Comparative Effectiveness Review
Number 201

Effectiveness of Indoor Allergen Reduction in Management of Asthma

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Effectiveness of Indoor Allergen Reduction in Management of Asthma

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Key Messages

Purpose of Review
To evaluate the effectiveness of indoor allergen reduction interventions on asthma outcomes.

Key Messages

- Evidence for single interventions designed to reduce indoor allergen exposure on asthma outcomes is lacking.
- Multicomponent interventions that bundle more than one strategy may improve some asthma outcomes, but it is unclear if specific combinations are more effective than others.
- Multicomponent interventions that include high-efficiency particulate air-filtration (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 utilization, pulmonary physiology, and asthma-related quality of life.

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The National Heart, Lung, and Blood Institute, one of the National Institutes of Health, requested that AHRQ conduct a systematic review of the effectiveness of allergen removal in treating asthma and provided funding for this.

The reports and assessments provide organizations with comprehensive, evidence-based information on common medical conditions and new health care technologies and strategies. They also identify research gaps in the selected scientific area, identify methodologic and scientific weaknesses, suggest research needs, and move the field forward through an unbiased, evidence-based assessment of the available literature. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review and public comment prior to their release as a final report.

AHRQ expects that the EPC evidence reports and technology assessments, when appropriate, will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

If you have comments on this evidence report, they may be sent by mail to the Task Order Officers named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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We appreciate the collaboration of our colleagues at the other EPCs preparing reports for NHLBI, and particularly thank Diana Sobieraj and others at the University of Connecticut EPC, who provided the table and references for minimally important differences in Appendix E.

Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers.

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Effectiveness of Indoor Allergen Reduction in Management of Asthma

Structured Abstract

Objectives. This review evaluates the effectiveness of allergen reduction interventions on asthma outcomes in adults and children.

Data sources. We systematically searched the gray literature and five bibliographic databases, MEDLINE®, Embase®, PubMed®, CINAHL®, and the Cochrane Library, through April 21, 2017.

Review methods. Eligible studies included systematic reviews, meta-analyses, randomized controlled trials (RCTs), and nonrandomized controlled interventional studies. Studies were evaluated for risk of bias using the Cochrane Risk of Bias instrument or the Newcastle-Ottawa scale, and the evidence base was assessed using the methods guidance established by the Evidence-based Practice Center Program. Qualitative comparative analysis was conducted to support the primary analysis.

Results. Our literature searches identified 72 publications describing interventions to reduce exposure to indoor allergens and their effects on asthma. This included 60 unique RCTs with data published in 64 articles, as well as 8 non-RCTs. Validated measures of asthma control were infrequently reported across studies, and findings were often inconclusive. Thirty-eight studies evaluated single component interventions. Use of acaricides (dust mite pesticides) was not shown to improve pulmonary function (moderate strength of evidence [SOE]). Air purification devices, used alone, improved quality of life (low SOE) but did not reduce exacerbations or health care utilization (low SOE) or improve pulmonary function (low SOE). Impermeable mattress covers were not associated with improved asthma control (moderate SOE) and did not reduce exacerbations or health care utilization (moderate SOE) or improve quality of life (high SOE). Single intervention studies did not adequately examine carpet removal, high-efficiency particulate air-filtration (HEPA) vacuums, mold removal, pet removal, and pest control.

Thirty studies assessed multicomponent interventions, but wide differences among study interventions (and combinations of interventions) precluded meta-analysis. When examined as a component within a broader set of interventions, use of air purification reduced school absenteeism (low SOE) but did not improve asthma control (low SOE), reduce exacerbations (high SOE), or improve quality of life (high SOE). HEPA vacuums, when included in a multicomponent approach, reduced exacerbations and improved quality of life (moderate SOE) for children. Mattress covers used within multicomponent interventions reduced school absenteeism and missed activities (low SOE) but had no effect on emergency department visits (low SOE), hospitalizations (high SOE), or quality of life (moderate SOE). Pest control strategies incorporated into multicomponent interventions reduced exacerbations (moderate SOE), improved quality of life (low SOE), and reduced school absenteeism (low SOE) but did not reduce emergency department visits (moderate SOE), hospitalizations (high SOE), or worker absenteeism (low SOE). Other multicomponent interventions included carpet, mold, and pet removal, but the evidence for these strategies was inconclusive.

Conclusions. Single intervention studies were not associated with improvement in clinical asthma outcomes, with most strategies showing inconclusive results or no effect. Multicomponent intervention studies demonstrated improvement in various outcomes, but no specific combination of interventions was identified as more effective than others. High or moderate strength evidence suggests that multicomponent interventions that include HEPA vacuums or pest control may be effective in reducing exacerbations and improving quality of life. For many primary outcomes for both single and multicomponent interventions, the evidence is inconclusive because of a lack of studies. Further research is needed examining well-defined (standardized) indoor allergen reduction interventions in comparative studies, with sufficient population size of well-characterized patients to detect clinically meaningful differences in validated and relevant asthma outcomes.

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Evidence Summary

Objectives and Rationale for Review

This report summarizes a systematic review, "Effectiveness of Indoor Allergen Reduction in Management of Asthma," and identifies needs for future research. This was one of the six high priority topics within asthma identified by a National Heart, Lung, and Blood Institute Advisory Council Asthma Expert Working group.[1]

The objective of the systematic review is to assess the effectiveness of allergen reduction interventions on asthma outcomes in adults and children.

Background

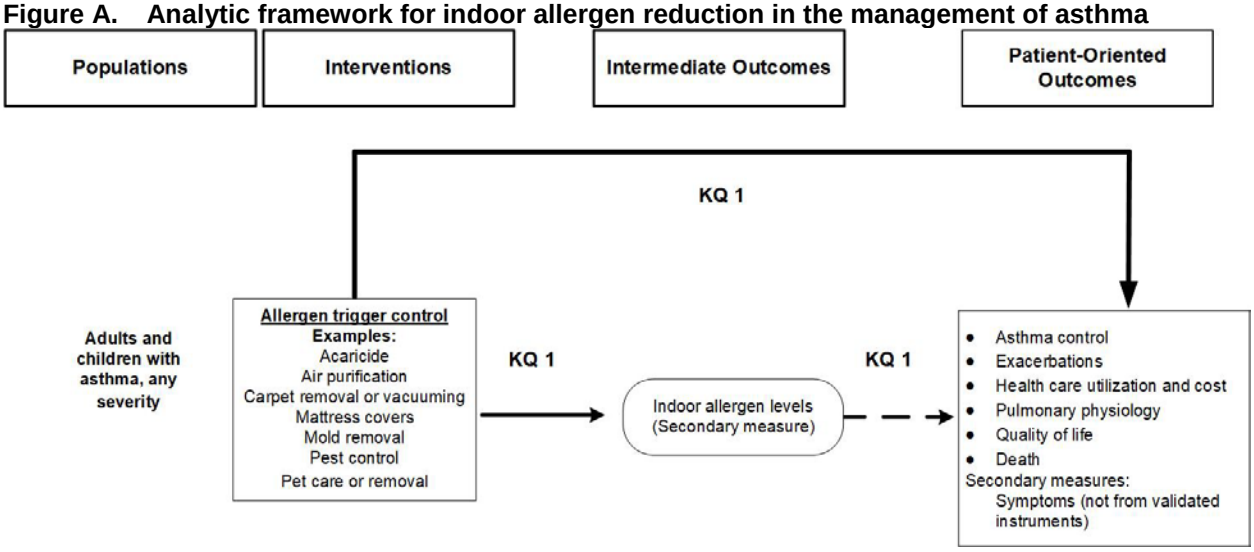
Control of environmental factors that may contribute to asthma is one of the four components of asthma management. Many common indoor inhalant allergens have been associated with increased risk of asthma exacerbations, including animal dander, house dust mites (HDMs), mice, cockroaches, and mold.[2] Numerous interventions have been designed to reduce exposure to allergens in the environment where patients with asthma live, work, learn, play, and sleep.[3] These interventions include use of acaricides (HDM pesticides), air purification systems, carpet removal or vacuuming, use of specially designed mattress covers and pillowcases, mold removal, pest control techniques, and containment or removal of family pets.

This report's main objective is to conduct a systematic review of the benefits and harms of interventions to reduce indoor inhalant allergens for the management of asthma in adults and children. In this review, we address the following Key Question:

Among individuals with asthma, what is the effectiveness of interventions to reduce or remove exposures to indoor inhalant allergens on asthma control, exacerbations, quality of life, and other relevant outcomes?

Figure A shows the analytic framework.

Figure A. Analytic framework for indoor allergen reduction in the management of asthma



KQ=Key Question
Dashed line indicates theoretical relationship

Data Sources

MEDLINE®, Embase®, PubMed®, CINAHL®, the Cochrane Library, and the gray literature were searched through April 21, 2017. The systematic review protocol is available online at https://effectivehealthcare.ahrq.gov/ehc/products/643/2318/asthma-nonpharmacologic-treatment-protocol-161004.pdf, and is registered in PROSPERO (http://www.crd.york.ac.uk/PROSPERO), with the registration number CRD42017055547.

Results

Thirty-eight comparative studies (n= 3,243) assessed individual (single component) interventions, and 30 comparative studies (n=4,907) assessed multicomponent interventions. The key findings of the review are listed below along with the strength of evidence (SOE).

- The evidence that either single or multicomponent interventions intended to reduce allergen exposure improve asthma outcomes is limited by a lack of high quality studies. Overall strength of evidence (SOE) for most comparisons and outcomes was either low, inconclusive, or no studies were available.
- No high or moderate strength evidence found improvement in patient-oriented outcomes resulting from single component interventions.
- Overall, multicomponent interventions performed better than single component interventions.
- Multicomponent strategies that included high-efficiency particulate air-filtration (HEPA) vacuums reduced exacerbations and improved quality of life (moderate SOE), while strategies that included mattress covers improved nonvalidated measures of respiratory symptoms (high SOE), and strategies that included pest control reduced exacerbations (moderate SOE).
- Mattress covers, when used without other interventions, did not affect asthma control (moderate SOE), exacerbations (moderate SOE), health care utilization (high SOE), pulmonary physiology (high SOE), quality of life (high SOE), or nonvalidated measures

of respiratory symptoms (high SOE), despite reducing the allergen burden detected on mattress surfaces (moderate SOE).

- Qualitative comparative analysis affirmed the general lack of robust findings of improved outcome effects. No single allergen interventions were determined to be necessary or sufficient for effectiveness. Multicomponent bundles were characterized by substantial heterogeneity, and no conclusions about the effectiveness of specific combinations were supported by the evidence.
- Important limitations of the evidence base include population heterogeneity (e.g., patient age and asthma severity), infrequent reporting of validated asthma outcome measures, poor data reporting, and variation in how interventions were implemented.
- Further research is needed examining indoor allergen reduction interventions in comparative studies with sufficient population sizes to detect clinically meaningful differences in relevant and validated asthma outcomes.

Discussion

We identified 60 randomized controlled trials (RCTs) and 8 additional studies (4 nonrandomized trials and 4 pre-post studies) that examined 8 types of interventions, alone or in combination, to reduce allergen levels in the home and improve the wellbeing of patients with asthma.

There was a high level of heterogeneity across studies, particularly related to patient characteristics such as allergen sensitization and disease severity, and the combinations of treatments examined, that limited our ability to assess the generalizability of our findings to the overall population of people with asthma. Other factors affecting the applicability of the results included potential exposure to indoor allergens in settings outside the home, as well as exposure to outdoor allergens or non-allergen irritants. We also found that few studies reported critical, discrete, validated outcome measures, which have established thresholds for clinical significance. The relative paucity of studies using current, standardized measures limited our interpretation of the primary outcome measures.

The overall evidence base is characterized by a lack of conclusive, consistent, high- or moderate-strength evidence that either favors interventions to reduce exposure to allergens, or demonstrates that these strategies have no effect. However, we note 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 the interventions evaluated. This does not indicate that the interventions are ineffective, but rather highlights the need for additional research.

Several evidence gaps could benefit from future research. First, there is insufficient information about several types of interventions, used alone or as part of multicomponent strategies. A substantial need exists for high-quality RCTs examining the effect of HEPA vacuums, pest control, carpet removal, pet removal, and mold removal. Research is also needed to evaluate multicomponent interventions more efficiently by standardizing sets of strategies that could be tested as bundles. The evidence base could also be evaluated with greater precision if outcome reporting were improved and standardized. For example, important, standardized measures of asthma control, exacerbations, healthcare utilization, and quality of life were often unreported in the included studies. We also need further research on the interaction between the effect size of outcome measures and meaningful clinical improvement.

Since asthma can significantly affect overall health and quality of life, patients and their families may be motivated to adopt interventions that are not physically invasive, such as use of mattress covers or air purifiers, to augment pharmacologic treatment. It is important for clinicians to consider the complexity of the patient population and the limitations of the evidence identified. Clinicians may also find it helpful to consider the severity of a patient's asthma and the extent of previous symptoms and exacerbations.

Conclusions

The evidence base addressing allergen-reduction interventions for patients with asthma spans 40 years and 4 continents and has included more than 7,000 patients. However, few conclusions can be reached about the effectiveness of interventions designed to reduce allergens in the home. Multicomponent interventions that include HEPA vacuums or pest control may be effective for reducing exacerbations and improving quality of life, although results were inconclusive for validated measures of asthma control. For many critical outcomes across the interventions, evidence was insufficient due to too few studies. Moreover, results that were conclusive tended to suggest lack of clinical effect. 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. Further research on many critical questions is needed. Future research should address these evidence gaps with comparative studies that enroll enough patients to detect clinically meaningful improvements in relevant, validated asthma outcomes.

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Introduction

Background

Asthma is a chronic inflammatory disorder of the airways, characterized by varying degrees of airflow obstruction. Bronchoconstriction, inflammatory cell infiltration, and airway edema reduce airflow intermittently, often in response to specific exposures, resulting in respiratory symptoms.[1] In the United States, asthma's prevalence has increased over the past decade, from an estimated 22.2 million Americans in 2005 to 24 million Americans in 2014.[2,3] Asthma can significantly affect patients' and families' quality of life and ability to pursue activities such as school, work, and exercise. Globally, asthma ranks 14th based on the burden of disease, as measured by disability-adjusted life years.[4] In the United States, asthma contributes significantly to health care resource utilization and associated costs. For example, in 2012, asthma was one of the top 20 leading diagnosis groups for primary care visits and was the main reason for 1.8 million emergency department visits and 439,000 hospitalizations. While the severity of disease varies between patients and over time in the same patient, asthma can be fatal, accounting for approximately 1 death per 100,000 Americans.[5]

Effectiveness of Indoor Inhalant Allergen Reduction

Control of environmental factors that may contribute to asthma is one of the four components of asthma management. Many common indoor inhalant allergens have been associated with increased risk of asthma exacerbations, including animal dander, house dust mites (HDMs), mice, cockroaches, and mold.[6] Numerous interventions have been designed to reduce exposure to allergens in the environment where patients with asthma live, work, learn, play, and sleep.[7] These interventions include use of acaricides (HDM pesticides), air purification systems, carpet removal or vacuuming, use of specially designed mattress covers and pillowcases, mold removal, pest control techniques, and containment or removal of family pets.

Evaluating the effectiveness of allergen exposure reduction interventions presents multiple challenges. Strategies to control environmental factors often include multicomponent approaches, which incorporate at least two different interventions resulting in difficulty identifying the effectiveness of individual component interventions. Moreover, a "single" intervention (e.g., vacuuming) may be expected to reduce or eradicate exposure to multiple allergens simultaneously and the effects on specific allergens may differ as a consequence of the same intervention. Other challenges in interpreting the literature include heterogeneity in the populations studied (e.g., documentation of sensitization to the targeted allergen, asthma severity and control) and inadequate descriptions of the interventions (e.g., lack of specificity with respect to the device used for air filtration, or compliance with use, or whether changes in allergen exposure were documented).

Purpose of the Systematic Review

In 1989, the National Heart, Lung, and Blood Institute (NHLBI) initiated the National Asthma Education and Prevention Program (NAEPP) to address growing concern about asthma in the United States. One of NAEPP's first accomplishments was to convene a panel of experts that produced a report in 1991, *The National Asthma Education and Prevention Program Expert Panel Report (EPR): Guidelines for the Diagnosis and Management of Asthma*. The guidelines address the diagnosis, evaluation, and treatment of asthma. Given that the most recent report,

EPR-3, was published in 2007,[1] NHLBI assessed the need for an update by requesting information from the public, NAEPP Coordinating Committee Members and its affiliates, and members of the 2007 Expert Panel. Collected information was provided to the NHLBI Advisory Council Asthma Expert Working Group, which produced a report to summarize the process and recommendations from their needs assessment.[8] The Working Group identified six high-priority topics that should be updated. For each topic, Key Questions meriting a systematic literature review were formulated. NHLBI engaged the Agency for Healthcare Research and Quality to perform the systematic reviews through its Evidence-Based Practice Centers. This document represents the systematic review of "The Effectiveness of Indoor Allergen Reduction in the Management of Asthma." The review also highlights areas of controversy and identifies needs for future research on this priority area.

Scope and Key Question

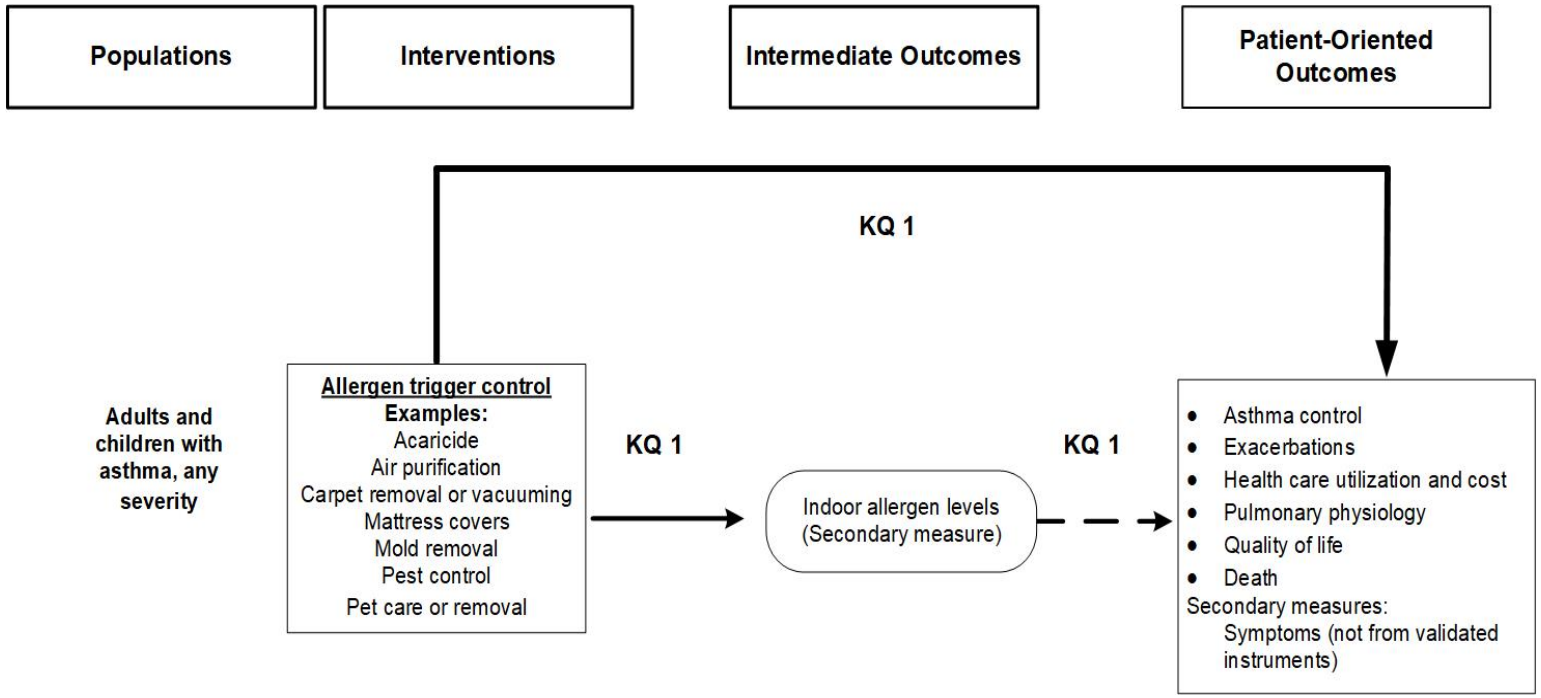
This report's main objective is to conduct a systematic review of the benefits and harms of interventions to reduce indoor inhalant allergens for the management of asthma in adults and children. In this review, we address the following Key Question:

Key Question: Among individuals with asthma, what is the effectiveness of interventions to reduce or remove exposures to indoor inhalant allergens on asthma control, exacerbations, quality of life, and other relevant outcomes?

Analytic Framework

We developed an analytic framework to guide the systematic review process (Figure 1).

Figure 1. Analytic framework for indoor allergen reduction in the management of asthma



KQ=Key Question
Dashed line indicates theoretical relationship

Organization of This Report

In the remaining three chapters of this report, we describe the methods for this systematic review, present the results, and discuss the overall findings. Within the Results chapter, we provide the results of the literature searches and screening procedures, as well as descriptions of included studies, key points, detailed syntheses of the studies, and strength-of-evidence tables. The Discussion chapter reviews the key findings and strength of evidence, places the findings in the context of previous systematic reviews, examines the general applicability of the studies, discusses implications for decisionmaking, describes limitations of the systematic review process and the evidence base, and identifies knowledge gaps that require further research.

A list of acronyms and abbreviations appears after the references, followed by five appendixes: Appendix A. Search Strategies; Appendix B. Excluded Studies; Appendix C. Evidence Tables; Appendix D. Qualitative Comparative Analysis; and Appendix E. Minimally Important Differences.

Methods

Protocol Development

The National Heart, Lung, and Blood Institute (NHLBI) nominated this topic, as described in the Introduction. We generated an analytic framework, a preliminary Key Question, and preliminary inclusion/exclusion criteria in the form of PICOTS (populations, interventions, comparators, outcomes, timing, and settings).

A Technical Expert Panel (TEP) was convened for this report. The TEP consisted of nine scientists and clinicians, including individuals with expertise in the clinical management of pediatric and adult asthma, and implementation of environmental control interventions to reduce exposure to allergens in the home. TEP members participated in conference calls and discussions through email to review the scope, analytic framework, Key Question, and PICOTS and provided input on the information and categories included in the evidence tables and analysis. A list of the TEP members is included in the front matter of the report. The final protocol was posted on the Effective Health Care Web site on October 11, 2016. A full version of our protocol for this systematic review is available online (https://effectivehealthcare.ahrq.gov/ehc/products/643/2318/asthma-nonpharmacologic-treatment-protocol-161004.pdf),[9] and is registered in PROSPERO (http://www.crd.york.ac.uk/PROSPERO), with the registration number CRD42017055547.[10]

Initially, the Key Question addressed in this report was intended for inclusion in a larger report on nonpharmacologic management of asthma. The scope of the broader report also examined the use of bronchial thermoplasty for patients with severe asthma. The larger report was divided into two distinct reports in response to peer review and public feedback about the draft report. However, the guidance provided by the TEP and the content included in the posted protocol reflect the larger scope of work as initially planned.

Literature Search Strategy

Search Strategy

Literature searches were performed by Medical Librarians at the Evidence-Based Practice Center Information Center and followed established systematic review protocols. Searches covered the literature published from database inception (dates vary, see Appendix A) through April 21, 2017.

We searched the following databases using controlled vocabulary and text words: Embase® and MEDLINE® (searched together on the Embase.com platform), PubMed® (In Process citations), CINAHL® (Cumulative Index to Nursing and Allied Health Literature), and the Cochrane Library.

We used text words to search gray literature sources and the Web sites of relevant organizations identified by the clinical experts on the project team. A complete list of the resources we searched is available in Appendix A.

Search resources, concepts, and strategies are available in Appendix A. Reference lists from systematic reviews and meta-analyses were reviewed and compared against our retrieved articles. If a systematic review contained references that appeared to meet our inclusion criteria, but had not been captured by our initial search results, the search strategy was refined to include

these articles. Supplemental Evidence and Data for Systematic Reviews (formerly known as Scientific Information Packets) submitted by interested parties were also reviewed.

Literature screening was performed in duplicate using the database Distiller SR (Evidence Partners, Ottawa, Ontario, Canada). Literature search results were initially screened for relevancy. Relevant abstracts were screened against the inclusion and exclusion criteria in duplicate. Studies that appeared to meet the inclusion criteria were retrieved in full and screened again in duplicate against the inclusion and exclusion criteria. All disagreements were resolved by consensus discussion between the two original screeners.

Inclusion and Exclusion Criteria

Publication Criteria

Included articles must have been published as full-length, peer-reviewed studies. Abstracts and meeting presentations were not included because they do not include sufficient details about experimental methods to permit an evaluation of study design and conduct; they may also contain only a subset of measured outcomes.[11,12] Additionally, it is not uncommon for abstracts that are published as part of conference proceedings to have inconsistencies compared with the final study publication or to describe studies that are never published as full articles.[13-17] To avoid double-counting patients, when several reports of the same or overlapping groups of patients were available, only outcome data from the report with the most patients were included. However, we included data from a smaller study when it either reported data on an outcome that the index report did not provide or when it provided longer followup data for a specific outcome.

When a study with an English abstract but published in a foreign language was identified, the abstract was assessed against the full set of inclusion/exclusion criteria. If the study appeared to fit the inclusion criteria, we evaluated whether excluding the study might result in language bias (e.g., if the findings differ from other included studies). If language bias seemed unlikely, we excluded the study.

Study Selection

We followed the PICOTS (Table 1) framework in developing the criteria for study inclusion. We included studies of patients of any age with a diagnosis of asthma. We included studies of asthma and other allergic conditions, when ≥85 percent of enrolled patients had asthma or when outcomes were reported separately for the subgroup with asthma. Studies that did not report whether patients were sensitized or allergic to indoor allergens were included. Studies had to report on one or more of the outcomes prespecified in our PICOTS. Study inclusion was not restricted by language of publication or treatment duration. Randomized controlled trials (RCTs) and nonrandomized interventional studies with concurrent controls (e.g., nonrandomized trials) or historical controls (e.g., pre-post studies) were considered for inclusion. We excluded *in vivo*, *in vitro*, and animal studies.

Table 1. PICOTS (populations, interventions, comparisons, outcomes, timing, and setting) criteria for including studies in the review

Category	Criteria
Populations	• All severity of asthma • Any age

Interventions	• Acaricide (house dust mite pesticide)
	  o Applied to carpet, mattresses, and/or furniture
	• Air quality
	  o Air purifiers
	  o Ventilation or duct cleaning
	• Carpet
	  o Removal
	  o Wall-to-wall versus area rugs
	  o Cleaning (professional services; high-efficiency particulate air-filtration (HEPA) vacuums)
	• Linens and furniture
	  o Pillow/mattress covers
	  o Furniture covers/"wipe-down" furniture
	  o Frequent laundering of linens
	• Mold removal
	• Animals and insects
	  o Pet bathing
	  o Pet removal or restriction of pet access
	  o Pest control (professional and lay interventions)
	• Multicomponent interventions
	  o Multiple strategies implemented concurrently

Comparators	• No intervention to reduce or eliminate exposure to indoor inhalant allergen(s) • Reduction or elimination of exposure to different indoor inhalant allergen(s) • Reduction or elimination of exposure to multiple indoor inhalant allergens

Outcomes	**Primary Outcomes**
	• Asthma control
	  o Asthma Control Test (ACT) / Childhood ACT
	  o Asthma Control Questionnaire
	• Exacerbations
	  o Systemic corticosteroids for asthma
	  o Asthma-specific hospitalizations
	  o Asthma-specific emergency department (ED) visits
	  o Asthma-specific urgent care visits (other than ED)
	  o Asthma-specific admissions to intensive care unit or intubations
	• Health care utilization and costs
	  o Asthma-specific ambulatory care visits
	  o Asthma-specific medication use (including medication name, dose, duration)
	  o Hospitalizations, ED visits, urgent care visits
	  ▪ All cause
	  ▪ Associated with potentially asthma-related complications
	  □ Pneumonia
	  □ Myocardial infarction
	  □ Steroid-induced hyperglycemia
	  o Asthma-specific days missed from work or school
	  o Participation in sports and recreational activities
	• Pulmonary physiology
	  o Peak expiratory flow
	  o Spirometry
	  o Airway hyper-responsiveness
	• Quality of life
	  o Asthma Quality of Life Questionnaire
	  o Pediatric Asthma Quality of Life Questionnaire
	  o Pediatric Asthma Caregivers Asthma Quality of Life Questionnaire
	• Death, asthma-specific, and all cause
	Secondary Measures
	• Patient-reported symptoms
	• Indoor inhalant allergen levels measured by formal testing

Category	Criteria
Timing	Studies with all lengths of followup duration will be considered
Setting	• Home • Work • School • Daycare

Data Extraction

Data were abstracted using Microsoft Word. Duplicate abstraction on a 10-percent random sample was used to ensure accuracy. All discrepancies were resolved by consensus discussion among the two original abstracters and an additional third person as needed. Elements abstracted included general study characteristics, patient characteristics, details of interventions, outcomes data, and risk of bias items.

In accordance with the approach used by the Guidelines for the Diagnosis and Management of Asthma,[1] we have defined "pediatric" or "child" populations as including patients age 11 or younger and "adult" populations as including youths age 12 or older and adults. Studies that include patients in both categories are described as having a "mixed population."

Risk of Bias Assessment of Individual Studies

We used the Cochrane Collaboration's tool for assessing risk of bias in RCTs.[18] Study characteristics were rated as introducing "low," "high," or "unclear" risk of bias. For nonrandomized studies, we used the Newcastle-Ottawa scale and rated study characteristics as "low," "moderate," "high," or "unclear."[19] Risk of bias was assessed by two independent reviewers, and discrepancies were addressed through consensus discussion.

We considered the funding source of individual studies as presenting a potentially important risk of bias. Therefore, for any study that reported receiving all or part of its funding from, or was coauthored by one or more employees of, a commercial manufacturer of an intervention, we noted that information in the risk of bias tables. We also rated the "Other Sources of Bias" component in the Cochrane scale as "high" in cases in which study funding presented a potential conflict of interest.

We created a summary assessment of "overall risk of bias" for each study by grouping the criteria included in the Cochrane tool into four categories based on the nature of their respective threats to validity. The four categories address: 1) participant enrollment (comprising "sequence generation" and "allocation concealment"); 2) blinding ("blinding participants and personnel" and "blinding outcome assessors"; 3) outcome data ("incomplete outcome data" and "selective outcome reporting"); and 4) other sources of bias. We then concluded that an individual study was at "high" overall risk of bias if it was assigned a "high" risk rating for one or more discrete criteria in at least two different categories. A study was determined to be at "medium" overall risk of bias if it was assigned a "high" risk rating in only one discrete criterion or in two criteria within the same category. Therefore, if a study was at "high" risk of bias for both "sequence generation" and "incomplete outcome data," the overall risk would be "high" because there is concern about two different categories. Conversely, if a study was at "high" risk of bias for "sequence generation" and "allocation concealment," then the overall risk would be "medium" because the two criteria are in the same category. If no criteria were assessed to be at "high" risk, then the overall risk of bias was "low." However, if we rated the risk as "unclear" in two or more categories, then the overall risk was "unclear."

Data Synthesis

Due to the heterogeneity of the included studies, we did not attempt to combine data from the studies quantitatively using meta-analyses. Additionally, some interventions were evaluated in only one study; thus, quantitative synthesis was not possible. Instead, we provide a narrative synthesis of the studies' general findings.

For the multicomponent studies, we organized the data synthesis and analysis by grouping studies according to their active components. We defined the "active component" as an intervention that was implemented in the intervention arm but not the study's control arm. Such interventions met inclusion criteria of this review, as shown in Table 1 above.

We have described outcomes as statistically significant when identified as such by the authors of the primary studies. Statistical significance, however, does not always equate with clinically significant changes in outcomes. In the strength of evidence (SOE) tables, we noted any cases in which a statistically significant result was not associated with an effect size that exceeded standard thresholds for clinical significance, as described in Appendix E; in the absence of published standards of minimal important differences, we identified outcomes that did not improve by an absolute difference of at least 10 percent (between groups or above baseline, depending on the comparison.)

SOE was assessed for the following validated outcomes: asthma-control measures, asthma-exacerbation measures, asthma-related health care utilization and costs, asthma-related pulmonary physiology, and asthma-related quality of life. Symptoms were included as an unvalidated secondary measure, and changes in allergen levels were reported as a measure of the effectiveness of the interventions.

Strength of the Body of Evidence

We graded the SOE of each comparison and outcome based on the guidance established by the Evidence-Based Practice Center (EPC) program. This approach incorporates five key domains: study limitations, consistency, directness, precision, and reporting bias. Overall SOE was graded as "high," "moderate," "low," or "insufficient." Evidence based on RCTs was assigned an initial SOE of "high," while evidence based on non-RCTs was assigned an initial SOE of "low." The SOE was then downgraded as appropriate based on the five domains as described below.

We determined study limitations by appraising the degree to which the included studies for the given comparison and outcome had adequate protection against bias (i.e., has good internal validity). In general, we downgraded for study limitations when 50 percent or more of the studies evaluated for a given outcome were at "high" overall risk of bias as described above. When 50 percent or more of the studies were at "medium," "low," or "unclear" risk of bias, we did not downgrade for study limitations. If the evidence permits a conclusion, then, all else being equal, a set of studies at low risk of bias yields a higher SOE rating than a set of studies at high risk of bias.

We assessed consistency of results for the same outcome among the available studies 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. In

some cases, we downgraded the SOE by two levels for substantial inconsistency, when we were unable to reconcile evidence favoring an intervention with evidence suggesting no effect.

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 may be affected by sample size, number of events, and width of confidence intervals. In some cases, we downgraded the SOE by two levels due to 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 the available data (e.g., 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 (and the lack of effect for interventions that were more widely studied), 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 and/or authorship, we also assessed the size and direction of any effect compared to the studies that did not receive commercial support, to identify possible publication or reporting bias.

Please note that the SOE synthesis approach enables reviewers to assess each individual component (i.e., study limitations, consistency, etc.) and then use their judgment to produce an overall SOE rating that represents a global assessment. Although the SOE domains are reported categorically, they represent concepts that are evaluated and integrated on a continuum. The final SOE assessment must be consistent with the domains, but they also reflect the interaction between components, the robustness of the findings, and the reviewer's confidence in the full body of evidence. Therefore, any two outcomes may have similar or identical limitations (such as inconsistency and imprecision) and nevertheless have different overall assessments.

Applicability

Several *a priori* factors may limit the applicability of findings. Many studies included children under age 11, youths age 12 or older, and adults, making it difficult to apply the findings to a single age group. Studies also often focused on patients at high risk for exposure to allergens, and this may not represent the general asthma population. Another important consideration is that many patients with asthma in the "real world" may have limited opportunities to implement some of the interventions examined in this report, such as structural changes like carpet removal.

Peer Review and Public Commentary

Experts in clinical management of asthma and strategies to minimize the presence and effect of indoor inhalant allergens were invited to provide external peer review of the draft report. AHRQ staff, an Associate Editor, and representatives from NHLBI reviewed the draft report before it was distributed for peer review. The draft report was also posted on the Agency for Healthcare Research and Quality (AHRQ) Web site from April 26, 2017, to May 25, 2017, for public comment. We revised the report based on peer and public feedback and noted these revisions in the Disposition of Comments Report. The disposition report is made available 3 months after the final review is posted on AHRQ's Web site.

Several important revisions were made to the report in response to peer review and public comment. First, as noted above, this review was initially designed to include the current Key Question as well as an additional Key Question addressing the effectiveness of bronchial thermoplasty. We separated the larger review into two independent reports in response to substantial feedback. Second, we expanded the Discussion chapter to address in greater depth some of the major limitations and contextual factors that are important for interpreting this evidence base. These issues include the distinction between patient sensitization to an allergen and actual allergic reaction; lack of established thresholds for determining clinically meaningful improvement for many of the primary and secondary outcome measures we evaluated; exposure to allergens outside a patient's home (especially at school, work, or other routine activities); and the key difference between a lack of evidence (i.e., few or no high-quality published studies addressing a question) and a lack of efficacy (i.e., evidence that an intervention was tested and did not improve outcomes). We also explored in more detail how our methods and findings compared with and differed from previous influential reviews and guidelines. Finally, in response to peer and public commentary as well as feedback from AHRQ staff, we conducted a Qualitative Comparative Analysis of the studies to provide additional insight into the multicomponent interventions.

Qualitative Comparative Analysis

We used qualitative comparative analysis (QCA) to further evaluate the studies. QCA uses formal logic to examine combinations of "conditions," such as the different strategies within multicomponent interventions, and assesses their relationship to important outcomes.[20-23] Single interventions or combinations of strategies can be evaluated simultaneously. Conditions may be determined to be necessary, sufficient, or both for a given outcome. A necessary condition must be present for an outcome to occur, but it might not guarantee the outcome if other conditions are also necessary. A sufficient condition ensures the outcome will occur; however, it may not always be necessary if more than one strategy or set of strategies is capable of achieving the outcome.

QCA uses formal logic and set theory rather than statistical theory and thus does not identify statistical associations. Rather, QCA helps identify various combinations of factors, or "recipes," that may yield a specific result. The QCA approach is designed to provide one or more "solutions," which are combinations of conditions that are necessary, sufficient, or both for a particular outcome. This analytic technique was incorporated into our review to determine whether specific bundles of allergen reduction interventions may be more likely to improve asthma outcomes. Strength of evidence assessment was not performed for the QCA results.

Specific analytic steps are described in Appendix D.

Results

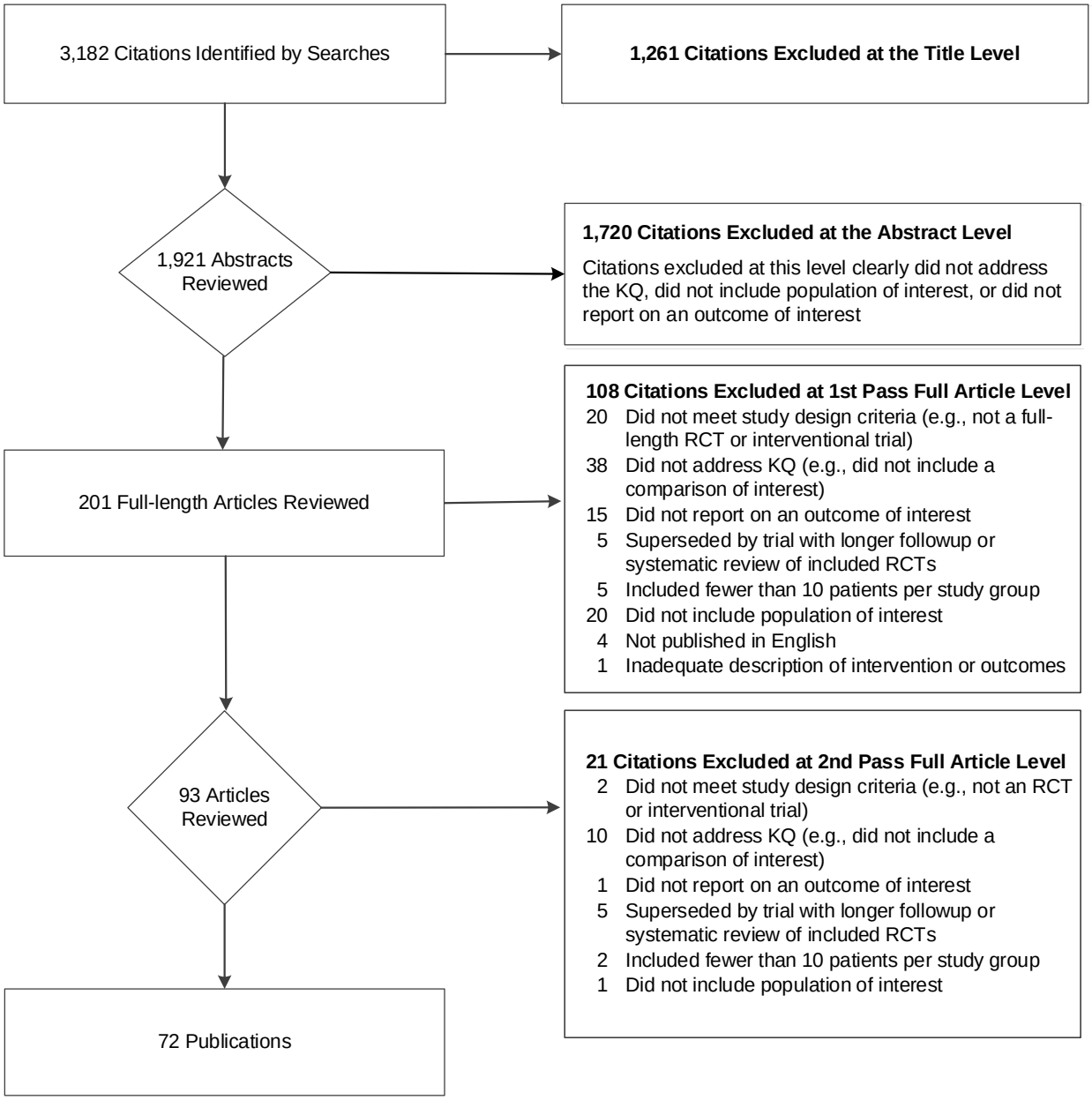
Introduction

We begin by describing the results of our literature searches. We then provide a brief general description of the included studies, followed by key summary points. Next, we provide a detailed analysis of the results for the single intervention studies, followed by the multicomponent studies. Finally, we present the results of the qualitative comparative analysis (QCA).

Results of Literature Searches

The literature searches identified 93 articles appropriate for comprehensive full-text review (see Figure 2). Seventy-two publications addressed the Key Question. The evidence base includes 60 randomized controlled trials (RCT) with data published in 64 articles and 8 non-RCTs. Articles that were excluded at the full-text level with reasons for their exclusion are listed in Appendix B.

Figure 2. Study attrition diagram



KQ=Key Question; RCT=randomized controlled trial

Key Question: Among individuals with asthma, what is the effectiveness of interventions to reduce or remove exposures to indoor inhalant allergens on asthma control, exacerbations, quality of life, and other relevant outcomes?

Description of Included Studies

Thirty-eight studies assessed individual (single component) interventions, and 30 studies assessed multicomponent interventions. The following specific interventions were evaluated:

- Acaricide (i.e., house dust mite [HDM] pesticide applied to carpets, mattresses, furniture)
- Air purification (i.e., devices designed to filter room air)
- Carpet removal (i.e., removal of carpeting or area rugs from one or more rooms)
- High-efficiency particulate air-filtration (HEPA) vacuum (i.e., routine use of HEPA vacuum for cleaning carpeting or rugs of any type)
- Mattress covers (i.e., impermeable covers placed on mattresses)
- Mold removal (i.e., professional cleaning of mold-covered surfaces)
- Pest control (i.e., traps, poison, and/or professional services designed to control common house pests such as cockroaches and mice)
- Pet removal (i.e., confinement to specific rooms within a house, or complete removal of furry pets such as dogs and cats)
- Multicomponent interventions with more than one strategy for reducing one or more allergen exposures

Mattress covers were the most frequently studied intervention, assessed in 17 single-intervention studies and 19 multicomponent trials. Conversely, we found the smallest body of evidence for pet removal, which was examined in only three studies. Twenty-two studies enrolled patients 12 years of age and above, while 9 studies were limited to children under 12. Thirty-six studies included patients above and below the age of 12. Thirty-four studies were conducted in Europe, 24 were performed in the United States, and the remaining 10 were conducted in Canada, Australia, New Zealand, or Asian countries. Table 2 provides an overview of the distribution of the studies. Figure 3 highlights the distribution of study designs by populations and complexity of the interventions.

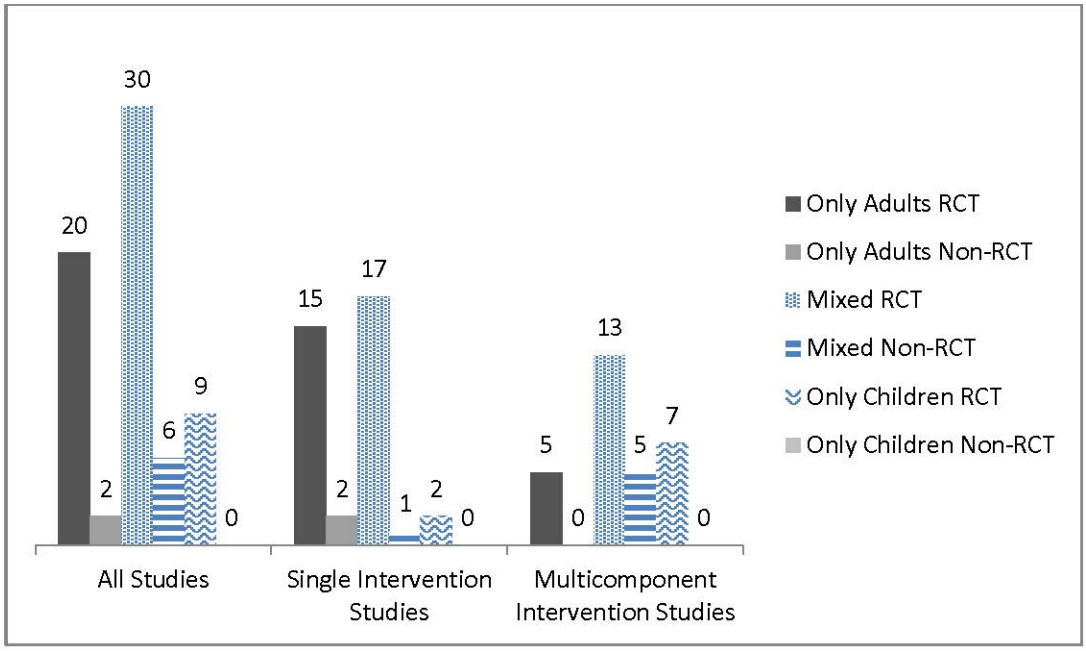
Table 2. Overview of interventional studies for reducing exposure to allergens

Intervention	Randomized Controlled Trials (number of studies, cumulative sample size, range of sample size)	Other Study Designs (number of studies, cumulative sample size)	Age Cohorts* (number of studies in each cohort)	Country/Region
Acaricides (dust mite pesticide)	6 n=229 (Range 26–62)	1 nonrandomized trial n=59	3 adult 4 mixed	6 Europe 1 Canada
Air purification	9 n=311 (Range 10–119)	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 n=60	0	1 mixed	1 Europe

Intervention	Randomized Controlled Trials (number of studies, cumulative sample size, range of sample size)	Other Study Designs (number of studies, cumulative sample size)	Age Cohorts* (number of studies in each cohort)	Country/Region
Mattress covers	17 n=2,287 (Range 20–1,122)	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 n=102	1 pre-post n=78	2 mixed	2 United States
Pet removal	0	1 nonrandomized trial (n=20)	1 adult	1 Asia
Other (1 study of bleach cleaning)	1 n=97	0	1 mixed	1 United States
Multicomponent	25 n=4,338 (Range 23–937)	3 pre-post (n=365) 2 nonrandomized controlled trials (n=204)	5 adult 7 pediatric 18 mixed	20 United States 9 Europe 1 Australia
Total	60	4 nonrandomized trials 4 pre-post	22 adult 9 pediatric 36 mixed 1 not reported	24 United States 1 Canada 34 Europe 5 Asia 4 Australia/ New Zealand

* Adult=all patients were ≥12 years old; Mixed=study included pediatric and adult patients; Pediatric=all patients were <12 years old
HEPA= high-efficiency particulate air-filtration

Figure 3. Number of included studies per study design and age group



RCT= Randomized controlled trial

Key Points

- The evidence that either single or multicomponent interventions intended to reduce allergen exposure improve asthma outcomes is limited by a lack of high quality studies. Overall strength of evidence (SOE) was either low, inconclusive, or no studies were available.
- No high or moderate strength evidence found improvement in clinical outcomes resulting from single component interventions.
- Overall, multicomponent interventions performed better than single interventions.
- Multicomponent strategies that included HEPA vacuums reduced exacerbations and improved quality of life (moderate SOE), while strategies that included mattress covers improved asthma symptoms (high SOE), and strategies that included pest control reduced exacerbations (moderate SOE).
- Mattress covers, when used without other interventions, did not affect asthma control (moderate SOE), exacerbations (moderate SOE), health care utilization (high SOE), pulmonary physiology (high SOE), quality of life (high SOE), or asthma symptoms (high SOE), despite reducing the allergen burden detected on mattress surfaces (moderate SOE).
- Qualitative comparative analysis affirmed the general lack of robust findings of improved outcome effects. No single allergen interventions were determined to be necessary or sufficient for effectiveness. Multicomponent bundles were characterized by substantial heterogeneity, and no conclusions about the effectiveness of specific combinations could be supported by the evidence.

- Important limitations of the evidence base include population heterogeneity (in terms of age and asthma severity), infrequent reporting of validated asthma outcome measures, poor data reporting, and variation in how interventions were implemented.
- Further research is needed examining indoor allergen reduction interventions in comparative studies with sufficient population sizes to detect clinically meaningful differences in relevant and validated asthma outcomes.

Table 3 summarizes the SOE for each intervention. Due to the heterogeneity of the included studies, we did not attempt to combine data from the studies quantitatively. Instead, we provide a narrative synthesis. Tables 4 through 10 address single component interventions, and Tables 11 and 12 address multicomponent interventions. Detailed evidence tables presenting information on the design of the studies, study populations, findings, and assessment of study limitations (risk of bias) are located in Appendix C.

Table 3. Allergen reduction interventions summary results and strength of evidence

Intervention (n=Studies)	Asthma Control	Exacerbations	Health Care Utilization	Absenteeism	Pulmonary Physiology	Quality of Life	Symptoms	Allergen Reduction
Acaricide only (n=7)	NA	NA	NA	NA	No effect (Moderate)	Inconclusive*	Inconclusive*	Inconclusive*
Acaricide multicomponent (n=6)	NA	Inconclusive*	Inconclusive*	NA	No effect (Moderate)	NA	No effect (High)	Improved (Low)
Air purification only (n=9)	Inconclusive*	No effect (Low)	No effect (Low)	NA	No effect (Low)	Improved (Low)	Inconclusive*	No effect (Low)
Air purification multicomponent (n=5)	No effect (Low)	No effect (High)	NA	Improved (Low)	Inconclusive*	No effect (High)	Improved (Low)	Improved (Moderate)
Carpet removal only (n=0)	NA	NA	NA	NA	NA	NA	NA	NA
Carpet removal multicomponent (n=8)	NA	Inconclusive*	Inconclusive*	NA	Inconclusive*	Inconclusive*	Inconclusive*	Improved (Moderate)
HEPA vacuum only (n=1)	NA	NA	NA	NA	Inconclusive*	NA	NA	Inconclusive*
HEPA vacuum multicomponent (n=8)	Inconclusive*	Improved (Moderate)	No effect (High)	Improved (Low)	Inconclusive*	Improved (Moderate)	Improved (Low)	Improved (Moderate)
Mattress cover only (n=17)	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)	Inconclusive*	No effect (High)	Inconclusive*	Improved (Low)	No effect (High)	No effect (Moderate)	Improved (High)	Improved (Low)
Mold removal only (n=0)	NA	NA	NA	NA	NA	NA	NA	NA
Mold removal multicomponent (n=6)	NA	Inconclusive*	Inconclusive*	NA	Inconclusive*	Inconclusive*	Improved (Low)	Inconclusive*
Pest control only (n=2)	Inconclusive*	Inconclusive*	NA	Inconclusive*	Inconclusive*	NA	Improved (Low)	Inconclusive*
Pest control multicomponent (n=13)	Inconclusive*	Improved (Moderate)	Inconclusive*	Improved (Low)	Inconclusive*	Improved (Low)	Improved (Low)	Improved (Low)
Pet removal only (n=1)	NA	Inconclusive*	Inconclusive*	NA	NA	NA	NA	NA
Pet removal multicomponent (n=2)	NA	NA	NA	NA	NA	NA	NA	NA

*Inconclusive due to insufficient evidence; HEPA=high-efficiency particulate air-filtration; NA=not applicable

Detailed Synthesis

Studies of Single Component/Individual Interventions

Individual interventions for which we identified studies include treatment of mattresses and carpets with acaricide, use of air purifiers, HEPA vacuuming, mattress covers, pest control, and pet removal. We also found one study of commercially available household cleaning products containing bleach or other disinfectants.

No adverse events were reported from the studies we examined. While many studies reported on pulmonary physiology, nonvalidated measures of respiratory symptoms, and allergen levels, few studies reported validated measures of asthma control or quality of life. Additionally, rates of exacerbations and health care utilization were often low or not reported.

Acaricide (Dust Mite Pesticide)

Four RCTs[24-27] compared the use of acaricide with placebo. One additional RCT[28] compared acaricide with other HDM-avoidance interventions. Another RCT[29] and a quasi-experimental study[30] had three arms comparing the use of acaricide with placebo and with other HDM-avoidance interventions. Treatments were used on carpets, upholstery, and mattresses in the bedroom and typically applied in the most commonly used residential room. Followup ranged from three to 6 months. The trials reported that all enrolled patients demonstrated allergic sensitization to HDM allergen. Six studies used skin-prick testing to confirm sensitization, while one trial used blood tests. Acaricide manufacturers funded two studies but did not report positive findings, and we did not detect publication or reporting bias in this evidence base. The studies did not report measures of asthma control, exacerbations, and health care utilization. Use of acaricide was associated with no change in pulmonary physiology compared with placebo (SOE: moderate) or other interventions (SOE: low). The findings for quality of life were inconclusive, and interpretation of the findings was limited by poor reporting of data and statistical analyses and small sample sizes. Table 4 presents the findings and SOE ratings for the outcomes these studies assessed.

Table 4. Acaricide (dust mite pesticide) interventions summary and strength of evidence

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
Acaricide vs. placebo	Asthma control	**Not evaluable:** Not reported in included studies.	NA	NA
	Exacerbations	**Not evaluable:** Not reported in included studies.	NA	NA
	Health care utilization	**Not evaluable:** Not reported in included studies.	NA	NA
	Pulmonary physiology: spirometry	**No effect:** No reported differences between acaricide and placebo for FEV_1, PEFR, or FVC measures.	4 RCTs[26-29] 1 non-RCT[30] n=219	Moderate (Imprecise)
	Pulmonary physiology: airway hyper-responsiveness	**Inconclusive:** RCT found no difference between acaricide and placebo; non-RCT reported a statistically significant but not clinically significant improvement in PC_{20} following use of acaricide.	1 RCT[25] 1 non-RCT[30] n=93	Insufficient (Inconsistent, Imprecise) **Substantial imprecision
	Quality of Life	**Inconclusive:** Small RCT showed no between-group difference in quality of life; data shown graphically with no estimation of variability.	1 RCT[29] n=62	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Symptoms (secondary measure)	**Inconclusive:** Small RCT found improvements in both parent and physician ratings of child's asthma severity, but no differences in frequency of wheezing.	1 RCT[24] n=35	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Allergen levels: Environmental measures (secondary measure)	**Inconclusive:** Small RCT[24] showed decreased levels of HDM allergens in both groups, with a greater decrease in the acaricide group. Another small RCT[26] showed no difference between groups for allergens in carpet or mattress, but found a reduction of allergens in other areas of the house. The remaining studies found no differences between groups.	4 RCTs[24,26,27,29] 1 non-RCT[30] n=228	Insufficient (Inconsistent, Imprecise)
Acaricide vs. other mite-avoidance interventions	Asthma control	**Not evaluable:** Not reported in included studies.	NA	NA
	Exacerbations	**Not evaluable:** Not reported in included studies.	NA	NA
	Health care utilization	**Not evaluable:** Not reported in included studies.	NA	NA
	Pulmonary physiology	**No effect:** No reported differences between acaricide and other mite-avoidance interventions for FEV_1, PEFR, or FVC measures.	2 RCTs[28,29] 1 non-RCT[30] n=147	Low (Study limitations, Imprecise)
	Quality of life	**Not evaluable:** Not reported in included studies.	NA	NA
	Symptoms (secondary measure)	**Not evaluable:** Not reported in included studies.	NA	NA
	Allergen levels (secondary measure)	**Inconclusive:** No studies showed between-group differences in allergen levels. Reported data did not allow assessment of precision.	2 RCTs[28,29] 1 non-RCT[30] n=147	Insufficient (Study limitations, Imprecise) **Unable to determine effect from reported data

*Outcomes of Asthma control, Exacerbations, Health care utilization, and Pulmonary physiology as defined by Asthma Outcomes workshop;[31] outcomes of Quality of life, Symptoms, and Allergen levels as defined by study authors.
**Criteria for downgrading strength of evidence is described as Rationale; when these criteria are insufficient for understanding the final strength of evidence, additional explanation is provided.
Der p=*dermatophagoides pteronyssinus* allergen; FEV_1=forced expiratory volume in one second; FVC=forced vital capacity; HDM=house dust mite; IgE=immunoglobulin E; NA=not available; PC_{20}=provocative concentration 20; PEFR=peak expiratory flow rate; RCT=randomized controlled trial

Air Purification Interventions

Seven of nine RCTs compared the use of air purification systems to either a sham intervention[32-36] or no intervention.[37,38] An additional RCT[39] compared the use of air filtration with other HDM-avoidance interventions. Finally, another study installed new mechanical heat-recovery ventilation in the home, with sham fans as a control.[40] Five of the studies implemented air purification in both bedrooms and living rooms, while three studies focused only on bedroom air (the mechanical ventilation study affected air throughout participants' homes.) Followup ranged from 4 weeks to 12 months. Six of the nine studies reported that all patients were sensitized to at least one allergen of interest that was potentially subject to the effects of the intervention, usually HDM, cat, or dog (four of these trials used skin- prick tests, and two used blood tests). Three other studies found that 70 to 95 percent of patients were sensitized to one of these allergens (two used skin-prick tests, and one used blood tests). Air filtration device manufacturers funded three studies, but we did not detect publication or reporting bias in this evidence base because the industry-funded studies were not associated with better results than non-industry-funded studies of air purifiers.

The effect of air purification interventions on asthma control was inconclusive, and exacerbations were not reported. There was no difference in health care utilization (SOE:lLow) and pulmonary physiology. For quality of life, one study found that Asthma Quality Control Questionnaire (AQLQ) scores improved (SOE: low), while two studies that used nonvalidated quality of life measures found no effect (SOE: low). Interpretation of all the findings reported for air purification interventions was limited by poor reporting of data and statistical analyses, lack of between-group comparisons, and small sample sizes. Table 5 presents the findings and SOE ratings for the outcomes these studies assessed.

Table 5. Air purification interventions summary and strength of evidence

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
Air filtration/air purifier vs. control	Asthma control	**Inconclusive:** 1 RCT with low risk of bias showed no differences in ACQ scores. 1 RCT with high risk of bias showed an improvement in combined asthma outcomes following use of air cleaners. 1 RCT[35] did not report differences in asthma scores between interventions.	3 RCTs[35,37,40] n=169	Insufficient (Inconsistent, Imprecise) **Unable to determine effect from reported data
	Exacerbations	**No effect:** Measures of ED visits and use of rescue medications did not differ between treatment conditions.	3 RCTs[32,35,40] n=167	Low (Study limitations, Imprecise)
	Health care utilization	**Not evaluable:** Not reported in included studies.	NA	NA
	Pulmonary physiology	**No effect:** 5 RCTs showed no differences in spirometry measures. 1 other RCT[40] showed improvements in evening peak flow, but in no other spirometry measures. 1 other RCT[34] showed improvements in peak flow variation and airway hyper-responsiveness but not in FEV_1.	7 RCTs[32-35,37,38,40] n=263	Low (Inconsistent, Imprecise)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Quality of life: mini-AQLQ	**Improvement:** 1 RCT[32] found significant improvement in mini-AQLQ scores for active air cleaners compared with placebo (mean difference in change [SEM], active – placebo = 0.54 (0.28); $p<0.05$).	1 RCT[32] n=28	Low (Study limitations, Unknown consistency)
	Quality of life: other measures	**No effect:** 2 RCTs showed no between-group differences in quality of life.	2 RCTs[33,40] n=155	Moderate (Imprecise)
	Symptoms (secondary measure)	**Inconclusive:** Following intervention, 1 small RCT[36] reported improvements in self-report asthma symptoms but provided no summary statistics.	1 RCT[36] n=18	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Allergen levels (secondary measure)	**No effect:** 4 RCTs[33,34,37,40] found no differences between treatment groups. 1 small RCT[35] showed decreased levels of Der p during the active intervention compared with placebo.	5 RCTs[33-35,37,40] n=225	Low (Imprecise)
Air filtration/air purifier vs. other mite avoidance interventions	Asthma control	**Not evaluable:** Not reported in included studies.	NA	NA
	Exacerbations	**Not evaluable:** Not reported in included studies.	NA	NA
	Healthcare utilization	**Not evaluable:** Not reported in included studies.	NA	NA
	Pulmonary physiology	**Inconclusive:** 1 RCT showed no differences for FEV_1, vital capacity, histamine PC_{20}. Data were shown graphically for the 2 groups with no estimate of variability; analyses for between-group comparisons not reported.	1 RCT[39] n=30	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Quality of life	**Not evaluable:** Not reported in included studies.	NA	NA
	Symptoms (secondary measure)	**Not evaluable:** Not reported in included studies.	NA	NA
	Allergen levels (secondary measure)	**Inconclusive:** Between-groups analyses not reported.	1 RCT[39] n=30	Insufficient (Unknown consistency, Imprecise) **Unable to determine effect from reported data

*Outcomes of Asthma control, Exacerbations, Healthcare utilization, and Pulmonary physiology as defined by Asthma Outcomes workshop;[31] outcomes of Quality of life, Symptoms, and Allergen levels as defined by study authors.

**Criteria for downgrading strength of evidence is described as Rationale; when these criteria are insufficient for understanding the final strength of evidence, additional explanation is provided.

ACQ=asthma control questionnaire; AQLQ=asthma quality of life questionnaire; Der p=*dermatophagoides pteronyssinus* allergen; ED=emergency department; FEV_1=forced expiratory volume in 1 second; HDM=house dust mite; NA=not available; PC_{20}=provocative concentration causing a 20% drop in FEV_1; RCT=randomized controlled trial; SEM=standard error of the mean

Carpet Removal

We did not identify any studies that examined carpet removal as a solitary intervention to improve asthma outcomes. Carpet removal was included as a strategy in several multicomponent interventions that are described in the multicomponent study section below.

HEPA Vacuum Interventions

One small RCT[41] compared the use of HEPA vacuums on carpets and soft furnishings with standard vacuums. Participants were instructed to vacuum the sofa, mattress, and living room and bedroom carpet at least once a week for up to one year. All patients were sensitized to HDM based on skin-prick tests, and a majority of those who owned a cat were also allergic to cat allergen. This study was not funded by an industry source, although one coauthor reported having received funding from a vacuum manufacturer. Measures of asthma control, exacerbations, health care utilization, or quality of life were not reported. Use of HEPA vacuums led to improvements in spirometry measures compared with the standard vacuums, but the overall SOE was Insufficient. Use of HEPA vacuums reduced the secondary measure of allergen levels compared with baseline for some areas of the home and some of the allergens measured, but most areas and allergens did not vary with use of the HEPA vacuum. In addition, between-group comparisons were not reported, limiting interpretation of the findings. Table 6 presents the findings and SOE ratings for the outcomes this study assessed.

Table 6. HEPA vacuum interventions summary and strength of evidence

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
HEPA vacuum vs. standard vacuum	Asthma control	**Not evaluable:** Not reported in included studies.	NA	NA
	Exacerbations	**Not evaluable:** Not reported in included studies.	NA	NA
	Health care utilization	**Not evaluable:** Not reported in included studies.	NA	NA
	Pulmonary physiology	**Inconclusive:** 1 RCT showed improvements in FEV_1 and peak flow, but only p-values were reported for between-group comparisons.	1 RCT[41] n=60	Insufficient (Unknown consistency, Imprecise) *Substantial imprecision
	Quality of life	**Not evaluable:** Not reported in included studies.	NA	NA
	Symptoms (secondary measure)	**Not evaluable:** Not reported in included studies.	NA	NA
	Allergen levels (secondary measure)	**Inconclusive:** Between-group comparisons not reported. Use of HEPA vacuum reduced allergen levels compared with baseline for some areas and allergens.	1 RCT[41] n=60	Insufficient (Unknown consistency, Imprecise) **Unable to determine effect from reported data

*Outcomes of Asthma control, Exacerbations, Healthcare utilization, and Pulmonary physiology as defined by Asthma Outcomes workshop;[31] outcomes of Quality of life, Symptoms, and Allergen levels as defined by study authors.
**Criteria for downgrading strength of evidence is described as Rationale; when these criteria are insufficient for understanding the final strength of evidence, additional explanation is provided.
FEV_1=forced expiratory volume in 1 second; HEPA=high-efficiency particulate air-filtration; NA=not available; RCT=randomized controlled trial

Mattress Cover Interventions

Seventeen RCTs examined the effectiveness of mattress covers or other interventions related to bedding. Ten of these RCTs[42-51] compared the use of impermeable mattress covers with placebo, and four other RCTs[52-55] compared covers with no intervention. We combined these 14 studies for analysis. An additional three RCTs evaluated different interventions: one[56] compared feather-filled pillows and quilts plus impermeable mattress covers with impermeable mattress covers alone; one[57] compared an impermeable pillow designed to resist HDM without any additional covering with a placebo pillow; and one[58] examined the effectiveness of boiling bed covers in hot water for 10 minutes and exposing them to sunlight for 3 hours every 2 weeks, compared with standard linen washing practices. None of the studies were conducted in the United States, and most were small; 9 studies included fewer than 50 patients, and only 5 studies included more than 100 patients. Ten studies included only patients age 12 or older, 6 included both adults and youths below age 12, and the study of the impermeable pillow enrolled only children. One study did not report the ages of enrolled participants.

Sixteen of the 17 studies confirmed that all patients demonstrated sensitization to HDM allergens, with 10 of these trials confirming sensitization using skin-prick tests. Only 7 studies described randomization and allocation practices, but 11 studies blinded both patients and outcome assessors. No studies reported direct funding by mattress cover manufacturers, although one study included two coauthors who had received funding from a manufacturer. Individual study risk of bias was not considered a limitation of the evidence base addressing mattress covers.

Mattress cover interventions showed no effect was observed for asthma control (SOE: moderate), exacerbations (SOE: moderate), use of inhaled corticosteroids (SOE: low), use of rescue medication (SOE: high), pulmonary physiology (SOE: high), or quality of life (SOE: high). However, the evidence suggests that HDM allergen exposure levels were significantly reduced by use of mattress covers (SOE: moderate) despite the lack of clinical improvement. Findings for the three studies that did not evaluate mattress covers were inconclusive. Table 7 presents the findings and SOE ratings for the outcomes these studies assessed.

Table 7. Mattress cover interventions summary and strength of evidence

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
Impermeable covers on mattress, pillow, and/or duvet vs. placebo covers or no intervention	Asthma control	**No effect:** No difference in ACQ scores in RCT of 126 adults and RCT of 284 mixed-population subjects.	2 RCTs[42,43] n=410	Moderate (Imprecise)
	Exacerbations	**No effect:** No difference in composite measure of hospitalization and/or rescue medication use in RCT of 1,122 adults. No difference in frequency of asthma attacks in RCT of 55 adults. Significant reduction in composite measure of hospitalization or ED visit in 1 RCT of 284 mixed-population subjects.	3 RCTs[42,47,48] n=1,461	Moderate (Inconsistent)
	Health care utilization: inhaled corticosteroid use	**No effect:** No difference for total dosage change in RCT of 126 adults. No difference for mean change in 28-day dose in RCT of 47 mixed-population subjects. Significantly greater reduction in mean daily dose in RCT of 60 mixed-population subjects.	3 RCTs[43,46,50] n=233	Low (Inconsistent, Imprecise)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Health care utilization: rescue medication use	**No effect:** No difference in 2 RCTs of 1,154 adults and 2 RCTs of 91 mixed-population subjects for beta agonist use or dose. No difference in use of undefined "rescue medication" in RCT of 30 adults.	5 RCTs[44,46,48,49,51] n=1,275	High
	Health care utilization and costs: work absenteeism	**Decreased workdays:** Significant decrease in missed days of work in RCT of 1,122 adults, but difference may not be meaningful: Mean difference: -0.15 days per month (95% CI: -0.29 to -0.02).	1 RCT[48] n=1,122	Low (Unknown consistency, Imprecise)
	Pulmonary physiology	**No effect:** No difference in morning or evening peak flow for 8 RCTs of 1,535 adults and 4 RCTs of 158 mixed-population subjects. Significant improvement reported in RCT of 25 adults.	13 RCTs[43-55] n=1,744	High
	Quality of life	**No effect:** No difference in 5 RCTs of 1,365 adults and 1 RCT of 284 mixed-population subjects; 2 used the Modified AQLQ-Marks; 1 used mini-AQLQ; 1 used St George's Respiratory Questionnaire; 1 used PACQLQ; 1 used Quality of Life for Respiratory Illness Questionnaire	6 RCTs[42-44,47-49] n=1,649	High
	Symptoms (secondary measure)	**No effect:** No difference in 7 RCTs (n=1,470; 4 in adults and 3 in mixed populations.) Significant improvement in RCT of 25 adults. Studies used similar but not identical sets of composite scores, ranging from 3 to 8 discrete items (e.g., cough, wheeze)	8 RCTs[43,44,46,48-52] n=1,473	High
	Allergen levels (secondary measure)	**Allergen reduction:** Significant reduction in Der p and/or Der f allergen in 6 RCTs of 1,387 adults and 3 RCTs of 375 mixed-population subjects. No difference in 2 RCTs of 141 adults.	11 RCTs[42-49,51,52,55] n=1,928	Moderate (Inconsistent)
Feather-filled pillow and quilt vs. impermeable cover on mattress, pillow, and quilt	Asthma control	**Not evaluable:** Not reported in included studies.	NA	NA
	Exacerbations	**Not evaluable:** Not reported in included studies.	NA	NA
	Health care utilization	**Not evaluable:** Not reported in included studies.	NA	NA
	Pulmonary physiology	**Not evaluable:** Not reported in included studies.	NA	NA
	Quality of life	**Inconclusive:** No difference for overall quality of life: Adjusted difference effect: 0.04 (95% CI: -0.27 to 0.35; p=0.80).	1 RCT[56] n=197	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Symptoms (secondary measure)	**Inconclusive:** No difference for frequent wheeze, speech-limiting wheeze, or sleep disturbance caused by wheeze.	1 RCT[56] n=197	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Allergen levels (secondary measure)	**Inconclusive:** No difference for Der p 1 allergen: Median exposure: 16.0 pg-m3 (IQR: 1.0 to 54.1) vs. 28.0 pg-m3 (IQR: 1.0 to 66.8, p=0.30).	1 RCT[56] n=197	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
Impermeable pillow vs. placebo pillow	Asthma control	**Not evaluable:** Not reported in included studies.	NA	NA
	Exacerbations	**Inconclusive**: No difference in number of asthma attacks (data reported in graph and cannot be evaluated).	1 RCT[57] n=20	Insufficient (Unknown consistency, Imprecise, Reporting Bias Detected)
	Health care utilization	**Not evaluable:** Not reported in included studies.	NA	NA
	Pulmonary physiology	**Not evaluable:** Not reported in included studies.	NA	NA
	Quality of life	**Not evaluable:** Not reported in included studies.	NA	NA
	Symptoms (secondary measure)	**Not evaluable:** Not reported in included studies.	NA	NA
	Allergen levels (secondary measure)	**Inconclusive:** No difference in IgE levels for HDM (data reported in graph and cannot be evaluated).	1 RCT[57] n=20	Insufficient (Unknown consistency, Imprecise, Reporting Bias Detected)
Cotton bed covers boiled and exposed to 3 hours of sunlight every 2 weeks vs. standard laundering	Asthma control	**Not evaluable:** Not reported in included studies.	NA	NA
	Exacerbations	**Inconclusive:** No difference in asthma attacks.	1 RCT[58] n=42	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Health care utilization	**Not evaluable:** Not reported in included studies.	NA	NA
	Pulmonary physiology	**Inconclusive:** No difference for morning or evening peak flow.	1 RCT[58] n=42	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Quality of life	**Not evaluable:** Not reported in included studies.	NA	NA
	Symptoms (secondary measure)	**Inconclusive:** No difference for frequency of cough, wheeze, or sputum. Significant reduction in frequency of dyspnea.	1 RCT[58] n=42	Insufficient (Study limitations, Unknown consistency, Imprecise)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Allergen levels (secondary measure)	**Inconclusive:** No difference between groups.	1 RCT[58] n=42	Insufficient (Study limitations, Unknown consistency, Imprecise)

*Outcomes of Asthma control, Exacerbations, Healthcare utilization, and Pulmonary physiology as defined by Asthma Outcomes workshop;[31] outcomes of Quality of life, Symptoms, and Allergen levels as defined by study authors.
**Criteria for downgrading strength of evidence is described as Rationale; when these criteria are insufficient for understanding the final strength of evidence, additional explanation is provided.
ACQ=asthma control questionnaire; AQLQ= asthma quality of life questionnaire; CI=confidence interval; Der f=*dermatophagoides farina* allergen; Der p=*dermatophagoides pteronyssinus* allergen; HDM=house dust mite; IgE=immunoglobulin E; IQR=interquartile range; NA=not available; PACQLQ= pediatric asthma caregivers asthma quality of life questionnaire; pg-m3=phosphoglucomutase 3 gene; RCT=randomized controlled trial

Mold Removal

We did not identify any studies that examined mold removal as a solitary intervention to improve asthma outcomes. Mold removal was included as a strategy in several multicomponent interventions that are described in the multicomponent study section below.

Pest Control Interventions

One RCT[59] and one pre-post study[60] examined pest-reduction interventions targeted primarily at cockroach (the RCT) and rodent (the pre-post study) elimination. The RCT[59] compared use of insecticide bait, placed in cockroach-sensitive areas by pest control professionals, with no intervention. Followup time was one year. Only 27 percent of patients were sensitized to cockroach allergen, while 12 percent were sensitized to mouse allergen and 50 percent were sensitized to HDM allergen, all based on blood tests.

The pre-post study[60] was conducted in public housing in Boston, Massachusetts, and consisted of a one-time deep-cleaning of the home, setting traps, sealing rodent access points, replacing mattresses, providing education about kitchen hygiene and food storage, reducing clutter, and communicating with housing authority and pest contractors. Followup times varied, with a maximum followup of 66 weeks. Sixty percent of patients were sensitized to HDM allergens, while 58 percent reported sensitization to cockroach allergen, as confirmed by skin-prick tests.

Measures of primary outcomes were inconclusive. However, respiratory symptoms were shown to improve. Lack of precision in reporting the findings and small sample size limit the ability to draw conclusions regarding effectiveness of the interventions. Table 8 presents the findings and SOE ratings for the outcomes these studies assessed

Table 8. Pest control interventions summary and strength of evidence

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
Pest reduction interventions pre- and post-treatment	Asthma control	**Inconclusive:** ACT score did not improve significantly in 1 RCT.	1 RCT[59] n=102	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Exacerbations	**Inconclusive:** ED or unscheduled clinic visits were significantly reduced after use of insecticide in 1 RCT, but hospitalizations did not improve; 1 pre-post study found no change in rates of exacerbations.	1 RCT[59] 1 pre-post study[60] n=180	Insufficient (Inconsistent, Imprecise) **Substantial imprecision
	Health care utilization	**Inconclusive:** Patients sensitized to cockroach allergen missed significantly fewer school days after use of insecticide.	1 RCT[59] n=102	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Pulmonary physiology	**Inconclusive:** FEV_1 improved significantly for patients after use of insecticide, but improvement was not significant for a subset of patients sensitized to cockroach allergen.	1 RCT[59] n=102	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Quality of life	**Not evaluable:** Not reported in included studies.	NA	NA
	Symptoms (secondary measure)	**Improvement:** Significant improvement in respiratory symptoms in RCT and in pre-post study.	1 RCT[59] 1 pre-post study[60] n=180	Low (Imprecise)
	Allergen levels (secondary measure)	**Inconclusive:** All allergens were reported to decrease from baseline, with no statistical analysis or description of statistical significance.	1 pre-post study[60] n=78	Insufficient (Unknown consistency, Imprecise) **Pre-post study

*Outcomes of Asthma control, Exacerbations, Healthcare utilization, and Pulmonary physiology as defined by Asthma Outcomes workshop;[31] outcomes of Quality of life, Symptoms, and Allergen levels as defined by study authors.
**Criteria for downgrading strength of evidence is described as Rationale; when these criteria are insufficient for understanding the final strength of evidence, additional explanation is provided.
ACT=asthma control test; ED=emergency department; FEV_1= forced expiratory volume in one second; NA=not available; RCT=randomized controlled trial

Pet Care and Removal

We identified one non-RCT[61] that examined pet removal as a solitary intervention to improve asthma outcomes. The intervention was conducted in patients with asthma in Japan and consisted of voluntary removal of pets from the home. The study involved two small cohorts of patients who removed pets following clinician advice and those who kept pets against clinician advice. Latency for pet removal from patient homes ranged from within 1 month of clinician advice up to 16 months following advice. Followup times varied, with a maximum followup of 43 months. All patients were sensitized to house pet allergens, based on skin-prick tests. Most patients were sensitized to other allergens, including cedar pollen, HDM, and grass pollens. Measures of asthma control, pulmonary physiology, and quality of life were not reported. The evidence for exacerbations and health care utilization was inconclusive. Over time, use of inhaled corticosteroid was eliminated in patients who removed their pets, and followup visits to the medical office were statistically significantly reduced in the pet-removal group compared with those who kept their pets. Lack of precision in reporting the findings and small sample size limit the ability to draw conclusions regarding effectiveness of the intervention. Table 9 presents the findings and SOE ratings for the outcomes this study assessed.

Table 9. Pet removal interventions summary and strength of evidence

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
Pet removal vs. keeping pets	Asthma control	**Not evaluable:** Not reported in included study.	NA	NA
	Exacerbations/ hospitalizations	**Inconclusive:** No patients in the removal group experienced exacerbations or hospitalizations. 2 patients who kept pets experienced either an exacerbation or hospitalization. No statistics presented in study.	1 non-RCT[61] n=20	Insufficient (Unknown consistency, Imprecise) **Non-RCT
	Health care utilization	**Inconclusive:** Both use of inhaled corticosteroids and followup visits to the medical office were statistically significantly reduced in the pet-removal group.	1 non-RCT[61] n=20	Insufficient (Unknown consistency) **Non-RCT
	Pulmonary physiology	**Not evaluable:** Not reported in included study.	NA	NA
	Quality of life	**Not evaluable:** Not reported in included study.	NA	NA
	Symptoms (secondary measure)	**Not evaluable:** Not reported in included study.	NA	NA
	Allergen levels (secondary measure)	**Not evaluable:** Not reported in included study.	NA	NA

*Outcomes of Asthma control, Exacerbations, Healthcare utilization, and Pulmonary physiology as defined by Asthma Outcomes workshop;[31] outcomes of Quality of life, Symptoms, and Allergen levels as defined by study authors.
** Criteria for downgrading strength of evidence is described as Rationale; when these criteria are insufficient for understanding the final strength of evidence, additional explanation is provided.
NA=not available; non-RCT=non-randomized controlled trial

Other Interventions: Cleaning Products

One RCT[62] examined the provision and use of common household cleaning products used for cleaning counters, floors, bathrooms, and other surfaces. These products were compared with no provision of or instructions regarding cleaning products. A manufacturer of cleaning products funded the study, and the authors did not report how many patients were sensitized to specific allergens. In this eight-week study, measures of asthma control and exacerbations were inconclusive. Health care utilization and pulmonary physiology outcomes were not reported. Furthermore, the main outcome of quality of life was improved in all groups, including the no-cleaning-product group, and the authors suggest the possibility of a placebo effect of keeping diaries on quality of life. Secondary asthma symptom outcomes were improved with use of any experimentally provided cleaner compared with no cleaning product. However, allergen levels measured in dust samples were not affected by cleaning products. Table 10 presents the findings and SOE ratings for the outcomes this study assessed.

Table 10. Cleaning products intervention summary and strength of evidence

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)
Cleaning products vs. no cleaning products	Asthma control	**Inconclusive:** Not possible to determine effectiveness of hypothesized effective intervention of sodium hypochlorite.	1 RCT[62] 97 families	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Exacerbations	**Inconclusive:** Overall rates of exacerbations described as low for all groups (data not shown).	1 RCT[62] 97 families	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Health care utilization	**Not evaluable:** Not reported in included studies.	NA	NA
	Pulmonary physiology	**Not evaluable:** Not reported in included studies.	NA	NA
	Quality of life	**Inconclusive:** Main outcome of quality of life was improved in all groups; authors note the possibility of placebo effect due to keeping diaries in-group with no cleaning products.	1 RCT[62] 97 families	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Symptoms (secondary measure)	**Not evaluable:** Not reported in included studies.	NA	NA
	Allergen levels (secondary measure)	**Inconclusive:** Levels of all dust allergens did not vary statistically as a function of treatment group. Comparative data not shown for cleaning compared with no cleaning in participants with asthma.	1 RCT[62] 97 families	Insufficient (Study limitations, Unknown consistency, Imprecise)

*Outcomes of Asthma control, Exacerbations, Healthcare utilization, and Pulmonary physiology as defined by Asthma Outcomes workshop;[31] outcomes of Quality of life, Symptoms, and Allergen levels as defined by study authors.
NA=not available; RCT=randomized controlled trial

Studies of Multicomponent Interventions

Twenty-five RCTs,[63-87] two nonrandomized trials with concurrent controls,[88,89] and three pre-post studies[90-92] examined interventions that bundled multiple allergen-avoidance strategies. Six of the 30 studies included application of an acaricide to carpeting. Five studies used air-filtration devices. Eight studies recommended or required removal of carpeting in living rooms, bedrooms, or both. Eight studies provided participants with HEPA vacuums. Nineteen studies included use of impermeable mattress covers. Six studies included an intervention intended to reduce or remove mold. Thirteen studies implemented pest control strategies. Two studies suggested pet removal to reduce pet-related allergens. In nine studies, patients were provided general cleaning supplies to help minimize allergens, dust, dirt, and other irritants. Additionally, 11 studies featured a community health worker, social worker, or study team member who visited patient homes to provide direct, tailored education about management of the home environment and offer instruction in the proper use of intervention tools such as mattress covers or vacuums. Finally, 13 studies included some other type of intervention as well, addressing a wide range of potential strategies.

Twenty of the 30 studies were conducted in the United States. Seven studies were conducted exclusively in children, 5 studies enrolled adults and youths age 12 or older, and the remaining

18 studies included all populations. Most of the studies have important limitations that increase potential risk of bias: only 7 of 25 RCTs described an acceptable randomization protocol, just 4 described a procedure for allocation concealment, and 9 included blinding of both patients and outcome assessors. Attrition was also a substantial limitation, with 12 RCTs reporting attrition rates exceeding 15 percent. Only one study reported funding from a commercial source that manufactured the intervention that was studied. Twenty studies judged risk of bias from selective outcome reporting to be low, and 13 studies judged risk of bias from incomplete data reporting to be low. Detailed information on risk of bias for all studies is found in Appendix C.

Another important factor is whether sensitization to the relevant allergen (targeted by the intervention) was assessed in participants before the intervention. Of the 25 RCTs, 11 reported that all enrolled patients were allergic to at least 1 allergen of interest (usually HDM), confirmed in 10 studies by a positive skin-prick test, and with blood tests in the other trial. Seven other RCTs reported that a majority of patients were sensitized (5 studies used skin-prick tests, and 2 used blood tests for confirmation), while four reported lower rates (3 used skin-prick tests, and 1 used blood tests for confirmation). Three studies did not report sensitization in the study participants.

Fifteen of 30 of the multicomponent intervention studies reported the secondary, intermediate outcome of allergen reduction in addition to at least 1 primary outcome. Ten of the studies demonstrated internal consistency between allergen reduction findings and clinical outcomes: seven studies showed significant reduction in allergen levels and significant improvement in at least one primary outcome, while three studies found no reduction in allergens detected and no improvement in clinical outcomes. Only five studies reported significant reductions in allergens but no corresponding improvement in primary outcomes, and no individual studies showed improvement in primary outcomes without evidence of reduced allergen levels.

Given the substantial heterogeneity in the combination of interventions used in these multicomponent studies, as well as variability in implementation and adherence to the interventions, we organized the SOE analysis according to the concept of "grouping by active component."[93] In this approach, each active component was examined by synthesizing the studies that shared a common element in the intervention arm (e.g., use of acaricide), without regard to the other active intervention components in those studies. The "active" components are interventions that were present in each study's intervention arm but not the control arm and are within this review's scope. These active components correlate with the single intervention studies described above: acaricide, air purification, carpet removal, HEPA vacuums, mattress covers, mold removal, pest control, and pet removal. A study that had three different active interventions (e.g., HEPA vacuum, mattress cover, pest control) would therefore be included in the SOE table three different times as it was combined with other studies that shared each respective active intervention. Although this approach limits our confidence in the results by temporarily attributing the outcomes of a complex study to only one of its components in each analysis, we believe this is the best approach to synthesize this evidence in the context of a highly heterogeneous evidence base.

We also considered two alternative analytic approaches. First, we attempted to group the studies into "bundles" that could be characterized by a set of shared components. This was not feasible, however, because the specific combinations of interventions were too diverse, and this approach would have yielded many sets of bundles with minimal numbers of studies in each set. A second approach was to compare studies that had positive findings (i.e., improvement in the primary clinical outcomes) with studies that found no effect and identify differences in the types

of interventions used. This analysis did not detect a pattern of intervention components that was more likely to be present in positive studies. After feedback from peer and public reviewers and AHRQ, we conducted QCA to supplement this assessment of the multicomponent interventions.

Some of the interventions that appear frequently in the studies are excluded from this analysis because they are outside the scope of the review (e.g., community health workers providing education beyond information on allergen reduction strategies). Additionally, pet removal was not assessed because it was a component of only two studies, and within those studies, pet ownership was not an inclusion criterion (i.e., any participants who had pets were encouraged to remove them or restrict their access, but the intervention was not standardized). Table 11 presents an overview of the interventions by study. Table 12 presents the findings and SOE for each primary active component and key outcomes.

Table 11. Multicomponent indoor allergen reduction interventions by study

Study	Acaricide (Dust Mite Pesticide)	Air Purification	Carpet Removal*	HEPA Vacuum	Mattress Covers	Mold Removal	Pest Control	Pet Removal*	Laundering Linens	Cleaning Supplies Provided	CHW Education/ Instruction	Other
Matsui et al. 2017[63]		✓			✓		✓					
DiMango et al. 2016[64]		✓		✓	✓					✓		
Shani et al. 2015[90]**					✓		✓			✓	✓	
Breysse et al. 2014[88]**			✓			✓						Weatherization
Turcotte et al. 2014[91]**				✓			✓			✓	✓	Professional cleaning
Sweet et al. 2013[92]**				✓	✓	✓	✓			✓	✓	Moisture control
El-Ghitany et al. 2012[87]	✓		✓		✓			✓	✓			Ventilation
Takaro et al. 2011[89]**		✓				✓						Ventilation
Bryant-Stephens et al. 2009[69]			✓		✓		✓			✓	✓	
Krieger et al. 2009[68]				✓						✓	✓	
Bryant-Stephens et al. 2008[70]			✓		✓		✓			✓	✓	
Parker et al. 2008[65]				✓	✓		✓			✓	✓	
Burr et al. 2007[82]						✓						Positive ventilation fan
Kercsmar et al. 2006[83]						✓						Moisture control
Williams et al. 2006[71]			✓		✓	✓	✓	✓			✓	Professional cleaning
Eggleston et al. 2005[78]		✓			✓		✓				✓	

Study	Acaricide (Dust Mite Pesticide)	Air Purification	Carpet Removal*	HEPA Vacuum	Mattress Covers	Mold Removal	Pest Control	Pet Removal*	Laundering Linens	Cleaning Supplies Provided	CHW Education/ Instruction	Other
Krieger et al. 2005[66]				✓			✓			✓	✓	
Morgan et al. 2004[67]		✓		✓	✓		✓					
Carter et al. 2001[79]					✓		✓		✓			
Htut et al. 2001[84]									✓			Ventilation; steam heating of mattress, duvet; new pillows
Warner et al. 2000[81]				✓								House-wide ventilation system
Cloosterman et al. 1999[74]	✓				✓							
Evans et al. 1999[86]					✓		✓				✓	
Shapiro et al. 1999[75]	✓				✓				✓			
Hayden et al. 1997[73]	✓		✓		✓				✓			
Carswell et al. 1996[76]	✓				✓				✓			
Marks et al. 1994[77]	✓				✓							
Walshaw et al. 1986[72]			✓		✓							Feather-based bedding replaced
Korsgaard et al. 1983[80]			✓						✓			Mattress vacuuming; pillows and quilts replaced; ventilation; clothes dried outdoors
Burr et al. 1980[85]									✓			Mattress vacuuming; quilts removed; feather pillows replaced
Total	**6**	**5**	**8**	**8**	**19**	**6**	**13**	**2**	**8**	**9**	**11**	

*Applied to some but not all study participants; **Not a randomized controlled trial; CHW= community health worker; HEPA= high-efficiency particulate air-filtration

Table 12. Multicomponent interventions summary and strength of evidence

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
Acaricide (dust mite pesticide) + other interventions vs. placebo	Asthma control	**Not evaluable:** Not reported in included studies.	NA	NA
	Exacerbations	**Inconclusive:** No difference in ED visits or hospitalizations in RCT of 44 mixed-population subjects. Significant reduction in hospitalizations in intervention group in RCT of 160 mixed-population subjects; no between-group comparison.	2 RCTs[75,87] n=204	Insufficient (Inconsistent, Imprecise) **Substantial imprecision
	Healthcare utilization	**Inconclusive:** Significantly less use of bronchodilator or any asthma medication in RCT of 70 children.	1 RCT[76] n=70	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Pulmonary physiology: peak flow	**No effect:** No difference in peak flow in 2 RCTs of 192 adults and RCT of 70 children. Improved peak flow reported in RCT of 23 mixed-population subjects. Improved peak flow in intervention group in RCT of 160 mixed-population subjects; no between-group comparison.	5 RCTs[73,74,76,77,87] n=445	Moderate (Inconsistent)
	Pulmonary physiology: FEV_1	**No effect:** No difference in FEV_1 in 2 RCTs of 192 adults and 2 RCTs of 67 mixed-population subjects. Significant increase in FEV_1 reported in RCT of 70 children. Significant increase in intervention group in RCT of 160 mixed-population subjects; no between-group comparison.	6 RCTs[73-77,87] n=489	Moderate (Inconsistent)
	Quality of life	**Not evaluable:** Not reported in included studies.	NA	NA
	Symptoms (secondary measure)	**No effect:** No difference in frequency of symptoms in 2 RCTs in 192 adults, RCT in 44 mixed-population subjects, and RCT in 70 children.	4 RCTs[74-77] n=306	High
	Allergen levels (secondary measure)	**Reduced allergen:** Significant reduction in HDM allergen found in RCT of 157 adults and RCT of 70 children. Significant reduction in intervention group in RCT of 160 mixed- population subjects; no between-group comparison. No difference in allergen levels in RCT of 35 adults and RCT of 44 mixed-population subjects.	5 RCTs[74-77,87] n=466	Low (Inconsistent, Imprecise)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
Air purification + other interventions vs. no intervention	Asthma control	**No effect:** No difference in ACT or childhood ACT score in RCT of 247 mixed-population subjects.	1 RCT[64] n=247	Low (Unknown consistency, Imprecise)
	Exacerbations	**No effect:** No difference in hospitalizations in 2 RCTs of 1,037 children and 1 RCT of 361 mixed-population subjects. No difference in ED visits in RCT of 937 children and RCT of 361 mixed-population subjects. No difference in "exacerbations" reported in RCT of 247 mixed-population subjects.	4 RCTs[63,64,67,78] n=1,645	High
	Health care utilization: acute care visits	**Inconclusive:** No difference in acute care visits (not defined) in RCT of 100 children.	1 RCT[78] n=100	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Health care utilization and costs: school absenteeism	**Improvement:** Significantly fewer days of missed school reported in RCT of 937 children.	1 RCT[67] n=937	Low (Unknown consistency, Imprecise)
	Pulmonary physiology	**Inconclusive**: No difference in FEV_1 % predicted in RCT of 361 mixed-population subjects.	1 RCT[63] n=361	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Quality of life	**No effect:** No difference in mini-AQLQ scores in RCT of 100 children and RCT of 247 mixed-population subjects.	2 RCTs[64,78] n=347	High
	Symptoms (secondary measure)	**Improved symptoms:** Significant reduction in symptoms in 2 RCTs of 1,037 children. No difference in 2 RCTs of 608 mixed-population subjects.	4 RCTs[63,64,67,78] n=1,645	Low (Inconsistent, Imprecise)
	Allergen levels (secondary measure)	**Allergen reduction:** Significant reduction for HDM, cockroach, cat, dog, and mouse allergen in RCT of 247 mixed-population subjects. Significant reduction in HDM, cockroach, and cat allergen in RCT of 937 children; no difference in dog allergen. Significant reduction in mouse allergen in RCT of 361 mixed-population subjects. No difference in allergens in RCT of 100 children.	4 RCTs[63,64,67,78] n=1,645	Moderate (Inconsistent)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
Carpet removal + other interventions vs. placebo or no intervention	Asthma control	**Not evaluable:** Not reported in included studies.	NA	NA
	Exacerbations	**Inconclusive:** No difference in ED visits or hospitalizations in 2 RCTs of 545 mixed- population subjects. Significant reduction in hospitalizations in intervention group in RCT of 160 mixed-population subjects; no between-group comparison.	3 RCTs[69,70,87] n=705	Insufficient (Study limitations, Inconsistent, Imprecise)
	Health care utilization	**Inconclusive:** Significant reduction in use of inhaled steroids in intervention group in RCT of 50 adults; no between-group comparison. Significant reduction in number of daytime terbutaline puffs in RCT of 46 adults; no difference in nighttime puffs or overall use.	2 RCTs[72,80] n=96	Insufficient (Study limitations, Imprecise) **Substantial imprecision
	Pulmonary physiology	**Inconclusive:** Improved peak flow in intervention group in RCT of 50 adults and RCT of 160 mixed-population subjects; no between-group comparison. No difference in RCT of 46 adults. Significant improvement in RCT in 23 mixed-population subjects.	4 RCTs[72,73,80,87] n=279	Insufficient (Inconsistent, Imprecise) **Substantial imprecision
	Quality of life	**Inconclusive:** Significant improvement in PACQLQ scores in nonrandomized trial of 102 mixed-population subjects.	1 non-RCT[88] n=102	Insufficient (Unknown consistency, Imprecise) **Non-RCT
	Symptoms (secondary measure)	**Inconclusive:** No difference in symptoms in RCT of 50 adults and 2 RCTs of 545 mixed- population subjects. Significant reduction in symptoms in RCT of 161 children. Significant reduction in daytime scores, no difference in nighttime scores in RCT of 46 adults.	5 RCTs[69-72,80] n=802	Insufficient (Study limitations, Inconsistent, Imprecise)
	Allergen levels (secondary measure)	**Allergen reduction:** Significant reduction in HDM allergen levels in 2 RCTs in 96 adults and RCT in 161 children. Significant reduction in intervention group in RCT of 160 mixed-population subjects; no between-group comparison.	4 RCTs[71,72,80,87] n=412	Moderate (Study limitations)
HEPA vacuum + other interventions vs. placebo or no intervention	Asthma control	**Inconclusive:** No difference in ACT or childhood ACT scores in RCT of 247 mixed- population subjects.	1 RCT[64] n=247	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Exacerbations: composite measure based on level of care	**Reduction:** Significant improvement in composite measure of hospitalization, ED visits, and acute care clinic visits in 3 RCTs of children.	3 RCTs[65-67] n=1,509	Moderate (Study limitations)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Exacerbations: unspecified	**No effect:** No difference in undefined "exacerbations" or "asthma attacks" in 2 RCTs of mixed-population subjects.	2 RCTs[64,68] n=556	Moderate (Imprecise)
	Health care utilization: medication use	**No effect:** No difference in use of rescue inhaler or beta agonists in 3 RCTs of mixed- population subjects.	3 RCTs[64,66,68] n=830	High
	Health care utilization and costs: school absenteeism	**No effect:** No difference in missed school days in 2 RCTs (n=583). Significant reduction in 1 RCT (n=937).	3 RCTs[66-68] n=1,520	Low (Inconsistent, Imprecise)
	Health care utilization and costs: work absenteeism	**No effect:** No difference in missed workdays.	2 RCTs[66,68] n=583	Moderate (Study limitations)
	Health care utilization and costs: missed activities	**Reduction:** Fewer days of missed activities in RCT of 937 children and RCT of 274 mixed- population subjects. No difference in RCT of 309 mixed-population subjects.	3 RCTs[66-68] n=1,520	Low (Inconsistent, imprecise)
	Pulmonary physiology: peak flow	**Inconclusive:** No difference in RCT of mixed- population subjects	1 RCT[81] n=40	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Pulmonary physiology: FEV_1	**Inconclusive:** No difference in RCT of mixed- population subjects.	1 RCT[64] n=247	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Quality of life: PACQLQ	**Improvement:** PACQLQ score improved significantly in 2 RCTs.	2 RCTs[66,68] n=583	Moderate (Study limitations)
	Quality of life: mini-AQLQ	**Inconclusive:** No difference in mini-AQLQ scores in RCT of mixed-population subjects.	1 RCT[64] n=247	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Quality of life: CHSA	**Inconclusive:** Significant improvement in CHSA scores in pre-post study of 170 mixed- population subjects.	1 pre-post[91] n=170	Insufficient (Unknown consistency, Imprecise) **Non-RCT
	Symptoms: children (secondary measure)	**Improved symptoms:** Significant decrease in symptom days in 2 RCTs (n=1,235). No difference in symptom days in 1 RCT (n=274).	3 RCTs[65-67] n=1,509	Low (Study limitations, Inconsistent)
	Symptoms: mixed populations (secondary measure)	**No effect:** No difference in 2 RCTs (n=287) in frequency of symptoms. Significant reduction in symptom days in 1 RCT (n=309).	3 RCTs[64,68,81] n=596	Moderate (Inconsistent)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Allergen levels: house dust mites (secondary measure)	**Inconclusive:** 3 RCTs did not specify Der p or Der f; 1 found significant reduction in allergen levels, 1 found no difference, and 1 found significant reduction in both intervention and control but had no comparison. A fourth RCT found reduced Der f but not Der p.	4 RCTs[64,65,67,81] n=1,522	Insufficient (Study limitations, Inconsistent, Imprecise)
	Allergen levels: cats and dogs (secondary measure)	**Inconclusive:** 1 RCT found significant reduction in cat levels but not dog; 1 RCT found significant reduction in dog but not cat; 1 RCT found significant reductions in cat and dog in intervention group, but had no between-group comparison.	3 RCTs[64,65,67] n=1,195	Insufficient (Inconsistent, Imprecise) **Substantial inconsistency
	Allergen levels: cockroach (secondary measure)	**Reduction:** 1 RCT found significant reduction in cockroach levels; 1 RCT found significant reduction in intervention group but had no between-group comparison.	2 RCTs[64,67] n=1,184	Moderate (Imprecise)
Mattress covers + other interventions vs. placebo or no intervention	Asthma control	**Inconclusive:** No difference in ACT or childhood ACT in 1 RCT (n=247).	1 RCT[64] n=247	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Exacerbations: ED visits	**No effect:** No difference in 3 RCTs (n=906).	3 RCTs[63,69,70] n=545	Low (Study limitations, Imprecise)
	Exacerbations: hospitalization	**No effect:** No difference in 6 RCTs (n=2,976).	6 RCTs[63,67,69,70,78,86] n=2,976	High
	Exacerbations: unscheduled care including ED, hospital, outpatient	**Inconclusive:** No difference in 3 RCTs (n=1,181) on composite measure of unscheduled care; significant reduction in 2 RCTs (n=1,235).	5 RCTs[65,67,75,79,86] n=2,416	Insufficient (Inconsistent, Imprecise) **Substantial inconsistency
	Health care utilization: acute care visits	**No effect:** No difference in 3 RCTs (n=1,318) of unscheduled acute care visits.	3 RCTs[67,70,78] n=1,318	Moderate (Study limitations)
	Health care utilization: medication use	**Inconclusive:** Reduced use of any asthma medication in 1 RCT (n=70); no difference in use of rescue inhaler in 1 RCT (n=247).	2 RCTs[64,76] n=317	Insufficient (Inconsistent, Imprecise) **Substantial imprecision
	Health care utilization and costs: school absenteeism	**Reduction:** Significantly fewer missed school days in 1 RCT (n=937).	1 RCT[67] n=937	Low (Unknown consistency, Imprecise)
	Health care utilization and costs: missed activities	**Reduction:** Fewer days of missed activities in 1 RCT (n=937).	1 RCT[67] n=937	Low (Unknown consistency, Imprecise)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Pulmonary physiology: peak flow	**Inconclusive:** Significant improvement in peak flow in 2 RCTs (n=321); no difference in 3 RCTs (n=262).	5 RCTs[65,73,74,76,77] n=583	Insufficient (Inconsistent, Imprecise) **Substantial inconsistency
	Pulmonary physiology: FEV_1	**No effect:** No difference in 7 RCTs (n=1,804); significant improvement in 1 RCT (n=70).	8 RCTs[63,64,67,73-77] n=1,874	High
	Quality of life	**No effect:** No difference in 1 RCT using AQLQ; no difference in 2 RCTs using unspecified quality-of-life scales.	3 RCTs[64,75,78] n=144	Moderate (Study limitations)
	Symptoms: composite symptom score (secondary measure)	**No effect:** No difference in 4 RCTs that used different sets of symptoms to derive composite scores (n=483).	4 RCTs[64,74,75,77] n=483	High
	Symptoms: symptom days (secondary measure)	**Reduction:** Significantly fewer days reported with symptoms in 4 RCTs (n=2,368); no effect reported in 1 RCT.	5 RCTs[63,65,67,78,86] n=2,729	High
	Symptoms: cough and wheeze (secondary measure)	**No effect:** No change in frequency of cough in 3 RCTs; reduced cough reported in 1 RCT; no change in frequency of wheeze reported in 4 RCTs; reduced wheeze reported in 1 RCT.	5 RCTs[65,67,69,70,76] n=1,850	Low (Study limitations, Inconsistent)
	Allergen reduction (secondary measure)	**Reduction:** Significant reduction in Der allergen reported in 4 RCTs (n=1,305); no effect reported in 4 RCTs (n=477).	8 RCTs[65,67,71,72,74,75,77,78] n=1,782	Low (Inconsistent, Imprecise)
Mold removal + other interventions vs. placebo or no intervention	Asthma control	**Not evaluable**: Not reported in included studies.	NA	NA
	Exacerbations	**Inconclusive:** No difference in number of urgent care or ED visits in RCT of 62 mixed- population subjects.	1 RCT[83] n=62	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Health care utilization	**Inconclusive:** Reduced need for relief medication in RCT of 232 mixed-population subjects.	1 RCT[82] n=232	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Pulmonary physiology	**Inconclusive:** No difference in peak flow variability in RCT of 232 mixed-population subjects.	1 RCT[82] n=232	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Quality of life	**Inconclusive:** No difference in mean CHSA scores in RCT of 62 mixed-population subjects.	1 RCT[83] n=62	Insufficient (Study limitations, Unknown consistency, Imprecise)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Symptoms (secondary measure)	**Improved symptoms:** Significant decrease in symptoms in RCT of 161 children and RCT of 62 mixed-population subjects.	2 RCTs[71,83] n=223	Low (Study limitations, Imprecise)
	Allergen levels (secondary measure)	**Inconclusive:** Significant reduction in mold scores in RCT of 62 mixed-population subjects.	1 RCT[83] n=62	Insufficient (Study limitations, Unknown consistency, Imprecise)
Pest control + other interventions vs. placebo or no intervention	Asthma control	**Inconclusive:** No difference in ACT or childhood ACT scores in pre-post study of 80 mixed-population subjects.	1 pre-post[90] n=80	Insufficient (Unknown consistency, Imprecise) **Pre-post study
	Exacerbations: Composite measure of urgent care	**Reduction:** Significant improvement in composite measure of hospitalization, ED visits, and acute care clinic visits in 3 RCTs of 1,509 children and RCT of 104 mixed- population subjects.	4 RCTs[65-67,79] n=1,613	Moderate (Study limitations)
	Exacerbations: Hospitalization	**No effect:** No difference in hospitalizations in 3 RCTs of 2,070 children and 2 RCTs of 625 mixed-population subjects. No difference in inpatient days in RCT of 281 mixed-population subjects.	6 RCTs[63,67,69,70,78,86] n=2,976	High
	Exacerbations: ED visits	**No effect:** No difference in ED visits in 1 RCT of 937 children and 3 RCTs of 906 mixed- population subjects.	4 RCTs[63,67,69,70] n=1,843	Moderate (Study limitations)
	Health care utilization: acute care clinic visits	**No effect:** No difference in clinic visits for acute care in 3 RCTs of 2,070 children.	3 RCTs[67,78,86] n=2,070	High
	Health care utilization: medication use	**Inconclusive:** No difference in use of beta-agonist or controller medications in RCT of 274 children.	1 RCT[66] n=274	Insufficient (Study limitations, Unknown consistency, Imprecise)
	Health care utilization and costs: school absenteeism/ patient activities	**Improvement:** Significantly fewer days with activity limitations in 2 RCTs of 1,211 youths. Significantly fewer missed school days in RCT of 937 children, but no difference in RCT of 274 children.	4 RCTs[65-67,78] n=1,609	Low (Study limitations, Inconsistent)
	Health care utilization and costs: work absenteeism/ caretaker plans	**No effect:** No difference in missed days of work or caretaker plans changed in 2 RCTs of 1,211 children.	2 RCTs[66,67]	Low (Study limitations, Imprecise)
	Pulmonary physiology: peak flow	**Inconclusive:** Significant increase in peak flow in RCT of 298 children. No difference in peak flow variability.	1 RCT[65] n=298	Insufficient (Study limitations, Unknown consistency, Imprecise)

Comparison	Outcome*	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale)**
	Pulmonary physiology: FEV_1	**Inconclusive:** Significant increase in FEV_1 from baseline (but no comparison between groups) in RCT of 298 children. No difference between groups in FEV_1 in RCT of 937 children and RCT of 361 mixed-population subjects.	3 RCTs[63,65,67] n=1,596	Insufficient (Inconsistent, Imprecise) **Substantial imprecision
	Quality of life: PACQLQ	**Improvement:** PACQLQ score improved significantly in RCT of 274 children.	1 RCT[66] N=274	Low (Study limitations, Unknown consistency)
	Quality of life: other measures	**Inconclusive:** No difference in RCT of 100 children in composite quality-of-life score (domains not described).	1 RCT[78] N=100	Insufficient (Unknown consistency, Imprecise) **Substantial imprecision
	Symptoms (secondary measure)	**Improved symptoms:** Significant decrease in symptom days or frequency of symptoms in 5 RCTs of 2,529 children. No difference in symptom days in RCT of 274 children and RCT of 361 mixed-population subjects. No difference in cough or wheeze in 2 RCTs of 545 mixed-population subjects.	9 RCTs[63,65-67,69-71,78,86] n=3,709	Low (Study limitations, Inconsistency)
	Allergen levels: cockroach (secondary measure)	**Reduction:** Significant reduction in cockroach allergen in RCT of 937 children. No difference in RCT of 100 children. Significant reduction at 4 and 8 months but not 12 months in RCT of 161 children.	3 RCTs[67,71,78] n=1,198	Low (Inconsistent, Imprecise)
	Allergen levels: mouse (secondary measure)	**Inconclusive:** Significant reduction in mouse allergen in RCT of 937 children and RCT of 361 mixed-population subjects. No difference in 2 RCTs of 398 children.	4 RCTs[65,67,78] n=1,696	Insufficient (Inconsistent, Imprecise) **Substantial inconsistency

*Outcomes of Asthma control, Exacerbations, Healthcare utilization, and Pulmonary physiology as defined by Asthma Outcomes workshop;[31] outcomes of Quality of life, Symptoms, and Allergen levels as defined by study authors.

** Criteria for downgrading strength of evidence is described as Rationale; when these criteria are insufficient for understanding the final strength of evidence, additional explanation is provided.

ACT=asthma control test; AQLQ=asthma quality of life questionnaire; Bla g=*blatella germanica* cockroach allergen; CHSA=children's health survey for asthma; Der f=*dermatophagoides farina* allergen; Der p=*dermatophagoides pteronyssinus* allergen; ED=emergency department; FEV_1=forced expiratory volume in 1 second; HDM=house dust mite; HEPA=high-efficiency particulate air-filtration; Mus m=*mus musculus* mouse allergen; NA=not available; PACQLQ=pediatric asthma caregivers asthma quality of life questionnaire; RCT=randomized controlled trial

Qualitative Comparative Analysis

Inputs

We included single intervention as well as multicomponent intervention studies in the analysis. Although the initial decision to conduct a qualitative comparative analysis (QCA) assessment was intended to refine our review of multicomponent interventions, we did not restrict the analysis to those studies. Including both single and multicomponent trials in the model provided two benefits: (1) expanding the number of studies enabled a more robust analysis; and (2) we could search for effects potentially associated with each intervention across single and multicomponent studies.

The analysis included 49 studies. We excluded studies that were not RCTs, studies that did not include one of the six interventions that we assessed for both single and multicomponent trials, and studies that did not report usable data for at least one primary outcome.

To simplify the model we created a composite outcome measure. Each study that demonstrated at least one statistically significant beneficial effect on any of the primary outcomes was coded as having a "positive outcome." Each study that found no effect on every primary outcome measure it reported was coded as having a "negative outcome." This dichotomous approach was selected to maximize the possibility of finding an effect and was expected to be necessary given the relatively few studies in this review that reported positive findings.

Step 1. Testing for Necessary or Sufficient Conditions

One parameter of fit-for-testing necessity and sufficiency of each discrete intervention is *consistency*, displayed in Table 13. Consistency assesses whether the causal pathway produces the outcome regularly. Consistency estimates for necessity range between 0.136 and 0.545. Consistency estimates for sufficiency range between 0.417 and 0.714. None of these values exceed the standard consistency threshold of ≥0.9. Thus, these results suggest that no individual intervention, whether implemented alone or as part of a multicomponent strategy, is either necessary or sufficient to improve asthma outcomes. This does not mean that these interventions are not effective; rather, it may suggest that further research is needed to better evaluate the effectiveness of both single and multicomponent strategies.

Table 13. Results of consistency analyses: necessity and sufficiency of interventions

Conditions	Necessity	Sufficiency
Acaricides (dust mite pesticide)	0.227	0.455
Air purification	0.227	0.417
Carpet removal	0.136	0.600
HEPA vacuum	0.227	0.714
Mattress covers	0.545	0.429
Pest control	0.227	0.500

HEPA=high-efficiency particulate air-filtration

Step 2. Constructing the Truth Table

We examined six interventions; therefore, the truth table has 2^6=64 rows representing all logically possible combinations of these conditions. The truth table is presented in Table 14. Only five configuration sets lead to the presence of a positive outcome (i.e., Outcome = 1), with high consistency scores. Conversely, there are many remainders, which are combinations of

interventions and outcomes that theoretically could exist, but were not present in any of the included studies. Also, six configurations lead to contradictory outcomes (i.e., Outcome = "C"), indicating that identical allergen reduction strategies resulted in some studies that found beneficial effects and others that did not.

Table 14. Truth table for allergen reduction interventions

Configuration	Acaricide	Air Purification	Carpet Removal	HEPA Vacuum	Mattress Cover	Pest Control	Outcome	n	Consistency
2	0	0	0	0	0	1	C	2	0.500
3	0	0	0	0	1	0	C	14	0.357
4	0	0	0	0	1	1	C	2	0.500
5	0	0	0	1	0	0	C	3	0.667
6	**0**	**0**	**0**	**1**	**0**	**1**	**1**	**1**	**1.000**
8	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**1**	**1.000**
9	**0**	**0**	**1**	**0**	**0**	**0**	**1**	**1**	**1.000**
12	0	0	1	0	1	1	0	2	0.000
17	0	1	0	0	0	0	C	9	0.444
20	0	1	0	0	1	1	0	1	0.000
23	0	1	0	1	1	0	0	1	0.000
24	**0**	**1**	**0**	**1**	**1**	**1**	**1**	**1**	**1.000**
33	1	0	0	0	0	0	0	5	0.200
35	1	0	0	0	1	0	C	4	0.500
43	**1**	**0**	**1**	**0**	**1**	**0**	**1**	**2**	**1.000**

For columns identifying interventions (Acaricide, Air Purification, Carpet Removal, HEPA Vacuum, Mattress Cover, and Pest Control), "1" indicates that the specific intervention was included in the given configuration, and "0" indicates that the specific intervention was not included in the given configuration; For the column identifying Outcome, "1" indicates that all studies using the given configuration reported a positive result for at least one primary outcome, "0" indicates that all studies using the given configuration reported no positive results for any primary outcome, and "C" indicates that the studies were contradictory, with at least one study reporting at least one positive result while at least one other study reported no positive results; Configurations where all included studies reported at least one positive result are in **bold**

HEPA= high-efficiency particulate air-filtration

Step 3. Solutions

Our analysis included 49 studies, with only 22 that showed significant improvement in at least 1 primary outcome. The Boolean analysis of the truth table found no conditions that were necessary, either individually or in combination. Therefore, no intervention or bundle of strategies appears to be required to produce improvement in asthma outcomes.

Analysis of sufficient combinations identified two solutions, each with 100 percent consistency. These solutions, shown in Figure 4, were use of carpet removal without use of pest control and combined use of a HEPA vacuum and pest control. The first solution may not have an empirical explanation and might be an artifact of the few studies evaluated. Three studies used carpet removal, did not use pest control, and found improvement in asthma outcomes. One of these studies used only carpet removal, while the other two studies also used mattress covers and acaricides. Conversely, two studies that used carpet removal as well as pest control found no improvements in outcomes, but these studies also used mattress covers. Further, five other included studies with positive results used pest control. We conclude that it is unlikely that avoidance of pest control is inherently associated with better asthma outcomes when carpet is removed.

The second solution includes use of a HEPA vacuum paired with pest control. Three studies used this combination, and all three resulted in improvement. However, these studies varied in study design. One of the three studies used only vacuums and pest control, one also used mattress covers, and a third used mattress covers and air purification devices, in addition to vacuums and pest control interventions. Therefore, although the combination of HEPA vacuums and pest control might logically improve outcomes by routinely addressing multiple types of allergens, the evidence base is too small to support any strong conclusions.

A final limitation of these solutions is the small coverage they provide. Coverage refers to how many studies with positive outcomes are included in the solutions, and thus demonstrates whether the solution combinations we identified can explain most of the positive findings in the literature. Taken together, our two solutions have 27 percent coverage, accounting for just 6 of the 22 studies that reported improvement in primary asthma outcomes. This is a very low estimate, and suggests that we cannot confidently determine whether specific combinations of interventions are likely to improve outcomes.

Figure 4. Solutions for qualitative comparative analysis

```
n OUT = 1/0/C: 6/9/34
  Total       : 49

p.sol: CARPET.REMOVAL*pest.control + HEPA.VACUUM*PEST.CONTROL

M1:    HEPA.VACUUM*PEST.CONTROL + CARPET.REMOVAL*pest.control => ANY.OUTCOME

                                incl   PRI    cov.r  cov.u
-------------------------------------------------------
1  CARPET.REMOVAL*pest.control  1.000  1.000  0.136  0.136
2  HEPA.VACUUM*PEST.CONTROL     1.000  1.000  0.136  0.136
-------------------------------------------------------
   M1                           1.000  1.000  0.273
```

cov.r= raw coverage, or how much of the outcome is represented by the given configuration; cov.u= unique coverage, or how much of the outcome is represented by only the given configuration and no other configurations; HEPA= high-efficiency particulate air-filtration; PRI= proportional reduction in inconsistency

Discussion

Key Findings and Strength of Evidence

We identified 60 randomized controlled trials (RCTs) and 8 additional studies (4 nonrandomized trials and 4 pre-post studies) that examined 8 types of interventions, alone or in combination, to reduce allergen levels in the home and improve the wellbeing of patients with asthma. Thirty-eight studies evaluated isolated interventions, and 30 studies used multicomponent strategies. Thirty-six studies enrolled patients above and below the age of 12, while 22 studies were limited to patients over 12 years old, and 9 studies were limited to patients less than 12 years old. Forty RCTs confirmed that all of their enrolled patients were sensitized to an allergen that was targeted by their intervention, and an additional 14 studies reported that a majority of patients were sensitized. Sensitization was confirmed through skin- prick testing in 43 of the 60 RCTs.

Seven studies examined the use of acaricide as the sole intervention designed to eliminate house dust mite (HDM) allergens. The evidence found no improvement in pulmonary physiology when comparing acaricide with placebo (strength of evidence [SOE]: moderate) or with other interventions (SOE: low), and other outcomes were inconclusive or not reported. Six multicomponent studies included acaricide and provide evidence suggesting no improvement in pulmonary physiology (SOE: moderate), while other primary outcomes were inconclusive or not reported. These multicomponent studies also found no improvement in the secondary outcome of asthma symptoms (SOE: high). However, acaricides were shown to reduce the secondary outcome of HDM allergen burden (SOE: low).

Nine studies evaluated the use of air purification as a single intervention. The evidence for asthma control and pulmonary physiology measures was inconclusive, while health care utilization was unchanged (SOE: low) and quality of life improved (SOE: low). Five additional studies included air purifiers within multicomponent strategies and observed no improvement in asthma control (SOE: low), exacerbations (SOE: high), or quality of life (SOE: high). However, school absenteeism was reduced (SOE: low). The secondary measures of asthma symptoms improved (SOE: low), and allergen levels were reduced (SOE: moderate).

No studies looked solely at removal of carpeting as an intervention. Eight multicomponent studies encouraged participants to remove carpets from their homes, but we could not determine from the studies how many patients actually removed carpeting or from which rooms. Evidence from these studies is inconclusive for clinical outcomes, although significant reduction in the secondary outcome of allergen levels was observed (SOE: moderate).

One small study examined high-efficiency particulate air-filtration (HEPA) vacuums alone, but the evidence base is insufficient to draw conclusions. Eight multicomponent studies included HEPA vacuums along with other strategies. The evidence was insufficient for asthma control and pulmonary physiology measures. Exacerbations were reduced (SOE: moderate) although medication use was unchanged (SOE: high), and no effect was seen for school absenteeism (SOE: low) or work absenteeism (SOE: moderate). Quality of life was improved among children (SOE: moderate). In addition, the multicomponent studies found that secondary measures of asthma symptoms improved among children (SOE: low) but not among mixed populations (SOE: low).

Seventeen studies focused on impermeable mattress covers or other approaches designed to limit HDM allergens on bedding. The evidence suggests no difference in exacerbations, health care utilization, pulmonary physiology, or quality of life (SOE: high), although these studies

suggest that the presence of HDM allergen was reduced significantly (SOE: moderate). Mattress covers were also used in 19 multicomponent intervention studies. In these studies, covers were associated with reduced school absenteeism and fewer missed activities (SOE: low), but no improvement was identified for emergency department use (SOE: low), hospitalizations (SOE: high), acute care visits (SOE: moderate), pulmonary physiology (SOE: high), or quality of life (SOE: moderate). Evidence was mixed for the secondary measure of asthma symptoms, with no difference detected for composite measures (SOE: high), but a reduction in symptomatic days was observed (SOE: high). Finally, allergen levels were reduced in the multicomponent studies that included mattress covers (SOE: low).

The single-intervention studies did not address mold removal, but six multicomponent studies did feature it. Secondary measures of asthma symptoms improved (SOE: low), but other outcomes were inconclusive.

One nonrandomized study used pest-control strategies alone. The findings of this study were insufficient to draw any conclusions. Thirteen multicomponent studies included pest-control efforts. The evidence was inconclusive for asthma control, pulmonary physiology measures, and medication use. Exacerbations were reduced when measured as a composite score (SOE: high), but no effect was observed when individual measures such as emergency department visits (SOE: moderate) and hospitalizations (SOE: high) were examined. Quality of life among children (SOE: low) was improved, and school absenteeism was reduced (SOE: low). The secondary outcome of asthma symptoms also showed improvement (SOE: low), and allergen levels were reduced (SOE: low).

One nonrandomized study examined pet removal as a single strategy. The evidence was inconclusive for exacerbations and health care utilization, and no other outcomes were reported. Two multicomponent interventions also included pet removal, but we did not evaluate the SOE because of the small number of studies.

One important factor in assessing the effectiveness of interventions is the role of the intermediate outcome of allergen reduction as measured on home surfaces. In the studies of single interventions, we found that evidence for allergen reduction was generally consistent with evidence for the primary clinical outcomes. Specifically, the evidence for primary outcomes was either inconclusive or showed low SOE for no effect, and our conclusions for the allergen reduction outcomes were similar. The only exception was the evidence for mattress covers. When mattress covers were used, we found moderate-strength evidence demonstrating significant reduction of allergen levels; however, this did not result in a corresponding improvement in the primary clinical outcomes, for which we found high- or moderate-strength evidence for no effect.

Within the studies of multicomponent interventions, 10 trials found that allergen reduction outcomes were consistent with primary outcomes, sharing either significant improvement or no change. Five studies, however, reported decreased allergen levels that did not lead to better clinical results, and no individual studies showed improved primary outcomes without reduced allergen levels. Unfortunately, half of the multicomponent intervention studies did not report the data needed to evaluate the interaction between allergen levels and patient outcomes.

Evaluation of the studies with qualitative comparative analysis (QCA) reinforces these findings. We developed a simplified model and used a low threshold for defining positive results, but nevertheless did not identify any single intervention of bundle of strategies that appears to reliably result in better outcomes for patients with asthma. The only empirically plausible solution we derived includes a combination of pest control with use of a HEPA vacuum, but the solution is based on three studies that are heterogeneous in other ways. Evaluation of the

published studies with QCA thus confirms that we lack strong evidence about the effectiveness of allergen reduction interventions.

Findings in Relation to What Is Already Known

These findings are generally consistent with previous Cochrane reviews. In 2011, Gotzsche and Johansen updated their Cochrane systematic review of strategies for controlling house dust mite (HDM) exposure, including mattress covers and acaricides.[94] Similar to our review, the authors found that these interventions were not associated with significant clinical effects, and they characterized the overall evidence base as lacking necessary rigor. In 2009, Kilburn and colleagues published a Cochrane review of air-filtration devices for reducing pet allergens.[95] They identified only two relevant studies, and neither demonstrated clinical benefit. The authors concluded that the evidence base was insufficient to draw any conclusions.

In contrast to our findings, a 2010 systematic review by Krieger et al. examined most of the same intervention types addressed in our review and found the evidence for some strategies to be compelling.[96] They conclude that multicomponent interventions that are tailored to a patient or family are effective. Their review also found that pest control and strategies to reduce moisture and mold were effective in reducing both mold and allergy symptoms. Although their review examined many of the same studies included in our current review, unlike our review, their review emphasized different outcomes, such as evidence suggesting reduced allergen levels on mattresses, floors, and carpets. In addition, they did not use a formal approach in their review of the evidence (such as the Evidence-based Practice Center (EPC) approach), and instead used a less formal approach incorporating expert opinion and epidemiologic evidence drawn from noninterventional studies. Likely because of these methodological differences, Krieger et al. concluded that individual interventions demonstrate consistent clinical benefits, while our review demonstrates limited strength of evidence based on the heterogeneity and inconsistent results among the studies that we evaluated.

Similarly, methodological differences in our respective approaches likely results in conclusions that vary from the review that was used to support the 2007 guidelines of the National Heart, Lung, and Blood Institute (NHLBI)[1] as well as clinical practice parameters published by the American Academy of Allergy, Asthma, and Immunology.[97-100] Whereas the prior review for the preparation of EPR-3 suggested there was greater benefit for the interventions intended to reduce exposure to allergens, our review identified deficits in the evidence base with low or insufficient strength of evidence (SOE). Our review differed in the studies included, with some publications after 2007 detecting no clinical effects of the interventions. In addition, our focus was intentionally restricted to studies with data on validated, clinical outcome measures, and we used alternative methods to assess the risk of bias, which also influenced the SOE ratings. Most importantly, we used the EPC approach to evaluate the evidence base, and our conclusions were therefore shaped by a methodology that was not used in the reviews that informed the earlier guidelines. These differences may account for variations between our assessment of the evidence and the preceding reviews.

Applicability

There was substantial variability in patients' baseline clinical characteristics suggesting that patients were not equally likely to benefit from the interventions we reviewed. Although sensitization to common indoor inhalant allergens was measured in most studies we evaluated, sensitization is a proxy measure that does not perfectly predict whether a patient will have an

allergic reaction when exposed under real-world conditions, nor does sensitization precisely identify the severity of a potential reaction. Therefore, although 40 of 60 randomized controlled trials (RCTs) reported that all enrolled patients were sensitized to at least 1 allergen, and an additional 14 trials reported that a majority of patients were sensitized, none of these studies identified how many patients exhibited signs or symptoms of allergic reaction. Moreover, variation in how sensitization is measured is an important related factor. Skin-prick testing is considered the most accurate method for assessing sensitization; 43 studies used this method. However, 13 studies measured sensitization using blood tests, which are viewed as a less reliable predictor of true allergy. Some patients in these studies were probably not actively allergic and therefore unlikely to benefit from the interventions. Inclusion of these patients may help explain the lack of effect observed across the evidence base. Due to these challenges in assessing the allergic status of patients included in clinical studies, we are limited in our ability to assess the applicability of the overall evidence base to real-world patients with asthma.

In addition to the potential utility of documenting sensitization status to characterize patients with asthma in these clinical studies, the generalizability of the findings is also likely affected by disease severity. Based on the outcomes defined in Table 1, we expect that underlying asthma severity influenced our ability to detect a treatment effect. For example, if patients with mild asthma are unlikely to have an exacerbation within any given 12–24 week period (even without treatment), then assessing the effect of allergen removal (versus no intervention) on exacerbations will not show a difference between the groups (because no one has exacerbations) even if the allergen removal is effective. In our review, only 18 RCTs classified the severity of participants' asthma: 11 studies included patients with moderate to severe asthma, 5 studies included patients with mild to moderate asthma, and 2 studies had populations with mixed severity. More importantly, 42 studies did not report asthma severity when characterizing the patient population. Therefore, it is possible that the results were affected by asthma severity (e.g., no effects were shown in patients with mild disease) and in most studies we have no information on disease severity to assess the impact of asthma severity on our conclusions. Similarly, we cannot draw conclusions regarding which patients are most likely to respond to allergen removal interventions based on disease severity or how long after the allergen removal clinical effects should be seen in the absence of consistent data.

A third major factor is the age of patients with asthma. Current clinical guidelines organize treatment recommendations along an age continuum in which "children" are identified as patients age 11 or younger, while youths 12 year of age or older are combined with adults. However, 33 studies we reviewed include patients from both groups. This is often due to studies enrolling populations that would, in other clinical contexts, be considered "pediatric" or "adolescent" (e.g., enrolling patients age 5 to 15 years old). It is therefore challenging to apply the results of studies in these "mixed" populations to the discrete categories of "child" or "adult." Given the limited robustness of most study results, however, it is unclear whether better alignment between study population age cohorts and treatment categories would result in different overall findings.

The applicability of our findings is also limited by the type of interventions we assessed. One important consideration is the challenge of implementing home-based interventions properly and completely. Many of the interventions we reviewed may be difficult for families to implement due to cost, language, technology, home ownership, and health literacy. Socioeconomic status can also play a role in implementation, as can the type of living unit (e.g., house or apartment, attached or detached, single family or multifamily). Nearly half of the multicomponent intervention studies, 13 of 30, included a community health worker who received specialized

training to educate patients on how to reduce home allergen exposure in a highly tailored way. Although we did not evaluate the direct impact of these health workers because they have traditionally focused on patient education activities, their role in the process of implementing home-based strategies may be important.

Similarly, it is difficult to measure fidelity to proper use of 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 these findings or discuss these challenges. In clinical practice, it is likely difficult to assess how successfully a patient adheres to use of an allergen-reduction strategy.

Another important factor is the potential exposure to indoor allergens outside the home. Patients with asthma may be exposed to allergens at work or school or while engaged in other activities. Such exposure may limit the effectiveness of interventions that are implemented only at home. This review was designed to include studies that evaluated interventions in work or school environments, but we did not identify any studies that fit those criteria.

An additional consideration is the role that exposure to outdoor allergens or non-allergen irritants may have on asthma outcomes. Inhalation of tobacco smoke, other pollutants, pollen, or microbes may trigger morbidity for patients with asthma and reduce the overall effectiveness of targeted interventions.

Finally, a major factor to consider is the distinction between single interventions that address a single allergen (e.g., acaricide for HDM allergen), single interventions that address multiple allergens (e.g., air purifiers), and multicomponent interventions that usually target more than one allergen. Since patients vary in their sensitization to different allergens, the interplay between allergen type, intervention type, and individual patient characteristics may strongly modify the effect of these interventions.

When considering the control or comparison conditions, a further limitation is the inherent difficulty in evaluating the relationship between individual interventions within a multicomponent strategy. Multicomponent studies represent nearly half of the evidence base, but interpretation of their results is challenging. Since we were unable to identify specific “bundles” of interventions, or detect patterns among the studies that reported positive results, our analytic approach focused on assessing active components separately. This strategy may under- or over-emphasize the role of specific interventions, and overlook the importance of their interaction. The evidence base is also limited by a lack of head-to-head comparisons between interventions. Almost all the studies we assessed compared a single intervention or a bundle of interventions with either a placebo group or no intervention. We are therefore unable to assess whether a particular intervention may be more effective than another active intervention.

With respect to outcomes, very few studies reported critical, discrete, validated outcome measures, which have established thresholds for clinical significance such as Asthma Control Test (ACT) or Asthma Quality of Life Questionnaire [AQLQ] (see Appendix E). While many studies reported data for forced expiratory volume in one second (FEV_1) or rescue medication use, they varied in their reporting, limiting meaningful comparisons across trials. Other studies employed composite metrics (e.g., a global measure of hospitalizations, emergency department visits, and urgent care visits). The relative paucity of studies using current, standardized measures limited our interpretation of the primary outcome measures.

Some of the validated, clinically important outcomes we used for our review also take an extended observation period to detect a change; whereas asthma symptoms may change in a matter of days in response to an intervention, lung function or health care utilization may take several months before the effect of removing an allergen is observed. Treatment duration in the

included studies ranged from 4 weeks to 3.5 years, with most studies falling within the range of 6 to 12 months. As maintaining an allergen-reduction strategy over time, particularly a multicomponent intervention, is challenging, studies employing short treatment times may not be reflective of real-world use of these interventions.

There was a high level of heterogeneity across studies, particularly related to patient characteristics and the combinations of treatments examined, that limited our ability to assess generalizability to the overall population of people with asthma.

Implications for Clinical and Policy Decisionmaking

This review highlights several important considerations for patients, clinicians, and policymakers. Since asthma can significantly affect overall health and quality of life, patients and their families may be motivated to adopt interventions that are not physically invasive, such as use of mattress covers or air purifiers, to augment pharmacologic treatment. It is important for clinicians to consider the complexity of the patient population and the limitations of the evidence that we have identified. Clinicians may also find it helpful to consider the severity of a patient's asthma and the extent of previous symptoms and exacerbations.

Allergen control interventions may be expensive or difficult for patients to purchase or use. Clinicians do not want patients—especially those with limited financial resources—to purchase interventions that are not helpful. Further research on the effectiveness of common allergen-control strategies, and the many patient- and household-level characteristics that may influence patient outcomes, is necessary.

Limitations of the Systematic Review Process

The scope of this review may have introduced two important limitations. First, because of the breadth of interventions we evaluated, we restricted our inclusion criteria to studies that directly evaluated an intervention. We therefore excluded all studies that presented either:
(1) observational data demonstrating an association between the presence or absence of a potential allergen source (such as a pet or carpeting) and clinical outcomes or (2) nonclinical studies that examined the level of allergens on a surface. These criteria contributed to the limited evidence base for many of the interventions examined. Second, although our review encompassed a broad range of interventions, we did not assess some potentially relevant strategies that were outside the scope of this review, such as the growing role of community health workers in the implementation of asthma control strategies. We also did not examine the impact of interventions aimed at reducing irritants, such as second-hand smoke or dust, which may influence asthma outcomes.

Limitations of the Evidence Base

The overall evidence base for interventions to reduce exposure to indoor allergens is characterized by a lack of conclusive, consistent, high- or moderate-strength evidence that either favors these strategies or demonstrates that they have no effect. We found inconclusive evidence for many comparisons and outcomes, and low-strength evidence of no effect for many others. In all of these cases, we must note 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 the interventions evaluated. This does not indicate that the interventions are ineffective, but rather highlights the need for additional research.

This evidence is limited in several other ways. Study size was small for many of the single-intervention studies, Heterogeneity of populations, interventions, allergens targeted, and outcomes were substantial, and we therefore did not conduct any meta-analyses of study outcomes. Results were also frequently reported in unusable ways, such as graphically without associated text or tables, or narratively without inclusion of quantitative estimates. A more systemic challenge is the lower prevalence of exacerbations and health care utilization among patients with more mild asthma. In some studies, the number of events was too small to support meaningful analysis.

Further, the risk of bias for individual studies was often difficult to assess because of incomplete reporting of important study characteristics such as randomization technique or blinding. A related consideration is the potential conflict of interest of studies funded by a manufacturer of an intervention (e.g., acaricides, air purifiers, mattress covers.) We identified only 8 out of 57 RCTs for which the funding source had a direct financial interest in the study outcomes; however, many studies did not report a funding source and/or may have received nonfinancial support through provision of study materials.

Another important limitation is the high attrition rate observed in many studies. This may be attributable partly to participants moving from one home to another or encountering instability in family life that may disrupt continuity. These challenges highlight some of the difficulties inherent in sustaining an allergen reduction strategy, in the context of both a controlled study and in real-world implementation.

Finally, researchers have been examining allergen reduction strategies for several decades. This long-term history presents its own challenge, because some of the studies we reviewed include earlier versions of interventions that have likely evolved since they were studied initially.

Evidence Gaps

Several evidence gaps could benefit from future research. First, there is insufficient information about several types of interventions, used alone or as part of multicomponent strategies. A substantial need exists for high-quality RCTs examining the effect of HEPA vacuums, pest control, carpet removal, pet removal, and mold removal. Research is also needed to evaluate multicomponent interventions more efficiently by standardizing sets of strategies that could be tested as bundles. Head-to-head studies of interventions are also missing from the current evidence base that consists almost entirely of comparisons with placebos or standard practices. Similarly, future research could attempt to directly compare single interventions with bundled interventions.

Additionally, the evidence base could be evaluated with greater precision if outcomes reporting were improved and standardized. Important, standardized measures of asthma control, exacerbations, healthcare utilization, and quality of life were often unreported in the included studies. Moreover, many of the studies we evaluated provided data that cannot be incorporated in a comparative analysis because of incomplete reporting or reliance on graphical representations of data that lack specificity. We also need further research on the interaction between the effect size of commonly reported measures and meaningful clinical improvement. Thresholds have been developed for some measures of important asthma outcomes such as asthma control, quality of life, lung function, and medication use (see Appendix E). However, there are no agreed upon standards for the outcomes that were most frequently reported as improved in the studies we reviewed, including measures of exacerbations, absenteeism, peak flow, asthma symptoms, and allergen reduction. Establishment of thresholds for identifying clinically significant change in a wide range of outcomes is needed.

Study methodology could also be reported more consistently and comprehensively. More than half the studies we included did not report important information about their methodology, introducing the possibility of risk of bias that cannot be adequately considered.

We also found it difficult to assess the consistency of the evidence for several interventions and for many critical outcomes, because we identified only one relevant study. The addition of new studies to the evidence base and more robust outcome reporting could improve the consistency, precision, and overall strength of our conclusions.

There are also evidence gaps related to misalignment between the published studies and the population of interest. Future research can also aim to explicitly adopt the National Asthma Education and Prevention Program framework for classifying patient populations by age categories. A consistent approach to identifying "children" and "adults" will enable more standardized and robust analyses of study data.

Setting is also important. All of the studies we evaluated were conducted in patients' homes. No studies were identified that implemented interventions in other settings where patients are routinely exposed to allergens, including workplaces, schools, and daycare.

We also highlight the need for studies that recognize the complex set of challenges that face low-income and minority groups who have the highest morbidity from asthma. Most of the studies included in this review do not describe the socioeconomic context of their patient population, and only a few seem likely to have included a substantial number of patients living in poverty and/or inner city settings despite the likelihood that these patients are at higher risk of allergen exposure and significant morbidity.

Similarly, it is important to improve our understanding of how allergen exposure interventions might directly influence health and whether they serve as markers for other influences that are not measured in these studies. For example, homes with pest infestation may be found more often in low-income neighborhoods where patients lack access to regular medical care, supermarkets with healthy foods, or social services, all of which may affect health in various ways that are not detected in the studies. More than half of the multicomponent intervention studies include a community health worker or social worker who provides education about the interventions but also link patients to a wide variety of other services. Further research on the optimal design of these community-based approaches and their impact would be useful.

We also need longitudinal studies that enable evaluation of how modifications to the home environment might have additive effects over time, or conversely, wane in effectiveness. Most of the studies we reviewed followed patients for 6 months to 1 year. Longer-term studies could help clarify the impact of these strategies and provide insight on their sustainability over time. Similarly, research is needed into how environmental interventions in childhood affect adult health. It could be important to know whether implementation of interventions at a young age can yield greater benefits as children grow.

Conclusions

The evidence base addressing allergen-reduction interventions for patients with asthma spans 40 years and 4 continents and has included more than 7,000 patients. However, few conclusions can be reached about the effectiveness of interventions designed to reduce allergens in the home. Multicomponent interventions that include HEPA vacuums or pest control may be effective for reducing exacerbations and improving quality of life, although results were inconclusive for validated measures of asthma control. For many critical outcomes across the interventions, evidence was insufficient due to too few studies. Moreover, results that were conclusive tended to suggest lack of clinical effect. 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. Further research on many critical questions is needed. Future research should address these evidence gaps with comparative studies that enroll enough patients to detect clinically meaningful improvements in relevant, validated asthma outcomes.

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Abbreviations and Acronyms

ACQ: Asthma Control Questionnaire
ACT: Asthma Control Test
AHRQ: Agency for Healthcare Research and Quality
AQLQ: Asthma Quality of Life Questionnaire
Can f 1: *canis familiaris* dog allergen 1
Bla g 1: *blattella germanica* cockroach allergen 1
CDC: Centers for Disease Control and Prevention
CHSA: Children's Health Survey for Asthma
CI: confidence interval
Der f 1: *Dermatophagoides farina* dust mite allergen 1
Der p 1: *Dermatophagoides pteronyssinus* dust mite allergen 1
ED: emergency department
FEF_{25-75}: average forced expiratory flow during the middle 25–75% portion of forced vital capacity
Fel d 1: *Felis domesticus* cat allergen 1
FeNO: fractional exhaled nitric oxide
FEV_1: forced expiratory volume in one second
FVC: forced vital capacity
GRADE: Grading of Recommendations Assessment, Development and Evaluation
HDM: house dust mite
HEPA: high-efficiency particulate air-filtration
ICS: inhaled corticosteroid
IgE: immunoglobulin E
IQR: interquartile range
mcg/g: micrograms per gram
Mini AQLQ: Mini Asthma Quality of Life Questionnaire
Mus m 1: *Mus musculus* mouse allergen 1
NAEPP: National Asthma Education and Prevention Program
NHLBI: National Heart, Lung, and Blood Institute
NR: not reported
OR: odds ratio
PACQLQ: Pediatric Asthma Caregiver's Quality of Life Questionnaire
PC_{20}: provocative concentration of methacholine causing a 20% drop in FEV_1
PEFR: peak expiratory flow rate
PFV: peak flow variability
PICOTS: patient populations, interventions, comparators, outcomes, timing, and settings
RAST: radioallergosorbent test
RCT: randomized controlled trial
RR: relative risk
SD: standard deviation
SE: standard error
SEM: standard error of the mean
SGRQ: St. George's Respiratory Questionnaire
SOE: strength of evidence
TEP: technical expert panel
u/g: units per gram

Appendix A. Search Strategies

Resources Searched

ECRI Institute information specialists searched the following databases for relevant information. Search terms and strategies for each resource appear below.

Table A-1. Databases searched

Name	Date Limits	Platform/Provider
The Cochrane Central Register of Controlled Trials (CENTRAL)	Inception [1999] through April 21, 2017	Wiley
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	Inception [1999] through April 21, 2017	Wiley
Cumulative Index of Nursing and Allied Health Literature (CINAHL)	Inception [1981] through April 21, 2017	EBSCOhost
Database of Abstracts of Reviews of Effects (DARE) (part of the Cochrane Library)	Inception [1999] through April 21, 2017	Wiley
EMBASE (Excerpta Medica)	Inception [1966] through April 21, 2017	Embase.com
Health Technology Assessment Database (HTA) (part of the Cochrane Library)	Inception [1999] through April 21, 2017	Wiley
MEDLINE	Inception [1966] through April 21, 2017	Embase.com
PUBMED (In Process citations)	Inception [1966] through April 21, 2017	NLM
U.K. National Health Service Economic Evaluation Database (NHS EED) (part of the Cochrane Library)	Inception [1999] through April 21, 2017	Wiley
Associations and Societies		
American Academy of Allergy, Asthma, and Immunology	June 29, 2016	https://www.aaaai.org/
Asthma and Allergy Foundation of America	June 30, 2016	http://www.aafa.org/
American Academy of Pediatrics	June 30, 2016	https://www.aap.org
American College of Allergy, Asthma, and Immunology	June 29, 2016	http://acaai.org/
Agency for Healthcare Research and Quality Technology Assessment Program	June 29, 2016	http://www.ahrq.gov/research/findings/ta/index.html
American Lung Association	June 29, 2016	http://www.lung.org/
American Public Health Association	June 29, 2016	https://www.apha.org/
American Thoracic Society	June 29, 2016	https://www.thoracic.org/
Centers for Disease Control and Prevention	June 28, 2016	https://www.cdc.gov/
Children's Health Protection Advisory Committee	June 30, 2016	https://www.epa.gov/children/childrens-health-protection-advisory-committee-chpac
Global Initiative for Asthma	June 30, 2016	http://ginasthma.org/
National Center for Healthy Housing	June 30, 2016	http://www.nchh.org/
National Academy of Medicine	June 28, 2016	https://nam.edu/
National Environmental Education Foundation	June 30, 2016	https://www.neefusa.org/
National Heart, Lung, and Blood Institute	June 30, 2016	https://www.nhlbi.nih.gov/
United States Environmental Protection Agency	June 28, 2016	https://www3.epa.gov/
United States National Institute of Environmental Health Sciences	June 29, 2016	http://www.niehs.nih.gov/
Other Gray Literature Resources		
ClinicalTrials.gov	Searched August 1, 2016	NIH
Centers for Medicare and Medicaid (CMS) - Medicare Coverage Database	Searched August 2, 2016	CMS
ECRI Institute Library Catalog	Searched August 2, 2016	ECRI Institute

Name	Date Limits	Platform/Provider
ECRI Institute Members Website	Searched August 2, 2016	ECRI Institute
Health Devices	Searched August 2, 2016	ECRI Institute
Healthcare Standards	Searched August 1, 2016	ECRI Institute
Internet	Searched August 3, 2016	Google; Bing
Medscape	Searched June 22, 2016	WebMD
National Guideline Clearinghouse™	Searched August 1, 2016	AHRQ
National Institute for Health and Care Excellence, U.K.	Searched August 1, 2016	NHS
TRIP (Turning Research Into Practice) Database	Searched August 4, 2016	Trip Database, Ltd.
U.S. Food and Drug Administration (FDA), including Medical Device databases	Searched August 1, 2016	FDA

Reimbursement

The following Web sites were searched for reimbursement policies: Aetna, Anthem BCBS, BCBS Florida, BCBS of Illinois, BCBS of Texas, BCBS of California, CIGNA, Humana, United Healthcare, Regence.

Hand Searches of Journal and Gray Literature

Journals and supplements maintained in ECRI Institute's collections were routinely reviewed. Nonjournal publications from professional organizations, private agencies, and government agencies were also screened. Other mechanisms used to retrieve additional relevant information included review of bibliographies/reference lists from peer-reviewed and gray literature. (Gray literature consists of reports, studies, articles, and monographs produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. These documents do not appear in the peer-reviewed journal literature.)

Topic-Specific Search Terms

The search strategies employed combinations of free-text keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. Strategies for each bibliographic database follow this table.

Table A-2. Topic-specific search terms

Concept	Controlled Vocabulary	Keywords
Asthma	**EMBASE (EMTREE)** asthma/exp 'allergic asthma'/exp 'asthmatic state'/exp 'extrinsic asthma'/exp 'intrinsic asthma'/exp 'mild intermittent asthma'/exp 'mild persistent asthma'/exp 'nocturnal asthma'/exp 'occupational asthma'/exp 'severe persistent asthma'/exp **MEDLINE/PubMed(MeSH)** Asthma[mh] **CINAHL** (MH "Asthma+")	Asthma*

Concept	Controlled Vocabulary	Keywords
	(MH "Asthma, Occupational")	
General Allergy terms	**EMBASE (EMTREE)** allergen/exp ‘disease exacerbation’/exp ‘environmental exposure’/exp ‘health hazard’/exp **MEDLINE/PubMed (MeSH)** Allergens[mh] “environmental exposure”[mh] **CINAHL** (MH "Allergens+") (MH "Disease Exacerbation") (MH "Environmental Exposure+")	Allergen exacerbation exacerbate irritant sensitive sensitivity trigger
Environmental and Household Allergens	**EMBASE (EMTREE)** 'airborne particle'/exp cat/exp cockroach/exp dander/exp dog/exp dust/exp household/exp mite/exp mould/exp 'pest insect'/exp 'pest organism'/exp 'pest rodent'/exp 'pet animal'/exp **MEDLINE/PubMed (MeSH)** "antigens, dermatophagoides"[mh] cats[mh] cockroaches[mh] dander[mh] “dermatophagoides farina”[mh] "dermatophagoides pteronyssinus"[mh] dogs[mh] dust[mh] fungi[mh] mites[mh] “mite infestations"[mh] pets[mh] "particulate matter"[mh] **CINAHL** (MH "Cats") (MH "Cockroaches") (MH "Dogs") (MH "Dust") (MH "Fungi+") (MH "Mites") (MH "Pets")	apartment cat cats chalk cockroach damp dander dermatophagoides daycare dog dogs dust dust mites fungus fungi home house housing housedust indoor insect mice mite mites moisture mold moldy mould mouldy mouse pet pets pest pests residence residential roach rodent school

Concept	Controlled Vocabulary	Keywords
Environmental Interventions	**EMBASE (EMTREE)** 'air filter'/exp bed/exp cleaning/exp 'environmental sanitation'/exp 'risk reduction'/exp vacuum/exp 'pests and pest control'/exp 'pest control'/exp ‘indoor residual spraying’/exp **MEDLINE/PubMed (MeSH)** "air filters"[mh] beds[mh] housekeeping[mh] "insect control"[mh] sanitation[mh] vacuum[mh] "pest control"[mh] "rodent control"[mh] ventilation[mh] **CINAHL** (MH "Air Filters") (MH "Beds and Mattresses+") (MH "Home Maintenance") (MH "Pest Control") (MH "Sanitation+") (MH "Vacuum") (MH "Ventilation+")	air filter air filtration air purification allergen reduction bath bathe bathing bed beds bedding clean cleaning comforter cover covering covers dehumidifier dehumidify duct cleaning duvet encase exterminate fabric feather futon HEPA high efficiency particulate arrestance hypoallergenic insulation launder laundering laundry linen mattress pet removal pet bathing pillow reduce sanitation sanitize sheet spray spraying sun sunlight remove removal vacuum ventilation wash washing wipe wiping

Concept	Controlled Vocabulary	Keywords
Carpet/Flooring	**EMBASE (EMTREE)** building/exp **MEDLINE/PubMed (MeSH)** “Floors and floorcoverings”[mh] **CINAHL** (MH “Floors and Floorcoverings”)	carpet* floor* rug rugs wood*

Search Strategies

Embase/Medline

Table A-3. Embase/MEDLINE

Set Number	Concept	Search Statement
1	Asthma	asthma/exp OR 'allergic asthma'/exp OR 'asthmatic state'/exp OR 'extrinsic asthma'/exp OR 'intrinsic asthma'/exp OR 'mild intermittent asthma'/exp OR 'mild persistent asthma'/exp OR 'nocturnal asthma'/exp OR 'occupational asthma'/exp OR 'severe persistent asthma'/exp OR asthma*:ti,ab,de
2	Environmental Allergens	(('allergen'/exp OR 'environmental exposure'/exp OR 'health hazard'/exp OR 'disease exacerbation'/exp OR allerg* OR irritant* OR trigger* OR exacerbat* OR sensitiv*) AND ('airborne particle'/exp OR 'cat'/exp OR 'cockroach'/exp OR 'dander'/exp OR 'dog'/exp OR 'dust'/exp OR 'household'/exp OR 'mite'/exp OR 'mould'/exp OR 'pest insect'/exp OR 'pest organism'/exp OR 'pest rodent'/exp OR 'pet animal'/exp OR cat OR cats OR cockroach* OR housedust* OR roach* OR damp* OR dander OR dermatophagoide* OR daycare OR dog OR dogs OR dust* OR home* OR house* OR indoor* OR insect* OR mite OR mites OR mold OR mould OR moldy OR mouldy OR mouse OR mice OR pet OR pets OR pest OR pests OR rodent* OR school* OR moist* OR fungus OR fungi OR chalk*))
	Household Allergens	OR (('household'/exp OR daycare OR home* OR house* OR indoor* OR residence OR residential OR apartment* OR housing) AND ('airborne particle'/exp OR 'cat'/exp OR 'cockroach'/exp OR 'dander'/exp OR 'dog'/exp OR 'dust'/exp OR 'mite'/exp OR 'mould'/exp OR 'pest insect'/exp OR 'pest organism'/exp OR 'pest rodent'/exp OR 'pet animal'/exp OR cat OR cats OR cockroach* OR housedust* OR roach* OR damp* OR dander OR dermatophagoide* OR dog OR dogs OR dust* OR insect* OR mite OR mites OR mold OR mould OR moldy OR mouldy OR mouse OR mice OR pet OR pets OR pest OR pests OR rodent* OR school* OR moist* OR fungus OR fungi OR chalk*))
3	Environmental Interventions	('air filter'/exp OR bed/exp OR cleaning/exp OR 'environmental sanitation'/exp OR vacuum/exp OR 'pests and pest control'/exp OR 'pest control'/exp OR 'indoor residual spraying'/exp) OR (air NEAR/2 (clean* OR filter* OR filtrat* OR purif*)) OR ventilat* OR insulat* OR (duct* NEAR/2 clean*) OR dehumid* OR bed OR beds OR bedding OR futon* OR clean* OR comforter* OR cover OR covers OR covering* OR duvet* OR encase* OR feather* OR linen* OR fabric OR pillow* OR mattress* OR sanita* OR sanitis* OR sanitiz* OR sheet* OR vacuum* OR sun OR sunlight* OR hypoallergenic OR remove OR removal OR bath* OR exterminat* OR spray* OR ((allergen OR pet OR pets OR pest*) NEAR/5 (reduc* OR avoid* OR eliminat*)) OR wipe OR wiping OR launder OR laundering OR laundry OR hepa OR 'high-efficiency particulate arrestance' OR 'high efficiency particulate arrestance' OR wash OR washing
4	Carpet/Flooring Removal	building/exp OR (carpet* OR floor* OR rug OR rugs OR wood*):ab,ti,de
5	Combine sets	1 AND 2 AND 3
6	Combine sets	1 AND 4
7	Combine sets	5 OR 6
8	Remove unwanted publication types	7 NOT (abstract:nc OR annual:nc OR book/de OR 'case report'/de OR 'case study'/de OR conference:nc OR 'conference abstract':it OR 'conference paper'/de OR 'conference paper':it OR 'conference proceeding':pt OR 'conference review':it OR congress:nc OR editorial/de OR editorial:it OR erratum/de OR letter:it OR note/de OR note:it OR meeting:nc OR sessions:nc OR 'short survey'/de OR symposium:nc)

Set Number	Concept	Search Statement
9	Controlled study filter	8 AND ('randomized controlled trial'/exp OR 'randomized controlled trial' OR 'randomization'/exp OR 'randomization' OR 'double blind procedure'/exp OR 'double blind procedure' OR 'single blind procedure'/exp OR 'single blind procedure' OR 'placebo'/exp OR 'placebo' OR 'latin square design'/exp OR 'latin square design' OR 'crossover procedure'/exp OR 'crossover procedure' OR 'triple blind procedure'/exp OR 'triple blind procedure' OR 'controlled study'/exp OR 'controlled study' OR 'clinical trial'/exp OR 'clinical trial' OR 'comparative study'/exp OR 'comparative study' OR 'cohort analysis'/exp OR 'cohort analysis' OR 'follow up'/exp OR 'follow up' OR 'intermethod comparison'/exp OR 'intermethod comparison' OR 'parallel design'/exp OR 'parallel design' OR 'control group'/exp OR 'control group' OR 'prospective study'/exp OR 'prospective study' OR 'retrospective study'/exp OR 'retrospective study' OR 'case control study'/exp OR 'case control study' OR 'major clinical study'/exp OR 'major clinical study' OR 'evaluation study'/exp OR 'evaluation study' OR random*:de OR random*:ti OR placebo* OR (singl* OR doubl* OR tripl* OR trebl* AND (dummy OR 'blind'/exp OR blind OR sham)) OR 'latin square' OR isrctn* OR actrn* OR (nct* NOT nct))
10	Systematic Review/Meta-analysis filter	8 AND ('research synthesis' OR pooled OR 'systematic review'/exp OR 'systematic review' OR 'meta analysis'/exp OR 'meta analysis' OR (('evidence base' OR 'evidence based'/exp OR 'evidence based' OR methodol* OR systematic OR quantitative* OR studies OR search*) AND ('review'/exp OR 'review' OR 'review'/it)))
11	Combine Sets	9 OR 10
12	Apply Limits	11 AND ('human'/de OR [adolescent]/lim OR [adult]/lim OR [aged]/lim OR [child]/lim OR [infant]/lim OR [middle aged]/lim OR [newborn]/lim OR [preschool]/lim OR [school]/lim OR [very elderly]/lim OR [young adult]/lim)

<u>EMBASE.com Syntax</u>:

*	=	truncation character (wildcard)
NEAR/*n*	=	search terms within a specified number (*n*) of words from each other in any order
NEXT/*n*	=	search terms within a specified number (*n*) of words from each other in the order specified
/	=	search as a subject heading
exp	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
mj	=	denotes a term that has been searched as a major subject heading
:de	=	search in the descriptors field (controlled terms and keywords)
:lnk	=	floating subheading
/lim	=	limiter
:it,pt.	=	source item or publication type
:ti.	=	limit to title
:ti,ab.	=	limit to title and abstract fields

PubMed (PreMEDLINE)

Table A-4. PubMed in process citations

Set Number	Concept	Search Statement
1	Asthma[mh] OR asthma*	Asthma[mh] OR asthma*
2	Environmental Allergens	("Allergens"[Mesh] OR "Environmental Exposure"[Mesh] OR allerg*[tiab] OR irritant*[tiab] OR trigger*[tiab] OR exacerbat*[tiab] OR sensitiv*[tiab]) AND ("Particulate Matter"[Mesh] OR "Cats"[Mesh] OR "Dander"[Mesh] OR "Dogs"[Mesh] OR "Cockroaches"[Mesh] OR "Dust"[Mesh] OR "Antigens, Dermatophagoides"[Mesh] OR "Dermatophagoides pteronyssinus"[Mesh] OR "Dermatophagoides farinae"[Mesh] OR "Mites"[Mesh] OR "Mite Infestations"[Mesh] OR "Fungi"[Mesh] OR "Pets"[Mesh] OR cat[tiab] OR cats[tiab] OR cockroach*[tiab] OR housedust*[tiab] OR roach*[tiab] OR damp*[tiab] OR dander[tiab] OR dermatophagoide*[tiab] OR daycare[tiab] OR dog[tiab] OR dogs[tiab] OR dust*[tiab] OR home*[tiab] OR house*[tiab] OR indoor*[tiab] OR insect*[tiab] OR mite[tiab] OR mites[tiab] OR mold[tiab] OR mould[tiab] OR moldy[tiab] OR mouldy[tiab] OR mouse[tiab] OR mice[tiab] OR pet[tiab] OR pets[tiab] OR pest[tiab] OR pests[tiab] OR rodent*[tiab] OR school*[tiab] OR moist*[tiab] OR fungus[tiab] OR fungi[tiab] OR chalk*[tiab])
	Household Allergens	OR (daycare OR home* OR house* OR indoor* OR residence OR residential OR apartment* OR housing) AND("Particulate Matter"[Mesh] OR "Cats"[Mesh] OR "Dander"[Mesh] OR "Dogs"[Mesh] OR "Cockroaches"[Mesh] OR "Dust"[Mesh] OR "Antigens, Dermatophagoides"[Mesh] OR "Dermatophagoides pteronyssinus"[Mesh] OR "Dermatophagoides farinae"[Mesh] OR "Mites"[Mesh] OR "Mite Infestations"[Mesh] OR "Fungi"[Mesh] OR "Pets"[Mesh] OR cat[tiab] OR cats[tiab] OR cockroach*[tiab] OR housedust*[tiab] OR roach*[tiab] OR damp*[tiab] OR dander[tiab] OR dermatophagoide*[tiab] OR dog[tiab] OR dogs[tiab] OR dust*[tiab] OR insect*[tiab] OR mite[tiab] OR mites[tiab] OR mold[tiab] OR mould[tiab] OR moldy[tiab] OR mouldy[tiab] OR mouse[tiab] OR mice[tiab] OR pet[tiab] OR pets[tiab] OR pest[tiab] OR pests[tiab] OR rodent*[tiab] OR school*[tiab] OR moist*[tiab] OR fungus[tiab] OR fungi[tiab] OR chalk*[tiab])

Set Number	Concept	Search Statement
3	Environmental Interventions	"Air Filters"[Mesh] OR "Beds"[Mesh] OR "Housekeeping"[Mesh] OR "Sanitation"[Mesh] OR "Vacuum"[Mesh] OR "Pest Control"[Mesh] OR "Insect Control"[Mesh] OR "Rodent Control"[Mesh] OR ventilation[Mesh] OR (air[tiab] AND (clean*[tiab] OR filter*[tiab] OR filtrat*[tiab] OR purif*[tiab])) OR ventilat*[tiab] OR insulat*[tiab] OR (duct*[tiab] AND clean*[tiab]) OR dehumid*[tiab] OR bed*[tiab] OR futon*[tiab] OR clean*[tiab] OR comforter*[tiab] OR cover[tiab] OR covers[tiab] OR covering*[tiab] OR duvet*[tiab] OR encase*[tiab] OR feather*[tiab] OR linen*[tiab] OR fabric[tiab] OR pillow*[tiab] OR mattress*[tiab] OR sanita*[tiab] OR sanitis*[tiab] OR sanitiz*[tiab] OR sheet*[tiab] OR vacuum*[tiab] OR hypoallergenic*[tiab] OR exterminat*[tiab] OR spray*[tiab] OR sun[tiab] [tiab] OR sunlight*[tiab] OR bath*[tiab] OR ((allergen*[tiab] OR pet[tiab] OR pets[tiab] OR pest*[tiab]) AND (reduc*[tiab] OR avoid*[tiab] OR eliminat*[tiab] OR remove OR removal)) OR wipe[tiab] OR wiping[tiab] OR launder[tiab] OR laundering[tiab] OR laundry[tiab] OR hepa[tiab] OR 'high-efficiency particulate arrestance'[tiab] OR 'high efficiency particulate arrestance'[tiab] OR wash[tiab] OR washing[tiab]
4	Carpet/Flooring removal	"Floors and Floorcoverings"[Mesh] OR (carpet*[tiab] OR floor*[tiab] OR rug[tiab] OR rugs[tiab] OR wood*[tiab])
5	Combine sets	1 AND 2 AND 3
6	Combine sets	1 AND 4
7	Combine sets	5 OR 6
8	Remove unwanted publication types	7 NOT (case reports[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR news[pt] OR "Textbooks" [pt] OR "Book Reviews"[pt]OR "Book Illustrations"[pt] OR book OR books OR textbook*)
9	In process citations	8 AND ("inprocess"[sb] OR publisher[sb] OR pubmednotmedline[sb])

PubMed Syntax:

*	=	truncation character (wildcard)
[mh]/[MesH]	=	controlled vocabulary term
[sb]	=	subset
[ti]	=	limit to title field
[tiab]	=	limit to title and abstract fields
[tw]	=	text word

CINAHL

English language, human, exclude MEDLINE records

Table A-5. CINAHL

Set Number	Concept	Search Statement
1	Asthma	(MH "Asthma+") OR (MH "Asthma, Occupational") OR asthma*
2	Household allergens	((MH "Allergens+") OR (MH "Disease Exacerbation") OR (MH "Environmental Exposure+") OR allerg* OR irritant* OR trigger* OR exacerbat* OR sensitiv*) AND ((MH "Dogs") OR (MH "Cats") OR (MH "Pets") OR (MH "Cockroaches") OR (MH "Dust") OR (MH "Mites") OR (MH "Fungi+") OR cat OR cats OR cockroach* OR housedust* OR roach* OR damp* OR dander OR dermatophagoide* OR daycare OR dog OR dogs OR dust* OR home* OR house* OR indoor* OR insect* OR mite OR mites OR mold OR mould OR moldy OR mouldy OR mouse OR mice OR pet OR pets OR pest OR pests OR rodent* OR school* OR moist* OR fungus OR fungi OR chalk*)
3	Environmental Interventions/Household Allergens	((MH "Air Filters") OR (MH "Beds and Mattresses+") OR (MH "Home Maintenance") OR (MH "Sanitation+") OR (MH "Vacuum") OR (MH "Pest Control") OR (MH "Ventilation+") OR (air AND (clean* OR filter* OR filtrat* OR purif*)) OR ventilat* OR insulat* OR (duct* AND clean*) OR dehumid* OR bed OR beds OR bedding OR futon* OR clean* OR comforter* OR cover OR covers OR covering* OR duvet* OR encase* OR feather* OR linen* OR fabric OR pillow* OR mattress* OR sanita* OR sanitis* OR sanitiz* OR sheet* OR vacuum* OR sun OR sunlight* OR hypoallergenic OR remove OR removal OR bath* OR exterminat* OR spray* OR ((allergen OR pet OR pets OR pest*) AND (reduc* OR avoid* OR eliminat*)) OR wipe OR wiping OR launder OR laundering OR laundry OR hepa OR “high-efficiency particulate arrestance” OR “high efficiency particulate arrestance” OR wash OR washing
4	Carpet/Flooring Removal	(MH "Floors and Floorcoverings") OR carpet* OR floor* OR rug OR rugs OR wood*
5	Combine sets Key Question 1	1 AND 2 AND 3
6	Combine sets Key Question 2	1 AND 4
7	Combine sets Key Question 1 OR Key Question 2	5 OR 6
8	Remove Medline records/ limit to academic journals	

<u>CINAHL Syntax</u>:

…+ = explode

* = truncation character (wildcard)

N*n* = search terms within a specified number (*n*) of words from each other in any order

TI = limit to title field

AB = limit to title and abstract fields

MH = MeSH heading

MJ = MeSH heading designated as major topic

PT = publication type

Appendix B. Excluded Studies

Belice PJ, Becker EA. Effective education parameters for trigger remediation in underserved children with asthma: a systematic review. J Asthma. 2016 Jun 15;1-16. Also available: http://dx.doi.org/10.1080/02770903.2016.1198374. PMID: 27304997. **Does not address Key Question**

Jassal MS, Diette GB, Dowdy DW. Cost-consequence analysis of multimodal interventions with environmental components for pediatric asthma in the state of Maryland. J Asthma. 2013 Aug;50(6):672-80. Also available: http://dx.doi.org/10.3109/02770903.2013.792351. PMID: 23614791. **Does not address Key Question**

Sauni R, Uitti J, Jauhiainen M, et al. Remediating buildings damaged by dampness and mould for preventing or reducing respiratory tract symptoms, infections and asthma (Review). Evidence-Based Child Health. 2013 May;8(3):944-1000. Also available: http://dx.doi.org/10.1002/ebch.1914. PMID: 23877912. **Does not address Key Question**

Singh M, Jaiswal N. Dehumidifiers for chronic asthma. Cochrane Database Syst Rev. 2013;(6):CD003563. PMID: 23760885. **Does not address Key Question**

Lanphear BP, Hornung RW, Khoury J, et al. Effects of HEPA air cleaners on unscheduled asthma visits and asthma symptoms for children exposed to secondhand tobacco smoke. Pediatrics. 2011 Jan;127(1):93-101. Also available: http://dx.doi.org/10.1542/peds.2009-2312. PMID: 21149427. **Irritant (smoke) not in scope**

Townsend KJ, George M. What is the evidence that environmental remediation programs are effective in urban children with allergic asthma? An integrated review. J Asthma Allergy Educ. 2011 Dec;2(6):295-305. Also available: http://dx.doi.org/10.1177/2150129711418826. **Does not address Key Question**

Krieger J, Jacobs DE, Ashley PJ, et al. Housing interventions and control of asthma-related indoor biologic agents: a review of the evidence. J Public Health Manag Pract. 2010 Sep-Oct;16(5 Suppl):S11-20. PMID: 20689369. **Systematic review**

Tzeng LF, Chiang LC, Hsueh KC, et al. A preliminary study to evaluate a patient-centred asthma education programme on parental control of home environment and asthma signs and symptoms in children with moderate-to-severe asthma. J Clin Nurs. 2010 May;19(9):1424-33. PMID: 20500352. **Education only**

Buczylko K, Korzycka-Zaborowska B, Michalak A. Influence of the acaricide - set on the improvement of mite allergy symptoms. Alergia Astma Immunologia. 2008 Mar;13(1):42-52. **Does not provide adequate data on asthma outcomes or allergen outcomes**

Gotzsche PC, Johansen HK. House dust mite control measures for asthma. Cochrane Database Syst Rev. 2008;(2):CD001187 Also available: http://dx.doi.org/10.1002/14651858.CD001187.pub3. PMID: 18425868. **Systematic review**

Howden-Chapman P, Pierse N, Nicholls S, et al. Effects of improved home heating on asthma in community dwelling children: Randomised controlled trial. BMJ. 2008 Oct 11;337(7674):852-5. Also available: http://dx.doi.org/10.1136/bmj.a1411. PMID: 18812366. **Does not focus on allergen removal**

Shedd AD, Peters JI, Wood P, et al. Impact of home environment characteristics on asthma quality of life and symptom scores. J Asthma. 2007 Apr;44(3):183-7. Also available: http://dx.doi.org/10.1080/02770900701209699. PMID: 17454335. **Not an RCT**

Bernstein JA, Bobbitt RC, Levin L, et al. Health effects of ultraviolet irradiation in asthmatic children's homes. J Asthma. 2006 May;43(4):255-62. Also available: http://dx.doi.org/10.1097/01.ede.0000209440.94875.42. PMID: 16809237. **Due to carry over effects, data analysis focused on the first treatment period; n<10**

Takaro TK, Krieger JW, Song L. Effect of environmental interventions to reduce exposure to asthma triggers in homes of low-income children in Seattle. J Expo Anal Environ Epidemiol. 2004;14 Suppl 1:S133-43. Also available: http://dx.doi.org/10.1038/sj.jea.7500367. PMID: 15118754. **Nonclinical data from Krieger study**

Hasan RA, Zureikat GY, Camp J, et al. The positive impact of a disease management program on asthma morbidity in inner-city children. Pediatr Asthma Allergy Immunol. 2003 Sep;16(3):147-54. **Only education**

Kilburn S, Lasserson TJ, McKean M. Pet allergen control measures for allergic asthma in children and adults. Cochrane Database Syst Rev. 2001;CD002989. PMID: 12535446. **Systematic review**

Rijssenbeek Nouwens LH, Oosting AJ, De Monchy JG, et al. The effect of anti-allergic mattress encasings on house dust mite-induced early- and late-airway reactions in asthmatic patients. A double-blind, placebo-controlled study. Clin Exp Allergy. 2002;32(1):117-25. Also available: http://dx.doi.org/10.1046/j.0022-0477.2001.01256.x. PMID: 12002728. **Preliminary report of included study**[1]

Singh M, Bara A, Gibson P. Humidity control for chronic asthma. Cochrane database of systematic reviews. 2002. PMID: 12076485. **Does not address Key Question**

Gotzsche PC, Hammarquist C, Burr M. House dust mite control measures in the management of asthma: Meta-analysis. Br Med J. 1998 Oct 24;317(7166):1105-10. PMID: 9784442. **Systematic review**

Wood RA, Johnson EF, Van Natta ML, et al. A placebo-controlled trial of a HEPA air cleaner in the treatment of cat allergy. Am J Respir Crit Care Med. 1998;158(1):115-20. PMID: 9655716. **<85% patients with asthma, data not reported separately**

Ehnert B, Lau-Schadendorf S, Weber A, et al. Reducing domestic exposure to dust mite allergen reduces bronchial hyperreactivity in sensitive children with asthma. J Allergy Clin Immunol. 1992 Jul;90(1):135-8. PMID: 1629503. **Fewer than 10 patients enrolled**

Reference List for Appendix B

1. Rijssenbeek-Nouwens LH, Oosting AJ, de Bruin-Weller MS, et al. 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 Sep;57(9):784-90. Also available: http://dx.doi.org/10.1136/thorax.57.9.784. PMID: 12200523.

Appendix C. Evidence Tables

Key Question 1: Allergen Reduction for Management of Asthma

Evidence Tables for Acaricide (Dust Mite Pesticide) Studies

Table C-1. Study characteristics of acaricide (dust mite pesticide) studies

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
Bahir et al. 1997[1]	***Arm 1*:** Acaricide (Acardust: esdepallethin/piperonyl butoxide) + avoidance ***Arm 2:*** Placebo + avoidance ***Arm 3*:** Avoidance measures alone Acaricide or placebo were applied to floors and mattresses at baseline and after 3 months	House dust mites Combined Der p 1 and Der f 1 as measured with Acarex test	***Type of study*:** RCT ***Population:*** 62 46 completed study Acardust: 13 Placebo: 17 Avoidance: 16 ***Attrition:*** 26% ***Setting:*** Home ***Country:*** Israel ***Followup:*** 6 months	***Age,*** mean (SD)**:** Acardust: 9.2 (2.4) Range: 6.5 to 13 Placebo: 10.4 (2.6) Range: 6 to 15 Avoidance: 11.8 (3.2) Range: 7 to 16.5 ***% Male:*** NR ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** Sites described as being in a "radius of 15 km along the seashore, [with] similar weather conditions with respect to air temperature and humidity."	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** Mild to moderate (Asthma score >2) ***Baseline spirometry*** (FEV_1 predicted): Acardust: 72% Placebo: 75% Avoidance: 72% ***Mean duration of asthma***, year (SD): Acardust: 7.3 (2.7) Placebo: 6.8 (2.6) Avoidance: 9.5 (4.3) ***Carpeted living room:*** Acardust: 38% Placebo: 53% Avoidance: 25% $Chi^2(2, 46)=9.271$; p=0.0097; presence of carpet statistically different among groups[a]

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
van der Heide et al. 1997[2]	***Arm 1***: Acaricide (Acarosan) ***Arm 2:*** Placebo (detergent) ***Arm 3*:** Mattress covers Acaricide or placebo was applied to textile-covered floors and mattresses; non-textile-covered floors were not treated	Der p 1	***Type of study:*** Quasi-RCT; participants randomized to acaricide or placebo, with participants who refused chemical intervention given mattress casings. ***Population:*** 59 Acaricide: 21 Placebo: 19 Mattress: 19 ***Attrition:*** NR ***Setting:*** Home ***Country:*** Netherlands ***Followup:*** 1 year	***Age,*** mean (SD): Acaricide: 31.5 (8.8) Placebo: 30.1 (7.2) Mattress: 32.3 (5.8) ***% Male:*** Acaricide: 44% Placebo: 53% Mattress: 42% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***FEV_1 % predicted***, mean (SD): Acaricide: 88.7 (13.6) Placebo: 89.4 (13.3) Mattress: 92.4 (12.8) ***PC_{20} histamine*** (mg/ml), mean (95% CI): Acaricide: 1.97 (1.22 to 3.16) Placebo: 2.23 (1.19 to 4.15) Mattress: 3.87 (2.24 to 6.62) ***Smokers*:** 16.9% ***Cigarette smoke exposed in home*:** 22% ***Animals in home:*** Acaricide: 43% Placebo: 58% Mattress: 58% ***Floor covering in bedroom:*** Acaricide: 77% Placebo: 89% Mattress: 52%* p<0.05 compared to other two groups
Chang et al. 1996[3]	***Arm 1*:** Acaricide (Acarosan: benzyl benzoate) + usual mite control ***Arm 2*:** Usual mite control (no placebo treatment given) Acarosan applied to mattress, bedroom carpet, carpet in most commonly used room Usual mite control included vinyl barriers on mattresses and pillows, vacuuming at least once per week, washing bed linens in hot water	House dust mite allergens Der p 1 and Der f 1	***Type of study:*** RCT ***Population:*** 26 11 children, 15 adults Acarosan: 12 Control: 14 ***Attrition:*** 0% ***Setting:*** Home ***Country:*** Canada ***Followup:*** 3 months	***Demographic data:*** NR; age ranges for adults and children not described ***Geographic environment:*** NR, patients enrolled in Vancouver and Winnipeg	***HDM Sensitization*** (skin prick test positive): 100% ***FEV_1, %*** baseline mean (SD***):*** Acarosan: 88% (11%) Control: 85% (11%) ***PEFR***, L/min, baseline mean (SD): Acarosan: 402 (69) Control: 381 (97) ***PC20****,* mg/mL, baseline mean (SD): Acarosan: 0.76 (1.93) Control: 0.47 (5.62)

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
Geller-Bernstein et al. 1995[4]	***Arm 1:*** Acaricide (Acardust) ***Arm 2:*** Placebo Acaricide or placebo were applied to bedrooms at baseline and after 3 months	House dust mite allergens Der p and Der f	***Type of study:*** RCT ***Population:*** 35 Acardust: 18 Placebo: 17 ***Attrition:*** 23% ***Setting:*** Home ***Country:*** Israel ***Followup:*** 6 months	***Age,*** mean (SD): Acardust: 9.74 (2.64) Placebo: 8.07 (2.58) Range 4 to 12 years ***% Male:*** 65.7% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** NR ***Mean duration of asthma****,* months (SD): Acardust: 83.7 (39.4) Placebo: 63.9 (40.9) ***Comorbidity:*** Rhinitis: Acardust: 94% Placebo: 88%
Sette et al. 1994[5]	***Arm 1:*** Acarosan ***Arm 2:*** Placebo ***Arm 3:*** No intervention Applied to mattresses at baseline and after 3 months	House dust mite allergen Der p 1	***Type of study:*** RCT ***Population:*** 34 Acarosan: 14 Placebo: 12 Control: 8 ***Attrition:*** NR ***Setting:*** Home ***Country:*** Italy ***Followup:*** 3 months	***Age,*** mean (SD): Acarosan: 12.5 (1.71) Placebo: 12.4 (1.57) Range: 13 to 58 years ***% Male:*** 69% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR
Dietemann et al. 1993[6]	***Arm 1:*** Acarosan ***Arm 2:*** Placebo Applied to carpets, upholstery, and mattresses at baseline and after 6 months	House dust mite allergens Der p 1 and Der f 1	***Type of study:*** RCT ***Population:*** 26 Acardust: 14 Placebo: 12 ***Attrition:*** 12% ***Setting:*** Home ***Country:*** France ***Followup:*** 12 months	***Age,*** mean (SD): Acardust: 36.8 (11) Placebo: 35.4 (6.7) Range: 13 to 58 years ***% Male:*** 35.7% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization:*** *Dp*-specific IgE (RAST), mean (SD): Acardust: 11.8 (2.7) Placebo: 14 (1.6) *Dp*-intradermal tests, mm, mean (SD): Acardust: 3.45 (0.3) Placebo: 3.72 (0.25) ***Asthma severity:*** Mean baseline FEV_1 (SD): Acardust: 63.45 (14.32) Placebo: 72.73 (16.4) Mean baseline FEF_{25-75} (SD) Acardust: 48 (16) Placebo: 56.34 (15.5) Mean morning PEFR (SD) Acardust: 67.85 (13.6) Placebo: 75.38 (11.6) Mean evening PEFR (SD) Acardust: 67.14 (13.3) Placebo: 79.25 (11.6) ***Mean duration of asthma*****,** years (SD): Acardust: 17.4 (10.6) Placebo: 13 (6.4)

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
Reiser et al. 1990[7]	***Arm 1:*** Natamycin ***Arm 2:*** Placebo Natamycin (500 mg/dose) or placebo spray applied to mattresses every 2 weeks for 3 months, for 6 total applications	House dust mite allergen Der p 1	***Type of study:*** RCT ***Population:*** 46 ***Attrition:*** NR ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 3 months	***Age,*** mean: NR Range: 5 to 16 ***% Male:*** 76% ***Race:*** NR ***Homeownership:*** 84% ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** Described as ranging from intermittent to chronic severe; no additional data reported ***Comorbidity:*** NR ***Carpet:*** 82% ***Pets:*** 36%

[a] Chi^2 test conducted by ECRI-Penn EPC to determine whether groups varied on important baseline factors.

CI=confidence interval; Der f 1=*Dermatophagoides farina* house dust mite allergen; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen; FEV_1=forced expiratory volume in one second; FEF_{25-75}=average forced expiratory flow during the middle 25–75% portion of forced vital capacity; HDM=house dust mite; IgE=immunoglobulin E; km=kilometer; mg/ml=milligrams per milliliter; NR=not reported; PEFR=peak expiratory flow rate; PC20=provocative concentration 20, assesses airway hyper-responsiveness; RAST=radioallergosorbent test; RCT=randomized controlled trial; SD=standard deviation

Table C-2. Outcomes of acaricide (dust mite pesticide) studies

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Bahir et al. 1997[1]	NR	NR	**Spirometry:** Comparison of arms showed no difference between treatments for any outcomes (data shown graphically; p>0.05) FEV_1, % mean (SD) Baseline: 73.5 (13.2)% 6 months: 78.2 (14.7)% Not statistically significant Morning PEFR, mean (SD): Baseline: 245 (85) 6 months: 282 (82) Not statistically significant Evening PEFR, mean (SD): Baseline: 253 (85) 6 months: 291 (83) Not statistically significant	NR	**Measurement:** Patient diaries, 12-point scale with lower scores showing fewer symptoms **Symptom scores**, mean (SD): Comparison of arms showed no difference between treatments (data shown graphically; p>0.05) Baseline: 2.6 (2) 6 months: 1.5 (1.5) p<0.001	**Measurement:** Patients collected dust samples by vacuuming mattresses and floors; samples collected 2 times: before and after study **Acarex score** (mean [SD]) improved within both treatment groups over time: Baseline: 3.5 (0.6) 6 months: 2.9 (0.9) p<0.001. Comparison of arms showed no difference between treatments (data shown graphically; p>0.05)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
van der Heide et al. 1997[2]	NR	NR	**FEV_1 and Vital Capacity:** Comparison of arms did not show difference between groups; data not shown **PC_{20} histamine:** No comparison between arms; statistically significant improvement over baseline in acaricide and mattress cover arms ($p<0.05$; data shown graphically); however, change was less than one doubling dose, which may not be clinically significant	NR	NR	NR
Chang et al. 1996[3]	NR	NR	**Spirometry at 3-month followup:** Comparison of arms showed no difference between arms or over time, for any outcomes. Test statistics NR. FEV_1, % mean (SD): Acarosan: 87% (20%) Control: 90% (15%) PEFR, L/min, mean (SD): Acarosan: 411 (75) Control: 383 (100) PC_{20}, mg/mL, mean (SD): Acarosan: 0.87 (2.29) Control: 0.82 (3.84)	NR	NR	**Measurement:** Dust samples collected by vacuuming mattresses and floors; study does not report who collected samples; samples were collected 5 times before and throughout the study period HDM allergen, Mattress mcg/g dust, (SD): Acarosan baseline: 2.17 (2.64) Acarosan 3 months: 0.06 (1.12) Control baseline: 1.68 (2.22) Control 3 months: 0.28 (1.32) Comparison of arms showed no difference, but allergen levels were reduced within both groups over baseline ($p<0.05$) HDM allergen, Floor mcg/g dust, (SD): Acarosan baseline: 2.38 (2.64) Acarosan 3 months: 0.50 (1.71) Control baseline: 2.05 (2.05) Control 3 months: 1.10 (2.17) Comparison of arms showed no difference, but allergen levels were reduced over baseline in Acarosan arm ($p<0.05$)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Geller-Bernstein et al. 1995[4]	NR	NR	NR	NR	**Measurement:** For the measures of daily activity disruption, and wheezing frequency, scores were derived from patient diaries (completed 2 times per week) using a 4-point Likert scale with lower scores showing fewer symptoms; for the measures of parent and doctor evaluation of severity, scores were derived from a 100-point visual analog scale completed 1 time each month, with lower scores showing less severity **Daily activity disruption**, mean: Acardust baseline: 1.17 Acardust 6 months: 0.13 Placebo baseline: 0.94 Placebo 6 months: 0.27 Acardust vs. placebo: p=0.02 **Wheezing frequency**, mean: Acardust baseline: 1.94 Acardust 6 months: 0.67 Placebo baseline: 2.06 Placebo 6 months: 0.73 Acardust vs. placebo: p=0.1 **Parent evaluation of severity**, mean: Acardust baseline: 34.83 Acardust 6 months: 5.47 Placebo baseline: 29.88 Placebo 6 months: 6.60 Acardust vs. placebo: p=0.001 **Doctor evaluation of severity**, mean: Acardust baseline: 34.56 Acardust 6 months: 4.20 Placebo baseline: 29.65 Placebo 6 months: 6.00 Acardust vs. placebo: p=0.04	**Measurement**: Patients collected dust samples by vacuuming mattresses; samples were collected 5 times before and throughout the study period HDM allergen mcg/g dust (SD) Acardust baseline: 10.05 (13.74) Acardust 6 months: 4.15 (6.51) Placebo baseline: 6.01 (8.01) Placebo 6 months: 3.01 (4.33) Allergen counts decreased to a greater degree over baseline in the Acardust group (p=0.02)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Sette et al. 1994[5]	NR	NR	**PC_{20}** change from baseline (mean, SEM) Study period 1 Acarosan: -2.39 (1.53) mg/mL Placebo: -0.07 (1.05) Control: -5.75 (4.42) Study period 2 Acarosan: -1.95 (1.19) Placebo: -1.82 (0.74) Control: -3.84 (3.12) p=not significant, actual p-value NR	NR	NR	**Serum IgE** change from baseline (no measure of variance provided) Study period 1 Acarosan: -1.41 Placebo: 0.45 Control: 9.60 p=not significant, actual p-value NR Study period 2 Acarosan: 1.10 Placebo: -0.50 Control: 0.50 p=not significant, actual p-value NR **Nasal IgE** Study period 1 Acarosan: 0.40 Placebo: 0.49 Control: 1.62 p=not significant, actual p-value NR Study period 2 Acarosan: 1.37 Placebo: 2.62 Control: -0.02 p=not significant, actual p-value NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Dietemann et al. 1993[6]	NR	NR	**FEV_1** change from baseline Acarosan: +14% Placebo: +0.08% Acarosan vs. placebo: p=not significant, actual p-value NR **FEF_{25-75}** change from baseline Acarosan: +24.6% Placebo: +12% Acarosan vs. placebo: p=not significant, actual p-value NR **Mean morning PEFR** change from baseline Acarosan: +0.05% Placebo: -0.014% Acarosan vs. placebo: p=not significant, actual p-value NR **Mean evening PEFR** change from baseline Acarosan: +0.03% Placebo: -0.02% Acarosan vs. placebo: p=not significant, actual p-value NR	NR	NR	**Measurement:** Member of study team collected dust samples by vacuuming mattresses, carpets, furniture; samples collected every 3 months throughout study period **Quantitative guanine** (mattress) change from baseline: Acarosan: -0.03% Placebo: -35% Acarosan vs. placebo: p=not significant, actual p-value NR **Der p 1 + Der f 1**, change from baseline: <u>Mattress</u> Acarosan: -19.7% Placebo: -17% Acarosan vs. placebo: p=not significant, actual p-value NR <u>Carpet</u> Acarosan: -74% Placebo: -27% Acarosan vs. placebo: p=not significant, actual p-value NR <u>Other</u> Acarosan: -67% Placebo: -61% Acarosan vs. placebo: p<0.05
Reiser et al. 1990[7]	NR	NR	**PEFR and FEV_1:** Comparison of arms showed no statistically significant difference (data reported in graph)	NR	**Measurement**: Patient diaries **Clinical symptoms:** Comparison of arms showed no statistically significant difference (data reported in graph)	**Measurement:** Member of study team collected dust samples by vacuuming mattresses; samples collected 2 times: before and after study period **Der p 1 allergen**, geometric mean difference from baseline to followup: Natamycin: 2659 Placebo: 1009 Natamycin vs. placebo: p=not significant, actual p-value NR

Der f 1=*Dermatophagoides farina* house dust mite allergen; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen; FEV_1=forced expiratory volume in one second; NR=not reported; PC_{20}=provocative concentration 20; PEFR=peak expiratory flow rate; SD=standard deviation; SEM=stand error of the mean

Table C-3. Risk of bias of acaricide (dust mite pesticide) randomized controlled trials

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Bahir et al. 1997[1]	Unclear	Unclear	Low	Unclear	High	Low	High	High	Insufficient description of randomization; placebo used; unclear if outcome assessors were blinded; 26% attrition; study funded by acaricide manufacturer
Chang et al. 1996[3]	Unclear	Unclear	High	High	Low	Low	Low	Medium	Insufficient description of randomization; no blinding; all patients completed followup
Geller-Bernstein et al. 1995[4]	Unclear	Unclear	Low	Low	High	Low	Low	Medium	Insufficient description of randomization; placebo used; 23% attrition
Sette et al. 1994[5]	Unclear	Unclear	Low	Low	Unclear	Low	Low	Unclear	Insufficient description of randomization; placebo used; attrition not reported
Dietemann et al. 1993[6]	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Insufficient description of randomization; placebo used; 12% attrition
Reiser et al. 1990[7]	Unclear	Unclear	Low	Low	Unclear	Low	High	Medium	Insufficient description of randomization; placebo used; attrition not reported; study funded by acaricide manufacturer

Table C-4. Risk of bias of acaricide (dust mite pesticide) non-randomized controlled trial

Study	Representativeness of the Study Population	Ascertainment of Exposure	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of Outcome	Followup Long Enough for Outcomes to Occur	Adequacy of Followup of Cohorts	Overall Risk of Bias	Comments
van der Heide 1997[2]	Low	Low	Low	Low	Low	Unclear	Low	Non-randomized but placebo controlled

Evidence Tables for Air Purification Studies

Table C-5. Study characteristics of air purification studies

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
Pedroletti et al. 2009[8]	***Arm 1:*** Airsonett Airshower filtering technique ***Arm 2:*** Placebo Airshower: Airflow over the bed is passed through a HEPA filter and cooled. Cool, filtered air is purported to displace allergens in the breathing space during sleep.	Pet (cat and/or dog; unspecified)	***Type of study:*** RCT, crossover design; ***Population:*** 28 enrolled; 22 completed both arms of crossover ***Attrition:*** 21% ***Setting:*** Home ***Country:*** Sweden ***Followup:*** Interventions were given for 10 weeks with 2 week washout in between	***Age*** (mean [SD]): 18.5 (6.6) Range: 12 to 33 ***% Male:*** 45.5% ***Race:*** Not specified ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): Pet (cat and/or dog): 100% FeNO, ppb (SD): 32.8 (24.1) ***FEV1 % predicted*** (SD): 77.9 (16.5) ***Asthma medication*** (N (%)): Daily (budesonide or fluticasone) Low: 13 (59.1) Medium: 8 (36.3) High: 1 (6.6) Dose ranges as defined by GINA Daily LABA: 19 (86) Daily LTRAL 7 (31.8) Mini AQLQ, mean score (SD): 5.18 (1.1)
Wright et al. 2009[9]	***Arm 1:*** Mechanical heat recovery ventilation (MHRV) ***Arm 2:*** Placebo ventilation system In the placebo arm, low-level electric motors were set to 'on' but were not connected to the ventilation fans For both groups, carpets were steam-cleaned and participants were provided with new pillows, comforters, and mattress covers	House dust mite: Der p 1	**Type of study***:* RCT ***Population:*** 119 MHRV: 60 Placebo: 59 ***Attrition:*** 15% ***Setting:*** Home ***Country:*** Scotland ***Followup:*** 12 months	***Age,*** mean ([SD): MHRV: 41.6 (9.6) Placebo: 42.3 (10.7) Min. age: 16 years ***% Male:*** 38.7% ***Race:*** Caucasian: 97.5% Asian: 2.5% ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization:*** Serum HDM IgE antibody, median (IQR): MHRV: 5.7 (1.6 to 13.1) Placebo: 6.1 (2.3 to 15.2) ***Asthma severity:*** Asthma control score (0–6), median (IQR): MHRV: 1.57 (1.18 to 2.54) Placebo: 1.86 (1.14 to 2.71) ***Baseline spirometry:*** Pre-bronchodilator FEV_1 % predicted, mean (SD): MHRV: 83.7 (18.0) Placebo: 82.7 (17.7) Post-bronchodilator FEV_1 % predicted, mean (SD): MHRV: 86.6 (18.1) Placebo: 89.5 (15.6) FVC % predicted- Pre-bronchodilator, mean (SD): MHRV: 93.5 (13.6) Placebo: 95.0 (15.4) ***Mean duration of asthma***, year, median (IQR): MHRV: 21.0 (9.2 to 30.7) Placebo: 16.0 (9.0 to 25.0) ***Comorbidity,*** n: MHRV Hay fever/nasal allergy: 44

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
					Eczema: 15 Hypertension: 5 Angina: 2 Diabetes: 3 Prior stroke: 1 Other respiratory: 0 Prior myocardial infarction: 0 Placebo Hay fever/nasal allergy: 47 Eczema: 14 Hypertension: 8 Angina: 3 Diabetes: 2 Prior stroke: 2 Other respiratory: 1 Prior myocardial infarction: 1 ***Current smoker***, n***:*** MHRV: 12 Placebo: 17
Sulser et al. 2008[10]	***Arm 1:*** HEPA air cleaners ***Arm 2:*** Placebo Air cleaners were placed in living rooms and bedrooms, with filters changed after 6 months of use	Fel d 1 and/or Can f 1	***Type of study:*** RCT ***Population:*** 36 HEPA: 18 Placebo: 18 ***Attrition:*** 12% ***Setting:*** Home ***Country:*** Germany ***Followup:*** 12 months	***Age,*** median: 12 years Range: 6 to 17 years ***% Male:*** 25% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization:*** Mite sensitization was an exclusion criterion Serum IgE to cat, median kU/l: HEPA: 33.89 Placebo: 32.40 Serum IgE to dog, median kU/l: HEPA: 19.2 Placebo: 5.7 ***Carpet in home:*** 100% Exposure to Fel d 1 and/or Can f 1 >500 ng/g in home carpet dust
Francis et al. 2003[11]	***Arm 1:*** HEPA air cleaner and HEPA vacuum ***Arm 2:*** HEPA vacuum alone Air cleaners were placed in living rooms and bedrooms, and participants were instructed to vacuum carpets at least twice per week	Fel d 1 and/or Can f 1	***Type of study:*** RCT ***Population:*** 30 Air cleaner: 15 Control: 15 ***Attrition:*** 0% ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 12 months	***Age,*** mean (95% CI): Air cleaner: 36.8 (29.3 to 44.3) Control: 41.6 (34.4 to 48.9) Age range: 18 to 65 years ***% Male:*** 23.3% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization:*** (skin prick test positive): Can f 1: n=29/30 Fel d 1: n=29/30 ***FEV_1 % predicted***, mean (95% CI): Air cleaner: 87.3 (80.3 to 94.2) Control: 88.8 (76.8 to 100.8) ***PC_{20}***, geometric mean (95% CI): Air cleaner: 0.19 (0.07 to 0.56) Control: 0.23 (0.08 to 0.68) ***Current smoker***, n***:*** Active: 1 Control: 3 ***Atopy***

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
					Alternaria: n=25/30 HDM: n=30/30 Grass pollen: n=30/30 Enrollment criterion: All enrolled participants kept a cat or dog in the home against medical advice
van der Heide et al. 1999[12]	***Arm 1:*** Air cleaners ***Arm 2:*** Sham air cleaners Air cleaners were placed in living rooms and bedrooms.	Fel d 1 and/or Can f 1	***Type of study:*** RCT, crossover ***Population:*** 20 ***Attrition:*** 0% ***Setting:*** Home ***Country:*** Netherlands ***Followup:*** 3 months per arm; no washout	***Age,*** mean (SD): 11.7 (2.2) ***% Male:*** 60% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (serum IgE RAST class ≥2): Can f 1: n=17/20 Fel d 1: n=18/20 ***FEV_1 % predicted***, mean (SD): 90.2 (11.2) ***PC_{20}***, geometric mean (95% CI): 5.39 (2.64 to 11.00) HDM: 20/20 ***Use of mattress covers:*** n=11/20 ***Smoking in home:*** n=7/20 ***Carpet in living room:*** n=8/20 ***Carpet in bedroom:*** n=10/20 ***Enrollment criterion:*** All enrolled participants had pets to which they were sensitized in the house
van der Heide et al. 1997[13]	***Arm 1:*** Air cleaners ***Arm 2:*** Placebo air cleaners + mattress covers ***Arm 3:*** Air cleaners + mattress covers Air cleaners or placebo air cleaners were placed in living room and bedroom	Der p 1	***Type of study:*** RCT ***Population:*** 45 Air cleaners: 15 Mattress covers: 15 Air cleaners + mattress covers: 15 ***Attrition:*** 0% ***Setting:*** Home ***Country:*** Netherlands ***Followup:*** 6 months	***Age***, mean: Air cleaners: 32 Mattress covers: 32 Air cleaners + Mattress covers: 33 ***Age***, range: Air cleaners: 18 to 35 Mattress covers: 19 to 45 Air cleaners + mattress covers: 18 to 45 ***% Male:*** 37.8% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): HDM: 24.4% HDM + pollen: 68.9% HDM + pets: 57.8% HDM + pets + pollen: 48.9% ***FEV_1 % predicted***, mean (range): Air cleaners: 95 (65 to 119) Mattress covers: 93 (75 to 107) Air cleaners + mattress covers: 3.87 (78 to 124) ***PC_{20} histamine*** (mg/ml), mean (range): Air cleaners: 6.06 (0.08 to 32) Mattress covers: 8.44 (0.48 to 32) Air cleaners + mattress covers: 7.31 (0.15 to 124) ***Cigarette smoke exposed in home:*** 33.3% ***Animals in home:*** 33.3% ***Floor covering in living room:*** 80% ***Floor covering in bedroom:*** 57.8%

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
Warner et al. 1993[14]	***Arm 1:*** Ionizer ***Arm 2:*** Placebo ionizer Air cleaner placed in the living room during day and bedroom at night	Der p 1	***Type of study:*** RCT, crossover ***Population:*** 20 ***Attrition:*** 0% ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 6 weeks per arm; no washout	***Age,*** median: 9 years Range: 3 to 11 ***% Male:*** NR ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): HDM: 100%
Mitchell et al. 1980[15]	***Arm 1:*** Electrostatic precipitator ***Arm 2:*** No air cleaner Electrostatic precipitator was run in the bedroom on high (air-flow rate 8,500 l/min) for 3 hours before child's bedtime, then run on low (3,800 l/min) overnight	Der p 1 Der f 1	***Type of study:*** RCT, crossover ***Population:*** 10 ***Attrition:*** 0% ***Setting:*** Home ***Country:*** New Zealand ***Followup:*** 4 weeks per arm; no washout	***Age:*** Range: 6.9 to 13.5 ***% Male:*** 40% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization (***skin prick test positive): HDM: 100% **Asthma severity*:*** Moderate to severe
Zwemer et al. 1973[16]	***Arm 1:*** Pure-zone System (head-board mounted air filtration system) ***Arm 2:*** Placebo system Filtered air was passed over the bed during sleeping hours	Not specified	***Type of study:*** RCT, crossover ***Population:*** 18 ***Attrition:*** 0% attrition, usable data from 66.7% ***Setting:*** Home ***Country:*** United States ***Followup:*** 4 weeks per arm; no washout, with follow-on open trial (40 weeks, n=4)	***Age,*** range: 6 to 16 ***% Male:*** 38.9% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization:*** Skin prick test positive to HDM and "other indoor allergic materials"

Can f 1=*Canis familiaris* dog allergen; CI=confidence interval; Der f 1=*Dermatophagoides farina* house dust mite allergen; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen; Fel d 1=*Felis domesticus* cat allergen 1; FEV_1=forced expiratory volume in one second; FeNO=fraction exhaled nitric oxide; FVC=forced vital capacity; GINA=Global Initiative for Asthma; HDM=house dust mite; HEPA=high efficiency particulate air filter; IgE=immunoglobulin E; IQR=interquartile range; LABA=long acting beta-agonists; LTRA=leukotriene receptor antagonist; MHRV=mechanical heat recovery ventilation; Mini AQLQ=Mini Asthma Quality of Life Questionnaire; NR=Not reported; PC20=provocative concentration 20; PPB=parts per billion; RAST= radioallergosorbent test; RCT=randomized controlled trial; SD=standard deviation

Table C-6. Outcomes of air purification studies

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Pedroletti et al. 2009[8]	NR	8 exacerbations reported (Airshower: n=4; placebo: n=4; 3 exacerbations occurred in the same participant)	**FeNO** (ppb, mean difference in change (SEM), intervention – placebo): -6.4 (2.5); p<0.05 **FEV_1,** % predicted, mean difference in change: 1.14%; p=not significant **PEFR**, mean difference in change: 3.44%; p=not significant	**Mini AQLQ**, mean difference in change (SEM): 0.54 (0.28); p<0.05	NR	NR
Wright et al. 2009[9]	**ACQ**, adjusted difference between groups (95% CI): -0.25 (-0.57 to 0.08); p=not significant	**Oral steroids**, adjusted difference between groups (95% CI): 0.51 (0.21 to 1.22); p=not significant **Emergency department visits**, adjusted difference between groups (95% CI): 1.78 (0.31 to 10.16) **General practitioner visits**, adjusted difference between groups (95% CI): 0.90 (0.42 to 1.93); p=not significant **Hospitalizations**, n: MHRV: 0 Placebo: 4 p=0.12 **Rescue medicine puffs,** adjusted difference between groups (95% CI): -0.04 (-1.00 to 0.92); p=not significant	**FEV_1**, % predicted, adjusted difference between groups (95% CI): 1.32 (-2.56 to 5.19); p=not significant **Morning PEFR,** l/min, adjusted difference between groups (95% CI): 13.59 (-2.66 to 29.85); p=not significant **Evening PEFR**, l/min, adjusted difference between groups (95% CI): 24.56 (8.97 to 40.15); p=0.002; favors MHRV **Serum HDM IgE antibody:** 2.09 (-5.67 to 9.85); p=not significant	**SGRQ**, adjusted difference between groups (95% CI): -2.83 (-7.82 to 2.16); p=not significant	NR	**Measurement**: Study team collected dust samples by vacuuming mattresses, bedroom floors, and living room floors; samples were collected 2 times: before and after study **Der p 1**, adjusted difference between groups (95% CI): Bed: -0.32 (-0.84 to 0.21); p=not significant Bedroom: 1.46 (-2.65 to 5.57); p=not significant Living room: 0.1 (-0.8 to 0.9); p=not significant **Der p 2**, adjusted difference between groups (95% CI): Bed: -0.04 (-0.16 to 0.08); p=not significant Bedroom: 1.07 (-1.63 to 3.76); p=not significant Living room: 0.56 (-0.65 to 1.77); p=not significant
Sulser et al. 2008[10]	NR	NR	**Change in FEV_1,** before and after cold air challenge: Data presented graphically, did not differ between groups; p=0.544	Quality of life scores did not vary between groups, data not shown	NR	**Measurement**: Parents collected dust samples by vacuuming mattresses and floors; samples were collected 3 times; **Can d 1 and Fel d 1**: levels of allergens did not vary between groups, data presented graphically

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Francis et al. 2003[11]	NR	NR	**Improvement in combined asthma outcome** (PC_{20} and treatment requirement, with a beneficial response defined as at least one: 2 or more doubling dose improvement in histamine reactivity and/or at least a one-step reduction in treatment medication): Air purifier: 10/15 Control: 3/15 Air purifier vs. control: p=0.01 **FEV_1**, L, mean (SD) at 12 months: Air purifier: 2.84 (0.87) Control: 2.59 (0.89) Air purifier vs. control: p=not significant **FVC**, L, mean (SD) at 12 months: Air purifier: 3.71 (0.96) Control: 3.52 (0.95) Air purifier vs. control: p=not significant **Mean peak flow**, L/min, mean (SD) at 12 months: Air purifier: 390 (130) Control: 404 (109) Air purifier vs. control: p=not significant	NR	NR	**Measurement**: Dust samples were collected by use of a high volume air sampler placed above the floor for 1 hour, and by vacuuming living room and bedroom carpets; study did not report who collected samples; samples were collected 3 times **Can f 1**, geometric mean (SD): Airborne, mcg/m^3 Air purifier baseline: 22.1 (2.6) Air purifier 12 months: 2.8 (3.7) Control baseline: 40.1 (1.4) Control 12 months: 3.69 (5.4) Air purifier vs. control: p=not significant, actual p-value NR Bedroom carpet, mcg/g Air purifier baseline: 8.6 (3.4) Air purifier 12 months: 20.2 (15.5) Control baseline: 39.7 (4.1) Control 12 months: 134.1 (18.5) Air purifier vs. control: p=not significant, actual p-value NR Living room carpet, mcg/g: Air purifier baseline: 198.2 (3.0) Air purifier 12 months: 145.2 (3.3) Control baseline: 494.1 (2.3) Control 12 months: 317.5 (7.5) Air purifier vs. control: p=not significant, actual p-value NR **Fel d 1**, geometric mean (SD): Airborne, mcg/m^3 Air purifier baseline: 8.7 (4.6) Air purifier 12 months: 3.1 (3.4) Control baseline: 15.1 (3.9) Control 12 months: 6.7 (3.0) Air purifier vs. control: p=not significant, actual p-value NR Bedroom carpet, mcg/g Air purifier baseline: 73.8 (5.9) Air purifier 12 months: 13.2 (21.5) Control baseline: 77.1 (8.5)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
						Control 12 months: 82.1 (9.2) Air purifier vs. control: p=not significant, actual p-value NR Living room carpet, mcg/g: Air purifier baseline: 156.7 (6.3) Air purifier 12 months: 92.0 (3.4) Control baseline: 207.0 (9.6) Control 12 months: 52.0 (18.7) Air purifier vs. control: p=not significant, actual p-value NR
van der Heide et al. 1999[12]	NR	NR	**FEV_1:** No change (data not shown) **PC_{20}:** Geometric mean increased from 5.69 to 13.01 mg/mL (p=0.003) with use of air purifier and returned to baseline levels in the absence of the air purifier (data shown graphically) **Peak flow variation:** Decreased after use of air purifier (p=0.045; data shown graphically)	NR	NR	**Measurement:** Dust samples were collected by vacuuming mattresses and bedroom and living room floors; study did not report who collected the samples; samples were collected 3 times. **Can d 1 and Fel d 1:** Allergen levels in floor dust did not vary with treatment (data not shown)
van der Heide et al. 1997[13]	NR	NR	**FEV_1 and Vital Capacity:** Did not differ between-groups; data not shown **PC_{20} histamine**: Statistically significant improvement over baseline in the Air filter + Mattress cover arm (p<0.05); improvements described as less than one doubling dose	NR	NR	**Measurement:** Dust samples were collected by vacuuming mattresses and bedroom and living room floors; study did not report who collected the samples; samples were collected 3 times. **Der p 1:** For patients with air filters and mattress covers, Der p 1 decreased from baseline; data shown graphically with no estimate of variance, and study arms were not compared

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Warner et al. 1993[14]	NR	**Bronchodilator use**, mean SEM (SD): no difference between ionizer and placebo Ionizer: 0.48 (0.18) Placebo: 0.53 (0.25) Ionizer vs. placebo : 0.275	**Morning PEFR** l/min, mean (SEM): Ionizer: 232.6 (23.4) Placebo: 231.3 (25.8) Ionizer vs. placebo: p=not significant **Evening PEFR** l/min, mean (SEM): Ionizer: 239.2 (24.5) Placebo: 232.8 (26.1) Ionizer vs. placebo: p=not significant	NR	**Measurement**: Patient diaries using 4-point Likert scale **Daytime wheeze**, mean (SEM): Ionizer: 0.20 (0.07) Placebo: 0.185 (0.09) Ionizer vs. placebo: p=not significant **Night time wheeze**, mean (SEM): Ionizer: 0.19 (0.08) Placebo: 0.198 (0.07) Ionizer vs. placebo: p=not significant **Night time cough**, mean (SEM): Ionizer: 0.43 (0.19) Placebo: 0.139 (0.04) Ionizer vs. placebo: p=not significant **Day activity**, mean (SD): Ionizer: 0.06 (0.03) Placebo: 0.06 (0.04)	**Measurement:** Dust samples collected by use of “Casella personal sampler”, collected during 3 hour intervals in bedrooms and living rooms; study did not report who collected the samples; samples were collected 3 times throughout each ionizer cycle. **Der p 1**: airborne levels were lower during use of the active ionizer (p<0.001; data shown graphically)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Mitchell et al. 1980[15]	NR	NR	**Mean PEFR** did not vary with treatment condition (no summary statistics shown)	NR	NR	NR
Zwemer et al. 1973[16]	NR	**Medication utilization reduced**: 5/18 patients **School absence**, n (total days): Pure-zone: 0 (0); Control: 3 (15)	NR	NR	**Measurement:** Patient self-report **Asthma symptoms:** Improved with use of Pure-zone (no summary statistics shown) **Uninterrupted sleep**, total nights/per condition: Pure-zone: 140 Control: 45	NR

ACQ=Asthma control questionnaire: Range 0 to 6; Can f 1=*Canis familiaris* dog allergen I; Der f 1=*Dermatophagoides farina* house dust mite allergen; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen; Fel d 1=*Felis domesticus* cat allergen 1; FEV_1=forced expiratory volume in one second; FEF_{25-75}=average forced expiratory flow during the middle 25–75% portion of forced vital capacity (FVC); FeNO=exhaled nitric oxide; HDM=house dust mite; IgE=immunoglobulin E; MHRV=mechanical heat recovery ventilation; Mini AQLQ=Mini Asthma Quality of Life Questionnaire; NR=not reported; PC_{20}=provocative concentration 20; PEFR=peak expiratory flow rate; Ppb=parts per billion; SD=standard deviation; SEM=standard error of the mean; SGRQ=St. George's Respiratory Questionnaire

Table C-7. Risk of bias of air purification randomized controlled trials

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Pedroletti et al. 2009[8]	Unclear	Unclear	Low	Low	High	Low	High	High	Insufficient description of randomization; placebo used; 22% attrition; study funded by device manufacturer
Wright et al. 2009[9]	Low	Low	Low	Low	Low	Low	Low	Low	Placebo used; 15% attrition and intent-to-treat analysis
Sulser et al. 2008[10]	Unclear	Unclear	Low	Low	Low	Unclear	Low	Unclear	Insufficient description of randomization; placebo used; 12% attrition; data not shown or presented only in graph form
Francis et al. 2003[11]	Unclear	Unclear	High	Low	Low	Low	Low	Medium	Insufficient description of randomization; patients not blinded; all patients completed followup
van der Heide et al. 1999[12]	Low	Low	Low	Low	Low	High	High	High	Placebo used; all patients completed study; data not shown or presented only in graph form; study funded by device manufacturer
van der Heide et al. 1997[13]	Low	Unclear	Low	Low	Low	Low	High	Medium	Allocation not described; placebo used; all patients completed followup; study funded by device manufacturer
Warner et al. 1993[14]	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Insufficient description of randomization; placebo used; all patients completed followup
Mitchell et al. 1980[15]	Unclear	Unclear	High	High	Low	High	Low	High	Insufficient description of randomization; no blinding; all participants completed followup; minimal reporting of data
Zwemer et al. 1973[16]	Unclear	Unclear	Unclear	Low	High	Low	Low	Medium	Insufficient description of randomization; patients were blinded but blinding broken in some cases

Evidence Tables for High-Efficiency Particulate Air-Filtration (HEPA) Vacuum Studies

Table C-8. Study characteristics of HEPA vacuum study

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
Popplewell et al. 2000[17]	***Arm 1:*** High-efficiency (Electrolux) vacuum ***Arm 2:*** Standard model (Electrolux) vacuum Participants instructed to vacuum sofa, mattress, living room, and bedroom carpet at least once per week	Cat: Fel d 1 Dog: Can f 1 Dust mite: Der p 1	***Type of study:*** RCT ***Population:*** 60 21 children, 39 adults ***Attrition:*** 15% ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean: NR Range: Children: 5 to 15 years Adults: 22 to 63 years ***% Male:*** NR ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick positive test): 100% house dust mite 10 of 15 cat owners sensitized to cat 8 participants owned a dog, none described as sensitized to dog ***Asthma severity:*** NR ***Comorbidity:*** NR ***Pet owners:*** 30%

Can f 1=*Canis familiaris* dog allergen I; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen; Fel d 1=*Felis domesticus* cat allergen 1; HEPA=high=efficiency particulate air-filtration; NR=Not reported; RCT=randomized controlled trial

Table C-9. Outcomes of HEPA vacuum study

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (median difference; 95% CI; p) (secondary measure)
Popplewell et al. 2000[17]	NR	NR	**FEV_1:** HEPA vs. standard vacuum: p=0.027 **PEFR:** HEPA vs. standard vacuum: p=0.001 (data shown graphically)	NR	NR	**Measurement:** Patients collected dust samples by vacuuming mattresses, bedroom and living room carpets, and sofas; samples were collected 2 times: before and after study **Der p 1** (mean ng/m^2 [95% CI]): <u>Living room carpet</u> HEPA: 117 (-2 to 269); pre-post p=0.089 Standard: 64 (-12 to 320); pre-post p=0.247 <u>Bedroom carpet</u> HEPA: 10 (-375 to 321); pre-post p=0.803 Standard: 19 (-278 to 96); pre-post p=0.58 <u>Sofa</u> HEPA: 94 (-96 to 842); pre-post p=0.325 Standard: 64 (-12 to 320); pre-post p=0.247 <u>Mattress</u> HEPA: 22 (-71 to 1264); pre-post p=0.179 Standard: 10 (-65 to 1497); pre-post p=0.377 **Fel d 1** (mean ng/m^2 (95% CI): <u>Living room carpet</u> HEPA: -185 (-674 to -15); pre-post p=0.046 Standard: -261 (-712 to 106); pre-post p=0.111 <u>Bedroom carpet</u>

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (median difference; 95% CI; p) (secondary measure)
						HEPA: -193 (-68 to -1848); pre-post p=0.003 Standard: -180 (-1320 to -15); pre-post p=0.061 Sofa HEPA: -728 (-3700 to -30); pre-post p=0.005 Standard: -570 (-1647 to 720); pre-post p=0.247 Mattress HEPA: -491 (-1216 to -23); pre-post p=0.013 Standard: -580 (-1702 to -23); pre-post p=0.009 **Can f 1** (ng/m^2 (95% CI): Living room carpet HEPA: 10 (-388 to 203); pre-post p=0.958 Standard: 21 (-118 to 2812); pre-post p=0.443 Bedroom carpet HEPA: -78 (-258 to 22); pre-post p=0.116 Standard: -23 (-93 to 44); pre-post p=0.511 Sofa HEPA: -140 (-791 to 469); pre-post p=0.542 Standard: 30 (-373 to 2035); pre-post p=0.617 Mattress HEPA: -58 (-726 to -28); pre-post p=0.028 Standard: -14 (-185 to 46); pre-post p=0.685

Can f 1=*Canis familiaris* dog allergen I; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen; CI=confidence interval; Fel d 1=*Felis domesticus* cat allergen 1; FEV1=forced expiratory volume in one second; HEPA=high-efficiency particulate air-filtration; NR=not reported; PEFR=peak expiratory flow rate

Table C-10. Risk of bias of HEPA vacuum randomized controlled trial

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Popplewell et al. 2000[17]	Unclear	Unclear	Low	Unclear	Low	Low	Low	Unclear	Insufficient description of randomization; placebo used; unclear in outcome assessors were blinded; 15% attrition

Evidence Tables for Mattress Cover Studies

Table C-11. Study characteristics of mattress cover studies

Study	Intervention	Study Design	Demographic Factors	Clinical Factors
Murray et al. 2017[18]	***Arm 1:*** Impermeable covers (Astex Pristine) on mattresses, pillows, duvets ***Arm 2:*** Placebo covers	***Type of study:*** RCT ***Population:*** 284 ***Attrition:*** 15% ***Age cohort:*** Mixed ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean (SD): Mattress covers: 7.11 (3.49) Placebo: 7.45 (3.55) Range: 3–17 ***% Male:*** 66% ***Race:*** White: 64% Asian: 25% Other: 11% ***Homeownership:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity***, % GINA step 1/2/3/4/5: Mattress cover: 6.8% / 45.2% / 33.6% / 14.4% / 0.0% Placebo: 3.6% / 48.6% / 34.8% / 12.3% / 0.7% ***Comorbidity:*** Hay fever: Mattress cover: 35.7% Placebo: 30.6% Eczema: Mattress cover: 40.7% Placebo: 51.8% ***Carpeted bedrooms:*** NR ***Cat/dog in home and sensitized:*** Mattress cover: 21.2% Placebo: 21.0% ***Smoker in home:*** Mattress cover: 45.9% Placebo: 41.3%
Tsurikisawa et al. 2016[19]	***Arm 1*:** Microfine covers on pillows and mattresses/futons ***Arm 2:*** Vacuum with a nozzle designed to collect HDM on mattresses/futons ***Arm 3:*** No intervention Participants in the intervention groups were also given allergen avoidance instructions which included guidance on frequency and quality of vacuuming/cleaning/laundering, removal of bedroom carpets, and controlling humidity	***Type of study:*** RCT ***Population*:** 111 Pillow/mattress covers: 50 Vacuum: 13 Control: 23 ***Attrition:*** 22.5% ***Age cohort:*** Adult ***Country:*** Japan ***Followup:*** 1 year	***Age,*** mean (SD): Pillow/mattress covers: 48.2 (13.4) Vacuum: 53.1 (15.3) Control: 48.9 (13.7) ***% Male:*** Pillow/mattress covers: 34% Vacuum: 23.1% Control: 34.8% ***Race:*** Asian ***Homeownership:*** NR ***Geographic environment:*** NR	***HDM Sensitization,*** (serum IgE) mean (SE): Pillow/mattress covers: 2.430 (0.549) Vacuum: 2.366 (0.505) Control: 2.421 (0.612) ***Asthma severity:*** Step 1/2/3/4 severity of asthma (n/n/n/n per category): Pillow/mattress covers: 2/15/17/16 Vacuum: 0/4/5/4 Control: 4/6/5/8 Daily dose of ICS (mg; converted to CFC-BDP equivalents): Pillow/mattress covers: 1092.0 (757.2) Vacuum: 1138.5 (727.5) Control: 1055.1 (672.3) FeNO, ppb, Mean (SD) Pillow/mattress covers: 32.1 (18.1) Vacuum: 36.0 (32.8) Control: 33.9 (21.2) PEF variability, mean (SD) % during 2-week baseline assessment: Pillow/mattress covers: 12.4 (9.4) Vacuum: 8.2 (4.0) Control: 12.0 (9.0)

Study	Intervention	Study Design	Demographic Factors	Clinical Factors
				Duration of asthma (years [SD]) Pillow/mattress covers: 21.1 (16.0) Vacuum: 19.5 (13.2) Control: 17.7 (16.1) ***Comorbidity:*** <u>Atopic rhinitis</u> Pillow/mattress covers: 70% Vacuum: 69.2% Control: 69.6% <u>Atopic conjunctivitis</u> Pillow/mattress covers: 52% Vacuum: 69.2% Control: 56.5% <u>Atopic dermatitis</u> Pillow/mattress covers: 30% Vacuum: 56.5% Control: 26.1%
Tsurikisawa et al. 2013[20]	***Arm 1:*** Microfine fiber covers (Microguard) on mattresses, futons, pillows + recommendations for routine cleaning of linens, furniture, and floors + recommendations to remove carpeting, pets, and stuffed/soft toys ***Arm 2:*** No intervention or recommendations	***Type of study:*** RCT ***Population:*** 25 ***Attrition:*** 0% ***Age cohort:*** Adult ***Country:*** Japan ***Followup:*** 1 year	***Age,*** mean: 47 years ***% Male:*** 36% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (serum IgE): 100% ***Asthma severity:*** 44% severe; 36% moderate; 20% mild persistent ***Comorbidity:*** 72% atopic rhinitis 68% atopic conjunctivitis 36% atopic dermatitis ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 28% kept pet ***Smoker in home:*** NR
Glasgow et al. 2011[21]	***Arm 1:*** Feather-filled pillows and feather-filled quilt + impermeable cover on mattresses ***Arm 2:*** Impermeable covers on mattress, pillows, quilts	***Type of study:*** RCT ***Population:*** 197 ***Attrition:*** 4% ***Age cohort:*** Mixed ***Country:*** Australia ***Followup:*** 1 year	***Age,*** mean: 10 years Range: 7 to 14 ***% Male:*** 65% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR, but patients were excluded from study if allergic to cat while keeping pet ***Smoker in home:*** 28%
Nambu et al. 2008[22]	***Arm 1:*** Impermeable pillow (Yamasei; the pillow is designed to be house dust mite-impermeable without an additional cover) ***Arm 2:*** Placebo pillow	***Type of study:*** RCT ***Population:*** 20 ***Attrition:*** 0% ***Age cohort:*** Child ***Country:*** Japan ***Followup:*** 1 year	***Age,*** median: 7 vs. 6 years Range: 4 to 11 ***% Male:*** 80% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (serum IgE): 100% ***Asthma severity:*** NR ***Comorbidity:*** 20% dermatitis 15% rhinitis ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR

Study	Intervention	Study Design	Demographic Factors	Clinical Factors
de Vries et al. 2007[23] and van den Bemt et al. 2007[24]	***Arm 1:*** Non-polyurethane impermeable covers (Cara C'air) on mattresses, pillows, duvets ***Arm 2:*** Placebo covers	***Type of study:*** RCT ***Population:*** 126 ***Attrition:*** 17% ***Age cohort:*** Adult ***Country:*** Netherlands ***Followup:*** 2 years	***Age,*** mean: 42 years Range of eligible patients: 16 to 60 ***% Male:*** 58% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (serum IgE): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR, but patients were excluded from study if allergic to cat or dog while keeping pet ***Smoker in home:*** 7% of patients were current smokers
Dharmage et al. 2006[25]	***Arm 1:*** Impermeable covers on mattresses, pillows, doonas ***Arm 2:*** Placebo cotton covers	***Type of study:*** RCT ***Population:*** 32 ***Attrition:*** 6% ***Age cohort:*** Adult ***Country:*** Australia ***Followup:*** 6 months	***Age,*** mean: Intervention: 30 years Control: 33 years Range: 18 to 47 ***% Male:*** 37% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** 75% ***Cat/dog in home:*** 23% had cats ***Smoker in home:*** NR, but current smokers not eligible for enrollment
van den Bemt et al. 2004[26]	***Arm 1:*** Non-polyurethane impermeable covers on mattresses, pillows, duvets ***Arm 2:*** Placebo covers	***Type of study:*** RCT ***Population:*** 52 ***Attrition:*** 0% ***Age cohort:*** Adult ***Country:*** Netherlands ***Followup:*** 9 weeks	***Age,*** mean: 34 years Range of eligible patients: 12 to 60 ***% Male:*** 52% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization:*** (serum IgE): 100% ***Asthma severity:*** NR, but mean symptom score was 2.1 on a scale of 0 to 60 ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR, but patients were excluded from study if allergic to cat or dog while keeping pet ***Smoker in home:*** 21% of patients were current smokers
Halken et al. 2003[27]	***Arm 1:*** Semi-permeable polyurethane covers (Allergy Control) on mattresses, pillows ***Arm 2:*** Placebo cotton covers	***Type of study:*** RCT ***Population:*** 60 ***Attrition:*** 17% ***Age cohort:*** Mixed ***Country:*** Denmark ***Followup:*** 1 year	***Age,*** mean: NR Range of eligible patients: 5 to 15 ***% Male:*** NR ***Race*** NR***:*** ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR, but patients were excluded from study if allergic to cat or dog while keeping pet ***Smoker in home:*** NR
Lee 2003[28]	***Arm 1:*** Cotton bed covers boiled for 10 minutes every 2 weeks, and exposed to sunlight for more than 3 hours every 2 weeks ***Arm 2:*** No intervention	***Type of study:*** RCT ***Population:*** 42 ***Attrition:*** NR ***Age cohort:*** NR **Country*:*** Korea ***Followup:*** 4 weeks	***Age,*** mean: 43% <30 years ***% Male:*** 55% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 36% ***Smoker in home:*** NR
Luczynska et al. 2003[29]	***Arm 1:*** Microfiber impermeable covers (Allerguard) on mattresses, pillows, duvets ***Arm 2:*** Placebo covers	***Type of study:*** RCT ***Population:*** 55 ***Attrition:*** 18% ***Age cohort:*** Adult ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean: 36 years Range of eligible patients: 18 to 54 ***% Male:*** 49% ***Race:*** NR ***Geographic environment:*** Urban	***HDM Sensitization*** (serum IgE): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR, but patients were excluded from study if allergic to cat or dog while keeping pet ***Smoker in home:*** NR

Study	Intervention	Study Design	Demographic Factors	Clinical Factors
Woodcock et al. 2003[30]	***Arm 1:*** Impermeable covers (Allergy Control Products) on mattresses, pillows, quilt covers ***Arm 2***: Placebo polyester-cotton covers	***Type of study:*** RCT ***Population:*** 1,122 ***Attrition:*** 16% ***Age cohort:*** Adult ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean: 37 years Range of eligible patients: 18 to 50 ***% Male:*** 36% ***Race:*** 98% White ***Geographic environment:*** NR	***HDM Sensitization*** (serum IgE): 65% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 55% ***Smoker in home:*** 23%
Rijssenbeek-Nouwens et al. 2002[31]	***Arm 1:*** Impermeable covers (Cara C'air) on mattresses, pillows, bedding ***Arm 2***: Placebo covers	***Type of study:*** RCT ***Population:*** 30 ***Attrition:*** 21% ***Age cohort:*** Adult (but 2 patients were 11 years old) ***Country:*** Netherlands ***Followup:*** 1 year	***Age,*** mean: 29 years Range: 11 to 51 ***% Male:*** 57% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive or serum IgE): 100% ***Asthma severity:*** All patients moderate or severe ***Comorbidity:*** 67% rhinitis ***Carpeted bedrooms:*** Patients with carpeted bedrooms were excluded from the study ***Cat/dog in home:*** NR, but patients were excluded from study if allergic to cat or dog while keeping pet ***Smoker in home:*** Smokers were excluded from the study
Sheikh et al. 2002[32]	***Arm 1:*** Impermeable covers (Allerayde) on mattresses, pillows, duvets ***Arm 2:*** Placebo covers	***Type of study:*** RCT ***Population:*** 47 ***Attrition:*** 8% ***Age cohort:*** Mixed ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean: 11 years Range of eligible patients: 5 to 14 ***% Male:*** 62% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** Pet owners were excluded from study ***Smoker in home:*** NR
Frederick et al. 1997[33]	***Arm 1:*** Impermeable covers (Intervent) on mattresses, pillows, duvets ***Arm 2:*** Placebo polycotton covers	***Type of study:*** RCT, crossover: intervention for 3 months, then 1 month wash-out period, then groups switched for 3 months ***Population:*** 31 ***Attrition:*** NR ***Age cohort:*** Mixed ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean: 9 years Range: 5 to 15 ***% Male:*** 65% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive or serum IgE): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 23% ***Smoker in home:*** NR
Burr et al. 1980[34]	***Arm 1:*** Impermeable plastic covers on mattresses + provision of new bedding and pillow ***Arm 2:*** No intervention	***Type of study:*** RCT, crossover: intervention for 1 month, then groups switched for 1 month ***Population:*** 21 ***Attrition:*** 0% ***Age cohort:*** Mixed ***Country:*** United Kingdom ***Followup:*** NR	***Age,*** mean: NR ***% Male:*** NR ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR

Study	Intervention	Study Design	Demographic Factors	Clinical Factors
Burr et al. 1976[35]	***Arm 1:*** Impermeable plastic covers on mattresses ***Arm 2:*** Vacuuming of upholstered furniture + recommendation to vacuum carpet regularly	***Type of study:*** RCT, crossover: intervention for 6 weeks, then groups switched for 6 weeks ***Population:*** 32 ***Attrition:*** NR% ***Age cohort:*** Adult ***Country:*** United Kingdom ***Followup:*** NR	***Age,*** mean: 33 ***% Male:*** 56% ***Race:*** NR ***Geographic environment:*** NR	***HDM Sensitization*** (skin prick test positive): 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR

CFC-BDP=chlorofluorocarbon-propelled beclomethasone dipropionate; Der f 1=*Dermatophagoides farina* house dust mite allergen; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen; FeNO=fraction exhaled nitric oxide; GINA=Global Initiative for Asthma; HDM=house dust mite; IgE= immunoglobulin E; NR=not reported; PEF=peak exploratory flow; PPB=parts per billion; RCT=randomized controlled trial; SD=standard deviation; SE=standard error

Table C-12. Outcomes of mattress cover studies

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Murray et al. 2017[18]	**ACQ**, mean difference (95% CI): No significant difference between arms, but there was significant reduction from baseline in mattress cover arm: Mattress covers: -0.56 (-0.18 to -0.93) Placebo: -0.25 (-0.61 to 0.11)	**Hospitalization or ED visit requiring systemic corticosteroids** (composite measure): Statistically significant difference: Mattress covers: 29.3% Placebo: 41.5% Mattress covers vs. placebo: OR: 0.58 (95% CI: 0.34 to 0.99), p=0.047 **Use of systemic corticosteroids for 3 or more days** (including inpatient and outpatient use): No statistically significant difference: Mattress covers: 48.8% Placebo: 50.0% Mattress covers vs. placebo: p=0.85	NR	**PACQLQ**, mean difference (95% CI): No statistically significant difference between arms, but there was a statistically significant reduction in each arm from baseline: Mattress covers: 0.50 (0.14 to 0.80) Placebo: 0.57 (0.12 to 1.02)	NR	**Measurement:** Study team collected dust samples by vacuuming mattresses and living room floors; samples collected 2 times: before and after study period **Der p 1:** <u>Mattress dust</u>: Statistically significant reduction in mattress cover arm compared with placebo arm: Mattress cover: 84% reduction Placebo: No reduction Mattress cover vs. placebo: p<0.001, data shown graphically <u>Living room floor dust</u>: No difference in either arm: p=0.48, data shown graphically

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Tsurikisawa et al. 2016[19]	NR	NR	**FeNO,** ppb, mean (SD): No statistically significant differences between arms: Mattress cover: 36.3 (23.3) Vacuum: 29.1 (22.3) Control: 35.8 (19.4) **PEFR variability**, mean (SD), % during 2-week final assessment: No statistically significant differences between arms: Mattress cover: 10.3 (6.7) Vacuum: 10.7 (6.3) Control: 14.1 (10.3)	NR	NR	**Measurement**: samples collected with tape from mattress, and in petri dish 100 cm above bedroom floor Mattress samples, log Der 1 (log ng/m^2) mean (SD): No statistically significant differences between arms: Mattress cover: 1.281 (0.830) Vacuum: 1.179 (1.072) Control: 1.262 (0.946) Bedroom air samples, log Der 1 (log ng/m^2) mean (SD): No statistically significant differences between arms Mattress cover: 2.039 (0.749) Vacuum: 1.872 (1.365) Control: 2.031 (0.838)
Tsurikisawa et al. 2013[20]	NR	NR	**PEFR:** Statistically significant increase in minimum % PEFR in mattress cover arm compared with control arm: p<0.01 (data reported in figure)	NR	**Measurement:** Patient questionnaires **Symptom score** (cough, wheeze, sneezing, sputum, dyspnea, use of short-acting beta stimulants, and ED visits): Statistically significant decrease in symptoms in mattress cover arm compared with control arm: p<0.01 (data reported in figure)	**Measurement:** Patients collected dust samples using petri dishes and tape, in the bedroom and on the mattress; samples were collected 2 times: before and after the study period **Der p 1 and Der f 1** Statistically significant reduction in allergen levels on mattresses in mattress cover arm compared with control arm: p<0.01 (data reported in figure)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Glasgow et al. 2011[21]	NR	NR	NR	**Juniper Paediatric Quality of Life Questionnaire**, difference effect between intervention arm and control arm (95% CI): Overall score: 0.04 (-0.27 to 0.35), p=0.80 Activity: 0.17 (-0.23 to 0.57), p=0.41 Symptoms: 0.04 (-0.28 to 0.36) Emotional function: -0.01 (-0.33 to 0.31), p=0.97	**Measurement**: Patient questionnaires **Frequent wheeze** (≥4 times), OR (95% CI): No statistically significant difference between arms: OR: 1.51 (0.83 to 2.76), p=0.17 **Speech-limiting wheeze**, OR (95% CI): No statistically significant difference between arms: OR: 0.70 (0.32 to 1.48), p=0.35 **Sleep disturbance caused by wheeze**, OR (95% CI): No statistically significant difference between arms: OR: 1.17 (0.64 to 2.13), p=0.61	**Measurement**: Patients collected dust samples by wearing nasal air samplers for four nights; samples were also collected by mechanical air filters **Der p 1**, median (IQR), pg/m^3: No statistically significant difference between arms Intervention: 16.0 (1.0 to 54.1) Control: 28.0 (1.0 to 66.8) Intervention vs. control: p=0.3
Nambu et al. 2008[22]	NR	**Asthma attacks:** No statistically significant difference between arms (data reported in figure)	NR	NR	NR	**Eosinophil levels:** No statistically significant difference between arms in IgE levels for HDM (data reported in figure)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
de Vries et al. 2007[23] van den Bemt et al. 2007[24]	**ACQ,** mean: No significant difference between arms, or within arms over baseline: Mattress cover baseline: 1.13 Mattress cover followup: 1.03 Placebo baseline: 1.05 Placebo followup: 1.71 Mattress cover vs. placebo: p=0.27	**Inhaled corticosteroids**, estimated total difference between mattress cover and placebo arms (95% CI): No statistically significant difference for total ICS doses over study period (Most commonly used ICS was budesonide 200 mcg with Turbuhaler®. Dose equivalents for different types of ICS and delivery devices were calculated.) -830.8 mcg (-1646.2 to 92.3), p=0.08	**Morning PEFR:** No statistically significant difference between mattress cover and placebo arms (p=0.52, data not shown) **Peak flow variability:** No statistically significant difference between mattress cover and placebo arms (p=0.36, data not shown)	**Mini Asthma Quality of Life Questionnaire:** No statistically significant difference between arms, and within arms over baseline Incremental change: -0.03, p=0.82	**Measurement:** Patient diaries **Cough:** No statistically significant difference between arms: (p=0.41, data not shown) **Wheeze:** No statistically significant difference between arms: (p=0.77, data not shown) **Dyspnea:** No statistically significant difference between arms: (p=0.46, data not shown)	**Measurement:** Study team collected dust samples by vacuuming mattresses; samples were collected 3 times throughout study period **Der p 1 concentration**, ng/g: Statistically significantly lower allergen levels in mattress cover arm compared with placebo arm Mattress cover baseline: 863 Mattress cover followup: 115 Placebo baseline: 806 Placebo followup: 895 Mattress cover vs. placebo: p<0.01 **Der p 1 density**, ng/m^2: Statistically significantly lower allergen density in mattress cover arm compared with placebo arm Mattress cover baseline: 52 Mattress cover followup: 10 Placebo baseline: 61 Placebo followup: 115 Mattress cover vs. placebo: p<0.01

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Dharmage et al. 2006[25]	NR	**Puffs per day, mean change (95% CI):** No statistically significant difference between arms, or within arms over baseline: Mattress cover: 0.36 (-0.14 to 0.85) Placebo: 0.20 (-0.02 to 0.43)	**Peak flow variability**, mean change (95% CI): No statistically significant difference between arms, or within arms over baseline Mattress cover: 1.95 (-0.05 to 3.9) Placebo: 0.50 (-1.50 to 2.50)	**Quality of life:** (measurement scale not described) No statistically significant difference between arms, but there was improvement over baseline in both arms ($p<0.05$; data reported in figure)	**Measurement:** Patient diaries **Daytime symptom score**, mean change (95% CI): (wheeze, cough, sleep disturbance, activity restriction) No statistically significant difference between arms or within arms over baseline: Mattress cover: 0.02 (-0.03 to 0.07) Placebo: 0.04 (-0.02 to 0.10) **Nighttime symptom score**, mean change (95% CI): No statistically significant difference between arms or within arms over baseline: Mattress cover: 0.20 (-0.08 to 0.49) Placebo: 0.14 (-0.17 to 0.45)	**Measurement:** Study team collected dust samples by vacuuming mattresses; samples were collected 3 times throughout the study period **Der p 1**, mcg/g: Statistically significant difference between arms: Mattress cover baseline: 19.2 Mattress cover followup: 7.3 Placebo baseline: 18.9 Placebo followup: 21.2 Mattress cover vs. placebo: $p<0.05$

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
van den Bemt et al. 2004[26]	NR	NR	**PEFR:** Statistically significant improvement between arms at followup: p=0.01 (data reported in figure); however, repeated measurement analysis showed change not sustained over time	NR	NR	**Measurement:** Study team collected dust samples by vacuuming mattresses; samples were collected 3 times throughout the study period **Der p 1**, geometric mean, mcg/m^2 (95 % CI): Statistically significant difference between arms Mattress cover baseline: 0.96 (0.40 to 2.31) Mattress cover followup: 0.04 (0.02 to 0.11) Placebo baseline: 0.70 (0.32 to 1.53) Placebo followup: 0.46 (0.18 to 1.17) Mattress cover vs. placebo: p<0.05
Halken et al. 2003[27]	NR	**Beta-agonist doses per 2 weeks**, change from baseline: Mattress cover: -8 Placebo: -7 Mattress cover vs. placebo: p=not significant **Systemic steroids**: No patients required use **ICS dose:** <u>% patients with dose reduced ≥50%:</u> Mattress cover: 73% Placebo: 24% Mattress cover vs. placebo: p<0.01 <u>Change in mean ICS dose</u>, mcg (budesonide or fluticasone): Mattress cover: -181 Placebo: -39 Mattress	**PEFR:** No statistically significant difference between arms (data not shown) Statistically significant increase in both arms over baseline: p<0.01 **FEV_1:** No statistically significant difference between arms (data not shown) Statistically significant increase in both arms over baseline: p<0.01	NR	**Measurement:** Patient diaries **Daytime symptom score**, mean: No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 1.62 Mattress cover followup: 1.73 Placebo baseline: 3.33 Placebo followup: 2.57 **Nighttime symptom score**, mean: No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 0.46 Mattress cover followup:	**Measurement:** Patients collected dust samples by vacuuming mattresses; samples were collected 6 times throughout the study period **Total house dust mite (Der p 1, Der f 1, Der m 1)**, geometric mean, ng/g dust: Statistically significant reduction in mattress cover arm compared with placebo arm: Mattress cover baseline: 15,604 Mattress cover followup: 1,456 Placebo baseline: 8,791 Placebo followup: 4,311 Mattress cover vs. placebo: p=0.03

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
		cover vs. placebo: p<0.01			1.08 Placebo baseline: 1.48 Placebo followup: 1.90	
Lee 2003[28]	NR	**Asthma attacks**, mean (SD): No statistically significant difference between arms, or within arms over baseline: Intervention baseline: 0.32 (1.49) Intervention followup: 0.14 (0.47) Control baseline: 0.95 (4.25) Control followup: 0.75 (3.13)	**Morning PEFR**, mean (SD): No statistically significant difference between arms, or within arms over baseline: Intervention baseline: 86.45 (14.89) Intervention followup: 88.60 (13.66) Control baseline: 92.45 (13.92) Control followup: 89.43 (17.33) Intervention vs. control: p=0.10 **Evening PEFR**, mean (SD): No statistically significant difference within arms, or between arms over baseline: Intervention baseline: 88.09 (13.88) Intervention followup: 90.27 (13.46) Control baseline: 93.50 (12.42) Control followup: 91.10 (17.28) Intervention vs. control: p=0.095	NR	**Measurement:** Patient diaries **Cough**, mean (SD): No statistically significant difference between arms, or within arms over baseline: Intervention baseline: 41.14 (81.68) Intervention followup: 22.27 (50.05) Control baseline: 38.95 (48.29) Control followup: 36.85 (63.44) **Wheeze**, mean (SD): No statistically significant difference between arms, but significant improvement within arms, over baseline: Intervention baseline: 2.23 (4.87) Intervention followup: 0.27 (1.08) Control baseline: 3.40 (11.48) Control followup: 2.00 (6.70) **Dyspnea**, mean (SD): Statistically significant improvement in intervention arm compared with control: Intervention baseline: 2.55 (5.19) Intervention followup: 1.18 (2.79) Control baseline: 0.85	**Measurement:** Study team collected dust samples by vacuuming mattresses and bedroom floors; samples were collected 2 times: before and after the study period **Der p 1**, ng/g of dust (SD): Statistically significant increase in allergen level in intervention arm: Intervention baseline: 220.8 (318.5) Intervention followup: 330.5 (627.8) Control baseline: 1687.4 (4741.1) Control followup: 1484.9 (4599.6) Intervention vs. control: p=0.02 **Der f 1**, ng/g of dust (SD): Statistically significant reduction in allergen level in intervention arm” Intervention baseline: 19877.7 (14726.4) Intervention followup: 14054.6 (9949.6) Control baseline: 18314.1 (17358.8) Control followup: 16394.5 (19432.4) Intervention vs. control: p<0.01

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
					(3.57) Control followup: 2.20 (4.69) **Sleep disturbance**, mean (SD): Statistically significant increase in symptom in intervention arm: Intervention baseline: 1.86 (7.43) Intervention followup: 3.09 (14.28) Control baseline: 1.15 (4.69) Control followup: 2.05 (6.49)	
Luczynska et al. 2003[29]	NR	**Asthma attacks**: No statistically significant difference between arms, or within arms over baseline (data NR) **Medication use**: No statistically significant difference between arms, or within arms over baseline (data NR)	**PEFR**, mean (95% CI): No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 325 (295 to 382) Mattress cover followup: 367 (289 to 445) Placebo baseline: 347 (322 to 372) Placebo followup: 388 (350 to 428)	**Marks Asthma Quality of Life Questionnaire**, mean decrease in square root of score (95% CI): No statistically significant difference between arms: Mattress cover: 0.44 (-0.25 to 1.14) Placebo: 0.69 (-0.04 to 1.42)	**Measurement:** Patient diaries **Chest tightness**, mean days (95% CI): No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 7.17 (5.26 to 9.08) Mattress cover followup: 4.88 (2.32 to 7.44) Placebo baseline: 6.05 (4.09 to 8.01) Placebo followup: 5.93 (2.98 to 8.88)	**Measurement:** Study team collected dust samples by vacuuming mattresses; samples were collected 3 times throughout the study period **Der p 1**, geometric mean (95% CI): No statistically significant difference between arms, but significant reduction in allergen levels within each arm over baseline: Mattress cover baseline: 18.90 (9.41 to 37.97) Mattress cover followup: 0.38 (0.13 to 1.18) Placebo baseline: 25.05 (11.56 to 54.59) Placebo followup: 2.31 (1.11 to 4.82)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Woodcock et al. 2003[30]	NR	**Exacerbations**, % 1 hospital visit or 1 course of oral corticosteroids in prior 6 months: No statistically significant difference between arms: Mattress cover: 10.3% Placebo: 12.0% Mattress cover vs. placebo: RR (95% CI): 0.85 (0.60 to 1.21) p=0.38 **Daytime beta-agonist**, mean number of puffs: No statistically significant difference between arms, but significant decrease within each arm over baseline: Mattress cover baseline: 2.91 Mattress cover followup: 2.24 Placebo baseline: 2.73 Placebo followup: 2.26 Mattress cover vs. placebo: Adjusted difference (95%): -0.15 (-0.32 to 0.02) p=0.08 **Nighttime beta-agonist**, mean number of puffs: No statistically significant difference between arms, but significant decrease within each arm over baseline: Mattress cover baseline: 1.36 Mattress	**Peak flow**, mean liters/minute: No statistically significant difference between arms, but significant improvement in both arms over baseline: Mattress cover baseline: 410.7 Mattress cover followup: 419.1 Placebo baseline: 417.8 Placebo followup: 427.4 Mattress cover vs. placebo: Adjusted difference (95% CI): -1.6 (-5.9 to 2.7), p=0.46	**St. George's Respiratory Questionnaire**, % of patients reporting that their quality of life had improved: No statistically significant difference between arms: Mattress cover: 71.3% Placebo: 71.7% Mattress cover vs. placebo: RR (95% CI): 1.00 (0.92 to 1.08), p=0.90	**Measurement:** Patient diaries **Daytime symptom score**, mean (components not described): No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 1.32 Mattress cover followup: 1.07 Placebo baseline: 1.33 Placebo followup: 1.09 Mattress cover vs. placebo: Adjusted difference (95% CI): -0.02 (-0.10 to 0.06), p=0.65 **Nighttime symptom score**, mean (components not described): No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 0.92 Mattress cover followup: 0.76 Placebo baseline: 0.94 Placebo followup: 0.76 Mattress cover vs. placebo: Adjusted difference (95% CI): 0.01 (-0.06 to 0.08), p=0.77	**Measurement:** Study team collected dust samples by vacuuming mattresses; samples were collected 3 times throughout the study period **House dust mite allergens**, geometric mean, µg/g: Statistically significant reduction in allergen levels in mattress cover arm compared with placebo arm: Mattress cover: 0.58 Placebo: 1.71 Mattress cover vs. placebo: p=0.01

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
		cover followup: 1.17 Placebo baseline: 1.47 Placebo followup: 1.27 Mattress cover vs. placebo: Adjusted difference (95%): -0.02 (-0.13 to 0.10) p=0.78 **Missed days of work**, mean days per prior month: Statistically significant reduction in mattress cover arm: Mattress cover: 0.11 Placebo: 0.25 Mattress cover vs. placebo: Unadjusted difference (95% CI): -0.15 (-0.29 to -0.02)				

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Rijssenbeek-Nouwens et al. 2002[31]	NR	**Rescue medication use**: No statistically significant difference between arms, or within arms over baseline (data not shown)	**Morning PEFR**, median (range): No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 426 (226 to 727) Mattress cover followup: 440 (246 to 740) Placebo baseline: 432 (292 to 581) Placebo followup: 416 (240 to 600) **Evening PEFR**, median (range): No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 422 (225 to 683) Mattress cover followup: 425 (247 to 748) Placebo baseline: 434 (228 to 625) Placebo followup: 406 (236 to 700)	**Quality of Life for Respiratory Illness Questionnaire**: No statistically significant difference between arms, but significant improvement within each arm over baseline (data not shown)	**Measurement:** Patient diaries **Pulmonary symptoms score**, median (range): (cough, wheeze, dyspnea, expectoration) No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 2.04 (0.0 to 8.25) Mattress cover followup: 1.46 (0.0 to 7.07) Placebo baseline: 1.27 (0.0 to 8.35) Placebo followup: 0.36 (0.0 to 10.92) **Nasal symptoms score**, median (range): (nasal blockage, sneezing, itching, rhinorrhea) No statistically significant difference between arms, but significant improvement within mattress cover arm over baseline: Mattress cover baseline: 1.67 (0.0 to 6.57) Mattress cover followup: 0.79 (0.0 to 5.21) Placebo baseline: 1.93 (0.0 to 11.16) Placebo followup: 1.43 (0.0 to 10.92)	**Measurement:** Study team collected dust samples by vacuuming mattresses; samples were collected 4 times throughout the study period **Der p 1**, mcg/g: Statistically significant reduction in allergen level in mattress cover arm, compared with placebo: Mattress cover baseline: 26.19 Mattress cover followup: 2.79 Placebo baseline: 23.28 Placebo followup: 25.11

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Sheikh et al. 2002[32]	NR	**Systemic steroid dose:** No statistically significant differences between arms or within each arm over baseline **Hospitalizations:** None reported in either arm **ICS dose** (agent not specified**)**, mean change in 28-day dose, mcg (SD): No statistically significant difference between arms: Mattress cover: -1815.91 (3861.45) Placebo: -1039.00 (1881.15) Mattress cover vs. placebo: p=0.41	**PEFR**, mean change liters/min (SD): No statistically significant difference between arms: Mattress cover: 16.38 (25.62) Placebo: 13.68 (43.14) Mattress cover vs. placebo: p=0.81	NR	**Measurement:** Patient diaries **Asthma symptoms score**, mean change (SD): (cough, wheeze, shortness of breath, chest tightness) No statistically significant difference between arms: Mattress cover: -3.40 (29.50) Placebo: -18.10 (27.80) Mattress cover vs. placebo: p=0.12 **Nighttime waking**, mean change, episodes per month (SD): No statistically significant difference between arms: Mattress cover: -0.64 (3.00) Placebo: -0.94 (2.30) Mattress cover vs. placebo: p=0.43	NR
Frederick et al. 1997[33]	NR	**Beta-agonist use**, median (range), µg: No statistically significant difference between arms, or within arms over baseline: Mattress cover baseline: 120 (0.0 to 986) Mattress cover followup: 80 (0.0 to 312) Placebo baseline: 60 (0.0 to 542) Placebo followup: 40 (0.0 to 372)	**Morning PEFR**, median (range), L/min: No statistically significant differences within arms over baseline; no between-arm comparisons conducted: Mattress cover baseline: 262 (132 to 389) Mattress cover followup: 257 (177 to 391) Placebo baseline: 269 (141 to 390)	NR	**Measurement:** Patient diaries **Asthma score for previous night**, median (range): No statistically significant differences within arms over baseline; no between-arm comparisons conducted: Mattress cover baseline: 0.2 (0.0 to 1.9) Mattress cover followup: 0.1 (0.0 to 0.8) Placebo baseline: 0.09 (0.0 to 2.5)	**Measurement:** Dust samples were collected by vacuuming mattresses; study does not report who collected samples; samples were collected 4 times throughout the study period **Der p 1:** Statistically significant reduction in allergen concentration on mattresses, pillows, and duvets, for mattress cover arm compared with placebo arm: p<0.01

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
			Placebo followup: 282 (155 to 428) **Evening PEFR**, median (range), L/min: No statistically significant differences within arms over baseline; no between-arm comparisons conducted: Mattress cover baseline: 265 (142 to 402) Mattress cover followup: 258 (174 to 407) Placebo baseline: 274 (160 to 418) Placebo followup: 307 (167 to 432) **FEV**, median (range): No statistically significant difference within mattress cover arm: Mattress cover baseline: 86% (43 to 123) Mattress cover followup: 85% (53 to 114)		Placebo followup: 0.09 (0.0 to 1.7) **Daytime wheeze score**, median (range): No statistically significant differences within arms over baseline; no between-arm comparisons conducted: Mattress cover baseline: 0.4 (0.0 to 1.2) Mattress cover followup: 0.3 (0.0 to 1.1) Placebo baseline: 0.3 (0.0 to 2.1) Placebo followup: 0.2 (0.0 to 1.1) **Exercise tolerance score**, median (range): No statistically significant differences within arms over baseline; no between-arm comparisons conducted: Mattress cover baseline: 0.4 (0.0 to 1.6) Mattress cover followup: 0.2 (0.0 to 1.1) Placebo baseline: 0.2 (0.0 to 2.1) Placebo followup: 0.2 (0.0 to 1.2)	

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Burr et al. 1980[34]	NR	NR	**Morning PEFR**, mean coefficient of variation (SE): No statistically significant differences between arms, or within arms over baseline: Mattress cover: 11.6 (1.4) No intervention: 14.6 (1.6) **Evening PEFR**, mean coefficient of variation (SE): No statistically significant differences between arms, or within arms over baseline: Mattress cover: 12.2 (1.4) No intervention: 12.9 (1.3)	NR	NR	NR
Burr et al. 1976[35]	NR	NR	**PEFR**, mean (SE), liters/min: No statistically significant difference between arms: Mattress cover: 335 (19.6) Control: 329 (20.8)	NR	NR	NR

ACQ=asthma control questionnaire; CI=95% confidence interval; Der f 1=*dermatophagoides farina* house dust mite allergen; Der p 1: *dermatophagoides pteronyssinus* house dust mite allergen; ED=emergency department; FEV_1=forced expiratory volume in 1 second; IQR=interquartile range; mcg/g=micrograms per gram; NR=not reported; OR=odds ratio; PACQLQ=pediatric asthma caregivers asthma quality of life questionnaire; PEFR=peak expiratory flow rate; PFV=peak flow variability; pg/m^3=phosphoglucomutase 3; RCT=randomized controlled trial; RR=relative risk; SD=standard deviation; SE=standard error

Table C-13. Risk of bias of mattress cover randomized controlled trials

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Murray et al. 2017[18]	Low	Low	Low	Low	Low	Low	Low	Low	Placebo; patients and assessors blinded; 15% attrition; intent-to-treat analysis; pre-specified outcomes reported
Tsurikisawa et al. 2016[19]	Unclear	Unclear	High	Unclear	High	Low	Low	High	Insufficient description of randomization; patients not blinded; unclear if outcome assessors were blinded; 23% attrition; no intent-to-treat analysis
Tsurikisawa et al. 2013[20]	Unclear	Unclear	High	High	Low	Low	Low	Medium	Insufficient description of randomization; no blinding; all patients completed study
Glasgow et al. 2011[21]	Low	Low	Low	Low	Low	Low	Low	Low	Placebo; patients and assessors blinded; low attrition; intent-to-treat analysis; pre-specified outcomes reported
Nambu et al. 2008[22]	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Insufficient description of randomization; placebo; patients and assessors blinded; all patients completed study
de Vries et al. 2007[23]	Low	Low	Low	Low	Unclear	Low	Low	Low	Placebo; patients blinded and most outcomes patient-reported; moderate attrition rate of 17% but intent-to-treat analysis used; pre-specified outcomes reported; study funded in part by pharmaceutical manufacturers
Dharmage et al. 2006[25]	Low	Low	Low	Low	Low	Low	Low	Low	Placebo; participants and assessors blinded; low attrition; pre-specified outcomes reported
van den Bemt et al. 2004[26]	Unclear	Unclear	Low	Low	Low	High	Low	Medium	Insufficient description of randomization; placebo; patients blinded and most outcomes patient-reported; intent-to-treat analysis used; did not report followup symptom score because baseline scores were very low
Halken et al. 2003[27]	Low	Low	Low	Low	High	Low	Low	Medium	Placebo; participants and assessors blinded; 17% attrition
Lee 2003[28]	Unclear	Unclear	High	High	High	High	Low	High	Insufficient description of randomization; no placebo; no blinding; 30% attrition

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Luczynska et al. 2003[29]	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Insufficient description of randomization; placebo; patients blinded and most outcomes patient-reported; intent-to-treat analysis found similar results; pre-specified outcomes reported
Woodcock et al. 2003[30]	Low	Low	Low	Low	Low	Low	Low	Low	Placebo; participants and assessors blinded; 16% attrition;
Rijssenbeek-Nouwens et al. 2002[31]	Unclear	Unclear	Low	Low	High	Low	Low	Medium	Insufficient description of randomization; placebo; patients blinded and most outcomes patient-reported; 21% attrition with no apparent intent-to-treat analysis; pre-specified outcomes reported
Sheikh et al. 2002[32]	Low	Low	Low	Low	Low	Low	Low	Low	Placebo; participants and assessors blinded; low attrition; pre-specified outcomes reported
Frederick et al. 1997[33]	Unclear	Unclear	Low	High	Unclear	Low	High	High	Insufficient description of randomization; patients only blinded; attrition not described; pre-specified outcomes reported; 3/5 authors funded or employed by relevant industry
Burr et al. 1980[34]	Unclear	Unclear	High	High	Low	High	Low	High	Insufficient description of randomization; no blinding; no placebo; attrition not described, very few outcomes reported
Burr et al. 1976[35]	Unclear	Unclear	High	High	Unclear	High	Low	High	Insufficient description of randomization; no blinding; no placebo; attrition not described, very few outcomes reported

Evidence Tables for Pest Control Studies

Table C-14. Study characteristics of pest control study

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
Rabito et al. 2016[36]	***Arm 1:*** Insecticide bait placed throughout home by pest control professionals ***Arm 2:*** No intervention	Bla g 1 Bla g 2	***Type of study:*** RCT ***Population:*** 102 ***Attrition:*** NR ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age***, mean (SD): 9.3 years Range of eligible patients: 5 to 17 ***% Male***: 65% ***Race:*** Black: 62% Hispanic: 30% Other: 8% ***Homeownership:*** 74% of insecticide arm lived in detached houses, but 54% of control arm lived in multifamily dwellings ***Geographic environment***: Urban	***Sensitization*** (serum IgE): Cockroach allergen: 27% HDM allergen: 50% Mouse allergen: 12% At least 1 allergen: 64% 2 or more allergens: 58% ***Asthma severity:*** All patients moderate to severe ***Comorbidity:*** NR ***Carpet in home:*** NR ***Pets in home:*** NR ***Smoker in home:*** 35%
Levy et al. 2006[37]	Intervention consisted of one-time deep cleaning, including HEPA vacuuming, setting traps, sealing rodent access points, replacement of mattresses, education about kitchen hygiene and food storage, reducing clutter, and communicating with housing authority and pest contractors	Bla g 1 Bla g 2 Can f 1 Der f 1 Der p 1 MUP Alternaria	***Type of study:*** Pre-post ***Population:*** 78 enrolled Competed: 50 (41 households) ***Attrition:*** 35.9% ***Setting:*** Home ***Country:*** United States ***Followup:*** Up to 66 weeks	***Age,*** mean: Intervention: 7.5 years Control: 7.6 years Range: 4 to 17 ***% Male:*** Intervention: 58% Control: 67.1% ***Race:*** Hispanic: 70% African American: 28% Caucasian: 2% ***Homeownership:*** Public housing ***Geographic environment:*** Urban	***Sensitization*** (skin prick test positive): Any allergen: 77% Cockroach allergen: 58% HDM: 60% ***Asthma severity:*** Baseline symptoms reported graphically ***Comorbidity:*** NR

Bla g 1, Bla g 2=*Blatella germanica* cockroach allergens; Can f 1=*Canis familiaris* dog allergen; Der f 1=*dermatophagoides farina* house dust mite allergen; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen; Fel d 1=*Felis domesticus* cat allergen; IgE=immunoglobulin E; HDM=house dust mite; HEPA=high-efficiency particulate air-filtration; MUP=mouse urinary protein; NR=not reported

Table C-15. Outcomes of pest control study

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Rabito et al. 2016[36]	**ACT score <19**: Sensitized patients only No significant difference between arms: OR (95% CI), control vs. insecticide: 2.65 (0.29 to 24.14), p=0.39	**ED or unscheduled clinic visits**: Sensitized patients only Statistically significant improvement: beta coefficient (95% CI), control vs. insecticide: 2.67 (0.35 to 4.99), p=0.02 All patients Statistically significant improvement: beta coefficient (95% CI), control vs. insecticide: 0.1.17 (0.11 to 2.24) p=0.03 **Hospitalizations:** Sensitized patients only No difference: OR (95% CI), control vs. insecticide: 1.24 (0.09 to 16.74), p=0.87 All patients No difference: OR (95% CI), control vs. insecticide: 1.89 (0.41 to 8.80), p=0.42 **Missed school days:** Sensitized patients only Statistically significant improvement: beta coefficient (95% CI), control vs. insecticide: 0.35 (0.28 to 1.64), p=0.01 All patients No difference: beta coefficient (95% CI), control vs. insecticide: 0.24 (-0.09 to 0.56), p=0.15	**FEV_1 <80% predicted:** Sensitized patients only No difference: OR (95% CI), control vs. insecticide: 13.09 (0.79 to 217.47) p=0.07 All patients Statistically significant improvement: OR (95% CI), control vs. insecticide: 5.74 (1.60 to 20.57), p=0.01	NR	**Measurement:** Computer-assisted telephone questionnaires **Maximum symptom days/2 weeks**, mean: Sensitized patients only Statistically significant improvement: beta coefficient (95% CI): 4.13 (0.25 to 8.01), p=0.04 All patients Statistically significant improvement: beta coefficient (95% CI): 1.82 (0.14 to 3.50), p=0.03	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Levy et al. 2006[37]	NR	No changes (data not shown; rates described as low)	NR	**Asthma related quality of life** (7-point scale): Clinically significant mean improvement of 1.32 points (no variance reported)	**Measurement:** Patient questionnaires, scored on an 8-point scale (not described) **Respiratory symptoms,** mean score (no variance reported): Pre-intervention: 2.6 Post-intervention: 1.5 Pre vs. post: p=0.0002	**Measurement:** Dust samples were collected by vacuuming mattresses and by use of an electrostatic precipitator; study did not report who collected samples; samples were collected 5 times throughout study **Percentage of allergen decrease,** baseline-final measurement; no statistical analysis presented: Bla g 1 Air: 57% Bed: 58% Kitchen: 61% Bla g 2 Air: 62% Bed: 56% Kitchen: 65% Can f 1 Air: 42% Bed: 37% Der f 1 Air: 43% Bed: 61% Der p 1 Air: 49% Bed: 52% Fel d 1 Air: 49% Bed: 62% MUP Air: 51% Bed: 46% Kitchen: 42% *Alternaria* Air: 49% Bed: 38%

ACT=asthma control test; Bla g 1, Bla g 2=*Blatella germanica* cockroach allergen; Can f 1=*Canis familiaris* dog allergen I; CI=confidence interval; Der f 1=*Dermatophagoides farina* house dust mite allergen; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen 1; Fel d 1=*Felis domesticus* cat allergen 1; MUP=mouse urinary protein; NR=not reported; OR=odds ratio

Table C-16. Risk of bias of pest control randomized controlled trial

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Rabito et al. 2016[36]	Low	Unclear	High	High	Unclear	Low	Low	Medium	No placebo, no blinding, attrition not reported

Table C-17. Risk of bias of pest control non-randomized study

Study	Representativeness of the Study Population	Ascertainment of Exposure	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of Outcome	Followup Long Enough for Outcomes to Occur	Adequacy of Followup of Cohorts	Overall Risk of Bias	Comments
Levy et al. 2006[37]	Low	Low	Low	Low	Low	High	Medium	Non-randomized pre-post study; all patients were Hispanic or African-American; minimum followup of 3 months

Evidence Tables for Pet Removal Studies

Table C-18. Study characteristics of pet removal study

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
Shirai et al. 2005[38]	All patients were instructed to remove all pets from the home. Pet removal was voluntary. Timing of pet removal relative to baseline ranged up to 16 months after enrollment.	Cat Dog Ferret Hamster	***Type of study:*** Non-randomized controlled trial ***Population:*** Removal group: 10 Keeping group: 10 ***Attrition:*** NR ***Setting:*** Home ***Country:*** Japan ***Followup:*** Up to 43 months	***Age:*** Mean (SD): Removal: 29 (6) years Keeping: 36 (3) years ***% Male:*** Removal: 20% Keeping: 30% ***% Smokers*** (including ex-smokers) Removal: 90% Keeping: 60%	***Sensitization*** (skin prick test positive): Animal allergen: 100% Cedar pollen: 70% HDM: 70% Grass pollen: 40% Other: 20% ***Asthma severity:*** Predominantly Step 2 ***Comorbidity:*** NR

HDM=house dust mite; NR=not reported; SD=standard deviation

Table C-19. Outcomes of pet removal study

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Shirai et al. 2005[38]	NR	Patients reported as having either exacerbation or hospitalization: Removal: 0% Keeping: 20% Administered inhaled corticosteroids at followup, %: Removal: 0% Keeping: 90% Removal vs. keeping: p<0.001 Regular followup visits and medication (% quit): Removal: 100% Keeping: 20% Removal vs. keeping: p<0.01	**FEV_1, % predicted**, mean (SD): Removal: 100.1 (14.0) Keeping: 96.2 (20.6) Removal vs. keeping: p=not significant **PEFR variability**, %, mean (SD): Removal: 11.3 (7.1) Keeping: 10.6 (9.5) Removal vs. keeping: p=not significant **PC_{20},** mg/mL, mean (SD): Removal: 8.3 (8.1) Keeping: 2.1 (6.3) Removal vs. keeping: p<0.05	NR	NR	NR

FEV_1=forced expiratory volume in one second; NR=not reported; PEFR=peak expiratory flow rate; PC_{20}=provocative concentration 20—following methacholine challenge, the dose that produces a 20% decrease in FEV_1; SD=standard deviation

Table C-20. Risk of bias of pet removal non-randomized study

Study	Representativeness of the Study Population	Ascertainment of Exposure	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of Outcome	Followup Long Enough for Outcomes to Occur	Adequacy of Followup of Cohorts	Overall Risk of Bias	Comments
Shirai et al. 2005[38]	Low	Low	Medium	Low	Medium	Low	Medium	Non-randomized study. Implementing the intervention (pet removal) was voluntary and timing of pet removal varied over a range of 16 months. Some lack of comparability of cohorts. Outcome assessors were blinded.

Evidence Tables for Other/Miscellaneous Intervention Studies

Table C-21. Study characteristics of other/miscellaneous intervention study

Study	Intervention	Allergen(s)	Study Design	Demographic Factors	Clinical Factors
Barnes et al. 2008[39]	***Arm 1:*** Regular products containing household bleach ***Arm 2:*** Regular products plus three additional products with dilute 0.09% hypochlorite; ***Arm 3:*** No cleaning products given Cleaning protocol not described Cleaning products from Clorox Corp: Ultra Clorox Bleach, Clorox Clean Up, Clorox Disinfecting Wipes, Ready Mop, Clorox Toilet Bowl Cleaner, Clorox Disinfecting Spray, and Clorox Toilet Bowl Automatic Cleaning Tablets. Trial funded by Clorox Corp.	Bacteria, fungi, and protein allergens	***Type of study:*** RCT ***Population:*** 97 families ***Attrition:*** 6.2% ***Setting:*** Home ***Country:*** United States ***Followup:*** 8 weeks Study included arm of participants with no diagnosis of asthma, data not reported here	***Age:*** NR, enrollment required "at least one person between 2 and 17 years" in the household ***% Male:*** NR ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** Urban core: 40% Suburban: 55% Rural: 5%	**Sensitization:** NR **Asthma severity:** NR; participants with asthma recruited from asthma clinic (single site) **Carpet in home:** 89% **Pets in home** (at least one): Cats: 18% Dogs: 58%

NR=not reported; RCT=randomized controlled trial

Table C-22. Outcomes of other/miscellaneous intervention study

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)	Other
Barnes et al. 2008[39]	NR	**Controller medication use at night:** Product: 3.73 (6.06) Control: 4.17 (6.57) Product vs. control: p=0.38 **Controller medication use in morning:** Product: 4.03 (6.06) Control: 5.12 (7.21) Product vs. control: p=0.04	NR	Quality of life scores improved within both arms over baseline: p<0.05 Data shown graphically with no estimate of variance; between-arm analysis not presented	**Measurement:** Patient questionnaires, scored on a 7-point Likert scale, mean (SD): **Wheeze in evening:** Product: 1.70 (2.27) Control: 2.47 (3.42) Product vs. control: p=0.001 **Wheeze in morning:** Product: 1.67 (2.59) Control: 2.10 (2.90) Product vs. control: p=0.05 **Cough in morning:** Product: 3.47 (4.53) Control: 4.14 (5.13) Product vs. control: p=0.08 **Cough in evening:** Product: 3.44 (4.39) Control: 2.47 (3.42) Product vs. control: p=0.004 **Breathing trouble in evening:** Product: 2.18 (3.31) Control: 4.61 (5.54) Product vs. control: p=0.001 **Breathing trouble in morning:** Product: 2.02 (2.95) Control: 2.86 (3.85) Product vs. control: p=0.02	**Measurement:** Study team collected dust samples from multiple sites throughout each house; method of collection not described; samples were collected 3 times throughout study. **Levels of all dust allergens** did not vary statistically as a function of treatment group. Comparative data of allergens not shown for cleaning vs. control in asthma participants alone.	Data reported here for population with asthma only. Main outcome of quality of life was improved in all groups; authors note possibility of placebo effect due to keeping diaries in control group. Because asthma symptoms are not reported separately for each type of cleaning product, it is not possible to evaluate the primary hypothesis that products containing sodium hypochlorate affect allergen levels.

NR=not reported; SD=standard deviation

Table C-23. Risk of bias of other/miscellaneous randomized controlled trial

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Barnes et al. 2008[39]	Unclear	Unclear	High	High	Low	High	High	High	Insufficient description of randomization; no blinding; 6% attrition; data not reported for primary intervention group separately; study funded by manufacturer of cleaning supplies

Evidence Tables for Multicomponent Intervention Studies

Table C-24. Study characteristics of multicomponent intervention studies

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Matsui et al. 2017[40]	***Arm 1:*** • Professional pest control • Impermeable mattress covers • Air purifier • Education on pest control strategies (e.g., use of traps, sealing of entry points, house cleaning) ***Arm 2:*** Education on pest control strategies	Der p or f Bla g Fel d Can f Mus m Mold	***Type of study:*** RCT ***Population:*** 361 ***Attrition:*** 7% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** mean (SD): 10 (3.2) years Range of eligible patients: 5 to 17 ***% Male:*** 62% **Race*:*** 79% Black 21% Hispanic 11% White ***Homeownership:*** 71% in houses, ownership NR 29% in apartments ***Geographic environment:*** Urban	***Sensitization*** (skin prick test positive): HDM: 44% Cockroach: 55% Cat: 54% Dog: 23% Mold: 34% Mouse (skin prick test or IgE): 100% ***Asthma severity:*** 12% step 1 19% step 2 15% step 3 5% step 4 49% step 5 ***Comorbidity:*** NR ***Carpeted bedroom:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR
DiMango et al. 2016[41]	***Arm 1:*** • Impermeable covers (brand NR) on mattresses • Vacuum (Electrolux; not specified if HEPA-filtered) • HEPA air purifier (Orek) • Mops (Swiffer WetJet) • Cleaning products (not specified) • Education and instruction about allergen reduction strategies given by 'intervention counselors' ***Arm 2:*** Education unrelated to allergen reduction given by 'intervention counselors'	Der p or f Bla g Fel d Can f Mus m Mold	***Type of study:*** RCT ***Population:*** 247 ***Attrition:*** 16% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 40 weeks	***Age,*** mean: NR 45% age 6 to 17, 55% age 18 to 69 Range: 6 to 69 years ***% Male:*** 45% ***Race:*** 56% Hispanic 37% Black 3% White ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization*** (skin prick test positive): 100% of participants sensitized to at least 1 allergen ***Asthma severity:*** 67% step 4–6 33% step 1–3 ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** 31%
Shani et al. 2015[42]	***Pre-post, 1 Arm:*** • Hypoallergenic covers (brand NR) on mattresses, pillows • Cockroach and mouse bait • Cleaning products (not specified) • Education and instruction about allergen reduction strategies given by community health workers	Der p or f Bla g Fel d Can f Mus m	***Type of study:*** Pre-post ***Population:*** 80 ***Attrition:*** 41% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 6 months	***Age,*** mean: 7 years Range of eligible patients: 2 to 17 ***% Male:*** 54% ***Race:*** "most children identified as African American" ***Homeownership:*** "most of the families were renters" ***Geographic environment:*** NR	***Sensitization:*** NR ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** 44%

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Breysse et al. 2014[43]	***Arm 1:*** • Weatherization-related interventions, including, as needed: replacing carpet with laminate, vinyl, hardwood, or low-volatile-organic-compound carpet; insulation of home, pipes, ductwork; plumbing repair; door replacement or weather-stripping; replacing bathroom fans and/or installing fan timers; replacement of range and dryer hoods; and additional interventions • Hypoallergenic covers (brand NR) on mattresses, pillows • HEPA vacuums • Cleaning supplies (not specified) • Education and instruction about allergen reduction strategies and asthma self-management given by community health workers ***Arm 2*** *(matched historical comparison group)****:*** • Hypoallergenic covers (brand NR) on mattresses, pillows • HEPA vacuums • Cleaning supplies (not specified) • Education and instruction about allergen reduction strategies and asthma self-management given by community health workers	Der p or f Bla g Fel d Can f Mus m Mold	***Type of study:*** Quasi-experimental ***Population:*** 102 ***Attrition:*** 24% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** mean: NR Range of eligible patients: 3 to 17 ***% Male:*** 60% ***Race:*** 46% Hispanic 21% Vietnamese 15% African American 9% Asian 8% White ***Homeownership:*** 0% ***Geographic environment:*** Urban	***Sensitization:*** NR ***Asthma severity:*** 53% “not well controlled” 47% “very poorly controlled” ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 20% ***Smoker in home:*** 3%
Turcotte et al. 2014[44]	***Pre-post, 1 Arm:*** • HEPA vacuums • Integrated pest management • Professional cleaning • Cleaning supplies (not specified) • Education and instruction about allergen reduction strategies given by community health workers	Der p or f Bla g Fel d Can f Mus m	***Type of study:*** Pre-post ***Population:*** 170 ***Attrition:*** 31% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** mean: 6 years Range of eligible patients: 15 years or younger ***% Male:*** 60% ***Race:*** 53% Hispanic 15% Asian 12% White 5% Black ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization:*** NR ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** 16%

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Sweet et al. 2013[45]	***Pre-post, 1 Arm:*** • Hypoallergenic covers (brand NR) on mattresses, pillows, box springs • HEPA vacuum • Integrated pest control • Cleaning supplies (mop, bucket, floor soap, vinegar, baking soda, spray bottle, scrub pad) • Mold removal • Dehumidifier and ventilation if necessary • Education and instruction about allergen reduction strategies and asthma self-management given by community health workers	Der p or f Bla g Fel d Can f Mus m Mold	***Type of study:*** Pre-post ***Population:*** 115 ***Attrition:*** NR ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 6 months	***Age,*** mean: 7 years Range: 1 to 18 ***% Male:*** 58% ***Race:*** 72% African American 17% White 5% Hispanic ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization:*** NR ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR
El-Ghitany et al. 2012[46]	***Arm 1:*** • Hypoallergenic covers on mattresses, pillows • Carpet removal or vacuuming more than 1 time per week • Ventilation • Removal of pets ***Arm 2:*** No interventions	Der p	***Type of study:*** RCT ***Population:*** 160 ***Attrition:*** 0% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** Egypt ***Followup:*** 16 weeks There was an initial 8 month cross-sectional study prior to conducting the RCT	***Age,*** mean: 8 years Range***:*** 5 to 12 ***% Male:*** 56% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** Urban: 40%	***Sensitization*** (skin prick test positive): HDM: 100% ***Asthma severity:*** 43% uncontrolled ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 46% ***Smoker in home:*** 30%

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Takaro et al. 2011[47]	***Arm 1:*** • Occupancy in "Breathe-Easy-Home," features include exterior with moisture proofing, interior finishes and flooring that minimizes dust, and heat-exchange ventilation system with filtration • Hypoallergenic covers (brand NR) on mattresses, pillows • HEPA vacuums • Cleaning supplies (not specified) • Education and instruction about allergen reduction strategies and asthma self-management given by community health workers ***Arm 2*** *(matched historical comparison group)****:*** • Hypoallergenic covers (brand NR) on mattresses, pillows • HEPA vacuums • Cleaning supplies (not specified) • Education and instruction about allergen reduction and asthma self-management given by community health workers	Der p or f Bla g Fel d Can f Mus m Mold	***Type of study:*** Quasi-experimental ***Population:*** 102 ***Attrition:*** NR ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** mean: NR Range of eligible patients: 3 to 17 ***% Male:*** 69% ***Race:*** 35% Hispanic 22% Black 17% Vietnamese 13% Asian 6% White ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization:*** NR ***Asthma severity:*** 19% severe 32% moderate persistent 36% mild persistent 15% intermittent ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 16% ***Smoker in home:*** 6%
Bryant-Stephens et al. 2009[48]	***Crossover RCT, 1 Arm:*** • Hypoallergenic covers (brand NR) on mattresses, pillows • Cockroach and mouse bait • Tiles to replace carpet • Cleaning supplies (not specified) • Education and instruction about allergen reduction strategies and asthma self-management given by community health workers	Der p or f Bla g Fel d Can f Mus m	***Type of study:*** RCT, crossover ***Population:*** 264 ***Attrition:*** 23% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 6 months	***Age,*** mean: 6 years Range of eligible patients: 2 to 16 ***% Male:*** 66% ***Race:*** 94% Black ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization:*** NR ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** 53% ***Cat/dog in home:*** 41% ***Smoker in home:*** 50%

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Krieger et al. 2009[49]	***Arm 1:*** • Impermeable covers (brand NR) on mattresses, pillows • Low emission vacuum (brand NR) • Cleaning supplies (not specified) • Commercial-quality door mats • Education and instruction about allergen reduction strategies and asthma self-management given by community health workers, including up to 5 home visits ***Arm 2:*** • Impermeable covers (brand NR) on mattresses, pillows • Asthma self-management education given by clinic nurses	Der p or f Bla g Fel d Can f Mus m Mold	***Type of study:*** RCT ***Population:*** 309 ***Attrition:*** 12% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** mean: 8 years Range of eligible patients: 3 to 13 ***% Male:*** 64% ***Race:*** 48% Hispanic 20% African-American 11% White 11% Vietnamese 6% Other Asian ***Homeownership:*** 23% ***Geographic environment:*** Urban	***Sensitization*** (skin prick test positive): 61% for one or more allergen ***Asthma severity:*** 9% severe 30% moderate 41% mild persistent 20% mild intermittent ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 23% ***Smoker in home:*** 42%
Bryant-Stephens et al. 2008[50]	***Arm 1:*** • Hypoallergenic covers (brand NR) on mattresses, pillows • Cockroach and mouse bait • Carpet removal if applicable and preferred by family • Vacuum cleaner bags and cleaning supplies (not specified) • Education and instruction about allergen reduction strategies given by community health workers ***Arm 2:*** No interventions ***Arm 3:*** Patients who declined consent for the study were enrolled in a case-matched control group with no intervention	Der p or f Bla g Fel d Can f Mus m	***Type of study:*** RCT ***Population:*** 281 in Arm 1 and Arm 2; 115 in Arm 3 ***Attrition:*** 29% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** mean: 6 years Range of eligible patients: 2 to 16 ***% Male:*** 60% ***Race:*** 100% African American ***Homeownership:*** 39% ***Geographic environment:*** Urban	***Sensitization:*** NR ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** 49% ***Cat/dog in home:*** NR ***Smoker in home:*** NR
Parker et al. 2008[51]	***Arm 1:*** • Impermeable covers (brand NR) on mattresses, pillows • HEPA filtered vacuum (Eureka SmartVac) • Household cleaning supplies provided • Integrated pest management • Education and instruction about allergen reduction strategies given by community health workers ***Arm 2:*** No interventions	Der p or f Bla g Fel d Can f Mus m	***Type of study:*** RCT ***Population:*** 298 ***Attrition:*** 24% ***Age cohort:*** Child ***Setting:*** Home ***Country:*** United States ***Followup:*** 3 months	***Age,*** mean: 9 years Range of eligible patients: 7 to 11 ***% Male:*** 58% ***Race:*** 81% African American 10% Latino 4% Caucasian ***Homeownership:*** 36% ***Geographic environment:*** Urban	***Sensitization:*** (skin prick test positive): HDM: 38% Bla g: 21% Fel d: 23% Can f: 8% Mus m: 13% ***Asthma severity:*** 48% moderate-severe 28% mild persistent 20% mild intermittent ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** 38%

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Burr et al. 2007[52]	***Arm 1:*** • 2-step mold removal process: 1) application of aqueous preparation (RLT Bactdet) containing detergent and fungicide (sodium dichlorophen) to remove mold from surfaces; 2) application of surface-penetrating aqueous preparation (RLT Halophen) containing fungicide (dialkyl dimethylammonium chloride) • Installation of positive ventilation fan (Drimaster) ***Arm 2:*** No interventions	Mold	***Type of study:*** RCT ***Population:*** 232 patients, 164 houses ***Attrition:*** 22% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean: 27 years Range: 3 to 61 ***% Male:*** NR ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): 41 % of patients mold-sensitized ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** 39% of homes had at least one smoker
Kercsmar et al. 2006[53]	***Arm 1:*** • Removal of mold from hard surfaces • Preventive measures against mold growth and moisture infiltration tailored to each patient's house; examples of interventions include: repair of leaks, disconnection and redirection of downspouts, furnace repairs, improving air exhaust from kitchens and bathrooms, and similar efforts ***Arm 2:*** No interventions	Mold	***Type of study:*** RCT ***Population:*** 62 ***Attrition:*** 18% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** mean: 7 years Range of eligible patients: 2 to 17 ***% Male:*** 60% ***Race:*** 76% Black 23% White ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization*** (serum IgE): Mold-sensitized: 31% HDM: 29% Bla g: 16% Mus m: 11% ***Asthma severity:*** 11% severe 19% moderate 48% mild 21% intermittent ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 39% any pet ***Smoker in home:*** 31%
Williams et al. 2006[54]	***Arm 1:*** • Impermeable covers (brand NR) on mattresses, pillows, box springs • Pest control with hydramethylnon gel • One-time professional cleaning of homes at outset of study • Education and instruction about allergen reduction strategies and asthma self-management given by community health workers • If applicable and preferred by family, any of the following: carpet removal; pet removal or bathing; removal of fungal growth; control of moisture/humidity ***Arm 2:*** Education from community health workers, no other interventions	Der p or f Bla g Fel d Can f	***Type of study:*** RCT ***Population:*** 161 ***Attrition:*** 77% ***Age cohort:*** Child ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** median: 8 years Range of eligible patients: 5 to 12 ***% Male:*** 59% ***Race:*** 99% Black ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization*** (serum IgE): HDM: 58% Bla g: 36% Fel d: 18% Can f: 15% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** 50%

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Eggleston et al. 2005[55]	***Arm 1:*** • Impermeable covers (Mission: Allergy) on mattresses, pillows • HEPA filter in bedroom • Integrated pest management (including fipronil bait gel for cockroach and bromadialone bait traps for mouse) • Education and instruction about allergen reduction strategies given by community health workers ***Arm 2:*** No interventions	Der p or f Bla g Fel d Mus m	***Type of study:*** RCT ***Population:*** 100 ***Attrition:*** 9% ***Age cohort:*** Child ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** median: 8 years Range: 6 to 12 ***% Male:*** 46% ***Race:*** 99% African American ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization*** (skin prick test positive): HDM: 29% Bla g: 42% Fel d: 22% Mus m: 9% ***Asthma severity:*** 24% moderate-severe symptoms ***Comorbidity:*** NR ***Carpeted bedrooms:*** 43% ***Cat/dog in home:*** 39% ***Smoker in home:*** 69%
Krieger et al. 2005[56]	***Arm 1:*** • Impermeable covers (brand NR) on mattresses, pillows • Low emission vacuum (brand NR) • Rodent traps and roach bait • Cleaning kits • Commercial-quality door mats • Education and instruction about allergen reduction strategies given by community health workers, including up to 9 home visits ***Arm 2:*** • Impermeable covers (brand NR) on mattresses, pillows • Single visit from community health worker for education • Patients were offered all interventions at study conclusion	Der p or f Bla g Fel d Can f Mus m Mold	***Type of study:*** RCT ***Population:*** 274 ***Attrition:*** 22% ***Age cohort:*** Child ***Setting:*** Home ***Country:*** United States ***Followup:*** 6 months	***Age,*** mean: 7 years Range of eligible patients: 4 to 12 ***% Male:*** 59% ***Race:*** 30% African American 24% Vietnamese 17% Hispanic 17% White 7% Other Asian ***Homeownership:*** 18% ***Geographic environment:*** Urban	***Sensitization:*** NR ***Asthma severity:*** 28% severe 34% moderate 14% mild persistent 24% mild intermittent ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 24% ***Smoker in home:*** 42%

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Morgan et al. 2004[57] Pongracic et al. 2008[58]	***Arm 1:*** • Impermeable covers (Allergy Control Products) on mattresses, pillows, box springs • HEPA filtered vacuum (Miele) • HEPA air purifier (Holmes Products) for patients exposed to pets, mold, or tobacco smoke • Professional pest control (Terminix) ***Arm 2:*** No interventions	Der p or f Bla g Fel d Can f Mus m Mold	***Type of study:*** RCT ***Population:*** 937 ***Attrition:*** 12% ***Age cohort:*** Child ***Setting:*** Home ***Country:*** United States ***Followup:*** 2 years	***Age,*** mean: 8 years Range: 5 to 11 ***% Male:*** 63% ***Race:*** 40% Black 40% Hispanic ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization*** (skin prick test positive: HDM: 63% Bla g: 69% Fel d: 44% Can f: 22% Mus m: 33% Mold: 50% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 22% dog, 18% cat ***Smoker in home:*** 48%
Carter et al. 2001[59]	***Arm 1:*** • Impermeable covers (Allergy Control Products) on mattresses, pillows • Cockroach bait (Combat) • Instruction to wash bedding weekly in hot water, and education about cleaning to control house dust mites and cockroaches ***Arm 2:*** • Placebo covers on mattresses, pillows • Ineffective cockroach bait • Instruction to wash bedding in cold or cool water ***Arm 3:*** No interventions or placebo	Der p or f Bla g	***Type of study:*** RCT ***Population:*** 104 ***Attrition:*** 18% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	***Age,*** mean: 11 years Range: 6 to 16 ***% Male:*** NR ***Race:*** NR, but enrolling clinic treats population that is 92% African American ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization*** (either skin prick test positive or serum IgE): HDM: 74% Bla g: 56% Fel d: 26% Mus m: 2% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR
Htut et al. 2001[60]	***Arm 1:*** • Steam heating applied to mattresses, duvets, upholstered furniture, carpet • New pillows provided • Linens washed ***Arm 2:*** • Steam heating as in Group 1 • Installation of positive ventilation system (Nuaire) above bedroom ***Arm 3:*** Placebo treatment of surfaces	Der p or f	***Type of study:*** RCT ***Population:*** 30 ***Attrition:*** 23% ***Age cohort:*** Adult ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean: NR Range of eligible patients: 18 to 45 ***% Male:*** NR ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): HDM: 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Warner et al. 2000[61]	***Arm 1:*** • Installation of whole-house mechanical ventilation system with heat recovery (ADM Indux) • HEPA vacuums (Miele) ***Arm 2:*** Ventilation system only ***Arm 3:*** HEPA vacuum only ***Arm 4:*** No interventions	Der p or f	***Type of study:*** RCT ***Population:*** 40 27 children, 13 adults ***Attrition:*** NR ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean: Children***:*** 10 years Adults: 40 years Range: 4 to 67 ***% Male:*** 65% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): HDM: 100% ***Asthma severity:*** All patients moderate or severe ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR
Cloosterman et al. 1999[62]	***Arm 1:*** • Impermeable covers (Intervent Bedding Systems) on mattresses, pillows, duvets • Carpet treated with Acarosan powder (benzyl benzoate) ***Arm 2:*** • Mattresses et al. covered with cotton placebos • Carpet treated with water spray	Der p or f	***Type of study:*** RCT ***Population:*** 157 ***Attrition:*** 23% ***Age cohort:*** Adult ***Setting:*** Home ***Country:*** Netherlands ***Followup:*** 20 weeks	***Age,*** mean: 33 years Range of eligible patients: 16 to 60 ***% Male:*** 57% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): HDM: 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** 66% ***Cat/dog in home:*** NR ***Smoker in home:*** 18%
Evans et al. 1999[63]	***Arm 1:*** • Impermeable covers (brand NR) on mattresses, pillows • Professional application of abamectin insecticide in homes of patients with positive Bla g skin test • Monthly contact with social workers to discuss allergen control, symptom management, access to medical care ***Arm 2:*** No interventions	Der p or f Bla g	***Type of study:*** RCT ***Population:*** 1,033 ***Attrition:*** 7% at 1 year, 14% at 2 years ***Age cohort:*** Child ***Setting:*** Home ***Country:*** United States ***Followup:*** 2 years	***Age,*** mean: 8 years Range: 5 to 11 ***% Male:*** 64% ***Race:*** 75% Black 17% Hispanic ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization*** (skin prick test positive: 86% sensitized to at least one allergen ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** 42%
Shapiro et al. 1999[64]	***Arm 1:*** • Impermeable covers (Allergy Control Products, Inc.) on mattresses, pillows, box springs • Laundry service delivery of clean blanket and linens monthly • Carpet treated with tannic acid ***Arm 2:*** Carpet treated with placebo	Der p or f	***Type of study:*** RCT ***Population:*** 44 ***Attrition:*** 11% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 1 year	**Age,** mean: 10 years Range: 6 to 15 ***% Male:*** 39% ***Race:*** 58% White; 25% African-American; 17% Other ***Homeownership:*** NR ***Geographic environment:*** Urban	***Sensitization*** (skin prick test positive): HDM: 100% ***Asthma severity:*** Mild or Moderate ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Hayden et al. 1997[65]	***Arm 1:*** • Impermeable covers (Allergy Control Products) on mattresses, pillows, box springs • Carpet in bedroom replaced with hardwood or vinyl flooring • Carpet in living room or family room treated with 3% tannic acid spray every 3 months • Instruction to wash bedding weekly in hot water ***Arm 2:*** • Placebo cotton covers on mattresses, pillows, box springs • Carpet treated with water spray • Instruction to wash bedding in cold water	Der p or f Bla g Fel d	***Type of study:*** RCT ***Population:*** 23 ***Attrition:*** 8% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United States ***Followup:*** 6 months	***Age,*** mean: 9 years Range: 5 to 16 ***% Male:*** 61% ***Race:*** 52% White 48% African American ***Homeownership:*** 87% ***Geographic environment:*** Suburban	***Sensitization*** (serum IgE): HDM: 65% Bla g: 9% Fel d: 13% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 30% indoor pet ***Smoker in home:*** 22%
Carswell et al. 1996[66]	***Arm 1:*** • Mattresses, pillows, duvets, and upholstered furniture vacuumed, then treated with Acarosan foam (benzyl benzoate 2.6%) • Cotton covers coated with polyurethane on mattresses, pillows, duvets • Bed linen washed at 60° C • Carpet vacuumed, treated with Acarosan powder (benzyl benzoate 5%) • Soft toys removed or washed ***Arm 2:*** • Mattresses et al. treated with water spray • Mattresses et al. covered with cotton placebos • Bed linen washed at 40° C • Carpet treated with chalk dust	Der p or f	***Type of study:*** RCT ***Population:*** N=70 ***Attrition:*** 13% ***Age cohort:*** Child ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 24 weeks	***Age,*** mean: 10 years Range: 7 to 10 ***% Male:*** 63% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): HDM: 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** 10% ***Smoker in home:*** NR
Marks et al. 1994[67]	***Arm 1:*** • Mattresses, pillows, duvets, blankets, and furniture treated with a tannic acid/acaricide solution (Allersearch DMS), applied by hand-held spray pump • Impermeable covers (Coolguard and Medisoft) on mattresses, pillows, duvets • Carpet treated with same tannic acid/acaricide solution ***Arm 2:*** Mattresses et al. treated with inactive placebo spray	Der p or f	***Type of study:*** RCT ***Population:*** 35 ***Attrition:*** 14% ***Age cohort:*** Adult ***Setting:*** Home ***Country:*** Australia ***Followup:*** 6 months	***Age,*** mean: 34 vs. 37 years Range of eligible patients: 13 to 60 ***% Male:*** 49% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): HDM: 94% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** 1 smoker

Study	Intervention	Allergen	Study Design	Demographic Factors	Clinical Factors
Walshaw et al. 1986[68]	***Arm 1:*** • Plastic covers on mattresses, pillows • Feather duvets, quilts and woolen blankets replaced with other materials • Bedroom carpet either replaced with linoleum or vacuumed regularly ***Arm 2:*** No interventions	Der p or f	***Type of study:*** RCT ***Population:*** 50 ***Attrition:*** 16% ***Age cohort:*** Adult ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 1 year	***Age,*** mean: 33 years ***% Male:*** 44% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (serum IgE): HDM: 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR
Korsgaard 1983[69]	***Arm 1:*** • Mattress vacuumed 2 times per week • Linens laundered 2 times per week • All pillows and quilts replaced with synthetic products • Carpet replaced with linoleum or wood flooring; floor cleaned 2 times per week • Bedroom and living room aired out for 20 minutes per day • Clothes dried outdoors when possible ***Arm 2:*** No interventions	Der p or f	***Type of study:*** RCT ***Population:*** 46 ***Attrition:*** 0% ***Age cohort:*** Adult ***Setting:*** Home ***Country:*** Denmark ***Followup:*** 6 months	***Age,*** median: 30 years Range of eligible patients: 15+ years ***% Male:*** 70% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): HDM: 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** 85% ***Cat/dog in home:*** NR ***Smoker in home:*** NR
Burr et al. 1980[70]	***Arm 1:*** • Mattress vacuumed weekly • Blankets laundered at beginning of study, then beaten in open air every 2 weeks • Linens laundered weekly • Feather pillows replaced with synthetic pillows, or encased in impermeable covers, and beaten in open air weekly • Quilts removed • Soft toys removed, or washed, brushed, and vacuumed weekly • Carpet in bedroom vacuumed several times per week, while upholstered furniture vacuumed every 2 weeks ***Arm 2:*** • Special dusters issued for dusting • Upholstered furniture vacuumed or brushed 2 times per week • Carpet vacuumed daily	Der p or f	***Type of study:*** RCT ***Population:*** 53 ***Attrition:*** 4% ***Age cohort:*** Mixed ***Setting:*** Home ***Country:*** United Kingdom ***Followup:*** 8 weeks	***Age,*** mean: 9 years Range: 4 to 14 ***% Male:*** 68% ***Race:*** NR ***Homeownership:*** NR ***Geographic environment:*** NR	***Sensitization*** (skin prick test positive): HDM: 100% ***Asthma severity:*** NR ***Comorbidity:*** NR ***Carpeted bedrooms:*** NR ***Cat/dog in home:*** NR ***Smoker in home:*** NR

Bla g=*Blatella germanica* cockroach allergen; Can f=*Canis familiaris* cat allergen; Der f=*Dermatophagoides farina* house dust mite allergen; Der p=*Dermatophagoides pteronyssinus* house dust mite allergen; Fel d=F*elis catus* cat allergen; HEPA=high-efficiency particulate air-filtration; Mus m 1=*Mus musculus* mouse allergen; NR=not reported; RCT=randomized controlled trial

Table C-25. Outcomes of multicomponent intervention studies

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Matsui et al. 2017[40]	NR	**ED visits**, median (IQR): No statistically significant difference between arms: Arm 1 baseline: 1 (1 to 3) Arm 1 12 months: 0 (0 to 1) Arm 2 baseline: 1 (0 to 2) Arm 2 12 months: 0 (0 to 1) Arm 1 vs. Arm 2: RR (95% CI): 1.15 (0.72 to 1.83) **Hospitalizations**, median (IQR): No statistically significant difference between arms: Arm 1 baseline: 0 (0 to 0) Arm 1 12 months: 0 (0 to 0) Arm 2 baseline: 0 (0 to 1) Arm 2 12 months: 0 (0 to 0) Arm 1 vs. Arm 2: RR (95% CI): 1.28 (0.50 to 3.31)	**FEV_1 % predicted**, mean (SD): No statistically significant difference between arms: Arm 1 baseline: 89.2 (13.9) Arm 1 12 months: 87.9 (14.0) Arm 2 baseline: 86.4 (19.0) Arm 2 12 months: 85.9 (14.2) Arm 1 vs. Arm 2: Beta coefficient (95% CI): 2.29 (-1.63 to 6.22)	NR	**Measurement:** Patient questionnaires **Maximal symptom days/ 2 weeks**, median (IQR): No statistically significant difference between arms: Arm 1 baseline: 2.5 (1.0 to 5.3) Arm 1 12 months: 2.0 (0.7 to 4.7) Arm 2 baseline: 3.0 (0 to 7.0) Arm 2 12 months: 2.7 (1.3 to 5.0) Arm 1 vs. Arm 2: Ratio of symptom frequencies (95% CI): 0.86 (0.69 to 1.06)	**Measurement:** NR **Airborne mouse allergen**, geometric mean (95% CI): Statistically significant difference between arms: Arm 1: 2.19 (1.77 to 2.71) Arm 2: 4.68 (3.72 to 5.90) Arm 1 vs. Arm 2: beta coefficient (95% CI): -1.08 (-1.51 to -0.65) **Bed dust mouse allergen**, geometric mean (95% CI): Statistically significant difference between arms: Arm 1: 0.58 (0.47 to 0.72) Arm 2: 0.75 (0.61 to 0.92) Arm 1 vs. Arm 2: beta coefficient (95% CI): -0.43 (-0.84 to -0.02) **Bedroom floor mouse allergen**, geometric mean (95% CI): No statistically significant difference between arms: Arm 1: 2.0 (1.6 to 2.5) Arm 2: 2.5 (2.0 to 3.3) Arm 1 vs. Arm 2: beta coefficient (95% CI): -0.42 (-0.91 to 0.07)
DiMango et al. 2016[41]	**ACT score**, mean (SE): No statistically significant difference between arms: Arm 1: 20.1 (0.38) Arm 2: 20.9 (0.40) Arm 1 vs. Arm 2: p=0.12 **Childhood ACT**, mean (SE):	**Exacerbations:** No difference in patients reporting exacerbations (criteria NR): 8 in each Arm; p=0.96 **Rescue inhaler days/2 weeks**, mean (SE): No statistically significant difference between arms: Arm 1: 2.32 (0.23) Arm 2: 2.15 (0.24) Arm 1 vs. Arm 2: p=0.61	**FEV_1**, mean (SE): No statistically significant difference between arms: Arm 1: 89.8 (1.58) Arm 2: 89.2 (1.64) Arm 1 vs. Arm 2: p=0.79	**Mini-AQLQ**, mean (SE): No statistically significant difference between arms: Arm 1: 5.41 (0.13) Arm 2: 5.63 (0.14) Arm 1 vs. Arm 2: p=0.26	**Measurement:** Patient questionnaires **Composite asthma score**, components not described, mean (SE): No statistically significant difference between arms: Arm 1: 5.64 (0.25) Arm 2: 5.66 (0.27) Arm 1 vs. Arm 2: p=0.97 **Nighttime awakening**, mean incidents (SE):	**Measurement:** Study team collected dust samples by vacuuming mattresses, bedroom floors, and kitchens; samples were collected 3 times throughout the study. No between-arm comparisons were reported. Arm 1: Statistically significant reduction from baseline was reported for all allergens:

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
	No statistically significant difference between arms: Arm 1: 22.6 (0.58) Arm 2: 22.9 (0.62) Arm 1 vs. Arm 2: p=0.71				No statistically significant difference between arms: Arm 1: 1.08 (0.16) Arm 2: 0.81 (0.17) Arm 1 vs. Arm 2: p=0.26 **Treatment step**, mean (SE): No statistically significant difference between arms: Arm 1: 3.50 (0.16) Arm 2: 3.43 (0.17) Arm 1 vs. Arm 2: p=0.76	Der f 1, Bla g, Fel d 1, Can f 1, Mus m 1 Arm 2: Statistically significant reduction from baseline was reported for: Der f 1, Bla g 2, and Mus m 1; no difference was reported for Fel d 1 or Can f 1
Shani et al. 2015[42]	**ACT and CACT score**, mean increase over baseline (SE): No improvement in ACT score: 2.31 (1.15), p=0.06 No improvement in CACT score: 0.94 (0.52), p=0.08 In subgroup analysis of patients with "severe" baseline scores below 20, there was significant improvement in ACT score (mean increase): 4.22 (1.83), p=0.05 and CACT score (mean increase): 3.45 (0.81) p<0.01	**ED visits**, mean difference (SE): Significant reduction between arms: -0.51 (0.18), p<0.01 **Hospitalizations**, mean difference (SE): No difference between arms: -0.18 (0.12), p=0.14 **Doctor visits**, mean difference (SE): No difference between arms: -0.11 (0.16), p=0.48 **Use of rescue medication**, mean difference (SE): Significant reduction between arms: -1.00 (0.50), p<0.05 **Missed school days**, mean difference (SE): Significant reduction between arms: -4.73 (1.73), p<0.01	NR	NR	NR	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Breysse et al. 2014[43]	NR	**Asthma attacks, use of urgent care, use of rescue medicine:** No statistically significant difference between arms; Statistically significant improvement over baseline was reported for intervention arm **Days with limited activity:** No statistically significant difference between arms, but significant improvement over baseline in both arms	NR	**PACQLQ**: Statistically significant improvement compared to control: p<0.01	**Measurement:** Patient questionnaires **% "asthma not well controlled or very poorly controlled",** decrease from baseline: Statistically significant improvement in Arm 1 vs. Arm 2: Arm 1 decrease: 71% Arm 2 decrease: 48% Arm 1 vs. Arm 2: p<0.05 **Symptom free days and nights:** No difference between arms for symptom-free days (p=0.67); No difference between arms for nights with symptoms (p=0.38); Statistically significant improvement over baseline, within each arm, for symptom-free days (p<0.01), and for nights with symptoms (p<0.01)	**Measurement:** Study team collected dust samples by vacuuming bedrooms, living rooms, and kitchens; samples were collected 2 times: before and after study No between-group comparisons; Der p 1 baseline: 75% Der p 1 followup: 44% Der p 1 baseline vs. followup: p=0.06 Der p 2 baseline: 94% Der p 2 followup: 75% Der p 2 baseline vs. followup: p=0.83 Mus m 1 (kitchen) baseline: 5% Mus m 1 (kitchen) followup: 62% Mus m 1 (kitchen) baseline vs. followup: p=0.14 Mus m 1 (living room) baseline: 37% Mus m 1 (living room) followup: 81% Mus m 1 (living room) baseline vs. followup: p=0.08
Turcotte et al. 2014[44]	**CHSA,** mean score: Statistically significant improvement in all 5 domains, as reported by authors (data shown in figure)	**ED visits/4 weeks**, mean: Baseline: 0.20; Followup: 0.04 **Hospitalizations/4 weeks**, mean: Baseline: 0.05; Followup: 0.00 **Asthma attacks/4 weeks**, mean: Baseline: 0.80; Followup: 0.20 **Doctor visits/4 weeks**, mean: Baseline: 0.70; Followup: 0.20 Authors report that all improvements were statistically significant, but analysis not shown	NR	NR	NR	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Sweet et al. 2013[45]	NR	**ED visits/3 months**, mean (SD): Statistically significant reduction: Baseline: 1.17 (3.06) Followup: 0.50 (0.67) Baseline vs. followup: p<0.01 **Hospitalizations/3 months**, mean (SD): No statistically significant difference: Baseline: 0.15 (0.67) Followup: 0.08 (0.53) Baseline vs. followup: p=0.33 **Albuterol use/2 weeks**, mean (SD): Statistically significant reduction: Baseline: 4.58 (4.73) Followup: 2.17 (3.24) Baseline vs. followup: p<0.01 **Days with limited activity/2 weeks**, mean (SD): Statistically significant reduction: Baseline: 3.84 (4.61) Followup: 1.62 (3.53) Baseline vs. followup: p<0.01 **Missed school days/6 months**, mean (SD): Statistically significant reduction: Baseline: 6.24 (12.82) Followup: 2.81 (5.94) Baseline vs. followup: p<0.01 **Missed work days/6 months**, mean (SD): Statistically significant reduction: Baseline: 3.41 (4.58) Followup: 0.83 (1.70) Baseline vs. followup: p<0.05	NR	**Survey**: Statistically significant improvement in responses to 7 of 9 questions on caregiver quality of life survey	**Measurement:** Patient questionnaires **Symptom days/2 weeks**, mean (SD): Statistically significant reduction: Baseline: 5.01 (4.27) Followup: 2.66 (3.86) Baseline vs. followup: p<0.01 **Nighttime awakening/ 2 weeks**, mean (SD): Statistically significant reduction: Baseline: 3.18 (3.91) Followup: 1.31 (2.72) Baseline vs. followup: p<0.01	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
El-Ghitany et al. 2012[46]	NR	**Number of hospitalizations**, median (interquartile range), compared to baseline: Arm 1: 0.50 (0 to 1) Arm 1 vs. baseline: p<0.01 Arm 2: 1.3 (1 to 2) Arm 2 vs. baseline: p=0.58	**PEFR**, mean difference from baseline, l/min: Arm 1: 6.82 Arm 1 vs. baseline: p=0.0 Arm 2: 1.62 Arm 2 vs. baseline: p=0.0 **FEV_1 % predicted**, mean difference from baseline: Arm 1: 2.55 Arm 1 vs. baseline: p=0.0 Arm 2: -0.15 Arm 2 vs. baseline: p=0.73 Between-arms analyses not presented.	NR	NR	**Measurement:** Study team collected dust samples by vacuuming mattresses and floors; samples were collected 2 times: before and after study period. Between-arms analysis not presented. Authors report statistically significant reduction from baseline of HDM allergen levels in Arm 1.
Takaro et al. 2011[47]	NR	**Urgent care use, asthma attacks, rescue medicine use:** No statistically significant difference between arms reported	**FEV_1:** No statistically significant difference between arms (p=0.93), but there was statistically significant improvement over baseline within arms	**PACQLQ** No statistically significant difference between arms, but there was statistically significant improvement over baseline within arms	**Measurement:** Patient self-report; not specified if diaries or questionnaires **Symptom-free days/ 2 weeks**, mean: No statistically significant difference between arms Arm 1 baseline: 8.6 Arm 1 followup: 12.4 Arm 2 baseline: 8.2 Arm 2 followup: 11.2 Arm 1 vs. Arm 2: p=0.53 **Nights with symptoms/ 2 weeks**, mean: Statistically significant improvement in arm 1: Arm 1 baseline: 4.4 Arm 1 followup: 1.0 Arm 2 baseline: 2.6 Arm 2 followup: 1.1 Arm 1 vs. Arm 2: p=0.44	NR
Bryant-Stephens	NR	**ED visits**, estimated difference (SD): No statistically significant difference	NR	NR	**Measurement:** Patient diaries	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
et al. 2009[48]		between arms: 0.02 (0.13), p=0.89 but significant decrease in each arm **Hospitalizations**, estimated difference (SD): No statistically significant difference between arms: -0.04 (0.16), p=0.81 but significant decrease in each arm			**Nighttime cough**, frequency: No statistically significant difference between arms: p=0.11, but significant improvement in each arm **Wheeze**, frequency: No statistically significant difference between arms: p=0.32, but significant improvement in each arm	
Krieger et al. 2009[49]	NR	**Need for urgent health care**, OR (95% CI): No statistically significant difference between arms: 0.69 (0.38 to 1.26), p=0.23, but significant reduction from baseline in each arm **Asthma attacks/3 months**, beta-coefficient (95% CI): No statistically significant difference between arms: -0.50 (-1.04 to 0.04), p=0.07, but significant reduction from baseline in Arm 1 **Days using beta-agonist/2 weeks**, beta-coefficient (95% CI): No statistically significant difference between arms: -0.59 (-1.45 to 0.26), p=0.18, but significant reduction from baseline in Arm 1 **Reduced activity days/2 weeks**, beta-coefficient (95% CI): No statistically significant difference between arms: -0.22 (-0.79 to 0.36), p=0.46, but significant reduction from baseline in each arm **Missed school days/2 weeks**, OR (95% CI): No statistically significant difference	NR	**PACQLQ**, beta-coefficient (95% CI): Statistically significant difference between arms: 0.22 (0.0 to 0.44), p=0.049	**Measurement**: Patient self-report, but not specified if diary or questionnaire **Symptom-free days/ 2 weeks**, beta-coefficient (95% CI), symptoms: (wheeze, cough, tightness in chest, shortness of breath, slowing down activity, nighttime awakening): Statistically significant difference between arms: 0.94 (0.02 to 1.86), p=0.046	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
		between arms: 0.81 (0.35 to 1.88), p=0.62, but significant reduction from baseline in each arm **Missed work days/2 weeks**, OR (95% CI): No statistically significant difference between arms: 0.60 (0.20 to 1.78), p=0.35, but significant reduction from baseline in each arm				
Bryant-Stephens et al. 2008[50]	NR	**ED visits:** Arm 1 (intervention) vs. Arm 2 (no intervention): No statistically significant difference: p=0.99 Arm 1 vs. Arm 3 (matched case-control patients): Statistically signification reduction: p<0.01 **Inpatient days:** Arm 1 (intervention) vs. Arm 2 (no intervention): No statistically significant difference: p=0.95 Arm 1 vs. Arm 3 (matched case-control patients): Statistically signification reduction: p<0.05 **Sick visits:** Arm 1 (intervention) vs. Arm 2 (no intervention): No statistically significant difference: p=0.26 Arm 1 vs. Arm 3 (matched case-control patients): Statistically signification reduction: p<0.05	NR	NR	**Measurement**: Patient diaries **Cough or wheeze**: No statistically significant difference between arms (data shown graphically)	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Parker et al. 2008[51]	NR	**Needed unscheduled medical care,** OR (95% CI): Statistically significant decrease, arm 1 vs. arm 2: 0.40 (0.22 to 0.74), p<0.01	**PEFR % predicted,** adjusted intervention effect (95% CI), pre- vs. post-intervention: Statistically significant improvement: 8.2 (1.1 to 15.2), p=0.02 **PEFR variability**, adjusted intervention effect (95% CI), pre- vs. post-intervention: No statistically significant difference: -2.1 (-5.0 to 0.8), p=0.15 **FEV_1 % predicted,** adjusted intervention effect (95% CI), pre- vs. post-intervention: Statistically significant improvement: 10.0 (0.9 to 19.1), p=0.03 **FEV_1 variability**, adjusted intervention effect (95% CI), pre- vs. post-intervention: No statistically significant difference: -1.3 (-5.8 to 3.1), p=0.56	**Caregiver depressive symptoms,** Center for Epidemiologic Studies Depression Scale, mean**:** Statistically significant reduction: Arm 1 baseline: 1.62 Arm 1 followup: 1.54 Arm 2 baseline: 1.58 Arm 2 followup: 1.64 Arm 1 vs. arm 2: p=0.02	**Measurement**: Patient questionnaires **Persistent cough**, mean: Statistically significant decrease: Arm 1 baseline: 3.81 Arm 1 followup: 3.36 Arm 2 baseline: 3.48 Arm 2 followup: 3.44 Arm 1 vs. arms 2: p=0.03 **Cough with exercise**, mean: Statistically significant decrease: Arm 1 baseline: 4.27 Arm 1 followup: 3.69 Arm 2 baseline: 3.80 Arm 2 followup: 3.66 Arm 1 vs. arms 2: p=0.02 **Wheeze, shortness of breath, chest tightness or heaviness, or sleep disturbance**, mean: No statistically significant differences (data NR)	**Measurement:** Study team collected dust samples by vacuuming child's bedroom; samples were collected 2 times: before and after study. **Can f**, median, ng/g: Statistically significant reduction: Arm 1 baseline: 130.9 Arm 1 followup: 9.6 Arm 2 baseline: 37.2 Arm 2 followup: 10.3 Arm 1 vs. arm 2: p<0.001 **HDM, Fel d, Mus m:** No statistically significant differences, p<0.001 Data NR
Burr et al. 2007[52]	NR	**Asthma relief medication use/ last 4 weeks**, change in use: Statistically significant difference: Arm 1: 20% of patients reported reduced need Arm 2: 2% of patients reported reduced need Arm 1 vs. arm 2: p=0.02	**Morning PEFR variability**, change in mean coefficient of variation, (SD): No statistically significant difference: Arm 1: -1.62 (6.47) Arm 2: -2.08 (5.96) Arm 1 vs. arm 2, difference (95% CI):	NR	**Measurement:** Patient questionnaires **Wheezing /last 4 weeks:** No statistically significant difference: Arm 1: 17% of patients reported improvement Arm 2: 20% of patients reported improvement Arm 1 vs. arm 2, net	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
			0.46 (-1.58 to 2.50) **Evening PEFR variability**, change in mean coefficient of variation, (SD): No statistically significant difference: Arm 1: -1.30 (6.04) Arm 2: -2.72 (6.30) Arm 1 vs. arm 2, difference (95% CI): 1.42 (-0.58 to 3.43)		difference (95% CI): -3 (-19 to 12)	
Kercsmar et al. 2006[53]	**CHSA**, mean score: No statistically significant difference between arms (data reported in figure)	**Acute care visits,** mean (SD): No statistically significant difference: Arm 1: 0.28 (SD 0.80) Arm 2: 0.91 (SD 1.79) Arm 1 vs. arm 2: p=0.06	NR	NR	**Measurement:** Patient questionnaires **Symptom days:** Statistically significant reduction after adjusting for baseline severity: Arm 1 vs. arm 2: p<0.01 (data reported in figure)	**Measurement:** "standardized visual assessment tool" to score the extent of mold **Mold scores**, mean (SD): Statistically significant reduction: Arm 1: 0.75 (0.99) Arm 2: 1.68 (1.32) Arm 1 vs. arm 2: p<0.01

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Williams et al. 2006[54]	NR	NR	NR	NR	**Measurement:** Patient questionnaires **Overall symptoms:** No statistically significant difference (data NR) **Functional severity score** (component of symptom scale including wheeze, nighttime awakening, occurrence of severe asthma attack, limited home and sports activities): Statistically significant difference: Arm 1: median score decreased by 33% Arm 2: median score decreased by 20% Arm 1 vs. arm 2: p<0.01	**Measurement:** Study team collected dust samples by vacuuming mattresses, floors, furniture; samples were collected 4 times throughout the study period. **Der p 1 or Der f 1 on mattresses**: Statistically significant difference, arm 1 vs. arm 2: p<0.05 (data reported in figure) **Bla g:** No statistically significant difference (data reported in figure)
Eggleston et al. 2005[55]	NR	**Acute care visits:** No statistically significant difference: Arm 1: 15% reduction Arm 2: 13% reduction **Hospitalizations:** No statistically significant difference (data NR)	NR	**Quality of life** (scale not described), mean score: No statistically significant difference: Arm 1: 4.70 Arm 2: 5.00	**Measurement**: Patient questionnaires **Daytime symptoms/ 2 weeks**: Statistically significant difference: Arm 1 baseline: 58% Arm 1 12 months: 55% Arm 2 baseline: 50% Arm 2 12 months: 59% Arm 1 vs. arm 2: p<0.05 **Nighttime symptoms 2 weeks**: No statistically significant difference (p-value NR): Arm 1 baseline: 42% Arm 1 12 months: 30% Arm 2 baseline: 36% Arm 2 12 months: 31% **Symptoms with exercise/2 weeks**: No statistically significant difference (p-value NR):	**Measurement:** Study team collected samples by vacuuming mattresses and floors; samples were collected 3 times throughout the study period. **HDM**, ng/g, median (IQR): No statistically significant difference (p-value NR): Arm 1 baseline: 0.05 (below detection level to 0.4) Arm 1 12 months: below detection level Arm 2 baseline: 0.07 (below detection level to 0.3) Arm 2 12 months: 0.07 (below detection level to 0.2) **Bla g 1**, U/g, median (IQR): No statistically significant difference (p-value NR): Arm 1 baseline: 4.9 (1.1 to 14)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
					Arm 1 baseline: 58% Arm 1 12 months: 33% Arm 2 baseline: 51% Arm 2 12 months: 38% **Symptoms interfering with activity/2 weeks:** No statistically significant difference (p-value NR): Arm 1 baseline: 71% Arm 1 12 months: 43% Arm 2 baseline: 60% Arm 2 12 months: 41%	Arm 1 12 months: 2.9 (below detection level to 11) Arm 2 baseline: 2.8 (0.8 to 18) Arm 2 12 months: 7.1 (1.0 to 24) **Fel d 1,** µg/g, median (IQR): No statistically significant difference (p-value NR): Arm 1 baseline: 0.5 (0.2 to 3.0) Arm 1 12 months: 0.5 (0.2 to 2.2) Arm 2 baseline: 0.5 (0.15 to 3.4) Arm 2 12 months: 2.4 (0.4 to 26) **Mus m 1**, µg/g, median (IQR): No statistically significant difference (p-value NR): Arm 1 baseline: 4.3 (1.2 to 10) Arm 1 12 months: 4.5 (2.6 to 10) Arm 2 baseline: 3.7 (0.67 to 1.3) Arm 2 12 months: 2.5 (0.68 to 14)
Krieger et al. 2005[56]	NR	**Need for urgent care/2 weeks:** Statistically significant difference: Arm 1 baseline: 23.4% Arm 1 followup: 8.4% Arm 2 baseline: 20.2% Arm 2 followup: 16.4% Arm 1 vs. arm 2, OR (95% CI): 0.38 (0.16 to 0.89), p=0.03 **Days using beta-agonist/2 weeks**, mean: No statistically significant difference: Arm 1 baseline: 7.5 Arm 1 followup: 4.0 Arm 2 baseline: 6.9	NR	**PACQLQ**, mean score: Statistically significant difference: Arm 1 baseline: 4.0 Arm 1 followup: 5.6 Arm 2 baseline: 4.4 Arm 2 followup: 5.4 Arm 1 vs. arm	**Measurement:** Patient questionnaires **Symptom days/2 weeks**, mean (symptoms include: wheeze, cough, tightness in chest, shortness of breath, slowing down activity, nighttime awakening): No statistically significant difference: Arm 1 baseline: 8.0 Arm 1 followup: 3.2 Arm 2 baseline: 7.8	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
		Arm 2 followup: 4.0 Arm 1 vs. arm 2, GEE coefficient (95% CI): -0.23 (-1.88 to 1.42) **Days with limited activity/ 2 weeks,** mean: Statistically significant difference: Arm 1 baseline: 5.6 Arm 1 followup: 1.5 Arm 2 baseline: 4.3 Arm 2 followup: 1.7 Arm 1 vs. arm 2, OR (95% CI): 0.22 (0.06 to 0.86), p=0.03 **Missed school days/2 weeks:** No statistically significant difference: Arm 1 baseline: 31.1% Arm 1 followup: 12.2% Arm 2 baseline: 28.4% Arm 2 followup: 20.3% Arm 1 vs. arm 2, OR (95% CI): 0.46 (0.18 to 1.18), p=0.11 **Missed work days/2 weeks:** No statistically significant difference: Arm 1 baseline: 13.1% Arm 1 followup: 11.2% Arm 2 baseline: 21.0% Arm 2 followup: 13.0% Arm 1 vs. arm 2, OR (95% CI): 1.07 (0.40 to 2.85), p=0.89		2, GEE coefficient (95% CI): 0.58 (0.18 to 0.99), p=0.005	Arm 2 followup: 3.9 Arm 1 vs. arm 2, GEE coefficient (95% CI): -1.24 (-2.9 to 0.4), p=0.138	

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Morgan et al. 2004[57] Pongracic et al. 2008[58]	NR	**Unscheduled ED or clinic visits per year,** mean (SE): Statistically significant reduction at 12 months: Arm 1: 2.22 (0.12) Arm 2: 2.57 (0.13) Arm 1 vs. arm 2: p=0.04 No difference at 2-year followup: 1.39 (0.10) vs. 1.66 (0.10), p=0.07 **Hospitalizations** No statistically significant difference at 12 months: Arm 1: 17.1% Arm 2: 15.5% Arm 1 vs. arm 2: p=0.56 No difference at 2-year followup: Arm 1: 10.6% Arm 2: 13.5% Arm 1 vs. arm 2: p=0.19 **Reduced activity days/2 weeks,** mean (SE): Statistically significant difference at 12 months: Arm 1: 2.34 (0.10) Arm 2: 2.84 (0.10) Arm 1 vs. arm 2, p<0.01 Significant difference at 2-year followup: Arm 1: 1.67 (0.10) Arm 2: 2.13 (0.10), p<0.01 **Missed school days/2 weeks**, mean (SE): Statistically significant reduction in missed school days at 12 months: Arm 1: 0.65 (0.04) Arm 2: 0.82 (0.04) Arm 1 vs. arm 2: p<0.01 Significant difference at 2 years: Arm 1: 0.54 (0.04) Arm 2: 0.71 (0.04) Arm 1 vs. arm 2: p<0.01 **Days caretaker changed plans/**	**FEV_1,** mean (SE): No statistically significant difference: Arm 1: 87.0 (0.77) Arm 2: 87.4 (0.78), Arm 1 vs. arm 2: p=0.69	NR	**Measurement:** Patient questionnaires **Symptom days/2 weeks**, mean (SE): Days with symptoms (wheeze, cough, tightness in chest): Statistically significant difference at 12 months: Arm 1: 3.39 (0.12) Arm 2: 4.20 (0.12) Arm 1 vs. arm 2: p<0.01 Maintained at 2 years: Arm 1: 2.62 (0.12) Arm 2: 3.21 (0.13) Arm 1 vs. arm 2: p<0.01 Days with wheeze: Statistically significant difference at 12 months: Arm 1: 2.65 (0.11) Arm 2: 3.43 (0.11) Arm 1 vs. arm 2: p<0.01 Maintained at 2 years: Arm 1: 2.28 (0.11) Arm 2: 2.87 (0.11) Arm 1 vs. arm 2: p<0.01 Nighttime awakenings: Statistically significant difference at 12 months: Arm 1: 1.55 (0.08) Arm 2: 2.17 (0.08) Arm 1 vs. arm 2: p<0.01 Maintained at 2 years: Arm 1: 1.27 (0.08) Arm 2: 1.57 (0.08) Arm 1 vs. arm 2: p=0.01	**Measurement:** Study team collected dust samples by vacuuming mattresses and bedroom floors. Samples were collected 5 times throughout the study period. **Der p 1 on bed**, % reduction from baseline: Statistically significant difference: Arm 1: 37% Arm 2: 18% Arm 1 vs. arm 2: p=0.007 **Der f 1 on bed:** Statistically significant difference: Arm 1: 59% Arm 2: 14% Arm 1 vs. arm 2: p<0.001 **Bla g 1 on bed:** No statistically significant difference: Arm 1: 44% Arm 2: 34% Arm 1 vs. arm 2: p=0.13) **Fel d 1 on bed:** Statistically significant difference: Arm 1: 28% Arm 2: increase of 15% Arm 1 vs. arm 2: p<0.001 **Can f 1 on bed:** No statistically significant difference: Arm 1: increase of 10% Arm 2: increase of 24% Arm 1 vs. arm 2: p=0.29 **Der p 1 on floor:** No statistically significant difference: Arm 1: 21% Arm 2: 13%

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
		2 weeks, mean (SE): No statistically significant difference at 12 months: Arm 1: 0.91 (0.07) Arm 2: 1.22 (SE 0.07) Arm 1 vs. arm 2: p<0.01 No difference at 2-year followup: Arm 1: 0.72 (0.06) Arm 2: 0.87 (SE 0.06) Arm 1 vs. arm 2: p=0.09				Arm 1 vs. arm 2: p=0.28 **Der f 1 on floor:** Statistically significant difference: Arm 1: 34% Arm 2: 10% Arm 1 vs. arm 2: p=0.004 **Bla g 1 on floor:** Statistically significant difference: Arm 1: 53% Arm 2: 19% Arm 1 vs. arm 2: p<0.001 **Fel d 1 on floor:** Statistically significant difference: Arm 1: 14% Arm 2: increase of 15% Arm 1 vs. arm 2: p=0.02 **Can f 1 on floor:** No statistically significant difference: Arm 1: increase of 10% Arm 2: increase of 18% Arm 1 vs. arm 2: p=0.56
Carter et al. 2001[59]	NR	**Need for acute care,** including ED visit, hospitalization, clinic visit: No statistically significant difference between Arm 1 and placebo. Statistically significant reduction between Arm 1 and Arm 3 (no intervention and no placebo), p<0.01	NR	NR	NR	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Htut et al. 2001[60]	NR	NR	**PD_{20}**: Arm 1 (steam cleaning): No statistically significant difference from baseline: p-value NR (data reported in figure Arm 2 (ventilation and steam cleaning): Statistically significant improvement from baseline: p=0.05 (data reported in figure) Arm 3 (placebo): Statistically significant worsening from baseline: p=0.05 (data reported in figure)	NR	NR	**Measurement:** Dust samples were collected by vacuuming mattresses and living room floors. Samples were collected 4 times throughout the study period. **HDM**, geometric mean (SD), ng/g: Arm 1 (steam cleaning): Statistically significant reduction from baseline: Baseline: 7.4 (SD 1.3) Followup: 3.3 (SD 1.6) Arm 2 (ventilation and steam cleaning): Statistically significant reduction from baseline: Baseline: 6.5 (SD 1.4) Followup: 2.2 (SD 1.8) Arm 3 (placebo): No change over baseline (data reported in figure): Arms 1 and 2 vs. arm 3: statistically significant reduction: p=0.03
Warner et al. 2000[61]	NR	NR	**PEFR:** No statistically significant difference between arms (data NR) **PC_{20}:** No statistically significant difference between arms (data reported in figure)	NR	**Measurement:** Patient diaries **Symptom scores** (daytime wheeze, nighttime wheeze, cough, activity): No statistically significant difference between arms (data NR)	**Measurement:** Study team collected dust samples by vacuuming mattresses and floors. Samples were collected 7 times throughout the study period. Ventilation: Statistically significant reduction in HDM allergen on bedroom carpets (p<0.01), mattresses (p=0.03), and sofas (p=0.03), but not living room carpets HEPA vacuum: statistically significant reduction in HDM allergen on bedroom carpets (p=0.04) but not other surfaces

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Cloosterman et al. 1999[62]	NR	NR	**Peak flow variability:** No statistically significant difference, arm 1 vs. arm 2: p=0.62 (data reported in figure) **FEV_1:** No statistically significant difference, arm 1 vs. arm 2: p=0.82 (data reported in figure)	NR	**Measurement:** Patient diaries **Symptom score** (composite of sleep disturbance, cough, breathlessness, wheeze, expectoration, tiredness): No statistically significant difference: p=0.55 (data reported in figure)	**Measurement:** Study team collected dust samples by vacuuming mattresses and bedroom and living room floors. Samples were collected 4 times throughout the study period. **HDM on mattresses:** Statistically significant reduction: Arm 1: 90.6% decrease from baseline Arm 2: 31.5% decrease from baseline Arm 1 vs. arm 2: p<0.01
Evans et al. 1999[63]	NR	**Hospitalizations**, %: No statistically significant difference at 12 months: Arm 1: 15% Arm 2: 19% Arm 1 vs. arm 2: p=0.07 No difference at 2 years: Arm 1: 10% Arm 2: 14% Arm 1 vs. arm 2: p=0.08 **Unscheduled visits per year**, mean: No statistically significant difference at 12 months: Arm 1: 2.64 Arm 2: 2.85 Arm 1 vs. arm 2: p=0.32 No difference at 2 years: Arm 1 : 1.89 Arm 2: 2.24 Arm 1 vs. arm 2: p=0.08	NR	NR	**Measurement:** Patient questionnaires **Symptom days/2 weeks,** mean: Statistically significant difference at 12 months: Arm 1: 3.51 Arm 2: 4.06 Arm 1 vs. arm 2: p<0.01 Improvement maintained at 2 years: Arm 1: 2.64 Arm 2: 3.16 Arm 1 vs. arm 2: p<0.01	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Shapiro et al. 1999[64]	NR	**Hospitalizations, emergency department visits, steroid bursts:** No statistically significant difference between arms (data NR)	**FEV_1:** No statistically significant difference between arms (data NR) **PD_{20}:** Statistically significant increase in doubling of PD_{20} methacholine: Arm 1: 47% Arm 2: 23% Arm 1 vs. arm 2: p<0.05	**Quality of life:** No statistically significant difference between arms in 14-point quality of life scale (name of scale and data NR)	**Measurement:** Patient diaries **Symptom score:** No statistically significant difference between arms (components not described; data NR)	**Measurement***:* Study team collected dust samples by vacuuming mattresses, floors, furniture. **HDM:** No statistically significant difference between arms: Arm 1: 20% reduction from baseline Arm 2: 33% increase over baseline Arm 1 vs. arm 2: p=0.20 Allergen concentrations were categorized as low (<2 µg/g dust), moderate (2 to <10 µg/g dust), or high (≥10 µg/g dust). Significant improvement in % of homes that moved to a lower concentration category: Arm 1: 50% Arm 2: 17% Arm 1 vs. arm 2: p=0.03
Hayden et al. 1997[65]	NR	NR	**PEFR:** Statistically significant difference: Arm 1: 15.1% increase Placebo: 4.4% increase Arm 1 vs. placebo: p<0.05 **FEV_1:** No statistically significant difference: Arm 1: 83% Placebo: 86%	NR	NR	NR

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Carswell et al. 1996[66]	NR	**Medication use:** Use of any asthma medication Statistically significantly reduction: Arm 1: 50% Arm 2: 80% Arm 1 vs. arm 2: p<0.02 Bronchodilator use Statistically significant reduction: Arm 1: 17% Arm 2: 54% Arm 1 vs. arm 2: p<0.01 Use of inhaled steroid No statistically significant difference (actual p-value NR): Arm 1: 13% Arm 2: 35%	**PEFR:** No statistically significant difference between arms (data reported in figure) **FEV_1:** % predicted (SD): Statistically significant difference Arm 1 baseline: 102.7 % (5.8) Arm 1 followup: 105.0% (10.2) Arm 2 baseline: 101.8% (11.8) Arm 2 followup: 98.6% (15.3) Arm 1 vs. arm 2: p<0.05	NR	**Measurement:** Patient diaries **Symptoms, any:** Statistically significantly fewer patients in arm 1 reported any asthma symptoms compared with arm 2, but no significant difference between arms for frequency of daytime wheeze or cough (data reported in figure)	**Measurement:** Dust samples were collected on petri dishes pre-treated with teleosten gelatin and exposed to bedroom air for 2 weeks. Samples were collected 4 times throughout the study period. **HDM, mattresses:** Statistically significant difference: Arm 1 reduction from baseline: 100% Arm 2 reduction from baseline: 53% Arm 1 vs. arm 2: p<0.001
Marks et al. 1994[67]	NR	NR	**Peak flow variability**, mean difference from baseline (95% CI): No statistically significant difference: Arm 1: 1.3 (-0.9 to 3.6) Arm 2: 1.2 (-1.4 to 3.9) Arm 1 vs. arm 2: p=0.94 **FEV_1, % predicted,** mean difference from baseline (95% CI): No statistically significant difference: Arm 1: 4.37 (-1.9 to 10.6) Arm 2: 2.80 (-4.1 to 9.7) Arm 1 vs. arm 2: p=0.72	NR	**Measurement:** Patient diaries **Symptom score** (composite of sleep disturbance, cough, chest tightness, wheeze, breathlessness), square root transformed (95% CI): No statistically significant difference: Arm 1: 0.14 (-0.08 to 0.37) Arm 2: -0.06 (-0.31 to 0.19) Arm 1 vs. arm 2: p=0.20	**Measurement:** Study team collected dust samples by vacuuming mattresses and bedroom and living room floors. Samples were collected 5 times throughout the study period. **HDM:** No statistically significant difference between arms: p=0.76 (data reported in figure)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Walshaw et al. 1986[68]	NR	**Inhaled steroids,** inhalations/ day, mean (SEM): Statistically significant reduction from baseline in arm 1: Arm 1 baseline: 1.83 (0.55) Arm 1 followup: 1.00 (0.47) Arm 1 pre-post: p<0.05 Arm 2 baseline: 2.80 (0.75) Arm 2 followup: 2.40 (0.76) Arm 2 pre post: p=not significant (actual p-value NR) No between-arm analysis provided	**PEFR**, l/min, mean (SEM): Statistically significant improvement from baseline in arm 1: Arm 1 baseline: 391 (31) Arm 1 followup: 423 (31) Arm 1 pre-post: p<0.05 Arm 2 baseline: 376 (27) Arm 2 followup: 372 (31) Arm 2 pre post: p=not significant (actual p-value NR) No between-arm analysis provided	NR	**Measurement:** Patient questionnaires **Symptom ranking** (components and scoring scale not described): Authors report "progressive improvement" in symptoms, but no statistically significant difference between arms (data reported in figure)	**Measurement:** Study team collected dust samples by vacuuming mattresses and living room and bedroom floors. Samples were collected 4 times throughout the study period. **HDM:** Authors report a "significant and sustained" reduction from baseline in HDM allergens for arm 1, with no change for arm 2 (all data reported in figures)

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Korsgaard 1983[69]	NR	**Bronchodilator use** Number of daily puffs, median (IQR): Statistically significant difference: Arm 1 baseline: 3.5 (0.5 to 8.5) Arm 1 followup: 2.0 (0 to 5.5) Arm 2 baseline: 2.5 (0.5 to 5.5) Arm 2 followup: 2.0 (0 to 7.5) Arm 1 vs. arm 2: p=0.03 Nightly use, median (IQR): No statistically significant difference: Arm 1 baseline: 1.5 (0 to 4.0) Arm 1 followup: 0 (0 to 1.5) Arm 2 baseline: 0.5 (0 to 2.5) Arm 2 followup: 0 (0 to 2.5) Arm 1 vs. arm 2: p=0.15	**Morning PEFR**, median (IQR), l/min: No statistically significant difference: Arm 1 baseline: 460 (400 to 540) Arm 1 followup: 490 (420 to 560) Arm 2 baseline: 450 (380 to 530) Arm 2 followup: 460 (390 to 530) Arm 1 vs. arm 2: p=0.33 **Evening PEFR**, median (IQR), l/min: No statistically significant difference: Arm 1 baseline: 470 (430 to 590) Arm 1 followup: 490 (430 to 600) Arm 2 baseline: 475 (410 to 540) Arm 2 followup: 490 (410 to 550) Arm 1 vs. arm 2: p=0.82	NR	**Measurement:** Patient diaries **Daily symptom score**, median (IQR): (composite of cough, wheeze, and shortness of breath, rated on 4-point Likert scale, and summed over 1 week): Statistically significant difference: Arm 1 baseline: 9.0 (5.5 to 14.5) Arm 1 followup: 3.0 (1.0 to 10.5) Arm 2 baseline: 9.0 (3.0 to 16.5) Arm 2 followup: 7.5 (2.0 to 10.5) Arm 1 vs. arm 2: p=0.02 **Nighttime symptom score**, median (IQR): No statistically significant difference: Arm 1 baseline: 5.0 (0 to 8.5) Arm 1 followup: 0.5 (0 to 4.0) Arm 2 baseline: 4.0 (0 to 9.5) Arm 2 followup: 3.0 (0 to 7.0) Arm 1 vs. arm 2: p=0.07	**Measurement:** Study team collected dust samples by vacuuming mattresses and bedroom and living room floors. Samples were collected before and after the study period. **HDM, mattress**, median (IQR): No statistically significant difference: Arm 1 baseline: 55 (23 to 346) Arm 1 followup: 122 (18 to 230) Arm 2 baseline: 44 (5 to 398) Arm 2 followup: 64 (8 to 378) Arm 1 vs. arm 2: p=0.15 **HDM, bedroom floor**, median (IQR): Statistically significant reduction: Arm 1 baseline: 52 (8 to 204) Arm 1 followup: 16 (5 to 30) Arm 2 baseline: 47 (6 to 201) Arm 2 followup: 74 (21 to 463) Arm 1 vs. arm 2: p<0.001 **HDM, living room floor**, median (IQR): No statistically significant difference: Arm 1 baseline: 6 (2 to 41) Arm 1 followup: 14 (4 to 71) Arm 2 baseline: 8 (2 to 49) Arm 2 followup: 8 (3 to 70) Arm 1 vs. arm 2: p=0.676

Study	Asthma Control	Exacerbations and Healthcare Utilization	Pulmonary Physiology	Quality of Life	Symptoms (secondary measure)	Allergen Levels (secondary measure)
Burr et al. 1980[70]	NR	NR	**PEFR variability:** No statistically significant difference: Morning PEFR: Arm 1: 109.2 Arm 2: 107.4 Evening PEFR: Arm 1: 107.7 Arm 2: 105.5	NR	NR	NR

ACT=asthma control test; Bla g 1=*Blatella germanica* cockroach allergen; CACT=children's asthma control test; Can f 1=*Canis familiaris* allergen 1; CHSA=children's health survey for asthma; CI=confidence interval; Der f 1=*Dermatophagoides farina* house dust mite allergen; Der p 1=*Dermatophagoides pteronyssinus* house dust mite allergen; ED=emergency department; Fel d 1=*Felis domesticus* allergen; FEV_1=forced expiratory volume in 1 second; HDM=house dust mite; Mus m 1=*Mus musculus* mouse allergen 1; NR=not reported; OR=odds ratio; PACQLQ=pediatric asthma caregivers asthma quality of life questionnaire; PEFR=peak expiratory flow rate; SD=standard deviation; SE=standard error

Table-C-26. Risk of bias of multicomponent intervention randomized controlled trials

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Matsui et al. 2017[40]	Low	Low	High	High	Low	Low	Low	Medium	No blinding
DiMango et al. 2016[41]	Unclear	Unclear	High	High	Low	Low	Low	Medium	Insufficient description of randomization; no blinding; attrition 16% but intent-to-treat analysis; pre-specified outcomes and subgroup analyses
El-Ghitany et al. 2012[46]	Low	Unclear	High	Low	Low	Low	Low	Medium	Allocation not described; patients not blinded but outcome assessors were; all patients completed followup
Bryant-Stephens et al. 2009[48]	Unclear	Unclear	High	High	High	Low	Low	High	Insufficient description of randomization; no blinding; 23% attrition
Krieger et al. 2009[49]	Low	Low	High	High	Low	Low	Low	Medium	No blinding; 12% attrition and intent-to-treat analysis; pre-specified outcomes reported
Bryant-Stephens et al. 2008[50]	Unclear	Unclear	High	Unclear	High	Low	Low	High	Insufficient description of randomization; no blinding of patients; most outcomes extracted from electronic health record but no description of whether extractors were blinded; 29% attrition

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Parker et al. 2008[51]	Low	Unclear	High	High	High	Low	Low	High	No description of allocation; no blinding; 24% attrition and dropouts differed from completers on homeownership
Burr et al. 2007[52]	Unclear	Unclear	High	High	High	High	Low	High	Insufficient description of randomization; no blinding; 22% attrition
Kercsmar et al. 2006[53]	Low	Low	High	High	High	Low	Low	High	No blinding; 22% attrition
Williams et al. 2006[54]	Low	Unclear	High	Unclear	High	High	Low	High	No description of allocation; no blinding; unclear if outcome assessors were blinded; 77% attrition; major positive finding was a post-hoc analysis
Eggleston et al. 2005[55]	Unclear	Unclear	High	High	Low	Unclear	Low	Medium	Insufficient description of randomization; no blinding; 9 attrition; some data now shown and quality of life scales not described
Krieger et al. 2005[56]	Unclear	Unclear	High	High	High	Low	Low	High	Insufficient description of randomization; no blinding; 22% attrition
Morgan et al. 2004[57]	Low	Unclear	High	Low	Low	Low	Low	Medium	No description of allocation; patients not blinded, but study evaluators blinded; 12% attrition
Carter et al. 2001[59]	Unclear	Unclear	Low	Low	High	Low	Low	Medium	Insufficient description of randomization; placebo used; outcomes assessors blinded; 18% attrition;
Htut et al. 2001[60]	Low	Low	Low	Low	High	Low	High	High	Placebo used; outcomes assessors blinded; 23% attrition; ventilation equipment provided by manufacturer
Warner et al. 2000[61]	High	Unclear	High	High	Unclear	High	Low	High	Randomization was suspended for several participants whose homes were not suited to one of the study arms; no description of allocation; no blinding; attrition not reported; not all data reported

Study	Sequence Generation	Allocation Concealment	Blinding Participants and Personnel	Blinding Outcome Assessors	Incomplete Outcome Data	Selective Outcome Reporting	Other Sources of Bias	Overall Risk of Bias	Comments
Cloosterman et al. 1999[62]	Unclear	Unclear	Low	Low	High	Low	Low	Medium	Insufficient description of randomization; placebo used; 23% attrition; study funded in part by pharmaceutical manufacturers
Evans et al. 1999[63]	Low	Unclear	High	Low	Low	Low	Low	Medium	No description of allocation; outcomes assessors blinded but patients were not; low attrition
Shapiro et al. 1999[64]	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Insufficient description of randomization; placebo used; 11% attrition
Hayden et al. 1997[65]	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Insufficient description of randomization; placebo used; 8% attrition
Carswell et al. 1996[66]	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Insufficient description of randomization; placebo used; 13% attrition
Marks et al. 1994[67]	Unclear	Unclear	Low	Low	High	Low	Low	Medium	Insufficient description of randomization; placebo used; 14% attrition but many data sets incomplete due to patients not completing daily symptom reports
Walshaw et al. 1986[68]	Unclear	Unclear	High	Unclear	Low	High	Low	High	Insufficient description of randomization; no blinding of patients; unclear in outcome assessors were blinded; some data or between-group comparisons not reported
Korsgaard 1983[69]	Unclear	Unclear	High	High	Low	Low	Low	Medium	Insufficient description of randomization; no blinding; no drop-outs
Burr et al. 1980[70]	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Insufficient description of randomization; placebo used; outcomes assessor blinded; 4% attrition

Table C-27. Risk of bias of multicomponent intervention non-randomized controlled trials

Study	Representativeness of the Study Population	Ascertainment of Exposure	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of Outcome	Followup Long Enough for Outcomes to Occur	Adequacy of Followup of Cohorts	Overall Risk of Bias	Comments
Shani et al. 2015[42]	Low	Low	Low	Low	Low	High	Medium	17% of participants were lost to followup and another 24% had incomplete data
Breysse et al. 2014[43]	Low	Low	Low	Low	Low	High	Medium	24% of participants were lost to followup
Turcotte et al. 2014[44]	Low	Low	Low	Low	Low	High	Medium	31% of participants were lost to followup
Sweet et al. 2013[45]	Low	Low	Low	Low	Low	Unclear	Low	Attrition rate not reported
Takaro et al. 2011[47]	Low	Low	Low	Low	Low	Unclear	Low	Attrition rate not reported

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Appendix D. Qualitative Comparative Analysis

The analytic steps of the qualitative comparative analysis (QCA) are described below:

1. Specifying the configural questions. For this review, we asked, "What allergen reduction intervention or combination of intervention components is present in studies demonstrating improved asthma outcomes?"

2. Identifying cases for use in analysis. Randomized controlled trials were included if they: a) examined one of the six types of interventions that were previously evaluated as a single intervention, or a strategy within multicomponent intervention studies (i.e., acaricide, air purification, carpet removal, HEPA vacuum, mattress cover, and pest control); and b) reported data on a primary outcome (i.e., asthma control, exacerbations, healthcare utilization, quality of life, and pulmonary physiology.)

3. Specifying and calibrating condition sets. Condition and outcome sets are calibrated by establishing thresholds and decision rules for membership in a condition. In a crisp set, a value of 1 indicates that a case is fully in the condition set; a value of 0 indicates that a case is fully out of a condition set. We employed a crisp set, where each intervention either was, or was not, used in each study. A value of 1 indicated that an intervention was used in the active arm but not the control arm of a study, while a value of 0 indicated that a given intervention was not examined in that study.

   We also considered other sets of conditions for analysis, in addition to specific intervention strategies. We were especially interested in whether outcomes varied by any of the following characteristics: (a) study population age; (b) use of a single strategy compared with multicomponent interventions; and (c) use of strategies that targeted only one type of allergen compared with interventions that addressed multiple allergens. Therefore, we classified studies according to whether the population was exclusively pediatric (under the age of 12, per our methods for this review), and whether an intervention was implemented in isolation or as part of a multicomponent approach. We also coded studies based on whether their included intervention(s) would be expected to reduce exposure to a single type of allergen, such as acaricide for house dust mites, or multiple allergens, as would apply to air purifiers.

   Although we had 49 studies for analysis, only 22 reported positive findings for a primary outcome. We therefore needed to limit the number of conditions we could test. Because QCA examines all possible combinations of conditions, adding conditions to a model increases the number of possible combinations exponentially (by 2 to the *k*th power, where *k* is the number of conditions. Thus, three conditions produce eight combinations, four conditions produce 16 combinations, and so on). After preliminary analysis, we discovered that inclusion of population and study characteristics as described above did not result in useful findings, and diluted the QCA model. We therefore removed these conditions from the model, and completed the analysis by examining only the six types of interventions discussed above.

4. Specifying the outcome set. We assigned a value of 1 if a study reported significant improvement in at least one measure of one primary outcome (i.e., asthma control, exacerbations, healthcare utilization, pulmonary physiology, or quality of life,) even if other measures or outcomes within the study found no effect. We assigned a value of 0 to cases that did not demonstrate any statistically significant improvement in any measure of

any primary outcome. Table D-1 presents the intervention and outcome inputs for each study.

5. Constructing and analyzing the truth table. The truth table is the main analytic device in QCA. Analysis of the truth table helps to determine which interventions or combination of conditions are consistently present in studies that report improved outcomes. We used R Set Methods and QCA packages to identify "solutions," which are combinations of conditions that are necessary or sufficient to produce a given outcome. This analysis also included examination of two parameters of fit: consistency and coverage. *Consistency* assesses the proportion of studies with a given intervention that achieved the outcome, within an individual solution or across solutions. High consistency indicates that all or most studies that included a given intervention achieved the desired outcome. *Coverage* examines variation in how well a solution accounts for outcomes across all studies. High coverage indicates that a given intervention (or combination of interventions) is present in all or most of the studies that reported a desired outcome.

   The results of a QCA analysis are statements of necessity and sufficiency. We assessed each individual condition for necessity and sufficiency, examined the necessary and sufficient combinations of conditions that resulted in significant improvements, and calculated consistency and coverage. We explored three types of solutions, which differ based on the assumptions that the model makes about the "remainders," which are the combinations of conditions that theoretically could exist but were not present in any of the included studies. These solutions are categorized as conservative, intermediate, and parsimonious. We implemented a 0.80 consistency level for including combinations in the final minimization model. As is typical in QCA practice, we report the intermediate solution in the Results of the report. The conservative and parsimonious solutions, which are a subset and a superset (respectively) of the intermediate solution, are shown in Figure D-1 and Figure D-2.

Figure D-1. Conservative solution

```
n OUT = 1/0/C: 6/9/34
  Total      : 49

Number of multiple-covered cases: 1

M1: acaricide*air.purification*carpet.removal*HEPA.VACUUM*PEST.CONTROL +
acaricide*carpet.removal*HEPA.VACUUM*MATTRESS.COVERS*PEST.CONTROL +
    acaricide*air.purification*CARPET.REMOVAL*hepa.vacuum*mattress.covers*pest.control +
ACARICIDE*air.purification*CARPET.REMOVAL*hepa.vacuum*MATTRESS.COVERS*pest.control
    => ANY.OUTCOME

                                                                                    incl   PRI    cov.r  cov.u  cases
-----------------------------------------------------------------------------------------------------------------------
1  acaricide*air.purification*carpet.removal*HEPA.VACUUM*PEST.CONTROL               1.000  1.000  0.091  0.045  8; 6
2  acaricide*carpet.removal*HEPA.VACUUM*MATTRESS.COVERS*PEST.CONTROL                1.000  1.000  0.091  0.045  6; 9
3  acaricide*air.purification*CARPET.REMOVAL*hepa.vacuum*mattress.covers*pest.control  1.000  1.000  0.045  0.045  18
4  ACARICIDE*air.purification*CARPET.REMOVAL*hepa.vacuum*MATTRESS.COVERS*pest.control  1.000  1.000  0.091  0.091  2,15
-----------------------------------------------------------------------------------------------------------------------
   M1                                                                               1.000  1.000  0.273
```

Figure D-2. Parsimonious solution

```
n OUT = 1/0/C: 6/9/34
  Total      : 49

M1: CARPET.REMOVAL*pest.control + HEPA.VACUUM*PEST.CONTROL => ANY.OUTCOME

                                incl   PRI    cov.r  cov.u
-----------------------------------------------------------
1  CARPET.REMOVAL*pest.control  1.000  1.000  0.136  0.136
2  HEPA.VACUUM*PEST.CONTROL     1.000  1.000  0.136  0.136
-----------------------------------------------------------
   M1                           1.000  1.000  0.273
```

Table D-1. QCA input table

Study	Acaricide	Air Purification	Carpet Removal	HEPA Vacuum	Mattress Covers	Pest Control	Primary Outcome
Matsui et al. 2017[1]	0	0	0	0	0	1	0
Rabito et al. 2017[2]	0	0	0	0	0	1	1
DiMango et al. 2016[3]	0	1	0	1	1	0	0
El-Ghitany et al. 2012[4]	1	0	1	0	1	0	1
Bryant-Stephens et al. 2009[5]	0	0	1	0	1	1	0
Krieger et al. 2009[6]	0	0	0	1	0	0	1
Bryant-Stephens et al. 2008[7]	0	0	1	0	1	1	0
Parker et al. 2008[8]	0	0	0	1	1	1	1
Eggleston et al. 2005[9]	0	1	0	0	1	1	0
Krieger et al. 2005[10]	0	0	0	1	0	1	1
Morgan et al. 2004[11]	0	1	0	1	1	1	1
Carter et al. 2001[12]	0	0	0	0	1	1	1
Warner et al. 2000[13]	0	0	0	1	0	0	0
Cloosterman et al. 1999[14]	1	0	0	0	1	0	0
Evans et al. 1999[15]	0	0	0	0	1	1	0
Shapiro et al. 1999[16]	1	0	0	0	1	0	1
Hayden et al. 1997[17]	1	0	1	0	1	0	1
Carswell et al. 1996[18]	1	0	0	0	1	0	1
Marks et al. 1994[19]	1	0	0	0	1	0	0
Korsgaard et al. 1983[20]	0	0	1	0	0	0	1
Bahir et al. 1997[21]	1	0	0	0	0	0	0
Chang et al. 1996[22]	1	0	0	0	0	0	0
Sette et al. 1994[23]	1	0	0	0	0	0	1
Dietemann et al. 1993[24]	1	0	0	0	0	0	0
Reiser et al. 1990[25]	1	0	0	0	0	0	0
Pedroletti et al. 2009[26]	0	1	0	0	0	0	1
Wright et al. 2009[27]	0	1	0	0	0	0	1
Sulser et al. 2008[28]	0	1	0	0	0	0	0
Francis et al. 2003[29]	0	1	0	0	0	0	1
Van der Heide et al. 1999[30]	0	1	0	0	0	0	1
Van der Heide et al. 1997[31]	0	1	0	0	0	0	0
Warner et al. 1993[32]	0	1	0	0	0	0	0
Mitchell et al. 1980[33]	0	1	0	0	0	0	0

Study	Acaricide	Air Purification	Carpet Removal	HEPA Vacuum	Mattress Covers	Pest Control	Primary Outcome
Zwemer et al. 1973[34]	0	1	0	0	0	0	0
Popplewell et al. 2000[35]	0	0	0	1	0	0	1
Murray et al. 2017[36]	0	0	0	0	1	0	1
Tsurikisawa et al. 2016[37]	0	0	0	0	1	0	0
Tsurikisawa et al. 2013[38]	0	0	0	0	1	0	1
de Vries et al. 2007[39]	0	0	0	0	1	0	0
Dharmage et al. 2006[40]	0	0	0	0	1	0	0
van den Bemt et al. 2004[41]	0	0	0	0	1	0	1
Halken et al. 2003[42]	0	0	0	0	1	0	1
Luczynska et al. 2003[43]	0	0	0	0	1	0	0
Woodcock et al. 2003[44]	0	0	0	0	1	0	1
Rijssenbeek-Nouwens et al. 2002[45]	0	0	0	0	1	0	0
Sheikh et al. 2002[46]	0	0	0	0	1	0	0
Frederick et al. 1997[47]	0	0	0	0	1	0	0
Burr et al. 1980[48]	0	0	0	0	1	0	0
Burr et al. 1976[49]	0	0	0	0	1	0	0
Total (N=49)	**11**	**12**	**5**	**7**	**28**	**10**	**22**

HEPA=high-efficiency particulate air-filtration

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Appendix E. Minimally Important Differences

It is important to evaluate whether a measured change in an asthma outcome is clinically meaningful as well as statistically significant. Thresholds for determining clinically significant improvement have been established for some measures of asthma control, asthma-related quality of life, pulmonary physiology, and healthcare utilization, and are presented in Table E-1. The data in this table are reproduced with permission from the AHRQ EPC report, "Systematic Review of Intermittent Inhaled Corticosteroids and of Long-acting Muscarinic Antagonists for Asthma", by the University of Connecticut Evidence-based Practice Center.

Table E-1. Thresholds for clinical significance

Instrument/ Outcome	Range (points)	Final score	Threshold
ACT	5 to 25	Well-controlled: ≥20 Not well-controlled: ≤19	≥12 y: Δ 3 points[1]
ACQ5, ACQ6	0 to 6	Uncontrolled: ≥1.5 Well-controlled: <0.75	≥18 y: Δ 0.5 points[2]
ACQ7	0 to 6	Uncontrolled: ≥1.5 Well-controlled: <0.75	≥6 y: Δ 0.5 points[2,3]
AQLQ,AQLQ(S), AQLQ-mini	1 to 7	Severe impairment = 1 No impairment= 7	≥18 y: Δ 0.5 points[4-6]
AQLQ12+	1 to 7	Severe impairment = 1 No impairment= 7	≥12 y: Δ 0.5 points[7,8]
PAQLQ, PACQLQ	1 to 7	Severe impairment = 1 No impairment= 7	7-17 y: Δ 0.5 points[9,10]
FEV1	Continuous measure, L	NA	≥18 y: -0.2 L[11]
Rescue medication use	Continuous measure, puffs per unit of time	NA	≥18 y: -0.81 puffs/day[11]

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