

Dust Mites: Using Data from an Intervention Study to Suggest Future Research Needs and Directions

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Abstract: *Dermatophagoides farinae* (Der f 1; referred as Der f hereafter) and *D. pteronyssinus* (Der p 1; referred as Der p hereafter) are common allergy-causing mites found in homes worldwide. Mites are more prevalent in humid climates, but are rare or absent in drier climates. Levels of dust mite sensitivity have been reported between 48% and 63% for asthmatic children. Dose-response relations between levels of dust-mite exposure and sensitivity have been reported; yet, relatively high levels of dust mite sensitivity (50%-60%) have been found in populations exposed to concentrations below the proposed cut-point sensitization concentration of 2 µg dust mite per gram of dust. A meta-analysis of 49 trials involving 2733 patients found that interventions for dust mite-control did not result in any clinical benefit to mite-sensitive asthmatics. We assessed the impact of replacing old mattresses with dust-mite resistant mattresses on dust-mite levels, and to a more limited extent, on health outcomes. Replacement mattresses were provided to 44 asthmatic children residing in public housing in inner city Boston, Massachusetts. At baseline, we found concentrations to exceed the cut point of 2 µg g⁻¹ in only 9% of beds for Der p and 16% for Der f. Only 7% of beds for Der f and 5% for Der p exceeded 10 µg g⁻¹. Dust-mite allergy levels were high in these asthmatic children (54% for Der f and 62% for Der p) despite low baseline mattress levels. Our intervention reduced Der p (p=0.026) and Der f (p<0.001) below their low starting levels. Investigations are needed that (1) evaluate the reduction of dust-mite levels below the suggested cut-points for sensitization and exacerbation; (2) assess the impact of reduction of multiple antigens; (3) assess exposure to dust mites outside of the home; and (4) test bundled interventions.

Keywords: dust mites; mattresses; public housing; allergy; asthma; interventions

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INTRODUCTION

Asthma is a complex disease in terms of causation, exacerbation, diagnosis, expression, and management. The disease is responsive to a range of clinical, educational, and environmental interventions, but with varying degrees of success /1-2/. Success may depend on an ability to recognize and address the specific environmental factors to which the asthmatic is allergic and that are present in their environment /3/. The success of interventions can be complicated because present living conditions may differ from prior living conditions in which the initial asthma sensitization took place.

Intervention and, more recently, prevention measures have sought to recognize and address the matrix of direct and indirect causative and exacerbating influences for asthma. Intervention and prevention measures can be categorized as pharmacological or non-pharmacological, the later typically involving educational and environmental intervention strategies to reduce the exposure concentrations of the relevant allergens /4/.

Dermatophagoides farinae (Der f 1; referred as Der f hereafter) and *D. pteronyssinus* (Der p 1; referred as Der p hereafter) are common allergy-causing mites found in homes worldwide. The most prevalent mite species and associated allergens that

are found in homes differ geographically, between homes within a geographical region and by areas within a home. Mites are more prevalent in humid climates but are rare or absent in drier climates unless humidity is artificially raised /5/. Housing characteristics and types of floor coverings have been found to influence the prevalence of dust mite allergens /6/. Levels of Der f and Der p are usually lower in apartments than in houses, likely due to the higher ambient temperatures and lower relative humidity typically found in apartment buildings /7/. Der f is more common than Der p and is more common in the cooler, less humid northern climates./6/.

Levels of dust mite sensitivity between 48% and 63% have been reported for asthmatic children /8-9/. Dose-response relations between levels of dust-mite exposure and sensitivity have been reported; yet, relatively high levels of dust mite sensitivity (50% to 60%) have been observed in populations exposed to concentrations below the proposed sensitization cut-point of 2 µg dust mite per gram of dust /10/.

A meta-analysis of 49 trials involving 2733 patients found that interventions for dust-mite control did not demonstrate any clinical benefit to mite-sensitive asthmatics. The outcome most commonly assessed was morning peak flow, but many other outcomes—symptom scores, FEV1 (forced expiratory volume in 1 second), and others—were similarly devoid of evidence of any beneficial effect. Thirty-one trials used physical methods of dust mite control, ten used chemical methods, and eight used a combination of physical and chemical. Mite reduction occurred in 13 trials, and reduction was unsuccessful in 24 and not measured or reported in the remaining 12 trials /11/.

A multi-tiered intervention that included dust-mite control, along with control of cockroaches, tobacco smoke, mold and other risk factors, was associated with reduced asthma symptom days. This study was not included in the meta-analysis. Although attributing the improvements to a particular component of the intervention is difficult,

reductions in the levels of cockroach allergen and dust mite allergen Der f in the bedroom were significantly correlated with reduced complications of asthma /9/.

The combination of the continued application of dust mite control measures in practice and the weak evidence that doing so has a beneficial health effect suggests that, despite numerous studies, further research is needed, particularly with respect to the role and impact of dust-mite control as a part of bundled interventions and the impact of interventions on low concentrations.

In the United States (US), the Healthy Public Housing Initiative (HPHI) was a four-year community-based participatory research project designed to engage the public housing residents in Boston, Massachusetts in a collaborative process to improve building conditions and the health and quality of life of residents. The HPHI conducted multi-tiered interventions primarily aimed at controlling cockroach infestation and for this purpose, measured the changes in health status of children with asthma, the results of which have been reported /12-13/.

In addition to integrated pest management, the children in the study were also provided with new mite-resistant mattresses. This study is the first of which we are aware to involve the provision of new replacement mattresses (as distinct from mattress encasements) designed to prevent dust-mite colonization. Here we report data from the study relevant to dust-mite control and use our findings to raise questions about several key issues related to dust-mite research.

METHODS

Study methods have been reported elsewhere /12, 14-15/. Briefly, asthmatic children ages 4-17 years were recruited from three public housing developments in Boston, MA, USA in 2002 and 2003. Asthma status was confirmed by a pediatric pulmonologist. Data collection and management of participation in the project was shared by trained

public-housing residents and university-based researchers. Participants were assessed for health, environmental factors and quality of life before and after the interventions.

Allergy skin testing was conducted on children enrolled in the study using the prick puncture method /14/. The allergens tested included cockroach (Bla g 1, Bla g 2) and dust mites (Der f, Der p), as well as cat, mouse, dog, 11-tree mix, 7-grass mix, and multiple fungi. Eighty-six (86) Simmons mattresses called BodyCare Kids, featuring proprietary 'microfiber' construction and reported by the manufacturer to be designed to withstand dust-mite growth, were installed in homes of asthmatic children living in the public housing developments. The mattresses were provided to each asthmatic child participating in the study and for the people sleeping in the same room (siblings or other relatives). Other bedding (sheets, comforters, pillows) was not replaced. Noteworthy is that dust mite studies have commonly not replaced bedding /16/.

In addition to the mattresses, each home enrolling in the study received an integrated pest-management intervention consisting of intensive cleaning (especially of the kitchen), sealing of cracks and crevices through which cockroaches might travel, room air filters, application of hydromethylnon gel (MaxForce), Abamectin gel granules, and boric acid, and in home resident education about pest management. Such environmental interventions were designed to address cockroach infestation /12/. Preceding the environmental interventions, the participants also received basic clinical guidance about proper asthma care and management.

Allergen dust samples were collected from old mattresses and bed linens at baseline. After the intervention, allergen dust samples were collected at up to three points in time from the new beds. Our assumption is that changes in dust-mite levels are almost entirely due to the mattress intervention because cockroach pest-management methods are unlikely to affect mattress dust-mite levels. Yet, possibly intensive cleaning could have secondary

benefits for dust resuspension and deposition on the bed. Highly likely, however, is that replacing the mattresses did affect the levels of cockroach and other antigens besides dust mites in the bed itself. Studies of dust mite control have largely not addressed how mattress covers, for example, would affect the distribution of antigens besides dust mite antigen.

Dust samples were collected based on the standard method for collecting dust outlined in the Inner-City Asthma Study (ICAS) Environmental Intervention Manual of Operations Version 1.0 (March 17, 1998). For bed samples, all layers of the bedding, including the mattress and pillows, were vacuumed for a total of five minutes.

Samples were analyzed for dust mite allergens (Der f and Der p) as well as for cockroach (Bla g 1, Bla g 2), cat (Fel d 1) and dog (Can f 1) allergens, mouse urinary protein (MUP), and *Alternaria* antigen. The primary analysis reported here is the evaluation and comparison of Der p and Der f levels in the bed samples before and after the replacement of mattresses. A sandwich enzyme-linked immunosorbent assay (ELISA) was used for the detection and quantification of antigens other than MUP and the fungi *Alternaria*, for which a competitive inhibition ELISA was used. For analysis, we used the sample taken at the furthest time from the intervention for each household.

At the start and the end of the study, caregivers were asked about the frequency in the last two weeks of wheeze/cough, slowing down or stopping play due to asthma, waking up at night due to asthma, and severe asthma attacks for their asthmatic children /14/.

Data Management and Statistical Methods

The data for baseline and post-intervention concentrations of Der p and Der f were not normally distributed and were, therefore, log transformed. We report untransformed values in tables for ease of comparison to environmental benchmarks but use transformed values in statistical

Table 1: *Detection of Der p 1 and Der f 1 (N = 44 mattresses) and Allergy Frequency (N = 37 children)*

Parameter studied	Der p	Der f
Allergy	62%	54%
Percent above LLOD	31%	80%
Frequency above sensitization concentration (2 µg g ⁻¹ dust)	9%	16%
Frequency above exacerbation concentration (10 µg g ⁻¹ dust)	5%	7%
Range of detected concentrations (µg g ⁻¹ dust) ¹	0.05 - 23.6	0.03 - 23.3
Mean (µg g ⁻¹ dust) ²	1.3	1.6
Median (µg g ⁻¹ dust) ²	LLOD	0.315

¹Excludes values < LLOD; ²Includes values < LLOD (0.03 µg g⁻¹)

analyses. Values below the limit of detection were replaced with random values between zero and half of the lower limit of detection (LLOD) /15-16/. Data were managed in Microsoft Excel, and the analyses were conducted in SPSS.

RESULTS

Dust Mite Mattress Concentrations

In total, baseline and post-intervention dust mite mattress concentrations were available for 44 mattresses from 37 households. Of a total of 86 mattresses originally distributed, 42 were left out of the analysis because of not having a post-intervention measurement of dust mite antigen or because the mattresses were given to children in the same room as the index asthmatic child, but who were not enrolled in the study. Consistent with the literature on inner city housing in the Northeastern US, dust-mite antigen concentrations were generally low at baseline, with only 9% and 16% of mattress concentrations exceeding the 2 µg g⁻¹ cut-point for sensitization for Der p and Der f, respectively. Only 5% and 7% of mattress con-

centrations at baseline exceeded the 10 µg g⁻¹ exacerbation cut point for Der p and Der f, respectively. Table 1 presents the frequency of detection and range of detected concentrations of Der p and Der f.

Der p was above the limit of detection (0.03 µg g⁻¹ at baseline) in 31% of mattresses at baseline. As expected given the cooler, less-humid northern climate, Der f was more commonly present, with baseline Der f concentrations in 80% of mattresses above the detection limit. Baseline Der p concentrations above the LLOD ranged from 0.05 to 23.6 µg g⁻¹ and baseline Der f concentrations above the LLOD ranged from 0.03 to 23.3 µg g⁻¹. In only one case was Der p detected above the detection limit in the absence of a corresponding detection of Der f. Baseline concentrations of Der p and Der f before the intervention were significantly correlated with each other (using log-transformed data, $p < 0.001$ for both). In reference to detects only, there was a statistically significant decrease in concentrations of Der p following the intervention (paired samples t-test comparison of log normalized means, $p < .0001$; Table 2).

Post-intervention concentrations of Der f also remained lower than baseline concentrations and

Table 2: Comparison of baseline and post-intervention concentrations of Der p 1 and Der f 1 (μg of dust mite per g of dust)

Detects Only	Baseline		Post-intervention		p-value
	mean	median	mean	median	
Der p	3.8	0.46	1.97	0.05	<.0001
Der f	1.9	0.64	0.49	0.04	<.0001
All samples	mean	median	mean	median	p-value
Der p	1.3	<LLOD	0.69	<LLOD	.026
Der f	1.6	0.315	0.41	<LLOD	<.0001

Table 3: Percentages of mattresses either having dust mite concentrations below the detection limit throughout the study or having concentrations reduced between the baseline and final post-intervention measurement

Mattresses with dust-mite concentrations...	Der p	Der f
Below detection limit pre- and post-intervention	59%	14%
Lower post-intervention than pre-intervention	30%	67%
Higher post-intervention than pre-intervention	11%	19%

decreases were statistically significant ($p < .0001$; Table 2). When including non-detects in the analysis, decreases of both Der p and Der f remained statistically significant ($p = .026$ and $p < .0001$, respectively). Concentrations either decreased or remained below the detection limit for 89% of mattresses for Der p and 81% for Der f (Table 3).

One problem with studying dust mite exposure is that the mites tend to vary by season, especially in locations where humidity varies seasonally. To determine whether changes we saw in our data could be explained by seasonal variation, we created 4 variables to test the potential impact of seasonal variation on changes in dust-mite antigen levels. The variables categorized individual participants according to the seasons at the time of the baseline and post intervention values. The

seasons were chosen in accordance with recorded relative humidity values recorded in the housing units: October-May (dry) and June-September (wet). The categories were: (1) Dry for both measurements; (2) Wet for both measurements; (3) Dry early and wet late; (4) Wet early and dry late. In regression analyses, the dependent variable was the difference in dust-mite levels from baseline to post intervention. No significant association with the seasonal variables was found in regression models (details not shown).

Dust Mite Sensitivity

Despite the low concentrations of dust-mite antigen found in their mattresses, allergy to dust mite was common among asthmatic children. The

allergy testing was conducted on 37 children who received new mattresses. The results indicated that of these children, 68% were allergic to cockroaches; 62% and 54% were allergic to Der p and Der f, respectively; and 51% were allergic to both cockroaches and dust mites. Sixteen percent of children were allergic only to cockroaches and 16% were allergic only to dust mites. In general, children who were allergic to dust mites demonstrated sensitivity to both Der p and Der f but nevertheless, five children exhibited sensitivity to only one form. The incidence of allergy was not significantly associated with baseline dust-mite concentrations for Der p or Der f ($p = .162$ and 0.67).

DISCUSSION

Strengths and Limitations

Our data were strongest with respect to assessing changes in levels of dust-mite antigen and comparing dust mite antigen levels to the allergic sensitivity of asthmatic children living in public housing apartments. For changes in dust-mite antigen levels, the primary limitation was our relatively small sample size. To assess the impact of dust-mite levels on the development of atopy effectively, it would have been necessary to conduct a longitudinal assessment starting before both the intervention and development of allergies. Our method of collecting bed samples was a composite sample taken from the mattress, pillow, and bed covers, yet, our interventions included only the introduction of new mattresses and did not address the other possible reservoirs of dust mites on the bed /17/.

In addition, our analysis was limited because the concentrations of allergens vary over time, given an intervention at a fixed point in time and the single post-intervention point used in this analysis. Previous analyses of our data demonstrated that although initial improvements were seen, in some cases cockroach and dust-mite levels

started to increase about 6 months after the intervention /15-16/. Future studies should assess more formally the longitudinal time course of dust-mite allergen levels, a factor not addressed in most dust-mite intervention studies.

In our sample population, the median concentrations of cockroach allergen were substantially above asthma sensitization and exacerbation levels in the kitchen and close to the exacerbation level for Bla g 2 in the bed /15/. In contrast, median dust-mite levels were well below the sensitization and exacerbation levels in the bed, and were not measured in the kitchen. Because ours was not a randomized controlled trial, it is not possible to infer causality, especially with regard to health outcomes. Similarly, the absence of a group receiving new mattresses without microfiber construction makes it difficult to disentangle the benefits of the technology from the benefits of simply replacing an old mattress.

Dust Mite Levels

Previous studies from the HPHI have shown that the public housing buildings included in this study have widespread overheating in winter, alternating with the use of gas ovens for heating during transitional weather. Steam-heating pipes in the apartments are often not insulated, and tenants routinely open windows in the winter to control the heat, leading to a very low indoor relative humidity. At one of the housing developments in our study, the relative humidity inside the apartments ranged from 24% to 39% from December to April /18/. Another of the housing developments may have less severe heating due to upgrades to the heating system but is still likely to have low relative humidity /19/.

Our findings of low dust-mite antigen levels in Boston public housing are consistent with the low relative humidity and with the findings of a prior Boston-based study. That study found that the dust-mite populations in beds were 19 to 31 times higher in houses than in apartments for Der p and

Der f, respectively. For cockroaches, apartments had levels 5 times higher than houses /7/. Similarly, Kitch et al /6/ found that homes in high poverty areas in Metropolitan Boston were more likely to have high (cut point 10 U g^{-1}) cockroach allergen levels than homes in the low poverty areas (51% vs. 3%) but less likely to have high dust mite allergen (16% vs. 53%).

Dust Mite Sensitization

Positive skin tests are influenced by a combination of exposure, atopic status, and total serum IgE. A dose-response relation has been reported between increasing exposure to house dust mites and the likelihood of having positive allergy skin test responses to mites, with odds ratios ranging from 3.3, 6.2, to 8.9 for low (less than $2 \text{ } \mu\text{g g}^{-1}$), moderate ($2\text{--}10 \text{ } \mu\text{g g}^{-1}$), and high (greater than $10 \text{ } \mu\text{g g}^{-1}$) dust mite levels, respectively. Most important for this report, children with low-level exposures between 0.020 and $2 \text{ } \mu\text{g g}^{-1}$ were found to have a high prevalence of skin sensitivity to dust mites /10/.

Consistent with our findings, a study of 114 inner-city children who lived in Boston found that dust mite sensitivity levels were 49.8% (Der p) and 44.9% (Der f) for those not exposed to levels above $2 \text{ } \mu\text{g g}^{-1}$, whereas dust mite sensitivity was 82% and 62% for those exposed to levels above $2 \text{ } \mu\text{g g}^{-1}$. The housing type was predominantly low-rise apartments (like those in our study), row houses, or duplex/triplex. Only 26% had a relative humidity over 50%, which is considered optimal for the survival of dust mites /8/. Our findings extend this association to public-housing residents who are a discrete subgroup compared with the subjects in the earlier and larger study. Taken together, these findings may cast doubt on the labeling of $2 \text{ } \mu\text{g g}^{-1}$ as a 'threshold' for risk of sensitization.

While it is possible that low levels of dust-mite antigen act as an effective sensitizer, it is possible that these inner-city populations are exposed to dust mites in other settings, such as schools or

daycare facilities, resulting in sensitization despite low residential exposure.

A higher risk of developing positive skin test responses to house dust mites or cockroaches has been found with increasing degrees of atopy as measured by the number of positive allergy skin test responses to allergens other than mites or cockroaches. Subjects with a positive family history of allergy also require exposure to much lower concentrations of allergens to achieve sensitization /20/. Seventy percent of the children assessed at baseline in the HPHI had a parent or grandparent with asthma, with 34% having a family history of eczema or hay fever, and 78% were sensitized to at least one allergen tested /14/. Although we could not assess it directly, it could be that in our study population, all of whom had asthma, the development of dust mite sensitivity (despite low levels in the home) may be affected by a predominance of atopic/genetically susceptible children.

Impact of the Mattress Intervention

The replacement mattresses were largely effective at reducing dust-mite antigen levels and keeping levels below the generally low levels at baseline for follow-up times ranging to almost a year. Although IPM interventions occurred simultaneously with mattress replacement, they were not expected to affect dust-mite levels in the bed to a significant degree. The use of replacement mattresses is a novel approach and possible alternative to mattress covers, which appear to be ineffective at reducing asthma symptoms—that deserves further investigation. Replacement pillows and bedding in addition to mattresses, which we did not supply, might further reduce allergen levels.

Health Impact

A previously reported analysis of the children in our study /12/ showed that, overall, respiratory-symptom scores improved significantly between the start and the end of the study. In multivariate

analyses, significant differences were found by development and cat allergy status, the latter of which was thought to proxy for levels of allergen reductions and other factors. Reductions in Bla g 2 and reductions of multiple allergens in the bed to which the child was allergic were of moderate significance, which supports the notion that the bed is an important allergen reservoir and suggests a need for intervention studies that reduce mite allergen levels even further.

Because multiple allergens were detected in the bed, the replacement mattresses had an impact on reducing more than the dust mites. Reductions in bed concentrations were observed for varying percentages of homes across allergens (ranging from 37% of homes with reductions for Can f 1 to 62% for Fel d 1). The presence of multiple antigens, all of which are affected by the bedding interventions, points to potential confounders that are not measured in most dust-mite studies.

CONCLUSIONS AND FUTURE DIRECTIONS

We have presented above data from the Healthy Public Housing Initiative nested within the literature on dust mites and asthma. Our analysis, in the context of other studies, illustrates some of the key issues facing researchers seeking to both reduce dust-mite levels and improve the health of persons with asthma. For example, our data show that the use of dust-mite resistant replacement mattresses within an IPM intervention reduces the levels of dust-mite antigen as well as other allergens. The impact of new mattresses, dust covers, or new bedding on multiple antigens should be assessed as part of studies aimed at controlling dust mites. Without evidence of the effect on cockroach, cat, and other antigens, there is a risk of missing important allergenic factors contributing to changes in health.

Interestingly, given the failure of most mite-intervention studies to show health effects, and the possibility that such a result is due to not lowering

antigen levels sufficiently, we have shown that mite-antigen levels can be reduced further, even when such levels started below what is commonly considered a 'threshold' for sensitization and the exacerbation of asthma. One possible area of future effort might focus on reducing dust-mite levels below 1 or even $0.5 \mu\text{g g}^{-1}$, as beneficial effects might not be seen until such low levels are achieved.

Based on the high prevalence of mite-antigen sensitivity despite low dust-mite antigen levels, a more rigorous assessment of multiple sources of exposure is necessary. For children with low dust-mite levels at home, are there other places where they spend time—preschools, daycare, relatives, school—at which they receive higher exposures? If not, then aiming to reduce antigen levels well below the currently cited sensitivity level of $2 \mu\text{g g}^{-1}$ could be the way forward. Gøtzsche et al /20/ agree with most of our conclusions. The authors also recommend trials that reduce dust-mite levels further than those in previous studies and also raise a concern, albeit with less specificity than we have, about multiple antigen exposures.

A final area of consideration is the use of bundled interventions addressing multiple allergens simultaneously. Possibly, mattress cover interventions did in fact reduce antigens other than dust mites, but less likely is that chemical applications affected other antigens. Given the need to address bed clothing, as well as mattresses, and the possibility that surfaces in homes must be cleaned to remove residual mite antigen, interventions aimed at reducing dust-mite levels further than those in previous studies will likely reduce the levels of other potentially allergenic antigens as well. Accordingly, more studies are needed that bundle interventions and use designs that attempt to disaggregate the impact of multiple antigens.

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