Original Article

Individualized Household Allergen Intervention Lowers Allergen Level But Not Asthma Medication Use: A Randomized Controlled Trial

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What is already known about this topic? Cockroach and mouse allergens appear to be the most important allergens associated with asthma morbidity in inner-city residents. Intervention trials for reducing household allergens report mixed results in terms of improving asthma morbidity.

What does this article add to our knowledge? Individualized household allergen intervention does not lead to incremental reduction in asthma step-level care.

How does this study impact current management guidelines? This study highlights the need for further studies to inform current guidelines for allergen avoidance in individuals with asthma.

BACKGROUND: Environmental exposures to indoor allergens are major contributors to asthma symptoms, particularly in inner cities. The effectiveness of household allergen reduction as an adjunct to National Asthma Education Prevention Program guideline–based pharmacologic therapy in asthma has not been prospectively studied.

OBJECTIVE: To study the effect of individualized allergen reduction on ability to reduce asthma pharmacologic therapy over 40 weeks.

METHODS: We performed a randomized controlled trial to determine the effect of multifaceted indoor allergen avoidance measures on the ability to reduce asthma controller therapy in adults and children residing in New York City who were both sensitized and exposed to at least 1 indoor allergen. Asthma treatment and control were optimized in all subjects before randomization.

RESULTS: A total of 125 subjects were randomized to receive individualized household allergen reduction and 122 received a sham intervention. Subjects in the intervention group significantly reduced all measured allergen levels (cat, dog, dust mite allergens in the bedroom, cockroach and mouse allergens in the kitchen and bedroom); those in the control group reduced only dust mite and mouse allergens in the bedroom and cockroach allergen in the kitchen. Participants in the intervention arm reduced National Asthma Education Prevention Program–based therapy from step 4.4 at randomization to 3.50 postintervention (range, 0-6); participants in the control arm reduced medication from step 4.4 to 3.4 ($P = .76$). There were no differences in other measured asthma outcomes.

CONCLUSIONS: Targeted allergen avoidance measures do not allow for reduction in asthma pharmacologic therapy compared with usual care in patients already receiving optimal controller therapy. **(J Allergy Clin Immunol Pract 2016;4:671-9)**

Key words: *Asthma; Allergens; Cockroach; Mouse; Asthma controller*

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Abbreviations used
ACT- Asthma Control Test
AQLQ- Asthma Quality of Life Questionnaire
ETS- environmental tobacco smoke
NAEPP- National Asthma Education and Prevention Program

Environmental exposures to indoor allergens are major contributors to asthma morbidity among individuals in all geographic regions. Household exposure to allergens is of particular concern among inner-city individuals, where time spent indoors and high incidence of sensitization to indoor allergens exist and correlate with asthma severity in a dose-dependent fashion.[1-8] Despite the effectiveness of existing pharmacologic treatments for most patients with asthma, there is heightened concern over the adverse effects of these agents over the short- and long-term, contributing to poor adherence to medication regimens.[9-13] Asthma management guidelines emphasize the need for individualized environmental control measures for the treatment of asthma, but there is conflicting evidence of the efficacy of such measures and widely variable adherence to these recommendations by patients and providers.[14,15]

Previously conducted studies demonstrate variable results regarding benefits of household allergen reduction on asthma morbidity.[2,5,16,17] Limitations of single household allergen avoidance trials have directed attention to multifaceted allergen reduction.[16-18] Limited numbers of clinical trials have evaluated multiple allergen avoidance, especially in adults. In 2004, the Inner-City Asthma Study reported on a multifaceted home-based environmental intervention for children with asthma, tailored to each patient's sensitization and environmental risk profile.[19] Individuals randomized to environmental intervention demonstrated significantly fewer symptoms days (0.8 fewer symptom days per 2-week period) compared with individuals in the control group.[5] However, in another multifaceted allergen avoidance study, Carter et al[20] studied the effect of avoidance of dust and cockroach in a group of inner-city children with asthma and demonstrated no improvement. Mouse allergen in the inner city has also received considerable attention given the prevalence of mouse allergen in 95% of inner-city households tested in the National Cooperative Inner-City Asthma Study and the dose-dependent correlation of mouse allergen with asthma morbidity.[3,21-24] However, intervention trials based on household mouse allergen have not be reported.

Further complicating the interpretation of study results is the fact that the effectiveness of multifaceted environmental intervention as an adjunct to guideline-based pharmacologic therapy has not been prospectively studied.[2,5,17,25] We hypothesized that household allergen reduction among patients with asthma living in New York City may improve asthma control and allow for significant reduction in need for pharmacologic therapy. We performed a randomized controlled trial in subjects receiving optimized asthma controller therapy to assess the effect of individualized, comprehensive, multifaceted indoor allergen avoidance measures on the ability to step down asthma controller therapy in adults and children with mild to severe persistent asthma who were both sensitized and exposed to specific indoor allergens.

METHODS

Participants

Nonsmoking adults and children with mild to severe persistent asthma (≥6 years) were invited to participate at either Columbia University Medical Center in New York, New York, or the Jacobi Medical Center in Bronx, New York, between March 2011 and July 2012. The study was approved by the institutional review board of each institution and was posted on clinicaltrials.gov (NCT0159311). Subjects were recruited from pediatric and adult asthma and primary care clinics at the institutions as well as through printed advertisements. Written informed consent was obtained from each subject or guardian. Adolescents aged 12 to 17 years provided assent. Enrolled subjects were either receiving controller therapy or had symptoms consistent with persistent asthma[26] if not receiving therapy. Additional inclusion criteria at screening included an FEV_1 value of 40% predicted or more and asthma confirmed by bronchodilator reversibility, defined as having a 12% or greater increase in FEV_1 15 minutes after the administration of 2 puffs of albuterol or a PC_{20} methacholine value of 8 mg/mL or less if not using inhaled corticosteroids or 16 mg/mL or less if using inhaled corticosteroids. Subjects had to sleep overnight at the same address at least 5 times per week, have a positive skin test result (or ImmunoCAP if $FEV_1 <$ 60% precluded skin testing) to protein extracts of at least 1 common indoor allergen including dust mite, German cockroach, mouse, Aspergillus mix, cat, and dog allergens. Skin testing was performed using the percutaneous MultiTest method (MultiTest II, Lincoln Diagnostics, Decatur, Ill). ImmunoCAP testing (ThermoFisher, Uppsala, Sweden) was performed as previously described.[27] Following screening, subjects continued their usual asthma therapy or its equivalent for 21 days to allow for characterization of asthma severity and control. For subjects not previously receiving controller therapy, the study physician determined appropriate therapy on the basis of National Asthma Education and Prevention Program (NAEPP) guidelines.[26] To standardize therapy, medications were transitioned on the basis of equivalency tables (Table I).[28,29] All medications were provided free of charge to the subjects; adherence was measured by built-in dose counter and pill count.

Home evaluation/dust collection

One to 10 days following screening, 2 trained home evaluators conducted a home visit. Visual assessment of the subject's home, recording evidence of exposure to second-hand environmental tobacco smoke (ETS), presence and number of pets, and condition of the living space, kitchen, bedroom, and bathroom, was performed. Two vacuumed settled dust samples were collected from the bed, bedroom floor, and kitchen as previously described[24] (see this article's Online Repository at www.jaci-inpractice.org for additional methods). Protein was extracted, and Musm1 (mouse), Bla g1 (cockroach), Der f1 (dust mite), Can f1 (dog), and Fel d1 (cat) allergen concentration was quantified by means of ELISA.[30] Evidence of exposure above a prespecified cutoff[31] (see Table E1 in this article's Online Repository at www.jaci-inpractice.org) to at least 1 allergen to which the subject was sensitized was required for study continuation. Subjects sensitized to only cat or dog were eligible only if they had a cat or dog in the home.

Run-in period (4 weeks)

At least 70% medication adherence was required to proceed to the run-in period. Asthma control was assessed on the basis of measured FEV_1 as well as subject recall of number of days with asthma symptoms, number of days with rescue medication use, and

TABLE I. Asthma treatment steps and associated controller therapy

Treatment step	Medication
0	Albuterol MDI as needed
1	Montelukast 5 mg daily for ages 6-11 y, 10 mg daily for ages ≥12 y
2	Fluticasone DPI 100 μg twice a day
3	Fluticasone DPI 200 μg twice a day
4	Fluticasone/salmeterol diskus 250 μg/50 μg twice a day
5	Fluticasone/salmeterol diskus 500 μg/50 μg twice a day
6	Fluticasone/salmeterol diskus 500 μg/50 μg plus montelukast 1 daily dosed by age

DPI, Dry powder inhaler; *MDI*, metered-dose inhaler.

number of nights with symptoms over the previous 2 weeks (Table II).[28,29] The most severe metric was used to determine control level, with level 1 denoting good control. A standardized NAEPP-guideline–based algorithm (see Table E2 in this article's Online Repository at www.jaci-inpractice.org) was used by the study physician to determine the appropriate treatment step (range, 1-6) required to achieve or maintain asthma control at the mild intermittent level (control level 1) during the subsequent run-in period.[28,29] The purpose of the 4-week run-in period was to allow transition to protocol-driven asthma management, ensure asthma control and adherence with therapy, and determine baseline symptoms and physiologic and inflammatory parameters.

Randomization

Subjects with optimal asthma control (control level 1 with FEV_1 modified to be ≥85% of FEV_1 at run-in visit) and 70% adherence were randomized and maintained on the same asthma treatment step level. If asthma control level was more than 1, controller therapy was increased on the basis of Table E2 and the run-in period was extended for 2 weeks. Subjects receiving step 6 with control level more than 1 were maintained on step 6 and randomized.

Treatment period

Subjects who were randomized to the intervention arm received an individualized home-based program by 2 intervention counselors using standardized modules targeting furry pets, cockroach, dust mites, rodents (ie, mice and rats), and mold as described by Morgan et al.[5] All subjects in the intervention group received all intervention modules including the Safe Sleeping Zone module, organized around reducing all allergen levels in the bedroom.[5] Subjects in the intervention arm received targeted education about how indoor allergens can affect asthma and education about strategies for reduction of allergens in the home. Intervention counselors provided materials needed for allergen reduction (eg, mattress covers, cleaning products, Electrolux vacuums, Swiffer WetJet mops, and Orek HEPA-air purifiers placed in the bedroom) and implemented the measures in the home while teaching the subjects how to maintain them. Any report or observation of ETS in the home prompted inclusion of the ETS remediation plan, which included strategies for avoiding ETS in the home and public places, a HEPA air purifier, and encouraging smokers to smoke outside the home. Follow-up visits by the intervention counselor with replacement of supplies occurred at weeks 18 and 32. The group assigned to the control arm also received a total of 3 visits by the intervention counselor where they received educational materials unrelated to asthma (eg, window guards), with no discussion of allergen avoidance. Subjects in the control arm were provided no information related to their own or their child's allergen sensitization or exposure. Two follow-up home evaluation visits for exposure assessment and dust collection were conducted for all subjects at weeks 20 and 36 following randomization. Home evaluators were distinct from intervention counselors.

TABLE II. Control level based on subject 2-wk recall

Level of control	No. of days with symptoms	No. of days with rescue albuterol use	No. of nights with asthma symptoms	FEV_1 (% predicted)*
1	0-3	0-3	0-1	≥85
2	4-9	4-9	2	80-84
3	10-13	10-13	3-4	70-79
4	14	14	5-14	<70

*Modified to reflect FEV_1 relative to FEV_1 at *run-in visit* for all visits following randomization.

Clinical assessments were performed at the study site at baseline and every 8 weeks thereafter (see Figure E1 in this article's Online Repository at www.jaci-inpractice.org). Questionnaires based on 2-week recall of symptoms, rescue bronchodilator use, and nocturnal awakenings were administered at each visit and mean for the 2-week period was calculated. Information regarding asthma exacerbations was collected at every visit. Spirometry was performed with a KoKo spirometer (nSpire Health, Longmont, Colo), and percent predicted values were determined using Hankinson equations. Fraction of exhaled nitric oxide levels was measured with the NIOX Mino (Aerocrine, Solana, Sweden) following American Thoracic Society guidelines.[32] All subjects completed an Asthma Control Test (ACT)[33] or childhood ACT if younger than 12 years,[34] and Juniper mini Asthma Quality of Life (mini-AQLQ)[35] at baseline, week 24, and week 40. Total and allergen specific IgE level was measured at randomization visit and at weeks 24 and 40. Composite asthma severity index was calculated as a composite measure of clinical characterization of asthma.[36]

Treatment reduction phase

During the 40-week treatment period, pharmacologic therapy was stepped up or down on the basis of control level at each visit by investigators blinded to the treatment arm, using Table E3 (in this article's Online Repository at www.jaci-inpractice.org), with the goal of achieving or maintaining asthma control at the mild intermittent range (control level 1). The following protocol was used[29]: if asthma control was at level 1, maintenance therapy was reduced 1 step. If asthma control level was more than 1, maintenance therapy was increased by an appropriate number of steps. The option to use a prednisone burst at any time during the study was at the discretion of the study physician or the treating physician. Once asthma control was achieved, reduction of 1 step at a time was repeated at each visit until the subject was using only albuterol as needed ("step 0") or until asthma became uncontrolled, at which point treatment was increased incrementally, 1 step at a time, until control was again achieved.

The primary outcome variable was reduction in asthma step therapy between randomization and 40 weeks of study treatment. Secondary outcomes included change in FEV_1, rescue albuterol use, asthma symptoms, fraction of exhaled nitric oxide, score on the ACT and mini-AQLQ, and total and allergen specific IgE levels.

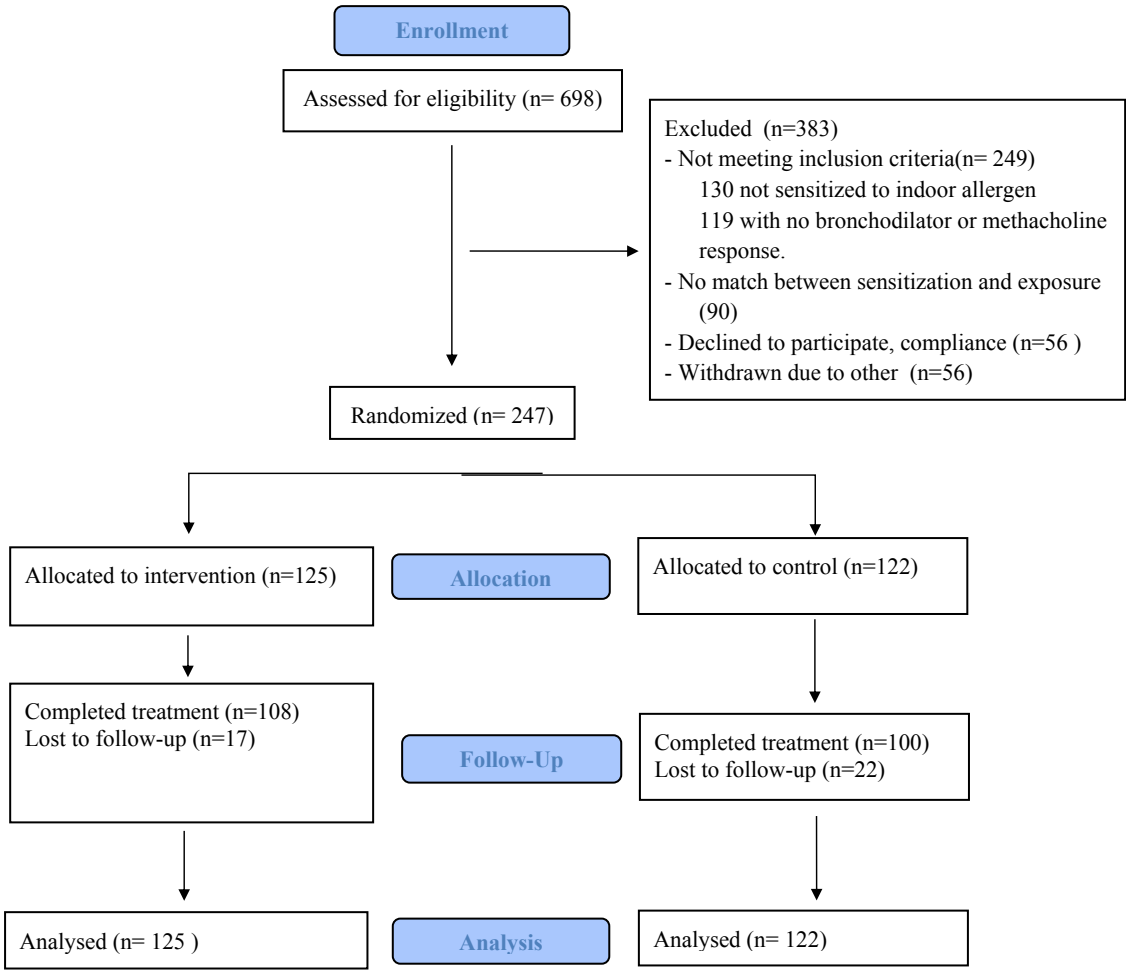

FIGURE 1. CONSORT diagram.

Prespecified subgroup analysis based on factors known to contribute to asthma outcomes, including baseline age (< or ≥18 years), body mass index (< or ≥30 kg/m^2), asthma control level (1 or >1), asthma therapy (steps 1-5 or step 6), ETS, and race, was conducted, as was post hoc analysis comparing subjects who, regardless of treatment group, did and did not have reduction in mouse and cockroach allergens, allergens most associated with inner-city asthma morbidity.[2,21]

It was estimated that 99 participants per group would be needed to achieve 80% power (2-sided type I error of 0.05) to detect a clinically meaningful difference of 20% in therapy reduction between groups. To allow sufficient power for subgroup analysis by age, a sample size of 150 subjects per group was estimated.

Statistical analysis

Summary statistics were calculated to describe sample characteristics. For baseline demographic characteristics, the chi-square test was used to compare categorical variables and the Wilcoxon rank-sum test was used to compare continuous variables. The mean postrandomization outcome variables for each group and group differences were analyzed with linear mixed-effects models with visit and group as fixed effects. For variables with skewed distribution, log transformation was performed and ratio was reported. The random effects included a random intercept to account for the within-subject correlation between repeated measures over time. The primary outcome, step therapy, was analyzed as a continuous outcome. Prespecified subgroup analyses were conducted to assess heterogeneity of treatment effects across 9 characteristics, with a statistical test for interaction following recommended guidelines for subgroup analyses.[37] Statistical analyses were performed with SAS software (version 9.3, SAS Institute, Carey, NC). The latent class mixed model analysis, to determine trajectory clusters for exposure to mouse and cockroach, was implemented using the lcmm software package[38] in R 3.2.1.[39] No adjustments for multiple comparisons were made given the *a priori* nature of the hypotheses tested. Analyses were performed according to intention to treat with a 2-sided alpha level of 0.05. Missing data were examined using linear mixed models. Mixed effect models were used for repeated measures over time.[40]

RESULTS

Baseline characteristics of participants

Six hundred ninety-eight subjects were screened; 130 subjects were excluded on the basis of negative allergen skin testing or ImmunoCAP, and 119 subjects were excluded on the basis of lack of bronchodilator reversibility or methacholine hyperresponsiveness; 90 were excluded because of absence of home allergen exposure corresponding to specific sensitization

TABLE III. Characteristics of the intention-to-treat participants at randomization*

Characteristic	Intervention (N = 125)	Usual care (N = 122)	*P* value
Age (y)			.99
6-17	56 (44.8%)	54 (44.3%)	
18-69	69 (55.2%)	68 (55.7%)	
Sex			.42
Female	73 (58.4%)	64 (52.5%)	
Male	52 (41.6%)	58 (47.5%)	
Race/ethnicity			.11
Hispanic	67 (55.4%)	72 (61.0%)	
Black (non-Hispanic)	47 (38.8%)	45 (38.1%)	
White (non-Hispanic)	7 (5.79%)	1 (0.85%)	
Borough			.60
Bronx	89 (71.8%)	81 (66.4%)	
Manhattan	29 (23.4%)	30 (24.6%)	
Brooklyn	4 (3.23%)	7 (5.74%)	
Queens	2 (1.61%)	4 (3.28%)	
Body mass index (kg/m^2)	28.9 ± 8.75	27.8 ± 8.72	.36
Asthma symptoms (days past 2 wk)	2.34 ± 3.00	1.87 ± 2.59	.19
Rescue (albuterol) inhaler (days past 2 wk)	2.10 ± 2.77	1.72 ± 2.74	.28
Awakened with asthma symptoms (days past 2 wk)	1.17 ± 2.98	0.79 ± 2.19	.25
ACT score (n = 175)	19.5 ± 4.14	20.2 ± 3.94	.23
Childhood ACT score (n = 69)	21.9 ± 4.74	22.7 ± 3.60	.45
Exhaled nitric oxide (ppb)	28.8 ± 25.5	27.0 ± 23.0	.61
Total IgE (kU/L)	416 ± 556	517 ± 632	.37
FEV_1/FVC ratio	0.76 ± 0.09	0.78 ± 0.11	.30
FEV_1 (% predicted) pre	85.4 ± 18.6	84.9 ± 18.1	.84
FEV_1 (% predicted) post	90.4 ± 22.0	90.4 ± 17.3	.99
FEV_1 (% predicted) change	6.79 ± 9.97	7.53 ± 10.2	.57
Reversibility 10%: Yes	36 (29.0%)	32 (26.4%)	.65
Control level			
1	69 (55.6%)	62 (51.2%)	.73
2	11 (8.87%)	11 (9.09%)	
3	17 (13.7%)	23 (19.0%)	
4	27 (21.8%)	25 (20.7%)	
Control level mean	2.02 ± 1.26	2.09 ± 1.24	.64
Treatment step at randomization (categorical)			.10
1	2 (1.61%)	3 (2.50%)	
2	17 (13.7%)	14 (11.7%)	
3	22 (17.7%)	21 (17.5%)	
4	19 (15.3%)	27 (22.5%)	
5	14 (11.3%)	3 (2.50%)	
6	50 (40.3%)	52 (43.3%)	
Treatment step at randomization (continuous)	4.42 ± 1.56	4.41 ± 1.57	.96
Juniper mini-AQLQ score†	5.03 ± 1.32	5.57 ± 1.26	.02
Reported smokers in home: Yes	43 (34.4%)	33 (27.0%)	.27
"Spend a lot of time with someone who smokes"	41 (33.3%)	30 (25.6%)	.24
Cat/dog/pet rodent in your home now or 6 mo prior: Yes	24 (35.3%)	21 (34.4%)	.99

FVC, Forced vital capacity; *ppb*, parts per billion.
*Values are count (percent) or mean ± SD.
†Higher score denotes better quality of life.

(Figure 1). Two hundred forty-seven subjects were randomized; 125 (56 children and 69 adults) into the intervention arm and 122 (54 children and 68 adults) into the control arm. There were no significant baseline differences between the control and intervention groups in all listed variables with the exception of the mini-AQLQ, score for which was higher in the control group (Table III). At the time of randomization, the ACT score in both groups revealed well-controlled asthma, defined as an ACT score of more than 19. Mean FEV_1 was 85.4% ± 18.6% predicted in the intervention group and 84.9% ± 18.1% predicted in the control group. The mean number of days in the 2-week interval on which subjects had symptoms was 2.34 ± 3.00 days in the

TABLE IV. Allergen reduction for each treatment group over the study period*

Exposure (μg/g)	Location	Usual care				Intervention			
		Week −2	16	32	*P* value	Week −2	16	32	*P* value
Bla g 2	Bedroom	0.05 (0.04-0.06)	0.04 (0.03-0.05)	0.04 (0.03-0.05)	.63	0.05 (0.04-0.06)	0.04 (0.03-0.04)	0.03 (0.02-0.04)	<.01
Can f 1		0.27 (0.18-0.40)	0.26 (0.17-0.38)	0.22 (0.15-0.32)	.36	0.28 (0.18-0.41)	0.19 (0.13-0.28)	0.17 (0.12-0.25)	.03
Der f 1		0.06 (0.05-0.08)	0.05 (0.04-0.06)	0.05 (0.04-0.05)	.04	0.07 (0.06-0.09)	0.05 (0.04-0.06)	0.05 (0.04-0.05)	<.01
Fel d 1		0.11 (0.08-0.16)	0.10 (0.07-0.15)	0.10 (0.07-0.14)	.87	0.11 (0.08-0.17)	0.08 (0.06-0.12)	0.07 (0.05-0.10)	.01
Mus m 1		0.48 (0.35-0.65)	0.24 (0.17-0.33)	0.33 (0.24-0.45)	.03	0.38 (0.28-0.51)	0.20 (0.15-0.28)	0.17 (0.13-0.23)	<.01
Bla g 2	Kitchen	0.64 (0.42-0.97)	0.38 (0.26-0.55)	0.32 (0.21-0.47)	<.01	0.73 (0.48-1.11)	0.49 (0.34-0.70)	0.30 (0.21-0.44)	<.01
Mus m 1		2.51 (1.68-3.74)	1.94 (1.24-3.04)	1.76 (1.17-2.65)	.10	1.66 (1.12-2.46)	1.47 (0.95-2.27)	1.02 (0.69-1.51)	.02

*Numbers are geometric means (95% CIs); the *P* value for trend is computed using linear mixed models.

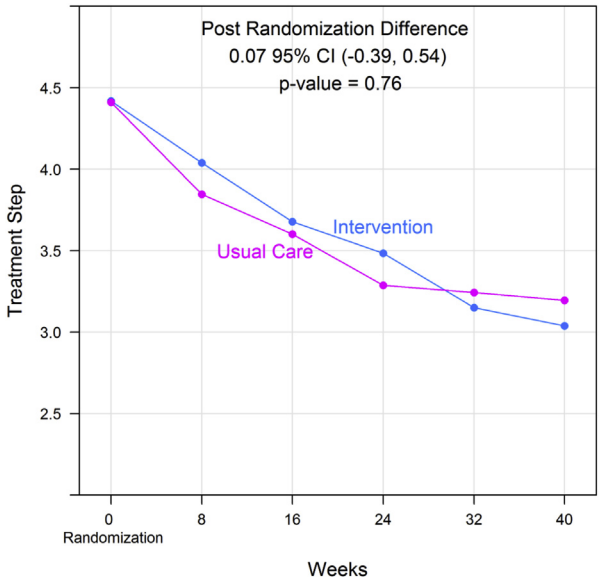

FIGURE 2. Change in asthma treatment step over the study period for each study group.

intervention group compared with 1.87 ± 2.59 days in the control group ($P = .19$). At baseline, slightly more than half the subjects had asthma control level of 1. Mean NAEPP treatment step required for optimal asthma control at baseline was similar in the 2 groups, 4.42 ± 1.56 in the intervention group and 4.41 ± 1.57 in the control group ($P = .96$), with similar numbers of subjects requiring step 6, or maximal therapy. A total of 23% of children were on step 5 or 6 and 69% of adults were on step 5 or 6. A total of 105 subjects in the intervention group (84%) and 97 subjects in the control group (80%) completed the study, with only 10% of completed subjects missing a clinic assessment.

Change in asthma outcomes in response to treatment group

There was a significant decline in all mean measured allergen levels in the intervention group (cat, dog, dust mite, cockroach, mouse); however, the control group demonstrated a significant decline in allergen levels only for dust mite and mouse in the bedroom and cockroach in the kitchen (Table IV). For the primary outcome, NAEPP treatment step, both groups reduced asthma step therapy, but there was no significant difference between treatment groups (Figure 2). Participants in the treatment group reduced NAEPP-based therapy from treatment step 4.4 to treatment step 3.50 over the study period; participants in the control group reduced medications from step 4.4 to step 3.43 ($P = .76$; 95% CI, −0.39 to 0.54). Table V presents the group-specific mean and mean difference in the primary and secondary outcomes over the 40-week postrandomization period. There was no significant difference in the mean number of days with asthma symptoms, nocturnal awakenings, or need for rescue bronchodilator therapy between groups. There was no significant difference in mean prebronchodilator or postbronchodilator FEV_1, childhood or adult ACT score, or the mini-AQLQ score between groups. Total serum IgE and allergen specific IgE levels were similar between the 2 treatment groups and did not significantly change over the course of the study period (see Table E4 in this article's Online Repository at www.jaci-inpractice.org). Eight subjects (6.4%) in the intervention group and 8 subjects (6.6%) in the control group experienced an exacerbation during the study period ($P = .96$). As a sensitivity analysis, we also calculated the effect of the intervention as a change from baseline (see Table E5 in this article's Online Repository at www.jaci-inpractice.org). Similarly, no intervention effect was observed as reflected by the *P* values for the differences between groups.

Prespecified subgroup analysis based on baseline age, body mass index, asthma control level, asthma step therapy, ETS, and race revealed no difference in ability to reduce step therapy between the intervention and control groups (see Table E6 in this article's Online Repository at www.jaci-inpractice.org). Sensitization and exposure for each allergen was similar between groups and is reported in Table E7 in this article's Online Repository at www.jaci-inpractice.org. When analyzing only those subjects exposed and sensitized to cockroach and mouse, there was no significant difference in ability to reduce step therapy between the intervention and control groups or any of the other measured outcomes.

Post hoc comparison of subjects for whom mouse and cockroach allergen reduction occurred during the study period with subjects for whom specific allergen reduction did not occur, regardless of intervention assignment, was performed using a longitudinal cluster analysis. For both mouse and cockroach exposure, a 2-group solution was found as optimal; subjects were clustered in with/without an allergen reduction throughout the study. Subjects who experienced significant reduction in mouse allergen in the kitchen (n = 122) were able to reduce asthma therapy from step 4.25 at the time of randomization to step 2.74

TABLE V. Treatment effect averaged over 40 wk of follow-up*

Asthma outcome	Intervention*	Usual care*	Effect† (95% CI)	*P* value
Treatment step final	3.50 ± 0.16	3.43 ± 0.17	0.07 (−0.39 to 0.54)	.76
Asthma symptoms (d/2 wk)	2.44 ± 0.22	2.38 ± 0.23	0.06 (−0.57 to 0.70)	.85
Rescue (albuterol) inhaler (d/2wk)	2.32 ± 0.23	2.15 ± 0.24	0.17 (−0.48 to 0.82)	.61
Awakened with asthma symptoms	1.08 ± 0.16	0.81 ± 0.17	0.27 (−0.20 to 0.73)	.26
ACT score (n = 175)	20.1 ± 0.38	20.9 ± 0.40	−0.85 (−1.93 to 0.24)	.12
Childhood ACT score (n = 69)	22.6 ± 0.58	22.9 ± 0.62	−0.31 (−2.01 to 1.39)	.71
Exhaled nitric oxide‡	23.6 ± 0.65	26.1 ± 0.75	0.90 (0.75 to 1.08)	.26
FEV_1 (% predicted) pre	83.8 ± 1.45	82.8 ± 1.51	1.03 (−3.09 to 5.15)	.62
FEV_1 (% predicted) post	89.8 ± 1.58	89.2 ± 1.64	0.60 (−3.87 to 5.06)	.79
Control level	1.57 ± 0.06	1.56 ± 0.06	0.01 (−0.16 to 0.18)	.92
Composite asthma score	5.64 ± 0.25	5.66 ± 0.27	−0.01 (−0.74 to 0.71)	.97
Exacerbations, n (%)	8 (6.4%)	8 (6.6%)	0	.96
Juniper mini-AQLQ	5.41 ± 0.13	5.63 ± 0.14	−0.22 (−0.61 to 0.16)	.26
Mite IgE (kU/L)‡	1.22 ± 0.09	1.09 ± 0.08	1.12 (0.69 to 1.84)	.64
Cat IgE (kU/L)‡	1.77 ± 0.15	1.78 ± 0.15	0.99 (0.57 to 1.72)	.98
Cockroach IgE (kU/L)‡	2.08 ± 0.17	1.75 ± 0.15	1.19 (0.69 to 2.06)	.53
Mouse IgE (kU/L)‡	1.16 ± 0.11	1.17 ± 0.10	0.99 (0.53 to 1.85)	.97
Dog IgE (kU/L)‡	1.47 ± 0.12	2.28 ± 0.19	0.64 (0.38 to 1.10)	.10
Total IgE (kU/L)‡	231.4 ± 13.6	250.3 ± 15.2	0.92 (0.63 to 1.36)	.69

SE, Standard error.
*Plus−minus values are means ± SE over the 40-wk treatment period.
†Unrounded values were used to determine the difference between groups for the 40-wk treatment.
‡Because of skewed distribution, log transformation was performed and the geometric mean and SEs are reported. For these variables, the ratio rather than the difference is reported.

at study completion; those subjects without a significant decline in kitchen mouse allergen (n = 125) reduced asthma therapy from step 4.57 to 3.47 (effect size, 0.53; 95% CI, 0.07-0.99; $P = .02$). Similar analysis comparing reduction in cockroach allergen in the kitchen or bedroom and reduction in mouse allergen in the bedroom did not lead to a significant difference in ability to reduce asthma treatment burden.

DISCUSSION

Exposure to indoor allergens among sensitized patients with asthma has been associated with worse asthma severity and increased health care utilization.[41-43] In inner-city communities particularly, exposure and sensitization to indoor allergens has been identified as an independent risk factor for poor asthma-related outcomes.[1-3,43,44] Efforts to reduce indoor allergens have been recommended in published guidelines as a treatment for asthma.[26] However, previously conducted environmental intervention studies have demonstrated conflicting results regarding the effectiveness of household allergen reduction. The effect of household allergen avoidance on real-world asthma management is not clear, partly because of the lack of control for concurrent asthma therapy as interventions are implemented. In one study, Halken et al[25] demonstrated that reduction in dust mite exposure led to a significant reduction in inhaled corticosteroid dose among dust mite−allergic children; however, the study was not designed to prospectively test this outcome and asthma therapy at baseline was not standardized before randomization.

Our study demonstrates that in a population of inner-city adults and children exposed and sensitized to common indoor allergens and receiving optimal guideline-based asthma therapy, environmental control measures effectively reduced levels of all measured household allergens (cockroach, mouse, dust mite, cat, and dog), but did not lead to further reduction in need for asthma controller therapy compared with a control group receiving a home visit that did not target allergies and asthma. However, in our study, the control group also experienced a significant reduction in the concentration of several allergens (dust mite, cockroach, and mouse in bedroom), thus making it difficult to assess the direct effect of allergen intervention measures on reduction in asthma therapy through reduced allergen exposure. Allergen reduction in the control group of our study may have been due to preparation by subjects for expected visits to the home. Some of the treatment reduction in both groups, beyond the effect of allergen reduction, may have been due to enrollment in a study with regular follow-up and dispensing of medications free of charge. The difference in our results compared with previously published studies showing an effect of environmental remediation may be due to the initial optimization of pharmacologic asthma therapy in our study. In addition, enrollment in our study required both sensitization and exposure to at least 1 indoor allergen, a criterion not used in many previous studies.

Although it is recognized that environments outside of the home may differ considerably between children and adults, exposure to household allergens is expected to be similar and thus both age groups were included in this trial. To our knowledge, our study is the first prospective allergen reduction study controlling for concurrent asthma medication use. Post hoc analysis showed that participants with a significant decline in mouse allergen in the kitchen, regardless of treatment arm, had a

significant reduction in NAEPP step therapy compared with those participants not experiencing a reduction in mouse allergen. This finding was not seen in those participants with reduction in cockroach allergen, another allergen often cited as a major contributor to asthma morbidity in the inner city. Ahluwalia et al[3] also recently reported on the strong association of mouse allergen, but not cockroach allergen, with poor asthma outcomes in inner-city children in Baltimore. Given the high prevalence of mouse allergen in inner-city homes,[23] these findings highlight the need to perform prospective studies targeting mouse allergen in the inner city. Some potential weaknesses of our study include the fact that our study was underpowered to detect differences in the effect of the intervention in children versus adults and did not include effects of air pollution and outdoor exposures.

Our study population required relatively high doses of controller therapy to achieve asthma control, consistent with advanced severity of asthma often noted in inner-city residents.[4,45] However, even among those patients requiring the highest asthma step therapy, household allergen reduction did not allow for a significant reduction in therapy or improvement in asthma control compared with the control group.

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Methods

Home dust collection. Two vacuumed dust samples were collected using a hand-held vacuum cleaner and a Dustream filter collection device (Indoor Biotechnologies, Charlottesville, Va). A total of 2-m^2 area on the floor beside and under the bed was vacuumed for a total of 5 minutes. A 1-m^2 area was delineated at the head of the bed for sampling. All bedding layers including the pillow were vacuumed for a total of 3 minutes.

Measurements. Scores on the Childhood ACT and the ACT were measured on scales of 0 to 27 and 5 to 25, respectively. A score of 19 or less on either test indicates that asthma is not well controlled. The minimally important difference for ACT equals 3 points; for Childhood ACT, a 3-point increase suggests a clinically relevant improvement in asthma control while a 2-point decrease suggests a clinically relevant worsening.[E1]

Scores on the Juniper mini-AQLQ were measured on a scale of 1 to 7, with higher scores reflecting better quality of life. The minimally important difference for the mini-AQLQ is 0.5.[E2,E3]

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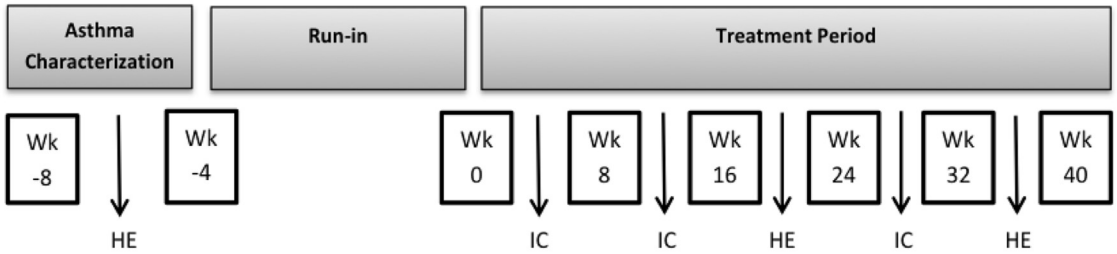

FIGURE E1. Flow diagram for study visits. *HE*, Home evaluator visit; *IC*, intervention counselor visit.

TABLE E1. Threshold allergen levels in settled dust

Allergen	Minimum accepted concentration (μg/g)
Der p1 + Der f1	2
Fel d1	1
Can f1	1
Mus m1	0.4
Bla 2	0.06

TABLE E2. Algorithm for prescribing treatment regimen at randomization

Current regimen	Current level of control	Regimen for run-in
Step 1	Control level 1	Step 1
	Control level 2	Step 2
	Control level 3	Step 2
	Control level 4	Step 3
Step 2	Control level 1	Step 2
	Control level 2	Step 3
	Control level 3	Step 3
	Control level 4	Step 4
Step 3	Control level 1	Step 3
	Control level 2	Step 4
	Control level 3	Step 4
	Control level 4	Step 5
Step 4	Control level 1	Step 4
	Control level 2	Step 5
	Control level 3	Step 5
	Control level 4	Step 6
Step 5	Control level 1	Step 5
	Control level 2	Step 6
	Control level 3	Step 6
	Control level 4	Step 6
Step 6	Control level 1	Step 6
	Control level 2	Step 6
	Control level 3	Step 6
	Control level 4	Step 6

TABLE E3. Algorithm for treatment period

Control level	Prescribed change in treatment
1	If on step 1, reduce to albuterol prn (as needed). If on steps 2-6, decrease controller regimen by 1 step
2	Increase controller regimen by 1 step; if on step 6, continue step 6
3	If on steps 1-4, increase controller regimen by 2 steps. If on step 5, increase to step 6. If on step 6, continue.
4	If on steps 1-3, increase controller regimen by 3 steps OR treat with 4-d prednisone burst and increase controller regimen by 2 steps. If on steps 4-5, increase to step 6 OR treat with step 6 AND 8-d prednisone burst. If on step 6, continue step 6 OR treat with step 6 and a 4-d prednisone burst

TABLE E4. Characteristics of the intention-to-treat participants at randomization for sensitization (allergen specific IgE) and exposure*

Baseline	Intervention (N = 125)	Usual care (N = 122)	*P* value
Total IgE (kU/L)	190 [105-540]	259 [138-622]	.33
Mite IgE (kU/L)	0.76 [0.25-9.94]	0.51 [0.25-3.72]	.43
Cat IgE (kU/L)	1.34 [0.25-5.12]	1.87 [0.25-17.1]	.41
Cockroach IgE (kU/L)	1.10 [0.25-7.87]	1.63 [0.25-8.07]	.90
Mouse IgE (kU/L)	0.25 [0.25-2.44]	0.25 [0.25-2.64]	.97
Dog IgE (kU/L)	1.27 [0.25-4.83]	2.61 [0.25-12.3]	.11
Mite positive >0.35 (kU/L): Yes	34 (59.6%)	42 (62.7%)	.87
Cat positive >0.35 (kU/L): Yes	36 (63.2%)	46 (68.7%)	.65
Cockroach positive >0.35 (kU/L): Yes	37 (64.9%)	44 (65.7%)	.99
Mouse positive >0.35 (kU/L): Yes	22 (38.6%)	23 (34.3%)	.76
Dog positive >0.35 (kU/L): Yes	36 (63.2%)	49 (73.1%)	.32
Bla g 2 bed (μg/g) (LOD, 0.034)	0.02 [0.02-0.09]	0.02 [0.02-0.09]	.3
Der f 1 bed (μg/g) (LOD, 0.069)	0.04 [0.04-0.15]	0.04 [0.04-0.04]	.54
Fel d 1 bed (μg/g) (LOD, 0.041)	0.06 [0.02-0.33]	0.05 [0.02-0.29]	.75
Mus m 1 bed (μg/g) (LOD, 0.034)	0.29 [0.12-1.13]	0.40 [0.13-1.64]	.21
Can f 1 bed (μg/g) (LOD, 0.069)	0.11 [0.04-1.71]	0.13 [0.04-1.15]	.67
Bla g 2 bed (μg/g) (LOD, 0.086)	0.60 [0.04-6.60]	0.45 [0.04-5.42]	.75
Mus m 1 bed (μg/g) (LOD, 0.17)	1.30 [0.20-10.2]	2.95 [0.40-19.7]	.10
Bla g 2 bed: Yes	57 (46.7%)	43 (35.5%)	.10
Der f 1 bed: Yes	33 (26.4%)	29 (24.0%)	.77
Fel d 1 bed: Yes	69 (55.2%)	63 (52.1%)	.72
Mus m 1 bed Yes/No: Yes	120 (96.0%)	120 (98.4%)	.45
Can f 1 bed Yes/No: Yes	72 (57.6%)	82 (67.2%)	.15
Bla g 2 bed Yes/No: Yes	90 (72.0%)	87 (72.5%)	.99
Mus m 1 bed Yes/No: Yes	104 (83.2%)	108 (88.5%)	.31
Dog in your home now or 6 mo prior: Yes	23 (28.7%)	29 (36.7%)	.37
Cat in your home now or 6 mo prior: Yes	18 (24.0%)	18 (26.5%)	.88
Rodent in your home now or 6 mo prior: Yes	9 (12.7%)	8 (12.3%)	.99

LOD, Limit of detection.
*Values are count (percent) or median [interquartile range].

TABLE E5. Treatment effect (change from baseline) during 48 wk of follow-up*: Change from baseline in outcomes (baseline visit minus final visit)

Baseline	Intervention*	Usual care*	Difference† (95% CI)	*P* value
Asthma symptoms (d/2 wk)	−0.14 ± 0.26	−0.52 ± 0.27	0.38 (−0.37 to 1.12)	.32
Rescue (albuterol) inhaler	−0.19 ± 0.23	−0.49 ± 0.24	0.29 (−0.37 to 0.96)	.39
Awakened with asthma symptoms	0.10 ± 0.22	−0.07 ± 0.23	0.17 (−0.46 to 0.8)	.60
ACT score	−0.61 ± 0.38	−0.33 ± 0.40	−0.29 (−1.36 to 0.79)	.60
Childhood ACT score	−0.37 ± 0.60	0.24 ± 0.63	−0.61 (−2.36 to 1.14)	.49
Treatment step	0.95 ± 0.11	0.96 ± 0.12	−0.02 (−0.34 to 0.31)	.92
Exhaled nitric oxide*	1.19 ± 0.07	1.05 ± 0.07	0.14 (−0.04 to 0.33)	.13
FEV_1 (% predicted) pre	1.70 ± 0.76	2.72 ± 0.79	−1.02 (−3.16 to 1.12)	.35
FEV_1 (% predicted) post	0.75 ± 0.90	1.88 ± 0.94	−1.13 (−3.69 to 1.44)	.39
Control level	0.43 ± 0.11	0.49 ± 0.12	−0.07 (−0.38 to 0.25)	.68
Composite asthma score	0.15 ± 0.19	−0.09 ± 0.20	0.24 (−0.30 to 0.78)	.38
Juniper mini-AQLQ	−0.32 ± 0.14	−0.08 ± 0.16	−0.24 (−0.66 to 0.18)	.27

*Plus−minus values are means ± standard error over the 48-wk treatment period. Change from baseline is calculated as baseline visit minus postbaseline visit.
†Unrounded values were used to determine the difference between groups for the 48-wk treatment.

TABLE E6. Subgroup analyses for the primary outcome (treatment step) using different *a priori* randomization characteristics*

	Group: No		Group: Yes		Interaction
Subgroup	Difference (intervention − control)	*P* value	Difference (intervention − control)	*P* value	*P* value*
Age	0.18 (0.32)	.57	−0.05 (0.29)	.85	.58
Body mass index > 30	−0.32 (0.28)	.26	0.44 (0.34)	.19	.09
ETS exposure	0.26 (0.28)	.36	−0.43 (0.43)	.32	.18
Non-Hispanic	−0.02 (0.32)	.95	0.09 (0.36)	.80	.81
Control level > 1	0.20 (0.27)	.47	0.09 (0.30)	.76	.80
Treatment step 6	0.15 (0.24)	.53	0.10 (0.28)	.71	.90
Cockroach sensitized and exposed	0.24 (0.36)	.50	−0.17 (0.32)	.59	.39
Mouse sensitized and exposed	0.10 (0.27)	.72	−0.39 (0.53)	.46	.41

*All subgroup analyses were prespecified before examination of the data and are presented in their entirety in this table. We used the recommended statistical method for assessing the heterogeneity of the effect among the subgroups using a statistical test for interaction, adjusting for the prespecified baseline characteristics. Because they were exploratory, subgroup analyses do not include adjustment for multiple comparisons.

TABLE E7. Sensitization and exposure to each allergen

Allergen (sensitized and exposed)	Intervention, n (%)	Control, n (%)	*P* value
Cockroach	70 (57.4)	64 (53.8)	.67
Mouse	35 (28.7)	21 (17.6)	.06
Cat	20 (16.0)	21 (17.4)	.91
Dog	14 (11.2)	25 (20.5)	.07
Dust	3 (2.4)	4 (3.3)	.72