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# New Strategies for Asthma: Exploring the 2020 Guidelines Update

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## Disclosures

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- I have no relevant disclosures



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I have read and am familiar with the 2020 asthma guideline updates



**PolLEv.com/ulpulm**



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Key Messages from Guideline Updates



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## Objectives

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- **Learn about the six focus areas addressed by the guidelines update**
- **Highlight guidance for intermittent ICS use in select children and adults**
- **Evaluate single maintenance and reliever therapy (SMART) use in general practice**

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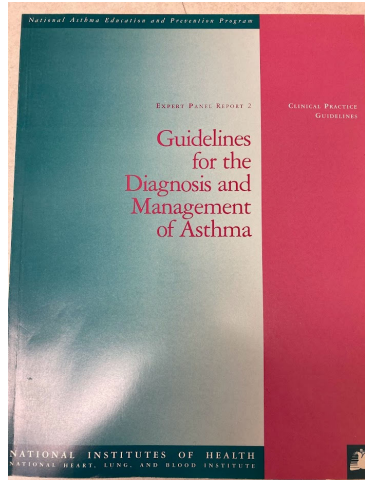
## Background

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- **First set of guidelines by NHLBI released in 1991**
- **Most recent revision was issued in 2007**
- **Multiple new asthma therapies, developments in asthma research since last update**
- **Other guidelines (notably GINA) have had multiple updates since 2007**
- **Intended to be an \*update\*; not a complete revision of last guidelines**
- **Six focus areas addressed; GRADE criteria used**

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# ERP-2 and Inhalers of that Era



## Commonly Used Metered-Dose Inhalers To Help You Breathe Better

| Anticholinergic/<br>Beta <sub>2</sub> -agonist<br>Combination                               | Anticholinergics  | Beta <sub>2</sub> -agonists  | Corticosteroids  | Other  |
|---|---|--|--|--|
| <b>Cumivent<sup>®</sup></b><br>Ipratropium bromide and albuterol sulfate inhalation aerosol | <b>Atrovent<sup>®</sup></b><br>Ipratropium bromide inhalation aerosol | <b>Albuterol<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol | <b>Aerobid<sup>®</sup></b><br>Beclomethasone dipropionate inhalation aerosol | <b>Intal<sup>®</sup></b><br>Disodium cromoglycate inhalation aerosol |
| <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol                        | <b>Ventolin<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol   | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol         | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol |
| <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol                        | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol  | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol         | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol |
| <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol                        | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol  | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol         | <b>Proventil<sup>®</sup></b><br>Albuterol sulfate inhalation aerosol |

### Effects Of Disease On Airways

**Normal**  
Larger airway

**Chronic Bronchitis**  
Larger airway

**Emphysema**  
Larger airway

**Asthma**  
Smaller airway

Boehringer Ingelheim logo and other product information at the bottom.

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# Respiratory Treatments

2021

Allergy & Asthma Network | College of Allergy, Asthma & Immunology | CHEST FOUNDATION

|   |  |   |  |
|---|--|---|--|
| <h3>SHORT-ACTING BETA<sub>2</sub>-AGONIST BRONCHODILATORS</h3> <p>relax tight muscles in airways and offer quick relief of symptoms such as coughing, wheezing and shortness of breath for 3-6 hours</p>  |  | <h3>LONG-ACTING BETA<sub>2</sub>-AGONIST BRONCHODILATORS</h3> <p>relax tight muscles in airways and offer lasting relief of symptoms such as coughing, wheezing and shortness of breath for at least 12 hours</p> |  |
| <p><b>ProAir<sup>®</sup></b> HFA<br/>90 mcg albuterol sulfate inhalation aerosol</p> <p><b>Digihaler<sup>®</sup></b><br/>90 mcg albuterol sulfate inhalation powder</p> <p><b>ProAir<sup>®</sup></b> HFA<br/>90 mcg albuterol sulfate inhalation aerosol</p> <p><b>ProAir<sup>®</sup></b> RespClick<sup>®</sup><br/>90 mcg albuterol sulfate inhalation powder</p> <p><b>Proventil<sup>®</sup></b> HFA<br/>90 mcg albuterol sulfate inhalation aerosol</p> <p><b>Ventolin<sup>®</sup></b> HFA<br/>90 mcg albuterol sulfate inhalation aerosol</p> <p><b>Xopenex<sup>®</sup></b> HFA<sup>®</sup><br/>80 mcg levalbuterol hydrochloride inhalation aerosol</p>  | <p><b>Serevent<sup>®</sup></b> Diskus<sup>®</sup><br/>50 mcg salmeterol xinafoate inhalation powder</p> <p><b>Serevent<sup>®</sup></b> RespiMat<sup>®</sup><br/>5.0 mcg salmeterol xinafoate inhalation powder</p>   | <h3>INHALED CORTICOSTEROIDS</h3> <p>reduce and prevent swelling of airway tissues and help reduce ongoing symptoms of coughing, wheezing and shortness of breath</p>  |  |
| <p><b>Alvesco<sup>®</sup></b> HFA<br/>85, 180 mcg budesonide inhalation aerosol</p> <p><b>ArmonAir<sup>®</sup></b> Digihaler<sup>®</sup><br/>85, 170, 330 mcg budesonide inhalation powder</p> <p><b>Arnuity<sup>®</sup></b> Ellipta<sup>®</sup><br/>90, 180, 360 mcg fluticasone propionate inhalation powder</p> <p><b>Asmanex<sup>®</sup></b> HFA<br/>90, 180, 270 mcg mometasone furoate inhalation powder</p> <p><b>Asmanex<sup>®</sup></b> Twisthaler<sup>®</sup><br/>90, 180, 270 mcg mometasone furoate inhalation powder</p> <p><b>Flovent<sup>®</sup></b> Diskus<sup>®</sup><br/>50, 100, 250 mcg fluticasone propionate inhalation powder</p> <p><b>Flovent<sup>®</sup></b> HFA<br/>45, 110, 220 mcg fluticasone propionate inhalation aerosol</p> <p><b>Pulmicort<sup>®</sup></b> Flexhaler<sup>®</sup><br/>90, 180 mcg budesonide inhalation powder</p> <p><b>QVAR<sup>®</sup></b> Redihaler<sup>®</sup><br/>40, 80 mcg beclomethasone dipropionate inhalation aerosol</p>   | <h3>MUSCARINIC ANTAGONISTS (ANTICHOLINERGIC)</h3> <p>relax tight muscles in airways and offer lasting relief of symptoms such as coughing, wheezing and shortness of breath</p>  |   | <h3>COMBINATION MEDICATIONS</h3> <p>contain both long-acting beta<sub>2</sub>-agonist and short-acting muscarinic antagonist</p> |
| <p><b>Atrovent<sup>®</sup></b> HFA<br/>10 mcg ipratropium bromide inhalation aerosol</p> <p><b>Incusep<sup>®</sup></b> Ellipta<sup>®</sup><br/>62.5 mcg tiotropium bromide inhalation powder</p> <p><b>Spiriva<sup>®</sup></b> HandiHaler<sup>®</sup><br/>18 mcg tiotropium bromide inhalation powder</p> <p><b>Spiriva<sup>®</sup></b> RespiMat<sup>®</sup><br/>1.8, 3.6 mcg tiotropium bromide inhalation powder</p> <p><b>Tudorza<sup>®</sup></b> Pressair<sup>®</sup><br/>400 mcg acetylsalicylic acid inhalation powder</p>  | <p><b>Combivent<sup>®</sup></b> RespiMat<sup>®</sup><br/>20/100 mcg ipratropium bromide and salmeterol xinafoate inhalation powder</p>   | <h3>COMBINATION MEDICATIONS</h3> <p>contain both long-acting beta<sub>2</sub>-agonist and long-acting corticosteroid</p>  |  |
| <p><b>Advair Diskus<sup>®</sup></b><br/>100/60, 250/60, 500/60 mcg fluticasone propionate and salmeterol xinafoate inhalation powder</p> <p><b>Advair<sup>®</sup></b> HFA<br/>250/10, 500/10, 750/10 mcg fluticasone propionate and salmeterol xinafoate inhalation aerosol</p> <p><b>AirDuo<sup>®</sup></b> Digihaler<sup>®</sup><br/>100/4, 250/4, 500/4 mcg fluticasone propionate and salmeterol xinafoate inhalation powder</p> <p><b>AirDuo<sup>®</sup></b> RespClick<sup>®</sup><br/>100/4, 250/4, 500/4 mcg fluticasone propionate and salmeterol xinafoate inhalation powder</p> <p><b>Brevo<sup>®</sup></b> Ellipta<sup>®</sup><br/>100/5, 250/5, 500/5 mcg budesonide and formoterol fumarate dihydrate inhalation powder</p> <p><b>Dufera<sup>®</sup></b><br/>100/5, 100/5, 250/5 mcg budesonide and formoterol fumarate dihydrate inhalation powder</p> <p><b>Symbicort<sup>®</sup></b><br/>100/6, 100/6, 200/6 mcg budesonide and formoterol fumarate dihydrate inhalation powder</p> <p><b>Wixela<sup>®</sup></b> Inhub<sup>®</sup><br/>100/50, 250/50 mcg fluticasone propionate and budesonide inhalation powder</p> | <p><b>Asmanex<sup>®</sup></b> Ellipta<sup>®</sup><br/>62.5/50, 125/50 mcg mometasone furoate and formoterol fumarate dihydrate inhalation powder</p> <p><b>Brevo<sup>®</sup></b> Pressair<sup>®</sup><br/>80/400, 160/400 mcg budesonide and formoterol fumarate dihydrate inhalation powder</p> <p><b>Duakir<sup>®</sup></b> Pressair<sup>®</sup><br/>400, 12 mcg budesonide and formoterol fumarate dihydrate inhalation powder</p> <p><b>Silofta<sup>®</sup></b> RespiMat<sup>®</sup><br/>2.5/2.5, 5.0/5.0 mcg budesonide and formoterol fumarate dihydrate inhalation powder</p> <p><b>Tyflo<sup>®</sup></b> Ellipta<sup>®</sup><br/>200/62.5/25, 400/125/50 mcg budesonide, formoterol fumarate dihydrate, and ipratropium bromide inhalation powder</p> <p><b>Brevo<sup>®</sup></b> Pressair<sup>®</sup><br/>100/50/50, 250/50/50 mcg budesonide, formoterol fumarate dihydrate, and ipratropium bromide inhalation powder</p> | <h3>COMBINATION MEDICATIONS</h3> <p>contain both long-acting beta<sub>2</sub>-agonist and long-acting corticosteroid</p>  |  |
| <h3>BIOLOGICS</h3> <p>target cells and pathways that cause airway inflammation, delivered by injection or IV</p> <p><b>Cinqair<sup>®</sup></b> mepolizumab</p> <p><b>Dupixent<sup>®</sup></b> dupilumab</p> <p><b>Fasenra<sup>®</sup></b> reslizumab</p> <p><b>Nucala<sup>®</sup></b> mepolizumab</p> <p><b>Xolair<sup>®</sup></b> omalizumab</p>   | <h3>BRONCHIAL THERMOPLASTY</h3> <p>A minimally invasive procedure that uses radiofrequency to reduce airway smooth muscle, leading to fewer severe asthma flares, ER visits, and days lost from activities.</p>  | <h3>PDE4 INHIBITORS</h3> <p>relax tight muscles in airways and reduce inflammation</p> <p><b>Daliresp<sup>®</sup></b> 300, 500 mcg roflumilast inhalation powder</p>  |  |

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## Six Priority Topics

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1. Fractional exhaled nitric oxide (FeNO) in diagnosis, medication selection, and monitoring of treatment response in asthma
2. Remediation of indoor allergens in asthma management
3. Adjustable medication dosing in recurrent wheezing and asthma
4. Long-acting muscarinic antagonists (LAMAs) as add-on therapy
5. Immunotherapy and the management of asthma
6. Bronchial thermoplasty in adult severe asthma



Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## Six Priority Topics (re-ordered!)

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1. Adjustable medication dosing in recurrent wheezing and asthma
2. Long-acting muscarinic antagonists (LAMAs) as add-on therapy
3. Fractional exhaled nitric oxide (FeNO) in diagnosis, medication selection, and monitoring of treatment response in asthma
4. Remediation of indoor allergens in asthma management
5. Immunotherapy and the management of asthma
6. Bronchial thermoplasty in adult severe asthma



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<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## Emerging Topics (but no new recommendations)

- Adherence
- Asthma action plans
- Asthma heterogeneity
- Biologic agents
- Biomarkers (other than FeNO)
- Classification of asthma severity
- Long-acting beta<sub>2</sub>-agonist (LABA) safety
- Physiological assessments
- Prevention of asthma onset
- Role of community health workers in asthma management
- Step-down from maintenance therapy

**Multiple new biologics in pediatrics**

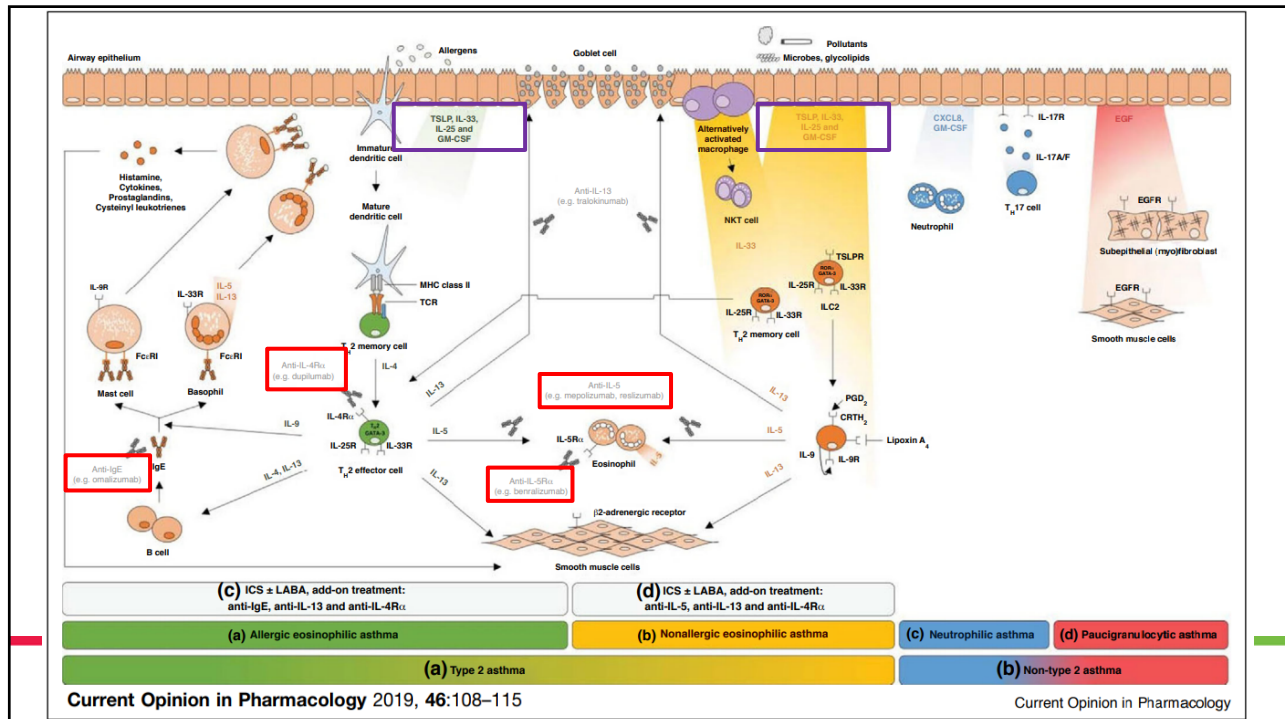
**Removal of black box warning in 2018 (but now a warning on montelukast)**



Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## Stepwise management (ages 0-4)

|  | Intermittent Asthma  | Management of Persistent Asthma in Individuals Ages 0-4 Years |                                    |   |   |  |
|--|--|---|------------------------------------|---|---|--|
| Treatment  | STEP 1   | STEP 2  | STEP 3                             | STEP 4  | STEP 5  | STEP 6   |
| <b>Preferred</b>   | PRN SABA and<br>At the start of RTI: Add short course daily ICS <sup>▲</sup> | Daily low-dose ICS and PRN SABA                               | Daily medium-dose ICS and PRN SABA | Daily medium-dose ICS-LABA and PRN SABA           | Daily high-dose ICS-LABA and PRN SABA           | Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA           |
| <b>Alternative</b>   |  | Daily montelukast* or Cromolyn,* and PRN SABA                 |                                    | Daily medium-dose ICS + montelukast* and PRN SABA | Daily high-dose ICS + montelukast* and PRN SABA | Daily high-dose ICS + montelukast* + oral systemic corticosteroid and PRN SABA |
| <small>For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5-11 Years diagram.</small>   |  |   |                                    |   |   |  |
| <b>Assess Control</b>  |  |   |                                    |   |   |  |
| <ul style="list-style-type: none"> <li>• First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.</li> <li>• <b>Step up</b> if needed; reassess in 4-6 weeks</li> <li>• <b>Step down</b> if possible (if asthma is well controlled for at least 3 consecutive months)</li> </ul> <p>Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.</p> |  |   |                                    |   |   |  |

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## Intermittent ICS in Children 0-4 with Recurrent Wheezing

- **Defined as: 3 lifetime episodes of infection-triggered wheezing or 2 in past year without symptoms between infections**
- **Two studies used nebulized budesonide 1mg BID x 7 days**
- **Reduced need for systemic steroids**
- **No increased asthma-related acute care visits**
- **Decreases overall exposure to ICS vs daily treatment**
- **Can be started at home by caregivers**

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## PRN SABA/ICS vs SABA alone

**Evidence Summary:** Intermittent Inhaled Corticosteroid with As-Needed Short-Acting Beta<sub>2</sub>-Agonist vs. As-Needed Short-Acting Beta<sub>2</sub>-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                       |
| <b>EXACERBATIONS (CRITICAL OUTCOME)</b>                  |  |                               |                          |                                       |   |
| Need for systemic corticosteroids<br>Follow-up: 52 weeks | 324 (3 RCTs) <sup>2-4</sup>                | High                          | RR: 0.67 (0.46 to 0.98)  | 79/140 (56.4%)                        | <b>Favors Intervention</b><br>70/184 (38.0%),<br>186 fewer per 1,000 (from 305 fewer to 11 fewer) |
| Asthma-related acute care visits<br>Follow-up: 52 weeks  | 324 (3 RCTs) <sup>2-4</sup>                | Moderate <sup>a</sup>         | RR: 0.90 (0.77 to 1.05)  | 92/140 (65.7%)                        | <b>No difference</b><br>106/184 (57.6%), 66 fewer per 1,000 (from 151 fewer to 33 more)           |



Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## Daily ICS vs PRN ICS + prn SABA

**Evidence Summary:** Intermittent Inhaled Corticosteroid with As-Needed Short-Acting Beta<sub>2</sub>-Agonist vs. Inhaled Corticosteroid Controller Therapy with As-Needed Short-Acting Beta<sub>2</sub>-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        |
| <b>EXACERBATIONS (CRITICAL OUTCOME)</b>                  |  |                               |                          |                                       |  |
| Need for systemic corticosteroids<br>Follow-up: 52 weeks | 278 (1 RCT) <sup>6</sup>                   | Moderate <sup>a</sup>         | RR: 0.99 (0.80 to 1.22)  | N = 139                               | <b>No difference</b><br>N = 139  |
| Asthma-related hospitalizations<br>Follow-up: 52 weeks   | 278 (1 RCT) <sup>6</sup>                   | Low <sup>b</sup>              | RR: 1.25 (0.34 to 4.56)  | 4/139 (2.9%)                          | <b>No difference</b><br>5/139 (3.6%), 7 more per 1,000 (from 19 fewer to 102 more) |



Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## Stepwise management ages 5-11

|                    | Intermittent Asthma | Management of Persistent Asthma in Individuals Ages 5-11 Years  |   |   |  |  |
|--------------------|---------------------|---|---|---|--|--|
| Treatment          | STEP 1              | STEP 2  | STEP 3  | STEP 4  | STEP 5   | STEP 6   |
| <b>Preferred</b>   | PRN SABA            | Daily low-dose ICS and PRN SABA   | Daily and PRN combination low-dose ICS-formoterol <sup>▲</sup>  | Daily and PRN combination medium-dose ICS-formoterol <sup>▲</sup>   | Daily high-dose ICS-LABA and PRN SABA  | Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA   |
| <b>Alternative</b> |                     | Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA   | Daily medium-dose ICS and PRN SABA<br>or<br>Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS + Theophylline,* and PRN SABA | Daily medium-dose ICS-LABA and PRN SABA<br>or<br>Daily medium-dose ICS + LTRA* or daily medium-dose ICS + Theophylline,* and PRN SABA | Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA | Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA |
|                    |                     | Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy <sup>▲</sup> |   |   | Consider Omalizumab <sup>**▲</sup>   |  |

<sup>▲</sup> Updated based on the 2020 guidelines.

\* Cromolyn, Nedocromil, LTRAs including montelukast, and Theophylline were not considered in this update and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a **Boxed Warning for montelukast in March 2020**.

**\*\* Omalizumab is the only asthma biologic currently FDA-approved for this age range.**

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## SMART

- S – Single**
- M – Maintenance**
- A – and**
- R – Reliever**
- T – Therapy**



**No albuterol (or other SABA)**




**Formoterol containing ICS/LABA inhaler ONLY**

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I am using SMART...



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**Poll Everywhere**

**PollEv.com/ulpulm**


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Barriers to SMART use in my practice are...



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**Poll Everywhere**

**PollEv.com/ulpulm**

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## SMART

- Preferred therapy for steps 3 and 4 for ages 5-11 and 12+
- Not recommended solely for PRN use
- Maximum inhalations per day is **8 puffs for 5-11** and **12 puffs for 12 and older**
- **WHY SMART?**
  - Easier therapy: no confusion between inhalers
  - Ensures patients receive anti-inflammatory treatment with symptoms
  - Part of the GINA guidelines since mid 2010s



Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## Evidence Base (SMART v ICS/LABA + SABA, 4-11)

| Outcomes   | Number of participants (number of studies) | Certainty of evidence (GRADE) | Relative effect (95% CI)   | Anticipated absolute effects (95% CI)  |  |
|--|--|-------------------------------|----------------------------|--|--|
|  |  |                               |                            | Risk with ICS-LABA controller and SABA quick relief therapy (same ICS dose) and/or N | Risk difference or mean difference with ICS-LABA controller and reliever therapy               |
| <b>EXACERBATIONS (CRITICAL OUTCOME)</b>  |  |                               |                            |  |  |
| Composite outcome comprising need for hospitalization, systemic corticosteroids, ED visits, or increased doses of ICS or other medications <sup>b</sup><br>Follow-up: 52 weeks | 235 <sup>a</sup><br>(1 RCT) <sup>2</sup>   | Moderate <sup>d</sup>         | RR: 0.28<br>(0.14 to 0.53) | 36/117 (30.8%)   | <b>Favors intervention</b><br>10/118 (8.5%), 222 fewer per 1,000 (from 265 fewer to 145 fewer) |
| <b>ASTHMA CONTROL (CRITICAL OUTCOME)</b>   |  |                               |                            |  |  |
| Not reported   |  |                               |                            |  |  |
| <b>QUALITY OF LIFE (CRITICAL OUTCOME)</b>  |  |                               |                            |  |  |
| Not reported   |  |                               |                            |  |  |

**Less steroid exposure (126 ug vs 320 ug/day) AND improved growth (mean difference 1cm)**

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## Evidence Base (SMART v ICS/LABA + SABA, 12+)

| Outcomes  | Number of participants (number of studies)   | Certainty of evidence (GRADE) | Relative effect (95% CI)   | Anticipated absolute effects (95% CI)  |  |
|---|--|-------------------------------|----------------------------|--|--|
|   |  |                               |                            | Risk with ICS-LABA controller and SABA quick-relief therapy (same ICS dose) and/or N | Risk difference or mean difference with ICS-LABA controller and reliever therapy                         |
| <b>EXACERBATIONS (CRITICAL OUTCOME)</b>   |  |                               |                            |  |  |
| Need for systemic corticosteroids<br>Follow-up: 48 to 52 weeks  | 3,792<br>(2 RCTs) <sup>15</sup>              | High                          | RR: 0.70<br>(0.57 to 0.86) | 311/1,891 (16.4%)  | <b>Favors intervention</b><br>219/1,901 (11.5%),<br>49 fewer per 1,000<br>(from 71 fewer to 23 fewer)    |
| Requiring hospitalization<br>Follow-up: 24 to 52 weeks  | 2,394 <sup>a</sup><br>(2 RCTs) <sup>16</sup> | Moderate <sup>b</sup>         | RR: 0.39<br>(0.18 to 0.85) | 35/1,194 (2.9%)  | <b>Favors intervention</b><br>13/1,200 (1.1%), 18<br>fewer per 1,000<br>(from 24 fewer to 4<br>fewer)    |
| Requiring ED visit<br>Follow-up: 52 weeks   | 2,091<br>(1 RCT) <sup>c</sup>                | High                          | RR: 0.74<br>(0.59 to 0.93) | 151/1,042 (14.5%)  | <b>Favors intervention</b><br>112/1,049 (10.7%),<br>38 fewer per 1,000<br>(from 59 fewer to 10<br>fewer) |
| Composite outcome of need for systemic corticosteroid treatment, hospitalization, or ED visit <sup>c,d</sup><br>Follow-up: 24 to 52 weeks | 8,483<br>(5 RCTs) <sup>17,e</sup>            | High                          | RR: 0.68<br>(0.58 to 0.80) | 843/4,257 (19.8%)  | <b>Favors intervention</b><br>572/4,226 (13.5%), 63<br>per 1,000 (from 83<br>fewer to 40 fewer)          |

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## Caveats...

- There were 16 randomized controlled trials in the Systematic Review with Meta-Analysis, relied upon by the NAEPF
- Only 1 employed the budesonide-formoterol MDI available in the US
- Another employed a beclomethasone-formoterol combination available
- The remaining 14 studies employed the budesonide-formoterol dry powder inhaler (Symbicort Turbuhaler) that delivers twice as much budesonide to the airways as the MDI
- There are no studies of SMART using mometasone-formoterol HFA MDI

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## Which products are SMART to use?

**YES!**



**Budesonide-formoterol**

**Mometasone-formoterol**

**NO!**



**Any ICS-salmeterol therapy**

**Any ICS/ultra-LABAs (Vilanterol)**



Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## Barriers to SMART implementation

- While endorsed by the guideline updates, formoterol/ICS products do not yet have specific FDA approval for use in acute bronchospasm
- Significant education for caregivers and other stakeholders is needed (pharmacies, schools, etc.)
- Payor acceptance required (for more than 1 ICS/LABA inhaler/month)
- Lack of evidence with spacing of rescue doses or dose for exercise pre-treatment

INDICATIONS AND USAGE

is a combination product containing a corticosteroid and a long-acting beta<sub>2</sub>-adrenergic agonist indicated for:

- Treatment of asthma in patients 6 years of age and older. (1.1)
- Maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and emphysema. (1.2)

Important limitations:

- Not indicated for the relief of acute bronchospasm. (1.1, 1.2)



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## Stepwise management for ages 12+

| Treatment          | STEP 1   | STEP 2   | STEP 3   | STEP 4  | STEP 5  | STEP 6 <sup>■</sup>   |
|--------------------|----------|--|--|---|---|---|
| <b>Preferred</b>   | PRN SABA | Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA ▲  | Daily and PRN combination low-dose ICS-formoterol ▲  | Daily and PRN combination medium-dose ICS-formoterol ▲  | Daily medium-high dose ICS-LABA + LAMA and PRN SABA ▲                                   | Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA |
| <b>Alternative</b> |          | Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA  | Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA,▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA | Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA ▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA | Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA            |   |
|                    |          | Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy ▲ |  |   | Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)** |   |

\*\* The AHRQ systematic reviews that informed this report did not include studies that examined the role of asthma biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13). Thus, this report does not contain specific recommendations for the use of biologics in asthma in Steps 5 and 6.

■ Data on the use of LAMA therapy in individuals with severe persistent asthma (Step 6) were not included in the AHRQ systematic review and thus no recommendation is made.

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## Stepwise management for ages 12+

- Option for prn low dose ICS + SABA for mild, persistent asthma (step 2)
  - Specifically mentions albuterol 2-4p followed by 80-250 mcg of beclomethasone equivalent q4h prn
  - Therapy can be started at home with follow up as needed
  - Not ideal for patients with very high or low perception of symptoms
- Option for LAMA use in steps 3-5 (preferred in step 5)
- SMART therapy steps 3-4 as discussed



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**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 |
| <b>EXACERBATIONS (CRITICAL OUTCOME)</b>                                |  |                               |                          |                                       |  |
| Need for systemic corticosteroids <sup>2b</sup><br>Follow-up: 52 weeks | 149 (1 RCT) <sup>2</sup>                   | Low <sup>c</sup>              | RR: 0.70 (0.30 to 1.64)  | N = 73                                | No difference<br>N = 76  |
| Asthma-related hospitalizations<br>Follow-up: 52 weeks                 | 149 (1 RCT) <sup>2</sup>                   | Very low <sup>d</sup>         | —                        | 0/73 (0.0%)                           | No events, (0/76 (0.0%))   |
| Asthma-related urgent care visits <sup>a</sup><br>Follow-up: 36 weeks  | 227 (1 RCT) <sup>3</sup>                   | Low <sup>c</sup>              | RR: 0.25 (0.05 to 1.16)  | N = 114                               | No difference<br>N = 113   |



Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>

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| 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  |
| <b>ASTHMA CONTROL (CRITICAL OUTCOME)</b>   |  |                               |                          |                                       |   |
| ACQ-7 scores of 0 for no impairment to 7 for maximum (MID for ages ≥18 years: 0.5 points) <sup>7</sup><br>Follow-up: 12 months | 149 (1 RCT) <sup>2</sup>                   | High                          | —                        | N = 73                                | No difference<br>N = 76<br>MD: 0.1 higher<br>(from 0.12 lower to 0.32 higher)   |
| <b>QUALITY OF LIFE (CRITICAL OUTCOME)</b>  |  |                               |                          |                                       |   |
| AQLQ scores of 1 for severe to 7 for no impairment (MID: 0.5 points)<br>Follow-up: 36 to 52 weeks                              | 376 (2 RCT) <sup>2,3</sup>                 | High                          | —                        | N = 187                               | No difference<br>N = 189<br>MD: 0.2 lower <sup>2</sup><br>(from 0.48 lower to 0.08 higher)<br>No difference<br>MD: 0.01 higher <sup>3</sup><br>(from 0.19 lower to 0.21 higher) |
| <b>RESCUE MEDICATION USE (IMPORTANT OUTCOME)</b>   |  |                               |                          |                                       |   |
| Albuterol puffs/day (MID for ages ≥18 years: -0.81 puffs/day)<br>Follow-up: 24 to 36 weeks                                     | 564 (2 RCT) <sup>3,4</sup>                 | High                          | —                        | —                                     | No difference<br>MD: 0.07 more <sup>4</sup><br>(from 0.13 fewer to 0.26 more)<br>No difference<br>MD: 0.04 fewer <sup>3</sup><br>(from 0.11 fewer to 0.03 more)                 |

Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>

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## ICS GRADE Summary

| Question | Intervention   | Comparator                          | Recommendation  | Certainty of Evidence |
|----------|--|-------------------------------------|---|-----------------------|
| 4.1      | Short-course daily ICS + as-needed SABA at start of RTI (Step 1) | As-needed SABA alone                | Recommendation 9: Conditional, in favor of the intervention for ages 0-4 years                                    | High                  |
|          |  | Daily ICS                           | No recommendation*  |                       |
|          |  | No therapy                          | No recommendation*  |                       |
| 4.2      | As-needed, concomitantly administered ICS + SABA                 | Daily ICS + as-needed SABA (Step 2) | Recommendation 10: Conditional, in favor of either the intervention or the comparator for ages 12 years and older | Moderate              |
|          |  |                                     | No recommendation* for ages 4-11 years  |                       |
|          | Intermittent, higher-dose ICS                                    |                                     | Recommendation 11: Conditional, against the intervention for ages 4 years and older                               | Low                   |



Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## SMART GRADE Summary

| Question | Intervention                                       | Comparator                                  | Recommendation   | Certainty of Evidence  |
|----------|--|---|--|--|
| 4.3      | Daily and as-needed ICS-formoterol (Steps 3 and 4) | Daily same-dose ICS + as-needed SABA        | No recommendation* for ages 4 years and older  |  |
|          |  | Daily higher-dose ICS + as-needed SABA      | Recommendation 12: Strong, in favor of the intervention for ages 4 years and older       | Moderate for ages 4-11 years<br>High for ages 12 years and older |
|          |  | Daily same-dose ICS-LABA + as-needed SABA   | Recommendation 12: Strong, in favor of the intervention for ages 4 years and older       | Moderate for ages 4-11 years<br>High for ages 12 years and older |
|          |  | Daily higher-dose ICS-LABA + as-needed SABA | No recommendation* for ages 4-11 years   |  |
|          |  |   | Recommendation 13: Conditional, in favor of the intervention for ages 12 years and older | High for ages 12 years and older                                 |

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I have used intermittent ICS in...



**PollEv.com/ulpulm**



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September 9, 2021

## Albuterol/Budesonide Fixed-Dose Combo Looks Promising in Asthma Trials



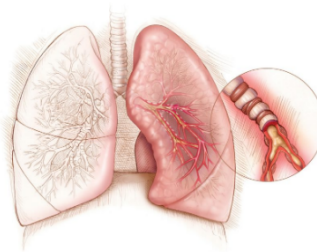
Brian Park, PharmD



Topline results were announced from two phase 3 studies evaluating a fixed-dose combination of albuterol, a short-acting beta2-agonist (SABA), and budesonide, an inhaled corticosteroid (ICS), in patients with asthma.

The multicenter, randomized, double-blind, parallel-group MANDALA trial (ClinicalTrials.gov Identifier: [NCT03769090](https://clinicaltrials.gov/ct2/show/study/NCT03769090)) evaluated the efficacy and safety of albuterol/budesonide on the time to first severe asthma exacerbation in 3132 patients aged 4 years and older with moderate to severe asthma who were receiving ICS with or without additional medications. Patients were randomly assigned 1:1:1: to receive albuterol/budesonide 180/160mcg, albuterol/budesonide 180/80mcg, or albuterol sulfate metered-dose inhaler 180mcg, as a rescue medication in response to symptoms.

Results showed that patients treated with albuterol/budesonide met the primary endpoint demonstrating statistically significant and clinically meaningful reductions in the risk of severe exacerbations compared with albuterol.



The investigational medicine is delivered in a pressurized metered-dose inhaler. Credit: Getty Images.

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## Comparison with GINA 2021

### Adults & adolescents 12+ years

**CONTROLLER and PREFERRED RELIEVER**  
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

**STEPS 1 – 2**  
As-needed low dose ICS-formoterol

**STEP 3**  
Low dose maintenance ICS-formoterol

**STEP 4**  
Medium dose maintenance ICS-formoterol

**STEP 5**  
Add-on LAMA  
Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R  
Consider high dose ICS-formoterol

RELIEVER: As-needed low-dose ICS-formoterol

**CONTROLLER and ALTERNATIVE RELIEVER**  
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

**STEP 1**  
Take ICS whenever SABA taken

**STEP 2**  
Low dose maintenance ICS

**STEP 3**  
Low dose maintenance ICS-LABA

**STEP 4**  
Medium/high dose maintenance ICS-LABA

**STEP 5**  
Add-on LAMA  
Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R  
Consider high dose ICS-LABA

RELIEVER: As-needed short-acting β<sub>2</sub>-agonist

Other controller options for either track

Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT

Medium dose ICS, or add LTRA, or add HDM SLIT

Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS

Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects

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## Long-acting muscarinic antagonists (LAMAs)

- FDA approved tiotropium as add on maintenance therapy down to age 6
- Guideline updates only address for 12+
- Add LABA to ICS first unless contraindication
- Adding on to ICS/LABA can improve symptoms in uncontrolled patients



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<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>  
Ann Allergy Asthma Immunol 124 (2020) 267e276

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## Fractional Exhaled Nitric Oxide (FeNO)



- **A measure of eosinophilic airway inflammation**
- **Not recommended for 4 and under**
- **May support an asthma diagnosis where uncertainty even with history, physical exam and spirometry (including bronchodilator testing)**
- **Should not be used in isolation for diagnosis or ongoing monitoring**



## Allergen Mitigation

- **Little evidence mitigation strategies are beneficial for improving outcomes across the board**
- **For patients with allergies to specific indoor substance (dust mites), multiple strategies needed concomitantly**
- **Recommend integrated pest management in those allergic and exposed to cockroaches or rodents**
- **No mitigation needed for patients without specific allergies to indoor substances**

| Intervention assessed in studies in the SR            | EtD table number | Evidence on use as a single-component strategy for allergen mitigation (certainty of evidence) | Evidence on use as part of a multicomponent strategy for allergen mitigation (certainty of evidence)* |
|---|------------------|--|---|
| Acaricide   | IV               | †  | Intervention makes no difference (moderate certainty of evidence)                                     |
| Impermeable pillow and mattress covers                | V                | Intervention makes no difference (moderate certainty of evidence)                              | Evidence favors intervention (moderate certainty of evidence)   |
| Carpet removal  | VI               | †  | Intervention makes no difference (low certainty of evidence)  |
| Integrated pest management (for cockroaches and mice) | VII              | Evidence favors intervention (low certainty of evidence)                                       | Evidence favors intervention (low certainty of evidence)  |
| Air filtration systems and air purifiers              | VIII             | Intervention makes no difference (low certainty of evidence)                                   | Intervention makes no difference (moderate certainty of evidence)                                     |
| HEPA vacuum cleaners                                  | IX               | †  | Evidence favors intervention (among children only; moderate certainty of evidence)                    |
| Cleaning products                                     | X                | †  | †   |
| Mold mitigation                                       | XI               | †  | Evidence favors intervention (low certainty of evidence)  |
| Pet removal   | XII              | †  | †   |

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## Subcutaneous Immunotherapy

- **Recommended as an adjunct therapy for people with allergic sensitization and worsening of asthma after exposures**
- **SCIT should not be administered in the setting of active symptoms or those with severe asthma**
- **SCIT should not be given at home**
- **Delayed reactions (after 30 mins) in 15% of patients**
- **Patients with history of significant reactions should carry Epi**
- **Currently no role for oral/sublingual immunotherapy**

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## Bronchial Thermoplasty

- In individuals ages 18 years and older with persistent asthma, the Expert Panel conditionally recommends against bronchial thermoplasty.
- The risks of BT include asthma exacerbations, hemoptysis, and atelectasis during the treatment period.
- Severe, delayed-onset complications could occur that have not yet been recognized because of the small numbers of individuals who have undergone the procedure.
- Offer the procedure in the setting of a clinical trial or a registry study to enable the collection of long-term data on the use of BT for asthma.

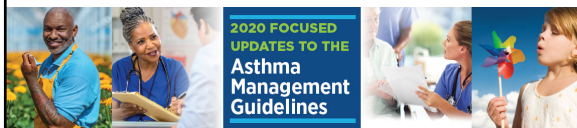


Cloutier, et al. J Allergy Clin Immunol 2020;146:1217-70.  
<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## Digital Toolkit / Resources



### CLINICIAN'S GUIDE

#### PURPOSE

This Clinician's Guide summarizes the 2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group to help clinicians integrate the new recommendations into clinical care. The full 2020 Report, which is focused on selected topics rather than a complete revision of the 2007 Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR-3), can be found at [nhlbi.nih.gov/asthmaguidelines](https://www.nhlbi.nih.gov/asthmaguidelines). This summary guide should be used in conjunction with the full report. The Guide is organized by the following topics:

- Intermittent Inhaled Corticosteroids
- Long-Acting Muscarinic Antagonists
- Indoor Allergen Mitigation
- Immunotherapy in the Treatment of Allergic Asthma
- Fractional Exhaled Nitric Oxide Testing
- Bronchial Thermoplasty



#### Fact Sheets

Share these fact sheets to help patients understand different treatment options and asthma management:

- [Asthma Management Guidelines and Your Care](#)
- [The Changing Role of Inhaled Corticosteroids in Asthma Management](#)
- [Long-Acting Muscarinic Antagonists \(LAMAs\)](#)
- [Reducing Allergens in Your Home](#)
- [Can Immunotherapy Help with the Treatment of Allergic Asthma?](#)
- [What is Fractional Exhaled Nitric Oxide \(FeNO\) Testing?](#)
- [Is Bronchial Thermoplasty Right for You?](#)
- [2020 Asthma Action Plan](#)



#### Asthma Action Plan

Use this worksheet in coordination with your health care provider to write down your plan to monitor your asthma and treat changing symptoms or attacks:

- [2020 Asthma Action Plan](#)



<https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates>



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## Take Home Points

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- **Guideline updates provide new flexibility in many populations**
- **Intermittent ICS + SABA may be used in 0-4 and 12+ in appropriate patients**
- **SMART is preferred Step 3 and 4 therapy for 5+ but barriers to implementation remain**
- **New recommendations on LAMAs, SCIT and allergy mitigation provide additional tools to achieve control**
- **Updates likely to become more frequent than previous**



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## Thank you!

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### Questions?



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