# **Supplementary Online Content**

Matsui EC, Perzanowski M, Peng RD, et al. Effect of an integrated pest management intervention on asthma symptoms among mouse-sensitized children and adolescents with asthma: a randomized clinical trial. JAMA. doi:10.1001/jama.2016.21048

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This supplementary material has been provided by the authors to give readers additional information about their work.

### **eMethods**

## Lung function

Pre- and post-bronchodilator spirometry was performed at the clinic visits according to American Thoracic Society guidelines. Post-bronchodilator spirometry was performed approximately 20 minutes after albuterol was administered by nebulizer (2.5mg/3cc). Predicted values were calculated using the Hankinson equations, which are applicable for children  $\geq 8$  years and adolescents. Analyses including lung function data were restricted to children who were at least 8 years of age at baseline. Bronchodilator reversibility was defined as an increase in FEV<sub>1</sub> by  $\geq 12\%$  following albuterol. All lung function data were reviewed by an investigator for acceptability.

### Other Clinical Data

Blood was collected by venipuncture at baseline and 12 months for measurement of mouse urine-specific IgE by ImmunoCAP (ThermoFisher). Race/ethnicity was captured by asking the primary caregiver to select all race/ethnicity options that he/she deemed appropriate for his/her child. An acute visit was defined as an urgent doctor visit, ED visit, or hospitalization for asthma symptoms in the previous 3 months and an oral corticosteroid burst was defined as parent report of the participant taking oral corticosteroids in the previous 3 months.

Controller medication data were obtained by reviewing medications brought to the study visit by the primary caregiver.

Participants were classified as taking a controller if they reported taking a controller medication in the previous 2 weeks. Treatment

step was determined by classifying controller medication regimen into one of 5 treatment steps: Step 1: short-acting beta-agonist only; Step 2: low dose inhaled corticosteroids (ICS); Step 3: low dose ICS + long-acting beta-agonist (LABA) Step 4: medium dose ICS+LABA; Step 5: high dose ICS ±LABA.

## Allergen Exposure

Exposure assessment of allergen levels in homes occurred every three months, at baseline, 3, 6, 9, and 12 months. Settled dust collection methods were standardized across recruitment sites through a common protocol established for this study based on many previous studies. Separate bed and bedroom floor dust samples were collected by portable canister vacuum cleaner (Oreck) using a standard protocol. At baseline, 6, and 12 months, air samplers (SKC, Inc.) were deployed in the child's bedroom for approximately 3 days at a flow rate of 4 liters per minute to collect airborne particulate matter ≤10 microns for measurement of mouse allergen. Mouse allergen (Mus m 1) was measured in all samples by ELISA (Indoor Biotechnologies). Cockroach allergen (Bla g 2) was measured in bed dust samples at all of the time points, and other major indoor allergens, cat (Fel d 1), dog (Can f 1), dust mites (Der p 1 and Der f 1), and rat (Rat n 1), were measured at baseline in bed dust samples. A validated commercially available assay was used throughout the study for baseline and follow-up samples. All samples were run in duplicate and at multiple dilutions. Because baseline home dust samples were assayed for mouse allergen content in real-time to determine eligibility for randomization, these

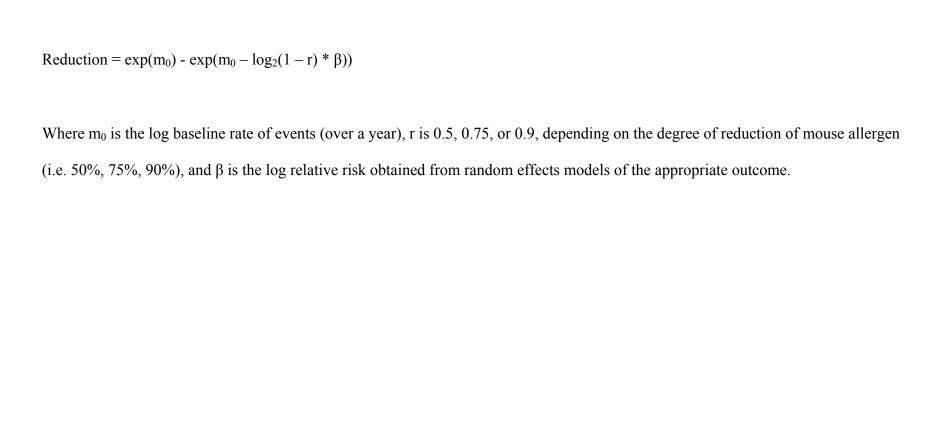
mouse allergen concentrations in these samples were examined over time to determine if there was a drift in assay performance, and the allergen concentrations remained stable over time.

Statistical Analyses

The Mouse Allergen and Asthma Intervention Trial was a one year, parallel arm, randomized clinical trial of an intensive, professionally-delivered IPM intervention. Missing data were evaluated to determine the quantity of missing data and whether participants who dropped out were reflective of the overall study population (eTable 6). Because the 16 participants who dropped were similar to the overall population with respect to socio-demographic characteristics, group assignment, and study site, but not maximal symptom days, an analysis was performed to determine if excluding (or including) participants in the analysis based on baseline maximal symptoms days would alter the result of the trial. An interaction term between group and baseline maximal symptom days was included in the statistical model for the primary analysis and was not statistically significant (p=0.26).

A pre-specified analysis was performed to examine the relationship between the within-person reduction in mouse allergen and asthma outcomes among the entire study population. First, random effects models were constructed to model the relationships between reduction in mouse allergen and asthma outcomes among the entire study population, irrespective of group assignment.

Second, to predict reductions in symptoms and acute health care use outcomes associated with mouse allergen reduction, the following approach was applied, where



## MAAIT integrated pest management treatment and education procedures

### 1. HOME PREPARATION FOR PEST MANAGEMENT

The following should be reviewed with the parent/guardian when scheduling the IPM visit.

Home preparation for rodent IPM is essential for success in controlling this pest. In order to find and see where mice are moving and harboring, obstacles need to be moved or removed. Advanced cleaning of mice and evidence of mice is <u>not necessary and should not be done</u> since we want to find <u>and</u> examine mouse evidence.

## Families should prepare as follows (keeping in mind that mice run along and inside walls):

- 1. Empty out beneath the kitchen sink and lower cabinets.
- 2. Clear the floors of closets and other storage areas;
- 3. Minimize clutter; place items into large, translucent, plastic storage containers which can be moved easily.
- 4. <u>IPM staff</u> will need to move furniture and large appliances 1-2 feet away from walls for inspection and treatment. Do not move them before the IPM visit, but have it possible for them to be moved (clear obstacles).
- 5. Allow access and inspection of the heating and other utility systems. This is very important because mice take advantage of these avenues to move in and out of other rooms and homes.
- 6. Provide access to the basement, attic, and storage areas. Have keys available if needed for access to these areas.
- 7. Provide access to the outside perimeter; this includes removing toys, equipment, vegetation, animal waste, trash, debris and rubble.

#### 2. IPM HOME VISIT

IPM procedures include placement of traps, application of rodenticide in holes and cracks, sealing of holes and cracks, targeted cleaning, and education. Additional procedures for the IPM intervention are mattress/pillow encasements and air purifiers. This standard operating procedure is focused on the extermination and sealing of entry points.

### **IPM Supplies:**

- 1. Rodenticide, tracking powder
- 2. Expanding foam
- 3. Stuff-It copper gauze
- 4. Duct tape
- 5. Screen
- 6. Traps: snap, glue and curiosity
- 7. Non-allergenic non-toxic bait for traps

#### The IPM Technician:

- 1. Asks the family about:
  - a. Recent pest activity/sightings.
  - b. The family's prior mouse control experiences at this home. Specifically, any previous success/failure with glue (box shape) and/or snap traps.
  - c. If there are pets or young children (<10 years old), in which case the IT will take extra care in placement of traps and use of rodenticide.
  - d. Access to areas of the home (ask if any area in the home if off limits or restricted, i.e. child napping).
- 2. Documents a walk-through of the living quarters:
  - a. Identify and draw/sketch the layout of the home (detailed instructions for completing the form are included in it).
  - b. Identify visual evidence of infestation, areas of pest harborage and movement, gaps providing access to pests, and food and water sources.
  - c. Identify and document impediments (i.e. closets or other areas are which are heavily cluttered). Removing clutter/impediments will maximize the ability to access these areas at the next IPM visit.
- 3. Implements IPM strategies:
  - a Start in the kitchen.

- 1) Request to move major appliances, including the stove and refrigerator, to look for evidence of current or prior infestation (mouse droppings, tunneling, rub marks) and previously placed rodent traps.
- 2) Add anticoagulant tracking powder into holes and cracks that can be sealed to prevent migration of tracking powder into the home where <u>pets and children could be exposed</u>. Treat voids, including pipe chases.
- 3) Fill and seal holes, cracks and crevices with Stuff IT (copper gauze) and Pur-fil/Hilti foam or both. Screening and duct tape can be used for larger openings.
- 4) Place traps (a minimum of 6 traps in the kitchen).
- b. Inspect remaining rooms (living room, bedrooms), particularly around the heating system. Request access to closets (check frames around doors) and cluttered areas. Treat with the following sequence:
  - 1) Put anticoagulant tracking powder into holes and/or cracks in walls which can be sealed to prevent the migration of the powder into the living space.
  - 2) Seal the holes and cracks using copper gauze and Pur-fill foam. Screen and duct tape can be used to seal large holes.
  - 3) Place traps (sticky or snap) behind furniture or in hidden areas. A minimum of 3 traps should be placed in <u>each</u> of these rooms.
- c. Inspect the attic, basement, crawl space and other void areas (document if you do not have access to these areas) and treat with same sequence as indicated for kitchen and other rooms above:
  - 1) Inspect insulation, looking for droppings and/or tunneling and old rodent baits. Look on sills, utility openings, near windows and doors.
  - 2) Place anticoagulant powder inside cracks or holes and then seal with copper gauze and foam.
  - 3) Place traps.
- d. Inspect outside perimeter of home(including under and around porches or stoops) for holes in the foundation, and treat with the same sequence as above:
  - 1) Put anticoagulant tracking powder into holes and/or cracks in walls which can be sealed to prevent the migration of the powder into the living space.
  - 2) Seal the holes and cracks using copper gauze and Pur-fil/Hilti foam. Screen and duct tape can be used to seal large holes.
  - 3) Place traps
- e. In general identify openings under the primary or other critical doors. Any gap which lets in light or is otherwise visible should be sealed. Door sweeps should be installed if these gaps are present.

The Booster Visit will follow the same protocol as Intervention Visit 1. This visit should be as intense as the first visit the 3, 6, or 9 month Home Assessment Visits:

#### 3. IPM EDUCATION

Examples of food storage containers, traps, copper mesh and foam are shown to the parent/guardian.

#### **Materials:**

- Samples of food storage containers
- Samples of mouse traps
- Copper mesh
- Spray foam

#### Information:

The following background information will be reviewed with the parent/guardian:

- Many children with asthma are allergic to mice.
- People who are allergic to mice are allergic to the allergen that the mice make.
- The allergen that mice make is excreted in their urine in very large amounts. The allergen can also be found on mouse dander.
- When the urine dries, the allergen becomes dust and floats in the air.
- The allergen gets all over the home in bedding, in furniture, in the air, on floors, and on walls.
- When children with mouse allergy breathe the dust, the mouse allergen goes into their lungs and causes irritation which makes their asthma worse.

The research assistant will review the 3 main approaches to reducing mouse allergen levels:

- Get rid of the mice which make the allergen
- Keep the mice from coming back
- Clean up the allergen that is already in the home

eTable 1. Comparison of baseline characteristics of participants excluded from the primary analysis to the overall study population

	Not in primary analysis (n=16)	Entire Study Population (n=350)
Gender-male, n (%)	11 (69)	218 (62)
Age, mean (SD)	10.7 (3.7)	9.8 (3.2)
Race-black, n (%)	13 (81)	278 (79)
Hispanic-yes, n (%)	3 (19)	75 (21)
Income, n (%)		
< \$30,000	9 (56)	232 (67)
\$ 30,000 - \$ 50,000	5 (31)	57 (16)
> \$50,000	2 (13)	31 (9)
Refused/unknown	0 (0)	30 (8)
Group-Integrated Pest Management, n (%)	10 (63)	176 (50)
Maximal symptoms days, median (Q1-Q3)	5.0 (3.8-11.0)	3.0 (0-6.8)
Site- Baltimore, n (%)	10 (63)	239 (68)

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eTable 2. Adverse Events

	IPM+Education	Education
Participants with at least 1 adverse event, n	132 (75%)	137 (79%)
Participants with ≥1 probably/definitely related AE, n	2 (1%)	2 (1%)
Probably/definitely related adverse events,* n	4	2

<sup>\*</sup>Integrated Pest Management+Education: 3 events were rash/pruritis related to skin testing prior to randomization, 1 event was mouth pain during saliva collection

**Education:** 1 event was itchy watery eyes and throat irritation after skin testing prior to randomization, 1 event was wheezing after spirometry prior to randomization

eTable 3. Estimated Effects of Decreasing Bedroom Floor Mouse Allergen on Asthma Morbidity<sup>¥</sup>

	Crude Ratio of Symptom Frequencies (95% Confidence Interval)	p-value	Adjusted* Ratio of Symptom Frequencies (95% Confidence Interval)	p-value
Asthma Symptom Outcomes				
Major Asthma Symptoms				
Wheezing, coughing, chest tightness	0.97 (0.96-0.99)	<0.001	0.97 (0.96-0.99)	<0.001
Slowed activity	0.95 (0.93-0.97)	<0.001	0.95 (0.93-0.97)	<0.001
Nocturnal wakening	0.95 (0.93-0.97)	<0.001	0.95 (0.93-0.97)	<0.001
Maximal symptom days <sup>€</sup>	0.96 (0.95-0.98)	<0.001	0.96 (0.95-0.98)	<0.001
Other symptoms and rescue medication use				
Cough without a cold	0.94 (0.92-0.96)	<0.001	0.94 (0.92-0.96)	<0.001
Exercise-related symptoms	0.92 (0.90-0.94)	<0.001	0.92 (0.90-0.94)	<0.001

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Difficulty speaking	0.89 (0.86-0.93)	<0.001	0.89 (0.86-0.93)	<0.001
Short-acting beta-agonist use	0.96 (0.95-0.98)	<0.001	0.96 (0.95-0.98)	<0.001
Asthma-related Health Care Us	se			
	Crude Relative Risk (95% Confidence Interval)	p-value	Adjusted Relative Risk (95% Confidence Interval)	p-value
Acute visit	0.93 (0.90 – 0.96)	<0.001	0.93 (0.90 – 0.96)	<0.001
ED visit	0.94 (0.90 – 0.98)	0.002	0.94 (0.91 – 0.98)	0.004
Hospitalization	0.93 (0.86 – 1.01)	0.10	0.94 (0.86 – 1.02)	0.14
<b>Lung Function, </b> Mouse-specific	e IgE, and Oral Corticosteroi	d Burst		
	β coefficient √ (95% Confidence Interval)	p-value	Adjusted* β coefficient  (95% Confidence Interval)	p-value
FEV1 % predicted	0.02 (-0.43 – 0.46)	0.94	0.06 (-0.38 – 0.51)	0.78
FVC % predicted	-0.14 (-0.55 – 0.27)	0.50	-0.12 (-0.53 – 0.29)	0.58

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FEV/FVC %	-0.02 (-0.25 – 0.22)	0.90	-0.01 (-0.25 – 0.22)	0.91
log2(mouse-specific IgE)	-0.16 (-0.200.11)	<0.001 -0.14 (-0.190.09)		<0.001
	Crude Odds Ratio (95% Confidence Interval)	p-value	Adjusted* Odds Ratio (95% Confidence Interval)	p-value
Bronchodilator reversibility**	0.99 (0.90- 1.09)	0.79	0.99 (0.90-1.09)	0.83
Oral corticosteroid burst	0.94 (0.89 – 1.00)	0.05	0.95 (0.90 – 1.01)	0.11

\*random effects models of relationships between log2(mouse allergen) and asthma symptoms, morbidity, lung function, and mouse-specific IgE; 1 unit reduction in log2(mouse allergen) is the reference increment for the ratios of relative symptom frequencies, Relative Risks and Odds Ratios, and is equivalent to a 50% reduction in mouse allergen; Poisson models were used for symptoms and acute care outcomes, logistic models for binary outcomes of oral corticosteroid burst and bronchodilator reversibility, and a linear model for log2(mouse-specific IgE); unadjusted analyses included all participants with at least one visit with both mouse allergen and outcome data and adjusted analyses included participants who also had a complete set of covariates

<sup>e</sup>highest number of days of symptoms in the previous two weeks among three types of symptoms (days of slowed activity due to asthma, number of nights of waking with asthma symptoms, and days of coughing, wheezing, or chest tightness)

<sup>\*</sup>models adjusted for controller medication, season, and cockroach allergen

<sup>&</sup>lt;sup>€</sup>lung function data reported for participants 8 years or older at baseline, n=211

 $<sup>^{\</sup>vee}\beta$  coefficients represent the differences in the mean of the corresponding lung function index across 6 and 12 months between groups or the log2(mouse-specific IgE) at 12 months

<sup>\*\* ≥12%</sup> increase in FEV1 following short-acting beta-agonist

**eTable 4.** Estimated Effects of Decreasing Airborne Mouse Allergen on Asthma Morbidity<sup>¥</sup>

	Crude Ratio of Symptom Frequencies (95% Confidence Interval)	p-value	Adjusted* Ratio of Symptom Frequencies (95% Confidence Interval)	p-value
Asthma Symptom Outcomes				
Major Asthma Symptoms				
Wheezing, coughing, chest tightness	0.97 (0.95-0.99)	0.01	0.97 (0.95-1.00)	0.03
Slowed activity	0.94 (0.91-0.96)	<0.001	0.95 (0.92-0.98)	0.001
Nocturnal wakening	0.98 (0.95-1.01)	0.18	0.98 (0.95-1.01)	0.20
Maximal symptom days $^{\epsilon}$	0.97 (0.95-0.99)	0.01	0.98 (0.95-1.00)	0.04
Other symptoms and rescue medication use				
Cough without a cold	0.93 (0.90-0.97)	<0.001	0.95 (0.91-0.98)	0.002
Exercise-related symptoms	0.92 (0.90-0.95)	<0.001	0.94 (0.91-0.97)	<0.001
Difficulty speaking	0.94	0.05	0.95	0.11

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	(0.88-1.00)		(0.89-1.01)	
Short-acting beta-agonist use	0.92 (0.90-0.94)	<0.001	0.93 (0.91-0.95)	<0.001
Asthma-related Health Care Use				
	Crude Relative Risk (95% Confidence Interval)	p-value	Adjusted* Relative Risk (95% Confidence Interval)	p-value
Acute visit	0.95 (0.91 – 0.98)	0.01	0.95 (0.91 – 0.99)	0.02
ED visit	0.93 (0.88 – 0.98)	0.01	0.93 (0.88 – 0.98)	0.01
Hospitalization	0.97 (0.87 – 1.08)	0.54	0.97 (0.87 – 1.08)	0.63
<b>Lung Function,</b> Mouse-specific IgE, and Oral	Corticosteroid Burst			
	β coefficient (95% Confidence Interval)	p-value	Adjusted* β coefficient <sup>\(\sigma\)</sup> (95% Confidence Interval)	p-value
FEV1 % predicted	0.39 (-0.14 – 0.92)	0.15	0.39 (-0.14 – 0.92)	0.15
FVC % predicted	0.57 (0.09 – 1.06)	0.02	0.56 (0.07 – 1.05)	0.03

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	β coefficient √ (95% Confidence Interval)	p-value	Adjusted* β coefficient <sup>\(\sigma\)</sup> (95% Confidence Interval)	p-value
FEV/FVC %	-0.03 (-0.31 – 0.25)	0.83	-0.04 (-0.33 – 0.24)	0.77
log2(mouse-specific IgE)	-0.06 (-0.13 - 0)	0.05	-0.05 (-0.12 – 0.01)	0.10
	Crude Odds Ratio (95% CI)	p-value	Adjusted* Odds Ratio (95% CI)	p-value
Bronchodilator reversibility**	1.04 (0.93 – 1.16)	0.47	1.05 (0.94 – 1.17)	0.41
Oral corticosteroid burst	0.91 (0.84 -0.98)	0.02	0.92 (0.85 – 0.99)	0.03

<sup>\*</sup>random effects models of relationships between log2(mouse allergen) and asthma symptoms, morbidity, lung function, and mouse-specific IgE; 1 unit reduction in log2(mouse allergen) is the reference increment for both the RRs and the ORs, and is equivalent to a 50% reduction in mouse allergen; Poisson models were used for symptoms and acute care outcomes, logistic models for binary outcomes of oral corticosteroid burst and bronchodilator reversibility, and a linear model for log2(mouse-specific IgE); unadjusted analyses included all participants with at least one visit with both mouse allergen and outcome data and adjusted analyses included participants who also had a complete set of covariates

<sup>&</sup>lt;sup>e</sup>highest number of days of symptoms in the previous two weeks among three types of symptoms (days of slowed activity due to asthma, number of nights of waking with asthma symptoms, and days of coughing, wheezing, or chest tightness)

<sup>\*</sup>models adjusted for controller medication, season, and cockroach allergen

flung function data reported for participants 8 years or older at baseline

 $<sup>^{\</sup>vee}\beta$  coefficients represent the differences in the mean of the corresponding lung function index across 6 and 12 months between groups or the log2(mouse-specific IgE) at 12 months

<sup>\*\* ≥12%</sup> increase in FEV1 following short-acting beta-agonist

eTable 5. Estimated Effects of Decreasing Bed Dust Mouse Allergen on Asthma Morbidity $^{\sharp}$ 

	Crude Relative Risk (95% Confidence Interval)	p-value	Adjusted* Relative Risk (95% Confidence Interval)	p-value
Asthma Symptom Outcomes		1		
Major Asthma Symptoms				
Wheezing, coughing, chest tightness	0.97 (0.95-0.98)	<0.001	0.97 (0.95-0.99)	<0.001
Slowed activity	0.94 (0.93-0.96)	<0.001	0.95 (0.93-0.97)	<0.001
Nocturnal wakening	0.96 (0.94-0.98)	0.001	0.96 (0.94-0.99)	0.004
Maximal symptom days <sup>€</sup>	0.96 (0.94-0.97)	<0.001	0.96 (0.95-0.98)	<0.001
Other Asthma Symptoms and Rescue Medication Use				
Cough without a cold	0.95 (0.93-0.97)	<0.001	0.95 (0.93-0.97)	<0.001
Exercise-related symptoms	0.91 (0.89-0.93)	<0.001	0.92 (0.90-0.94)	<0.001
Difficulty speaking	0.91	<0.001	0.92	0.001

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	(0.87-0.96)		(0.88-0.97)	
Short-acting beta-agonist use	0.99 (0.97-1.00)	0.11	0.99 (0.98-1.01)	0.37
Asthma-related Health Care Use				
	Crude Relative Risk (95% Confidence Interval)	p-value	Adjusted* Relative Risk (95% Confidence Interval)	p-value
Acute visit	0.96 (0.93 – 0.99)	0.02	0.96 (0.93 – 1.00)	0.03
ED visit	0.98 (0.93 – 1.02)	0.27	0.98 (0.94 – 1.02)	0.35
Hospitalization	0.93 (0.85 – 1.02)	0.11	0.93 (0.85 – 1.02)	0.13
<b>Lung Function,</b> € <b>Mouse-specific IgE, and Oral C</b>	Corticosteroid Burst		1	
	β coefficient √ (95% Confidence Interval)	p-value	Adjusted* β coefficient  (95% Confidence Interval)	p-value
FEV1 % predicted	0.40 (-0.13 – 0.91)	0.15	0.41 (-0.12 – 0.94)	0.13
FVC % predicted	0.30 (-0.18 – 0.78)	0.22	0.29 (-0.19 – 0.78)	0.23

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FEV/FVC %	0.14 (-0.14 – 0.41)	0.33	0.13 (-0.15 – 0.41)	0.36
Log2(mouse-specific IgE)	-0.15 (-0.210.09)	<0.001	-0.14 (-0.190.08)	<0.001
	Crude Odds Ratio (95% Confidence Interval)	p-value	Adjusted* Odds Ratio (95% Confidence Interval)	p-value
Bronchodilator reversibility**	1.00 (0.89 – 1.12)	0.99	1.01 (0.90 – 1.13)	0.90
Oral corticosteroid burst	0.94 (0.88 – 1.00)	0.05	0.95 (0.89 – 1.01)	0.13

Frandom effects models of relationships between log2(mouse allergen) and asthma symptoms, morbidity, lung function, and mouse-specific IgE; 1 unit reduction in log2(mouse allergen) is the reference increment for both the RRs and the ORs, and is equivalent to a 50% reduction in mouse allergen; Poisson models were used for symptoms and acute care outcomes, logistic models for binary outcomes of oral corticosteroid burst and bronchodilator reversibility, and a linear model for log2(mouse-specific IgE); unadjusted analyses included all participants with at least one visit with both mouse allergen and outcome data and adjusted analyses included participants who also had a complete set of covariates

<sup>&</sup>lt;sup>€</sup>highest number of days of symptoms in the previous two weeks among three types of symptoms (days of slowed activity due to asthma, number of nights of waking with asthma symptoms, and days of coughing, wheezing, or chest tightness)

<sup>\*</sup>models adjusted for controller medication, season, and cockroach allergen

flung function data reported for participants 8 years or older at baseline

 $<sup>^{\</sup>vee}\beta$  coefficients represent the differences in the mean of the corresponding lung function index across 6 and 12 months between groups or the log2(mouse-specific IgE) at 12 months

<sup>\*\* ≥12%</sup> increase in FEV1 following short-acting beta-agonist

eTable 6. Predicted Change in Asthma Symptoms and Morbidity for Different Degrees of Reduction in Mouse Allergen<sup>‡</sup>

	no. days per person-year (95% CI)  % reduction in bedroom floor mouse allergen		
	50%	75%	90%
Asthma Symptom Outcomes			
Maximum symptom days	-4.5	-8.7	-14.1
	(-5.6, -2.2)	(-10.9, -4.4)	(-17.4, -7.2)
Wheezing, coughing, chest tightness	-2.6	-5.2	-8.4
	(-3.5, -0.9)	(-6.8, -1.7)	(-11.0, -2.9)
Slowed activity	-3.6	-7.1	-11.4
	(-5.1, -2.2)	(-9.8, -4.3)	(-15.6, -7.0)
Cough without a cold	-3.9	-7.5	-11.9
	(-5.1, -2.6)	(-9.9, -5.0)	(-15.6, -8.2)
Exercise-related symptoms	-5.5	-10.6	-16.7
	(-6.9, -4.1)	(-13.1, -8.0)	(-20.4, -12.8)
Nocturnal wakening	-2.6	-5.0	-8.0
	(-3.6, -1.5)	(-6.9, -3.0)	(-10.9, -4.9)
Difficulty speaking	-1.5	-2.8	-4.2

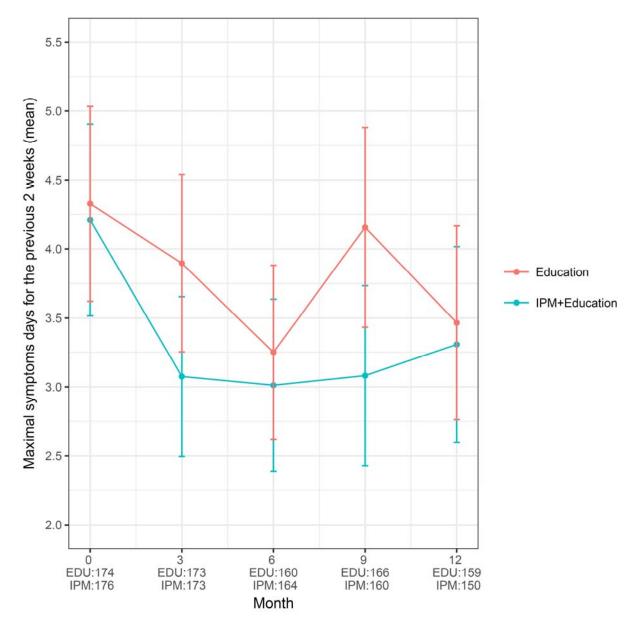
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	(-1.9, -0.9)	(-3.4, -1.8)	(-5.2, -2.8)	
Short-acting beta-agonist use	-5.2	-10.1	-16.4	
	(-6.5, -2.6)	(-12.6, -5.1)	(-20.3, -8.4)	
	number per person-year (95% CI)			
Asthma-related Health Care Use	e			
Acute visits	-0.27	-0.52	-0.82	
	(-0.38, -0.15)	(-0.73, -0.30)	(-1.13, -0.48)	
ED visits	-0.13	-0.26	-0.42	
	(-0.20, -0.04)	(-0.39, -0.09)	(-0.60, -0.15)	
Hospitalizations	-0.02	-0.04	-0.07	
	(-0.05, 0.01)	(-0.09, 0.01)	(-0.14, 0.02)	

<sup>\*</sup>effects estimated from random effects models of relationships between log2(mouse allergen) and asthma symptoms and morbidity; further details can be found in the Methods section of the Online Supplement Statistically significant findings indicated in **bold** 

eFigure. Maximal symptoms days in the previous 2 weeks at each time point, by group

Means and 95% confidence intervals are displayed and the number of participants contributing to the analysis at each time point is indicated below the x axis.



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