



Asthma and Allergies in the School Environment

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Abstract

The school is a complex microenvironment of indoor allergens, pollutants, and other exposures. The school represents an occupational model for children and exposures in this environment have a significant health effect. Current research establishes an association between school exposure and asthma morbidity in children. This review will focus on common school environmental exposures (cockroach, rodents, cat, dog, classroom pets, dust mite, fungus, and pollution) and their impact on children with allergies and asthma. Understanding and evaluation of school-based environments is needed to help guide school-based interventions. School-based interventions have the potential for substantial benefit to the individual, school, community, and public health. However, there is a paucity data on school-based environmental interventions and health outcomes. The studies performed to date are small and cross-sectional with no control for home exposures. Randomized controlled school-based environmental intervention trials are needed to assess health outcomes and the cost-effectiveness of these interventions. The School Inner-City Asthma Intervention Study (SICAS 2), a NIH/NIAID randomized controlled clinical trial using environmental interventions modeled from successful home-based interventions, is currently underway with health outcome results pending. If efficacious, these interventions could potentially help further guide school-based interventions potentially with policy implications. In the meanwhile, the allergist/immunologist can continue to play a vital role in improving the quality of life in children with allergies and asthma at school through the use of the ADA policy and Section 504 of the Rehabilitation Act as well as encouraging adoption of toolkits to build successful school-based asthma programs and asthma-friendly schools.

Keywords Asthma · Allergen · Environment · Pediatric asthma · Pollutant · School · School exposure · School-based intervention

Abbreviations

SICAS 1	School Inner-City Asthma Study
NIH	National Institutes of Health
NIAID	National Institute of Allergy and Infectious Disease
IPM	Integrated pest management
HEPA	High efficiency particulate arrestance
PM _{2.5}	Particulate matter 2.5

BC	Black carbon
NO ₂	Nitrogen dioxide
(CO)	Carbon monoxide
O ₃	Ozone
SICAS 2	School Inner-City Asthma Intervention Study

Introduction

Asthma is one of the leading chronic childhood diseases in the USA, affecting 8.4% of children [1]. Pediatric asthma is the most common reason for school absenteeism, accounting for the greatest loss of school days per year [2]. Asthma results in a significant economic burden to patients, families, and collectively, the country. The estimated cost of asthma in the USA is \$56 billion per year, with productivity losses accounting for \$3.8 billion and productivity losses due to mortality accounting for \$2.1 billion [3]. Children with asthma have higher health care utilization due to higher rates of hospitalizations, emergency department visits, and outpatient visits [4]. There is currently no cure for asthma, and it is expected that the burden of asthma will only increase in the future.

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Americans spend an average of 87% of their time indoors and about 6% of their time in enclosed vehicles [5]. Furthermore, toddlers and children spend a large proportion of their day (estimated between 7 and 12 h per day) indoors in daycare and school environments. Past research has established an association between environmental exposures at home and pediatric asthma morbidity [6–8]. Researchers have now expanded beyond the home to further understand environmental exposures in the school setting. This research has revealed an overlap in exposures between the home and school environment, including allergens and pollutants [9–14]. Studies have also demonstrated an association with environmental exposure at school and childhood asthma morbidity [13, 15–18]. Home-based strategies to reduce allergen and pollutant exposure have demonstrated improved asthma outcomes [19]. However, the efficacy of environmental interventions outside of the home is not as well understood. There are limited studies on school-based environmental interventions, and the benefits and cost-effectiveness of these interventions are not yet established.

This review will focus on common school environmental exposures and their impact on children with asthma. This review will discuss important exposures in the school setting including cockroach, rodents, cat, dog, classroom pets, dust mite, fungus, and pollution. Other exposures including endotoxin, tobacco, volatile organic compounds, plasticizers, crime, and stress/stressors were beyond the scope of the review and were not included. Additionally, school-based environmental intervention strategies intended to improve asthma morbidity will be reviewed.

Cockroach and Rodents

In the USA, epidemiologists and clinical researchers have consistently shown that the burden of asthma is significant in urban areas with high levels of poverty and large minority populations [20, 21]. It follows, therefore, that the inner-city home environment is an important area of study given the disparate burdens of asthma seen in children including increased asthma severity, morbidity, and associated healthcare use [22, 23]. Given the often crowded home environments of low-income families living in the inner-city, it is not surprising that high rates of both cockroach and mouse infestations exist [6, 24–28]. This is noteworthy as both cockroach and mouse allergen exposure in homes are linked to higher asthma morbidity [6, 29, 30].

The major cockroach allergens, Bla g 1 and Bla g 2, have been the primary focus of asthma and allergy research. Newer data suggests that the number of allergens relevant to cockroach allergy may actually be higher with implications for sensitization and clinical disease [31]. In the late 1990s, the National Cooperative Inner-City Asthma Study (NCICAS)

showed that urban children with asthma who were both sensitized and exposed to high levels of home cockroach allergen had increased asthma morbidity [6]. In a subsequent study, the Inner-City Asthma Study (ICAS) consortium demonstrated that implementation of an individualized, home-based, multifaceted environmental intervention effectively decreased cockroach and dust mite allergen exposure and improved asthma morbidity for inner-city children [19]. The term “multifaceted” has been used to describe interventions directed toward more than one asthma trigger or interventions with more than one component. Dimango et al. employed the same individualized multifaceted environmental intervention strategy in a randomized controlled trial of New York City homes and concluded that despite a significant reduction of measured allergen levels in the intervention group, it did not result in a reduction in asthma controller therapy [32]. In contrast, a single allergen intervention demonstrated that a single low-cost intervention to reduce cockroach exposure, the strategic placement of insecticidal bait in the homes of children with asthma, resulted in significant cockroach reduction and improved asthma outcomes when compared with the no intervention control group [33].

Similar to cockroach allergen, studies have shown that mouse allergen is prevalent in urban homes and that this exposure is associated with increased childhood asthma morbidity [24, 25, 29, 30]. Major mouse allergenic proteins are Mus m 1 and Mus m 2 and can be found in mouse urine, dander, and hair follicles. Home intervention strategies to reduce mouse allergen levels have incorporated a multidisciplinary approach utilizing a range of pest control methods known as integrated pest management (IPM). Some fundamental principles of IPM include (1) identifying and monitoring pest populations with sticky traps to find out where they are living and hiding (reservoirs); (2) blocking pest access and entryways; (3) preventing pests by eliminating food and water (facilitating factors); (4) controlling pests by selectively applying low-toxicity pesticides. Removing reservoirs such as carpeting, bedding, or other areas containing allergen may also be helpful. The Mouse Allergen and Asthma Intervention Trial (MAAIT) compared a year-long home IPM intervention plus pest management education compared with pest management education alone among mouse-sensitized and exposed children and observed a reduction in mouse allergen levels in both groups but no significant difference in maximal asthma symptom days between the two groups [34]. These and additional studies are highlighted in the recent workshop report, NIAID, NIEHS, NHLBI, and MCAN Workshop Report: The indoor environment and childhood asthma—implications for home environmental intervention in asthma prevention and management [35]. Please refer to this comprehensive workshop report for further details regarding home intervention studies and the implications for asthma prevention and management [35].

Since the majority of children in the USA spend between 7 and 12 h a day in school or daycare settings, researchers are now studying the school environment as an exposure risk for children with asthma. The majority of school-based studies assessing cockroach and mouse allergen exposures have been performed in urban schools [9, 10, 14, 36, 37] and have demonstrated findings similar to the indoor home environment. Chew et al. provided evidence that cockroach and mouse allergens are commonly detected in classroom dust samples of inner-city public high schools [9]. The School Inner-City Asthma Study (SICAS) is a NIH/NIAID-funded comprehensive prospective study of classroom- and school-specific exposures and asthma morbidity among students in the Northeast, adjusting for home exposures [38]. The SICAS findings revealed higher levels of mouse allergen from dust samples obtained in school classrooms linked to enrolled students with asthma when compared with the same students' homes [10]. Moreover, exposure to classroom mouse allergen was associated with increased asthma symptoms and decreased lung function [15]. Another interesting finding was that levels of cockroach allergen were undetectable to very low in SICAS samples from both schools and homes [10, 11]. In contrast, cockroach levels have been detected in schools located in Texas, Baltimore, and England [36, 39, 40]. This highlights the theory that allergen levels may vary by location even within a city, by race/ethnicity, and by shifts in poverty levels [37, 40, 41]. These initial SICAS findings were replicated when the SICAS researchers used another technique for aeroallergen collection and moist table wipes, to examine levels on desktop surfaces of inner-city preschools and elementary schools [14].

Given the prevalence of pest exposure in the school setting and its association with asthma morbidity, additional research is needed to determine if reducing allergen exposure in children results in improvements in asthma morbidity. The successful home-based interventions serve as the model for school-based interventions. Further research in the area is needed.

Cat and Dog

According to the American Pet Products Association's (APPA) National Pet Owner's survey, 68% of households in the USA owns a pet, which equates to 84.6 million homes [42]. This leads to significant animal exposure inside the home. However, that said, animal exposure occurs outside of the home setting as well in locations where animals are not present including hospitals, schools, public transportation, and/or other public buildings [40, 43, 44]. The major cat allergen is Fel d 1 and the major dog allergen is Can f 1. Cat (Fel d 1) and dog (Can f 1) allergens disperse readily being carried on small airborne particles and can adhere to many things

including textiles and carpeting. The transfer of allergens from pet owner to non-pet owner can occur through clothing as well as human hair [45, 46]. Allergen transfer through clothing is dependent on the washing frequency and the type of clothing; for example, woolen sweaters increased personal allergen exposure [45]. Interestingly, a recent study of teenagers revealed that the majority of cat-sensitized individuals did not live in a home with a cat [47]. Previous studies documented threshold levels of dog and cat exposure associated with sensitization and asthma symptoms. The threshold level for sensitization to cat (Fel d 1) is $> 1 \mu\text{g/g}$, and for asthma symptoms in sensitized individuals is $> 8 \mu\text{g/g}$ [43, 44]. The published threshold level for sensitization to dog (Can f 1) is $> 2 \mu\text{g/g}$, and the threshold level associated with asthma symptoms in sensitized individuals is $> 10 \mu\text{g/g}$ [43, 44].

Schools and daycares have been identified as sites of exposure to cat and dog allergens. Multiple studies have detected cat and dog allergens in the school setting, with levels exceeding thresholds associated with sensitization [43, 44, 48, 49]. Furthermore, cat and dog allergen levels were demonstrated to be higher in schools than in homes with no animals present [48–50]. In the school environment, the levels of exposure to cat and dog allergens vary extensively within schools and between schools. Past studies have found that the number of pet owners is one of the strongest predictors of elevated cat and dog allergen levels in schools [48, 51]. Additionally, carpeted and upholstered areas are associated with higher levels of exposure [37, 40, 44]. This may be more relevant for elementary school and preschool classrooms as they tend to have more carpeted and upholstered areas for classroom learning and play. Previously published SICAS studies demonstrated that dog and cat allergens were frequently detected in schools; however, these levels were found to be below past published threshold levels associated with asthma symptoms [10, 11, 15]. The researchers hypothesized that the relatively low absolute levels of dog and cat allergens detected in the schools may have been secondary to lower overall prevalence of household pet ownership in the inner-city setting [15]. Ongoing research is needed to assess the health effects of cat and dog allergen exposure in the school setting.

The primary home exposure to cat and dog is through pet ownership. Pet ownership and its role in the pathogenesis of atopic diseases are of considerable interest at this time. There is increasing interest in whether animal exposure can be beneficial or protective to the development of atopic disease. Recent studies suggest a protective association between early life exposure to dogs and cats and asthma [52–54]. This finding may be due to the effect of pets on the home microbiome which may, in turn, affect the gastrointestinal microbiome of the infant [35, 55]. This remains an area of active research. That said, it is evident that in sensitized individuals, exposure to cat and dog allergens are of significant concern and associated with increased asthma morbidity [18, 56].

Classroom Pets (Guinea Pigs, Hamsters, Rabbits, Etc.)

Many classrooms in schools throughout the USA have classroom pets; however, there has been limited research assessing the prevalence of animals in the classrooms. It has previously been reported that of the responding elementary school teachers, 25% reported having a classroom animal, mostly small vertebrates [57]. In 2015, the American Humane Association (AHA) performed an online survey and determined that the most common classroom pet adopted by surveyed teachers was fish (31%), followed by guinea pigs (13.7%) and hamsters (10.5%) [58]. There are no studies assessing exposure to these classroom pets (guinea pigs, hamsters, rabbits) and effects on sensitization and atopic disease. There is ample opportunity for future research in this area.

Dust Mites

Dust mites are a major, ubiquitous allergen source [59]. The most common dust mite species found in the USA are *Dermatophagoides farinae* (Der f 1) and *Dermatophagoides pteronyssinus* (Der p 1) [59]. Dust mites thrive in warm, humid environments. The body of a dust mite is 70–75% water by weight, and this must be maintained in order for the microscopic arthropods to reproduce [60]. Dust mites do not survive in relative humidity levels less than 50% [60]. Dust mite allergens are found in settled dust in bedding, carpeting, upholstered furniture, and less frequently in washed clothing [59]. The major site of dust mite exposure is in the bed; however, more recent studies have suggested significant exposures to dust mite during the day as well [61].

Previous studies have observed an association with dust mite allergen exposure and sensitization [62]. The defined threshold level of dust mite allergen exposure for sensitization is $> 2 \mu\text{g/g}$ (or potentially any level of exposure in a genetically predisposed individual) [62]. The threshold level of dust mite allergen exposure associated with asthma symptoms is $> 10 \mu\text{g/g}$ [63]. For children who are sensitized to dust mites, there is evidence of a causal relationship between exacerbations of asthma and exposure to dust mite allergen [56].

Dust mite allergen is present in the school setting with levels similar to slightly lower than corresponding levels in the home environment [64]. Within the school setting, there is variation in dust mite levels dependent on the location of the classroom. Dust mite levels are found to be higher in carpeted areas [65]. This finding is relevant for classrooms with more carpeted areas for classroom learning and plan (typically elementary and preschool classrooms). Additionally, past studies documented that the highest mite allergen levels in the daycare center were in the carpeted areas during the day when the center was occupied, suggesting that mite allergens become

airborne due to disruption of the reservoir with daily activity [66]. Dust mite allergen levels in schools and daycares have been found to be greater than threshold levels associated with sensitization [39, 66]. However, the mean or median concentrations have not exceeded previously determined threshold associated with asthma symptoms ($> 10 \mu\text{g/g}$) [10, 11, 14, 48, 63]. A direct association of dust mite allergen exposure in the school setting with respiratory health has not yet been identified. Dust mite interventions have been studied in the home environment, and this topic is reviewed in detail in the recently updated practice parameters [59]. Please refer to these practice parameters for further details. That said, there are no studies assessing effect of school-based interventions on dust mite allergen exposure.

Fungus

Fungi are ubiquitous microorganisms that are present in both outdoor and indoor air. These spores and their fragments enter indoor spaces through open windows, open doors, and fresh air intakes in buildings. Once these spores and fragments have entered, they can then accumulate on surfaces. Fungal growth is likely to occur in environments that contain nutrients and moisture adequate for growth. When inhaled, these particles are thought to contribute adverse health effects in sensitized individuals as well as other individuals with respiratory diseases susceptible to irritant effects from exposure. The threshold levels of fungus exposure associated with asthma symptoms in sensitized individuals are not known. It would be assumed that these levels would vary by different fungal species. Multiple studies and meta-analyses have identified an association between exposure to indoor fungus and dampness and the development or worsening of asthma [56, 67–71]. Most of these studies have focused on health effects from household exposures. Few studies have provided an assessment of fungus in the school environment.

Schools and classrooms provide unique environments that are susceptible to fungus exposure. In a SICAS study, Baxi et al. demonstrated that schools located in the Northeastern United States are a source of fungus exposure and that visible fungus may be a predictor for higher fungal spore counts [12]. In this study, the authors evaluated 180 classrooms in 12 schools for fungal spores using Burkard air samplers and found that all classrooms had varying amounts of fungal spores present [12]. Interestingly, classrooms within the same school had substantial variability in quantity of spores and species [12]. Studies from other countries have also identified fungal exposure in the classroom and found an association of fungal exposure and asthma morbidity. Simoni et al. evaluated 46 classrooms in 21 European schools and found viable mold and fungal DNA in all classrooms [72]. Furthermore, they found that *Aspergillus/Penicillium* was significantly

associated with wheeze and children exposed to high levels of viable mold had a higher risk for night cough [72]. In a nationwide school survey in Taiwan, Chen et al. investigated the correlation between fungal spores in classrooms and asthma in school children using Burkard personal air samplers to collect fungal spores [16]. They demonstrated that classroom *Aspergillus/Penicillium* and basidiospores were associated with current asthma and asthma with symptoms reduced on holidays [16]. In Portugal, investigators evaluated 71 classrooms in 20 schools using single-stage microbiologic impactors to determine fungal diversity [73]. Higher concentrations of *Penicillium* were found in classrooms with a higher number of children with atopic sensitization [73]. In contrast, investigators found that exposure to higher fungal diversity was protective against allergic sensitization but this was not seen for asthma [73].

Reducing indoor exposure, using a variety of interventions largely aimed at reducing moisture, killing fungi, and removing contaminated materials, has been shown to decrease the risk of asthma morbidity [74]. However, there are still many unknowns including (1) whether there are threshold levels that cause disease, (2) whether there is a dose-response relationship, (3) whether specific fungal genera are responsible for the effect, or (4) whether interventions to reduce exposure prevent asthma morbidity. Further research is necessary to determine whether efforts to decrease fungus exposure in schools can be effective at reducing adverse health effects.

Indoor Pollution and Air Quality

Exposures to ambient air pollution have been associated with adverse health effects including increased asthma symptoms, decreased lung function, increased medication use, increased hospitalizations, and increased mortality [75–79] [75–78, 80, 81]. In the school environment, some of the common exposures to pollution include particulate matter (PM), black carbon (BC), nitrogen dioxide (NO₂), carbon monoxide (CO), and ozone (O₃). PM is a complex mixture of microscopic particles and liquid droplets that are aerosolized and once inhaled can affect the heart and lungs [82]. BC is a sooty black substance emitted from diesel and gas engines, burning of wood and coal, and other sources that burn fossil fuel [82]. BC is released directly into the atmosphere in the form of particulate matter. NO₂ is one of the group of gases called nitrogen oxides and is used as the indicator for the larger group of nitrogen oxide gases [82]. High concentrations of these gases can irritate the airways and even short exposures can aggravate respiratory diseases. CO is a colorless and odorless gas released through combustion, such as the burning of fossil fuels, that can be harmful when inhaled in large amounts [82]. Breathing high concentrations of CO reduces the amount of oxygen that is transported to vital organs [82]. O₃ is a gas

composed of three oxygen atoms [82]. Harmful ozone is found at the ground level and is created by chemical reactions between nitrogen oxides and volatile organic compounds, and reaction can occur when emissions from vehicles or factories interact with sunlight [82]. The federal Clean Air Act requires the Environmental Protection Agency to set National Ambient Air Quality standards for pollutants like PM, NO₂, CO, and O₃.

Schools have a unique indoor environment with fewer sources of indoor pollutants, as most schools do not have fuel-burning kitchens and smoking is prohibited. However, indoor air quality in the classroom is an important issue, and traffic emissions are a source of pollutant exposure in the schools. Kingsley et al. examined the proximity of public and private schools in the USA and the nearest major roadway and demonstrated that 3.2 million students attended schools located within 100 m of a major roadway [83]. These students are potentially exposed to very high levels of traffic-related air pollution on a daily basis [83]. Additionally, there are often cars and buses idling for pick up and drop off [84]. The French 6-Cities Study assessed air quality in schools in six metropolitan French cities and found that air quality in the classroom was poor, with 30% of school children exposed to high levels of pollutants [85]. Madureira et al. assessed the indoor air quality of 73 classrooms in 20 schools in Porto, Portugal, and found frequent high levels of CO₂, PM_{2.5}, and PM₁₀, and low rates of ventilation [86]. From SICAS, Gaffin et al. described the relationship between indoor and outdoor levels of PM_{2.5} and BC in inner-city schools in 136 classrooms over 30 schools in the Northeastern United States [87]. They demonstrated a strong relationship between measured indoor classroom levels of PM_{2.5} and BC with matching outdoor levels [87]. Furthermore, they demonstrated that indoor sources of PM_{2.5} and BC within the school contributed significantly to indoor levels despite the absence of smoking and cooking at the locations [87]. In a similar cohort, Gaffin et al. described NO₂ levels in 218 classrooms within 37 schools and found that levels were relatively low compared with the US Environmental Protection Agency's air quality standards with a mean level of 11.1 ppb and mean of 10.4 ppb [13]. This study demonstrated that NO₂ levels greater than 8 ppb were significantly associated with airflow obstruction but not with asthma symptoms [13].

There have been few studies that have evaluated the impact of a school-based intervention on indoor air quality and health effects (Table 1). Pilotto et al. in a randomized control trial of 19 schools, an intervention replacing unflued gas heaters with electric heaters resulted in significant reduction in NO₂ levels and asthma symptoms in the intervention group [88]. Jhun et al. performed a small randomized control trial using an intervention of classroom-based air cleaners using high efficiency particulate air (HEPA) filters vs. a control of sham air cleaners [89]. In the intervention classrooms, PM_{2.5} and BC

Table 1 School-based Environmental Intervention Studies

Study	Design	Population	Intervention	Effectiveness of Intervention
Pilotto et al. [88] (2004)	Randomized control trial	Children (aged 8–9 y; Australia)	Replacement flued gas or electric heaters in schools	<ul style="list-style-type: none"> Reduction in NO₂ exposure Reduction in asthma symptoms
Jhun et al. [89] (2017)	Randomized control trial (Pilot Study)	Children (aged 6–10 y; USA)	Classroom based HEPA air cleaner intervention	<ul style="list-style-type: none"> Reductions in PM_{2.5} and BC No significant changes in FEV₁ and asthma symptoms Modest improvement in peak flow
Bernstein et al. [90] (2005)	Randomized control trial (Pilot Study)	Children (aged newborn–5 y; USA)	Dehumidification plus day care room based HEPA air cleaner	<ul style="list-style-type: none"> Lower average dew point from baseline for both day care A and B Reduction in fungal spore counts for day care A only No health outcomes assessed
Lignell et al. [91] (2007)	Longitudinal intervention study	Children (aged 7–12 y; Finland)	Damaged school renovated for all identified problems, mechanical exhaust and supply air ventilation system installed	<ul style="list-style-type: none"> 50% reduction in fungal concentrations Modest reduction in respiratory symptoms
Meklin et al. [92] (2005)	Longitudinal intervention study	Children (aged 6–17 y; Finland)	Damaged schools thoroughly cleaned, repaired, renovated, and mechanical exhaust and supply ventilation system installed	<ul style="list-style-type: none"> Normalization of indoor air fungal concentrations Reduction in respiratory and other symptoms
Karlsson et al. [93] (2004)	Intervention study	Children (aged 6–12 y; Sweden)	School clothing or pet-free classes. Two classes of children with special school clothing, one class of children with no pets, and three control classes.	<ul style="list-style-type: none"> 4–6 fold lower airborne cat allergen levels in intervention classes compared with controls. No health outcomes assessed
Nalyanya et al. [94] (2009)	Longitudinal intervention study	Children (USA)	Integrated pest management (IPM) or conventional pest control	<ul style="list-style-type: none"> Reduction in Bla g 1 concentrations in IPM-treated schools than in schools treated with conventional approaches. No health outcomes assessed

Abbreviations: NO₂: nitrogen dioxide; US: United States; HEPA: high efficiency particulate arrestance; PM_{2.5}: particulate matter 2.5; BC: black carbon; FEV₁: forced expiratory volume in 1 second; Bla g 1: *Blattella germanica*, German cockroach

levels were significantly reduced compared with the control classrooms [89]. The air cleaner intervention reduced $PM_{2.5}$ and BC levels during the follow-up periods, demonstrated modest improvement in peak flow, but did not demonstrate significant changes in FEV_1 or asthma symptoms [89]. Further large-scale studies are needed to evaluate the effectiveness in reducing pollutant levels in schools and whether this has a resultant effect on asthma morbidity.

School Environmental Intervention Strategies

School-based studies examining environmental interventions and health outcomes are lacking in the USA. The few published European studies are small and not adequately powered to comprehensively assess asthma morbidity outcomes [88–93]. Studies evaluating school-based environmental interventions are highlighted in Table 1. In addition to indoor air quality interventions previously discussed above [88, 89], other studies have assessed interventions targeted at fungi, pet allergens, and cockroach [90–94]. One study showed that banning pet ownership in Swedish schools and having dedicated school clothing resulted in four to six times lower airborne cat allergen levels in the intervention groups (classes with school clothing or pet ownership ban) compared with the control classes, thereby, reducing pet dander in schools [93]. Despite its efficacy in Sweden, this school-based environmental intervention is unlikely to find favor in the USA. In another Swedish study, other allergen prevention measures such as dedicated cleaning, removal of upholstery and curtains, and replacement of bookshelves with cupboards to lessen allergen load offered no significant change in cat allergen levels in school classrooms [95]. Two longitudinal Finnish studies, limited by the small number of schools assessed, demonstrated improvement in asthma symptoms through reparation of air filtration systems and moisture damage in schools, reduction in mold exposure, and other building maintenance [91, 92]. In one Australian school study, as previously mentioned, an intervention replacing unflued gas heaters with electric heaters effectively reduced NO_2 levels and improved asthma symptoms [88]. The use of air filtration systems to reduce environmental exposures is a potential effective school-based intervention [96]. One pilot study showed that HEPA air filters reduced mold spore counts in daycare centers by 50% [90]. Lastly, Nalyanya et al. demonstrated that IPM implementation in North Carolina schools was not only more effective at controlling cockroaches than conventional pest control but lead to long-term reductions in allergen concentrations [94]. Ongoing research is needed to better understand the health outcome effects of school-based IPM interventions.

Well-designed randomized, double-blinded, controlled school-based environmental intervention trials are needed. The majority of school-based intervention studies to date have

been cross-sectional with small sample sizes and with no control for home exposures [36, 37, 40, 41, 49, 97, 98] [99]. The School Inner-City Asthma Intervention Study (SICAS 2), is an NIH/NIAID-funded ([ClinicalTrials.gov NCT02291302](https://clinicaltrials.gov/ct2/show/study/NCT02291302)) randomized controlled clinical trial using an environmental intervention of classroom HEPA filters and school wide IPM to comprehensively determine health benefits on reducing asthma morbidity, adjusting for exposure in the home [100]. Pilot data from this SICAS 2 study revealed that a classroom-based air cleaner intervention led to significant reductions in $PM_{2.5}$ and BC, compared with sham filters [89]. This study demonstrated modest improvement in peak flow but no significant changes in FEV_1 and asthma symptoms [89]. The SICAS 2 research group is working to better understand the benefits of school-based interventions and associated health outcomes.

Challenges of School Environmental Intervention Studies

We know that the school environment contains a large reservoir of exposures such as indoor allergens and pollutants, and like homes, should also be considered for interventions. In schools throughout the country, there will be variation in exposures secondary to multiple factors including differing geographic, climate, socioeconomic conditions, distance from major highways and roadways, and the built environment, as well as many other factors. Given this, a single school-based environmental intervention strategy may not be realistic or generalizable for all schools. This is similar to the fact that an intervention strategy for one home may not be generalizable to all homes. This makes implementation of school-based environmental intervention strategies complicated. Additionally, to adequately study and demonstrate improved asthma outcomes in school based-intervention studies, multiple exposures must be taken into consideration. Although challenging, school-based environmental interventions have the potential to benefit a community of children. Past research in the state of Maryland demonstrated that single- and multi-component environmental strategies in the home were cost-saving relative to the standard of care [101]. Given that school-based interventions have the potential to impact a large number of children, if effective, these programs could be even more cost-effective.

The logistics of implementing these interventions in a classroom setting in an unobtrusive way should also be considered. HEPA filters need to be both obscure and noiseless so as not to disturb students in the classrooms. While it is possible for some school-based interventions to be blinded, such as sham versus active filters in the classrooms, large-scale interventions might be more difficult to blind. In addition, certain interventions such as IPM cannot be randomized from classroom to classroom but could be randomized between schools. Of utmost importance to the success of these school-based

environmental intervention studies is the involvement and commitment from the school systems as well as community buy-in. Support for school-based interventions must be attained from many sponsors including senior school administrators, principals, teachers, school nurses, facilities management, and the students and their families.

Policy and Policy Implications

It is evident that there is a relationship between school exposure and pediatric asthma morbidity and thus, policy changes could provide an important supplement to clinical care to improve the quality of life and health of students. Abramson's recent review [102] discussed potential policies to help reduce allergic triggers and improve care for patients with allergic rhinitis and allergic asthma. In this review, Abramson discussed occupational exposure policies with the school environment, as the school represents the occupational environment for many children [102]. We remain hopeful that SICAS 2, a prospective randomized, blinded, sham-controlled school environmental intervention trial currently underway, will help determine the efficacy of a school-based intervention to improve asthma control. If efficacious, these interventions could then further guide policy change.

The allergist/immunologist plays an important role in improving the quality of life at school. The allergist/immunologist can aid families through the ADA policy and Section 504 of the Rehabilitation Act that require schools to accommodate children with disabilities, including allergies. The allergist/immunologist can help facilitate a 504 plan and communicate with the school administrators and nurses to develop an action plan for the school [102]. The developed action plan for the school is variable patient to patient dependent on the allergens, issues in the school, and identifiable exposures.

External to the role of the allergist/immunologist, multiple toolkits have been developed to educate schools with the goal to build successful school-based asthma programs and asthma-friendly schools. The EPA has created the Indoor Air Quality Tools for Schools Program that provides recommendations to improve the quality of environmental conditions in the school setting [103]. These tools are available to all schools and the program recognizes effective implementation of these policies along with innovations in environmental control with EPA awards to schools [102, 104]. Additionally, the Centers for Disease Control and Prevention (CDC) Healthy Schools Program [105] and the School-Based Asthma Management Program (SAMPRO™) [106] offer toolkits to schools. These toolkit and reward programs are valuable and should continue; however, there remains a need for continued identifications of best practices for reducing allergenic exposures. This emphasizes the need for ongoing environmental health research to assess the efficacy of school interventions.

Conclusion

The home and school environments are both rich sources of allergen and pollutant exposures, and these exposures are associated with increased asthma morbidity. Past research has assessed the efficacy of environmental interventions in the home setting, but there is limited data on interventions in the school setting. Successful environmental interventions in the home serve as the model for interventions in the school. Through school-based interventions, the goal is to decrease exposure to multiple allergens and pollutants in the school and thereby improve health outcomes, including atopic diseases. However, there are many additional challenges and costs associated with school-based interventions and further research is necessary to assess the impacts of school-based interventions and the cost-effectiveness of these interventions. SICAS 2 is currently underway as a randomized controlled trial to determine the efficacy of a school-based intervention to improve asthma control.

The potential benefit of successful school-based interventions is substantial as many students, teachers, and staff are impacted by a school-based intervention. From a public health perspective, interventions in the schools have the potential to improve the health of a community instead of the focus on individual homes and families. Ongoing research is needed to determine the effectiveness of these interventions, but we remain optimistic in hopes to improve the health and lives of those attending schools. In the meanwhile, the allergist/immunologist can continue to play a vital role in improving the quality of life in children with allergies and asthma at school through the use of the ADA policy and Section 504 of the Rehabilitation Act as well as encouraging adoption of toolkits to build successful school-based asthma programs and asthma-friendly schools.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

- National Center for Health Statistics. Centers for disease control and prevention. Asthma. Available from: <https://www.cdc.gov/nchs/fastats/asthma.htm>. Accessed 22 Jan 2018
- Centers for Disease Control and Prevention. Asthma in schools. Available from: <https://www.cdc.gov/healthyschools/asthma/>. Accessed 22 Jan 2018
- Barnett SB, Nurmagambetov TA (2011) Costs of asthma in the United States: 2002–2007. *J Allergy Clin Immunol* 127(1):145–152
- Sullivan PW, Ghushchyan V, Navaratnam P, Friedman HS, Kavati A, Ortiz B et al (2017) The national cost of asthma among school-aged children in the United States. *Ann Allergy Asthma Immunol* 119(3):246–52.e1
- Klepeis NE, Nelson WC, Ott WR, Robinson JP, Tsang AM, Switzer P et al (2001) The National Human Activity Pattern Survey (NHAPS): a resource for assessing exposure to environmental pollutants. *J Expo Anal Environ Epidemiol* 11(3):231–252
- 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
- Crain EF, Walter M, O'Connor GT, Mitchell H, Gruchalla RS, Kattan M, Malindzak GS, Enright P, Evans R 3rd, Morgan W, Stout JW (2002) Home and allergic characteristics of children with asthma in seven U.S. urban communities and design of an environmental intervention: the Inner-City Asthma Study. *Environ Health Perspect* 110(9):939–945
- Kattan M, Mitchell H, Eggleston P, Gergen P, Crain E, Redline S, Weiss K, Evans R, Kaslow R, Kerckmar C, Leickly F, Malveaux F, Wedner HJ (1997) Characteristics of inner-city children with asthma: the National Cooperative Inner-City Asthma Study. *Pediatr Pulmonol* 24(4):253–262
- Chew GL, Correa JC, Perzanowski MS (2005) Mouse and cockroach allergens in the dust and air in northeastern United States inner-city public high schools. *Indoor Air* 15(4):228–234
- 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
- Sheehan WJ, Rangsitienchai PA, Muilenberg ML, Rogers CA, Lane JP, Ghaemghami J, Rivard DV, Otsu K, Hoffman EB, Israel E, Gold DR, Phipatanakul W (2009) Mouse allergens in urban elementary schools and homes of children with asthma. *Ann Allergy Asthma Immunol* 102(2):125–130
- Baxi SN, Muilenberg ML, Rogers CA, Sheehan WJ, Gaffin J, Permaul P, Kopel LS, Lai PS, Lane JP, Bailey A, Petty CR, Fu C, Gold DR, Phipatanakul W (2013) Exposures to molds in school classrooms of children with asthma. *Pediatr Allergy Immunol* 24(7):697–703
- Gaffin JM, Hauptman M, Petty CR, Sheehan WJ, Lai PS, Wolfson JM, Gold DR, Coull BA, Koutrakis P, Phipatanakul W (2017) Nitrogen dioxide exposure in school classrooms of inner-city children with asthma. *J Allergy Clin Immunol* 141(6):2249–2255
- Kanchongkittiphon W, Sheehan WJ, Friedlander J, Chapman MD, King EM, Martirosyan K, Baxi SN, Permaul P, Gaffin JM, Kopel L, Bailey A, Fu C, Petty CR, Gold DR, Phipatanakul W (2014) Allergens on desktop surfaces in preschools and elementary schools of urban children with asthma. *Allergy*. 69(7):960–963
- Sheehan WJ, Permaul P, Petty CR, Coull BA, Baxi SN, Gaffin JM, Lai PS, Gold DR, Phipatanakul W (2017) Association between allergen exposure in inner-city schools and asthma morbidity among students. *JAMA Pediatr* 171(1):31–38
- Chen CH, Chao HJ, Chan CC, Chen BY, Guo YL (2014) Current asthma in schoolchildren is related to fungal spores in classrooms. *Chest*. 146(1):123–134
- Holst GJ, Host A, Doekes G, Meyer HW, Madsen AM, Plesner KB et al (2016) Allergy and respiratory health effects of dampness and dampness-related agents in schools and homes: a cross-sectional study in Danish pupils. *Indoor Air* 26(6):880–891
- Almqvist C, Wickman M, Perfetti L, Berglund N, Renstrom A, Hedren M et al (2001) Worsening of asthma in children allergic to cats, after indirect exposure to cat at school. *Am J Respir Crit Care Med* 163(3 Pt 1):694–698
- 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
- Dutmer CM, Kim H, Searing DA, Zoratti EM, Liu AH (2018) Asthma in inner city children: recent insights: United States. *Curr Opin Allergy Clin Immunol* 18(2):139–147
- Poowuttikul P, Saini S, Seth D (2019) Inner-city asthma in children. *Clin Rev Allergy Immunol* 56(2):248–268
- Szeffler SJ, Gergen PJ, Mitchell H, Morgan W (2010) Achieving asthma control in the inner city: do the National Institutes of Health Asthma Guidelines really work? *J Allergy Clin Immunol* 125(3):521–526 quiz 7-8
- Bollinger ME, Butz A, Tsoukleris M, Lewis-Land C, Mudd S, Morpheus T (2019) Characteristics of inner city children with life-threatening asthma. *Ann Allergy Asthma Immunol* 122(4):381–386
- Ahluwalia SK, Peng RD, Breyse PN, Diette GB, Curtin-Brosnan J, Aloe C et al (2013) Mouse allergen is the major allergen of public health relevance in Baltimore City. *J Allergy Clin Immunol* 132(4):830–5.e1–2
- 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
- Gruchalla RS, Pongracic J, Plaut M, Evans R, Visness CM, Walter M et al (2005) Inner City Asthma Study: relationships among sensitivity, allergen exposure, and asthma morbidity. *J Allergy Clin Immunol* 115(3):478–485
- Sarpong SB, Hamilton RG, Eggleston PA, Adkinson NF Jr (1996) Socioeconomic status and race as risk factors for cockroach allergen exposure and sensitization in children with asthma. *J Allergy Clin Immunol* 97(6):1393–1401
- Olmedo O, Goldstein IF, Acosta L, Divjan A, Rundle AG, Chew GL et al (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):284–92.e7
- Phipatanakul W, Eggleston PA, Wright EC, Wood RA, Study NCI-CA (2000) Mouse allergen. II. The relationship of mouse allergen exposure to mouse sensitization and asthma morbidity in inner-city children with asthma. *J Allergy Clin Immunol* 106(6):1075–1080
- Grant T, Aloe C, Perzanowski M, Phipatanakul W, Bollinger ME, Miller R et al (2017) Mouse sensitization and exposure are associated with asthma severity in urban children. *J Allergy Clin Immunol Pract* 5(4):1008–14.e1
- Pomes A, Mueller GA, Randall TA, Chapman MD, Arruda LK (2017) New insights into cockroach allergens. *Curr Allergy Asthma Rep* 17(4):25
- DiMango E, Serebrisky D, Narula S, Shim C, Keating C, Sheares B et al (2016) Individualized household allergen intervention

- lowers allergen level but not asthma medication use: a randomized controlled trial. *J Allergy Clin Immunol Pract* 4(4):671–9.e4
33. 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
 34. 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
 35. Gold DR, Adamkiewicz G, Arshad SH, Celedon JC, Chapman MD, Chew GL et al (2017) NIAID, NIEHS, NHLBI, and MCAN Workshop Report: the indoor environment and childhood asthma-implications for home environmental intervention in asthma prevention and management. *J Allergy Clin Immunol* 140(4):933–949
 36. Sarpong SB, Wood RA, Karrison T, Eggleston PA (1997) Cockroach allergen (Bla g 1) in school dust. *J Allergy Clin Immunol* 99(4):486–492
 37. Amr S, Bollinger ME, Myers M, Hamilton RG, Weiss SR, Rossman M, Osborne L, Timmins S, Kimes DS, Levine ER, Blaisdell CJ (2003) Environmental allergens and asthma in urban elementary schools. *Ann Allergy Asthma Immunol* 90(1):34–40
 38. Phipatanakul W, Bailey A, Hoffman EB, Sheehan WJ, Lane JP, Baxi S et al (2011) The school inner-city asthma study: design, methods, and lessons learned. *J Asthma*. 48(10):1007–1014
 39. Abramson SL, Turner-Henson A, Anderson L, Hemstreet MP, Bartholomew LK, Joseph CL et al (2006) Allergens in school settings: results of environmental assessments in 3 city school systems. *J Sch Health* 76(6):246–249
 40. Custovic A, Green R, Taggart SC, Smith A, Pickering CA, Chapman MD et al (1996) Domestic allergens in public places. II: dog (can f1) and cockroach (Bla g 2) allergens in dust and mite, cat, dog and cockroach allergens in the air in public buildings. *Clin Exp Allergy* 26(11):1246–1252
 41. Tortolero SR, Bartholomew LK, Tyrrell S, Abramson SL, Sockrider MM, Markham CM, Whitehead LW, Parcel GS (2002) Environmental allergens and irritants in schools: a focus on asthma. *J Sch Health*. 72(1):33–38
 42. 2017–2018 APPA National Pet Owners Survey Statistics: pet ownership & annual expenses. Available from: http://americanpetproducts.org/press_industrytrends.asp. Accessed 18 Jan 2018
 43. Ingram JM, Sporik R, Rose G, Honsinger R, Chapman MD, Platts-Mills TA (1995) Quantitative assessment of exposure to dog (can f 1) and cat (Fel d 1) allergens: relation to sensitization and asthma among children living in Los Alamos, New Mexico. *J Allergy Clin Immunol* 96(4):449–456
 44. Custovic A, Fletcher A, Pickering CA, Francis HC, Green R, Smith A et al (1998) Domestic allergens in public places III: house dust mite, cat, dog and cockroach allergens in British hospitals. *Clin Exp Allergy* 28(1):53–59
 45. De Lucca SD, O'Meara TJ, Tovey ER (2000) Exposure to mite and cat allergens on a range of clothing items at home and the transfer of cat allergen in the workplace. *J Allergy Clin Immunol* 106(5):874–879
 46. Karlsson AS, Renstrom A (2005) Human hair is a potential source of cat allergen contamination of ambient air. *Allergy*. 60(7):961–964
 47. Perzanowski MS, Ronmark E, James HR, Hedman L, Schuyler AJ, Bjerg A, Lundback B, Platts-Mills TAE (2016) Relevance of specific IgE antibody titer to the prevalence, severity, and persistence of asthma among 19-year-olds in northern Sweden. *J Allergy Clin Immunol* 138(6):1582–1590
 48. Salo PM, Sever ML, Zeldin DC (2009) Indoor allergens in school and day care environments. *J Allergy Clin Immunol* 124(2):185–92.e9
 49. Perzanowski MS, Ronmark E, Nold B, Lundback B, Platts-Mills TA (1999) Relevance of allergens from cats and dogs to asthma in the northernmost province of Sweden: schools as a major site of exposure. *J Allergy Clin Immunol* 103(6):1018–1024
 50. Krop EJ, Jacobs JH, Sander I, Raulf-Heimsoth M, Heederik DJ (2014) Allergens and beta-glucans in dutch homes and schools: characterizing airborne levels. *PLoS One* 9(2):e88871
 51. Almqvist C, Larsson PH, Egmar AC, Hedren M, Malmberg P, Wickman M (1999) School as a risk environment for children allergic to cats and a site for transfer of cat allergen to homes. *J Allergy Clin Immunol* 103(6):1012–1017
 52. Litonjua AA, Milton DK, Celedon JC, Ryan L, Weiss ST, Gold DR (2002) A longitudinal analysis of wheezing in young children: the independent effects of early life exposure to house dust endotoxin, allergens, and pets. *J Allergy Clin Immunol* 110(5):736–742
 53. Ownby DR, Johnson CC, Peterson EL (2002) Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age. *JAMA*. 288(8):963–972
 54. Bufford JD, Reardon CL, Li Z, Roberg KA, DaSilva D, Eggleston PA, Liu AH, Milton D, Alwis U, Gangnon R, Lemanske RF Jr, Gern JE (2008) Effects of dog ownership in early childhood on immune development and atopic diseases. *Clin Exp Allergy* 38(10):1635–1643
 55. Azad MB, Konya T, Maughan H, Guttman DS, Field CJ, Sears MR, Becker AB, Scott JA, Kozyrskyj AL, CHILD Study Investigators (2013) Infant gut microbiota and the hygiene hypothesis of allergic disease: impact of household pets and siblings on microbiota composition and diversity. *Allergy Asthma Clin Immunol* 9(1):15
 56. Kanchongkittiphon W, Mendell MJ, Gaffin JM, Wang G, Phipatanakul W (2015) Indoor environmental exposures and exacerbation of asthma: an update to the 2000 review by the Institute of Medicine. *Environ Health Perspect* 123(1):6–20
 57. Rud AG Jr, Beck AM (2003) Companion animals in Indiana elementary schools. *Anthrozoös*. 16(3):241–251
 58. Association AH (2015) Pets in the classroom study: phase I findings report. Author Google Scholar, Washington, DC
 59. Portnoy J, Miller JD, Williams PB, Chew GL, Miller JD, Zaitoun F, Phipatanakul W, Kennedy K, Barnes C, Grimes C, Larenas-Linnemann D, Sublett J, Bernstein D, Blessing-Moore J, Khan D, Lang D, Nicklas R, Oppenheimer J, Randolph C, Schuller D, Spector S, Tilles SA, Wallace D, Joint Taskforce on Practice Parameters, Practice Parameter Workgroup (2013) Environmental assessment and exposure control of dust mites: a practice parameter. *Ann Allergy Asthma Immunol* 111(6):465–507
 60. Arlian LG, Bernstein D, Bernstein IL, Friedman S, Grant A, Lieberman P, Lopez M, Metzger J, Platts-Mills T, Schatz M, Spector S, Wasserman SI, Zeiger RS (1992) Prevalence of dust mites in the homes of people with asthma living in eight different geographic areas of the United States. *J Allergy Clin Immunol* 90(3 Pt 1):292–300
 61. Tovey ER, Willenborg CM, Crisafulli DA, Rimmer J, Marks GB (2013) Most personal exposure to house dust mite aeroallergen occurs during the day. *PLoS One* 8(7):e69900
 62. Platts-Mills TA, Vervloet D, Thomas WR, Aalberse RC, Chapman MD (1997) Indoor allergens and asthma: report of the Third International Workshop. *J Allergy Clin Immunol* 100(6 Pt 1):S2–S24
 63. (1989) Dust mite allergens and asthma—a worldwide problem. *J Allergy Clin Immunol* 83(2 Pt 1):416–427

64. Einarsson R, Munir AK, Dreborg SK (1995) Allergens in school dust: II. Major mite (Der p I, Der f I) allergens in dust from Swedish schools. *J Allergy Clin Immunol* 95(5 Pt 1):1049–1053
65. Zock JP, Brunekreef B (1995) House dust mite allergen levels in dust from schools with smooth and carpeted classroom floors. *Clin Exp Allergy* 25(6):549–553
66. Fernandez-Caldas E, Codina R, Ledford DK, Trudeau WL, Lockey RF (2001) House dust mite, cat, and cockroach allergen concentrations in daycare centers in Tampa, Florida. *Ann Allergy Asthma Immunol* 87(3):196–200
67. Fisk WJ, Lei-Gomez Q, Mendell MJ (2007) Meta-analyses of the associations of respiratory health effects with dampness and mold in homes. *Indoor Air* 17(4):284–296
68. Gent JF, Kezik JM, Hill ME, Tsai E, Li D-W, Leaderer BP (2012) Household mold and dust allergens: exposure, sensitization and childhood asthma morbidity. *Environ Res* 118:86–93
69. Karvonen AM, Hyvarinen A, Korppi M, Haverinen-Shaughnessy U, Renz H, Pfefferle PI, Remes S, Genuneit J, Pekkanen J (2015) Moisture damage and asthma: a birth cohort study. *Pediatrics*. 135(3):e598–e606
70. Mendell MJ, Mirer AG, Cheung K, Tong M, Douwes J (2011) Respiratory and allergic health effects of dampness, mold, and dampness-related agents: a review of the epidemiologic evidence. *Environ Health Perspect* 119(6):748–756
71. Quansah R, Jaakkola MS, Hugg TT, Heikkinen SAM, Jaakkola JJ (2012) Residential dampness and molds and the risk of developing asthma: a systematic review and meta-analysis. *PLoS One* 7(11): e47526
72. Simoni M, Cai GH, Norback D, Annesi-Maesano I, Lavaud F, Sigsgaard T, Wieslander G, Nystad W, Canciani M, Viegi G, Sestini P (2011) Total viable molds and fungal DNA in classrooms and association with respiratory health and pulmonary function of European schoolchildren. *Pediatr Allergy Immunol* 22(8):843–852
73. 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
74. Sauni R, Verbeek JH, Uitti J, Jauhiainen M, Kreiss K, Sigsgaard T (2015) Remediating buildings damaged by dampness and mould for preventing or reducing respiratory tract symptoms, infections and asthma. *Cochrane Database Syst Rev* (2):Cd007897
75. 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
76. Gauderman WJ, Urman R, Avol E, Berhane K, McConnell R, Rappaport E, Chang R, Lurmann F, Gilliland F (2015) Association of improved air quality with lung development in children. *N Engl J Med* 372(10):905–913
77. Strickland MJ, Darrow LA, Klein M, Flanders WD, Samat JA, Waller LA, Samat SE, Mulholland JA, Tolbert PE (2010) Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. *Am J Respir Crit Care Med* 182(3):307–316
78. Silverman RA, Ito K (2010) Age-related association of fine particles and ozone with severe acute asthma in New York City. *J Allergy Clin Immunol* 125(2):367–73.e5
79. Organization WH (2005) Effects of air pollution on children's health and development: a review of the evidence.
80. World Health Organization. Effects of air pollution on children's health and development. A review of the evidence. <http://www.euro.who.int/en/health-topics/environment-and-health/airquality/publications/pre2009/effects-of-air-pollution-on-childrens-health-and-development-a-review-of-theevidence>. Accessed 18 Jan 2018
81. Di Q, Wang Y, Zanobetti A, Wang Y, Koutrakis P, Choirat C et al (2017) Air pollution and mortality in the Medicare population. *N Engl J Med* 376(26):2513–2522
82. Environmental Protection Agency. Criteria air pollutants. Available from: <https://www.epa.gov/criteria-air-pollutants>. Accessed 22 Jan 2018
83. Kingsley SL, Eliot MN, Carlson L, Finn J, MacIntosh DL, Suh HH et al (2014) Proximity of US schools to major roadways: a nationwide assessment. *J Expo Sci Environ Epidemiol* 24(3): 253–259
84. Hochstetler HA, Yermakov M, Reponen T, Ryan PH, Grinshpun SA (2011) Aerosol particles generated by diesel-powered school buses at urban schools as a source of children's exposure. *Atmos Environ (Oxford, England : 1994)* 45(7):1444–1453
85. Annesi-Maesano I, Hulin M, Lavaud F, Raheison C, Kopferschmitt C, de Blay F, André Charpin D, Denis C (2012) Poor air quality in classrooms related to asthma and rhinitis in primary schoolchildren of the French 6 Cities Study. *Thorax*. 67(8):682–688
86. Madureira J, Paciencia I, Pereira C, Teixeira JP, Fernandes Ede O (2016) Indoor air quality in Portuguese schools: levels and sources of pollutants. *Indoor Air* 26(4):526–537
87. Gaffin JM, Petty CR, Hauptman M, Kang CM, Wolfson JM, Abu Awad Y, di Q, Lai PS, Sheehan WJ, Baxi S, Coull BA, Schwartz JD, Gold DR, Koutrakis P, Phipatanakul W (2017) Modeling indoor particulate exposures in inner-city school classrooms. *J Expo Sci Environ Epidemiol*. 27(5):451–457
88. Pilotto LS, Nitschke M, Smith BJ, Pisaniello D, Ruffin RE, McElroy HJ, Martin J, Hiller JE (2004) Randomized controlled trial of unflued gas heater replacement on respiratory health of asthmatic schoolchildren. *Int J Epidemiol* 33(1):208–211
89. Jhun I, Gaffin JM, Coull BA, Huffaker MF, Petty CR, Sheehan WJ et al (2017) School environmental intervention to reduce particulate pollutant exposures for children with asthma. *J Allergy Clin Immunol Pract* 5(1):154–9.e3
90. Bernstein JA, Levin L, Crandall MS, Perez A, Lanphear B (2005) A pilot study to investigate the effects of combined dehumidification and HEPA filtration on dew point and airborne mold spore counts in day care centers. *Indoor Air* 15(6):402–407
91. Lignell U, Meklin T, Putus T, Rintala H, Vepsäläinen A, Kalliokoski P et al (2007) Effects of moisture damage and renovation on microbial conditions and pupils' health in two schools—a longitudinal analysis of five years. *J Environ Monit* 9(3):225–233
92. Meklin T, Potus T, Pekkanen J, Hyvarinen A, Hirvonen MR, Nevalainen A (2005) Effects of moisture-damage repairs on microbial exposure and symptoms in schoolchildren. *Indoor Air* 15(Suppl 10):40–47
93. Karlsson AS, Andersson B, Renstrom A, Svedmyr J, Larsson K, Borres MP (2004) Airborne cat allergen reduction in classrooms that use special school clothing or ban pet ownership. *J Allergy Clin Immunol* 113(6):1172–1177
94. Nalyanya G, Gore JC, Linker HM, Schal C (2009) German cockroach allergen levels in North Carolina schools: comparison of integrated pest management and conventional cockroach control. *J Med Entomol* 46(3):420–427
95. Karlsson AS, Renstrom A, Hedren M, Larsson K (2004) Allergen avoidance does not alter airborne cat allergen levels in classrooms. *Allergy*. 59(6):661–667
96. Sublett JL (2011) Effectiveness of air filters and air cleaners in allergic respiratory diseases: a review of the recent literature. *Curr Allergy Asthma Rep* 11(5):395–402
97. Munir AK, Einarsson R, Schou C, Dreborg SK (1993) Allergens in school dust. I. the amount of the major cat (Fel d I) and dog (Can f I) allergens in dust from Swedish schools is high enough to probably cause perennial symptoms in most children with asthma

- who are sensitized to cat and dog. *J Allergy Clin Immunol* 91(5): 1067–1074
98. Chew GL, Burge HA, Dockery DW, Muilenberg ML, Weiss ST, Gold DR (1998) Limitations of a home characteristics questionnaire as a predictor of indoor allergen levels. *Am J Respir Crit Care Med* 157(5 Pt 1):1536–1541
99. Dotterud LK, Van TD, Kvammen B, Dybendal T, Elsayed S, Falk ES (1997) Allergen content in dust from homes and schools in northern Norway in relation to sensitization and allergy symptoms in schoolchildren. *Clin Exp Allergy* 27(3):252–261
100. Phipatanakul W, Koutrakis P, Coull BA, Kang CM, Wolfson JM, Ferguson ST, Petty CR, Samnaliev M, Cunningham A, Sheehan WJ, Gaffin JM, Baxi SN, Lai PS, Permaul P, Liang L, Thome PS, Adamkiewicz G, Brennan KJ, Baccarelli AA, Gold DR (2017) The school inner-city asthma intervention study: design, rationale, methods, and lessons learned. *Contemp Clin Trials* 60:14–23
101. Jassal MS, Diette GB, Dowdy DW (2013) Cost-consequence analysis of multimodal interventions with environmental components for pediatric asthma in the state of Maryland. *J Asthma* 50(6):672–680
102. Abramson SL (2018) Reducing environmental allergic triggers: policy issues. *J Allergy Clin Immunol Pract* 6(1):32–35
103. Indoor air quality tools for schools action kit. Available from: <https://www.epa.gov/iaq-schools/indoor-air-quality-tools-schools-action-kit>. Accessed 26 May 2018
104. US Environmental Protection Agency. EPA Environmental awards
105. Centers for Disease Control and Prevention (CDC) Healthy schools program: managing asthma in schools. Available from: <https://www.cdc.gov/healthyschools/asthma/index.htm>. Accessed 26 May 2018
106. Lemanske RF Jr, Kakumanu S, Shanovich K, Antos N, Cloutier MM, Mazyck D, Phipatanakul W, Schantz S, Szeffler S, Vandlik R, Williams P (2016) Creation and implementation of SAMPRO: a school-based asthma management program. *J Allergy Clin Immunol* 138(3):711–723

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