



# From inflammation to remission: Updates in adult asthma management

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## Objectives

- Apply evidence-based management of mild asthma, with a focus on AIR and MART therapy
- Identify and differentiate difficult-to-treat asthma from severe asthma
- Understand role of biologics in the treatment of severe asthma, with a potential to achieve clinical remission

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## Pediatric Objectives

- Recognize appropriate candidates for single maintenance and reliever therapy in a pediatric patient.
- Apply evidence-based medication management for intermittent asthma in a pediatric patient.
- Understand that there are multiple therapy options to treat pediatric asthma and therapy needs to be customized to the patient.

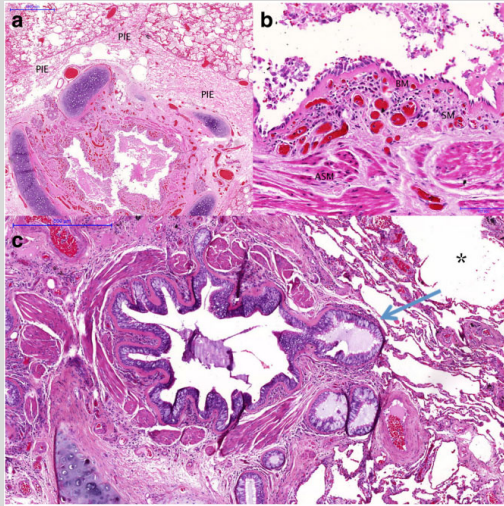
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## Disclosures

- No financial disclosures
- The use of budesonide-formoterol on an as needed basis, and as single maintenance and reliever therapy (SMART) is **off-label use** in the US

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## Asthma



“**Heterogenous** disease, usually characterized by **chronic airway inflammation**.”

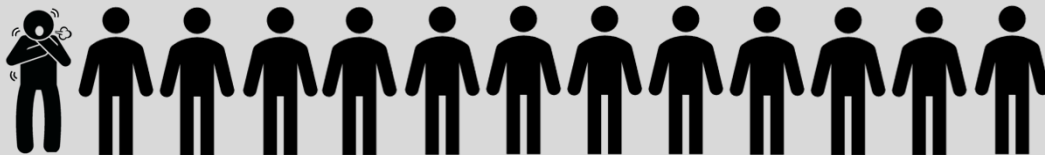
It is defined by the history of **respiratory symptoms** such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with **variable airflow limitation**.

One or more symptoms may predominate. **Airflow limitation may later become persistent.**”

GINA 2024  
Mauad et al. BMC Pulmonary Medicine 2018 <https://doi.org/10.1186/s12890-018-0615-7>

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## Asthma



1 million  
ER visits

3,518  
deaths

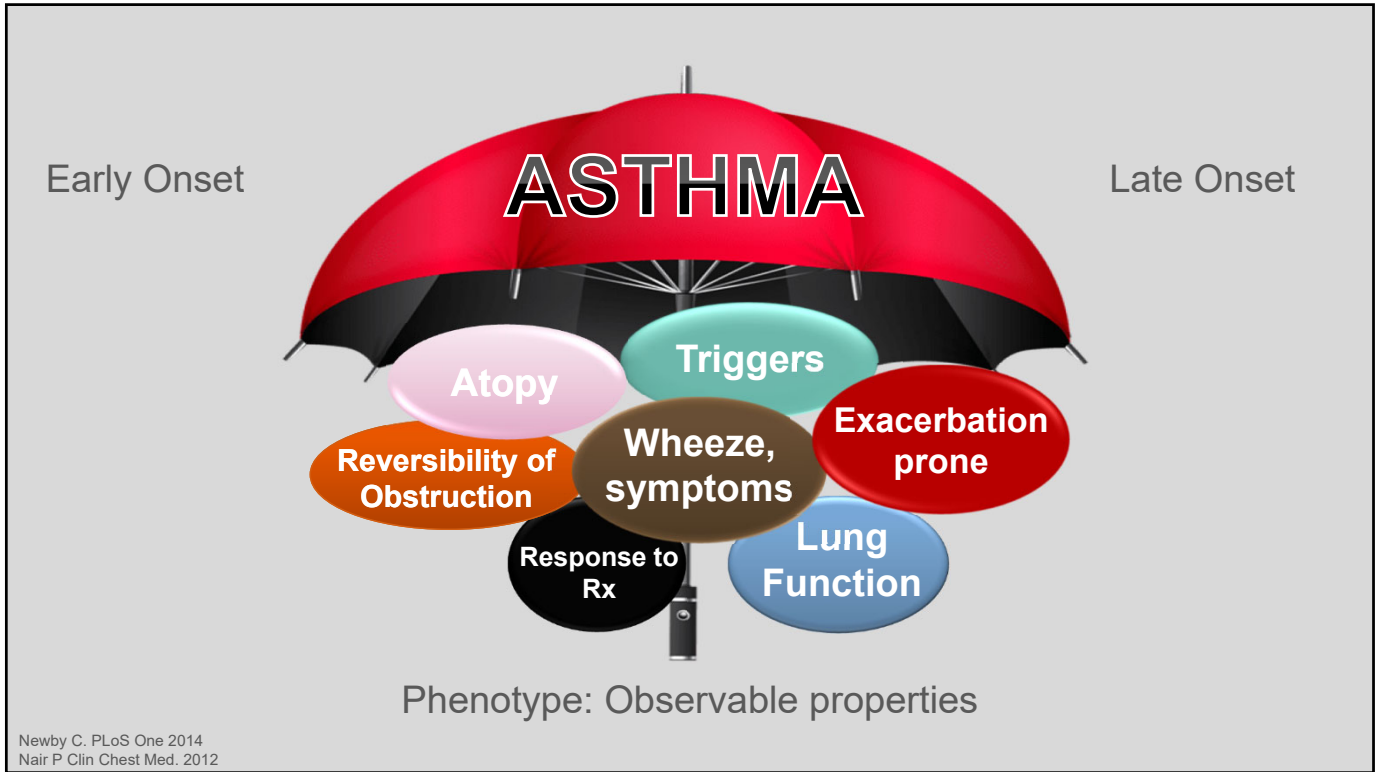
62%  
uncontrolled

30%  
misdiagnosed

>50%  
incorrect  
inhaler  
technique

cdc.gov- 2001-2021 data ; Aaron SD et al JAMA 2017 ; Melani AS et al Respir Med 2011; Souza ML J Bras Pneumol 2009

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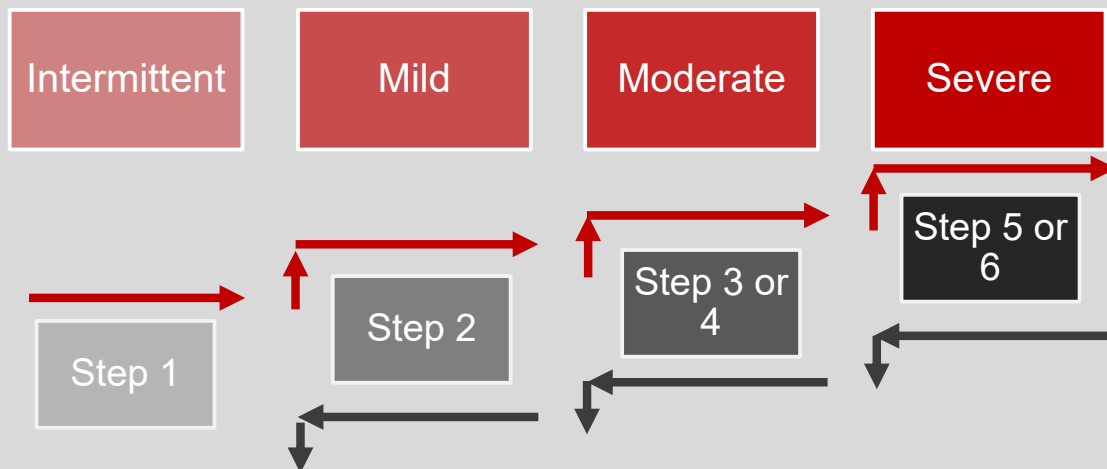


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## Definitions- asthma severity



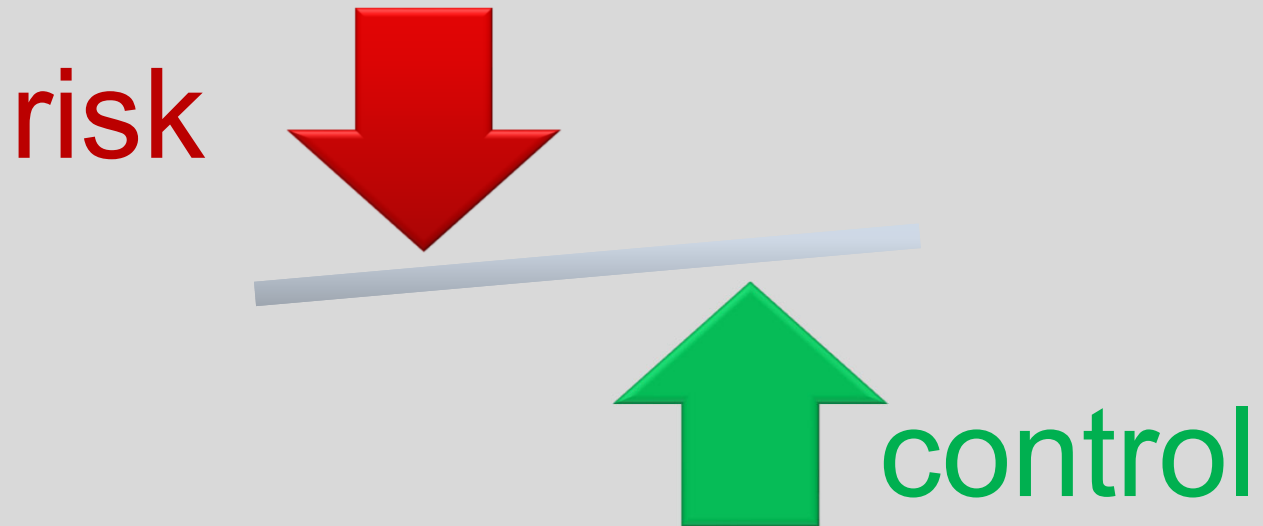
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## Definitions- treatment class

- **ICS: Inhaled Corticosteroid**
  - Budesonide, mometasone, fluticasone, beclomethasone etc
- **LABA: Long-Acting Beta Agonist**
  - Formoterol, salmeterol, vilanterol as ICS- combination therapy
- **SABA: Short-Acting Beta Agonist**
  - Albuterol, levalbuterol
- **LAMA: Long-Acting Muscarinic Antagonists**
  - Tiotropium, umeclidium, glycopyrrolate etc

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## Treatment Goals in Asthma



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## Definitions- treatment concepts

- (S)MART: single Maintenance and Reliever Therapy
  - Most data in budesonide-formoterol
  - “ICS-formoterol”
  - Not just a *single* inhaler- need 2! (*home and school/work*)

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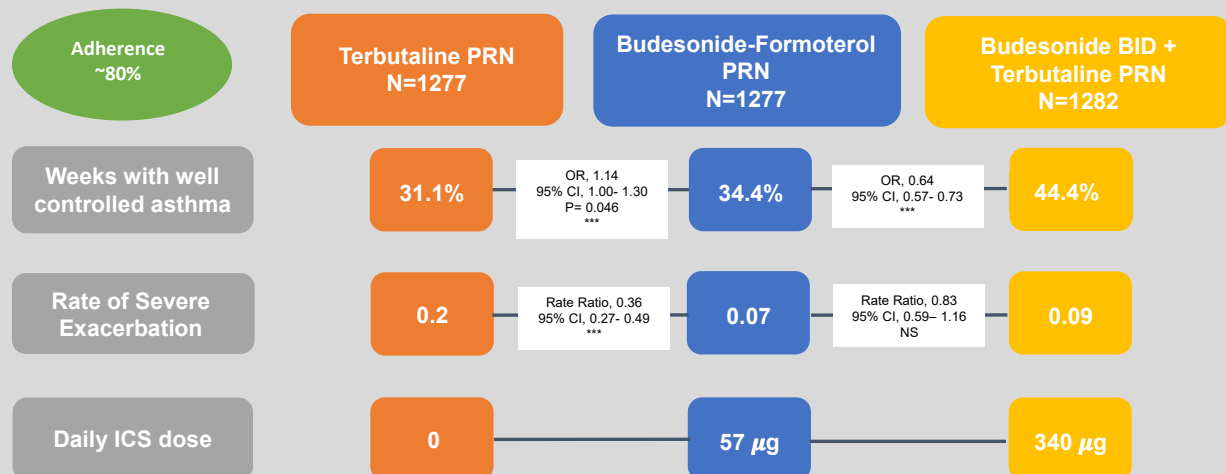
## Definitions- treatment concepts

- **(S)MART: single Maintenance and Reliever Therapy**
  - Most data in budesonide-formoterol
  - “ICS-formoterol”
  - Not just a *single* inhaler- need 2! (*home and school/work*)
- **AIR: Anti-inflammatory Reliever**
  - Inhaled corticosteroid- **formoterol**
  - Budesonide- albuterol
  - AIR- only, ICS LABA with AIR therapy, MART provides AIR

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## Symbicort Given As Needed in Mild Asthma 1

Mild asthma: SABA vs ICS-LABA PRN vs ICS BID



O'Byrne et al NEJM 2018

SYGMA 2 Bateman et al NEJM 2018  
 NOVEL START Beasley et al NEJM 2019  
 PRACTICAL Hardy J et al Lancet 2019

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## ICS- formoterol provides superior exacerbation reduction across asthma spectrum

Table I. Risk of severe asthma exacerbations with ICS/formoterol reliever vs SABA reliever according to maintenance treatment

ICS/formoterol alone vs SABA alone <sup>14</sup>	OR, 0.45; 95% CI, 0.34- 0.60
ICS/formoterol alone vs low-dose ICS plus SABA <sup>14</sup>	OR, 0.79; 95% CI, 0.59- 1.07
ICS/formoterol SMART vs same-dose ICS plus SABA <sup>13</sup>	RR, 0.64; 95% CI, 0.53- 0.78
ICS/formoterol SMART vs 2× dose ICS plus SABA <sup>13</sup>	RR, 0.59; 95% CI, 0.49- 0.71
ICS/formoterol SMART vs same-dose ICS/LABA plus SABA <sup>13</sup>	RR, 0.68; 95% CI, 0.58- 0.80
ICS/formoterol SMART vs 2× dose ICS/LABA plus SABA <sup>13</sup>	RR, 0.77; 95% CI, 0.60- 0.98

OR, Odds ratio; RR, risk ratio.

Beasley R J *Allergy Clin Immunol Pract.* 2023 - Creative Commons License

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## Anti-Inflammatory Reliever Therapy

- Deliver reliever with ICS
  - Treat symptoms and inflammatory etiology
- How to dose AIR:
  - Budesonide- Formoterol 160/4.5 mcg 1 puff PRN
  - Budesonide- Formoterol 80/4.5 mcg 2 puff PRN
  - As of 2024: Budesonide- Albuterol 80/90 2 puff PRN
  - *Max daily: 12 inhalations*

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## What about ICS-Albuterol?

- 12 + with uncontrolled moderate to severe asthma on scheduled ICS +/- LABA
- Budesonide-Albuterol 160/180 PRN reduced risk of severe exacerbation compared to albuterol 180 alone ( $n=3,123$ )
- Both albuterol and budesonide components contribute efficacy in improved lung function
- Ongoing trial using BUD-ALB as step 1 therapy

MANDALA Papi A NEJM 2022 | DENALI Chipps B CHEST 2023 | BATURA design LaForce C J Asthma Allergy 2024

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## Budesonide- albuterol labelling

- As needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients  $\geq 18$  years of age with asthma.
- **AIR added to maintenance ICS therapy**

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# Guiding Publications



GLOBAL INITIATIVE FOR ASTHMA



**U.S. Department of Health and Human Services**  
National Institutes of Health  
National Heart, Lung, and Blood Institute

NIH/NAEPP Expert Panel Report

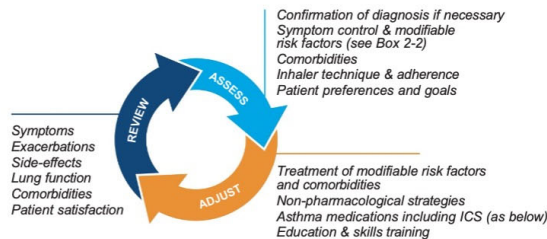
Ginasthma.org  
Nhlbi.nih.gov/AsthmaGuidelines

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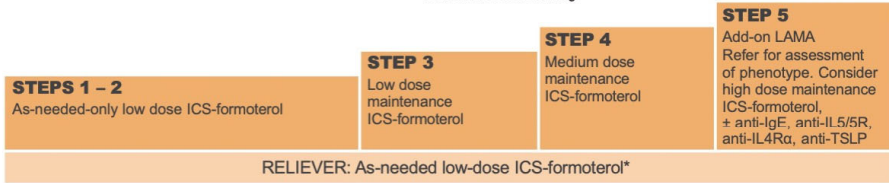
## GINA 2024 – Adults & adolescents 12+ years

### Personalized asthma management

Assess, Adjust, Review  
for individual patient needs

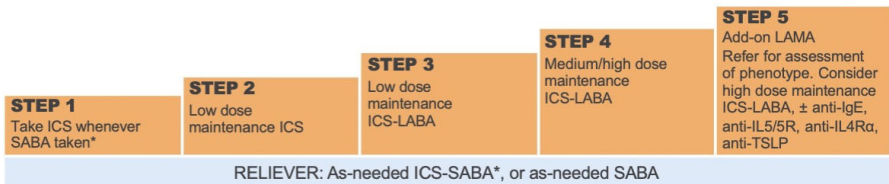


**TRACK 1: PREFERRED CONTROLLER and RELIEVER**  
Using ICS-formoterol as the reliever\* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen



See GINA severe asthma guide

**TRACK 2: Alternative CONTROLLER and RELIEVER**  
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment



Other controller options (limited indications, or less evidence for efficacy or safety – see text)

Low dose ICS whenever SABA taken*, or daily LTRA <sup>1</sup> , or add HDM SLIT	Medium dose ICS, or add LTRA <sup>1</sup> , or add HDM SLIT	Add LAMA or add LTRA <sup>1</sup> , or add HDM SLIT, or switch to high dose ICS-only	Add azithromycin (adults) or add LTRA <sup>1</sup> . As last resort consider adding low dose OCS but consider side-effects
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\*Anti-inflammatory reliever; <sup>1</sup>advise about risk of neuropsychiatric adverse effects

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## AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
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 <sup>▲</sup>	Daily and PRN combination low-dose ICS-formoterol <sup>▲</sup>	Daily and PRN combination medium-dose ICS-formoterol <sup>▲</sup>	Daily medium-high dose ICS-LABA + LAMA and PRN SABA <sup>▲</sup>	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, <sup>▲</sup> 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 <sup>▲</sup> 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 <sup>▲</sup>			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Nhlbi.nih.gov/AsthmaGuidelines  
Cloutier MM et al JACI 2020

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## SABA only therapy in adults: out of favor

- Adverse effects and clinical outcomes
- Even mild asthma at risk for severe exacerbation and fatal events
- Disease of bronchoconstriction **Inflammation**
  - Patient conceptualized primary treatment matters
- Pragmatic consideration: adherence to scheduled Rx

Dusser Allergy 2007 | Suissa S et al Am J Respir Crit Care Med 1994 | Aldridge RE et al Am J Respir Crit Care Med 2000 | Hancox RJ et al Respir Med 2000

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- Titration of ICS to symptoms more effective at preventing exacerbations
- Anti-inflammatory reliever across all steps of asthma therapy:
  - ICS-formoterol MART or
  - ICS-SABA
- Paradigmatic change

