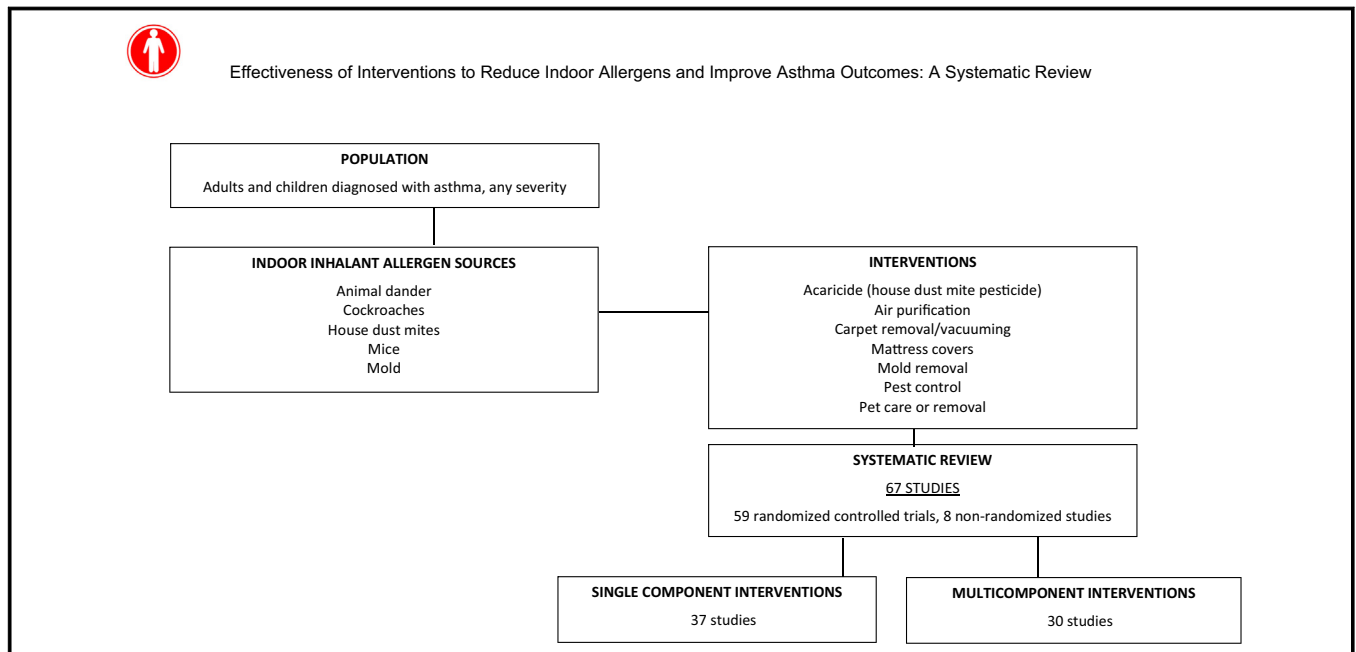


Effectiveness of indoor allergen reduction in asthma management: A systematic review



Brian F. Leas, MS, MA,^a Kristen E. D'Anci, PhD,^b Andrea J. Apter, MD, MSc,^c Tyra Bryant-Stephens, MD,^d Marcus P. Lynch, PhD,^b Janice L. Kaczmarek, MS,^b and Craig A. Umscheid, MD, MSCE^{a,c} *Philadelphia and Plymouth Meeting, Pa*

GRAPHICAL ABSTRACT



Background: This review will inform updated National Asthma Education and Prevention Program clinical practice guidelines. **Objective:** We sought to evaluate the effectiveness of allergen reduction interventions on asthma outcomes. **Methods:** We systematically searched the “gray literature” and 5 bibliographic databases. Eligible studies included systematic

reviews, randomized controlled trials, and nonrandomized interventional studies. Risk of bias was assessed by using the Cochrane Risk of Bias instrument and the Newcastle-Ottawa scale. The evidence base was assessed by using the approach of the Agency for Healthcare Research and Quality’s Evidence-based Practice Center program.

From ^athe Center for Evidence-based Practice, University of Pennsylvania Health System, Philadelphia; ^bthe ECRI Institute Plymouth Meeting; ^cthe Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia; and ^dChildren’s Hospital of Philadelphia.

Supported under contract no. 290-2015-00005-I from the Agency for Healthcare Research and Quality (AHRQ), US Department of Health and Human Services. The authors of this manuscript are responsible for its content. Statements in the manuscript should not be construed as endorsement by the AHRQ or the US Department of Health and Human Services. AHRQ retains a license to display, reproduce, and distribute the data and the report from which this manuscript was derived under the terms of the agency’s contract with the author. This topic was nominated by the National Heart, Lung, and Blood Institute (NHLBI) and selected by the AHRQ for systematic review by an Evidence-based Practice Center. A representative from AHRQ served as a Contracting Officer’s Technical Representative and provide technical assistance during the conduct of the full evidence report and provided comments on draft versions of the full evidence report. AHRQ did not directly participate in the literature search, determination of study eligibility criteria, data analysis or interpretation, or preparation, review, or approval of the manuscript for publication.

Disclosure of potential conflict of interest: B. F. Leas reports a grant from the Agency for Healthcare Research and Quality (AHRQ). K. E. D’Anci reports a grant from the AHRQ. A. J. Apter reports funding from the AHRQ (contract 290-2015-00005-1). T. Bryant-Stephens reports pending grants from the National Heart, Lung, and Blood Institute (NHLBI) and the Pennsylvania Department of Health. M. P. Lynch reports a grant from the AHRQ/NHLBI. C. A. Umscheid reports a grant from the AHRQ. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication November 8, 2017; revised January 16, 2018; accepted for publication February 2, 2018.

Available online February 13, 2018.

Corresponding author: Brian F. Leas, MS, MA, Center for Evidence-based Practice, University of Pennsylvania Health System, 3535 Market St, Suite 50, Philadelphia, PA 19104. E-mail: brian.leas@uphs.upenn.edu.

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0091-6749/\$36.00

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<https://doi.org/10.1016/j.jaci.2018.02.001>

Results: Fifty-nine randomized and 8 nonrandomized trials addressed 8 interventions: acaricide, air purification, carpet removal, high-efficiency particulate air filtration (HEPA) vacuums, mattress covers, mold removal, pest control, and pet removal. Thirty-seven studies evaluated single-component interventions, and 30 studies assessed multicomponent interventions. Heterogeneity precluded meta-analysis. For most interventions and outcomes, the evidence base was inconclusive or showed no effect. No interventions were associated with improvement in validated asthma control measures or pulmonary physiology. Exacerbations were diminished in multicomponent studies that included HEPA vacuums or pest control (moderate strength of evidence [SOE] for both). Quality of life improved in studies of air purifiers (SOE: low) and in multicomponent studies that included HEPA vacuums (SOE: moderate) or pest control (SOE: low).

Conclusions: Single interventions were generally not associated with improvement in asthma measures, with most strategies showing inconclusive results or no effect. Multicomponent interventions improved various outcomes, but no combination of specific interventions appears to be more effective. The evidence was often inconclusive because of a lack of studies. Further research is needed comparing the effect of indoor allergen reduction interventions on validated asthma measures, with sufficient population sizes to detect clinically meaningful differences. (*J Allergy Clin Immunol* 2018;141:1854-69.)

Key words: Asthma, allergens, environmental, house dust mites, carpet, pests, pets, air purification, high-efficiency particulate air filtration vacuums, mattress covers

Control of common environmental factors that contribute to asthma is an important component of asthma management. Many indoor inhalant allergens are associated with increased risk of asthma symptoms and exacerbations, including animal dander, cockroaches, house dust mites, mice, and mold.¹ Numerous interventions have been designed to reduce exposure to these allergens, including use of acaricides (dust mite pesticides), air-purification systems, carpet removal, high-efficiency particulate air filtration (HEPA) vacuums, allergen-impermeable mattress covers, mold removal, pest-elimination techniques, and removal of family pets.

In 1991, the National Asthma Education and Prevention Program (NAEPP), a project of the National Heart, Lung, and Blood Institute (NHLBI), produced clinical practice guidelines addressing the diagnosis, evaluation, and treatment of asthma, including reducing exposure to indoor inhalant allergens. The guidelines were updated subsequently, most recently in 2007.²

In 2016, the NHLBI convened a working group to oversee a new update of the guidelines. After receiving input from the public, NAEPP Coordinating Committee Members and affiliates, and members of the 2007 Expert Panel, the working group identified 6 high-priority topics for updating. For each topic, key questions were developed to guide new systematic literature reviews. The NHLBI engaged the Agency for Healthcare Research and Quality (AHRQ) to perform the systematic reviews through its Evidence-based Practice Centers (EPCs). In this article we summarize the resulting systematic review on

Abbreviations used

ACT:	Asthma Control Test
AHRQ:	Agency for Healthcare Research and Quality
EPC:	Evidence-based Practice Center
HEPA:	High-efficiency particulate air filtration
NAEPP:	National Asthma Education and Prevention Program
NHLBI:	National Heart, Lung, and Blood Institute
RCT:	Randomized controlled trial
SOE:	Strength of evidence

“Effectiveness of indoor allergen reduction in management of asthma.” The complete review is available at <https://effectivehealthcare.ahrq.gov/topics/asthma-nonpharmacologic-treatment/final-report-indoor-allergen-reduction>.

METHODS

We searched Embase, MEDLINE, PubMed, CINAHL, and the Cochrane Library up to April 21, 2017. We also browsed the Web sites of relevant agencies and organizations to identify “gray literature,” such as reports, white papers, dissertations, or other documents not published in peer-reviewed sources. Two independent reviewers performed abstract and full-text screening, with disagreements resolved by means of consensus.

We included only full-length peer-reviewed studies. Systematic reviews, meta-analyses, randomized controlled trials (RCTs), and nonrandomized interventional studies with concurrent controls (eg, nonrandomized trials) or historical controls (eg, pre-post studies) were eligible for inclusion. *In vivo*, *in vitro*, and animal studies were excluded. Studies published in a foreign language with English-language abstracts were considered for inclusion if they examined interventions or reported outcomes not sufficiently addressed in English-language studies or provided novel data that might affect our conclusions. Studies were excluded if more than 15% of participants were not given a diagnosis of asthma or if outcomes for asthmatic patients were not reported separately from patients without asthma.

In accordance with the approach used by the “Guidelines for the diagnosis and management of asthma,”² we defined “pediatric” or “child” populations as including patients aged 11 years or less and “adult” populations as including patients aged 12 years or older. Studies that included patients in both categories are described as having a “mixed population.”

We limited our review to studies that examined a single intervention or a set of interventions designed to decrease exposure to 1 or more of the following sources of indoor allergens: dust mites, household pets, rodents, cockroaches, or mold. Interventions addressing other indoor allergens or irritants, such as tobacco smoke, indoor pollution, and endotoxin, were excluded. We examined the following interventions selected to reflect the input of the NHLBI Advisory Council Asthma Expert Working Group³: acaricides, air-purification devices, carpet or rug removal, HEPA vacuums, impermeable mattress covers, mold removal, pest control, and pet removal.

Data elements abstracted included general study characteristics, patient characteristics, details of interventions, outcomes data, and risk of bias for each study. Risk of bias was assessed by 2 independent reviewers using the Cochrane Collaboration’s tool for RCTs⁴ and the Newcastle-Ottawa scale⁵ for nonrandomized studies. Because of the heterogeneity of the included studies, we did not attempt to combine data from the studies quantitatively.

Outcomes were selected to be consistent with the recommendations of the 2010 Asthma Outcomes Workshop.⁶ Primary outcomes included validated measures of asthma control (eg, the Asthma Control Questionnaire⁷ or Asthma Control Test [ACT]⁸), asthma-related exacerbations, asthma-related health care use and costs, pulmonary physiology (eg, spirometric measures), and asthma-related quality of life (eg, the Asthma Quality of Life Questionnaire [AQLQ]).⁹ Nonvalidated measures of asthma symptoms and allergen levels were assessed as secondary outcomes.

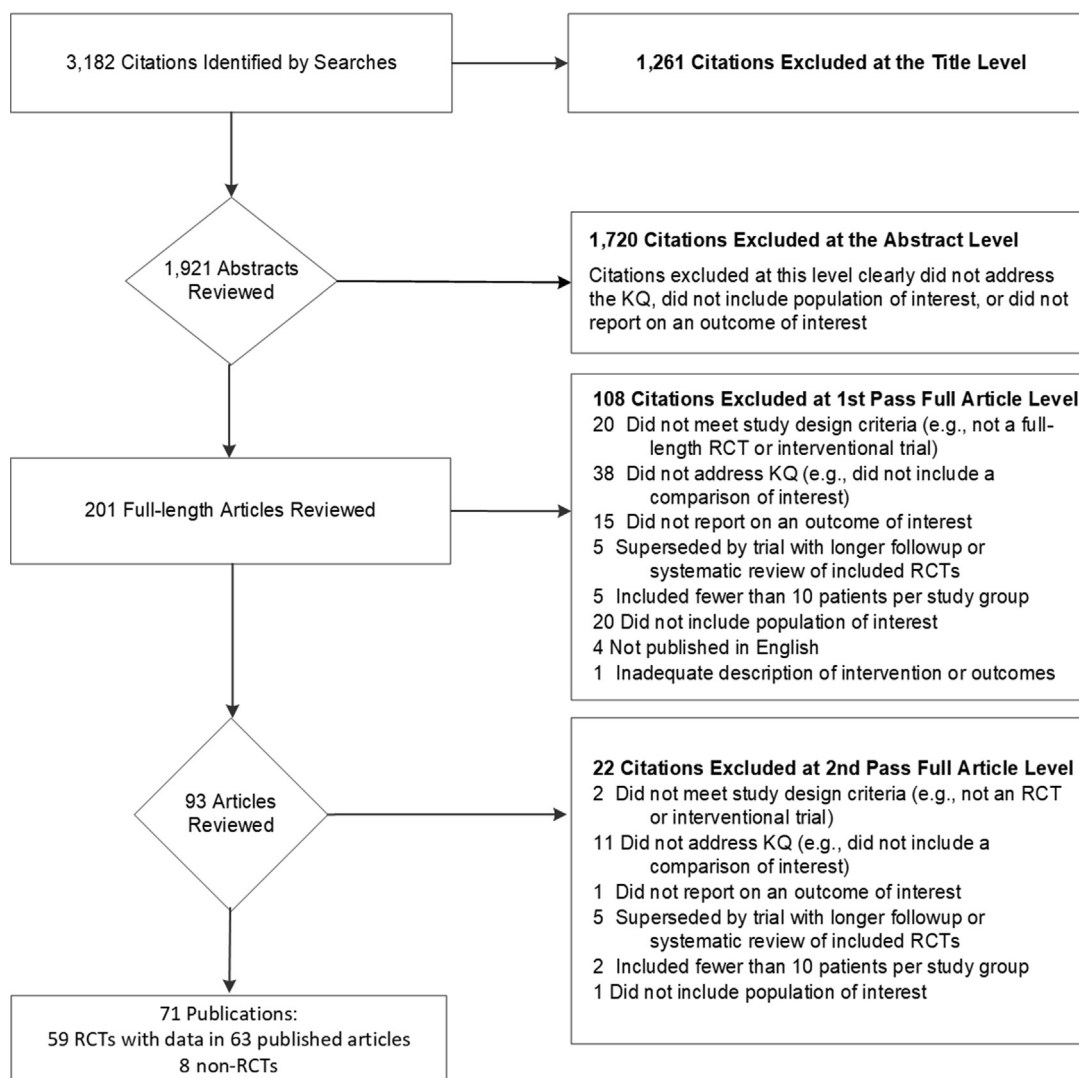


FIG 1. Study attrition diagram. *KQ*, Key question; *RCT*, randomized controlled trial.

We graded the strength of evidence (SOE) for each outcome based on guidance established by the EPC program.¹⁰ This approach incorporates 5 key domains: study limitations, consistency, directness, precision, and reporting bias. Overall SOE was evaluated as high, moderate, low, or insufficient. Evidence based on RCTs was assigned an initial SOE of “high,” whereas evidence based on non-RCTs was assigned an initial SOE of “low.” The SOE was then downgraded as appropriate based on the 5 domains.

We determined study limitations by appraising the degree to which the included studies for the given comparison and outcome had adequate protection against bias (ie, had good internal validity). In general, we downgraded for study limitations when 50% or more of the studies evaluated for a given outcome were at “high” overall risk of bias, as described above. When 50% or more of the studies were at “medium,” “low,” or “unclear” risk of bias, we did not downgrade for study limitations.

We assessed consistency of results in terms of the direction and magnitude of effect. In general, we downgraded for inconsistency when there was heterogeneity in the effects of an intervention across studies for a given outcome that could not be explained through identifiable differences in study characteristics. We downgraded for unknown consistency when only a single study was included for an outcome.

The evidence was considered indirect if the populations, interventions, comparisons, or outcomes used within studies did not directly correspond to the comparisons we were evaluating.

Precision is the degree of certainty surrounding an effect estimate with respect to a given outcome and might be affected by sample size, number of events, and width of CIs. In some cases we downgraded the SOE by 2 levels because of substantial imprecision resulting from very small samples or numbers of events or when it was not possible to assess an estimate of effect based on available data (eg, measures of variance were not included or results were presented graphically without reporting of specific data points).

Reporting bias includes publication bias, outcome-reporting bias, and analysis-reporting bias. Given the small number of studies we evaluated for most of the interventions, we did not examine funnel plots. We downgraded for reporting bias when we detected a likelihood of outcome reporting bias (important clinical outcomes appear to have been collected but not reported by the studies within a comparison) or analysis reporting bias (important comparisons were not analyzed). For studies that had commercial funding, authorship, or both, we also assessed the size and direction of any effect compared with the studies that did not receive commercial support to identify possible publication or reporting bias.

We also conducted a qualitative comparative analysis¹¹ to evaluate the studies. This analytic technique was incorporated to determine whether specific individual strategies or bundles of allergen reduction interventions might be more likely to improve asthma outcomes.

A complete description of the methods used in this review are included in the EPC report.

TABLE I. Overview of interventional studies for reducing allergen exposure

Intervention	RCTs and sample size	Other study designs and sample size	Age cohorts*	Country/region
Acaricides (dust mite pesticide)	6 ¹²⁻¹⁷ (total n = 229)	1 nonrandomized trial ¹⁸ (n = 59)	3 Adult 4 Mixed	6 Europe 1 Canada
Air purification	9 ¹⁹⁻²⁷ (total n = 311)	0	4 Adult 1 Pediatric 4 Mixed	1 United States 7 Europe 1 New Zealand
Carpet removal	0	0	Not applicable	Not applicable
HEPA vacuums	1 ²⁸ (n = 60)	0	1 Mixed	1 Europe
Mattress covers	17 ²⁹⁻⁴⁵ (total n = 2287)	0	9 Adult 1 Pediatric 6 Mixed 1 Not reported	11 Europe 4 Asia 2 Australia
Mold removal	0	0	Not applicable	Not applicable
Pest control	1 ⁴⁶ (n = 102)	1 Pre-post ⁴⁷ (n = 78)	2 Mixed	2 United States
Pet removal	0	1 Nonrandomized trial ⁴⁸ (n = 20)	1 Adult	1 Asia
Multicomponent	25 ⁴⁹⁻⁷³ (total n = 4338)	3 Pre-post ⁷⁴⁻⁷⁶ (n = 365) 2 Non-RCTs ^{77,78} (n = 204)	5 Adult 7 Pediatric 18 Mixed	20 United States 9 Europe 1 Australia
Total	59	4 Nonrandomized trials 4 Pre-post	22 Adult 9 Pediatric 35 Mixed 1 Not reported	23 United States 1 Canada 34 Europe 5 Asia 4 Australia/New Zealand

*Adult patients were 12 years old or older, pediatric patients were less than 12 years old, and mixed populations included pediatric and adult patients.

RESULTS

We reviewed 1921 abstracts and 201 full-text studies. We included 59 RCTs (with data published in 63 published articles) and 8 nonrandomized controlled studies in the review (Fig 1). Thirty-seven studies evaluated single interventions, and 30 studies examined multicomponent strategies. Use of mattress covers was the most frequently examined intervention and was included in 33 studies. Conversely, pet removal was implemented in just 3 studies. Twenty-two studies included only patients 12 years of age and older, whereas 9 studies were limited to children less than 12 years of age. Thirty-five studies enrolled patients greater than and less than age 12 years, and 1 study did not report age. Thirty-four studies were conducted in Europe, 23 were performed in the United States, and the remaining 10 were conducted in Canada, Australia, New Zealand, or Asian countries. In 40 studies all patients were sensitized to a relevant allergen, and an additional 14 studies reported that a majority of patients were sensitized. Sensitization was confirmed through skin prick tests in 43 RCTs and with blood tests in the remaining 11 trials.

Table I¹²⁻⁷⁸ provides an overview of the distribution of the studies. Table II⁴⁹⁻⁷⁸ shows the combinations of interventions used in multicomponent studies. Table III^{12-42,46-49,64} summarizes the SOE for each intervention.

A more detailed description of the analysis is presented in Tables IV (for single-intervention studies) and V (for multicomponent studies).^{49-62,64-72,74,75,77} Additional information for each included study is available in the complete AHRQ report (<https://effectivehealthcare.ahrq.gov/topics/asthma-nonpharmacologic-treatment/final-report-indoor-allergen-reduction>).

Acaricides

Seven studies examined use of acaricides on mattresses, carpets, and upholstery as a single intervention to eradicate house

dust mite allergens.¹²⁻¹⁸ There was no improvement in pulmonary physiology when comparing acaricides with placebo (moderate SOE) or with other interventions (SOE: low), and other outcomes were inconclusive or not reported. Six multicomponent studies also examined acaricides^{51,65,67-70} and suggested no improvement in pulmonary physiology (SOE: moderate) or asthma symptoms (SOE: high). Acaricides reduced dust mite allergen burden (SOE: low), but other outcomes were inconclusive or not reported.

Air purification

Nine studies evaluated air purification as a single intervention.¹⁹⁻²⁷ The evidence for asthma control was inconclusive, and no difference was observed for exacerbations or pulmonary physiology measures (SOE: low). For quality of life, 1 study found that AQLQ scores improved (SOE: low), whereas 2 studies that used nonvalidated quality of life measures found no effect (SOE: low). Five studies evaluated air purifiers within multicomponent interventions^{49,50,59,61,78} and reported no improvement in asthma control (SOE: low), exacerbations (SOE: high), or quality of life (SOE: high). However, school absenteeism decreased (SOE: low), asthma symptoms improved (SOE: low), and allergen levels were reduced (SOE: moderate).

Carpet removal

No studies looked solely at removal of carpeting; however, 8 multicomponent studies encouraged patients to remove carpet from their homes, but it is unclear how widely this recommendation was implemented.^{51,52,54,58,68,71,72,77} Allergen levels were reduced in these studies (SOE: moderate), but the evidence is inconclusive for the other outcomes.

TABLE II. Multicomponent indoor allergen-reduction interventions by study

Study	Acaricides (dust mite pesticide)	Air purification	Carpet removal*	HEPA vacuum	Mattress covers	Mold removal	Pest control	Pet removal*	Laundry linens	Cleaning supplies provided	CHW education/ instruction	Other
Matsui et al, 2017 ⁴⁹		✓			✓		✓					
DiMango et al, 2016 ⁵⁰		✓		✓	✓					✓		
Shani et al, 2015 ^{74†}					✓		✓			✓	✓	
Breyse et al, 2014 ^{77†}			✓			✓						Weatherization
Turcotte et al, 2014 ^{75†}				✓			✓			✓	✓	Professional cleaning
Sweet et al, 2013 ^{76†}				✓	✓	✓	✓			✓	✓	Moisture control
El-Ghitany and El-Salam, 2012 ⁵¹	✓		✓		✓			✓	✓			Ventilation
Takaro et al, 2011 ^{78†}		✓				✓						Ventilation
Bryant-Stephens et al, 2009 ⁵²			✓		✓		✓			✓	✓	
Krieger et al, 2009 ⁵³				✓						✓	✓	
Bryant-Stephens and Li, 2008 ⁵⁴			✓		✓		✓			✓	✓	
Parker et al, 2008 ⁵⁵				✓	✓		✓			✓	✓	
Burr et al, 2007 ⁵⁶						✓						Positive ventilation fan
Kercsmar et al, 2006 ⁵⁷						✓						Moisture control
Williams et al, 2006 ⁵⁸			✓		✓	✓	✓	✓			✓	Professional cleaning
Eggleston et al, 2005 ⁵⁹		✓			✓		✓				✓	
Krieger et al, 2005 ⁶⁰				✓			✓			✓	✓	
Morgan et al, 2004 ⁶¹		✓		✓	✓		✓					
Carter et al, 2001 ⁶²					✓		✓		✓			
Htut et al, 2001 ⁶³									✓			Ventilation, steam heating, new pillows
Warner et al, 2000 ⁶⁴				✓								House-wide ventilation system
Cloosterman et al, 1999 ⁶⁵	✓				✓							
Evans et al, 1999 ⁶⁶					✓		✓				✓	
Shapiro et al, 1999 ⁶⁷	✓				✓				✓			
Hayden et al, 1997 ⁶⁸	✓		✓		✓				✓			
Carswell et al, 1996 ⁶⁹	✓				✓				✓			
Marks et al, 1994 ⁷⁰	✓				✓							
Walshaw and Evans, 1986 ⁷¹			✓		✓							Feather-based bedding replaced
Korsgaard, 1983 ⁷²			✓						✓			Mattress vacuuming, new pillows and quilts, ventilation, clothes dried outdoors
Burr et al, 1980 ⁷³									✓			Mattress vacuuming, quilts removed, feather pillows replaced
Total	6	5	8	8	19	6	13	2	8	9	11	

CHW, Community health worker.

*Implemented by some, but not all, study participants.

†Not an RCT.

TABLE III. Allergen-reduction interventions: Summary results and SOE*

Intervention (no. of studies)	Asthma control	Exacerbations	Health care use	Absenteeism	Pulmonary physiology	Quality of life	Symptoms	Allergen reduction
Acaricide only (n = 7) ¹²⁻¹⁸	No studies	No studies	No studies	No studies	No effect (moderate)	Inconclusive	Inconclusive	Inconclusive
Acaricide multicomponent (n = 6) ^{51,65,67-70}	No studies	Inconclusive	Inconclusive	No studies	No effect (moderate)	No studies	No effect (high)	Improved (low)
Air purification only (n = 9) ¹⁹⁻²⁷	Inconclusive	No effect (low)	No effect (low)	No studies	No effect (low)	Improved (low)	Inconclusive	No effect (low)
Air purification multicomponent (n = 5) ^{49,50,59,61,78}	No effect (low)	No effect (high)	No studies	Improved (low)	Inconclusive	No effect (high)	Improved (low)	Improved (moderate)
Carpet removal only (n = 0)	No studies	No studies	No studies	No studies	No studies	No studies	No studies	No studies
Carpet removal multicomponent (n = 8) ^{51,52,54,58,68,71,72,77}	No studies	Inconclusive	Inconclusive	No studies	Inconclusive	Inconclusive	Inconclusive	Improved (moderate)
HEPA vacuum only (n = 1) ²⁸	No studies	No studies	No studies	No studies	Inconclusive	No studies	No studies	Inconclusive
HEPA vacuum multicomponent (n = 8) ^{50,53,55,60,61,64,75,76}	Inconclusive	Improved (moderate)	No effect (high)	Improved (low)	Inconclusive	Improved (moderate)	Improved (low)	Improved (moderate)
Mattress cover only (n = 17) ²⁹⁻⁴⁵	No effect (moderate)	No effect (moderate)	No effect (high)	Improved (low)	No effect (high)	No effect (high)	No effect (high)	Improved (moderate)
Mattress cover multicomponent (n = 19) ^{49-52,54,55,58,59,61,62,65-71,74,76}	Inconclusive	No effect (high)	Inconclusive	Improved (low)	No effect (high)	No effect (moderate)	Improved (high)	Improved (low)
Mold removal only (n = 0)	No studies	No studies	No studies	No studies	No studies	No studies	No studies	No studies
Mold removal multicomponent (n = 6) ^{56-58,76-78}	No studies	Inconclusive	Inconclusive	No studies	Inconclusive	Inconclusive	Improved (low)	Inconclusive
Pest control only (n = 2) ^{46,47}	Inconclusive	Inconclusive	No studies	Inconclusive	Inconclusive	No studies	Improved (low)	Inconclusive
Pest control multicomponent (n = 13) ^{49,52,54,55,58-62,66,74-76}	Inconclusive	Improved (moderate)	Inconclusive	Improved (low)	Inconclusive	Improved (low)	Improved (low)	Improved (low)
Pet removal only (n = 1) ⁴⁸	No studies	Inconclusive	Inconclusive	No studies	No studies	No studies	No studies	No studies
Pet removal multicomponent (n = 2) ^{51,58}	No studies	No studies	No studies	No studies	No studies	No studies	No studies	No studies

*Tables IV and V provide detailed information about the direction of effect and SOE.

HEPA vacuum

One study examined HEPA vacuums alone, but the evidence base is insufficient to support conclusions.²⁸ Eight multicomponent studies also evaluated HEPA vacuums.^{50,53,55,60,61,64,75,77} The evidence was insufficient for asthma control and pulmonary physiology measures. Exacerbations were reduced (SOE: moderate), medication use did not change (SOE: high), and no effect was observed for school (SOE: low) or work (SOE: moderate) absenteeism. Quality of life improved in studies of children less than 12 years old (SOE: moderate). In addition, asthma symptoms improved in children (SOE: low) but not among mixed populations of children, adolescents, and adults (SOE: moderate).

Mattress covers

Fourteen studies examined impermeable mattress covers,²⁹⁻⁴² and 3 studies evaluated other approaches designed to limit dust mite allergens on bedding.⁴³⁻⁴⁵ The evidence suggests no difference in asthma control (SOE: moderate), exacerbations (SOE: moderate), inhaled corticosteroid use (SOE: low), rescue medication use (SOE: high), pulmonary physiology (SOE: high), quality of life (SOE: high), or self-reported asthma symptoms (SOE: high). Conversely, these studies reported reductions in dust mite allergen levels (SOE: moderate). Mattress covers were also used in 19 multicomponent intervention studies.^{49-52,54,55,58,59,61,62,65-71,74,76} In these studies no improvement was found for emergency department use (SOE: low), hospitalizations (SOE: high), or acute care visits (SOE:

moderate). However, school absenteeism and missed activities decreased (SOE: low). No effect was observed for measures of pulmonary physiology (SOE: high) or quality of life (SOE: moderate).

Mold removal

There were no single-intervention studies examining mold removal. Six multicomponent studies examined mold removal^{56-58,76-78} and found that asthma symptoms improved (SOE: low), but findings for other outcomes were inconclusive.

Pest control

One RCT⁴⁶ and 1 nonrandomized study⁴⁷ examined pest-control strategies alone and the findings were insufficient to support any conclusions other than improvement in self-reported asthma symptoms (SOE: low). Thirteen multicomponent studies evaluated pest-control efforts.^{49,52,54,55,58-62,66,74-76} The evidence was inconclusive for asthma control, medication use, and pulmonary physiology measures. Exacerbations were reduced when measured as a composite score (SOE: moderate), but no effect was observed for discrete measures, including emergency department visits (SOE: moderate) and hospitalizations (SOE: high). School absenteeism decreased (SOE: low) and quality of life among children (SOE: low) improved. Asthma symptoms also improved (SOE: low), and allergen levels were reduced for some pests (eg, cockroaches; SOE: low).

TABLE IV. SOE for studies of individual interventions

Outcome	Conclusion	Study design and sample size	SOE (rationale)*
Acaricide compared with placebo (not reported in studies: asthma control, exacerbations, health care use)			
Pulmonary physiology: spirometry	No effect: no difference for FEV ₁ or peak flow	4 RCTs ^{13,15,17} 1 Non-RCT ¹⁸ n = 219	Moderate (imprecise)
Pulmonary physiology: airway hyperresponsiveness	Inconclusive	1 RCT ¹³ 1 non-RCT ¹⁸ n = 93	Insufficient (inconsistent, imprecise) Substantial imprecision*
Quality of life	Inconclusive	1 RCT ¹⁷ n = 62	Insufficient (study limitations, unknown consistency, imprecise)
Symptoms	Inconclusive	1 RCT ¹² n = 35	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Allergen levels	Inconclusive: 1 study found decreased allergen; 1 study found no difference on carpet or mattress and decreased allergen in other locations; other studies found no difference	4 RCTs ^{12,14,15,17} 1 Non-RCT ¹⁸ n = 228	Insufficient (inconsistent, imprecise) Substantial inconsistency*
Acaricide compared with other mite-avoidance interventions (not reported in studies: asthma control, exacerbations, health care use, quality of life, symptoms)			
Pulmonary physiology	No effect: no difference for FEV ₁ or peak flow	2 RCTs ^{16,17} 1 Non-RCT ¹⁸ n = 147	Low (study limitations, imprecise)
Allergen levels	Inconclusive: no estimate of precision provided in studies	2 RCTs ^{16,17} 1 Non-RCT ¹⁸ n = 147	Insufficient (study limitations, imprecise) Reported data insufficient for determining effect*
Air purification compared with placebo devices or no intervention (not reported in studies: health care use)			
Asthma control	Inconclusive: 1 study found no difference in ACQ scores; 1 study found improvement in composite asthma outcomes; 1 study did not report differences between arms	3 RCTs ^{24,27,64} n = 169	Insufficient (inconsistent, imprecise) Reported data insufficient for determining effect*
Exacerbations	No effect: ED visits and use of rescue medications did not differ	3 RCTs ^{19,27,64} n = 167	Low (study limitations, imprecise)
Pulmonary physiology	No effect: 5 studies found no difference in spirometry; 1 study found improved peak flow; 1 study found improved peak flow and airway hyperresponsiveness	7 RCTs ^{19-22,24,25,27} n = 263	Low (inconsistent, imprecise)
Quality of life: mini-AQLQ	Improvement: improved mini-AQLQ scores; mean difference in change (SEM): 0.54 (0.28); $P < .05$	1 RCT ¹⁹ n = 28	Low (study limitations, unknown consistency)
Quality of life: other measures	No effect: no difference	2 RCTs ^{20,27} n = 155	Moderate (imprecise)
Symptoms	Inconclusive	1 RCT ²³ n = 18	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Allergen levels	No effect: 4 studies found no difference; 1 study found decreased allergen	5 RCTs ^{20-22,24,27} n = 225	Low (imprecise)
HEPA vacuum compared with standard vacuum (not reported in studies: asthma control, exacerbations, health care use, quality of life, symptoms)			
Pulmonary physiology	Inconclusive	1 RCT ²⁸ n = 60	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Allergen levels	Inconclusive	1 RCT ²⁸ n = 60	Insufficient (unknown consistency, imprecise) Reported data insufficient for determining effect*
Impermeable mattress covers compared with placebo covers or no intervention			
Asthma control	No effect: no difference in ACQ scores	2 RCTs ^{29,31} n = 410	Moderate (imprecise)

(Continued)

TABLE IV. (Continued)

Outcome	Conclusion	Study design and sample size	SOE (rationale)*
Exacerbations	No effect: 1 study found no difference in composite measure (hospitalization/rescue medication); 1 study found improved composite measure (hospitalization/ED visit); 1 study found no difference in asthma attack frequency	3 RCTs ^{29,35,36} n = 1461	Moderate (inconsistent)
Health care use: inhaled corticosteroids	No effect: 1 study found no difference for total dose change; 1 study found no difference for mean dose change; 1 study found improvement in daily dose	3 RCTs ^{31,34,38} n = 233	Low (inconsistent, imprecise)
Health care use: rescue medication use	No effect: no difference in use of rescue medications	5 RCTs ^{32,34,36,37,39} n = 1275	High
Health care use and costs: work absenteeism	Decreased workdays: fewer missed days of work but difference might not be meaningful; mean difference, -0.15 days per month (95% CI, -0.29 to -0.02)	1 RCT ³⁶ n = 1122	Low (unknown consistency, imprecise)
Pulmonary physiology	No effect: no difference in peak flow in 12 studies; 1 study found improvement	13 RCTs ³⁰⁻⁴² n = 1744	High
Quality of life	No effect: no difference in quality of life	6 RCTs ^{29,31,32,35-37} n = 1649	High
Symptoms	No effect: no difference in 7 studies; 1 small study found improvement	8 RCTs ^{31,32,34,36-40} n = 1473	High
Allergen levels	Allergen reduction: 9 studies found reduced allergen; 2 studies found no difference	11 RCTs ^{29-37,39,40} n = 1928	Moderate (inconsistent)
Pest reduction interventions compared with no intervention (not reported in studies: quality of life)			
Asthma control	Inconclusive	1 RCT ⁴⁶ n = 102	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Exacerbations	Inconclusive	1 RCT ⁴⁶ 1 Pre-post ⁴⁷ n = 180	Insufficient (inconsistent, imprecise) Substantial imprecision*
Health care use	Inconclusive	1 RCT ⁴⁶ n = 102	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Pulmonary physiology	Inconclusive	1 RCT ⁴⁶ n = 102	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Symptoms	Improvement: improved respiratory symptoms	1 RCT ⁴⁶ 1 Pre-post ⁴⁷ n = 180	Low (imprecise)
Allergen levels	Inconclusive	1 Pre-post ⁴⁷ n = 78	Insufficient (unknown consistency, imprecise) Pre-post study*
Pet removal compared with no intervention (not reported in studies: asthma control, pulmonary physiology, quality of life, symptoms, allergen levels)			
Exacerbations/hospitalizations	Inconclusive	1 Non-RCT ⁴⁸ n = 20	Insufficient (unknown consistency, imprecise) Non-RCT*
Health care use	Inconclusive	1 Non-RCT ⁴⁸ n = 20	Insufficient (unknown consistency) Non-RCT*

ACQ, Asthma Control Questionnaire; AQLQ, Asthma Quality of Life Questionnaire; ED, emergency department.

*Criteria for downgrading SOE is described as (rationale); when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

Pet removal

One nonrandomized study focused on pet removal.⁴⁸ The evidence for hospitalizations, medication use, and follow-up

visits was inconclusive, and no other asthma outcomes were reported. Two multicomponent interventions encouraged pet removal,^{51,58} but we did not evaluate the SOE because of the

TABLE V. SOE for studies of multicomponent interventions

Outcome	Conclusion	Study design and sample size	SOE (rationale)*
Acaricide (dust mite pesticide) plus other interventions compared with placebo (not reported in studies: asthma control, quality of life)			
Exacerbations	Inconclusive: no difference in ED visits or hospitalizations in 1 study; no comparison between arms in other study	2 RCTs ^{51,67} n = 204	Insufficient (inconsistent, imprecise) Substantial imprecision*
Health care use	Inconclusive	1 RCT ⁶⁹ n = 70	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Pulmonary physiology: peak flow	No effect: no difference in peak flow in 3 studies; improved peak flow in 1 study; no comparison between arms in 1 study	5 RCTs ^{51,65,68-70} n = 445	Moderate (inconsistent)
Pulmonary physiology: FEV ₁	No effect: no difference in 4 studies; improved FEV ₁ in 1 study; no comparison between arms in 1 study	6 RCTs ^{51,65,67-70} n = 489	Moderate (inconsistent)
Symptoms	No effect: no difference in frequency of symptoms	4 RCTs ^{65,67,69,70} n = 306	High
Allergen levels	Reduced allergen: 2 studies found reduced allergens; 2 smaller studies found no difference; no comparison between arms in 1 study	5 RCTs ^{51,65,67,69,70} n = 466	Low (inconsistent, imprecise)
Air purification plus other interventions compared with no intervention			
Asthma control	No effect: no difference in ACT or childhood ACT scores	1 RCT ⁵⁰ n = 247	Low (unknown consistency, imprecise)
Exacerbations	No effect: no difference in hospitalizations in 3 studies; no difference in ED visits in 2 studies; no difference in undefined exacerbations in 1 study	4 RCTs ^{49,50,59,61} n = 1645	High
Health care use: acute care visits	Inconclusive	1 RCT ⁵⁹ n = 100	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Health care use and costs: school absenteeism	Improvement: fewer days of missed school	1 RCT ⁶¹ n = 937	Low (unknown consistency, imprecise)
Pulmonary physiology	Inconclusive	1 RCT ⁴⁹ n = 361	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Quality of life	No effect: no difference in mini-AQLQ scores	2 RCTs ^{50,59} n = 347	High
Symptoms	Improved: reduced symptoms in 2 studies; no difference in 2 other studies	4 RCTs ^{49,50,59,61} n = 1645	Low (inconsistent, imprecise)
Allergen levels	Allergen reduction: decreased allergens in 3 studies; no difference in 1 study	4 RCTs ^{49,50,59,61} n = 1645	Moderate (inconsistent)
Carpet removal plus other interventions compared with placebo or no intervention (not reported in studies: asthma control)			
Exacerbations	Inconclusive: no difference in ED visits or hospitalizations in 2 studies; no comparison between arms in 1 study	3 RCTs ^{51,52,54} n = 705	Insufficient (study limitations, inconsistent, imprecise)
Health care use	Inconclusive: reduced number of daytime terbutaline puffs in 1 study; no comparison between arms in 1 study	2 RCTs ^{71,72} n = 96	Insufficient (study limitations, imprecise) Substantial imprecision*
Pulmonary physiology	Inconclusive: improved peak flow in 1 study; no difference in 1 study; no comparison between arms in 2 studies	4 RCTs ^{51,68,71,72} n = 279	Insufficient (inconsistent, imprecise) Substantial imprecision*

(Continued)

TABLE V. (Continued)

Outcome	Conclusion	Study design and sample size	SOE (rationale)*
Quality of life	Inconclusive	1 Non-RCT ⁷⁷ n = 102	Insufficient (unknown consistency, imprecise) Non-RCT*
Symptoms	Inconclusive: no difference in 3 studies; reduced symptoms in 1 study; reduced daytime symptoms but no difference in nighttime symptoms in 1 study	5 RCTs ^{52,54,58,71,72} n = 802	Insufficient (study limitations, inconsistent, imprecise)
Allergen levels	Allergen reduction: decreased allergen levels in 3 studies; no comparison between arms in 1 study	4 RCTs ^{51,58,71,72} n = 412	Moderate (study limitations)
HEPA vacuum plus other interventions compared with placebo or no intervention			
Asthma control	Inconclusive	1 RCT ⁵⁰ n = 247	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Exacerbations: composite measure	Reduction: improved composite measure of hospitalization, ED visits, and acute care clinic visits	3 RCTs ^{55,60,61} n = 1509	Moderate (study limitations)
Exacerbations: unspecified	No effect: no difference in undefined “exacerbations” or “asthma attacks”	2 RCTs ^{50,53} n = 556	Moderate (imprecise)
Health care use: medication use	No effect: no difference in use of rescue inhaler or β -agonists	3 RCTs ^{50,53,60} n = 830	High
Health care use and costs: school absenteeism	No effect: no difference in missed school days in 2 studies; reduction found in 1 study	3 RCTs ^{53,60,61} n = 1520	Low (inconsistent, imprecise)
Health care use and costs: work absenteeism	No effect: no difference in missed workdays	2 RCTs ^{53,60} n = 583	Moderate (study limitations)
Health care use and costs: missed activities	Reduction: fewer days of missed activities in 2 studies; no difference in 1 study	3 RCTs ^{53,60,61} n = 1520	Low (inconsistent, imprecise)
Pulmonary physiology: peak flow	Inconclusive	1 RCT ⁶⁴ n = 40	Insufficient (study limitations, unknown consistency, imprecise)
Pulmonary physiology: FEV ₁	Inconclusive	1 RCT ⁵⁰ n = 247	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Quality of life: PACQLQ	Improvement: improved PACQLQ scores	2 RCTs ^{53,60} n = 583	Moderate (study limitations)
Quality of life: mini-AQLQ	Inconclusive	1 RCT ⁵⁰ n = 247	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Quality of life: CHSA	Inconclusive	1 Pre-post ⁷⁵ n = 170	Insufficient (unknown consistency, imprecise) Non-RCT*
Symptoms: children	Improvement: fewer symptom days in 2 studies; no difference in 1 study	3 RCTs ^{55,60,61} n = 1509	Low (study limitations, inconsistent)
Symptoms: mixed populations	No effect: no difference in symptom frequency in 2 studies; fewer symptom days in 1 study	3 RCTs ^{50,53,64} n = 596	Moderate (inconsistent)
Allergen levels: house dust mites	Inconclusive: no difference in 1 study; reduced allergen levels in 1 study; no comparison between arms in 1 study; fourth study found reduced <i>Dermatophagoides farinae</i> allergens but no difference for <i>Dermatophagoides pteronyssinus</i>	4 RCTs ^{50,55,61,64} n = 1522	Insufficient (study limitations, inconsistent, imprecise)

(Continued)

TABLE V. (Continued)

Outcome	Conclusion	Study design and sample size	SOE (rationale)*
Allergen levels: cats and dogs	Inconclusive: 1 study found reduction in cat but not dog allergens; 1 study found reduction in dog but not cat allergens; 1 study had no comparison between arms	3 RCTs ^{50,55,61} n = 1195	Insufficient (inconsistent, imprecise) Substantial imprecision*
Allergen levels: cockroach	Reduction: 1 study found decreased cockroach allergen levels; 1 study had no comparison between arms	2 RCTs ^{50,61} n = 1184	Moderate (imprecise)
Mattress covers plus other interventions compared with placebo or no intervention			
Asthma control	Inconclusive	1 RCT ⁵⁰ n = 247	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Exacerbations: ED visits	No effect: no difference	3 RCTs ^{49,52,54} n = 545	Low (study limitations, imprecise)
Exacerbations: hospitalization	No effect: no difference	6 RCTs ^{49,52,54,59,61,66} n = 2976	High
Exacerbations: unscheduled care	Inconclusive: no difference in 3 studies; reduction in 2 studies	5 RCTs ^{55,61,62,66,67} n = 2416	Insufficient (inconsistent, imprecise) Substantial imprecision*
Health care use: acute care visits	No effect: no difference	3 RCTs ^{54,59,61} n = 1318	Moderate (study limitations)
Health care use: medication use	Inconclusive: reduced use of asthma medication in 1 study; no difference in other study	2 RCTs ^{50,69} n = 317	Insufficient (inconsistent, imprecise) Substantial imprecision*
Health care use and costs: school absenteeism	Reduction: fewer missed school days	1 RCT ⁶¹ n = 937	Low (unknown consistency, imprecise)
Health care use and costs: missed activities	Reduction: fewer days of missed activities	1 RCT ⁶¹ n = 937	Low (unknown consistency, imprecise)
Pulmonary physiology: peak flow	Inconclusive: improved peak flow in 2 studies; no difference in 3 studies	5 RCTs ^{55,65,68-70} n = 583	Insufficient (inconsistent, imprecise) Substantial imprecision*
Pulmonary physiology: FEV ₁	No effect: no difference in 7 studies; improvement in 1 study	8 RCTs ^{49,50,61,65,67,70} n = 1874	High
Quality of life	No effect: no difference	3 RCTs ^{50,56,67} n = 144	Moderate (study limitations)
Symptoms: composite score	No effect: no difference	4 RCTs ^{50,65,67,70} n = 483	High
Symptoms: symptom days	Reduction: fewer days reported with symptoms in 4 studies; no difference in 1 study	5 RCTs ^{49,55,59,61,66} n = 2729	High
Symptoms: cough and wheeze	No effect: no difference in frequency of cough in 3 studies; reduced cough in 1 study; no difference in frequency of wheeze in 4 studies; reduced wheeze in 1 study	5 RCTs ^{52,54,55,61,69} n = 1850	Low (study limitations, inconsistent)
Allergen reduction	Reduction: decreased allergen levels in 4 studies; no difference in 4 smaller studies	8 RCTs ^{55,58,59,61,65,67,70,71} n = 1782	Low (inconsistent, imprecise)
Mold removal plus other interventions compared with placebo or no intervention (not reported in studies: asthma control)			
Exacerbations	Inconclusive	1 RCT ⁵⁷ n = 62	Insufficient (study limitations, unknown consistency, imprecise)
Health care use	Inconclusive	1 RCT ⁵⁶ n = 232	Insufficient (study limitations, unknown consistency, imprecise)
Pulmonary physiology	Inconclusive	1 RCT ⁵⁶ n = 232	Insufficient (study limitations, unknown consistency, imprecise)
Quality of life	Inconclusive	1 RCT ⁵⁷ n = 62	Insufficient (study limitations, unknown consistency, imprecise)
Symptoms	Improved symptoms: fewer symptoms	2 RCTs ^{57,58} n = 223	Low (study limitations, imprecise)
Allergen levels	Inconclusive	1 RCT ⁵⁷ n = 62	Insufficient (study limitations, unknown consistency, imprecise)

(Continued)

TABLE V. (Continued)

Outcome	Conclusion	Study design and sample size	SOE (rationale)*
Pest control plus other interventions compared with placebo or no intervention			
Asthma control	Inconclusive	1 Pre-post ⁷⁴ n = 80	Insufficient (unknown consistency, imprecise) Pre-post study*
Exacerbations: composite measure	Reduction: improved composite measure of hospitalization, ED visits, and acute care clinic visits	4 RCTs ^{55,60-62} n = 1613	Moderate (study limitations)
Exacerbations: hospitalization	No effect: no difference in hospitalizations in 5 studies; no difference in inpatient days in 1 study	6 RCTs ^{49,52,54,59,61,66} n = 2976	High
Exacerbations: ED visits	No effect: no difference	4 RCTs ^{49,52,54,61} n = 1843	Moderate (study limitations)
Health care use: acute care clinic visits	No effect: no difference in clinic visits for acute care	3 RCTs ^{59,61,66} n = 2070	High
Health care use: medication use	Inconclusive	1 RCT ⁶⁰ n = 274	Insufficient (study limitations, unknown consistency, imprecise)
Health care use and costs: school absenteeism/patient activities	Improvement: fewer days with activity limitations in 2 studies; fewer missed school days in 1 study but no difference in missed school days in other study	4 RCTs ^{55,59-61} n = 1609	Low (study limitations, inconsistent)
Health care use and costs: work absenteeism/plans	No effect: no difference in missed days of work or caretaker plans changed	2 RCTs ^{60,61} n = 1211	Low (study limitations, imprecise)
Pulmonary physiology: peak flow	Inconclusive	1 RCT ⁵⁵ n = 298	Insufficient (study limitations, unknown consistency, imprecise)
Pulmonary physiology: FEV ₁	Inconclusive: no difference in 2 studies; no comparison between arms in 1 study	3 RCTs ^{49,55,61} n = 1596	Insufficient (inconsistent, imprecise) Substantial imprecision*
Quality of life: PACQLQ	Improvement: improved PACQLQ scores	1 RCT ⁶⁰ n = 274	Low (study limitations, unknown consistency)
Quality of life: other measures	Inconclusive	1 RCT ⁵⁹ n = 100	Insufficient (unknown consistency, imprecise) Substantial imprecision*
Symptoms	Improvement: reduced symptom days or frequency of symptoms in 5 studies; no difference in symptom days in 2 studies; no difference in cough/wheeze in 2 studies	9 RCTs ^{49,52,54,55,58-61,66} n = 3709	Low (study limitations, inconsistent)
Allergen levels: cockroach	Reduction: decreased allergen levels in 2 studies; no difference in 1 study	3 RCTs ^{58,59,61} n = 1198	Low (inconsistent, imprecise)
Allergen levels: mouse	Inconclusive: decreased allergen levels in 2 studies; no difference in 2 studies	4 RCTs ^{46,55,59,61} n = 1696	Insufficient (inconsistent, imprecise) Substantial imprecision*

AQLQ, Asthma Quality of Life Questionnaire; CHSA, Children's Health Survey for Asthma; ED, emergency department; PACQLQ, Pediatric Asthma Caregivers Quality of Life Questionnaire.

*Criteria for downgrading SOE is described as (rationale); when these criteria are insufficient for understanding the final SOE, additional explanation is provided.

small number of studies and uncertainty regarding how widely this recommendation was implemented.

effects of most single interventions or multicomponent strategies on important asthma outcomes.

Qualitative comparative analysis

We included 30 multicomponent and 19 individual intervention studies in the qualitative comparative analysis. The results were not robust, and no intervention or bundle of interventions was necessary or sufficient for improvement in any primary outcome. Overall, the analysis reinforced the findings described in our SOE assessment: there is insufficient evidence demonstrating the

DISCUSSION

This systematic review identified 59 RCTs and 8 non-RCTs addressing 8 interventions for reducing home-based indoor allergen exposure and improving asthma outcomes. Thirty-seven studies evaluated single-component interventions, and 30 studies assessed multicomponent interventions. Overall, we found no high-strength evidence suggesting improvement in

any of the primary outcomes, but there was low- to moderate-strength evidence for some interventions. Validated measures of asthma control were reported infrequently.

Our findings are generally consistent with previous Cochrane reviews of similar interventions but differ from some other reviews. For example, in a Cochrane systematic review addressing mattress covers and acaricides⁷⁹ and another that examined air-purification devices,⁸⁰ evidence was generally lacking in rigor and insufficient to inform conclusions. Conversely, a 2010 systematic review⁸¹ found evidence supporting pest control, mold removal, and multicomponent interventions that are individually tailored to a patient or family. However, the authors did not use a formal approach for assessing the strength of the evidence base, and they incorporated expert opinion and epidemiologic evidence drawn from noninterventional studies into their conclusions. Also, they emphasized evidence showing reduced allergen levels on mattresses and floors when clinical outcomes were lacking.

Similarly, our assessment varies in key ways from the 2007 NAEPP guidelines² and clinical practice parameters of the American Academy of Allergy, Asthma & Immunology.⁸² We found that the evidence for most interventions was low strength or insufficient, whereas the previous guidelines found greater evidence of benefit associated with some interventions.

Several reasons can account for our different conclusions. Our review includes numerous studies published recently, some of which showed no intervention effect. Additionally, we did not always select the same studies as other reviewers because of differences in our respective inclusion criteria. We also prioritized outcomes and examined specific outcome measures differently from the American Academy of Allergy, Asthma & Immunology and the 2007 NAEPP, which affected how our findings were synthesized. Furthermore, our report used different instruments to assess the risk of bias of individual studies, which in turn affected our analysis of the SOE. Finally, the prior reviews did not use the EPC methodology¹⁰ or a similar Grading of Recommendations Assessment, Development and Evaluation (GRADE)⁸³ type of approach to evaluate the evidence base. These differences might account for variations between our assessment and the preceding reviews.

We found a high level of heterogeneity across studies, particularly related to patient characteristics and combinations of treatments examined, and this limited our ability to assess generalizability to the overall population of patients with asthma. First, variability in patients' baseline clinical characteristics suggests that patients were not equally likely to benefit from the interventions. Although 40 RCTs reported that all patients were sensitized to an allergen and 14 more trials confirmed sensitization in a majority of patients, only 43 studies used skin prick tests to confirm sensitization, whereas 13 studies measured sensitization by using blood tests (a less reliable predictor of true allergy). Therefore some patients in these studies might have been unlikely to benefit from the interventions if they were not allergic. This might affect the results of our analysis.

A similar consideration is variation in asthma severity. Only 18 RCTs classified the severity of participants' asthma. In 11 studies, most or all patients had moderate-to-severe asthma, whereas most patients had mild-to-moderate asthma in 5 studies. In 2 studies the populations were distributed evenly among patients with mild, moderate, and severe asthma. Unfortunately, because 41 RCTs

did not report severity, it is difficult to determine how disease severity might have affected our results and whether these studies are representative of the broader population of patients with asthma.

We also note that home-based interventions are difficult to implement properly and completely because cost, language, technology, home ownership, and health literacy can be barriers. Thirteen of the 30 multicomponent intervention studies included a community health worker who received specialized training to educate patients about reducing home allergen exposure in a highly tailored way. Although we did not evaluate the direct effect of these health workers, their role in the process might be important. Similarly, it is difficult to evaluate or ensure fidelity to a home-based intervention. Although several studies reported that adherence to study protocols was evaluated periodically (through surveys or home visits), most studies did not report such findings. Conversely, it is possible and even likely that some control group households adopted allergen-reducing interventions during their studies, potentially masking or minimizing differences in outcomes between study groups. The studies we evaluated did not address or adjust for this type of confounding.

It might also be difficult to maintain an allergen reduction strategy over time. Many studies had high attrition rates, which are attributable partly to participants moving from one home to another or encountering instability in family life that can disrupt continuity. Additionally, some of the interventions might have evolved over time. For example, contemporary air-purification devices might be different from those technologies available and examined 2 or 3 decades earlier, and this could introduce further heterogeneity into the results.

Another important factor is the potential exposure to indoor allergens outside the home. Asthmatic patients are exposed frequently to allergens at work or school or while engaged in other activities, which might limit the effectiveness of interventions used solely at home. Although our review was designed to include studies that evaluated interventions in work or school environments, we did not identify any eligible studies that fit those criteria.

We also note that standardized measures of asthma control, exacerbations, health care use, and quality of life were reported infrequently. Few studies included discrete and validated outcome measures that have established thresholds for clinical significance, such as the ACT or AQLQ. Furthermore, composite outcome measures were used frequently, but their components were not uniform. The relative paucity of studies using validated and standardized measures limited our interpretation of the results.

Overall, the most important limitation of the evidence base we reviewed is the lack of conclusive, consistent, high- or moderate-strength evidence that either favors or does not favor these interventions. We found inconclusive evidence for many comparisons and outcomes and low-strength evidence or no effect for many others. We must emphasize in this context the critical distinction between a lack of evidence and evidence of no effect. Throughout this review, we found that the evidence base lacks sufficient high-quality studies to inform useful conclusions for these interventions. This does not indicate that the interventions are ineffective but rather highlights the need for additional research.

We identified several evidence gaps that would benefit from future research. First, there has been insufficient evaluation of

several specific interventions, including HEPA vacuums, carpet removal, pet cleaning or removal, and mold removal. Head-to-head studies of interventions are also missing from the current evidence base, which consists almost entirely of comparisons with placebos or standard practices. Research is also needed to evaluate multicomponent interventions more efficiently. This might be accomplished by standardizing sets of strategies that could be tested as bundles. Additionally, future research could attempt to directly compare single interventions with bundled interventions.

We also need research to establish thresholds for clinically significant change in many of the asthma outcomes examined. Thresholds exist for some outcome measures, such as the ACT and AQLQ, but there are no agreed upon standards for the outcomes that were most frequently improved in the studies we reviewed, including measures of exacerbations, absenteeism, peak flow, asthma symptoms, and allergen reduction.

We also highlight the need for studies that recognize the complex set of challenges facing low-income and minority groups. Although these patients are at higher risk of allergen exposure and significant morbidity, most of the studies we reviewed did not describe the socioeconomic context of their patient population, and only 14 RCTs (24%) seem to have included a substantial number of patients living in poverty, inner-city settings, or both. Finally, assessment of differences in outcomes by age (ie, children versus adults) needs exploration. For example, younger patients are most likely to be truly allergic and have exacerbations related to allergen exposure, but these differences are not adequately addressed in the current literature.

This review highlights an important consideration for clinicians. Because asthma significantly affects overall health and quality of life, patients and their families are often motivated to augment medical treatment with interventions that reduce exposure to allergen triggers. It is important for clinicians to consider the complexity of their patient population and the limitations of the evidence we have identified. When recommending specific steps of action, clinicians might find it helpful to consider a patient's individual sensitization and reaction to specific allergens, as well as the severity of the patient's asthma and the extent of previous symptoms and exacerbations. Meanwhile, further research on the effectiveness of common allergen-control strategies and the many patient- and household-level characteristics that might influence patient outcomes is necessary.

Despite an extensive evidence base spanning several decades, the evidence base as a whole is insufficient to support meaningful conclusions about the effectiveness of many widely used products and strategies for improving patient outcomes by reducing environmental allergen exposure. For many important outcomes, evidence was insufficient because of too few studies. Moreover, results that were conclusive often suggested lack of clinical effect. Further research is needed and should address these evidence gaps with comparative studies that enroll enough patients to detect clinically meaningful improvements in important validated asthma outcomes.

We gratefully acknowledge Mary Butler, PhD, MBA, who served as AHRQ EPC Associate Editor; Leila Kahwati, MD, MPH, at RTI International, Yong Chen, PhD and Yulun Liu, PhD, of the University of Pennsylvania for their contributions to the qualitative comparative analysis; and the

following persons at the ECRI Institute for their contributions to this project: Katherine Donahue, Gina Giradi, Kristy McShea, Michael Phillips, and EPC Director Karen Schoelles. We also thank AHRQ Task Order Officers Aysegul Gozu, MD, MPH, and David W. Niebuhr, MD, MPH, MSc, and the following persons at the NHLBI: Janet M. DeJesus, MS, and Michelle Freemer, MD, MPH.

Key messages

- Evidence for single interventions designed to reduce indoor allergen exposure on asthma outcomes is lacking.
- Multicomponent interventions that bundle more than 1 strategy might improve some asthma outcomes, but it is unclear whether specific combinations are more effective than others.
- Multicomponent interventions that include HEPA vacuums or pest control reduce exacerbations and improve quality of life.
- The evidence for both single and multicomponent interventions does not address many other important outcomes, including asthma-related health care use, pulmonary physiology, and asthma-related quality of life.

REFERENCES

1. American Academy of Allergy Asthma & Immunology. Asthma overview. Available at: <http://www.aaaai.org/conditions-and-treatments/asthma>. Accessed November 7, 2017.
2. National Heart, Lung, and Blood Institute. Expert panel report 3: guidelines for the diagnosis and management of asthma. Available at: <https://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report>. Accessed November 7, 2017.
3. National Heart, Lung, and Blood Institute. Draft needs assessment report for potential update of the Expert Panel Report-3 (2007): guidelines for the diagnosis and management of asthma. Bethesda (MD): National Heart, Lung, and Blood Institute; 2015.
4. Cochrane handbook for systematic reviews of interventions. Version 5.1.0. Available at: <http://handbook.cochrane.org/>. Accessed November 7, 2017.
5. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis [manuals and scales. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm. Accessed November 7, 2017.
6. Busse WW, Morgan WJ, Taggart V, Togias A. Asthma outcomes workshop: overview. *J Allergy Clin Immunol* 2012;129(suppl):S1-8.
7. Juniper EF, Bousquet J, Abetz L, Bateman ED. The GOAL Committee. Identifying 'well-controlled' and 'now well-controlled' asthma using the Asthma Control Questionnaire. *Respir Med* 2006;100:616-21.
8. Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA, et al. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. *J Allergy Clin Immunol* 2006;117: 549-56.
9. Juniper EF, Guyatt GH, Epstein RS, Ferrie PJ, Jaeschke R, Hiller TK. Evaluation of impairment of health-related quality of life in asthma: development of a questionnaire for use in clinical trials. *Thorax* 1992;47:76-83.
10. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville (MD): Agency for Healthcare Research and Quality; 2014. AHRQ Publication no. 10(14)-EHC063-EF.
11. Kahwati L, Jacobs S, Kane H, Lewis M, Viswanathan M, Golin CE. Using qualitative comparative analysis in a systematic review of a complex intervention. *Syst Rev* 2016;5:82.
12. Geller-Bernstein C, Pibourdin JM, Domelas A, Fondarai J. Efficacy of the acaricide: acaridust for the prevention of asthma and rhinitis due to dust mite allergy, in children. *Allerg Immunol (Paris)* 1995;27:147-54.
13. Sette L, Comis A, Marcucci F, Sensi L, Piacentini GL, Boner AL. Benzyl-benzoate foam: effects on mite allergens in mattress, serum and nasal secretory IgE to *Dermatophagoides pteronyssinus*, and bronchial hyperreactivity in children with allergic asthma. *Pediatr Pulmonol* 1994;18:218-27.

14. Dietemann A, Bessot JC, Hoyet C, Ott M, Verot A, Pauli G. A double-blind, placebo controlled trial of solidified benzyl benzoate applied in dwellings of asthmatic patients sensitive to mites: clinical efficacy and effect on mite allergens. *J Allergy Clin Immunol* 1993;91:738-46.
15. Reiser J, Ingram D, Mitchell EB, Warner JO. House dust mite allergen levels and an anti-mite mattress spray (natamycin) in the treatment of childhood asthma. *Clin Exp Allergy* 1990;20:561-7.
16. Chang JH, Becker A, Ferguson A, Manfreda J, Simons E, Chan H, et al. Effect of application of benzyl benzoate on house dust mite allergen levels. *Ann Allergy Asthma Immunol* 1996;77:187-90.
17. Bahir A, Goldberg A, Mekori YA, Confino-Cohen R, Morag H, Rosen Y, et al. Continuous avoidance measures with or without acaricide in dust mite-allergic asthmatic children. *Ann Allergy Asthma Immunol* 1997;78:506-12.
18. van der Heide S, Kauffman HF, Dubois AE, de Monchy JG. Allergen-avoidance measures in homes of house-dust-mite-allergic asthmatic patients: effects of acaricides and mattress encasings. *Allergy* 1997;52:921-7.
19. Pedroletti C, Millinger E, Dahlén B, Soderman P, Zetterstrom O. Clinical effects of purified air administered to the breathing zone in allergic asthma: a double-blind randomized cross-over trial. *Respir Med* 2009;103:1313-9.
20. Sulser C, Schulz G, Wagner P, Sommerfeld C, Keil T, Reich A, et al. Can the use of HEPA cleaners in homes of asthmatic children and adolescents sensitized to cat and dog allergens decrease bronchial hyperresponsiveness and allergen contents in solid dust? *Int Arch Allergy Immunol* 2008;148:23-30.
21. van der Heide S, van Aalderen WM, Kauffman HF, Dubois AEJ, de Monchy JGR. Clinical effects of air cleaners in homes of asthmatic children sensitized to pet allergens. *J Allergy Clin Immunol* 1999;104:447-51.
22. Warner JA, Marchant JL, Warner JO. Double blind trial of ionisers in children with asthma sensitive to the house dust mite. *Thorax* 1993;48:330-3.
23. Zwemer RJ, Karibo J. Use of laminar control device as adjunct to standard environmental control measures in symptomatic asthmatic children. *Ann Allergy* 1973;31:284-90.
24. Francis H, Fletcher G, Anthony C, Pickering C, Oldham L, Hadley E, et al. Clinical effects of air filters in homes of asthmatic adults sensitized and exposed to pet allergens. *Clin Exp Allergy* 2003;33:101-5.
25. Mitchell EA, Elliott RB. Controlled trial of an electrostatic precipitator in childhood asthma. *Lancet* 1980;2:559-61.
26. van der Heide S, Kauffman HF, Dubois AE, de Monchy JG. Allergen reduction measures in houses of allergic asthmatic patients: effects of air-cleaners and allergen-impermeable mattress covers. *Eur Respir J* 1997;10:1217-23.
27. Wright GR, Howieson S, McSharry C, McMahon AD, Chaudhuri R, Thompson J, et al. Effect of improved home ventilation on asthma control and house dust mite allergen levels. *Allergy* 2009;64:1671-80.
28. Popplewell EJ, Innes VA, Lloyd-Hughes S, Jenkins EL, Khdir K, Bryant TN, et al. The effect of high-efficiency and standard vacuum-cleaners on mite, cat and dog allergen levels and clinical progress. *Pediatr Allergy Immunol* 2000;11:142-8.
29. Murray CS, Foden P, Sumner H, Shepley E, Custovic A, Simpson A. Preventing severe asthma exacerbations in children: a randomised trial of mite impermeable bedcovers. *Am J Respir Crit Care Med* 2017;196:150-8.
30. Tsurikisawa N, Saito A, Oshikata C, Yasueda H, Akiyama K. Effective allergen avoidance for reducing exposure to house dust mite allergens and improving disease management in adult atopic asthmatics. *J Asthma* 2016;53:843-53.
31. de Vries MP, van den Beemt L, Aretz K, Thoonen BP, Muris JW, Kester AD, et al. House dust mite allergen avoidance and self-management in allergic patients with asthma: randomised controlled trial. *Br J Gen Pract* 2007;57:184-90.
32. Dharmage S, Walters EH, Thien F, Bailey M, Raven J, Wharton C, et al. Encasement of bedding does not improve asthma in atopic adult asthmatics. *Int Arch Allergy Immunol* 2006;139:132-8.
33. van den Beemt L, van Knapen L, de Vries MP, Jansen M, Cloosterman S, van Schayck CP. Clinical effectiveness of a mite allergen-impermeable bed-covering system in asthmatic mite-sensitive patients. *J Allergy Clin Immunol* 2004;114:858-62.
34. Halken S, Host A, Niklassen U, Hansen LG, Nielsen F, Pedersen S, et al. Effect of mattress and pillow encasings on children with asthma and house dust mite allergy. *J Allergy Clin Immunol* 2003;111:169-76.
35. Luczynska C, Tredwell E, Smeeton N, Burney P. A randomized controlled trial of mite allergen-impermeable bed covers in adult mite-sensitized asthmatics. *Clin Exp Allergy* 2003;33:1648-53.
36. Woodcock A, Forster L, Matthews E, Martin J, Letley L, Vickers M, et al. Control of exposure to mite allergen and allergen-impermeable bed covers for adults with asthma. *N Engl J Med* 2003;349:225-36.
37. Rijssenbeek-Nouwens LH, Oosting AJ, de Bruin-Weller MS, Bregman I, de Monchy JGR, Postma DS. Clinical evaluation of the effect of anti-allergic mattress covers in patients with moderate to severe asthma and house dust mite allergy: a randomised double blind placebo controlled study. *Thorax* 2002;57:784-90.
38. Sheikh A, Hurwitz B, Sibbald B, Barnes G, Howe M, Durham S. House dust mite barrier bedding for childhood asthma: randomised placebo controlled trial in primary care [ISRCTN63308372]. *BMC Fam Pract* 2002;3:12.
39. Frederick JM, Warner JO, Jessop WJ, Enander I, Warner JA. Effect of a bed covering system in children with asthma and house dust mite hypersensitivity. *Eur Respir J* 1997;10:361-6.
40. Tsurikisawa N, Saito A, Oshikata C, Nakazawa T, Yasueda H, Akiyama K. Encasing bedding in covers made of microfine fibers reduces exposure to house mite allergens and improves disease management in adult atopic asthmatics. *Allergy Asthma Clin Immunol* 2013;9:44.
41. Burr ML, Neale E, Dean BV, Verrier-Jones ER. Effect of a change to mite-free bedding on children with mite-sensitive asthma: a controlled trial. *Thorax* 1980;35:513-4.
42. Burr ML, St Leger AS, Neale E. Anti-mite measurements in mite-sensitive adult asthma. A controlled trial. *Lancet* 1976;1:333-5.
43. Glasgow NJ, Ponsonby AL, Kemp A, Tovey E, van Asperen P, McKay K, et al. Feather bedding and childhood asthma associated with house dust mite sensitisation: a randomised controlled trial. *Arch Dis Child* 2011;96:541-7.
44. Nambu M, Shirai H, Sakaguchi M, Aihara M, Takatori K. Effect of house dust mite-free pillow on clinical course of asthma and IgE level—a randomized, double-blind, controlled study. *Pediatr Asthma Allergy Immunol* 2008;21:137-44.
45. Lee IS. Effect of bedding control on amount of house dust mite allergens, asthma symptoms, and peak expiratory flow rate. *Yonsei Med J* 2003;44:313-22.
46. Rabito FA, Carlson JC, He H, Werthmann D, Schal C. A single intervention for cockroach control reduces cockroach exposure and asthma morbidity in children. *J Allergy Clin Immunol* 2017;140:389-90.
47. Levy JJ, Brugge D, Peters JL, Clougherty JE, Saddler SS. A community-based participatory research study of multifaceted in-home environmental interventions for pediatric asthmatics in public housing. *Soc Sci Med* 2006;63:2191-203.
48. Shirai T, Matsui T, Suzuki K, Chida K. Effect of pet removal on pet allergic asthma. *Chest* 2005;127:1565-71.
49. Matsui EC, Perzanowski M, Peng RD, Wise RA, Balcer-Whaley S, Newman M, 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* 2017;317:1027-36.
50. DiMango E, Serebrisky D, Narula S, Shim C, Keating C, Sheares B, et al. Individualized household allergen intervention lowers allergen level but not asthma medication use: a randomized controlled trial. *J Allergy Clin Immunol Pract* 2016;4:671-9.e4.
51. El-Ghitany EM, El-Salam MM. Environmental intervention for house dust mite control in childhood bronchial asthma. *Environ Health Prevent Med* 2012;17:377-84.
52. Bryant-Stephens T, Kurian C, Guo R, Zhao H. Impact of a household environmental intervention delivered by lay health workers on asthma symptom control in urban, disadvantaged children with asthma. *Am J Public Health* 2009;99(suppl 3):S657-65.
53. Krieger J, Takaro TK, Song L, Beaudet N, Edwards K. A randomized controlled trial of asthma self-management support comparing clinic-based nurses and in-home community health workers: the Seattle-King County Healthy Homes II Project. *Arch Pediatr Adolesc Med* 2009;163:141-9.
54. Bryant-Stephens T, Li Y. Outcomes of a home-based environmental remediation for urban children with asthma. *J Natl Med Assoc* 2008;100:306-16.
55. Parker EA, Israel BA, Robins TG, Mentz G, Lin X, Brakefield-Caldwell W, et al. Evaluation of community action against asthma: a community health worker intervention to improve children's asthma-related health by reducing household environmental triggers for asthma. *Health Educ Behav* 2008;35:376-95.
56. Burr ML, Matthews IP, Arthur RA, Watson HL, Gregory CJ, Dunstan FDJ, et al. Effects on patients with asthma of eradicating visible indoor mould: a randomised controlled trial. *Thorax* 2007;62:767-72.
57. Kercsmar CM, Dearborn DG, Schluchter M, Xue L, Kirchner HL, Sobolewski J, et al. Reduction in asthma morbidity in children as a result of home remediation aimed at moisture sources. *Environ Health Perspect* 2006;114:1574-80.
58. Williams SG, Brown CM, Falter KH, Alverson CJ, Gotway-Crawford C, Homa D, et al. Does a multifaceted environmental intervention alter the impact of asthma on inner-city children? *J Natl Med Assoc* 2006;98:249-60.
59. Eggleston PA, Butz A, Rand C, Curtin-Brosnan J, Kanchanaraks S, Swartz L, et al. Home environmental intervention in inner-city asthma: a randomized controlled clinical trial. *Ann Allergy Asthma Immunol* 2005;95:518-24.
60. Krieger JW, Takaro TK, Song L, Weaver M. The Seattle-King County Healthy Homes Project: a randomized, controlled trial of a community health worker intervention to decrease exposure to indoor asthma triggers. *Am J Public Health* 2005;95:652-9.

61. Morgan WJ, Crain EF, Gruchalla RS, O'Connor GT, Kattan M, Evans R III, et al. Results of a home-based environmental intervention among urban children with asthma. *N Engl J Med* 2004;351:1068-80.
62. Carter MC, Perzanowski MS, Raymond A, Platts-Mills TAE. Home intervention in the treatment of asthma among inner-city children. *J Allergy Clin Immunol* 2001;108:732-7.
63. Htut T, Higenbottam TW, Gill GW, Darwin R, Anderson PB, Syed N. Eradication of house dust mite from homes of atopic asthmatic subjects: a double-blind trial. *J Allergy Clin Immunol* 2001;107:55-60.
64. Warner JA, Frederick JM, Bryant TN, Weich C, Raw GJ, Hunter C, et al. Mechanical ventilation and high-efficiency vacuum cleaning: a combined strategy of mite and mite allergen reduction in the control of mite-sensitive asthma. *J Allergy Clin Immunol* 2000;105:75-82.
65. Cloosterman SG, Schermer TR, Bijl-Hofland ID, van der Heide S, Brunekreef B, van den Elshout FJJ, et al. Effects of house dust mite avoidance measures on Der p 1 concentrations and clinical condition of mild adult house dust mite-allergic asthmatic patients, using no inhaled steroids. *Clin Exp Allergy* 1999;29:1336-46.
66. Evans R III, Gergen PJ, Mitchell H, Kattan M, Kercsmar C, Crain E, et al. A randomized clinical trial to reduce asthma morbidity among inner-city children: results of the National Cooperative Inner-City Asthma Study. *J Pediatr* 1999;135:332-8.
67. Shapiro GG, Wightton TG, Chinn T, Zuckerman J, Eliassen AH, Picciano JF, et al. House dust mite avoidance for children with asthma in homes of low-income families. *J Allergy Clin Immunol* 1999;103:1069-74.
68. Hayden ML, Perzanowski M, Matheson L, Scott P, Call RS, Platts-Mills TA. Dust mite allergen avoidance in the treatment of hospitalized children with asthma. *Ann Allergy Asthma Immunol* 1997;79:437-42.
69. Carswell F, Birmingham K, Oliver J, Crewes A, Weeks J. The respiratory effects of reduction of mite allergen in the bedrooms of asthmatic children—a double-blind controlled trial. *Clin Exp Allergy* 1996;26:386-96.
70. Marks GB, Tovey ER, Green W, Shearer M, Salome CM, Woolcock AJ. House dust mite allergen avoidance: A randomized controlled trial of surface chemical treatment and encasement of bedding. *Clin Exp Allergy* 1994;24:1078-83.
71. Walshaw MJ, Evans CC. Allergen avoidance in house dust mite sensitive adult asthma. *QJM* 1986;58:199-215.
72. Korsgaard J. Preventive measures in mite asthma. A controlled trial. *Allergy* 1983;38:93-102.
73. Burr ML, Dean BV, Merrett TG, Neale E, St Leger AS, Verrier-Jones ER. Effects of anti-mite measures on children with mite-sensitive asthma: a controlled trial. *Thorax* 1980;35:506-12.
74. Shani Z, Scott RG, Schofield LS, Johnson JH, Williams ER, Hampton J, et al. Effect of a home intervention program on pediatric asthma in an environmental justice community. *Health Promot Pract* 2015;16:291-8.
75. Turcotte DA, Alker H, Chaves E, Gore R, Woskie S. Healthy homes: in-home environmental asthma intervention in a diverse urban community. *Am J Public Health* 2014;104:665-71.
76. Sweet L, Polivka BJ, Chaudry RV, Bouton P. The impact of an urban home-based intervention program on asthma outcomes in children. *Public Health Nurs* 2014;31:243-53.
77. Breysse J, Dixon S, Gregory J, Philby M, Jacobs DE, Krieger J. Effect of weatherization combined with community health worker in-home education on asthma control. *Am J Public Health* 2014;104:e57.
78. Takaro TK, Krieger J, Song L, Sharify D, Beaudet N. The Breathe-Easy Home: the impact of asthma-friendly home construction on clinical outcomes and trigger exposure. *Am J Public Health* 2011;101:55-62.
79. Gotzsche PC, Johansen HK. House dust mite control measures for asthma. *Cochrane Database Syst Rev* 2008;2:CD001187.
80. Kilburn S, Lasserson TJ, McKean M. Pet allergen control measures for allergic asthma in children and adults. *Cochrane Database Syst Rev* 2001;(1):CD002989.
81. Krieger J, Jacobs DE, Ashley PJ, Baeder A, Chew GL, Dearborn D, et al. Housing interventions and control of asthma-related indoor biologic agents: a review of the evidence. *J Public Health Manag Pract* 2010;16:S11-20.
82. American Academy of Allergy, Asthma & Immunology. Available at: <https://www.aaaai.org/practice-resources/Statements-and-Practice-Parameters/Practice-parameters-and-other-guidelines-page>. Accessed November 7, 2017.
83. GRADE. The GRADE working group. Available at: www.gradeworkinggroup.org/#. Accessed November 7, 2017.