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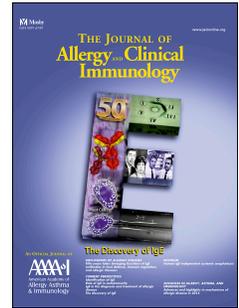
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45 **Abstract**

46

47 **Background:** This review will inform updated National Asthma Education and Prevention
48 Program clinical practice guidelines.

49 **Objective:** To evaluate the effectiveness of allergen reduction interventions on asthma
50 outcomes.

51 **Methods:** We systematically searched the gray literature and five bibliographic databases.
52 Eligible studies included systematic reviews, randomized controlled trials, and nonrandomized
53 interventional studies. Risk of bias was assessed using the Cochrane Risk of Bias instrument and
54 the Newcastle-Ottawa scale. The evidence base was assessed using the approach of the Agency
55 for Healthcare Research and Quality's Evidence-based Practice Center program.

56 **Results:** Fifty-nine randomized and 8 non-randomized trials addressed 8 interventions: acaricide,
57 air purification, carpet removal, high-efficiency particulate air-filtration (HEPA) vacuums,
58 mattress covers, mold removal, pest control, and pet removal. Thirty-seven studies evaluated
59 single component interventions, and 30 studies assessed multicomponent interventions.

60 Heterogeneity precluded meta-analysis. For most interventions and outcomes, the evidence base
61 was inconclusive or showed no effect. No interventions were associated with improvement in
62 validated asthma control measures or pulmonary physiology. Exacerbations were diminished in
63 multicomponent studies that included HEPA vacuums or pest control (moderate strength of
64 evidence [SOE] for both). Quality of life improved in studies of air purifiers (low SOE), and in
65 multicomponent studies that included HEPA vacuums (moderate SOE) or pest control (low
66 SOE).

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

73 **Key Messages:**

- 74
- 75 • Evidence for single interventions designed to reduce indoor allergen exposure on asthma
 - 76 outcomes is lacking.
 - 77 • Multicomponent interventions that bundle more than one strategy may improve some
 - 78 asthma outcomes, but it is unclear if specific combinations are more effective than others.
 - 79 • Multicomponent interventions that include high-efficiency particulate air-filtration (HEPA)
 - 80 vacuums or pest control reduce exacerbations and improve quality of life.
 - 81 • The evidence for both single and multicomponent interventions does not address many other
 - 82 important outcomes, including asthma-related health care utilization, pulmonary physiology,
 - 83 and asthma-related quality of life.
- 84

85

86 **Capsule summary:**

87

88 This systematic review assessed the effectiveness of interventions to reduce exposure to indoor

89 inhalant allergens on asthma outcomes in adults and children. No single or specific combination

90 of interventions was found to be conclusively effective.

91

92 **Keywords:** asthma; allergens; environmental; house dust mites; carpet; pests; pets; air

93 purification; high-efficiency particulate air filtration (HEPA) vacuums; mattress covers

94

95 **Introduction**

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

103 In 1991, the National Asthma Education and Prevention Program (NAEPP), a project of the
104 National Heart, Lung, and Blood Institute (NHLBI), produced clinical practice guidelines
105 addressing the diagnosis, evaluation, and treatment of asthma, including reducing exposure to
106 indoor inhalant allergens. The guidelines were subsequently updated, most recently in 2007.² In
107 2016, NHLBI convened a working group to oversee a new update of the guidelines. After
108 receiving input from the public, NAEPP Coordinating Committee Members and affiliates, and
109 members of the 2007 Expert Panel, the working group identified six high-priority topics for
110 updating. For each topic, key questions were developed to guide new systematic literature
111 reviews. NHLBI engaged the Agency for Healthcare Research and Quality (AHRQ) to perform
112 the systematic reviews through its Evidence-based Practice Centers (EPCs). In this article, we
113 summarize the resulting systematic review on “Effectiveness of Indoor Allergen Reduction in
114 Management of Asthma.” The complete review is available at: (INSERT when available)

115

116 **Methods**

117 We searched Embase, MEDLINE, PubMed, CINAHL, and the Cochrane Library up to April
118 21, 2017. We also browsed the websites of relevant agencies and organizations to identify “gray
119 literature” such as reports, white papers, dissertations, or other documents not published in peer-
120 reviewed sources. Two independent reviewers performed abstract and full text screening, with
121 disagreements resolved by consensus.

122 We included only full-length, peer-reviewed studies. Systematic reviews, meta-analyses,
123 randomized controlled trials (RCTs), and nonrandomized interventional studies with concurrent
124 controls (e.g., nonrandomized trials) or historical controls (e.g., pre-post studies) were eligible
125 for inclusion. In vivo, in vitro, and animal studies were excluded. Studies published in a foreign
126 language with English-language abstracts were considered for inclusion if they examined
127 interventions or reported outcomes not sufficiently addressed in English-language studies, or
128 provided novel data that might affect our conclusions. Studies were excluded if more than 15%
129 of participants were not diagnosed with asthma, or if outcomes for asthmatic patients were not
130 reported separately from patients without asthma. In accordance with the approach used by the
131 Guidelines for the Diagnosis and Management of Asthma², we defined “pediatric” or “child”
132 populations as including patients age 11 or younger, and “adult” populations as including
133 patients age 12 or older. Studies that included patients in both categories are described as having
134 a “mixed population.”

135 We limited our review to studies that examined a single intervention or a set of interventions
136 designed to decrease exposure to one or more of the following sources of indoor allergens: dust
137 mites, household pets, rodents, cockroaches, or mold. Interventions addressing other indoor
138 allergens or irritants, such as tobacco smoke, indoor pollution, and endotoxin, were excluded.

139 We examined the following interventions, selected to reflect the input of the NHLBI Advisory
140 Council Asthma Expert Working Group³:

- 141 • Acaricides
- 142 • Air purification devices
- 143 • Carpet or rug removal
- 144 • HEPA vacuums
- 145 • Impermeable mattress covers
- 146 • Mold removal
- 147 • Pest control
- 148 • Pet removal

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

154 Outcomes were selected to be consistent with the recommendations of the 2010 Asthma
155 Outcomes workshop.⁶ Primary outcomes included: validated measures of asthma control (e.g.,
156 the Asthma Control Questionnaire⁷ (ACQ) or Asthma Control Test⁸ (ACT)), asthma-related
157 exacerbations, asthma-related healthcare utilization and costs, pulmonary physiology (e.g.,
158 spirometry measures), and asthma-related quality of life (e.g., the Asthma Quality of Life
159 Questionnaire⁹ (AQLQ)). Non-validated measures of asthma symptoms and allergen levels were
160 assessed as secondary outcomes.

161 We graded the strength of evidence (SOE) for each outcome based on the guidance
162 established by the EPC program¹⁰. This approach incorporates five key domains: study
163 limitations, consistency, directness, precision, and reporting bias. Overall SOE was evaluated as
164 High, Moderate, Low, or Insufficient. Evidence based on RCTs was assigned an initial SOE of
165 “high,” while evidence based on non-RCTs was assigned an initial SOE of “low.” The SOE was
166 then downgraded as appropriate based on the five domains.

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

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

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

180 Precision is the degree of certainty surrounding an effect estimate with respect to a given
181 outcome and may be affected by sample size, number of events, and width of confidence
182 intervals. In some cases, we downgraded the SOE by two levels due to substantial imprecision
183 resulting from very small samples or numbers of events, or when it was not possible to assess an

184 estimate of effect based on the available data (e.g., measures of variance were not included, or
185 results were presented graphically without reporting of specific data points).

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

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

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

198

199 **Results**

200 We reviewed 1,921 abstracts and 201 full-text studies. We included 59 RCTs (with data
201 published in 63 published articles) and 8 non-randomized controlled studies in the review
202 (Figure 1). Thirty-seven studies evaluated single interventions and 30 studies examined
203 multicomponent strategies. Use of mattress covers was the most frequently examined
204 intervention and was included in 33 studies. Pet removal, conversely, was implemented in just
205 three studies. Twenty-two studies included only patients twelve years of age and older, while 9
206 studies were limited to children under 12. Thirty-five studies enrolled patients above and below
207 the age of 12 and one study did not report age. Thirty-four studies were conducted in Europe, 23
208 were performed in the United States, and the remaining 10 were conducted in Canada, Australia,
209 New Zealand, or Asian countries. In forty studies, all patients were sensitized to a relevant
210 allergen, while an additional 14 studies reported that a majority of patients were sensitized.
211 Sensitization was confirmed through skin-prick testing in 43 RCTs, and with blood tests in the
212 remaining 11 trials.

213 Table 1 provides an overview of the distribution of the studies. Table 2 shows the
214 combinations of interventions used in the multicomponent studies. Table 3 summarizes the
215 strength of evidence for each intervention.

216 A more detailed description of the analysis is presented in Table 4 (for single-intervention
217 studies) and Table 5 (for multicomponent studies). Additional information for each included
218 study is available in the complete AHRQ report (link when available).

219 Acaricide

220 Seven studies examined the use of acaricide on mattresses, carpets, and upholstery, as a
221 single intervention to eradicate house dust mite allergens.¹²⁻¹⁸ There was no improvement in
222 pulmonary physiology when comparing acaricide with placebo (SOE: Moderate) or with other
223 interventions (SOE: Low), and other outcomes were inconclusive or not reported. Six
224 multicomponent studies also examined acaricide,^{51,65,67-70} and suggested no improvement in
225 pulmonary physiology (SOE: Moderate) or asthma symptoms (SOE: High). Acaricides reduced
226 dust mite allergen burden (SOE: Low), but other outcomes were inconclusive or not reported.

227 Air purification

228 Nine studies evaluated air purification as a single intervention.¹⁹⁻²⁷ The evidence for asthma
229 control was inconclusive, and no difference was observed for exacerbations or pulmonary
230 physiology measures (SOE: Low). For quality of life, one study found that Asthma Quality
231 Control Questionnaire (AQLQ) scores improved (SOE: Low), while two studies that used
232 nonvalidated quality of life measures found no effect (SOE: Low). Five studies evaluated air
233 purifiers within multicomponent interventions,^{49,50,59,61,78} and reported no improvement in asthma
234 control (SOE: Low), exacerbations (SOE: High), or quality of life (SOE: High). However, school
235 absenteeism decreased (SOE: Low), asthma symptoms improved (SOE: Low), and allergen
236 levels were reduced (SOE: Moderate).

237 Carpet removal

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

HEPA vacuum

242
243 One study examined HEPA vacuums alone, but the evidence base is insufficient to support
244 conclusions.²⁸ Eight multicomponent studies also evaluated HEPA vacuums.^{50,53,55,60,61,64,75,77}
245 The evidence was insufficient for asthma control and pulmonary physiology measures.
246 Exacerbations were reduced (SOE: Moderate), medication use did not change (SOE: High), and
247 no effect was observed for school (SOE: Low) or work absenteeism (SOE: Moderate). Quality of
248 life improved in studies of children under age 12 (SOE: Moderate) In addition, asthma symptoms
249 improved in children (SOE: Low) but not among mixed populations of children, adolescents, and
250 adults (SOE: Moderate).

Mattress covers

251
252 Fourteen studies examined impermeable mattress covers²⁹⁻⁴² and three studies evaluated
253 other approaches designed to limit dust mite allergens on bedding.⁴³⁻⁴⁵ The evidence suggests no
254 difference in asthma control (SOE: Moderate), exacerbations (SOE: Moderate), use of inhaled
255 corticosteroids (SOE: Low), rescue medication use (SOE: High), pulmonary physiology (SOE:
256 High), quality of life (SOE: High), or self-reported asthma symptoms (SOE: High). Conversely,
257 these studies reported reduction in dust mite allergen levels (SOE: Moderate). Mattress covers
258 were also used in 19 multicomponent intervention studies.^{49-52,54,55,58,59,61,62,65-71,74,77} In these
259 studies, no improvement was found for emergency department use (SOE: Low), hospitalizations
260 (SOE: High), or acute care visits (SOE: Moderate). However, school absenteeism and missed
261 activities decreased (SOE: Low). No effect was observed for measures of pulmonary physiology
262 (SOE: High), or quality of life (SOE: Moderate).

263

264

265 Mold removal

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

269 Pest control

270 One RCT⁴⁰ and one nonrandomized study⁴⁷ examined pest-control strategies alone and the
271 findings were insufficient to support any conclusions other than improvement in self-reported
272 asthma symptoms (SOE: Low). Thirteen multicomponent studies evaluated pest-control
273 efforts.^{49,52,54,55,58-62,66,74-76} The evidence was inconclusive for asthma control, medication use,
274 and pulmonary physiology measures. Exacerbations were reduced when measured as a
275 composite score (SOE: Moderate), but no effect was observed for discrete measures including
276 emergency department visits (SOE: Moderate) and hospitalizations (SOE: High). School
277 absenteeism decreased (SOE: Low) and quality of life among children (SOE: Low) improved.
278 Asthma symptoms also improved (SOE: Low), and allergen levels were reduced for some pests
279 (e.g. cockroaches) (SOE: Low).

280 Pet removal

281 One nonrandomized study focused on pet removal.⁴⁸ The evidence for hospitalizations,
282 medication use, and follow-up visits was inconclusive, and no other asthma outcomes were
283 reported. Two multicomponent interventions encouraged pet removal,^{51,58} but we did not
284 evaluate the SOE because of the small number of studies and uncertainty regarding how widely
285 this recommendation was implemented.

286

287

288 **Qualitative Comparative Analysis (QCA)**

289 We included 30 multicomponent and 19 individual intervention studies in the QCA. The
290 results were not robust, and no intervention or bundle of interventions was necessary or
291 sufficient for improvement in any primary outcome. Overall, the analysis reinforced the findings
292 described in our SOE assessment: there is insufficient evidence demonstrating the effects of most
293 single interventions or multicomponent strategies on important asthma outcomes.

294 **Discussion**

295 This systematic review identified 59 RCTs and 8 non-RCTs addressing 8 interventions for
296 reducing home-based indoor allergen exposure and improving asthma outcomes. Thirty-seven
297 studies evaluated single component interventions, and 30 studies assessed multicomponent
298 interventions. Overall, we found no high-strength evidence suggesting improvement in any of the
299 primary outcomes, but there was low to moderate-strength evidence for some interventions.
300 Validated measures of asthma control were infrequently reported.

301 Our findings are generally consistent with previous Cochrane reviews of similar
302 interventions, but differs from some other reviews. For example, in a Cochrane systematic
303 review addressing mattress covers and acaricides,⁷⁹ and another that examined air purification
304 devices,⁸⁰ evidence was generally lacking in rigor and insufficient to inform conclusions.
305 Conversely, a 2010 systematic review⁸¹ found evidence supporting pest control, mold removal,
306 and multicomponent interventions that are individually tailored to a patient or family. The
307 authors, however, did not use a formal approach for assessing the strength of the evidence base,
308 and they incorporated expert opinion and epidemiologic evidence drawn from noninterventional
309 studies into their conclusions. Also, they emphasized evidence showing reduced allergen levels
310 on mattresses and floors, when clinical outcomes were lacking.

311 Similarly, our assessment varies in key ways from the 2007 NAEPP guidelines,² and clinical
312 practice parameters of the American Academy of Allergy, Asthma, and Immunology.⁸² We
313 found that the evidence for most interventions was low-strength or insufficient, while the
314 previous guidelines found greater evidence of benefit associated with some interventions.
315 Several reasons can account for our different conclusions. Our review includes numerous studies
316 published recently, some of which showed no intervention effect. Additionally, we did not

317 always select the same studies as other reviewers because of differences in our respective
318 inclusion criteria. We also prioritized outcomes and examined specific outcome measures
319 differently from the AAAAI and the 2007 NAEPP, which affected how our findings were
320 synthesized. Further, our report used different instruments to assess the risk of bias of individual
321 studies, which in turn affected our analysis of the SOE. Finally, the prior reviews did not employ
322 the EPC methodology¹⁰ or a similar GRADE (Grading of Recommendations Assessment,
323 Development and Evaluation⁸³) type of approach to evaluate the evidence base. These
324 differences may account for variations between our assessment and the preceding reviews.

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

335 A similar consideration is variation in asthma severity. Only 18 RCTs classified the severity
336 of participants' asthma. In 11 studies, most or all patients had moderate to severe asthma, while
337 most patients had mild to moderate asthma in 5 studies. In 2 studies, the populations were
338 distributed evenly among mild, moderate, and severe patients. Unfortunately, since 41 RCTs did

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

341 We also note that home-based interventions are difficult to implement properly and
342 completely, as cost, language, technology, home ownership, and health literacy can be barriers.
343 Thirteen of the 30 multicomponent intervention studies included a community health worker
344 who received specialized training to educate patients about reducing home allergen exposure in a
345 highly tailored way. Although we did not evaluate the direct impact of these health workers, their
346 role in the process may be important. Similarly, it is difficult to evaluate or ensure fidelity to a
347 home-based intervention. Although several studies reported that adherence to study protocols
348 was evaluated periodically (through surveys or home visits), most studies did not report such
349 findings. Conversely, it is possible and even likely that some control group households adopted
350 allergen-reducing interventions during their studies, potentially masking or minimizing
351 differences in outcomes between study groups. The studies we evaluated did not address or
352 adjust for this type of confounding. It may also be difficult to maintain an allergen-reduction
353 strategy over time. Many studies had high attrition rates, which are attributable partly to
354 participants moving from one home to another or encountering instability in family life that may
355 disrupt continuity. Additionally, some of the interventions may have evolved over time. For
356 example, contemporary air purification devices may be different from those technologies
357 available and examined two or three decades earlier, and this may introduce further
358 heterogeneity into the results.

359 Another important factor is the potential exposure to indoor allergens outside the home.
360 Patients with asthma are frequently exposed to allergens at work or school or while engaged in
361 other activities, which may limit the effectiveness of interventions used solely at home. Although

362 our review was designed to include studies that evaluated interventions in work or school
363 environments, we did not identify any eligible studies that fit those criteria.

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

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

378 We identified several evidence gaps that would benefit from future research. First, there has
379 been insufficient evaluation of several specific interventions, including HEPA vacuums, carpet
380 removal, pet cleaning or removal, and mold removal. Head-to-head studies of interventions are
381 also missing from the current evidence base, which consists almost entirely of comparisons with
382 placebos or standard practices. Research is also needed to evaluate multicomponent interventions
383 more efficiently. This might be accomplished by standardizing sets of strategies that could be

384 tested as bundles. Additionally, future research could attempt to directly compare single
385 interventions with bundled interventions.

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

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

399 This review highlights an important consideration for clinicians. Since asthma significantly
400 affects overall health and quality of life, patients and their families are often motivated to
401 augment medical treatment with interventions that reduce exposure to allergen triggers. It is
402 important for clinicians to consider the complexity of their patient population and the limitations
403 of the evidence that we have identified. When recommending specific steps of action, clinicians
404 may find it helpful to consider a patient's individual sensitization and reaction to specific
405 allergens, as well as the severity of the patient's asthma and the extent of previous symptoms and
406 exacerbations. Meanwhile, further research on the effectiveness of common allergen-control

407 strategies, and the many patient- and household-level characteristics that may influence patient
408 outcomes, is necessary.

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

416

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439 eligibility criteria, data analysis or interpretation, or preparation, review, or approval of the
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735 Figure 1 Legend: KQ=Key Question; RCT=randomized controlled trial

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736 **Table 1. Overview of interventional studies for reducing exposure to allergens**

Intervention	Randomized Controlled Trials and Sample Size	Other Study Designs and Sample Size	Age Cohorts ^a	Country/Region
Acaricides (dust mite pesticide)	6 ¹²⁻¹⁷ Total n=229	1 nonrandomized trial ¹⁸ n=59	3 adult 4 mixed	6 Europe 1 Canada
Air purification	9 ¹⁹⁻²⁷ Total n=311	0	4 adult 1 pediatric 4 mixed	1 United States 7 Europe 1 New Zealand
Carpet removal	0	0	Not applicable	Not applicable
HEPA vacuums	1 ²⁸ n=60	0	1 mixed	1 Europe
Mattress covers	17 ²⁹⁻⁴⁵ Total n=2,287	0	9 adult 1 pediatric 6 mixed 1 not reported	11 Europe 4 Asia 2 Australia
Mold removal	0	0	Not applicable	Not applicable
Pest control	1 ⁴⁶ n=102	1 pre-post ⁴⁷ n=78	2 mixed	2 United States
Pet removal	0	1 nonrandomized trial ⁴⁸ n=20	1 adult	1 Asia
Multicomponent	25 ⁴⁹⁻⁷³ Total n=4,338	3 pre-post ⁷⁴⁻⁷⁶ (n=365) 2 nonrandomized controlled trials ^{77,78} (n=204)	5 adult 7 pediatric 18 mixed	20 United States 9 Europe 1 Australia
Total	59	4 nonrandomized trials 4 pre-post	22 adult 9 pediatric 35 mixed 1 not reported	23 United States 1 Canada 34 Europe 5 Asia 4 Australia/ New Zealand

737 ^a "adult" patients were ≥12 years old, "pediatric" patients were <12 years old, and "mixed" populations
738 included pediatric and adult patients
739 HEPA: high-efficiency particulate air-filtration

740 **Table 2. Multicomponent indoor allergen reduction interventions by study**

Study	Acaricide (dust mite pesticide)	Air Purification	Carpet Removal ^a	HEPA Vacuum	Mattress Covers	Mold Removal	Pest Control	Pet Removal ^a	Laundering Linens	Cleaning Supplies Provided	CHW Education/ Instruction	Other
Matsui, 2017 ⁴⁹		✓			✓		✓					
DiMango, 2016 ⁵⁰		✓		✓	✓					✓		
Shani, 2015 ^{74,b}					✓		✓			✓	✓	
Breyse, 2014 ^{77,b}			✓			✓						Weatherization
Turcotte, 2014 ^{75,b}				✓			✓			✓	✓	Professional cleaning
Sweet, 2013 ^{76,d}				✓	✓	✓	✓			✓	✓	Moisture control
El-Ghitany, 2012 ⁵¹	✓		✓		✓			✓	✓			Ventilation
Takaro, 2011 ^{78,b}		✓				✓						Ventilation
Bryant-Stephens, 2009 ⁵²			✓		✓		✓			✓	✓	
Krieger, 2009 ⁵³				✓						✓	✓	
Bryant-Stephens, 2008 ⁵⁴			✓		✓		✓			✓	✓	
Parker, 2008 ⁵⁵				✓	✓		✓			✓	✓	
Burr, 2007 ⁵⁶						✓						Positive ventilation fan
Kercsmar, 2006 ⁵⁷						✓						Moisture control
Williams, 2006 ⁵⁸			✓		✓	✓	✓	✓			✓	Professional cleaning
Eggleston, 2005 ⁵⁹		✓			✓		✓				✓	
Krieger, 2005 ⁶⁰				✓			✓			✓	✓	
Morgan, 2004 ⁶¹		✓		✓	✓		✓					
Carter, 2001 ⁶²					✓		✓		✓			
Htut, 2001 ⁶³									✓			Ventilation; steam heating; new pillows
Warner, 2000 ⁶⁴				✓								House-wide ventilation system
Cloosterman, 1999 ⁶⁵	✓				✓							
Evans, 1999 ⁶⁶					✓		✓				✓	
Shapiro, 1999 ⁶⁷	✓				✓				✓			
Hayden, 1997 ⁶⁸	✓		✓		✓				✓			
Carswell, 1996 ⁶⁹	✓				✓				✓			
Marks, 1994 ⁷⁰	✓				✓							

Study	Acaricide (dust mite pesticide)	Air Purification	Carpet Removal ^a	HEPA Vacuum	Mattress Covers	Mold Removal	Pest Control	Pet Removal ^a	Laundering Linens	Cleaning Supplies Provided	CHW Education/ Instruction	Other
Walshaw, 1986 ⁷¹			✓		✓							Feather-based bedding replaced
Korsgaard, 1983 ⁷²			✓						✓			Mattress vacuuming; new pillows and quilts; ventilation; clothes dried outdoors
Burr, 1980 ⁷³									✓			Mattress vacuuming; quilts removed; feather pillows replaced
Total	6	5	8	8	19	6	13	2	8	9	11	

741 ^aimplemented by some but not all study participants

742 ^bnot an RCT

743 CHW: community health worker

744 HEPA: high-efficiency particulate air-filtration

745 **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) ¹²⁻¹⁸	No studies	No studies	No studies	No studies	No effect (Moderate)	Inconclusive	Inconclusive	Inconclusive
Acaricide multicomponent (n=6) ^{51,65,67-70}	No studies	Inconclusive	Inconclusive	No studies	No effect (Moderate)	No studies	No effect (High)	Improved (Low)
Air purification only (n=9) ¹⁹⁻²⁷	Inconclusive	No effect (Low)	No effect (Low)	No studies	No effect (Low)	Improved (Low)	Inconclusive	No effect (Low)
Air purification multicomponent (n=5) ^{49,50,59,61,78}	No effect (Low)	No effect (High)	No studies	Improved (Low)	Inconclusive	No effect (High)	Improved (Low)	Improved (Moderate)
Carpet removal only (n=0)	No studies	No studies	No studies	No studies	No studies	No studies	No studies	No studies
Carpet removal multicomponent (n=8) ^{51,52,54,58,68,71,72,77}	No studies	Inconclusive	Inconclusive	No studies	Inconclusive	Inconclusive	Inconclusive	Improved (Moderate)
HEPA vacuum only (n=1) ²⁸	No studies	No studies	No studies	No studies	Inconclusive	No studies	No studies	Inconclusive
HEPA vacuum multicomponent (n=8) ^{50,53,55,60,61,64,75,76}	Inconclusive	Improved (Moderate)	No effect (High)	Improved (Low)	Inconclusive	Improved (Moderate)	Improved (Low)	Improved (Moderate)
Mattress cover only (n=17) ²⁹⁻⁴⁵	No effect (Moderate)	No effect (Moderate)	No effect (High)	Improved (Low)	No effect (High)	No effect (High)	No effect (High)	Improved (Moderate)
Mattress cover multicomponent (n=19) ^{49-52,54,55,58,59,61,62,65-71,74,76}	Inconclusive	No effect (High)	Inconclusive	Improved (Low)	No effect (High)	No effect (Moderate)	Improved (High)	Improved (Low)
Mold removal only (n=0)	No studies	No studies	No studies	No studies	No studies	No studies	No studies	No studies
Mold removal multicomponent (n=6) ^{56-58,76-78}	No studies	Inconclusive	Inconclusive	No studies	Inconclusive	Inconclusive	Improved (Low)	Inconclusive
Pest control only (n=2) ^{46,47}	Inconclusive	Inconclusive	No studies	Inconclusive	Inconclusive	No studies	Improved (Low)	Inconclusive
Pest control multicomponent (n=13) ^{49,52,54,55,58-62,66,74-76}	Inconclusive	Improved (Moderate)	Inconclusive	Improved (Low)	Inconclusive	Improved (Low)	Improved (Low)	Improved (Low)
Pet removal only (n=1) ⁴⁸	No studies	Inconclusive	Inconclusive	No studies	No studies	No studies	No studies	No studies
Pet removal multicomponent (n=2) ^{51,58}	No studies	No studies	No studies	No studies	No studies	No studies	No studies	No studies

746 *Tables 4 and 5 provide detailed information about the direction of effect and strength of evidence

747 HEPA: high-efficiency particulate air-filtration; green shading=improvement, red=no effect, yellow=inconclusive

748 **Table 4. Strength of evidence for studies of individual interventions**

Outcome	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale) ^a
Acaricide compared with placebo (not reported in studies: asthma control, exacerbations, healthcare utilization)			
Pulmonary physiology: spirometry	No effect: No difference for FEV ₁ or peak flow	4 RCTs ^{13-15,17} 1 non-RCT ¹⁸ (n=219)	Moderate (Imprecise)
Pulmonary physiology: airway hyperresponsiveness	Inconclusive	1 RCT ¹³ 1 non-RCT ¹⁸ (n=93)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision
Quality of Life	Inconclusive	1 RCT ¹⁷ (n=62)	Insufficient (Study limitations, Unknown consistency, Imprecise)
Symptoms	Inconclusive	1 RCT ¹² (n=35)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Allergen levels	Inconclusive: 1 study found decreased allergen; 1 study found no difference on carpet or mattress and decreased allergen in other locations; other studies found no difference	4 RCTs ^{12,14,15,17} 1 non-RCT ¹⁸ (n=228)	Insufficient (Inconsistent, Imprecise) ^a Substantial inconsistency
Acaricide compared with other mite- avoidance interventions (not reported in studies: asthma control, exacerbations, healthcare utilization, quality of life, symptoms)			
Pulmonary physiology	No effect: No difference for FEV ₁ or peak flow	2 RCTs ^{16,17} 1 non-RCT ¹⁸ (n=147)	Low (Study limitations, Imprecise)
Allergen levels	Inconclusive: No estimate of precision provided in studies	2 RCTs ^{16,17} 1 non-RCT ¹⁸ (n=147)	Insufficient (Study limitations, Imprecise) ^a Reported data insufficient for determining effect
Air purification compared with placebo devices or no intervention (not reported in studies: healthcare utilization)			
Asthma control	Inconclusive: 1 study found no difference in ACQ scores; 1 study found improvement in composite asthma outcomes; 1 study did not report differences between arms	3 RCTs ^{24,27,64} (n=169)	Insufficient (Inconsistent, Imprecise) ^a Reported data insufficient for determining effect
Exacerbations	No effect: ED visits and use of rescue medications did not differ	3 RCTs ^{19,27,64} (n=167)	Low (Study limitations, Imprecise)
Pulmonary physiology	No effect: 5 studies found no difference in spirometry; 1 study found improved peak flow; 1 study found improved peak flow and airway hyper-responsiveness	7 RCTs ^{19-22,24,25,27} (n=263)	Low (Inconsistent, Imprecise)

Outcome	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale) ^a
Quality of life: mini-AQLQ	Improvement: Improved mini-AQLQ scores; mean difference in change (standard error of the mean): 0.54 (0.28); p<0.05	1 RCT ¹⁹ (n=28)	Low (Study limitations, Unknown consistency)
Quality of life: other measures	No effect: No difference	2 RCTs ^{20,27} (n=155)	Moderate (Imprecise)
Symptoms	Inconclusive	1 RCT ²³ (n=18)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Allergen levels	No effect: 4 studies found no difference; 1 study found decreased allergen	5 RCTs ^{20-22,24,27} (n=225)	Low (Imprecise)
HEPA vacuum compared with standard vacuum (not reported in studies: asthma control, exacerbations, healthcare utilization, quality of life, symptoms)			
Pulmonary physiology	Inconclusive	1 RCT ²⁸ (n=60)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Allergen levels	Inconclusive	1 RCT ²⁸ (n=60)	Insufficient (Unknown consistency, Imprecise) ^a Reported data insufficient for determining effect
Impermeable mattress covers compared with placebo covers or no intervention			
Asthma control	No effect: No difference in ACQ scores	2 RCTs ^{29,31} (n=410)	Moderate (Imprecise)
Exacerbations	No effect: 1 study found no difference in composite measure (hospitalization/ rescue medication); 1 study found improved composite measure (hospitalization/ ED visit); 1 study found no difference in asthma attack frequency	3 RCTs ^{29,35,36} (n=1,461)	Moderate (Inconsistent)
Health care utilization: inhaled corticosteroids	No effect: 1 study found no difference for total dose change; 1 study found no difference for mean dose change; 1 study found improvement in daily dose	3 RCTs ^{31,34,38} (n=233)	Low (Inconsistent, Imprecise)
Health care utilization: rescue medication use	No effect: No difference in use of rescue medications	5 RCTs ^{32,34,36,37,39} (n=1,275)	High
Health care utilization and costs: work absenteeism	Decreased workdays: Fewer missed days of work, but difference may not be meaningful: Mean difference: -0.15 days per month (95% confidence interval: -0.29 to -0.02)	1 RCT ³⁶ (n=1,122)	Low (Unknown consistency, Imprecise)

Outcome	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale) ^a
Pulmonary physiology	No effect: No difference in peak flow in 12 studies; 1 study found improvement	13 RCTs ³⁰⁻⁴² (n=1,744)	High
Quality of life	No effect: No difference in quality of life	6 RCTs ^{29,31,32,35-37} (n=1,649)	High
Symptoms	No effect: No difference in 7 studies; 1 small study found improvement	8 RCTs ^{31,32,34,36-40} (n=1,473)	High
Allergen levels	Allergen reduction: 9 studies found reduced allergen; 2 studies found no difference	11 RCTs ^{29-37,39,40} (n=1,928)	Moderate (Inconsistent)
Pest reduction interventions compared with no intervention (not reported in studies: quality of life)			
Asthma control	Inconclusive	1 RCT ⁴⁶ (n=102)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Exacerbations	Inconclusive	1 RCT ⁴⁶ 1 pre-post ⁴⁷ (n=180)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision
Health care utilization	Inconclusive	1 RCT ⁴⁶ (n=102)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Pulmonary physiology	Inconclusive	1 RCT ⁴⁶ (n=102)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Symptoms	Improvement: Improved respiratory symptoms	1 RCT ⁴⁶ 1 pre-post ⁴⁷ (n=180)	Low (Imprecise)
Allergen levels	Inconclusive	1 pre-post ⁴⁷ (n=78)	Insufficient (Unknown consistency, Imprecise) ^a Pre-post study
Pet removal compared with no intervention (not reported in studies: asthma control, pulmonary physiology, quality of life, symptoms, allergen levels)			
Exacerbations/hospitalizations	Inconclusive	1 non-RCT ⁴⁸ (n=20)	Insufficient (Unknown consistency, Imprecise) ^a Non-RCT
Health care utilization	Inconclusive	1 non-RCT ⁴⁸ (n=20)	Insufficient (Unknown consistency) ^a Non-RCT

749 ^aCriteria for downgrading strength of evidence is described as (Rationale); when these criteria are
750 insufficient for understanding the final strength of evidence, additional explanation is provided

751 ACQ: Asthma Control Questionnaire

752 AQLQ: Asthma Quality of Life Questionnaire

753 ED: emergency department

754 FEV₁: forced expiratory volume in 1 second

755 HEPA: high-efficiency particulate air-filtration

756 RCT: randomized controlled trial

757

Table 5. Strength of evidence for studies of multicomponent interventions

Outcome	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale) ^a
Acaricide (dust mite pesticide) + other interventions compared with placebo (not reported in studies: asthma control, quality of life)			
Exacerbations	Inconclusive: No difference in ED visits or hospitalizations in 1 study; no comparison between arms in other study	2 RCTs ^{51,67} (n=204)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision
Healthcare utilization	Inconclusive	1 RCT ⁶⁹ (n=70)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Pulmonary physiology: peak flow	No effect: No difference in peak flow in 3 studies; improved peak flow in 1 study; no comparison between arms in 1 study	5 RCTs ^{51,65,68-70} (n=445)	Moderate (Inconsistent)
Pulmonary physiology: FEV ₁	No effect: No difference 4 studies; improved FEV ₁ in 1 study; no comparison between arms in 1 study	6 RCTs ^{51,65,67-70} (n=489)	Moderate (Inconsistent)
Symptoms	No effect: No difference in frequency of symptoms	4 RCTs ^{65,67,69,70} (n=306)	High
Allergen levels	Reduced allergen: 2 studies found reduced allergens; 2 smaller studies found no difference; no comparison between arms in 1 study	5 RCTs ^{51,65,67,69,70} (n=466)	Low (Inconsistent, Imprecise)
Air purification + other interventions compared with no intervention			
Asthma control	No effect: No difference in ACT or childhood ACT scores	1 RCT ⁵⁰ (n=247)	Low (Unknown consistency, Imprecise)
Exacerbations	No effect: No difference in hospitalizations in 3 studies; no difference in ED visits in 2 studies; no difference in undefined exacerbations in 1 study	4 RCTs ^{49,50,59,61} (n=1,645)	High
Health care utilization: acute care visits	Inconclusive	1 RCT ⁵⁹ (n=100)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Health care utilization and costs: school absenteeism	Improvement: Fewer days of missed school	1 RCT ⁶¹ (n=937)	Low (Unknown consistency, Imprecise)
Pulmonary physiology	Inconclusive	1 RCT ⁴⁹ (n=361)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Quality of life	No effect: No difference in mini-AQLQ scores	2 RCTs ^{50,59} (n=347)	High

Outcome	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale) ^a
Symptoms	Improved: Reduced symptoms in 2 studies; no difference in 2 other studies	4 RCTs ^{49,50,59,61} (n=1,645)	Low (Inconsistent, Imprecise)
Allergen levels	Allergen reduction: Decreased allergens in 3 studies; no difference in 1 study	4 RCTs ^{49,50,59,61} (n=1,645)	Moderate (Inconsistent)
Carpet removal + other interventions compared with placebo or no intervention (not reported in studies: asthma control)			
Exacerbations	Inconclusive: No difference in ED visits or hospitalizations in 2 studies; no comparison between arms in 1 study	3 RCTs ^{51,52,54} (n=705)	Insufficient (Study limitations, Inconsistent, Imprecise)
Health care utilization	Inconclusive: Reduced number of daytime terbutaline puffs in 1 study; no comparison between arms in 1 study	2 RCTs ^{71,72} (n=96)	Insufficient (Study limitations, Imprecise) ^a Substantial imprecision
Pulmonary physiology	Inconclusive: Improved peak flow in 1 study; no difference in 1 study; no comparison between arms in 2 studies	4 RCTs ^{51,68,71,72} (n=279)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision
Quality of life	Inconclusive	1 non-RCT ⁷⁷ (n=102)	Insufficient (Unknown consistency, Imprecise) ^a Non-RCT
Symptoms	Inconclusive: No difference in 3 studies; reduced symptoms in 1 study; reduced daytime symptoms but no difference in nighttime symptoms in 1 study	5 RCTs ^{52,54,58,71,72} (n=802)	Insufficient (Study limitations, Inconsistent, Imprecise)
Allergen levels	Allergen reduction: Decreased allergen levels in 3 studies; no comparison between arms in 1 study	4 RCTs ^{51,58,71,72} (n=412)	Moderate (Study limitations)
HEPA vacuum + other interventions compared with placebo or no intervention			
Asthma control	Inconclusive	1 RCT ⁵⁰ (n=247)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Exacerbations: composite measure	Reduction: Improved composite measure of hospitalization, ED visits, and acute care clinic visits	3 RCTs ^{55,60,61} (n=1,509)	Moderate (Study limitations)
Exacerbations: unspecified	No effect: No difference in undefined “exacerbations” or “asthma attacks”	2 RCTs ^{50,53} (n=556)	Moderate (Imprecise)
Health care utilization: medication use	No effect: No difference in use of rescue inhaler or beta agonists	3 RCTs ^{50,53,60} (n=830)	High

Outcome	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale) ^a
Health care utilization and costs: school absenteeism	No effect: No difference in missed school days in 2 studies; reduction found in 1 study	3 RCTs ^{53,60,61} (n=1,520)	Low (Inconsistent, Imprecise)
Health care utilization and costs: work absenteeism	No effect: No difference in missed workdays	2 RCTs ^{53,60} (n=583)	Moderate (Study limitations)
Health care utilization and costs: missed activities	Reduction: Fewer days of missed activities in 2 studies; no difference in 1 study	3 RCTs ^{53,60,61} (n=1,520)	Low (Inconsistent, Imprecise)
Pulmonary physiology: peak flow	Inconclusive	1 RCT ⁶⁴ (n=40)	Insufficient (Study limitations, Unknown consistency, Imprecise)
Pulmonary physiology: FEV ₁	Inconclusive	1 RCT ⁵⁰ (n=247)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Quality of life: PACQLQ	Improvement: Improved PACQLQ scores	2 RCTs ^{53,60} (n=583)	Moderate (Study limitations)
Quality of life: mini-AQLQ	Inconclusive	1 RCT ⁵⁰ (n=247)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Quality of life: CHSA	Inconclusive	1 pre-post ⁷⁵ (n=170)	Insufficient (Unknown consistency, Imprecise) ^a Non-RCT
Symptoms: children	Improvement: Fewer symptom days in 2 studies; no difference in 1 study	3 RCTs ^{55,60,61} (n=1,509)	Low (Study limitations, Inconsistent)
Symptoms: mixed populations	No effect: No difference in symptom frequency in 2 studies; fewer symptom days in 1 study	3 RCTs ^{50,53,64} (n=596)	Moderate (Inconsistent)
Allergen levels: house dust mites	Inconclusive: No difference in 1 study; reduced allergen levels in 1 study; no comparison between arms in 1 study; 4 th study found reduced Der f allergens but no difference for Der p	4 RCTs ^{50,55,61,64} (n=1,522)	Insufficient (Study limitations, Inconsistent, Imprecise)
Allergen levels: cats and dogs	Inconclusive: 1 study found reduction in cat but not dog allergens; 1 study found reduction in dog but not cat allergens; 1 study had no comparison between arms	3 RCTs ^{50,55,61} (n=1,195)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision

Outcome	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale) ^a
Allergen levels: cockroach	Reduction: 1 study found decreased cockroach allergen levels; 1 study had no comparison between arms	2 RCTs ^{50,61} (n=1,184)	Moderate (Imprecise)
Mattress covers + other interventions compared with placebo or no intervention			
Asthma control	Inconclusive	1 RCT ⁵⁰ (n=247)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Exacerbations: ED visits	No effect: No difference	3 RCTs ^{49,52,54} (n=545)	Low (Study limitations, Imprecise)
Exacerbations: hospitalization	No effect: No difference	6 RCTs ^{49,52,54,59,61,66} (n=2,976)	High
Exacerbations: Unscheduled care	Inconclusive: No difference in 3 studies; reduction in 2 studies	5 RCTs ^{55,61,62,66,67} (n=2,416)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision
Health care utilization: acute care visits	No effect: No difference	3 RCTs ^{54,59,61} (n=1,318)	Moderate (Study limitations)
Health care utilization: medication use	Inconclusive: Reduced use of asthma medication in 1 study; no difference in other study	2 RCTs ^{50,69} (n=317)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision
Health care utilization and costs: school absenteeism	Reduction: Fewer missed school days	1 RCT ⁶¹ (n=937)	Low (Unknown consistency, Imprecise)
Health care utilization and costs: missed activities	Reduction: Fewer days of missed activities	1 RCT ⁶¹ (n=937)	Low (Unknown consistency, Imprecise)
Pulmonary physiology: peak flow	Inconclusive: Improved peak flow in 2 studies; no difference in 3 studies	5 RCTs ^{55,65,68-70} (n=583)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision
Pulmonary physiology: FEV ₁	No effect: No difference in 7 studies; improvement in 1 study	8 RCTs ^{49,50,61,65,67-70} (n=1,874)	High
Quality of life	No effect: No difference	3 RCTs ^{50,56,67} (n=144)	Moderate (Study limitations)
Symptoms: composite score	No effect: No difference	4 RCTs ^{50,65,67,70} (n=483)	High
Symptoms: symptom days	Reduction: Fewer days reported with symptoms in 4 studies; no difference in 1 study	5 RCTs ^{49,55,59,61,66} (n=2,729)	High

Outcome	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale) ^a
Symptoms: cough and wheeze	No effect: No difference in frequency of cough in 3 studies; reduced cough in 1 study; no difference in frequency of wheeze in 4 studies; reduced wheeze in 1 study	5 RCTs ^{52,54,55,61,69} (n=1,850)	Low (Study limitations, Inconsistent)
Allergen reduction	Reduction: Decreased allergen levels in 4 studies; no difference in 4 smaller studies	8 RCTs ^{55,58,59,61,65,67,70,71} (n=1,782)	Low (Inconsistent, Imprecise)
Mold removal + other interventions compared with placebo or no intervention (not reported in studies: asthma control)			
Exacerbations	Inconclusive	1 RCT ⁵⁷ (n=62)	Insufficient (Study limitations, Unknown consistency, Imprecise)
Health care utilization	Inconclusive	1 RCT ⁵⁶ (n=232)	Insufficient (Study limitations, Unknown consistency, Imprecise)
Pulmonary physiology	Inconclusive	1 RCT ⁵⁶ (n=232)	Insufficient (Study limitations, Unknown consistency, Imprecise)
Quality of life	Inconclusive	1 RCT ⁵⁷ (n=62)	Insufficient (Study limitations, Unknown consistency, Imprecise)
Symptoms	Improved symptoms: Fewer symptoms	2 RCTs ^{57,58} (n=223)	Low (Study limitations, Imprecise)
Allergen levels	Inconclusive	1 RCT ⁵⁷ (n=62)	Insufficient (Study limitations, Unknown consistency, Imprecise)
Pest control + other interventions compared with placebo or no intervention			
Asthma control	Inconclusive	1 pre-post ⁷⁴ (n=80)	Insufficient (Unknown consistency, Imprecise) ^a Pre-post study
Exacerbations: Composite measure	Reduction: Improved composite measure of hospitalization, ED visits, and acute care clinic visits	4 RCTs ^{55,60-62} (n=1,613)	Moderate (Study limitations)
Exacerbations: Hospitalization	No effect: No difference in hospitalizations in 5 studies; no difference in inpatient days in 1 study	6 RCTs ^{49,52,54,59,61,66} (n=2,976)	High
Exacerbations: ED visits	No effect: No difference	4 RCTs ^{49,52,54,61} (n=1,843)	Moderate (Study limitations)
Health care utilization: acute care clinic visits	No effect: No difference in clinic visits for acute care	3 RCTs ^{59,61,66} (n=2,070)	High
Health care utilization: medication use	Inconclusive	1 RCT ⁶⁰ (n=274)	Insufficient (Study limitations, Unknown consistency, Imprecise)

Outcome	Conclusion	Study Design and Sample Size	Strength of Evidence (Rationale) ^a
Health care utilization and costs: school absenteeism/patient activities	Improvement: Fewer days with activity limitations in 2 studies; fewer missed school days in 1 study, but no difference in missed school days in other study	4 RCTs ^{55,59-61} (n=1,609)	Low (Study limitations, Inconsistent)
Health care utilization and costs: work absenteeism/plans	No effect: No difference in missed days of work or caretaker plans changed	2 RCTs ^{60,61} (n=1,211)	Low (Study limitations, Imprecise)
Pulmonary physiology: peak flow	Inconclusive	1 RCT ⁵⁵ (n=298)	Insufficient (Study limitations, Unknown consistency, Imprecise)
Pulmonary physiology: FEV ₁	Inconclusive: No difference in 2 studies; no comparison between arms in 1 study	3 RCTs ^{49,55,61} (n=1,596)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision
Quality of life: PACQLQ	Improvement: Improved PACQLQ scores	1 RCT ⁶⁰ (n=274)	Low (Study limitations, Unknown consistency)
Quality of life: other measures	Inconclusive	1 RCT ⁵⁹ (n=100)	Insufficient (Unknown consistency, Imprecise) ^a Substantial imprecision
Symptoms	Improvement: Reduced symptom days or frequency of symptoms in 5 studies; no difference in symptom days in 2 studies; no difference in cough/wheeze in 2 studies	9 RCTs ^{49,52,54,55,58-61,66} (n=3,709)	Low (Study limitations, Inconsistent)
Allergen levels: cockroach	Reduction: Decreased allergen levels in 2 studies; no difference in 1 study	3 RCTs ^{58,59,61} (n=1,198)	Low (Inconsistent, Imprecise)
Allergen levels: mouse	Inconclusive: Decreased allergen levels in 2 studies; no difference in 2 studies	4 RCTs ^{46,55,59,61} (n=1,696)	Insufficient (Inconsistent, Imprecise) ^a Substantial imprecision

758 ^aCriteria for downgrading strength of evidence is described as (Rationale); when these criteria are
759 insufficient for understanding the final strength of evidence, additional explanation is provided

760 ACT: Asthma Control Test

761 AQLQ: Asthma Quality of Life Questionnaire

762 CHSA: Children's Health Survey for Asthma

763 ED: emergency department

764 FEV₁: forced expiratory volume in 1 second

765 PACQLQ: Pediatric Asthma Caregivers Quality of Life Questionnaire

766 RCT: randomized controlled trial

