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Indoor Environmental Interventions for Furry Pet Allergens, Pest Allergens, and Mold: Looking to the Future

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Abstract

Over the last 2–3 decades, significant advances have been made in understanding the role that indoor allergen exposures play with regard to respiratory health. Multiple studies have confirmed that sensitization and exposure to indoor allergens can be a risk factor for asthma morbidity. Environmental interventions targeting key indoor allergens have been evaluated with the aims of examining their causal effects upon asthma-related outcomes and identifying clinically efficacious interventions to incorporate into treatment recommendations. Historically, it appeared the most successful intervention, as performed in the Inner-City Asthma Study (ICAS), was individually-tailored, targeting multiple allergens in a predominantly low-income, minority, and urban pediatric population. Recent studies suggest that single allergen interventions may be efficacious when targeting the most clinically relevant allergen for a population. In this article, we review recent literature on home environmental interventions and their effects upon specific indoor allergen levels and asthma-related outcomes.

Keywords

indoor allergens; environmental interventions; asthma; furry pet allergens; mouse allergen; cockroach allergen; fungal allergens; inner-city asthma; childhood asthma

Introduction

Over the last 2–3 decades, significant advances have been made in understanding the role that indoor allergen exposures play with regard to respiratory health. Epidemiologic studies

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have confirmed that asthmatic individuals with sensitization to indoor allergens tend to have a more severe asthma phenotype, and that sensitization and exposure to allergens can be a driving factor in asthma morbidity (1–6). Modern society has shifted toward spending more and more time indoors (7), making these correlations between allergen exposure and disease severity increasingly relevant. Many studies have evaluated various indoor environmental interventions targeting key indoor allergens with the aims of examining their causal effects upon asthma-related outcomes and identifying clinically efficacious interventions to incorporate into treatment recommendations. However, synthesizing the home environmental intervention literature is difficult because of the heterogeneity of these types of studies (8).

Environmental intervention studies are tailored to specific populations, designed to evaluate specific interventions, and powered to measure specific outcomes, and these features vary from one study to another. Even though the majority of US based studies are performed in low-income, urban populations, and generally involve children, there are still substantial differences between studies in the allergens targeted, the methods used to intervene on those allergens, and the outcomes evaluated. In addition, since the clinical relevance of an allergen varies based on ecology, geography, and housing stock among other factors, outcomes from one population may not be reproducible in another geographically or ecologically different population or location. Furthermore, studies approach the environmental interventions to reduce these allergens with myriad techniques. While some studies take the approach of using pragmatic, easily deliverable interventions targeted at allergen reduction (i.e. single interventions or simply education for participants about how allergens can be reduced), others are designed as multi-faceted complex interventions targeting multiple allergens in the home environment along with provision of education about allergens. The methods by which studies measure everything from study eligibility (presence of allergen in the home, sensitization status of participants, evidence of clinical reactivity to the allergen, etc.) to allergen reduction (decrease in major allergen levels, decrease in report of pest sightings, etc.) to clinical outcomes (healthcare utilization, symptoms, medication usage, etc.) also vary. Although this degree of heterogeneity among study designs makes it difficult to draw broad conclusions about the efficacy of indoor environmental interventions generally, the literature is informative for understanding which allergens are likely to be most relevant for a patient or a community, which patients or communities would be most likely to benefit from allergen interventions, and which interventions are most likely to result in clinically meaningful reductions in the target allergen. In this article, we review recent literature on home environmental interventions and their effects upon specific indoor allergen levels and asthma-related outcomes.

Furry Pet Allergens

Cats and dogs are the most common furry pets found in American homes. Market research statistics published by animal food suppliers estimate that approximately 50% of households in developed countries have pets, with slightly higher dog ownership (~47%) than cat ownership (~37%) (9). Fel d 1 and Can f 1, the respective major allergens for cats and dogs, are found in the saliva, skin, and hair follicles of these animals. These pet allergens are predominantly carried on small particles (<10–20 um), allowing them to remain airborne for long periods of time and adhere to clothing and surfaces (10). As a result, pet allergens are carried long distances, and are passively transferred to environments where no pets may be present. Can f 1 and Fel d 1 can be found in almost all homes, although the concentrations are 10–1000 times higher in homes with pets than in homes without pets (11,12). These pet allergens are also ubiquitous in public places such as schools and office buildings (13,14).

Allergic sensitization to cat and dog is quite common; approximately 12% of the general population and 25–65% of children with persistent asthma are sensitized to cat or dog allergens (1, 2, 15–17). Pet allergen exposure has been linked to worse asthma outcomes in animal-sensitized adults and children with asthma (4, 17,18).

The most effective long-term strategy for environmental remediation in pet-sensitized individuals is to remove pets from the home (19). Even after removing a pet from the home, it can take several months before significant reductions in allergen levels are achieved (20). The only study of pet removal was a prospective, controlled, but non-randomized trial of pet removal for 20 adults with newly diagnosed pet-allergic asthma, which demonstrated that pet removal was associated with substantial reductions in controller medication needs. At 1 year follow-up, none of the subjects in the pet removal group required inhaled corticosteroids (ICS) compared to 9/10 in the control group that kept their pets ($p<0.001$) (21). While removing the pet from the home is an effective strategy, it is difficult to implement in practice due to most patients' reluctance to give up their pets. As a result, there have been several studies examining the efficacy of other interventions aimed at reducing indoor pet allergen levels to improve asthma in sensitized individuals.

Frequent washing of animals has been evaluated as a means of reducing airborne allergen levels. Unfortunately, washing cats demonstrated no benefit or transient benefit in airborne Fel d 1 levels that was not sustained, even at 1 week post-washing (22,23). Dog washing reduced recoverable allergen levels from dog hair and dander, but the results were short-lived unless the dog was washed twice a week (24). Given the difficulty in maintaining regular washing of animals, particularly cats, along with the transient benefit, these interventions have understandably not been widely embraced.

Evaluation of HEPA air filters for the purpose of reducing airborne pet allergen levels and thereby theoretically improving asthma has also been performed with largely negative results. Although use of HEPA filters has been associated with approximately 30–40% reduction in airborne cat allergen levels as compared with placebo filters, settled dust pet allergen levels do not appear to be affected, and minimal to no corresponding significant improvement in asthma or allergic rhinitis symptoms has been reported (12,25). Together, these findings suggest that the degree of allergen exposure reduction may be insufficient to result in clinical improvements. Use of free standing HEPA air filters in multiple rooms of a home, along with frequent vacuuming, has been correlated with improvements in asthma outcomes in one study, despite minimal change in settled dust allergen levels (26), suggesting that the air filters may have reduced airborne pet allergen or another airborne contaminant or pollutant.

Patients will commonly ask about obtaining “hypoallergenic” dog breeds if they (or their children) are known to be dog allergic. Unfortunately, there is no evidence to support the claim that any breed of dog is “hypoallergenic” (27). In fact, in a study of Can f 1 levels in the hair and homes of various breeds of dogs, there was no difference in airborne levels of Can f 1 in homes with “hypoallergenic” breeds vs other breeds. In fact, the purportedly “hypoallergenic” breeds actually had higher Can f 1 levels in hair and coat samples than the “non-hypoallergenic” breeds (28). Thus, there is no evidence to suggest that “hypoallergenic” dogs would be of benefit in the dog-sensitized patient.

For patients with allergic asthma and known sensitization to furry pet allergens, pet removal/relocation from the home remains the most effective method for obtaining reductions in pet allergen reductions in the home over the long-term (19).

Mouse allergen

Mice are ubiquitous in many urban environments, and their role in respiratory allergic disorders in community-based populations has become firmly established in the last 10–15 years (2, 29–31). The major mouse allergen, Mus m 1, is excreted in mouse urine. Mus m 1 is carried on small particles, mainly <10 microns; thus, it remains airborne for prolonged periods of time (32–34).

Several studies have demonstrated that in some low-income, urban communities, particularly in the Northeastern and Midwestern United States, mouse allergen exposure, as assessed in settled dust samples, is virtually ubiquitous, while about 75–80% of suburban homes have detectable mouse allergen in settled dust. Perhaps more importantly, concentrations of mouse allergen in settled dust are 100–1000-fold higher among certain low-income, urban neighborhoods than among suburban neighborhoods. (2, 3, 5, 6, 30, 31, 35). Certain home characteristics have been associated with higher concentrations of mouse allergen, including presence of holes or cracks in the walls or doors; report of mouse sightings; and presence or report of cockroaches (30, 35, 36). However, mouse allergen can be present even without reported mouse sightings in the home, particularly in neighborhoods where mouse infestation is endemic. The presence of a cat in the home is associated with lower mouse allergen concentrations; however, most individuals with asthma demonstrate sensitization to both mouse and cat (2, 3, 5), making acquisition of a cat a poor solution for improving asthma outcomes.

Sensitization to mouse is quite common; it is estimated that 18–51% of urban, low income children are sensitized to mouse (2, 3, 5, 30). In urban children with asthma, sensitization to mouse has been independently associated with rhinitis (37). Furthermore, mouse allergen sensitization and exposure has also been linked to a higher risk of asthma morbidity in multiple studies, and it may play a greater role in asthma morbidity than other allergens in cities such as Baltimore and New York City (2, 3, 6, 31, 38).

Given this understanding of the role mouse allergen plays in asthma morbidity, the next logical step has been to intervene with the aim of reducing the concentration of this allergen in the home. Studies aimed at reducing mouse allergen concentration have generally employed integrated pest management (IPM). IPM is a multifaceted interventional approach that includes vigorous cleaning, meticulous food disposal, sealing of holes and cracks in housing structures, setting traps, and if necessary, application of rodenticide, with the aim of reducing mouse allergen concentrations in homes with mouse infestation. A variety of approaches to implementing IPM, including education, provision of IPM materials (along with demonstrations of how to use them) to participants, and professional delivery of pest management interventions, have been employed in studies involving IPM interventions (39).

The first IPM study, to our knowledge, was a pilot study of professionally-delivered IPM that resulted in ~75% reduction in mouse allergen concentrations in the intervention group and an increase in mouse allergen concentrations in the control group (40). Building on this finding, the Mouse Allergen and Asthma Intervention Trial (MAAIT) compared a similar professionally-delivered IPM intervention to education about IPM and observed ~70% reductions in mouse allergen in both groups (41). However, other studies that tested IPM educational interventions as a part of multi-faceted interventions observed little change in allergen concentrations between the IPM education groups and the control groups, suggesting that IPM education in the context of a multi-faceted intervention may be ineffective in reducing mouse allergen concentrations (31, 38).

Several of these studies have observed a direct link between substantial reductions in mouse allergen and clinical benefit. Sufficiently large (≥50–75%) reductions in mouse allergen concentrations are correlated with significant and clinically meaningful improvements in measures of asthma outcomes, while smaller reductions in the mouse allergen concentration may not be associated with any significant effects on asthma morbidity (31, 38, 41). Taken together, these studies suggest that it is feasible to reduce mouse allergen concentrations and have an impact on asthma morbidity. Furthermore, it is possible that IPM education alone, as a single allergen intervention, may be effective; thus, use of IPM education deserves further study. In particular, this approach is attractive for community-level interventions because it is more readily scalable than individually-tailored multi-allergen interventions, and it can be targeted to communities with a high asthma morbidity burden where mouse allergen is known to be a major contributor to asthma morbidity.

Interestingly, while large relative reductions in mouse allergen concentrations have been achieved along with correlating meaningful improvement in asthma in MAAIT, the concentration of mouse allergen tended to remain in a range that is known to be associated with increased risk of asthma morbidity (41). This observation underscores the need for further work on intervention methods that could provide even greater reductions in mouse allergen concentrations; such interventions could include home renovations or housing mobility programs to support moving to better housing in non-poor neighborhoods.

For now, patients with allergic asthma and evidence of mouse sensitization and exposure can be provided education about implementing IPM. In some cities, there are local resources provided by the health department or non-profit organizations, which sometimes include home visiting and comprehensive education about implementing IPM. In addition, families who rent should be encouraged to also request that their landlord provide pest management services. If a family is having difficulty engaging the landlord, housing regulations provide a path for compelling the landlord to remediate health hazards in the home. And finally, in a few cities, housing mobility programs exist whereby organizations aid families in moving from high poverty neighborhoods to better housing in low poverty neighborhoods.

Cockroach allergen

The two most common cockroaches in US homes are the German cockroach (*Blatella germanica*) and the American cockroach (*Periplaneta Americana*). The major allergens for these species (Bla g 1, Bla g 2, and Per a 1) of cockroach are found in the saliva, secretions, debris, and fecal material. Cockroach infestation is associated with presence of highly dense population, urban environment, and low socio-economic status (42). At least half of urban, low income homes have a clinically relevant level of cockroach allergen, and as many as 30% of suburban, middle class homes may also have detectable levels of cockroach allergen (43, 44). However, the levels in suburban homes are generally much lower than in urban, low income homes (45).

In low income, urban populations, 60–80% of children with asthma are sensitized to cockroach (1, 46), and in one suburban population, the sensitization rate was 21% (45). Cockroach allergen has also been repeatedly linked to poorer asthma outcomes in low income, urban children with asthma, including increased asthma related health-care utilization (1, 43, 47). However, recent studies in Baltimore and New York City have suggested that cockroach allergen may be less clinically important than mouse allergen in these populations (2, 38). It is important to note, however, that the lack of population-level clinical effect of cockroach allergen does not mean that an individual in the population is not affected by cockroach allergen exposure.

Substantial (80–90%) reductions in cockroach allergen levels can be achieved using an IPM approach to target cockroach infestation in the home (48–51). IPM approaches targeting cockroach allergen in the home generally employ multiple modalities including application of pesticide, sealing of cracks and holes, vigorous cleaning aimed at reducing allergen reservoir, and meticulous food disposal. When compared to no intervention, these approaches are successful in producing substantial reduction in cockroach allergen levels in homes of low income, urban children with asthma (49–52). However, an entomologist-led intervention of placement of insecticidal bait alone, without the other components of integrated pest management, appears to be highly effective, as it has been associated with 80–90% reductions in measures of cockroach exposure (53–54). In one randomized, controlled 3-arm trial, entomologist-led cockroach intervention produced significantly lower trapped cockroach counts than both a commercial pest control company cockroach intervention and a control that received no intervention (53), indicating that use of a single, strategic intervention can be highly effective.

Findings from at least two randomized, controlled trials in children with asthma have supported a link between reduction in cockroach exposure and improvement in markers of asthma morbidity. Clinical benefit has been observed with sufficiently large (≥50–90%) reductions in cockroach exposure, as measured by decreases in cockroach allergen concentrations or mean trapped cockroach counts (51,54). While the correlation between decreases in cockroach exposure and clinical benefit has been strongest in children both sensitized and exposed to cockroach allergen, some benefit has also been suggested in children who are exposed but not sensitized to cockroach (54). Contrary to these studies, a recent randomized, controlled multi-allergen interventional study targeting cockroach allergen (among other allergens) in homes of children with asthma in New York City demonstrated no change in asthma controller medication correlating with cockroach allergen reduction (38). However, the reductions in the level of cockroach allergen in settled dust from bedroom and kitchen appeared similar in the control and intervention groups, indicating that the intervention was not successful in reducing targeted allergen levels; thus, no change in asthma control would be expected.

For patients with allergic asthma and evidence of cockroach sensitization and exposure, strategic use of gel bait insecticides containing fipronil or indoxacarb targeted to areas with cockroach activity (54) (ie. Darks spaces, cracks, and crevices) may be the most effective strategy to decrease cockroach allergen burden in a home. Insecticide sprays should be avoided. Insecticide gel bait products are sold directly to the consumer, but pest management professionals may also be engaged and asked to employ this approach

Dampness and Molds

Fungi, commonly known as “molds,” are ubiquitous in the indoor and outdoor environments. Over 100,000 fungi have been described to date, but true fungal diversity is likely to be an order of magnitude greater than what is already known (55–57). Common outdoor fungi include *Alternaria* and *Cladosporium*, while fungi more commonly associated with indoor dampness and water damage include *Penicillium* and *Aspergillus* (58). “Outdoor” fungi are commonly found indoors, as they can be tracked in through open windows and doors, and on clothing and pets. Total fungal exposure in a home is difficult to measure, as there is no standard method to identify and quantify fungus. Direct microscopy and culture-based volumetric air sampling can be used to identify spores and/or measure fungal metabolites. Immunoassays, quantitative PCR and genomic sequencing have been employed to assess fungal diversity, as well. Methods used to quantify and assess fungi are not consistent across studies.

The best predictors for indoor concentrations of fungi are 1) outdoor concentrations when windows are open, and 2) overall dampness in a home when windows are closed (59). Significant problems with mold in buildings are a direct result of excessive moisture, which can result from water intrusion, inadequate ventilation, defective plumbing or other building problems; concentration of fungal allergens in settled dust correlate with carbon dioxide levels, a marker of building ventilation, and they are highest at ambient temperatures of 20°C to 22.5°C (60). Organic building material such as wood, cellulose, dry wall, and cardboard are most vulnerable to fungi (61). Assessment tools and questionnaires have been created to assist physicians in determining when home assessments for potential mold exposure are warranted (62, 63).

Although most fungi are not implicated in human disease, some have been linked to asthma and atopy. True sensitization rates to fungi are difficult to ascertain, as it is believed that most fungal species have not yet even been identified (56,57). General population estimates of overall sensitization to fungal allergens range from 8–14% (64–66), but the estimates are considerably higher in atopic individuals. In one study, 50% of children with asthma demonstrated sensitization to at least one fungal allergen (67), while 76% of individuals with multiple hospitalizations for asthma were noted to have sensitization to fungal allergens in another study (68). Interestingly, associations between exposure to fungi and risk of respiratory symptoms have been found regardless of sensitization status, but sensitization to fungi is believed to increase the risk of morbidity (67, 69). This observation suggests fungi may also have biologic effects through non-IgE mediated mechanisms as fungal components can directly activate the innate immune system.

Exposure to dampness and molds in the home has been associated with increased asthma morbidity in multiple studies involving both children and adults, and multiple meta-analyses and systematic reviews have concluded that enough evidence exists to demonstrate this association (70–72). Poor asthma control in children has also been linked to the presence of visible mold or mold odor in the home (73). In children with sensitization and exposure to fungus, exposure to *Penicillium* has been correlated with increased asthma exacerbations (17, 67). Sensitivity to *Aspergillus fumigatus* has been associated with severe persistent asthma in adults (74). Exposure and sensitization to Alternaria species has been associated with increases in asthma symptoms, bronchial hyperresponsiveness, and severe asthma exacerbations (75–80).

Interventional studies have suggested a role for remediation of dampness and mold to reduce adverse respiratory health effects associated with dampness and mold exposure (81–83). The interventions employed have included multiple of the following modalities: removal of mold from hard surfaces, elimination of rainwater intrusion, installation of ventilation systems, and repair of plumbing leaks. These randomized, controlled interventional studies, together, have demonstrated improvement in asthma outcomes, including fewer asthma symptom days, less acute healthcare utilization, and decreased asthma medication usage associated with improved ventilation, decreased dampness, and decreased mold for both children and adults with asthma, irrespective of sensitization status to mold (81, 82). One observational study followed children with asthma who moved into “Breathe Easy Homes” (BEHs) with structural features to prevent moisture intrusion, interior materials that minimized dust, and ventilation systems with filters. In this study, levels of exposure to mold, dampness, and also rodents were significantly decreased in the BEHs; after 1 year in the BEHs, participants were noted to have less asthma symptoms days, less acute healthcare utilization for asthma, and improved caretaker quality of life (84). Systematic reviews have also concluded that sufficient evidence exists to recommend dampness and mold remediation in homes to help reduce asthma symptoms in both children and adults (85, 86). While these interventions all target much more than just dampness and mold, likely affecting the levels of other pollutants and allergens in the home, they have shown promise in improving asthma health outcomes.

For patients with allergic asthma and mold sensitization, use of a central HVAC system with properly maintained filters can help reduce transport of outdoor fungal spores indoors. In addition, decreasing dampness through fixing leaks and water extravasation along with removal of visible mold can be of benefit in decreasing mold allergen burden within the home. Care must be exercised when attempting to remove visible mold and when using chlorine-based bleach products to kill mold spores. The National Institute of Occupational Safety and Health (NIOSH) recommends use of an N-95 mask at minimum when removing visible mold. When using chlorine-based bleach products, respirators with specific chemical cartridges are necessary to prevent injury to the lung from the chemical fumes (87). Many commercial companies offer mold remediation services. The Centers for Disease Control recommends the following: 1) ensure the contractor has experience cleaning up mold, 2) ensure the contractor is willing to use guidelines and recommendations set forth for mold remediation by either the Environmental Protection Agency (EPA), American Conference of Governmental Industrial Hygienists (ACGIH), or guidelines set forth by another governmental institution or agency (88).

Further Considerations

Since the landmark Inner-city Asthma Study (ICAS) in 2004 provided high level evidence to support the efficacy of an individually-tailored, multi-faceted home environmental intervention for inner-city children with asthma, several trials have been conducted that have highlighted the complexity of implementing these interventions, the challenge of interpreting their results, and the need for well-designed studies focused on implementation of these types of interventions, in particular pragmatic clinical trials (Table 1). In the past 5 years, 4 clinical trials have been conducted that have targeted pet allergens, pest allergens, or mold, in multi-allergen and single allergen interventions (Table 1) and are instructive for the issues discussed below.

Interpreting Environmental Intervention Trial Results

Environmental intervention trials are distinctly different from trials that test a drug because the framework of these trials is that the intervention being performed is intended to reduce allergen exposure, and it is the reduction of allergen exposure that is expected to have the direct clinical benefit. This feature increases the complexity of conducting, reporting, and interpreting environmental intervention trials. There are some studies that suggest a mediating effect of allergen reduction upon asthma morbidity because of the greater improvement in asthma in the intervention group than in the control group (38, 41, 51). However, without understanding the effect of the intervention on the targeted allergen exposure, it is difficult to determine whether the intervention improved asthma outcomes by reducing exposure or through an effect on some other factor, such as medication adherence. As such, all trials should include measurement of the exposure(s) that are intended to be targeted as well as an assessment of the degree of exposure reduction in each group and whether the changes in exposure(s) between groups are statistically significant and clinically meaningful. In addition, an exploration of whether changes in other factors, aside from the targeted exposure(s), may explain the effect of the intervention on the clinical outcomes would also help in evaluating the likelihood that the intervention's health effects were mediated by reductions in the targeted exposure(s). More sophisticated statistical approaches have also been developed to evaluate whether it is the reduction in the environmental exposure that results in the improvement in health outcomes, or whether the intervention exerts its health effects through another factor such as improved awareness of the medical condition, improved medication adherence, or more frequent visits to medical providers (89, 90).

Single vs. Multi-allergen Interventions

The National Asthma Education and Prevention Program Expert Panel Report 3 (NAEPP EPR-3) endorses a multifaceted, multi-allergen approach to indoor aeroallergen trigger reduction, largely based on the ICAS trial results (51). However, some evidence from recent single allergen intervention studies suggest that interventions targeting a single allergen exposure may be effective in both reducing allergen levels and in decreasing asthma morbidity, and this approach deserves further study (41, 54). In addition, a recent intervention trial by DiMango and colleagues that used the same intervention approach used in ICAS that targeted multiple allergens did not show any effect on controller medication treatment step, the primary outcome (36). Unlike the ICAS trial, the DiMango trial appeared to have little effect on indoor allergen levels, suggesting that the lack of clinical efficacy may have been due to lack of effect on allergen exposure. Together these studies suggest that both multi-allergen and single allergen interventions can be successful in improving asthma outcomes if they are able to achieve substantial reductions in the targeted allergen(s), but more work is needed to optimize intervention methods so that they consistently achieve substantial reductions in the targeted allergen(s). The current intervention methods may be optimized, for instance, through simplification to reduce costs, improve adherence, and improve the feasibility of delivering the intervention on a population-level; or we may find that we need to develop entirely new intervention methods to effect large, clinically meaningful reductions in the allergens that are targeted.

Pragmatic Clinical Trials and Implementation Research

Another consideration is the challenge of implementing these environmental interventions in medical and public health settings. Although there are several studies evaluating public health programs that incorporate both asthma education and a home environmental component of some kind, these types of programs typically do not incorporate a comparison group and/or do not measure allergen exposure (91–95). Thus, there is an evidence gap that lies between clinical trials and public health practice, which needs to be filled with pragmatic clinical trials and other rigorous implementation research. Single allergen interventions are particularly attractive for community-level, public health oriented pragmatic trials, as they are more easily scaled than multi-allergen interventions. Community-level interventions also provide an opportunity to intervene in other indoor spaces in a neighborhood, such as schools, where clinically significant allergen exposure can occur (4, 96).

Cost Effectiveness and Payment of Environmental Interventions

A related issue is that cost-effectiveness data are lacking, due, at least in part, to the existence of only a few large trials that demonstrated efficacy of the intervention. One cost-effectiveness analysis of the ICAS trial found the cost per year per family ($750 to $1000) to implement the intervention was equivalent to the cost of midrange inhaled corticosteroid and albuterol for a child with moderate to severe asthma (97). It is possible that this cost provides benefit to more than one child for the one year period of the intervention since the clinical benefit of the intervention persisted for one year beyond the intervention period; in many low-income, urban communities, multiple household members have allergic asthma, and they may also benefit from a home environmental intervention. Since single allergen interventions are likely to be less costly to implement than multifaceted interventions, cost-effectiveness studies for this environmental intervention approach are needed. Not surprisingly, given the limited cost effectiveness data, insurers have generally have not covered the outreach, education, environmental assessments, or durable goods and services integral to home environmental interventions. However, given the recent focus on implementing value-based payment models, and the endorsement of home based environmental interventions by the NAEPP-EPR-3 guidelines, several pilot programs are evaluating the cost-effectiveness of a variety of payment models for environmental interventions (98).

Conclusion

Environmental interventions have had mixed results, but are successful in some settings and populations in reducing indoor allergen levels and in reducing asthma symptoms and exacerbations. Until recently, it appeared the most successful intervention was one that was individually-tailored and targeted multiple allergens in a predominantly low-income, minority, and urban pediatric population (51). Newer studies have suggested that single allergen interventions may be efficacious when targeting the most clinically relevant allergen for a population (38, 41, 54). In addition, whether the intervention targets a single allergen or multiple allergens, findings across multiple studies suggest that substantial reductions in allergen levels may be required to observe a clinical effect. Areas that need further study include the sustainability of both the exposure and clinical effects of the interventions. In addition, community- and population-level pragmatic clinical trials will provide insight into whether, and how, the successes that have been achieved can be effectively translated to practice. Use of single interventions, in particular, is an attractive approach to allergen abatement at a population level. Our challenge, moving forward, is to identify the interventions that are most effective at both reducing allergen exposure and at decreasing asthma morbidity with an eye toward evaluating how best to implement them in medical and public health practice.

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ABBREVIATIONS

ICAS	Inner-city Asthma Study
IPM	Integrated Pest Management
MAAIT	Mouse Allergen and Asthma Intervention Trial
BEH	Breathe-easy Home

NAEPP-EPR-3	National Asthma Education and Prevention Program Expert Panel Report 3

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Table 1

Clinical trials of home-based pet, pest, and/or mold allergen exposure interventions for asthma morbidity from the past 5 years Ahluwali a 31

			The Head-off Environmental Asthma in Louisiana Study **Mitchell** **2012**	**Individually-tailored, multi-faceted intervention** **DiMango** **2016**	**Mouse Allergen and Asthma Intervention Trial** **Matsui** **2017**	**NO-Roach** **Rabito** **2017**
GENERAL STUDY DESIGN	**Study Design**	Randomized?	Non-randomized	Randomized	Randomized	Randomized
		Control?	Control: none	Control: Education	Control: Education	Control: Not explicitly described
		Single, double blinded?		Unblinded	Unblinded	
		Clinical or Pragmatic Trial?	trial study	clinical trial	clinical trial	clinical trialBlinding not described
		Duration?	1 year	40 weeks	1 year	1 year
	Exposures targeted	Single or multi-exposure intervention?	Multiple exposures	Multiple exposures	Single exposure	Single exposure
		Which allergen(s)?	Major indoor allergens, including mold	Major indoor allergens	Mouse allergen	Cockroaches
INTERVENTION METHODS	**General approach**	Education or other behavioral intervention	Asthma counselor-delivered education & educational indoor allergen intervention modules.	Educational indoor allergen intervention modules.	Education about IPM & pest management.	No educational component.
		Provision of intervention by study				
		Both educational/behavioral and provision of intervention	Included supplies provided by study staff	Included supplies provided by study staff	Other goods and services provided by study staff	Intervention performed by study staff
	Specific intervention goods/services	Air cleaners	Two educational allergen intervention modules delivered by study staff, provision of supplies. air cleaner, mattress and pillow encasements	Repeated educational allergen intervention modules delivered by study staff, provision of supplies, air cleaners, safe sleeping zone	Repeated IPM, including trap setting, application of rodenticide, targeted cleaning, sealing holes and cracks. Allergen-proof mattress and pillow encasements. Air cleaners	Repeated, targeted insecticidal baiting performed by study team
		Cleaning, washing				
		Allergen-proof mattress & pillow encasements				
		IPM				
		Other				
STUDY POPULATION	**Study Population**	Sample size	182 children in New Orleans with moderate to severe persistent asthma. Predominantly black and low-income. 62% of homes had water damage from hurricane Katrina. ~60% of homes had high Alternaria concentrations.	147 children & adults in New York City with persistent asthma. Predominantly minority. Sensitized to at least one major indoor allergen & highly exposed to at least one allergen to which the participant was sensitized.	361 children & adolescents in Baltimore and Boston with persistent asthma & recent exacerbation. Predominantly minority, low-income. All sensitized to mouse and with high levels of mouse allergen in home.	102 children and adolescents in New Orleans with moderate to severe asthma & cockroaches trapped in home. Predominantly black and low-income. ~1/4 sensitized to cockroach.
		Inclusion/exclusion criteria				
		Sociodemographic characteristics				
		Asthma characteristics				
		Allergic sensitization characteristics				
		Allergen exposure characteristics				

			The Head-off Environmental Asthma in Louisiana Study **Mitchell** **2012**	**Individually-tailored, multi-faceted intervention** **DiMango** **2016**	**Mouse Allergen and Asthma Intervention Trial** **Matsui** **2017**	**NO-Roach** **Rabito** **2017**
ALLERGEN EXPOSURE	**Allergen exposure assessment**	Any exposure assessment?	Mold spore counts, major indoor allergens measured in settled dust samples	Major indoor allergens measured in settled dust samples	Mouse allergen measured in settled dust and air samples	Cockroach counts in traps
		Method used: questionnaire, environmental measurements, counts of pests, etc.				
	Degree of exposure reduction	Was the exposure reduced overall? By group?	~50% reductions in bedroom spore counts & Alternaria allergen levels from baseline to 12 months.	Cockroach, dog, dust mite, cat, mouse all decreased in intervention group by ~30–50%. Dust mite and mouse allergen also decreased in control group by ~20–30%. Differences in changes in indoor allergens between groups were not assessed.	Mouse allergen exposure reduced by ~70% in both groups.	Cockroach counts were markedly reduced in both groups, but to a greater extent in the intervention group.
		Were there differences in degree of exposure reduction between the control and intervention groups?				
		What was the magnitude of difference of reduction between the intervention and control groups?				No intervention homes had cockroaches at 12 months vs. 22% of control homes
CLINICAL OUTCOMES	**Clinical outcomes**	What outcomes were measured?	Primary outcome: “Maximal symptoms days”	Primary outcome: reduction in asthma step therapy between randomization and 40 weeks of study treatment.	Primary outcome: “Maximal symptoms days”	Primary outcome: “Maximum symptom days”, not validated
		What methods were used to measure the outcomes, and are they validated methods?	Statistically significant ~3 day decrease in maximal symptoms days/2 weeks from baseline to 12 months	No difference between groups in the primary outcome measure or any secondary asthma outcomes	No difference between groups in the primary outcome measure or any secondary asthma outcomes	Statistically significant improvements in maximum symptom days, unscheduled visits, proportion with FEV1<80% predicted in intervention vs. control groups. Reduction in unscheduled visits clinically meaningful (~1 visit), 1.8 days fewer of symptoms/2 weeks. No effect on missed school days, lost caregiver sleep, asthma control, FENO. Effects were largely explained by effects observed among cockroach sensitized sub-group.
		What degree of clinical improvement was observed overall, and in each group?				
		Were there differences in clinical improvement between groups?				
		Were the differences statistically significant? Clinically meaningful?				
OTHER CONSIDERATIONS	**Allergen exposure reduction as mediator of clinical effects**	Was there an analysis of the association between allergen reduction and clinical outcomes?	No analyses performed	Post-hoc analyses performed examining effect of mouse and cockroach allergen reduction on treatment step. Reduction in mouse was associated with a greater reduction in treatment step compared to those who did not have a reduction in mouse allergen. There was no effect of a reduction of cockroach allergen exposure.	Pre-specified exploratory analysis across all participants demonstrated correlations between reduction in mouse allergen and improvements in most asthma outcomes, including symptoms and acute care. Clinically meaningful effects on asthma outcomes were observed with >50% reduction in mouse allergen.	No analyses performed
	Comments	Limitations (loss-to-follow-up, comparison groups, assessment of other	Without a control group, not possible to know whether	There may not have been a greater reduction of indoor allergens in the	Findings suggest that IPM education alone may be	Striking reduction of cockroach counts in control group as well as the

			The Head-off Environmental Asthma in Louisiana Study **Mitchell** **2012**	**Individually-tailored, multi-faceted intervention** **DiMango** **2016**	**Mouse Allergen and Asthma Intervention Trial** **Matsui** **2017**	**NO-Roach** **Rabito** **2017**
		mediators that may explain effect of intervention on health outcomes, etc.)	reductions in mold were due to the intervention. The authors note, though, that the magnitude of the reduction in maximum symptoms days was similar to what has been observed in RCTs with control groups.	intervention group than the control group. If so, the lack of clinical effect could be due to lack of effect of the intervention on allergen exposure.	effective, but no comparison group that received no IPM education. Striking reductions in mouse allergen in both the control group (Education) and the intervention group.	intervention group. Unclear if other things may have changed along with the elimination of cockroaches that may have explained the clinical effect.

Table 2

Recommendations for Allergen Abatement

Indoor Allergen	**Recommended Intervention for Allergen Reduction**
Furry Pets	Removal of the pet from the home
Cockroach	Integrated pest management; strategic use of gel bait insecticides containing fipronil or indoxacarb targeted to areas with cockroach activity
Mouse	Integrated pest management; comprehending education about implementing IPM
Fungi/Molds	Decreasing dampness through fixing leaks and water extravasation along with removal of visible mold