIOS...was the PIAMA intervention study intervened upon? Allergy 60(8):1083–1086
90. Permaul P, Hoffman E, Fu C, Sheehan W, Baxi S, Gaffin J, Lane J, Bailey A, King E, Chapman M, Gold D, Phipatanakul W (2012) Allergens in urban schools and homes of children with asthma. Pediatr Allergy Immunol 23(6):543–549
91. Hauptman M, Phipatanakul W (2016) Recent advances in environmental controls outside the home setting. Curr Opin Allergy Clin Immunol 16(2):135–141