Evidence to Decision Table V — Pillow and Mattress Cover Interventions vs. No Intervention for Individuals with Asthma

Background

Many common indoor inhalant allergens—including animal dander, house dust mites, mice, cockroaches, and mold—are associated with an increased risk of asthma exacerbations. Numerous interventions have been designed to reduce exposure to allergens in the environments where individuals with asthma live, work, learn, play, and sleep. These interventions include use of acaricides (house dust mite pesticides), air purification systems, carpet removal or vacuuming, specially designed mattress covers and pillowcases, mold mitigation, pest control techniques, and containment or removal of pets.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	When pillow and mattress covers are used alone, they do not reduce the number of exacerbations or improve asthma control or quality of life (in comparison with different comparators). As part of a multicomponent intervention, pillow and mattress covers make no difference or their effects on critical outcomes are inconclusive; however, the findings for asthma symptoms support the intervention as having a small benefit.	

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Trivial	In most studies, no undesirable effects were identified. Cost and reduced comfort could be undesirable effects, but none of the studies examined these outcomes.	

Certainty of evidence: What is the overall certainty of the evidence of effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Moderate	For single-component interventions, moderate certainty of evidence shows that pillow and mattress covers are not beneficial. However, when used as part of a multicomponent intervention, the small benefits of pillow and mattress covers have moderate certainty of evidence.	

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no important uncertainty or variability		

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Varies		

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes	Because the intervention is associated with minimal harm, most stakeholders are likely to find it acceptable.	

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes		

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no impact		

Evidence Summary: Impermeable Covers on Mattresses, Pillows, Quilts, and Duvets vs. Feather-Filled Pillows, Quilts, and Duvets with Impermeable Covers on Mattresses for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Not reported				
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
Not reported				
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Based on PACQLQ scores Follow-up: 26 weeks	197 (1 RCT)[11]	Low[a]	—	**No difference** MD: 0.04 higher (from 0.27 lower to 0.35 higher) in 1 RCT in children.
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Frequent wheezing, speech-limiting wheezing, and sleep disturbance caused by wheezing Follow-up: 26 weeks[b]	197 (1 RCT)[11]	Low[a]	—	**No difference** No difference in frequent wheezing, speech-limiting wheezing, or sleep disturbance caused by wheezing.
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Health care utilization (rescue medication use)				**Not reported**

Abbreviations: ACQ, Asthma Control Questionnaire; AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; ED, emergency department; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MD, mean difference; PACQLQ, Pediatric Asthma Caregiver's Quality of Life Questionnaire; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. The Agency for Healthcare Research and Quality systematic review report rated this outcome down for imprecision.

b. The Expert Panel also reviewed studies that collected data on asthma symptoms using various nonvalidated symptom scales.

Evidence Summary: Impermeable Pillows vs. Placebo Pillows for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Asthma attacks Follow-up: 104 weeks	20 (1 RCT)[12]	Very low[a]	—	**Inconclusive** No difference in number of asthma attacks (data were reported in a graph, and the Expert Panel therefore could not evaluate these data).
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
Not reported				
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Not reported				
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Not reported				
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Health care utilization (rescue medication use)				Not reported

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. The Agency for Healthcare Research and Quality systematic review report rated this outcome down for imprecision (data were reported in a graph and could not be evaluated).

Evidence Summary: Cotton Bed Covers that Are Boiled and Exposed to Three Hours of Sunlight Every 2 Weeks vs. Covers that Undergo Standard Laundering for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Asthma attacks Follow-up: 104 weeks	42 (1 RCT)[13]	Very low[a]	—	**Inconclusive** No difference in asthma attacks.
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
Not reported				
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Not reported				
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Frequency of cough, wheezing, sputum, and dyspnea Follow-up: 104 weeks[b]	42 (1 RCT)[13]	Very low[a]	—	**Inconclusive** No difference in frequency of cough, wheezing, or sputum. Significantly lower frequency of dyspnea.
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Health care utilization (rescue medication use)				**Not reported**

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. The Agency for Healthcare Research and Quality systematic review report rated this outcome down for study limitations and imprecision.

b. The Expert Panel also reviewed studies that collected data on asthma symptoms using various nonvalidated symptom scales.

Evidence Summary: Mattress Covers as Part of Multicomponent Intervention vs. Placebo or No Mattress Interventions for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
ED visits Follow-up: 26 to 52 weeks	545 (3 RCTs)[14-16]	Low[a]	—	No differences in 3 RCTs
Hospitalizations Follow-up: 26 to 104 weeks	2,976 (6 RCTs)[14-19]	High	—	No differences in 6 RCTs
Unscheduled ED, hospital, and outpatient care Follow-up: 13 to 104 weeks	2,416 (5 RCTs)[18-22]	Very low[b]	—	Three RCTs[18,20,22] (N = 1,181) found no differences in a composite measure of unscheduled care. Two RCTs (N = 1,235)[19,21] showed reductions.
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
ACT or childhood ACT scores Follow-up: 40 weeks	247 (1 RCT)[23]	Very low[b]	—	**Inconclusive** No difference in ACT scores or childhood ACT scores in 1 RCT.
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
AQLQ and unspecified quality-of-life scales Follow-up: 40 to 52 weeks	144 (3 RCTs)[17,22,23]	Moderate[c]	—	**No difference** One RCT[23] found no difference in AQLQ scores. Two RCTs found no difference in scores in unspecified quality-of-life scales.

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Composite score Follow-up: 20 to 52 weeks[d]	483 (4 RCTs)[22-25]	High	—	**No difference** Four RCTs (total N = 483) found no differences in composite scores made up of different sets of symptoms.
Symptom days Follow-up: 13 to 104 weeks[d]	2,729 (5 RCTs)[16-19,21]	High		**Favors intervention** Four RCTs (total N = 2,368) found significantly fewer days with reported symptoms. One RCT[16] found no effect.
Frequency of cough and frequency of wheezing Follow-up 13 to 104 weeks[d]	1,850 (5 RCTs)[14,15,19,21,26]	Very low[e]		**Inconclusive** Three RCTs showed no change in coughing frequency, and one RCT found reduced coughing frequency. Four RCTs show no change in wheezing frequency, and one RCT shows reduced wheezing frequency.
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Health care utilization (acute care visits) Follow-up: 52 to 104 weeks	1,318 (3 RCTs)[15,17,19]	Low	—	**No difference** No difference in unscheduled acute care visits in 3 RCTs.
Health care utilization (rescue medication use) Follow-up: 24 to 40 weeks	317 (2 RCTs)[23,26]	Very low[b]	—	**Inconclusive** One study (N = 70)[26] found that the intervention reduced the use of any asthma medication. Another study (N = 247)[23] found no difference in use of a rescue inhaler.

Abbreviations: ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ED, emergency department; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down for study limitations and imprecision.
b. The AHRQ systematic review report rated this outcome down for inconsistency and imprecision.
c. The AHRQ systematic review report rated this outcome down for study limitations.
d. The Expert Panel also reviewed studies that collected data on asthma symptoms using various nonvalidated symptom scales.
e. The AHRQ systematic review report rated this outcome down for study limitations and inconsistency.

Harms: No harms in the studies were reported.

New evidence

No.

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Evidence to Decision Table VI — Carpet Removal (with or without Other Interventions) vs. Placebo or No Carpet Intervention for Individuals with Asthma

Background

Many common indoor inhalant allergens—including animal dander, house dust mites, mice, cockroaches, and mold—are associated with an increased risk of asthma exacerbations. Numerous interventions have been designed to reduce exposure to allergens in the environments where individuals with asthma live, work, learn, play, and sleep. These interventions include use of acaricides (house dust mite pesticides), air purification systems, carpet removal or vacuuming, specially designed mattress covers and pillowcases, mold mitigation, pest control techniques, and containment or removal of pets.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	The Expert Panel did not review any studies of single-component interventions. The evidence was mixed for the impact of multicomponent interventions on exacerbations, rescue medication use, and asthma symptoms.	

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Moderate	The intervention might increase exacerbations as a result of exposure to aeroallergens and irritants released by carpet removal.	Although carpet removal is a one-time intervention, its costs may be relevant, depending on the amount of carpeting in the residence and the potential additional cost of flooring to replace the carpets. In apartments, carpet removal can increase noise levels as well. Potential adverse effects from the replacement flooring include the release of semivolatile compounds (e.g., phthalates).

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Very low	This judgment is based on multicomponent strategies.	

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Possibly important uncertainty or variability	The decision of whether removal of carpet is worth the effort may be a value assessment. Different individuals may value carpet removal differently depending on the severity of their asthma, the amount of carpeting in the residence, and the cost associated with removal.	

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Does not favor either the intervention or the comparator		

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes		

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Varies	The intervention may not be feasible if the individual with asthma rents the residence or for other reasons.	

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Varies	Carpet removal may incur a one-time cost, and replacement of flooring is an added cost.	

Evidence Summary: Carpet Removal (Single Component Interventions)

The Agency for Healthcare Research and Quality systematic review report found no data on *important* or *critical* outcomes.

Evidence Summary: Multicomponent Interventions that Include Carpet Removal[a] vs. Placebo or No Multicomponent Intervention for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
ED visits or hospitalizations Follow-up: 16 to 52 weeks	705 (3 RCTs)[1-3]	Very low[b,c,d]	—	**No difference** No difference in ED visits or hospitalizations in two RCTs in 545 mixed-population participants. Significant reduction in hospitalizations in 1 RCT[3] in 160 mixed-population participants, but this study did not compare outcomes between groups.
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
Not reported				
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Severe to no impairment based on PACQLQ 1–7 (MID: 0.5 points) Follow-up: 52 weeks	102 (1 nonrandomized trial)[4]	Very low[c,d]	—	**Inconclusive** Significant improvement in PACQLQ scores in 1 nonrandomized trial in 102 mixed-population participants.
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Varies[e] Follow-up: 26 to 52 weeks[b]	802 (5 RCTs)[1,2,5-7]	Very low[b,c,d]	—	**Inconclusive** No difference in symptoms in 1 RCT[6] in 50 adults and 2 RCTs in 545 mixed-population participants.[1,2] Significant reduction in symptoms in 1 RCT in 161 children.[7] Significant reduction in daytime scores, but no difference in nighttime scores in 1 RCT in 46 adults.[5]

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Health care utilization (rescue medication use: use of bronchodilator or any asthma medication) Follow-up: 26 to 52 weeks	96 (2 RCTs)[5,6]	Very low[b,f]	—	**No difference** Significant reduction in use of inhaled corticosteroids in 1 RCT[6] in 50 adults, but this RCT did not conduct a between-group comparison. Significant reduction in number of daytime terbutaline puffs in 1 RCT[5] in 46 adults; no difference in nighttime puffs or overall use.

Abbreviations: CI, confidence interval; ED, emergency department; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MID, minimally important difference; PACQLQ, Pediatric Asthma Caregiver's Quality of Life Questionnaire; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. Other interventions included combinations of mold mitigation, mattress covers, laundering of linens, pest control, pet removal, and provision of cleaning supplies.

b. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down for risk of bias, commonly related to lack of blinding, high attrition rates, and/or insufficient information about randomization.

c. The AHRQ systematic review report rated this outcome down for inconsistency.

d. The AHRQ systematic review report rated this outcome down for imprecision.

e. The Expert Panel reviewed studies that collected data on asthma symptoms using various nonvalidated symptom scales.

f. The Expert Panel rated this outcome down twice for imprecision because the AHRQ systematic review report noted "substantial imprecision."

Harms: No harms in the studies were reported.

New evidence

No.

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Evidence to Decision Table VII — Integrated Pest Management with or without Other Interventions vs. Placebo or No Pest Management Interventions for Individuals with Asthma

Background

Many common indoor inhalant allergens—including animal dander, house dust mites, mice, cockroaches, and mold—are associated with an increased risk of asthma exacerbations. Numerous interventions have been designed to reduce exposure to allergens in the environments where individuals with asthma live, work, learn, play, and sleep. These interventions include acaricides (house dust mite pesticides), air purification systems, carpet removal or vacuuming, specially designed mattress covers and pillowcases, mold mitigation, pest control techniques, and containment or removal of pets.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	Single-component intervention studies (1 RCT and one pre- and postintervention study) found reductions in exacerbations and asthma symptoms. Studies of multicomponent interventions had variable results. Some evidence of improvement was found in studies that used a composite metric for exacerbations, quality of life, and asthma symptoms, but the results were not statistically significant.	Single-component intervention studies compared pest control interventions with no intervention. The interventions were implemented by pest control technicians. The multicomponent interventions studied included education, cleaning, and mattress covers. Multicomponent studies included mixed populations.

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Trivial	Study reports did not report any harms. Pest management interventions could be associated with harms if they use chemicals or toxins.	No insurance plans cover the costs of these interventions, so individuals with asthma pay for these services out of pocket. Some pest control products (e.g., permethrins) may trigger asthma and/or be hazardous to children.

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Very low	This judgment is based on multicomponent strategies.	

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no important uncertainty or variability	Even for individuals with asthma who do not have sensitization to pests, good housing and public health practice is to reduce exposure to pests. A majority of individuals with asthma would want the intervention.	

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably favors the intervention	No harms were reported. The studies compared the intervention to no intervention or to allergy education. Results were mixed on whether the intervention improves clinical outcomes; however, both single-component and multicomponent intervention studies showed a trend toward slight improvement in outcomes, particularly for asthma symptoms, but the improvements were not statistically significant.	Potential placebo effect can explain reductions in reported symptoms of individuals with asthma.

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes		Whether the strategy is safe for the environment and imposes minimal risk on young children and pets is a consideration for the type of pest-control strategy used.

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes	This intervention raises cost considerations. For individuals with asthma who live in a multifamily rental unit, the intervention's feasibility and success might depend on the landlord and whether the landlord implements the intervention in all of the rental units in addition to the unit where the individual with asthma resides.	

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably increased	Even if the intervention does not improve asthma-related outcomes, it is a good public health practice.	

Evidence Summary: Integrated Pest Management for Cockroaches and Rodents vs. No Pest Management Interventions for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
ED visits, unscheduled clinic visits, hospitalizations, or rates of exacerbations Follow-up: 52 weeks	180 (1 RCT,[1] 1 pre- and postintervention study[2])	Low[a]	—	**Favors intervention** Insecticide use significantly reduced ED and unscheduled clinic visits, but hospitalizations did not decline in 1 RCT. One pre- and postintervention study found no change in rates of exacerbations.
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
ACT Follow-up: 52 weeks	102 (1 RCT)[1]	Low[b]	—	**No difference** ACT scores did not improve in 1 RCT.
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Not reported				
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Follow-up: 52 weeks[c]	180 (1 RCT,[1] 1 pre- and postintervention study[2])	Moderate[d]	—	**Favors intervention** Respiratory symptoms declined in both studies.
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Not reported				

Abbreviations: ACT, Asthma Control Test; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ED, emergency department; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. The Expert Panel rated this outcome up from the rating in the Agency for Healthcare Research and Quality (AHRQ) systematic review report (which rated the evidence for this outcome as insufficient).

b. The Expert Panel rated this outcome down for risk of bias and imprecision.

c. The studies reporting data on asthma symptoms used nonvalidated scales.[1,2]

d. The AHRQ systematic review report rated this outcome down for imprecision.

Evidence Summary: Integrated Pest Management with Other Interventions[a] vs. Placebo or No Pest Management Interventions for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Composite measure of hospitalizations, ED visits, and acute care visits Follow-up: 12 to 104 weeks[b]	1,613 (4 RCTs)[3-6]	Moderate[c]	—	**Favors intervention** Improvement in composite measure in 3 RCTs in 1,509 children and 1 RCT[3] in 104 mixed-population participants.
Leading to hospitalization Follow-up: 26 to 104 weeks	2,976 (6 RCTs)[5,7-11]	High	—	**No difference** No difference in hospitalization rates in 3 RCTs in 2,070 children[5,9,10] and 2 RCTs[7,11] in 625 mixed-population participants. No difference in inpatient days in 1 RCT in a mixed population of 281 participants.[8]
Leading to ED visits Follow-up: 26 to 104 weeks	1,843 (4 RCTs)[5,7,8,11]	Moderate[d]	—	**No difference** No difference in ED visits in 1 RCT in children (N = 937)[5] and 3 RCTs in a mixed-population of 906 participants.

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
ACT (MID: ≥3 points for individuals ages 12 years and older) Follow-up: 26 weeks	80 (1 observational study)[12]	Very low[e]	—	**Inconclusive** No difference in ACT or childhood ACT scores in 1 observational study in a mixed population.
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
PACQLQ (MID: ≥0.5 points) Follow-up: 26 weeks	274 (1 RCT)[4]	Moderate[d]	—	**Favors intervention** PACQLQ score improved significantly in 1 RCT in children.
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Symptom days or coughing and wheezing Follow-up: 12 to 104 weeks[b]	3,709 (9 RCTs)[4-11,13]	Low[f]	—	**Favors intervention** Decrease in symptom days or frequency of symptoms in 5 RCTs[5,6,9,10,13] in 2,529 children. No difference in symptom days in 1 RCT[4] in 274 children and 1 RCT[11] in 361 mixed population participants. No difference in coughing or wheezing in 2 RCTs[7,8] in 545 mixed-population participants.
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Health care utilization (rescue medication use) Follow-up: 26 weeks	274 (1 RCT)[4]	Low[g]	—	**No difference** No difference in use of beta-agonist or controller medication in 1 RCT in children.

Abbreviations: ACT, Asthma Control Test; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MID, minimally important difference; PACQLQ, Pediatric Asthma Caregiver's Quality of Life Questionnaire; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. Other interventions included combinations of mattress covers, air purifiers, high-efficiency particulate air (HEPA) vacuum cleaners, provision of cleaning supplies, mold mitigation, or carpet removal.

b. The Expert Panel also reviewed a study (N = 18) that collected data on asthma symptoms using various nonvalidated symptom scales and found reductions in respiratory symptoms.

c. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down for risk of bias.

d. The AHRQ systematic review report rated this outcome down for study limitations.

e. The AHRQ systematic review report rated this outcome down for risk of bias and imprecision.

f. The AHRQ systematic review report rated this outcome down for risk of bias and inconsistency.

g. The Expert Panel rated this outcome down for risk of bias and imprecision.

Harms: No harms in the studies were reported.

New evidence

No.

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Evidence to Decision Table VIII — Air Filtration Systems and Air Purifiers (with or without Other Interventions) vs. Control Conditions, Other Mite Mitigation Interventions, or No Air Cleaning Intervention for Individuals with Asthma

Background

Many common indoor inhalant allergens—including animal dander, house dust mites, mice, cockroaches, and mold—have been associated with an increased risk of asthma exacerbations. Numerous interventions have been designed to reduce exposure to allergens in the environments where individuals with asthma live, work, learn, play, and sleep. These interventions include use of acaricides (house dust mite pesticides), air purification systems, carpet removal or vacuuming, specially designed mattress covers and pillowcases, mold mitigation, pest control techniques, and containment or removal of pets.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	For single-component interventions, the evidence indicates no benefit for critical and important outcomes. For multicomponent interventions, the evidence shows no benefit for exacerbations, asthma control, or quality of life. In children, studies of multicomponent interventions that included air filtration systems and air purifiers in addition to other allergen-mitigation modalities showed possible reductions in symptoms.	Nine randomized controlled trials were examined that demonstrated no benefit for *critical* or *important* outcomes. Air purifiers were used to address multiple allergens. No studies examined the impact of air purifiers on patients sensitized to a single allergen. The studies included mixed populations.

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Trivial	Studies found no undesirable anticipated effects.	Cost and comfort could be considerations but were not examined by any of the studies.

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Low		

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no important uncertainty or variability	Although different individuals with asthma might value the critical outcomes differently, these differences are unlikely to affect their decision-making regarding the intervention. Most of the studies found no differences, except for symptoms in children with multicomponent interventions.	Potential concern with regard to cost and burden of cleaning and/or purchasing new filters.

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Does not favor the intervention or the comparison		

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes	The intervention is probably acceptable to primary care providers and patients. However, insurers are unlikely to cover the costs of this intervention.	

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes		

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably increased		The intervention's cost may have implications for equity, fidelity of use, and equipment maintenance.

Evidence Summary: Single-Component Air Filtration System and Air Purifier Interventions vs. Control Interventions for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
ED visits and use of rescue medications Follow-up: 6 to 52 weeks	167 (3 RCTs)[1-3]	Low[a,b]	—	**No difference** One study (N = 119) with a low risk of bias found no significant differences in use of rescue medications.[3] One study (N = 28) with a high risk of bias found equal numbers of exacerbations with treatment and placebo.[1] One study (N = 20) with a low risk of bias found no differences in ED visits or use of rescue medications.[2]
ASTHMA CONTROL AND SYMPTOMS (*CRITICAL* OUTCOME)				
ACQ and symptom measures[c] Follow-up: 6 to 52 weeks	169 (3 RCTs)[2-4]	Low[b,d]	—	**No difference** One RCT (N = 119) with a low risk of bias found no difference in ACQ scores.[3] One RCT (N = 30) with a medium risk of bias found improvements in combined asthma outcomes after use of air purifiers.[4] One RCT (N = 20) found no differences in asthma scores.[2]
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Mini-AQLQ (MID: 0.5 points)[e] Follow-up: 10 weeks	28 (1 RCT)[1]	Very low[f,g]		**Inconclusive** Improvement in mini-AQLQ scores in 1 study with a crossover design (MD [SEM]: 0.54 [0.28])
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Not reported				

Abbreviations: ACQ, Asthma Control Questionnaire; AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; ED, emergency department; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MD, mean difference; MID, minimally important difference; RCT, randomized controlled trial; SEM, standard error of mean.

Footnotes, including GRADE explanations

a. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down for risk of bias because one of the three RCTs by Pedroletti et al. (2009)[1] had a high attrition rate and unclear sequence generation and allocation concealment.

b. The AHRQ systematic review report rated this outcome down for imprecision.

c. An additional RCT by Zwemer et al. (N = 18)[5] showed reductions in self-reported asthma symptoms, but the report provided no summary statistics.

d. The AHRQ systematic review report rated this outcome down for inconsistency.

e. Two RCTs, one by Sulser et al. (2009, N = 36)[6] and one by Wright et al. (2009, N = 155),[3] found no between-group differences in quality of life based on other measures.

f. The AHRQ systematic review report rated this outcome down for risk of bias because the Pedroletti et al. (2009) study[1] had a high attrition rate and unclear sequence generation and allocation concealment.

g. The Expert Panel rated this outcome down twice for imprecision because of the very small sample.

Evidence Summary: Single-Component Air Filtration System and Air Purifier Interventions vs. Other Mite-Mitigation Interventions for Individuals with Asthma

The Agency for Healthcare Research and Quality systematic review report found no data on *important* or *critical* outcomes for this comparison

Evidence Summary: Multicomponent Interventions that Include Air Filtration Systems and Air Purifiers vs. No Intervention for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Hospitalizations, ED visits, and unspecified exacerbations[a] Follow-up: 40 to 104 weeks	1,645 (4 RCTs)[7-10]	High	—	**No difference** No difference in hospitalizations in 2 RCTs[8,10] in 1,037 children and 1 RCT[9] in 361 mixed-population participants. No difference in ED visits in 1 RCT[10] in 937 children and 1 RCT[9] on 361 mixed-population participants. No difference in exacerbations in 1 RCT[7] in 247 mixed-population participants.
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
ACT or childhood ACT (MID: 3 points) Follow-up: 40 weeks	247 (1 RCT)[7]	Moderate[b]	—	**No difference** No difference in ACT or childhood ACT score in 1 RCT in 247 mixed-population participants.

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Mini-AQLQ (MID: 0.5 points) Follow-up: 40-52 weeks	347 (2 RCTs)[7,8]	High	—	**No difference** No difference in mini-AQLQ scores in 1 RCT[8] in 100 children and 1 RCT[7] in 247 mixed-population participants.
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Varies[c] Follow-up: 40 to 104 weeks	1,645 (4 RCTs)[7-10]	Low[b,d]	—	**Favors intervention** Reductions in symptoms in 2 RCTs[8,10] in 1,037 children, but no difference in 2 RCTs[7,9] in 608 mixed-population participants.
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Not reported				

Abbreviations: ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; ED, emergency department; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MID, minimally important difference; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. One RCT by Eggleston et al. (2005, N=100)[8] in children showed no difference in acute care visits.

b. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down for imprecision.

c. The Expert Panel reviewed 4 RCTs whose investigators reported data on asthma symptoms using various nonvalidated symptom scales and found reductions in symptoms among children in 2 RCTs (total N = 1,037).

d. The AHRQ systematic review report rated this outcome down for inconsistency.

Harms: No adverse events were reported.

New evidence

No.

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Evidence to Decision Table IX — High-Efficiency Particulate Air Vacuum Cleaners (with or without Other Interventions) vs. Placebo or No Vacuum Intervention for Individuals with Asthma

Background

Many common indoor inhalant allergens—including animal dander, house dust mites, mice, cockroaches, and mold—are associated with an increased risk of asthma exacerbations. Numerous interventions have been designed to reduce exposure to allergens in the environments where individuals with asthma live, work, learn, play, and sleep. These interventions include use of acaricides (house dust mite pesticides), air purification systems, carpet removal or vacuuming, specially designed mattress covers and pillowcases, mold mitigation, pest control techniques, and containment or removal of pets.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	No single-component intervention studies were found. Studies of multicomponent interventions provide evidence of improvement with multicomponent interventions from 3 RCTs in children (Krieger et al. 2005, Morgan et al. 2004, Parker et al. 2008). Two RCTs provide no data on asthma control (DiMango et al. 2016, Krieger et al. 2009), and 2 RCTs found improvement in PACQLQ scores in children (Krieger et al. 2005, Warner et al. 2000). Results were mixed for asthma symptoms in studies that used nonvalidated scales.	

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	Time and costs are associated with HEPA vacuum cleaner use. The vacuum cleaners need to be purchased one time only, but users need to clean and change the filters and to use the vacuum cleaner frequently.	

Certainty of evidence: What is the overall certainty of the evidence of effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Moderate		

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no important uncertainty or variability		

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably favors the intervention		

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes		

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes		

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Varies	The impact varies by prices for vacuum cleaners and filters.	

Abbreviations: HEPA, high-efficiency particulate air; PACQLQ, Pediatric Asthma Caregiver's Quality of Life Questionnaire; RCT, randomized controlled trial.

Evidence Summary: High-Efficiency Particulate Air Vacuum Cleaners with Other Interventions[a] vs. Placebo or No Vacuum Intervention for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Composite measure Follow-up: 13 to 104 weeks	1,461 (3 RCTs in children)[1-3]	Moderate[b]	—	**Favors intervention** Significant improvement in composite measure of hospitalizations, ED visits, and acute care clinic visits.
Unspecified Follow-up: 40 to 52 weeks	556 (2 RCTs in mixed populations)[4,5]	Moderate[b]	—	**No difference** No difference in undefined "exacerbations" or "asthma attacks."
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
Not reported				
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
PACQLQ (MID: 0.5 points) Follow-up: 26-52 weeks	583 (2 RCTs)[1,5]	Moderate[b]		**Favors intervention** Significant improvement in PACQLQ scores.
Mini-AQLQ (MID: 0.5 points) Follow-up: 40 weeks	247 (1 RCT in mixed populations)[4]	Very low[c]		**Inconclusive** No difference in mini-AQLQ scores.
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Varies[d] Follow-up: 13-104 weeks	1,509 (3 RCTs in children)[1-3]	Low[b,c]		**Favors intervention** Significant decrease in symptom days in 2 RCTs[2,3] (N = 1,235). No difference in symptom days in 1 RCT[1] (N = 274).
Varies[d] Follow-up: 40 to 52 weeks	596 (3 RCTs in mixed populations)[4-6]	Very low[e]		**Inconclusive** No difference in 2 RCTs[4,6] (total N = 287) in frequency of symptoms; significant reduction in symptom days in 1 RCT[5] (N = 309).

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Health care utilization (rescue) Follow-up: 26 to 52 weeks	830 (3 RCTs in mixed populations)[1,4,5]	High		**No difference** No difference in use of rescue inhaler or beta-agonists

Abbreviations: AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; ED, emergency department; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MID, minimally important difference; PACQLQ, Pediatric Asthma Caregiver's Quality of Life Questionnaire; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. Other interventions included combinations of air filtration systems and air purifiers, mattress covers, pest control, provision of cleaning supplies, and mold mitigation.

b. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down for risk of bias.

c. The AHRQ systematic review report rated this outcome down for imprecision and inconsistency.

d. The AHRQ systematic review report rated this outcome down for inconsistency.

e. The Expert Panel rated this outcome down for risk of bias and imprecision.

Harms: No harms were reported in the studies.

New evidence

No.

References

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Evidence to Decision Table X — Cleaning Products vs. No Cleaning Products for Individuals with Asthma

Background

Many common indoor inhalant allergens—including animal dander, house dust mites, mice, cockroaches, and mold—are associated with an increased risk of asthma exacerbations. Numerous interventions have been designed to reduce exposure to allergens in the environments where individuals with asthma live, work, learn, play, and sleep. These interventions include use of acaricides (house dust mite pesticides), air purification systems, carpet removal or vacuuming, specially designed mattress covers and pillowcases, mold mitigation, pest control techniques, and containment or removal of pets. The verification code for this document is 990813

Desirable effects: How substantial are the desirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Don't know		Insufficient evidence is available.

Undesirable effects: How substantial are the undesirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Don't know		Insufficient evidence is available.

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Very low		

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Possibly important uncertainty or variability	No data were reported regarding how individuals with asthma value the use of cleaning products or alternatives.	Preferences of individuals with asthma may vary regarding the use of bleach products as opposed to other cleaning options, including environmentally safe products.

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Don't know		

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Varies		

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Varies	The intervention is an affordable product that is widely available.	

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Don't know		

Evidence Summary: Single-Component Cleaning Product[a] Interventions vs. No Cleaning Products for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Not clearly defined Follow-up: 8 weeks	97 families (1 RCT)[1]	Very low[b,c]	—	**Inconclusive** Low rates of exacerbations in intervention and control groups.
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
Not clearly defined Follow-up: 8 weeks	97 families (1 RCT)[1]	Very low[b,c]	—	**Inconclusive** Not possible to determine the intervention's effectiveness.
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Scale not identified Follow-up: 8 weeks	97 families (1 RCT)[1]	Very low[b,c]	—	**Inconclusive** Quality of life improved in all groups, but no between-group analysis results were provided. Results could be explained by the placebo effect because members of the group that did not receive cleaning products kept a diary.
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Not reported				
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Not reported				

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. The cleaning products contained household bleach or 0.09% diluted hypochlorite.

b. The Agency for Healthcare Research and Quality systematic review report rated this outcome down for risk of bias.

c. The Expert Panel rated this outcome down twice for imprecision because of the small sample.

Harms: No adverse events were reported.

New evidence

No.

Reference

1. Barnes CS, Kennedy K, Gard L, Forrest E, Johnson L, Pacheco F, et al. The impact of home cleaning on quality of life for homes with asthmatic children. Allergy Asthma Proc. 2008;29(2):197-204.

Evidence to Decision Table XI — Mold Mitigation with or without Other Interventions vs. Placebo or No Mold Mitigation Interventions for Individuals with Asthma

Background

Many common indoor inhalant allergens—including animal dander, house dust mites, mice, cockroaches, and mold—are associated with an increased risk of asthma exacerbations. Numerous interventions have been designed to reduce exposure to allergens in the environments where individuals with asthma live, work, learn, play, and sleep. These interventions include use of acaricides (house dust mite pesticides), air purification systems, carpet removal or vacuuming, specially designed mattress covers and pillowcases, mold mitigation, pest control techniques, and containment or removal of pets.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	No single-component intervention studies were available. Data from multicomponent intervention studies show reductions in self-reported use of relief medications and symptoms but no reductions in exacerbations or improvements in quality of life.	Two of the mold mitigation multicomponent interventions focused on fungal mitigation as well as maintenance of pest removal (e.g., through moisture reduction and repairs of leaks).

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Varies	Costs depend on mold location and which interventions are needed to remove the mold and prevent it from returning.	Mitigation may involve a one-time cost, but removal of all mold may be difficult, and continuous monitoring to prevent regrowth may be costly.

Certainty of evidence: What is the overall certainty of the evidence of effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Very low	The overall certainty of evidence is based on multicomponent intervention studies.	

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no important uncertainty or variability		

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably favors the intervention		

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes	Even for individuals who are not sensitized to mold, removing mold from residences is a good public health and housing practice.	

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Varies	Removal of mold is only one part of the process. Steps need to be taken to prevent mold regrowth and to reduce the spread of mold to other areas of the residence.	The intervention's feasibility depends on the structure of the residence, surrounding residences, and whether the individual with asthma owns or rents the residence.

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably increased		Mold removal from residences is a good public health and housing practice.

Evidence Summary: Mold Mitigation vs. Placebo or No Mold Mitigation Intervention for Individuals with Asthma

No studies are available.

Evidence Summary: Mold Mitigation with Other Interventions[a] vs. Placebo or No Mold Mitigation Interventions for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Number of exacerbations requiring ED or urgent care visits Follow-up: 52 weeks	62 (1 RCT in mixed populations)[1]	Very low[b]	—	**Inconclusive** No differences in numbers of urgent care or ED visits.
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
Not reported				
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
CHSA Follow-up: 52 weeks	62 (1 RCT in mixed-populations)[1]	Very low[b]	—	**Inconclusive** No difference in mean CHSA scores.
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Asthma symptoms measured by patient questionnaires Follow-up: 52 weeks[d]	223 (2 RCTs: 1 RCT in mixed population participants and 1 RCT in children)[1,2]	Low[b,c]	—	**Inconclusive** One RCT found some improvement in symptoms.[1] Another RCT found no difference in overall symptoms.[2]

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Health care utilization (self-reported relief medication use) Follow-up: 52 weeks (last 4 weeks)	232 (1 RCT in mixed populations)[3]	Low[d]	—	**Favors intervention** The intervention reduced self-reported need for relief medication use.

Abbreviations: CHSA, Children's Health Survey for Asthma; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. Other interventions included combinations of carpet removal, mattress covers, high-efficiency particulate air (HEPA) vacuum cleaners, pest control, air purification, or pet removal.

b. The Agency for Healthcare Research and Quality systematic review report rated this outcome down for study limitations, unknown consistency, and imprecision.

c. The Expert Panel reviewed studies that reported data on asthma symptoms using various nonvalidated symptom scales.

d. The Expert Panel rated this outcome down for unknown consistency and imprecision.

Harms: No harms were reported in the studies.

New evidence

No.

References

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2. Williams SG, Brown CM, Falter KH, Alverson CJ, Gotway-Crawford C, Homa D, et al. Does a multifaceted environmental intervention alter the impact of asthma on inner-city children? J Natl Med Assoc. 2006;98(2):249-60.
3. Burr ML, Matthews IP, Arthur RA, Watson HL, Gregory CJ, Dunstan FD, et al. Effects on patients with asthma of eradicating visible indoor mould: a randomised controlled trial. Thorax. 2007;62(9):767-72.

Evidence to Decision Table XII — Pet Removal vs. No Pet Removal for Individuals with Asthma

Background

Many common indoor inhalant allergens—including animal dander, house dust mites, mice, cockroaches, and mold—are associated with an increased risk of asthma exacerbations. Numerous interventions have been designed to reduce exposure to allergens in the environments where individuals with asthma live, work, learn, play, and sleep. These interventions include use of acaricides (house dust mite pesticides), air purification systems, carpet removal or vacuuming, specially designed mattress covers and pillowcases, mold mitigation, pest control techniques, and containment or removal of pets.

Desirable effects: How substantial are the desirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Don't know		

Undesirable effects: How substantial are the undesirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Small		

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Very low	The overall certainty of evidence was based on single-component and multicomponent intervention studies.	Despite very low certainty of evidence, the opinion of the Expert Panel is that reducing exposure to animal dander may lead to improvements in asthma outcomes in most individuals with asthma, but some asthma outcomes might not improve in those who have developed tolerance to the exposure.

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Possibly important uncertainty or variability		

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Don't know		

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes		Individuals with asthma may be reluctant to remove pets from their homes.

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes		

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no impact		

Evidence Summary: Pet Removal vs. No Pet Removal for Individuals with Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Exacerbations or hospitalizations Follow-up: up to 43 months	20 (1 non-RCT)[1]	Very low[a]	—	**Inconclusive** The study report presented no statistics. No participant in the pet-removal group experienced exacerbations or hospitalizations. Two participants who kept pets experienced an exacerbation or hospitalization.
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
Not reported				
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Not reported				
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Not reported				
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Health care utilization (use of inhaled corticosteroids and follow-up visits to the medical office) Follow-up: up to 43 months	20 (1 non-RCT)[1]	Very low[a]	—	**Inconclusive** Rates of use of inhaled corticosteroids and follow-up visits to the medical office were significantly lower in the pet-removal group.

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. The Agency for Healthcare Research and Quality systematic review report rated this outcome down for imprecision.

Evidence Summary: Pet Removal with Other Interventions vs. No Pet Removal for Individuals with Asthma[a]

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Narrative summary of results
EXACERBATIONS (*CRITICAL* OUTCOME)				
Exacerbations or hospitalizations Follow-up: 16 weeks	160 (1 RCT)[2]	Very low[a,b]	—	**Inconclusive** Only within-group comparisons were reported. The number of hospitalizations was significantly lower in the intervention group and showed no significant change from baseline in the control group.
ASTHMA CONTROL (*CRITICAL* OUTCOME)				
Not reported				
QUALITY OF LIFE (*CRITICAL* OUTCOME)				
Not reported				
ASTHMA SYMPTOMS (*CRITICAL* OUTCOME)				
Overall symptoms and functional severity Follow-up: 52 months	161 (1 RCT)[3]	Very low[a,b]	—	**Inconclusive** No difference in overall symptoms. Significant difference in functional severity score.
OTHER OUTCOMES (IMPORTANT OUTCOME)				
Not reported				

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; RCT, randomized controlled trial.

Footnotes, including GRADE explanations

a. Other interventions included combinations of carpet removal, mattress covers, high-efficiency particulate air vacuum cleaners, pest control, and air purification.

b. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down twice for imprecision.

c. The AHRQ systematic review report rated this outcome down for indirectness because not all study participants in the intervention group removed their pets.

Harms: No harms were reported in the studies.

New evidence

No.

References

1. Shirai T, Matsui T, Suzuki K, Chida K. Effect of pet removal on pet allergic asthma. Chest. 2005;127(5):1565-71.
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3. Williams SG, Brown CM, Falter KH, Alverson CJ, Gotway-Crawford C, Homa D, et al. Does a multifaceted environmental intervention alter the impact of asthma on inner-city children? J Natl Med Assoc. 2006;98(2):249-60.

Evidence to Decision Table XIII — Intermittent Inhaled Corticosteroid vs. No Treatment, Pharmacologic Therapy, or Nonpharmacologic Therapy in Children Ages 0–4 with Recurrent Wheezing

Background

In the *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma,* published in 2007, scheduled, daily ICS dosing was the preferred pharmacologic controller therapy for persistent asthma in individuals of all ages.[1] The report suggested that intermittent ICS dosing schedules may be useful in some settings, but the evidence at that time was insufficient to support a recommendation beyond expert consensus for intermittent ICS dosing.[1] In 2015, the National Heart, Lung, and Blood Advisory Council Working Group determined that a sufficient number of studies had been published on intermittent ICS dosing to warrant a systematic literature review. This table addresses comparisons of intermittent ICS treatment with pharmacologic therapy, nonpharmacologic therapy, or no treatment in children ages 0–4 years old with recurrent wheezing.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Moderate	In studies that compared short courses of ICS with no treatment or pharmacologic therapy (including daily ICS, SABA, or no treatment), the opinion of the Expert Panel is that the desirable effects were moderate.	

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	Ducharme et al. (2009) found a 5% lower gain in height and weight in children with asthma receiving intermittent fluticasone (750 mcg twice daily at the onset of an upper respiratory tract infection for up to 10 days) than in children receiving placebo. A significant correlation between the cumulative dose of fluticasone and the change in height was noted. In contrast, Bacharier et al. (2008) did not find an effect on linear growth in children treated with budesonide inhalation suspension (1 mg twice daily for 7 days) who had an "identified respiratory tract illness" compared with placebo. Whether these differences were due to differences in drugs, doses, duration of treatment, or other factors is not clear.	

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
High	ICS compared with no treatment or pharmacologic treatment (SABA or ICS controller): ▪ High certainty of evidence in comparison with SABA ▪ Moderate certainty of evidence in comparison with ICS controller ▪ Very low certainty of evidence in comparison with no treatment	Although quality of life was also a critical outcome, the indirect assessments by caregivers for this age group lessen the importance of this outcome in this age group in the opinion of the Expert Panel.

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
No important uncertainty or variability	There is no uncertainty or variability in how much individuals with asthma value the main outcomes.	

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably favors the intervention	The beneficial effect was substantial, but evidence on the undesirable effects was contradictory.	The Expert Panel included in the explanation of the recommendation the specific short-course regimens used in the studies and their outcomes.

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes	Although the Expert Panel could not cite specific studies, clinical experience suggests that parents and caregivers of children with asthma are willing to use this type of therapy when the child who has experienced prior infections that have caused wheezing now develops signs of an apparent upper respiratory tract infection.	

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Yes	Home modification of treatment seems feasible in most circumstances. Action plans recommended by guidelines often address increased symptom frequency or severity, supporting the feasibility of this approach.	

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Don't know	Exacerbations are more common in ethnic minority populations and individuals with lower socioeconomic status. Therefore, reductions in exacerbations by an intervention might disproportionately affect such individuals. In contrast, members of these populations might have less access to care, which could limit the benefits of the intervention.	

Abbreviations: ICS, inhaled corticosteroid; SABA, short-acting beta$_2$-agonist

Evidence Summary: Intermittent Inhaled Corticosteroid with As-Needed Short-Acting Beta$_2$-Agonist vs. As-Needed Short-Acting Beta$_2$-Agonist in Children Ages 0–4 with Recurrent Wheezing

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with as-needed SABA and/or N	Risk difference or mean difference with intermittent ICS and as-needed SABA
EXACERBATIONS (*CRITICAL* OUTCOME)					
Need for systemic corticosteroids Follow-up: 52 weeks	324 (3 RCTs)[2-4]	High	RR: 0.67 (0.46 to 0.98)	79/140 (56.4%)	**Favors intervention** 70/184 (38.0%), 186 fewer per 1,000 (from 305 fewer to 11 fewer)
Asthma-related acute care visits Follow-up: 52 weeks	324 (3 RCTs)[2-4]	Moderate[a]	RR: 0.90 (0.77 to 1.05)	92/140 (65.7%)	**No difference** 106/184 (57.6%), 66 fewer per 1,000 (from 151 fewer to 33 more)

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with as-needed SABA and/or N	Risk difference or mean difference with intermittent ICS and as-needed SABA
Asthma-related hospitalizations Follow-up: 52 weeks	324 (3 RCTs)[2-4]	Low[b]	RR: 0.77 (0.06 to 9.68)	21/140 (15.0%)	**No difference** 17/184 (9.2%), 34 fewer per 1,000 (from 141 fewer to 1,000 more)
ASTHMA CONTROL (*CRITICAL* OUTCOME)					
Not reported					
QUALITY OF LIFE (*CRITICAL* OUTCOME)					
PACQLQ scores of 1 for severe to 7 for no impairment (MID: 0.5 points)[c] Follow-up: 52 weeks	270 (2 RCTs)[2,3]	Low[d,e]	—	**No difference** MD: 0.10 lower[3] (from 0.36 lower to 0.34 higher) **Favors intervention** MD: 0.49 higher[2] (from 0.10 higher to 0.86 higher)	
RESCUE MEDICATION USE (IMPORTANT OUTCOME)					
Daytime rescue medication use, number of inhalations/day (MID: 0.81 puffs/day)[f,g] Follow-up: 12 weeks	166 (1 RCT)[5]	Moderate[h]	—	N = 56	**No difference** N = 110 MD: 0.08 fewer (from 0.21 fewer to 0.05 more)
Nighttime rescue medication use, number of inhalations/day (MID: 0.81 puffs/day)[f,i] Follow-up: 12 weeks	166 (1 RCT)[5]	Moderate[h]	—	N = 56	**No difference** N = 110 MD: 0.04 fewer (from 0.11 fewer to 0.03 more)

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICS, inhaled corticosteroid; MD, mean difference; MID, minimally important difference; PACQLQ, Pediatric Asthma Caregiver's Quality of Life Questionnaire; RCT, randomized controlled trial; RR, relative risk; SABA, short-acting beta$_2$-agonist.

Footnotes, including GRADE explanations

a. The Expert Panel rated this outcome down for imprecision because the confidence interval was wide and the boundaries of the confidence interval showed both benefit and harm.

b. The Expert Panel rated this outcome down twice for imprecision because of very wide confidence intervals and boundaries of the confidence interval showed both benefit and harm.

c. The PACQLQ has not been validated for children ages 0–4 years. The established MID is for caregivers of individuals ages 7–17 years.

d. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down for inconsistency. Ducharme et al. (2009)[2] found a difference that was almost clinically meaningful, while Bacharier et al. (2008)[3] found no difference.

e. The AHRQ systematic review report rated this outcome down for imprecision. Ducharme et al. (2009)[2] was rated down for imprecision because the lower boundary of the confidence interval suggested no difference, but the upper boundary suggested a potentially clinically meaningful difference. Bacharier et al. (2008),[3] which had good precision, found no difference.

f. The MID for rescue medication use was defined for adults ages 18 years and older and was not stratified by daytime or nighttime use. Whether the MID changes by timing of use is not clear.

g. In Papi et al. (2009),[5] the number of uses of daytime rescue medication at baseline was 0.35 (0.41) for the ICS with as-needed SABA treatment group and 0.25 (0.25) for the as-needed SABA treatment group.

h. The Expert Panel rated this outcome down for risk of bias. Papi et al. (2009)[5] had an unclear risk of bias for sequence generation and allocation concealment.

i. In Papi et al. (2009),[5] the number of uses of nighttime rescue medication at baseline was 0.15 (0.17) for the ICS with as-needed SABA treatment group and 0.17 (0.19) for the as-needed SABA treatment group.

Evidence Summary: Intermittent Inhaled Corticosteroid with As-Needed Short-Acting Beta$_2$-Agonist vs. Inhaled Corticosteroid Controller Therapy with As-Needed Short-Acting Beta$_2$-Agonist in Children Ages 0–4 with Recurrent Wheezing

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with as-needed SABA and/or N	Risk difference or mean difference with intermittent ICS and as-needed SABA
EXACERBATIONS (*CRITICAL* OUTCOME)					
Need for systemic corticosteroids Follow-up: 52 weeks	278 (1 RCT)[6]	Moderate[a]	RR: 0.99 (0.80 to 1.22)	N = 139	**No difference** N = 139
Asthma-related hospitalizations Follow-up: 52 weeks	278 (1 RCT)[6]	Low[b]	RR: 1.25 (0.34 to 4.56)	4/139 (2.9%)	**No difference** 5/139 (3.6%), 7 more per 1,000 (from 19 fewer to 102 more)
ASTHMA CONTROL (*CRITICAL* OUTCOME)					
Not reported					
QUALITY OF LIFE (*CRITICAL* OUTCOME)					
Not reported					
RESCUE MEDICATION USE (IMPORTANT OUTCOME)					
Daytime rescue medication use, number of inhalations/day (MID: -0.81 puffs/day)[c,d] Follow-up: 12 weeks	220 (1 RCT)[5]	Moderate[e]	—	N = 110	**No difference** N = 110 MD: 0.07 more (from 0.4 fewer to 1.8 more)

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with as-needed SABA and/or N	Risk difference or mean difference with intermittent ICS and as-needed SABA
Nighttime rescue medication use, number of inhalations/day (MID: -0.81 puffs/day)[c,f] Follow-up: 12 weeks	220 (1 RCT)[5]	Moderate[e]	—	N = 110	**No difference** N = 110 MD: 0.02 fewer (from 0.7 fewer to 0.30 more)

Abbreviations: CI, confidence interval; ICS, inhaled corticosteroid; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MD, mean difference; MID, minimally important difference; RCT, randomized controlled trial; RR, relative risk; SABA, short-acting beta$_2$-agonist.

Footnotes, including GRADE explanations

a. The Expert Panel rated this outcome down for imprecision because the confidence interval was wide and the boundaries of the confidence interval showed both benefit and harm.

b. The Expert Panel rated this outcome down twice for imprecision because the confidence interval was very wide and the boundaries of the confidence interval showed both benefit and harm.

c. The MID for rescue medication use was defined for adults ages 18 years and older, but different MIDs have not been defined for daytime or nighttime use; whether the MID is different when the therapy is used at different times is not known.

d. In Papi et al. (2009),[5] the number of uses of daytime rescue medication at baseline was 0.35 (0.41) in the ICS with as-needed SABA treatment group and 0.26 (0.29) in the intermittent ICS with as-needed SABA treatment group.

e. The Expert Panel rated this outcome down for risk of bias concerns. Papi et al. (2009)[5] had an unclear risk of bias for sequence generation and allocation concealment.

f. In Papi et al. (2009),[5] the number of uses of nighttime rescue medication at baseline was 0.15 (0.17) in the ICS with as-needed SABA treatment group and 0.16 (0.18) in the intermittent ICS with as-needed SABA other treatment group.

Evidence Summary: Intermittent Inhaled Corticosteroid with As-Needed Short-Acting Beta$_2$-Agonist vs. No Treatment in Children Ages 0–4 Years with Recurrent Wheezing[a]

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with no treatment and/or N	Risk difference or mean difference with intermittent ICS and as-needed SABA
EXACERBATIONS (*CRITICAL* OUTCOME)					
Requiring systemic corticosteroids Follow-up: After 4 URTIs	26 (1 RCT)[7]	Very low[b,c]	RR: 0.54 (0.12 to 2.44)	4/13 (30.8%)	**No difference** 2/12 (16.7%), 142 fewer per 1,000 (from 271 fewer to 443 more)
Asthma-related ED visits Follow-up: After 4 URTIs	25 (1 RCT)[7]	Very low[b,c]	RR: 0.27 (0.04 to 2.10)	4/13 (30.8%)	**No difference** 1/12 (8.3%), 225 fewer per 1,000 (from 295 fewer to 338 more)
Asthma-related hospitalizations Follow-up: After 4 URTIs	26 (1 RCT)[7]	Very low[b,d]	—	0/13	No events 0/12
ASTHMA CONTROL (*CRITICAL* OUTCOME)					
Not reported					
QUALITY OF LIFE (*CRITICAL* OUTCOME)					
Not reported					
RESCUE MEDICATION USE (IMPORTANT OUTCOME)					
Not reported					

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICS, inhaled corticosteroid; RCT, randomized controlled trial; RR, relative risk; SABA, short-acting beta$_2$-agonist; URTI, upper respiratory tract infection.

Footnotes, including GRADE explanations

a. One small RCT (Ghirga et al. 2002)[7] informed this patient/population/problem, implementation/indicator, comparison/control, outcome question. This RCT enrolled individuals ages 7 to 12 months who presented with a history of recurrent wheezing during a respiratory tract infection. The study randomized 26 infants, and 25 completed the study.

b. The Expert Panel rated this outcome down for risk of bias because the study was open label and did not use blinding.

c. The Expert Panel rated this outcome down twice for imprecision because of very wide confidence intervals that showed both benefit and harm.

d. The Expert Panel rated this outcome down twice for imprecision because of sparse data with no events.

Evidence Summary: Intermittent Inhaled Corticosteroid with As-Needed Short-Acting Beta$_2$-Agonist vs. Nonpharmacologic Therapy in Children Ages 0–4 Years with Recurrent Wheezing

The Expert Panel was unable to find any data or information on this question.

Harms: Three articles in the systematic review addressed a potential adverse effect of study treatment on growth (Ducharme et al. 2009;[2] Bacharier et al. 2008;[3] Zeiger et al. 2011[6]). Ducharme et al. found a 5% lower gain in height and weight in individuals with asthma receiving intermittent fluticasone (750 mcg twice daily at the onset of an upper respiratory tract infection and continued for up to 10 days) compared with individuals receiving placebo.[2] The study showed a significant correlation between the cumulative dose of fluticasone and the change in height. In contrast, Bacharier et al. (2008) did not find an effect on linear growth in children treated with budesonide inhalation suspension (1 mg twice daily for 7 days) who had an identified respiratory tract illness in comparison with placebo.[3] Whether these differences were due to differences in drugs, doses, duration of treatment, or other factors is not clear. The third study compared intermittent budesonide inhalation suspension (1 mg twice daily for 7 days) "starting early during a predefined respiratory tract illness" with nightly budesonide (0.5 mg) for 1 year (Zeiger et al. 2011).[6] The results showed no differences in changes in height, weight, or head circumference, but this study did not include a placebo group.

Ducharme et al.[2] did not find any difference in bone density between intermittent fluticasone (750 mcg twice daily at onset of an upper respiratory tract infection for up to 10 days) and placebo. None of the other study reports provided bone density results.

Finally, the four studies with data on serious adverse events found no differences in rates of these events attributed to the study drug (Ducharme et al. 2009;[2] Ghirga et al. 2002;[7] Papi et al. 2009;[5] Zeiger et al. 2011[6]).

New evidence

No.

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Evidence to Decision Table XIV — Intermittent Inhaled Corticosteroids vs. Daily Inhaled Corticosteroid Controller Therapy in Individuals Ages 12 Years and Older with Mild Persistent Asthma

Background

In *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma,* published in 2007, scheduled, daily ICS dosing was the preferred pharmacologic controller therapy for persistent asthma in individuals of all ages.[1] The report suggested that intermittent ICS dosing schedules may be useful in some settings, but the evidence at that time was insufficient to support a recommendation for intermittent ICS dosing.[1] In 2015, the National Heart, Lung, and Blood Advisory Council Working Group determined that a sufficient number of studies had been published on intermittent ICS dosing to warrant a systematic literature review. This table addresses comparisons of intermittent ICS treatment with ICS controller therapy in individuals ages 12 years and older with mild persistent asthma.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	Asthma control, quality of life, and rescue therapy use were not different between users of two types of intermittent ICS therapy (ICS paired with albuterol in 2 studies and a 10-day course of ICS for increased symptoms in the other study) and users of regular ICS. The rate of exacerbations did not differ between groups in any of the studies.	Individuals had mild persistent asthma in 2 studies and mild-to-moderate persistent asthma in the other, but their asthma was controlled by low-dose ICS. Before randomization, individuals with asthma in the study by Boushey et al. (2005) underwent treatment for 10–14 days with 0.5 mg/kg prednisone, 800 mcg budesonide twice daily, and 20 mg zafirlukast twice daily.

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Trivial	Rates of severe adverse events did not differ between groups.	

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Low	The certainty of evidence was low for exacerbations and high for asthma control and quality of life.	

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
No important uncertainty or variability	There is no uncertainty or variability in how much individuals with asthma value the main outcomes.	

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Does not favor either the intervention or the comparison	The evidence showed no significant differences between groups for any of the outcomes.	

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Yes	In the opinion of the Expert Panel based on clinical experience (including low adherence rates for regular ICS use), most individuals with asthma and parents and caregivers of children with asthma would find symptom-based ICS therapy very acceptable. Some individuals might prefer symptom-driven therapy to regular therapy.	

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Yes	Home modification of treatment seems feasible in most circumstances. Action plans are commonly recommended in guidelines to address increased symptoms, and these recommendations support the feasibility of this approach.	

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no impact	It is not clear whether either treatment would affect health equity, but neither treatment is likely to do so.	

Evidence Summary: Intermittent Inhaled Corticosteroid vs. Daily Inhaled Corticosteroid Controller Therapy in Individuals Ages 12 Years and Older with Mild Persistent Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with ICS controller and/or N	Risk difference or mean difference with intermittent ICS treatment
EXACERBATIONS (*CRITICAL* OUTCOME)					
Need for systemic corticosteroids[a,b] Follow-up: 52 weeks	149 (1 RCT)[2]	Low[c]	RR: 0.70 (0.30 to 1.64)	N = 73	**No difference** N = 76
Asthma-related hospitalizations Follow-up: 52 weeks	149 (1 RCT)[2]	Very low[d]	—	0/73 (0.0%)	No events, (0/76 (0.0%)
Asthma-related urgent care visits[e] Follow-up: 36 weeks	227 (1 RCT)[3]	Low[c]	RR: 0.25 (0.05 to 1.16)	N = 114	**No difference** N = 113

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with ICS controller and/or N	Risk difference or mean difference with intermittent ICS treatment
ASTHMA CONTROL (*CRITICAL* OUTCOME)					
ACQ-7 scores of 0 for no impairment to 7 for maximum (MID for ages ≥18 years: 0.5 points)[f] Follow-up: 12 months	149 (1 RCT)[2]	High	—	N = 73	**No difference** N = 76 MD: 0.1 higher (from 0.12 lower to 0.32 higher)
QUALITY OF LIFE (*CRITICAL* OUTCOME)					
AQLQ scores of 1 for severe to 7 for no impairment (MID: 0.5 points) Follow-up: 36 to 52 weeks	376 (2 RCTs)[2,3]	High	—	N = 187	**No difference** N = 189 MD: 0.2 lower[2] (from 0.48 lower to 0.08 higher) **No difference** MD: 0.01 higher[3] (from 0.19 lower to 0.21 higher)
RESCUE MEDICATION USE (IMPORTANT OUTCOME)					
Albuterol puffs/day (MID for ages ≥18 years: −0.81 puffs/day) Follow-up: 24 to 36 weeks	564 (2 RCTs)[3,4]	High	—	—	**No difference** MD: 0.07 more[4] (from 0.13 fewer to 0.26 more) **No difference** MD: 0.04 fewer[3] (from 0.11 fewer to 0.03 more)

Abbreviations: ACQ, Asthma Control Questionnaire; CI, confidence interval; ICS, inhaled corticosteroid; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MD, mean difference; MID, minimally important difference; OR, odds ratio; RCT, randomized controlled trial; RR, relative risk.

Footnotes, including GRADE explanations

a. One RCT (Papi et al. 2007, N = 228)[4] provided data on mild (RR: 0.87; 95% CI, [0.29 to 2.61]) and severe exacerbations (Peto OR: 0.11; 95% CI, 0.01 to 1.11).

b. While developing the clinical guidelines, the Expert Panel did not have access to the raw data on this outcome from one study.[2] At least one exacerbation occurred in 10/73 individuals taking regular budesonide and 8/76 individuals taking intermittent therapy. Four exacerbations in the intermittent arm required corticosteroids, as did five in the controller arm (possibly 5.3% vs. 6.8%). The RR came from the Agency for Healthcare Research and Quality (AHRQ) systematic review report.

c. The Expert Panel rated this outcome down twice for imprecision because the confidence intervals were very wide and showed both benefit and harm.

d. The AHRQ systematic review report considered the evidence to be insufficient because no events occurred. This outcome had very low certainty of evidence based on GRADE.

e. While developing the clinical guidelines, the Expert Panel reviewed Calhoun et al. (2012)[3] whose raw data for this outcome were not available. The authors of this study defined exacerbations as "unscheduled medical contact for increased asthma symptoms that results in use of oral corticosteroids, increased inhaled corticosteroids, or additional medications for asthma." Information on urgent care visits was not reported separately in the publication. For the composite measure, asthma exacerbation rates were 0.23 events per person-year for the treatment group with physician assessment-based adjustments and 0.12 events per person-year for the treatment group with symptom-based adjustments (hazard ratio: 2.0; 97.5% CI, 0.8 to 5.4). The RR came from the AHRQ systematic review report.

f. One study (Calhoun et al. 2012, N=227)[3] also provided data on the asthma control outcome based on the five-item ACQ (mean difference: 0.01 lower; 95% CI, 0.17 lower to 0.15 higher).

Harms: No significant differences between groups were reported for serious adverse events in the three studies with data on this outcome (Boushey et al. 2005;[2] Papi et al. 2007;[4] and Calhoun et al. 2012[3]).

New evidence

No.

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Evidence to Decision Table XV — Intermittent Inhaled Corticosteroids vs. Daily Inhaled Corticosteroid Controller Therapy in Children Ages 4–11 Years with Persistent Asthma

Background

In *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma,* published in 2007, scheduled, daily ICS dosing was the preferred pharmacologic controller therapy for persistent asthma in individuals of all ages.[1] The report suggested that intermittent ICS dosing schedules may be useful in some settings, but the evidence at that time was insufficient to support a recommendation for intermittent ICS dosing.[1] In 2015, the National Heart, Lung, and Blood Advisory Council Working Group determined that a sufficient number of studies had been published on intermittent ICS dosing to warrant a systematic literature review. This table addresses comparisons between intermittent ICS and ICS controller therapy in children ages 4–11 years with persistent asthma.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	One study (Martinez et al. 2011) found no differences in rates of exacerbations or quality of life between the two groups, but the report did not provide data on asthma control.	The study by Martinez et al. (2011) used albuterol plus beclomethasone as rescue therapy for the intermittent ICS group. In the Turpeinen et al. (2008) study, all children received daily ICS treatment for the first 6 months. For the next 12 months, children were randomized to receive either intermittent ICS treatment or continued daily low-dose ICS treatment. The continuous ICS group had fewer exacerbations per child (0.97) than the intermittent ICS group (1.69).

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	In the Turpeinen et al. (2008) study, increases in height were greater in the intermittent ICS group after 6 months of daily therapy than in the group that continued daily therapy in months 7–18.	

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Low		

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
No important uncertainty or variability	There is no uncertainty or variability in how much individuals with asthma value the main outcomes. Informed individuals with asthma and parents and caregivers of children with asthma are likely to make similar treatment decisions.	

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Does not favor either the intervention or the comparison		

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes	Results from focus groups with individuals with asthma and parents and caregivers of children with asthma are mixed; some prefer intermittent ICS therapy, and others prefer daily ICS therapy.	

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Yes	Home modification of treatment seems feasible in most circumstances. Action plans are commonly recommended in guidelines to address increased symptoms, and these recommendations support the feasibility of this approach.	

Equity: What would be the impact on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably reduced	Exacerbations are more common in members of ethnic minority groups and individuals with asthma with lower socioeconomic status. Therefore, reductions in exacerbations by an intervention might disproportionately affect such individuals. In contrast, access to care may be lower in such individuals, which could limit the benefit of the intervention.	

Evidence Summary: Intermittent Inhaled Corticosteroid vs. Daily Inhaled Corticosteroid Controller Therapy in Children Ages 4–11 Years with Persistent Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with ICS controller and/or N	Risk difference or mean difference with intermittent ICS treatment
EXACERBATIONS (*CRITICAL* OUTCOME)					
Need for systemic corticosteroids[a] Follow-up: 44 weeks	143 (1 RCT)[2]	Low[b,c]	RR: 1.27 (0.78 to 2.07)	20/72 (27.8%)	**No difference** 25/71 (35.2%), 75 more per 1,000 (from 61 fewer to 297 more)
ASTHMA CONTROL (*CRITICAL* OUTCOME)					
Not reported					
QUALITY OF LIFE (*CRITICAL* OUTCOME)					
PAQLQ scores of 1 for severe to 7 for no impairment (MID: 0.5 points) Follow-up: 44 weeks	143 (1 RCT)[2]	Low[b,d]	—	N = 72	**No difference** N = 71 MD: 0.04 higher (from 0.25 lower to 0.33 higher)

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with ICS controller and/or N	Risk difference or mean difference with intermittent ICS treatment
RESCUE MEDICATION USE (IMPORTANT OUTCOME)					
Albuterol puffs/day (MID for ≥18 years: –0.81 puffs/day) Follow-up: 44 weeks	143 (1 RCT)[2]	Low[b,d]	—	N = 72	**No difference** N = 71 MD: 0.003 more (from 0.24 fewer to 0.25 more)

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICS, inhaled corticosteroid; MD, mean difference; MID, minimally important difference; PAQLQ Pediatric Asthma Quality of Life Questionnaire; RCT, randomized controlled trial; RR, relative risk.

Footnotes, including GRADE explanations

a. One study (Martinez et al. 2011, N = 143)[2] also provided data on treatment failure as an outcome. The relative risk was 3.04 (95% CI, 0.64 to 14.57).

b. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down for indirectness because Martinez et al. (2011)[2] enrolled individuals with asthma ages 5 to 18 years (mean ages 10.4 years for rescue ICS group and 10.8 years for daily ICS group).

c. The AHRQ systematic review report rated this outcome down for imprecision because the confidence interval was wide and showed both benefit and harm.

d. The AHRQ systematic review report rated this outcome down for imprecision because the confidence interval was wide and showed both benefit and harm.

Harms: For the comparison between daily and intermittent ICS treatment, one study (Turpeinen et al. 2008)[3] measured growth in children ages 5–10 years. In that study, all children were treated with daily ICS for the first 6 months. For the next 12 months, children were randomized to intermittent ICS or daily low-dose ICS treatment. In Months 7–18, the height velocity was greater in the intermittent than in the low-dose daily ICS group. Another study (Camargos et al. 2018)[4] that measured growth in children ages 6–18 years did not find any difference between groups, but this study only lasted 16 weeks.

New evidence

Yes[4]

References

1. National Asthma Education and Prevention Program. Third Expert Panel on the Diagnosis and Management of Asthma. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda, Maryland: National Heart, Lung, and Blood Institute (US). Aug. 2007. 440 pp. https://www.ncbi.nlm.nih.gov/books/NBK7232/.
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Evidence to Decision Table XVI — Intermittent Inhaled Corticosteroid with Inhaled Corticosteroid Controller Therapy vs. Inhaled Corticosteroid Controller Therapy in Children Ages 4–11 Years with Mild Persistent Asthma

Background

In *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma*, published in 2007, scheduled, daily ICS dosing was the preferred pharmacologic controller therapy for persistent asthma in individuals of all ages.[1] The report suggested that intermittent ICS dosing schedules may be useful in some settings, but the evidence at that time was insufficient to support a recommendation for intermittent ICS dosing.[1] In 2015, the National Heart, Lung, and Blood Advisory Council Working Group determined that a sufficient number of studies had been published on intermittent ICS dosing to warrant a systematic literature review. This table addresses comparisons of the combination of ICS controller therapy with intermittent ICS therapy vs. ICS controller therapy alone in children ages 4–11 years with mild persistent asthma.

Desirable effects: How substantial are the desirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Trivial	The intervention did not significantly reduce rates of exacerbations or of asthma hospitalizations or improve asthma quality of life.	

Undesirable effects: How substantial are the undesirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Small	In 1 long-term (48-week) study in children ages 4–11 years, the growth rate in the intervention group was lower, but this difference did not reach statistical significance.	

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Low		

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
No important uncertainty or variability		

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably favors the comparison	The potential for the intervention to suppress growth and the absence of demonstrated efficacy of the intervention in the reviewed articles led to the recommendation against this intervention in this age group.	

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Yes	Although the Expert Panel could not cite specific studies, clinical experience suggests that individuals with asthma, caregivers, and providers want to use rescue therapy to relieve symptoms and prevent further deterioration in the patient's condition.	

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Yes	Home modification of treatment seems feasible in most circumstances. Action plans are commonly recommended in guidelines to address increased symptoms, and these recommendations support the feasibility of this approach.	

Equity: What would the impact be on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no impact	Exacerbations are more common in ethnic minority populations and individuals with asthma with lower socioeconomic status. Therefore, an intervention that reduces the number of exacerbations might disproportionately affect such individuals. In contrast, these individuals might have less access to care, which could limit the benefits of the intervention. However, the intervention's lack of efficacy makes this question moot.	

Abbreviations: ICS, inhaled corticosteroid.

Evidence Summary: Intermittent Inhaled Corticosteroid with Inhaled Corticosteroid Controller Therapy vs. Inhaled Corticosteroid Controller Therapy in Children Ages 4–11 Years with Mild Persistent Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with ICS controller and/or N	Risk difference or mean difference with intermittent ICS and ICS controller therapy
EXACERBATIONS (*CRITICAL* OUTCOME)					
Requiring systemic corticosteroids[a]	143 (1 RCT)[2]	Low[b,c]	RR: 1.12 (0.67 to 1.86)	20/72 (27.8%)	**No difference** 22/71 (31.0%), 33 more per 1,000 (from 92 fewer to 239 more)
Requiring hospitalization Follow-up: 52 weeks	29 (1 RCT)[3]	Very low[d,e]	Peto OR: 0.14 (0.003 to 7.31)	1/15 (6.6%)	**No difference** 0/14 (0.0%), 57 fewer per 1,000 (from 66 fewer to 276 more)
ASTHMA CONTROL (*CRITICAL* OUTCOME)					
Not reported					
QUALITY OF LIFE (*CRITICAL* OUTCOME)					
PAQLQ scores of 1 for severe to 7 for no impairment (MID for ages 7–17 years: 0.5 points) Follow-up: 44 weeks	143 (1 RCT)[2]	Moderate[b]	-	N = 72	**No difference** N = 71, MD: 0.003 lower (from 0.25 lower to 0.25 higher)
RESCUE MEDICATION USE (IMPORTANT OUTCOME)					
Albuterol puffs/day (MID for ages ≥18 years: –0.81 puffs/day) Follow-up: 44 weeks	143 (1 RCT)[2]	Moderate[b]	-	N = 72	**No difference** N = 71, MD: 0.04 higher (from 0.33 lower to 0.40 higher)

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICS, inhaled corticosteroid; MD, mean difference; MID, minimally important difference; OR, odds ratio; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; RCT, randomized controlled trial; RR, relative risk.

Footnotes, including GRADE explanations:

a. The Martinez et al. study (2011, N = 143)[2] also provides data on treatment failure (not included in this table). The RR was 2.03 (95% CI, 0.39 to 10.72).

b. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated Martinez et al. (2011) down for indirectness because of a low enrollment rate for individuals with asthma ages 5–18 years (mean 11.4 for combined daily and intermittent use and 10.8 years for daily use only).[2]

c. The AHRQ systematic review report rated this outcome down for imprecision because the confidence interval was wide and showed both benefit and harm.

d. The AHRQ systematic review report rated this outcome down for risk of bias because the study by Colland et al. (2004) was judged to have an unclear risk of bias.[3]

e. The Expert Panel rated this outcome down for imprecision because events were sparse.

Harms:

For the comparison between daily inhaled corticosteroid (ICS) plus rescue ICS therapy vs. daily ICS plus short-acting beta$_2$-agonist (SABA) therapy, two studies addressed growth rate. One 48-week study by Jackson et al. (2018)[4] administered two puffs twice daily of ICS rescue therapy (fluticasone 220 mcg/puff) for 7 days. The growth rate in children in the rescue ICS group was 5.43 cm per year, which was 0.23 cm per year lower than the rate (5.65 cm per year) in children in the low-dose group (P = 0.06). This study did show a potential for growth suppression over the long term with intermittent, high-dose, rescue ICS therapy. In the study by Camargos et al. (2018),[5] rescue ICS therapy consisted of 1,000 mcg daily (1 puff of 250 mcg every 6 hours) of beclomethasone for 7 days. This study found no statistically significant difference (P = 0.35) in linear growth between groups; the rescue ICS group grew 1.6 cm (standard deviation [SD]: 1.4 cm), whereas the comparison group grew 1.4 cm (SD: 1.6 cm). However, this study lasted only 16 weeks.

Three studies that collected data on serious adverse events did not find differences between groups.[2,4,6] In the McKeever et al. (2018) study,[7] the most common serious adverse event consisted of asthma hospitalizations; three participants in the rescue ICS (quadrupled dose) group and 18 in the other group were hospitalized, and these hospitalizations were included in the primary outcome. The quadrupled-dose group had five events, and the other group had six events involving pneumonia or lower respiratory tract infections in the 4 weeks after use of rescue ICS therapy. One participant in the quadrupled-dose group died of severe pneumonia.

New evidence

Yes.[4,5,7]

References

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Evidence to Decision Table XVII — Intermittent Inhaled Corticosteroid with Inhaled Corticosteroid Controller Therapy vs. Inhaled Corticosteroid Controller Therapy in Individuals Ages 12 Years and Older with Persistent Asthma

Background

In *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma*, published in 2007, scheduled, daily ICS dosing was the preferred pharmacologic controller therapy for persistent asthma in individuals of all ages.[1] The report suggested that intermittent ICS dosing schedules may be useful in some settings, but the evidence at that time was insufficient to support a recommendation for intermittent ICS dosing.[1] In 2015, the National Heart, Lung, and Blood Advisory Council Working Group determined that a sufficient number of studies had been published on intermittent ICS dosing to warrant a systematic literature review. This table addresses comparisons of ICS controller therapy plus intermittent ICS therapy with ICS controller therapy in individuals ages 12 years and older with persistent asthma.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Trivial	The intervention did not significantly reduce the number of exacerbations (3 RCTs) or asthma hospitalizations (1 RCT). No data were reported on asthma control or quality of life from studies in the systematic review report. However, in a new large study (N = 1,871) from 2018 by McKeever et al. that was not included in the AHRQ systematic review report for this priority topic, the results showed a modest but significant reduction in time to severe exacerbation and in the rates of oral corticosteroid use and unscheduled health care consultations in patients whose action plan included a quadrupling of the ICS dose.	Unlike the studies in the AHRQ systematic review report, the new study did not have a placebo group, did not use blinding, and had a low baseline adherence rate.

Undesirable effects: How substantial are the undesirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Small	The rate of serious adverse events was low and similar in both groups.	

Certainty of evidence: What is the overall certainty of the evidence of effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Low		

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
No important uncertainty or variability	There is no uncertainty or variability in how much people value the main outcomes.	

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Does not favor either the intervention or the comparison	Studies included in the AHRQ systematic review report found no differences in efficacy or safety between groups, and methodologic issues make the New evidence from the study completed after completion of the AHRQ systematic review report less compelling.	

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Yes	Although the Expert Panel could not cite specific studies, clinical experience suggests that individuals with asthma and their providers want rescue therapy to relieve symptoms and prevent further deterioration in their condition.	

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Yes	Home modification of treatment seems feasible in most circumstances. Action plans are commonly recommended in guidelines to address increased symptoms, and these recommendations support the feasibility of this approach.	

Equity: What would the impact be on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably no impact	Exacerbations are more common in ethnic minority populations and individuals with asthma with lower socioeconomic status. Therefore, an intervention that reduces the number of exacerbations might disproportionately affect such individuals. In contrast, these individuals might have less access to care, which could limit the benefits of the intervention. However, the intervention's lack of efficacy makes this question moot.	

Abbreviations: AHRQ, Agency for Healthcare Research and Quality; ICS, inhaled corticosteroid; RCT, randomized controlled trial.

Evidence Summary: Intermittent Inhaled Corticosteroid with Inhaled Corticosteroid Controller Therapy vs. Inhaled Corticosteroid Controller Therapy in Individuals Ages 12 Years and Older with Persistent Asthma

Outcomes	Number of participants (number of studies)	Certainty of evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)	
				Risk with ICS controller therapy and/or N	Risk difference or mean difference with intermittent ICS and ICS controller therapy
EXACERBATIONS (*CRITICAL* OUTCOME)					
Need for oral corticosteroids[a] Follow-up: 52 weeks	908 (3 RCTs)[2-4]	Low[b,c]	RR: 0.68 (0.31 to 1.49)	80/463 (17.3%)	**No difference** 53/445 (11.9%), 55 fewer per 1,000 (from 119 fewer to 85 more)
Asthma-related hospitalizations Follow-up: 52 weeks	115 (1 RCT)[3]	Low[b,d]	RR: 0.70 (0.12 to 4.05)	3/59 (5.1%)	**No difference** 2/56 (3.6%), 15 fewer per 1,000 (from 45 fewer to 155 more)
ASTHMA CONTROL (*CRITICAL* OUTCOME)					
Not reported					
QUALITY OF LIFE (*CRITICAL* OUTCOME)					
Not reported					
RESCUE MEDICATION USE (IMPORTANT OUTCOME)					
Not reported					

Abbreviations: CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; ICS, inhaled corticosteroids; RCT, randomized controlled trial; RR, relative risk.

Footnotes, including GRADE explanations:

a. Additional data have been published on the exacerbation outcome of requiring an oral corticosteroid only in individuals starting to take the study inhaler, other individual exacerbation outcomes (asthma-related outpatient visits, unstable asthma, two or three exacerbations requiring oral corticosteroids, and fall in peak expiratory flow of less than 70% from the baseline rate), and a composite exacerbation outcome (need for oral corticosteroids, unscheduled doctor visit, or emergency department visit, or unstable asthma). Each study found no differences between groups, except in asthma-related outpatient visits, for which results were inconsistent in the two studies with data on this outcome. The RR of asthma-related outpatient visits from the Lahdensuo et al. (1996) study was 0.53 (95% CI, 0.29 to 0.96) and was 1.14 (95% CI, 0.71 to 1.83) in the Harrison et al. (2004) study.[2,3] For the composite exacerbation outcome, the RR from the one contributing study from Fitzgerald et al. (2004) was 1.03 (95% CI, 0.63 to 1.65).[5]

b. The Agency for Healthcare Research and Quality (AHRQ) systematic review report rated this outcome down for imprecision because the confidence intervals were wide and showed both benefit and harm.

c. The Expert Panel rated this outcome down for risk of bias because the Lahdensuo et al. (1996) study, which had the most favorable point estimate, also had a medium risk of bias.[3]

d. The AHRQ systematic review report rated this outcome down for risk of bias because the Lahdensuo et al. (1996) study had a medium risk of bias.[3]

Harms:
The three studies with data on serious adverse events—by Martinez et al. (2011), Oborne et al. (2009), and Jackson et al. (2018)[4,6,7]—found no differences in rates of these events between groups. In the McKeever et al. study, the most common serious event consisted of three asthma hospitalizations in the rescue ICS (quadrupled-dose) group and 18 asthma hospitalizations in the other group; asthma hospitalizations were also included in the primary outcome.[8] Five events in the quadruple-dose group and six in the other group involved pneumonia or lower respiratory tract infection in the 4 weeks after rescue ICS use, and one participant in the quadruple-dose group died of severe pneumonia.[8]

New evidence
Yes.[6,8]

References

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8. McKeever T, Mortimer K, Wilson A, Walker S, Brightling C, Skeggs A, et al. Quadrupling Inhaled Glucocorticoid Dose to Abort Asthma Exacerbations. N Engl J Med. 2018;378(10):902-10.

Evidence to Decision Table XVIII — Inhaled Corticosteroid and Long-Acting Beta$_2$-Agonist Controller and Reliever Therapy vs. Inhaled Corticosteroid and Short-Acting Beta$_2$-Agonist for Quick-Relief Therapy in Individuals Ages 4 Years and Older with Persistent Asthma

Background

In *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma*, published in 2007, scheduled, daily ICS dosing was the preferred pharmacologic controller therapy for persistent asthma in individuals of all ages.[1] The report suggested that intermittent ICS dosing schedules may be useful in some settings, but the evidence at that time was insufficient to support a recommendation for intermittent ICS dosing.[1] In 2015, the National Heart, Lung, and Blood Advisory Council Working Group determined that a sufficient number of studies had been published on intermittent ICS dosing to warrant a systematic literature review. This table addresses comparisons of ICS with LABA used as both controller and reliever therapy vs. ICS as controller therapy with SABA as quick-relief therapy in individuals ages 5 years and older with persistent asthma.

Desirable effects: How substantial are the desirable anticipated effects?

JUDGMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Large	▪ Two studies comparing SMART to higher-dose ICS therapy found a 40% relative risk reduction in exacerbations based on a composite outcome in individuals ages 12 years or older (Scicchitano et al. 2004; O'Byrne et al. 2005), and 1 study found a 57% reduction (Bisgaard et al. 2006) in individuals ages 4–11 years. ▪ The evidence provides no asthma control or quality-of-life data measured with validated scales. Data using multiple nonvalidated asthma symptom scales favored the intervention in individuals ages 12 years and older and, to a lesser degree, in individuals ages 4–11 years.	No studies used the same ICS dose in the active intervention and comparator groups.

Undesirable effects: How substantial are the undesirable anticipated effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Trivial	Growth data favored the intervention compared with daily higher-dose ICS therapy. Results showed no differences in serious adverse events.	

Certainty of evidence: What is the overall certainty of the evidence of effects?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
High	The certainty of evidence was high for individuals ages 12 years and older and moderate for individuals ages 4–11 years.	

Values: Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
No important uncertainty or variability	There is no uncertainty or variability in how much individuals with asthma value the main outcomes.	

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Favors the intervention	There is substantial benefit with respect to exacerbations, and the undesirable effects are trivial.	

Acceptability: Is the intervention acceptable to key stakeholders?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Yes	Using the same medication for controller and reliever therapy should be at least as logistically acceptable as using one inhaler for control and a separate inhaler for quick-relief therapy. Using ICS-formoterol in the same inhaler as needed for relief may be more expensive than using albuterol, depending on the individual's insurance coverage.	

Feasibility: Is the intervention feasible to implement?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably yes	Using the same medication for controller and reliever therapy should be easier than using two different inhalers. However, not all insurance plans might cover use of ICS-formoterol for reliever therapy.	

Equity: What would the impact be on health equity?		
JUDGMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Probably increased	Exacerbations are more common in ethnic minority populations and individuals with asthma with lower socioeconomic status. Therefore, an intervention that reduces the number of exacerbations might disproportionately affect such individuals. In contrast, these individuals might have less access to care, which could limit the benefits of the intervention.	

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; SABA, short-acting beta$_2$-agonist; SMART, single maintenance and reliever therapy.