Asthma Management: Control is the Goal

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Outline

- What is asthma
  - Defining asthma
  - Diagnosing asthma
  - Staging asthma
- How is asthma managed
  - Baseline asthma
  - Acute exacerbations
- How is severe or refractory asthma managed
  - What is an asthma endotype?
  - What do I do with these abnormal labs in my severe asthma patient?

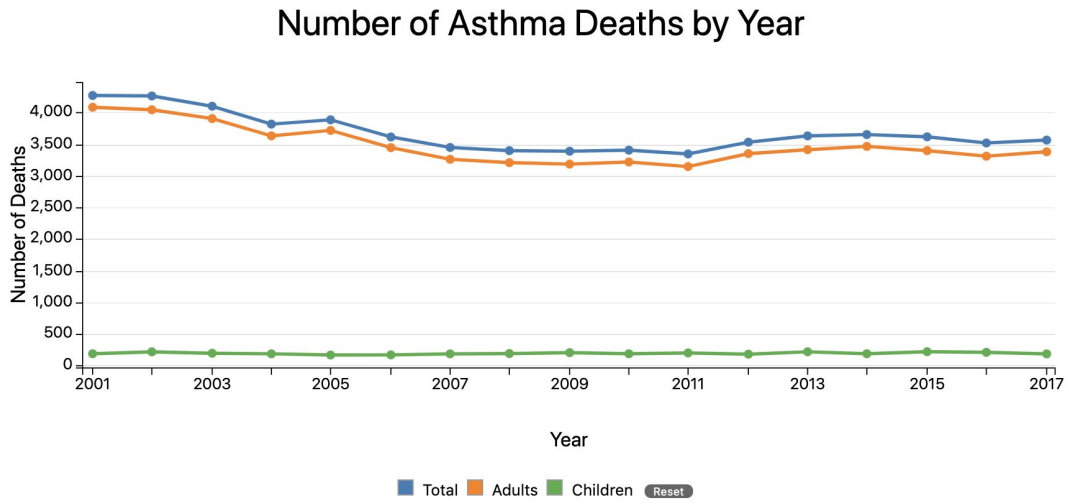
NHIS 2016-2018 Asthma Stats Summary

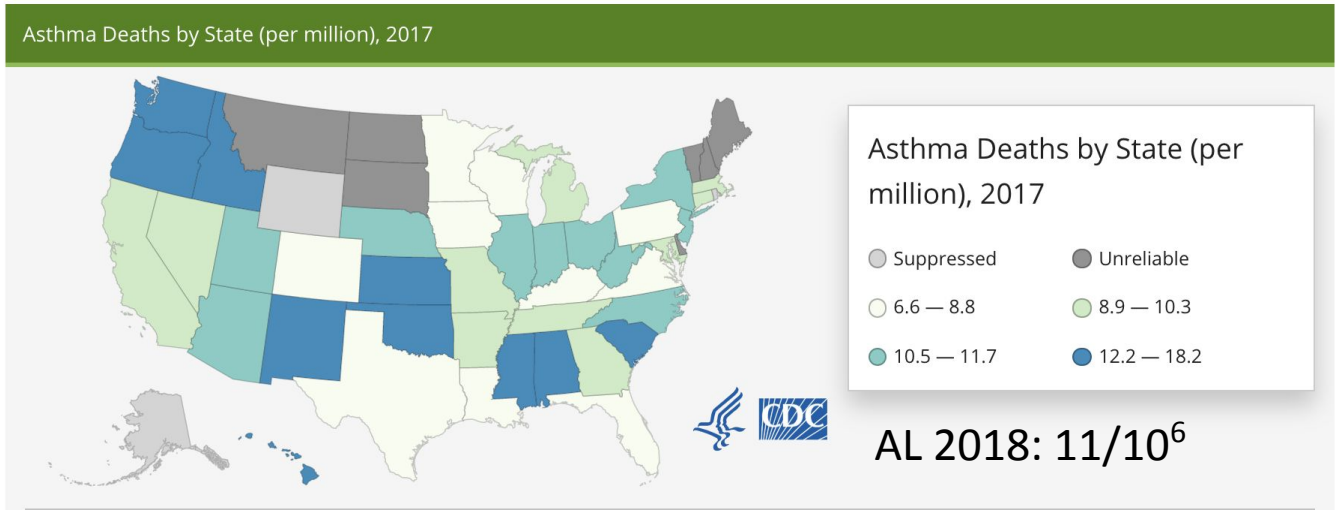
- Prevalence varies by
  - age
    - 11% of 15-19 yo, 6.5% of 25-34 yo
    - otherwise **~8%** for 5yo+
  - ethnicity
    - Highest rates in black (14% child, 9.6% adult), native (10.2%, 10.5%), and Puerto Rican (13.6%, 14.2%)
    - Caucasian rates 6.8% (child) 8.2% (adult)
  - SES
    - Below 100% poverty threshold 10.8%
    - 450% above poverty threshold 6.5%

- Asthma mortality impacted by
  - Age
    - 18-24 ($3.8/10^6$), 25-34 ($5.2/10^6$), 35-64 ($11/10^6$), 65+yo ($29/10^6$)
    - Adult male 10.8, Adult female 15
  - Ethnicity
    - Black ($21.8/10^6$), Native ($11.3/10^6$), Caucasian ($9.5/10^6$), Asian/Pacific Islander ($8.5/10^6$), Hispanic ($6.3/10^6$)

2016-2018 National Health Interview Survey (NHIS)
https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm

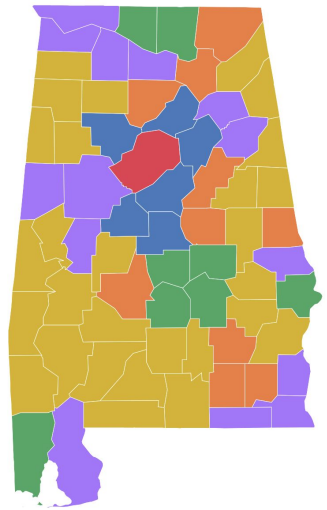
US deaths





AL 2018: $11/10^6$

Urban-Rural Classification of Counties with Corresponding Current Asthma Prevalence Among Adults in Alabama, 2016–2018



Urban-Rural Classification	Prevalence
Large Central Metropolitan	8.7%
Large Fringe Metropolitan	8.7%
Medium Metropolitan	11.3%
Small Metropolitan	10%
Micropolitan	11.6%
Noncore	11.1%

Data Source: 2013 National Center for Health Statistics (NCHS) Urban-Rural Classification Scheme for Counties and 2016–2018 Behavioral Risk Factor Surveillance System (BRFSS)

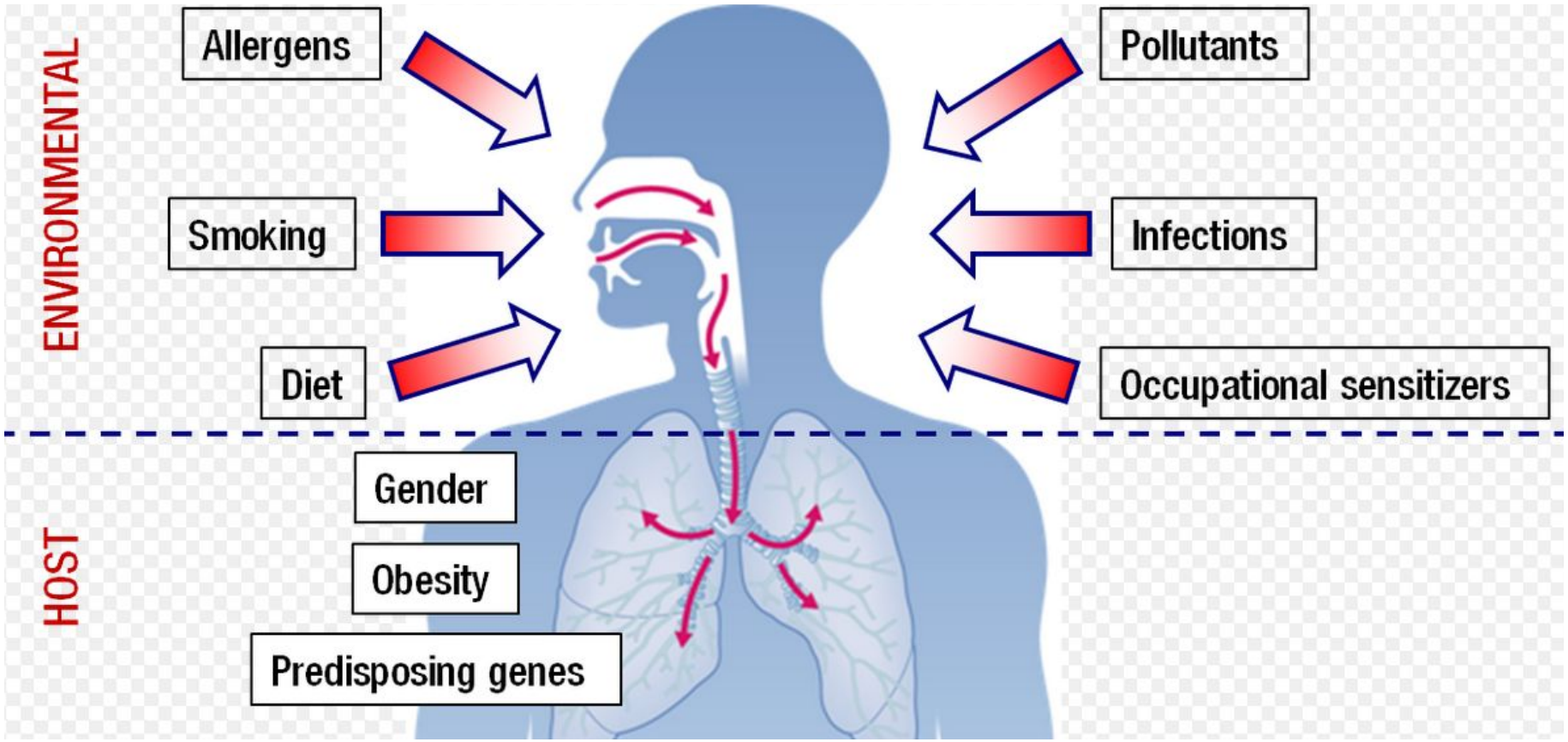
https://www.cdc.gov/asthma/data-visualizations/mortality-data.htm

https://www.cdc.gov/asthma/national-surveillance-data/a-prevalence-state-classification.htm

NHLBI NAEPP EPR 3 + GINA Definition of Asthma

- “a heterogeneous disease, (usually) characterized by chronic airway inflammation
  - The cellular elements driving inflammation include mast cells, eosinophils, T lymphocytes, neutrophils, and epithelial cells
- Characterized by
  - respiratory symptoms such as wheezing, shortness of breath, chest tightness, and cough that vary over time and in intensity
  - variable expiratory airflow limitation
    - Often reversible
    - may progress to persistent airflow limitation or fixed airway obstruction in a subset of patients

NHLBI NAEPP EPR 3 Guidelines, 2007; Global Initative for Asthma (GINA) Global Strategy for Asthma Management and Prevention 2019



NHLBI NAEPP EPR 3 Guidelines, 2007

US asthma guidelines

- EPR3 (2007)
  1. Intro (methods)
  2. Definition, pathophysiology, and natural history of asthma; implications for management
  3. Asthma management
     1. Measures of asthma assessment and monitoring
     2. Education
     3. Control of environmental triggers and comorbidities that affect asthma
     4. Medications
  4. Long term management of asthma
     - By age group
     - Achieving initial control, maintaining control, step up therapy
  6. Managing asthma exacerbations

NHLBI NAEPP EPR 3 Guidelines, 2007

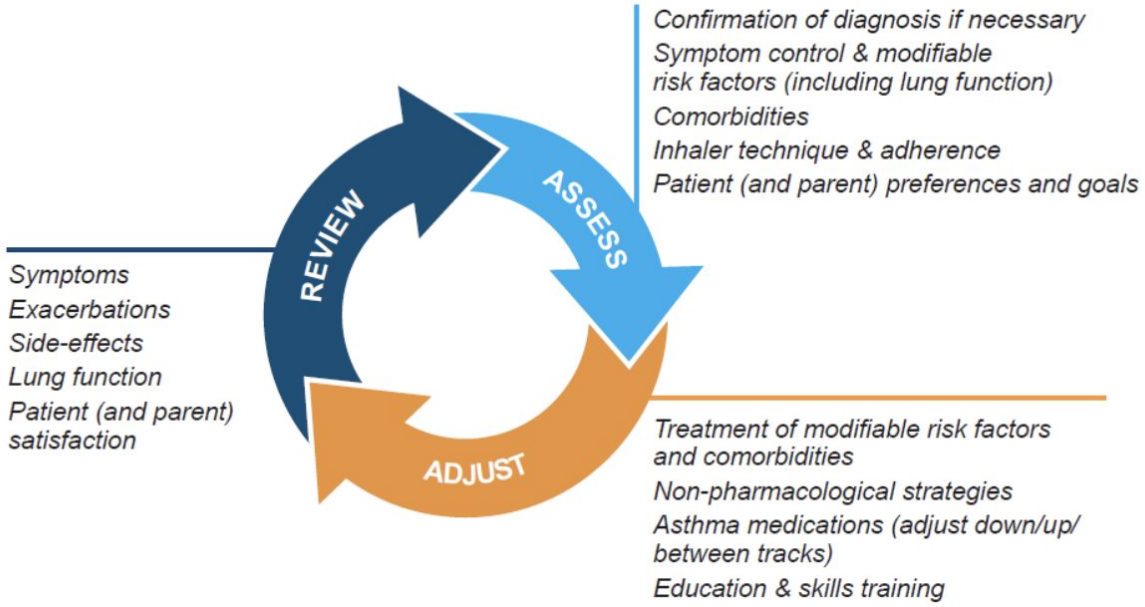
US asthma guidelines

- EPR4 (2020) – focused update to EPR3
- 6 priority topics
  - Using inhaled corticosteroids when needed for recurrent wheezing or persistent asthma
  - Using long-acting antimuscarinic agents (LAMAs) with inhaled corticosteroids for long-term asthma management
  - Using one or more methods to reduce exposure to indoor asthma triggers
  - Allergen immunotherapy
  - Using fractional exhaled nitric oxide (FeNO) tests to help manage asthma or to help confirm a diagnosis in some patients when the diagnosis is unclear
  - Using bronchial thermoplasty (BT) to treat selected adults with persistent asthma

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020

Global initiative for asthma (GINA) guidelines

- Launched 1993 as a collaboration with NHLBI, NIH and WHO
- Funded from 2014 onward through sale of its documents/resources
- Annual release of updated recommendations



www.ginasthma.org

Diagnosing asthma

- History
- Physical exam
- Confirm airflow obstruction is at least partially reversible or that airway hyper-responsiveness is present
  - *Airflow obstruction may be incompletely reversible in some patients*
- Evaluate for comorbid conditions and exclude alternative diagnoses

NHLBI NAEPP EPR 3 Guidelines, 2007

BOX 3–1. KEY INDICATORS FOR CONSIDERING A DIAGNOSIS OF ASTHMA

Consider a diagnosis of asthma and performing spirometry if any of these indicators is present.* These indicators are not diagnostic by themselves, but the presence of multiple key indicators increases the probability of a diagnosis of asthma. Spirometry is needed to establish a diagnosis of asthma.

- Wheezing—high-pitched whistling sounds when breathing out—especially in children. (Lack of wheezing and a normal chest examination do not exclude asthma.)
- History of any of the following:
  - Cough, worse particularly at night
  - Recurrent wheeze
  - Recurrent difficulty in breathing
  - Recurrent chest tightness
- Symptoms occur or worsen in the presence of:
  - Exercise
  - Viral infection
  - Animals with fur or hair
  - House-dust mites (in mattresses, pillows, upholstered furniture, carpets)
  - Mold
  - Smoke (tobacco, wood)
  - Pollen
  - Changes in weather
  - Strong emotional expression (laughing or crying hard)
  - Airborne chemicals or dusts
  - Menstrual cycles
- Symptoms occur or worsen at night, awakening the patient.

NHLBI NAEPP EPR 3 Guidelines, 2007

Confirmatory testing

- Reversible airflow limitation and airway hyper-responsiveness
  - Bronchodilator reversibility at 400ug salbutamol
    - Increase in FEV1 or FVC by 12% AND 200ml
  - Positive methacholine challenge test
    - Reduction in FEV1 by 20% of baseline
  - Change in FEV1 by >20% over time
  - EIB shows 10% reduction in FEV1 after exercise

ATS/ERS Spirometry Guidelines, 2005

Confirmatory testing

- FeNO may play a supportive role in those 5yo and up who have an uncertain diagnosis of asthma or are unable to perform spirometry
  - Complete H&P and spirometry should be done prior to FeNO
    - FeNO should not be done alone to diagnose asthma
  - Clinical context is important
    - Elevated FeNO ddx: Allergic rhinitis, atopy
    - avoid for >1h prior: cigarettes, caffeine, alcohol, nitrate-rich foods
  - In corticosteroid naïve individual, a FeNO of < 20 ppb has high sens. & spec. to r/o asthma
    - Sens. 0.79, spec. 0.77, OR 12.5
  - “Corticosteroid treatment should not be withhold solely based on a low FeNO”

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020

Confirmatory testing – supportive role for FeNO

Table II: Interpretations of FeNO Test Results for Asthma Diagnosis in Nonsmoking Individuals Not Taking Corticosteroids*

FeNO Level		
<25 ppb (<20 in children ages 5–12)	**25–50 ppb (20–35 in children ages 5–12)**	**>50 ppb (>35 in children ages 5–12)**
▪ Recent or current corticosteroid use ▪ Alternative diagnoses ▪ Phenotype less likely to benefit from ICS ▪ Noneosinophilic asthma ▪ COPD ▪ Bronchiectasis ▪ CF ▪ Vocal cord dysfunction ▪ Rhinosinusitis ▪ Smoking ▪ Obesity	▪ Evaluate in clinical context ▪ Consider other diagnoses ▪ Consider other factors influencing result ▪ Eosinophilic asthma less likely	▪ Eosinophilic airways inflammation likely ▪ Phenotype more likely to respond to ICS ▪ Allergic asthma ▪ Eosinophilic bronchitis

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020

Assess for contributory factors

- Medication compliance/inhaler technique
- Rhinosinusitis/Allergies
- Obesity
- Obstructive sleep apnea
  - Chronic rhinitis is comorbid with both OSA and obstructive lung disease
  - Albuterol use frequently at night d/t waking from sleep coughing
  - Asymptomatic during the day
- GERD
  - SARA (adult) and SARCA (peds) do not support PPI for poorly controlled asthma in the absence of GERD symptoms
- AERD

NHLBI NAEPP EPR 3 Guidelines 2007, Quezada W *et al. Ann Allergy Asthma Immunol* 2016

Exclude alternative or additional diagnosis

- COPD
- Vocal cord dysfunction
- Eosinophilic Granulomatosis with Polyangiitis (EGPA)
- Sarcoidosis
- Cystic fibrosis
- Alpha 1 antitrypsin deficiency
- Allergic bronchopulmonary aspergillosis (ABPA)

NHLBI NAEPP EPR 3 Guidelines, 2007

Outline

- What is asthma
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- How is asthma managed
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  - What is an asthma endotype?
  - What do I do with these abnormal labs in my severe asthma patient?

KEY POINTS: OVERVIEW OF MEASURES OF ASTHMA ASSESSMENT AND MONITORING

- The functions of assessment and monitoring are closely linked to the concepts of severity, control, and responsiveness to treatment:
  - Severity: the intrinsic intensity of the disease process. Severity is measured most easily and directly in a patient not receiving long-term-control therapy.
  - Control: the degree to which the manifestations of asthma (symptoms, functional impairments, and risks of untoward events) are minimized and the goals of therapy are met.
  - Responsiveness: the ease with which asthma control is achieved by therapy.
- Both severity and control include the domains of current impairment and future risk:
  - Impairment: frequency and intensity of symptoms and functional limitations the patient is experiencing or has recently experienced
  - Risk: the likelihood of either asthma exacerbations, progressive decline in lung function (or, for children, reduced lung growth), or risk of adverse effects from medication

NHLBI NAEPP EPR 3 Guidelines, 2007

Severity or Control

Assessing a patient's asthma severity or control depends on whether or not they are already taking asthma medications.

If a patient is ***not*** receiving long-term medications,

- **severity is assessed during the first visit** and control is assessed during all subsequent visits.

If a patient is ***already*** receiving long-term medications to control asthma,

- the asthma severity is already masked. Therefore, **control is assessed during the first and all subsequent visits.**

NHLBI NAEPP EPR 3 Guidelines, 2007

EPR-3 Chart: Asthma Severity in Age 12 and Older

Components of Severity		Classification of Asthma Severity ≥ 12 years of age (Not currently taking long-term contol medication)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting beta2-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily, and not >1x/on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Normal FEV1/FVC: 8-19 yr 85% 20-39 yr 80% 40-59 yr 75% 60-80 yr 70%	Lung function	• Normal FEV1 between exacerbations • FEV1>80% predicted • FEV1/FVC normal	• FEV1>80% predicted • FEV1/FVC normal	• FEV1>60% but <80% predicted • FEV1/FVC reduced 5%	• FEV1 <60% predicted • FEV1/FVC reduced > 5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year(see note)	≥2/year (see note)		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV1			
Recommended Step for Initiating Therapy (See figure 4-1b for treatment steps.)		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	Step 4
		In 2-6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

NHLBI NAEPP EPR 3 Guidelines, 2007

EPR-3 Chart: Asthma Control in Age 12 and Older

Components of Control		Classification of Asthma Control (≥ 12 years of age)		
		Well Controlled	**Not Well Controlled**	**Very Poorly Controlled**
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤2x/month	1-3x/week	≥4x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting beta2-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
	FEV1 or peak flow	>80% predicted/ personal best	60-80% predicted/ personal best	<60% predicted/ personal best
	Validated Questionnaires ATAQ ACQ ACT	 0 ≤0.75* ≥20	 1-2 ≥1.5 16-19	 3-4 N/A ≤15
Risk	Exacerbations	0-1/year	≥2/year (see note)	
		Consider severity and interval since last exacerbation.		
	Progressive loss of lung function	Evaluation requires long-term followup care		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment		• Maintain current step • Regular followup every 1-6 months to maintain control. • Consider step down if well controlled for at least 3 months	• Step up 1 step and • Reevaluate in 2-6 weeks. • For side effects: consider alternative treatment options.	• Consider short course of oral systemic corticosteroids. • Step up 1-2 steps, and • Reevaluate in 2 weeks. • For side effects, consider alternative treatment options.

NHLBI NAEPP EPR 3 Guidelines, 2007

KEY POINTS: OVERVIEW OF MEASURES OF ASTHMA ASSESSMENT AND MONITORING

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NHLBI NAEPP EPR 3 Guidelines, 2007

Severe asthma definition: risk + control

TABLE 3 Definition of severe asthma for patients aged ⩾6 years

Asthma which requires treatment with guidelines suggested medications for GINA steps 4–5 asthma (high dose ICS[#] and LABA or leukotriene modifier/theophylline) for the previous year or systemic CS for ⩾50% of the previous year to prevent it from becoming "uncontrolled" or which remains "uncontrolled" despite this therapy

Uncontrolled asthma defined as at least one of the following:

1) Poor symptom control: ACQ consistently >1.5, ACT <20 (or "not well controlled" by NAEPP/GINA guidelines)
2) Frequent severe exacerbations: two or more bursts of systemic CS (>3 days each) in the previous year
3) Serious exacerbations: at least one hospitalisation, ICU stay or mechanical ventilation in the previous year
4) Airflow limitation: after appropriate bronchodilator withhold FEV_1 <80% predicted (in the face of reduced FEV_1/FVC defined as less than the lower limit of normal)

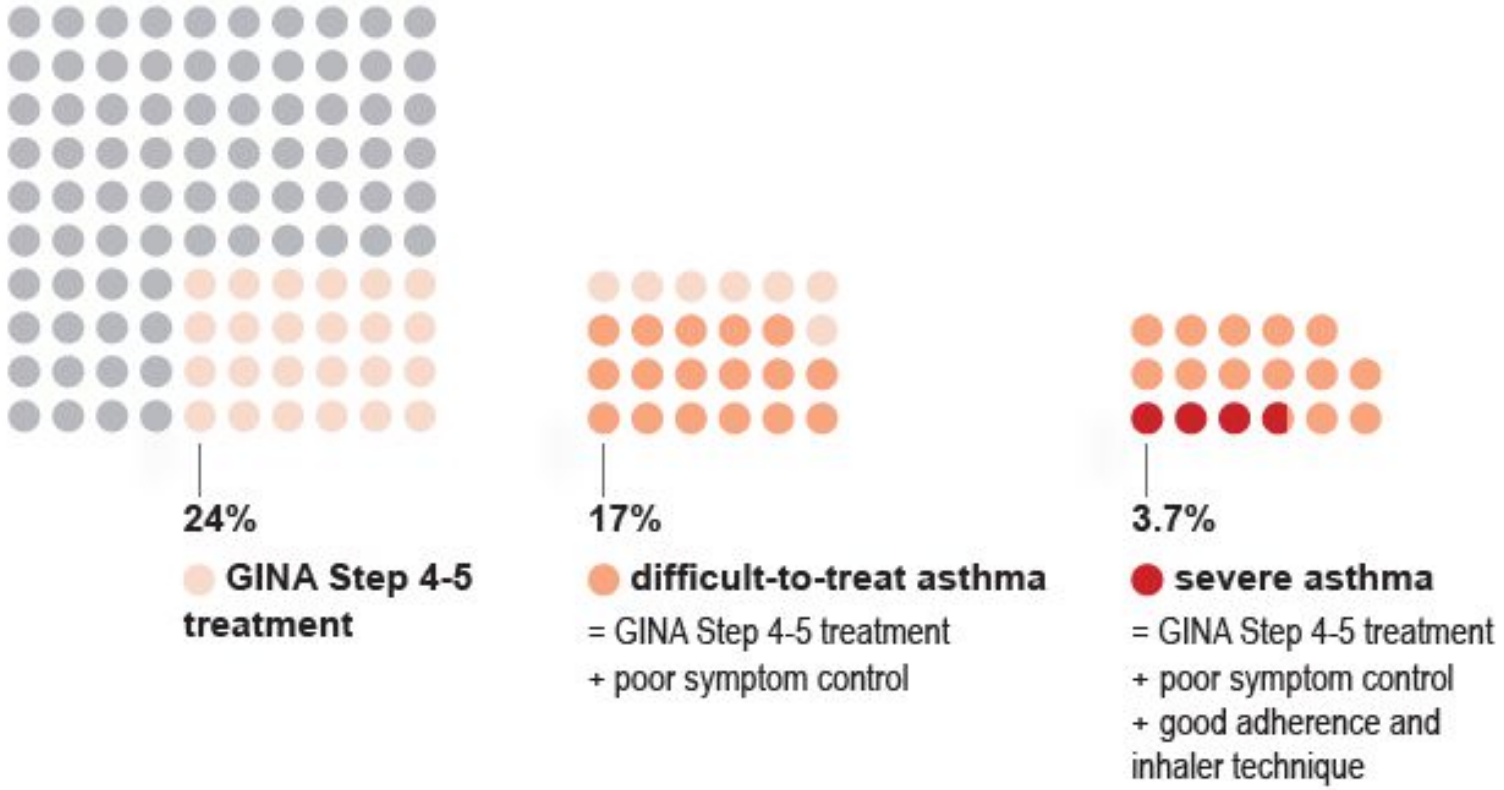
Controlled asthma that worsens on tapering of these high doses of ICS or systemic CS (or additional biologics)

#: the definition of high dose inhaled corticosteroids (ICS) is age-specific (table 4). GINA: Global Initiative for Asthma; LABA: long-acting β_2-agonists; CS: corticosteroids; ACQ: Asthma Control Questionnaire; ACT: Asthma Control Test; NAEPP National Asthma Education and Prevention Program.

Chung et al. ATS/ERS statement severe asthma, 2013

How common is severe asthma?

Box 1. What proportion of adults have difficult-to-treat or severe asthma?



These data are from a Dutch population survey of people ≥18 years with asthma[2]

Hekking et al, JACI 2015

Outline

- What is asthma
  - Defining asthma
  - Diagnosing asthma
  - Staging asthma

- How is asthma managed
  - Baseline asthma (EPR3 v EPR4)
    1. Measures of asthma assessment and monitoring
    2. Education
    3. Control of environmental triggers and comorbidities that affect asthma
    4. Medications
  - Acute exacerbations

- How is severe or refractory asthma managed
  - What is an asthma endotype?
  - What do I do with these abnormal labs in my severe asthma patient?

Asthma measurement and monitoring

- EPR3
  - Asthma self-management education
  - Asthma information and training in asthma management skills
  - Self-monitoring (either symptom– or peak flow–based)
  - Written asthma action plan regular assessment by a consistent clinician
  - Shared decision-making

- EPR4
  - Added *conditional recommendation* for FeNO use in patients to:
    - Select anti-inflammatory medications
    - aid in adjusting anti-inflammatory medications or omalizumab (not other biologics)
  - trend FeNO q2-3 mo to reduce asthma exacerbations
    - does not improve asthma control or QOL
  - Recommend against isolated use of FeNO

NHLBI NAEPP EPR 3 Guidelines, 2007

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020

Education

- Personalized asthma action plans
  - Endorsed by EPR3, CDC and GINA
  - Cochrane review (Gatheral T.L. *et al.* 2017):
    - Low quality evidence for or against
    - evidence does not clearly indicate benefit versus other education techniques

CDC.gov/ASTHMA

NHLBI NAEPP EPR 3 Guidelines, 2007

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020

Doing Well

- I don't have cough, wheezing, chest tightness, or trouble breathing at any time.
- I can do all the things I usually do.
- When I use a peak flow meter my peak flow* is more than 80 percent or more of my best peak flow.
- Continue taking your long-term control medicine.

Asthma Is Getting Worse

- I have some cough, wheezing, chest tightness, or trouble breathing. Or
- I wake up at night because of my asthma. Or
- I can't do some of the things I usually do. Or
- When I use a peak flow meter my peak flow* is half to three quarters of my best peak flow.
- Add your quick-relief medicine and continue your long-term control medicine.
- If your symptoms get better after an hour keep checking them and continue your long-term control medicine.

Medical Alert!

- I have a lot of trouble breathing. Or
- My quick-relief medicines don't help. Or
- I can't do any of the things I usually do. Or
- I was in the yellow zone for 24 hours and I'm not getting better. Or
- When I use a peak flow meter my peak flow* is less than half of my best peak flow.
- Add the other medicines your doctor has prescribed and call your doctor.
- If your symptoms don't get better and you can't reach your doctor, go to the hospital.

*Peak flow measurement is a quick test to measure air flowing out of the lungs.

Education

- Inhaler technique assessment and teaching
  - Endorsed by EPR3, CDC and GINA
  - RTs and nurses can perform this role in clinic
  - Online resources
    - ALA
    - Uptodate
    - CDC/asthma
  - Can also direct patients to commercial pharmacies with questions after they return home

Control of environmental factors

Key Differences in Recommendations in the 2007 (EPR-3) and 2020 Asthma Guidelines, by Topic Area

TOPIC AREA	2007 GUIDELINE	2020 GUIDELINE
Allergen Mitigation	Patients who have asthma at any level of severity should reduce, if possible, exposure to allergens to which the patient is sensitized and exposed	Conditional recommendation against allergen mitigation interventions as part of routine asthma management in individuals with asthma who do not have sensitization to specific indoor allergens or who do not have symptoms related to exposure to specific indoor allergens **(Recommendation 5)**
	Patients who have asthma at any level of severity should know that effective allergen avoidance requires a multifaceted, comprehensive approach; individual steps alone are generally ineffective (Evidence A)	Conditional recommendation for a multicomponent allergen-specific mitigation intervention in individuals with asthma who are exposed and have symptoms related to exposure to identified indoor allergens, confirmed by history taking or allergy testing **(Recommendation 6)**
	Recommended cockroach control measures if the patient is sensitive to cockroaches and the home has an infestation	Conditional recommendation for the use of integrated pest management alone or as part of a multicomponent allergen-specific mitigation intervention in individuals with asthma who are exposed and have sensitization or symptoms related to exposure to pests (cockroaches and rodents) **(Recommendation 7)**
	Recommended the following mite-control measures: ▪ Encase mattress in an allergen-impermeable cover ▪ Encase pillow in an allergen-impermeable cover or wash pillow weekly ▪ Wash sheets and blankets weekly in hot water	Conditional recommendation for impermeable pillow/mattress covers only as part of a multicomponent allergen mitigation intervention, not as a single-component intervention, in individuals with asthma who have sensitization or symptoms related to exposure to dust mites **(Recommendation 8)**

Key points:

Tailor advice to allergy testing results & symptoms

* pets: tolerance?

Pest management and mold abatement are recommended

Multicomponent strategies are recommended

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020

Asthma medications 101

Inhaled corticosteroids
Long-acting beta-agonist
Leukotriene receptor antagonist
Long-acting muscarinic antagonist

Inhaled corticosteroids

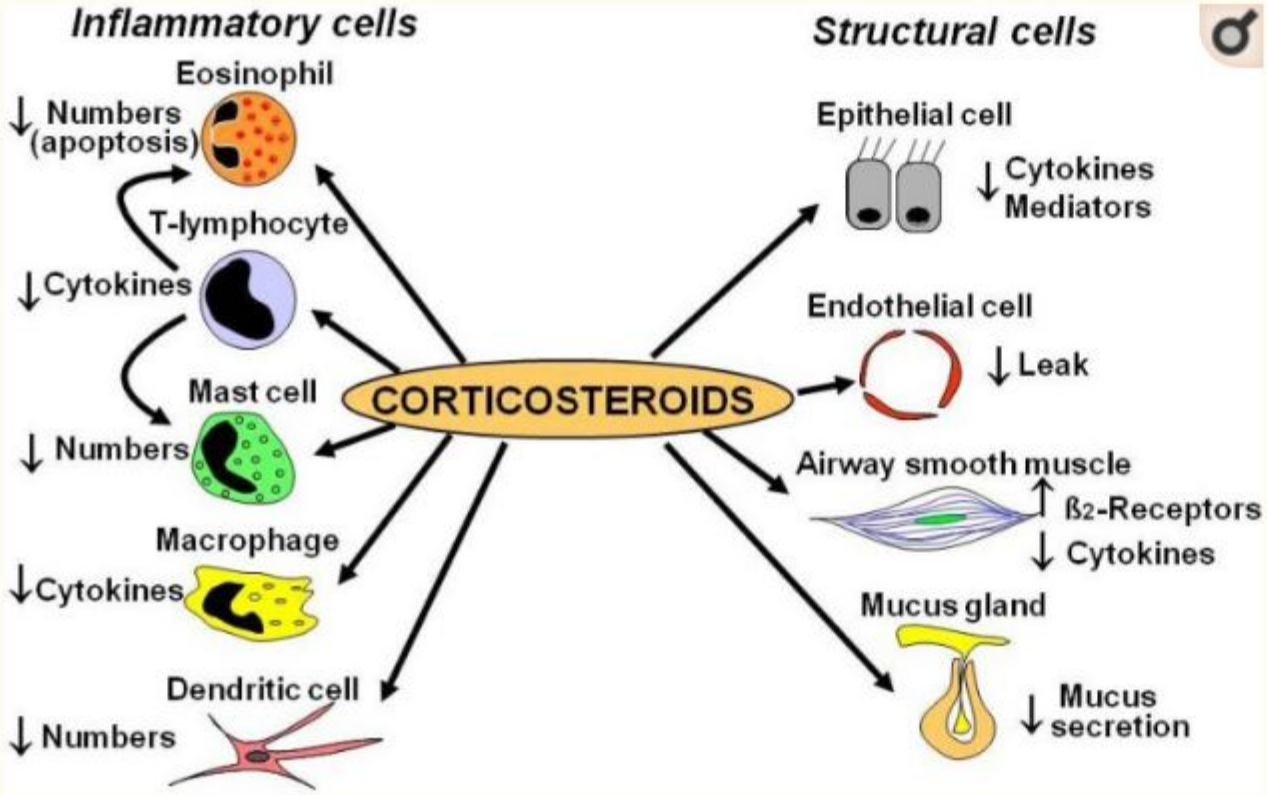


Figure 1

Cellular effect of corticosteroids.

Barnes, *Pharmaceuticals*, 2010

Leukotriene receptor antagonists

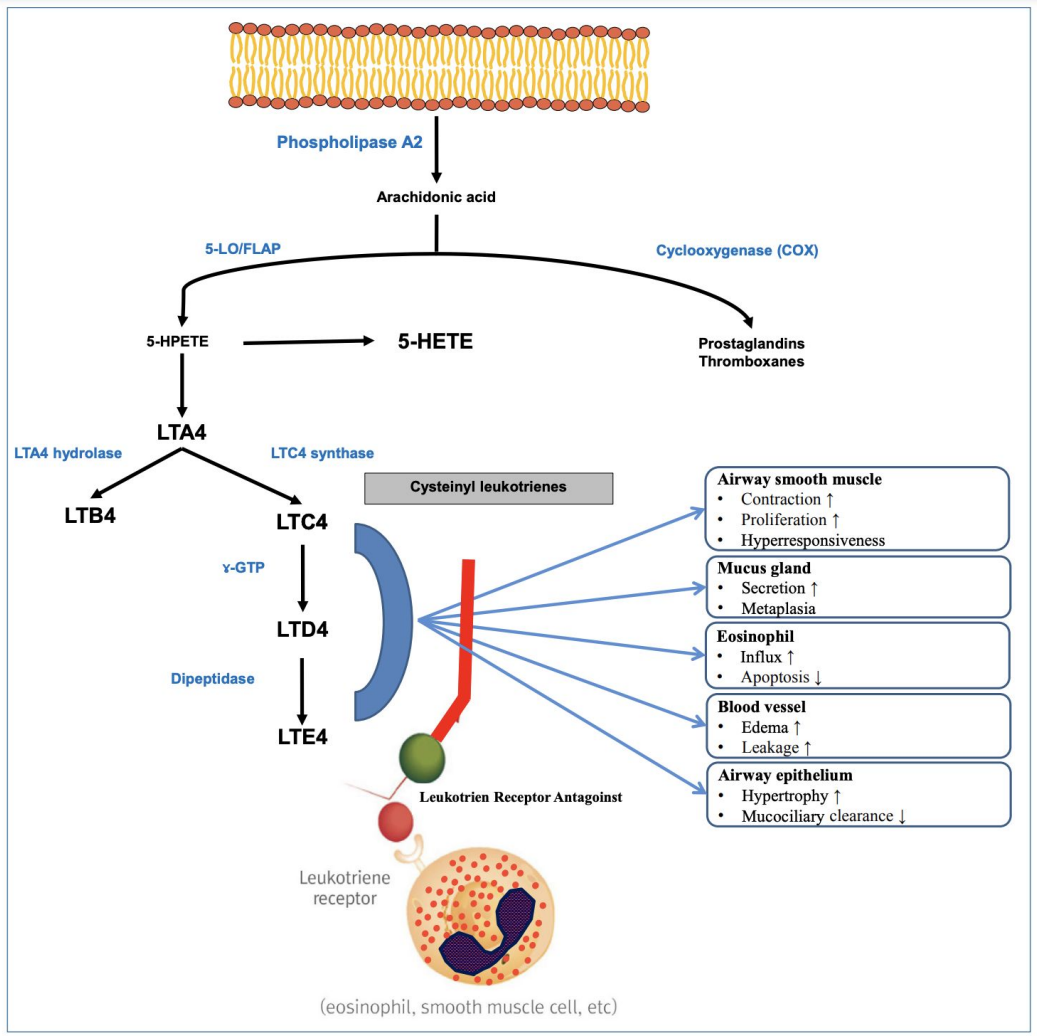
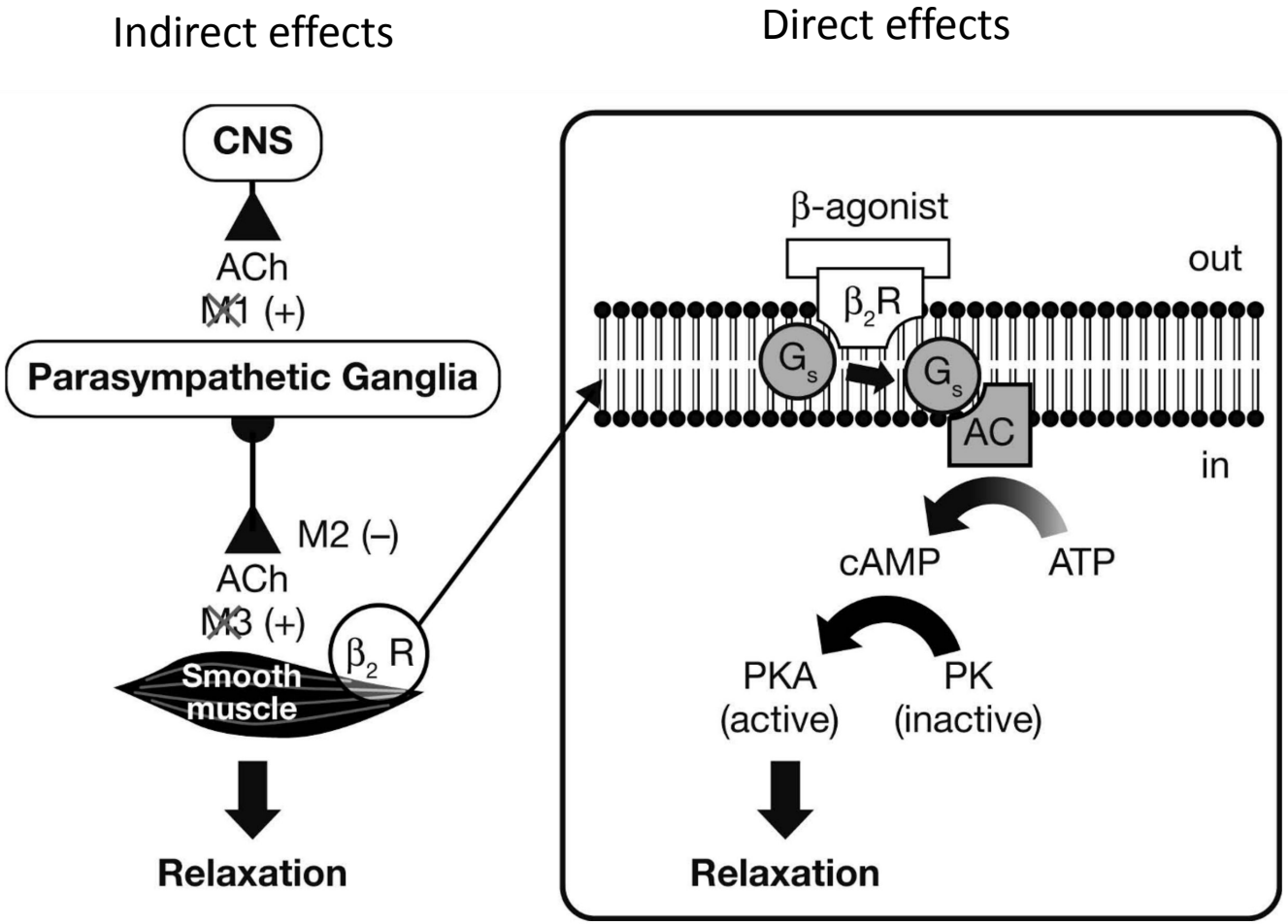


Fig. 1. Biosynthesis and role of leukotrienes. 5-LO, 5-lipoxygenase; FLAP, 5-LO-activating protein; 5-HPETE, 5-hydroperoxyeicosatetraenoic acid; 5-HETE, 5-hydroxyeicosatetraenoic acid; LT, leukotriene; GTP, glutamyl transpeptidase.

Y.J. Lee and C.K. Kim, *Clin. Exp. Pediatrics* 2020

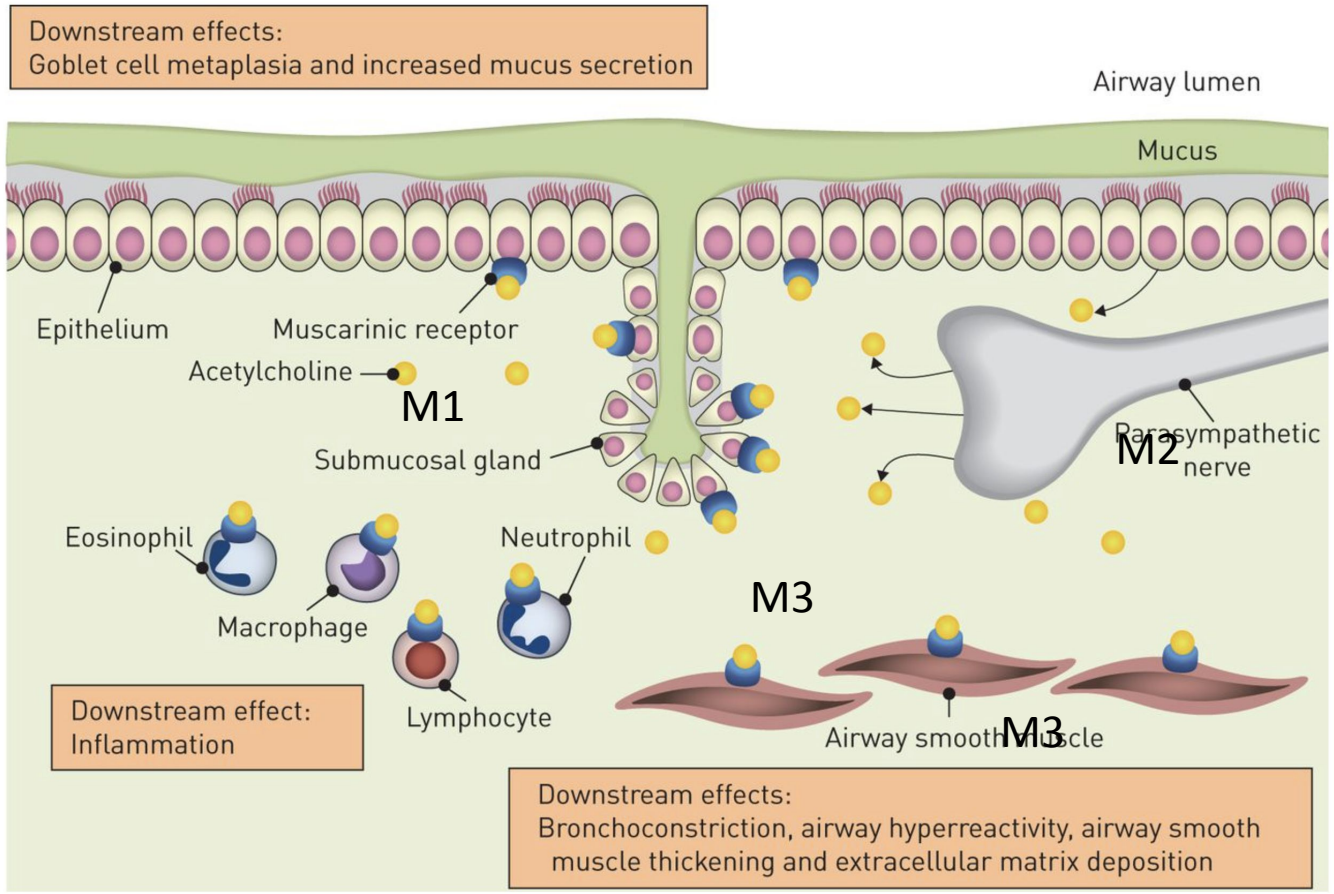
LABA

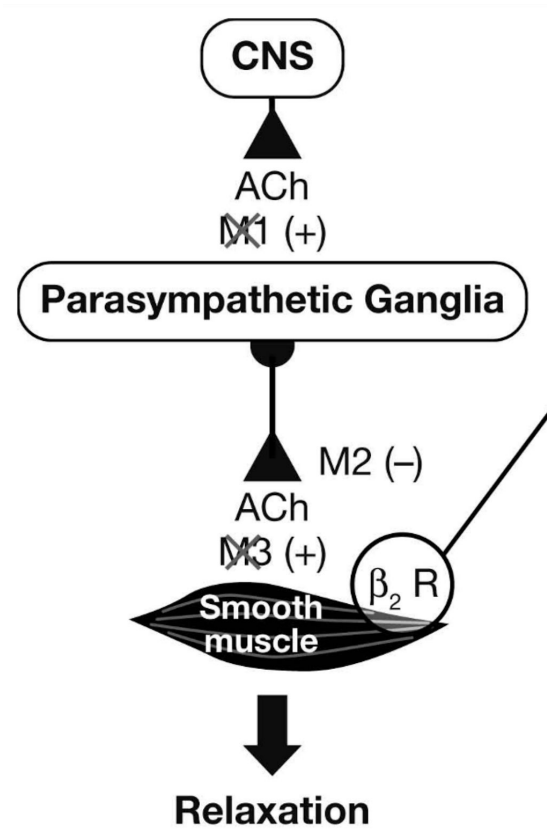


D.P. Tashkin and L.M. Fabry, *Respiratory Research* 2011

FDA Drug Safety Communication: FDA review finds no significant increase in risk of serious asthma outcomes with long-acting beta agonists (LABAs) used in combination with inhaled corticosteroids (ICS)

LAMA





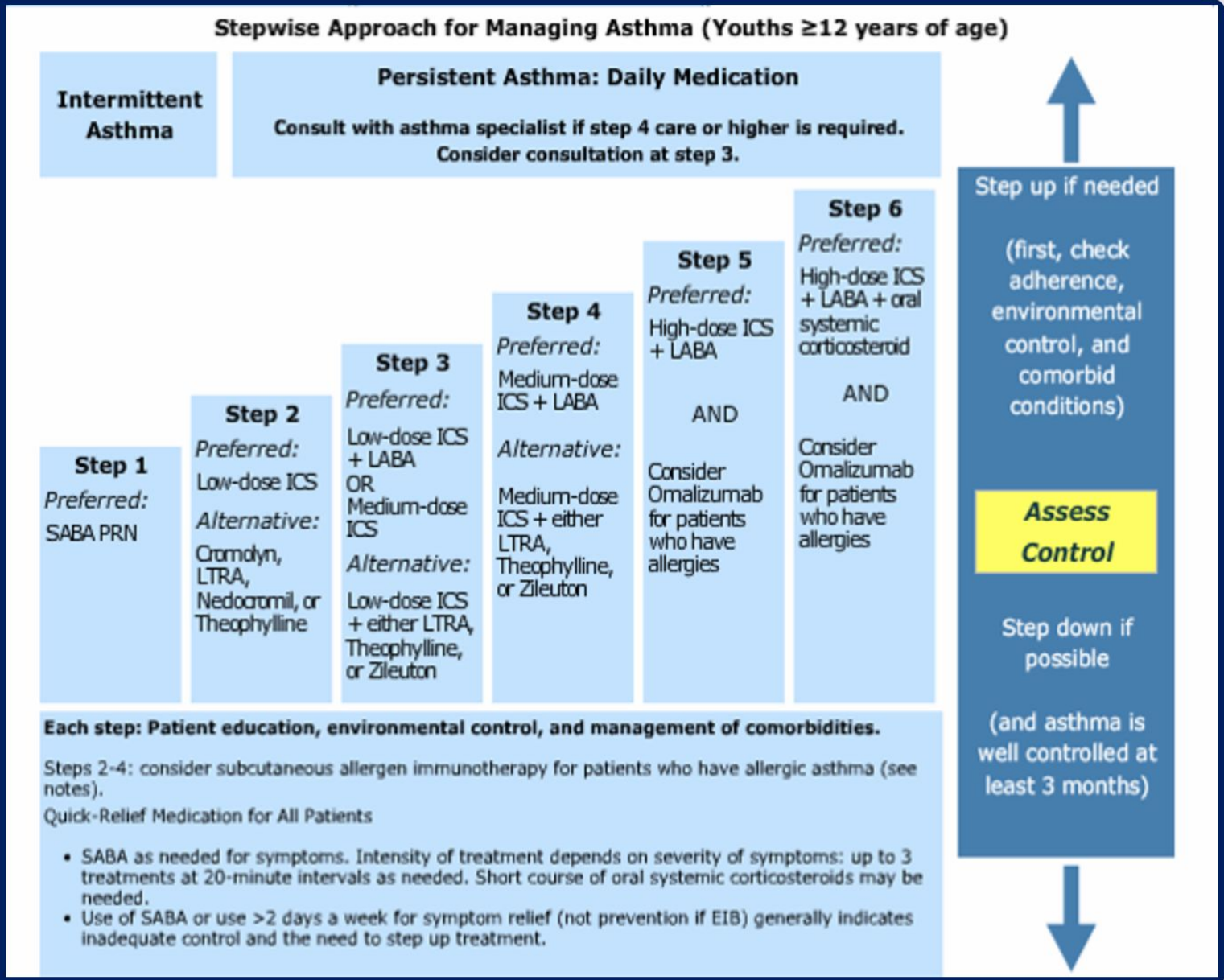
Ipratroprium (+SABA): nonselective

Tiotroprium (+ICS/LABA): M3 selective

R. Gosens, N. Gross, *ERS* 2018

D.P. Tashkin and L.M. Fabry, *Respiratory Research* 2011

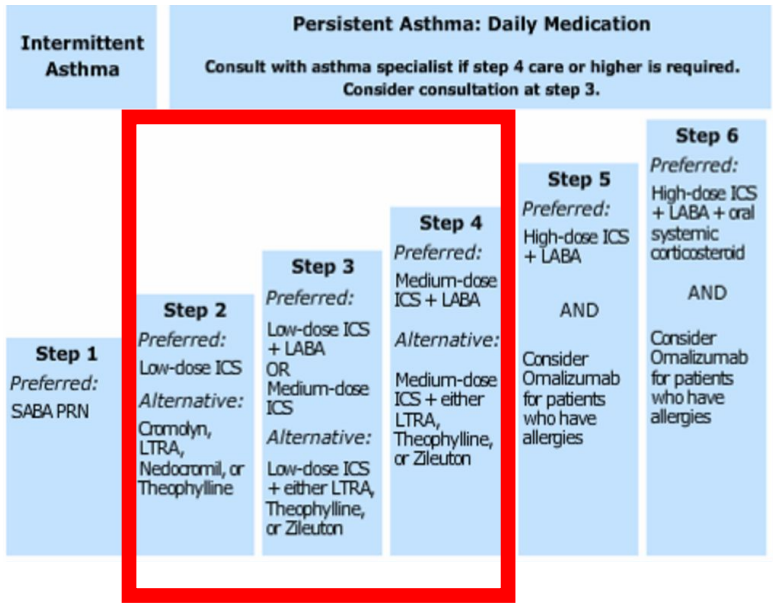
EPR3 Chart: Asthma Medications in Age 12 and Older



NHLBI NAEPP EPR 3 Guidelines, 2007

EPR4: updates to steps 2-4 of EPR3

EPR3



AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Treatment	Intermittent Asthma: STEP 1	Management of Persistent Asthma in Individuals Ages 12+ Years: STEP 2	STEP 3	STEP 4	STEP 5	STEP 6 ■
Preferred	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
Alternative		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)**	

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 2–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Allergen immunotherapy (EPR4 steps 2-4)

Key Differences in Recommendations in the 2007 (EPR-3) and 2020 Asthma Guidelines, by Topic Area (cont'd)

TOPIC AREA	2007 GUIDELINE	2020 GUIDELINE
Immunotherapy	Consider allergen immunotherapy for persistent asthma in the presence of symptoms and sensitization (one combined recommendation)	Conditional recommendation for use of SCIT as an adjunct treatment to standard pharmacotherapy in individuals ages 5 years and older with mild to moderate allergic asthma whose asthma is under control at the initiation, build-up, and maintenance phases of immunotherapy **(Recommendation 17)** Conditional recommendation against use of SLIT for asthma treatment in individuals with persistent allergic asthma **(Recommendation 18)**

SCIT – subcutaneous immunotherapy (shots)
SLIT – sublingual immunotherapy (drops, sprays, or tablets; only tablets are FDA approved)

Fatal and near-fatal reactions in SCIT patients are more likely in poorly controlled asthmatics

AAAAI Practice Parameters: Allergen Immunotherapy 2011

NHLBI NAEPP EPR 3 Guidelines, 2007

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020

Mild persistent asthma, 12yo and up (Step 2) *updated in EPR4*

- EPR3:
  - Preferred low-dose ICS
- EPR4 (12yo and up)
  - Either lose-dose ICS + SABA rescue
  - OR prn concomitant ICS + SABA
    - 2-4 puffs albuterol + 80-250 mcg beclomethasone
    - Not recommended for poor symptom perceivers

Step 2

Preferred:

Low-dose ICS

Alternative:

Cromolyn, LTRA, Nedocromil, or Theophylline

Treatment	STEP 1	STEP 2
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA

NHLBI NAEPP EPR 3 Guidelines, 2007

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020

Moderate persistent asthma, 12yo and up (Step 3-4) *updated in EPR4*

- EPR3
  - Preferred low-dose ICS/LABA or medium-dose ICS + prn SABA
- EPR4
  - Preferred daily ICS/formoterol + prn ICS/formoterol

    Strong recommendation

    Versus

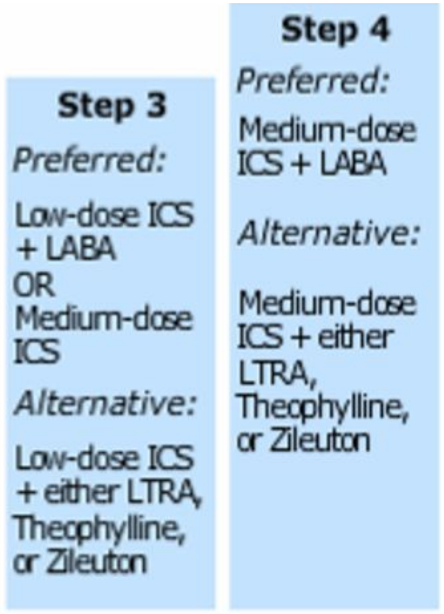
    higher dose ICS + prn SABA

    Same dose ICS/LABA + prn SABA

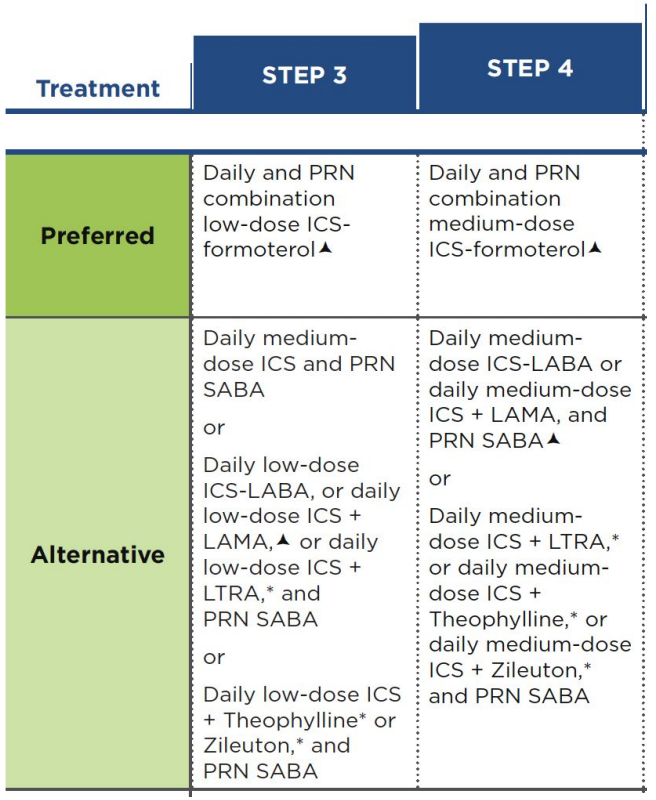
    Conditional recommendation

    Versus

    high-dose ICS/LABA + prn SABA



EPR3



Treatment	STEP 3	STEP 4
Preferred	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲
Alternative	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

EPR4

NHLBI NAEPP EPR 3 Guidelines, 2007

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020

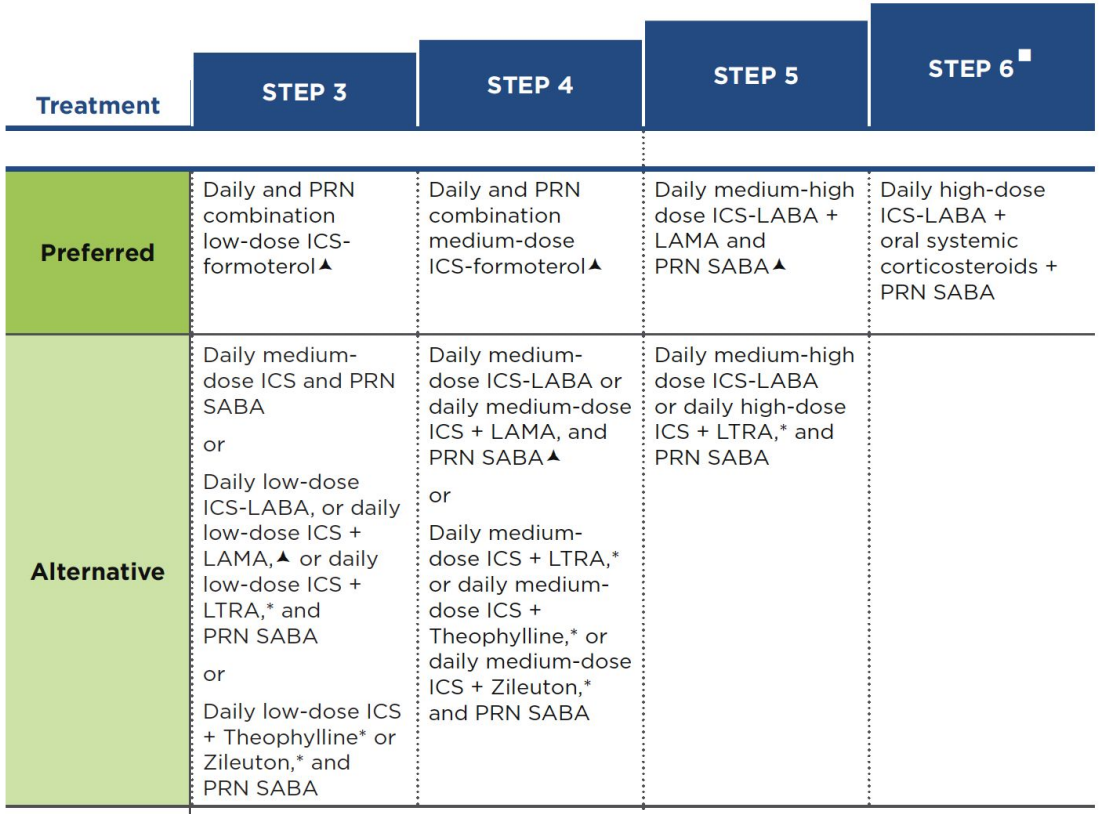
Which inhalers contain ICS + formoterol?

- Symbicort (budesonide/formoterol fumarate dihydrate)
- Dulera (mometasone/formoterol fumarate dihydrate)

- Are ICS/formoterol inhalers FDA approved for rescue use?
  - Not currently in US

Moderate to severe persistent asthma, 12yo and up (Step 4 and 5) *updated in EPR4*

- EPR3 – nil re: LAMA
- EPR4
  - *Conditional recommendation:*
  - ICS/LABA preferred to ICS/LAMA
    - If unable to tolerate LABA then LAMA is acceptable
  - ICS/LAMA preferred to ICS
  - ICS/LAMA/LABA preferred to increasing ICS/LABA dose
    - Qol, control improve; exac. do not
- Avoid: glaucoma, urinary retention



Treatment	STEP 3	STEP 4	STEP 5	STEP 6■
Preferred	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
Alternative	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	

NHLBI NAEPP EPR 4 Focused Update to Asthma Guidelines, 2020