Asthma Management: From Inhalers to Biologics

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Disclosure

I have no financial interests or relationships to disclose.

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01

Be able to discuss proper diagnosis of asthma and identify obstruction on spirometry

02

Be able to differentiate asthma from vocal cord dysfunction and COPD

03

Be able to discuss new GINA and NAEPP recommendations for asthma management

04

Be able to discuss role of biologics in severe asthma

Learning Objectives

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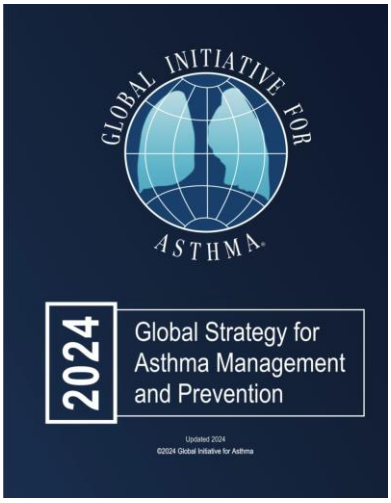

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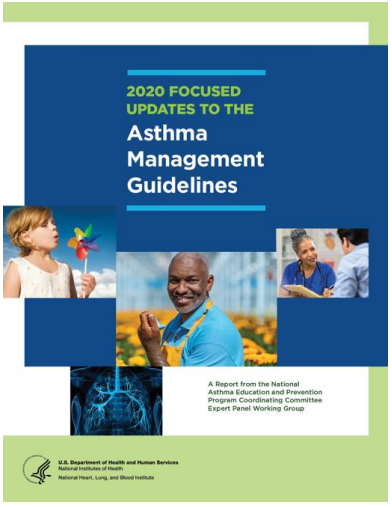

NAEPP

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Diagnosis of Asthma

Take Home Point:

Make sure the patient really has asthma

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Box 2. Features used in making the diagnosis of asthma

1. A history of variable respiratory symptoms
Typical symptoms are wheeze, shortness of breath, chest tightness, cough • People with asthma generally have more than one of these symptoms • The symptoms occur variably over time and vary in intensity • The symptoms often occur or are worse at night or on waking • Symptoms are often triggered by exercise, laughter, allergens or cold air • Symptoms often occur with or worsen with viral infections

Diagnosis of Asthma

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Lung Function Measurements

- Essential for optimal management
  - symptoms and physical exam often correlate poorly with lung function
- Spirometry
  - all patients with persistent asthma should have baseline spirometry
- Peak Flow Meters
  - not capable of detecting obstruction in all patients
  - very effort dependent

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Evidence of Reversible Obstruction

Criteria for obstruction on spirometry

- **FEV1/FVC ratio < LLN (lower limit of normal)**
- **Ratio < 80% is not a criteria for obstruction**

Defining Reversibility

- FEV1 or FVC increase by 10%
- After bronchodilator
- After corticosteroid therapy

The greater the variability or more excess variation seen, more confident in asthma diagnosis

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		Ref	LLN/ULN	Pre	% Ref	Post	% Ref	%Chg
Spirometry								
FVC	Liters	3.60	(2.9 - 4.3)	2.90	80	3.07	85	6
FEV1	Liters	2.97	(2.4 - 3.6)	1.79	60	2.03	68	13
FEV1/FVC	%	83	(73.4 - 92.0)	62		66		
FEF25-75%	L/sec	3.25	(1.9 - 4.6)	0.83	26	1.10	34	31
PEF	L/sec	6.90	(4.9 - 8.9)	6.45	93	6.71	97	4

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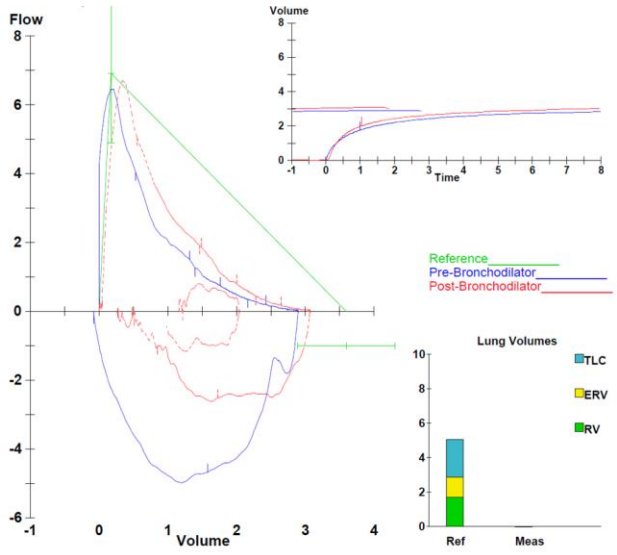

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Case Study

44 yo obese woman with 3 year history of severe asthma. Frequent exacerbations with coughing/wheezing that sometimes improve with albuterol but not always. Triggers strong odors and exertion. Intubated 3 times but all for ~ 1 day. In between attacks usually symptom free. High dose ICS/LABA ineffective. 10 pack year smoker quit 1 year ago.

What Is the Most Likely Diagnosis?

A. Severe asthma
B. Obesity
C. COPD
D. VCD

Differential Diagnosis of Asthma: Top 3

Vocal cord dysfunction

Obesity/Deconditioning

- Dyspnea on exertion, with rare symptoms at rest
- Restrictive physiology
- Symptoms improve quickly with rest
- Laughing is not a trigger

COPD

Others

- Hyperventilation syndrome, eosinophilic bronchitis, hypereosinophilic syndromes, ischemic heart disease, CHF, pulmonary embolus, interstitial lung disease

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Vocal Cord Dysfunction (a.k.a. Inducible Laryngeal Obstruction (ILO))

Definition

- involuntary paradoxical movement of the true vocal cords (or arytenoids) during the respiratory cycle resulting in airway symptoms mimicking a variety of upper and lower airway diseases

May masquerade as asthma, exercise-induced asthma, or anaphylaxis

Functional disorder of the vocal cords

- patients generally unable to reproduce symptoms

Pathogenesis unclear

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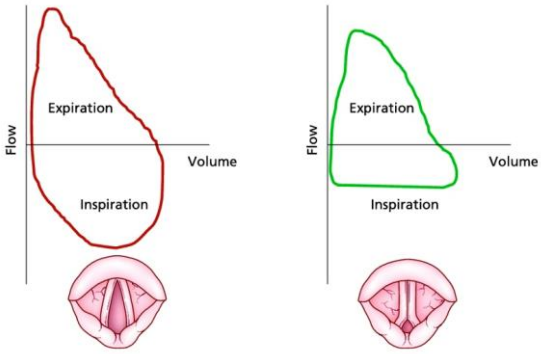

Variable Extrathoracic Obstruction in VCD

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Clues to Diagnosing Vocal Cord Dysfunction

- Attacks sudden and usually dramatic
- Localization of difficulty breathing to the throat
- Stridor (inspiratory/expiratory)
- Wheezing loudest over trachea but may be diffuse
- Change in voice
- Poor response to asthma medications
- Asymptomatic in between
- Female
- May have true asthma

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Pittsburgh VCD Score

Symptom	Assigned Score
Dysphonia	2
Absence of wheeze	2
Throat tightness	4
Triggered by odors	3

Score ≥4: specificity of 95% and sensitivity of 83%

J Allergy Clin Immunol Pract. 2014;2(1):65-9.

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Treatment of Vocal Cord Dysfunction

- Speech therapist
  - Breathing exercises
  - Relaxation methods
- Treat any underlying psychiatric disorder

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Asthma or COPD or Both?

Features of Asthma
- Onset < 40
- Variable symptoms
- Reversible obstruction

Features of COPD
- Onset > 40
- Significant tobacco exposure
- No prior asthma diagnosis

Asthma-COPD Overlap
- Tobacco exposure
- Prior history of asthma

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Methacholine Challenge

Assesses non-specific bronchial hyperresponsiveness (BHR)

Increasing doses inhaled with positive test resulting in fall of FEV1 ≥ 20% (PC/PD_{20})

Helpful in excluding asthma in those with normal spirometry (great NPV)

Many false positives
- COPD, allergic rhinitis, recent URI, CF, etc.

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Management of Asthma

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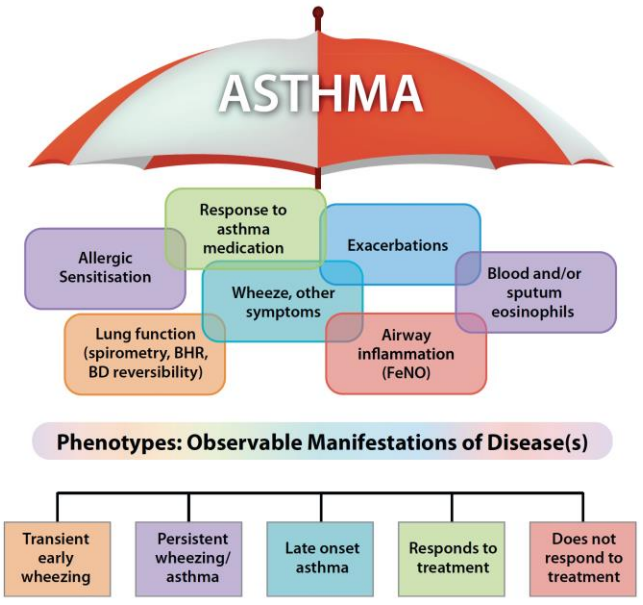
Asthma Phenotypes



Custovic A et al. J Allergy Clin Immun. 2019;144(1):25-33.

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35 yo Man Develops Rhinitis, then Nasal Polyp Disease. After 1 Year He Develops New Onset Asthma. One Year Later He Has an Asthma Attack 30 Minutes After Taking Ibuprofen for a Knee Injury.

What Medication Would Be Most Likely Tolerated?

A. aspirin
B. celecoxib
C. meloxicam
D. naproxen

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Aspirin-Exacerbated Respiratory Disease (AERD)

- Associated with asthma, rhinitis, sinusitis, nasal polyposis (Samters triad)
- Associated with excess leukotriene production and enhanced sensitivity
  - leukotriene modifiers often helpful
- Acute symptoms with NSAID's (< 1hr)
  - Rhinorrhea, conjunctivitis, bronchospasm
- Dependent on COX-1 inhibition
  - Need to avoid all NSAIDs and ASA
- COX-2 inhibitors generally safe

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Assessing Risk factors for Poor Asthma Outcomes

Assess risk factors at diagnosis and periodically at least every 1-2 years, especially for those with exacerbation

Measure FEV1 at start of treatment and after 3-6 months of controller treatment to record personal best lung function

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Risk Factors for Poor Asthma Outcomes

Uncontrolled asthma

Modifiable risk factors

- Medications
  - High SABA use, inadequate ICS, poor adherence, incorrect inhaler technique
- Comorbidities
  - Obesity, chronic rhinosinusitis, GERD, pregnancy
- Exposures
  - Smoking, air pollution, allergens
- Psychological/Socioeconomic problems
- Lung Function
  - Low FEV1, high BD reversibility

Others

- Intubation, ICU

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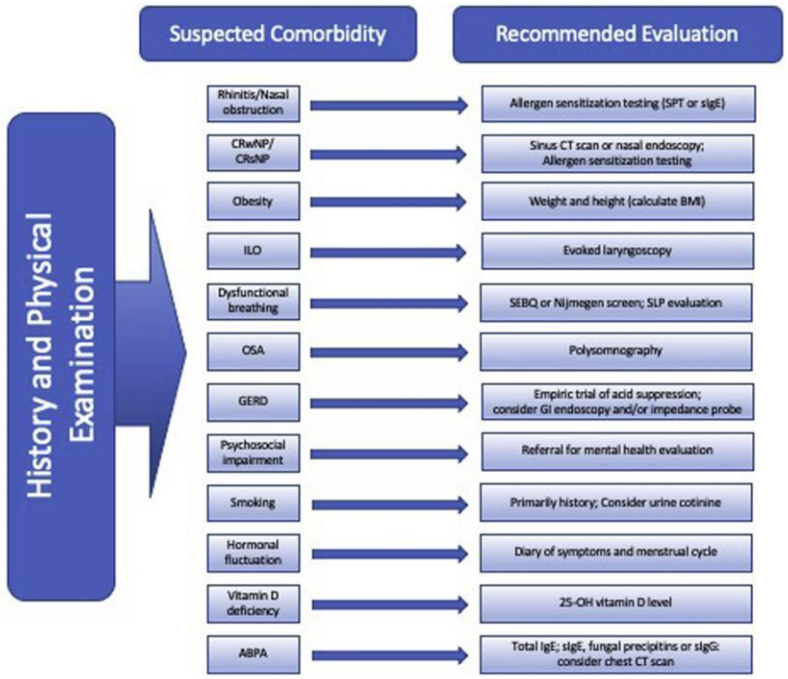
Comorbidities in Asthma



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Reviewing Inhaler Technique

80% of patients do not demonstrate proper technique

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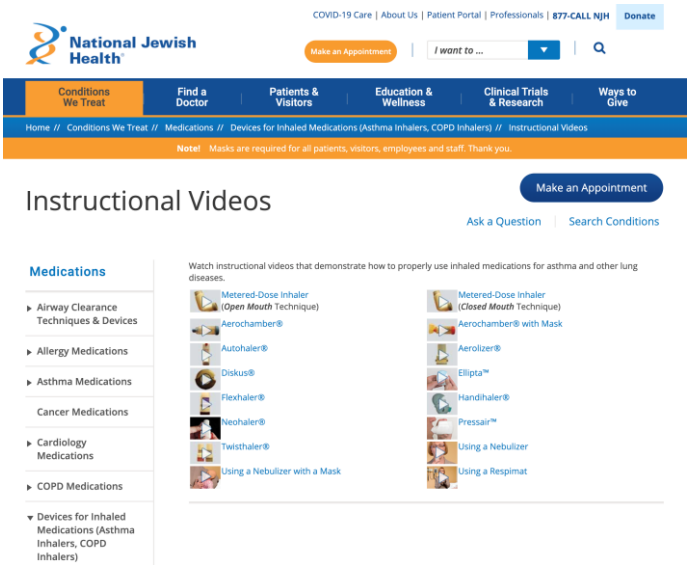

Multiple Inhaler Devices with Different Methods

https://www.nationaljewish.org/conditions/medications/inhaled-medication-asthma-inhaler-copd-inhaler/instructional-videos

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Inhaler Technique Education

- Choose appropriate inhaler
  - Consider spacer if difficulty coordinating inhalation
- Check inhaler technique routinely
- Correct inhaler technique
- Re-check at subsequent visits, especially if not controlled

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Improving Adherence

50% of asthma patients have poor adherence

To identify adherence issues

- Ask an empathetic question
  - "Its hard to take an inhaler every day, how often do you miss doses in a week?"
  - Check prescribing, pharmacy dispensing records
  - Ask about attitudes and beliefs of medications

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Investigating Uncontrolled Asthma in Primary Care

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Pharmacotherapy of Asthma

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About the GINA Strategy

- Recommendations are framed, not as answers to isolated PICO questions, but as part of an integrated strategy, in relation to:
  - goals of preventing deaths and exacerbations, as well as improving symptom control
  - Implementation in clinical practice
- For new therapies, 2 good quality studies + indication by EMA/FDA are required
  - For existing medications with established safety profile, GINA may sometimes make off-label recommendations for new indications (e.g. macrolides for severe asthma)

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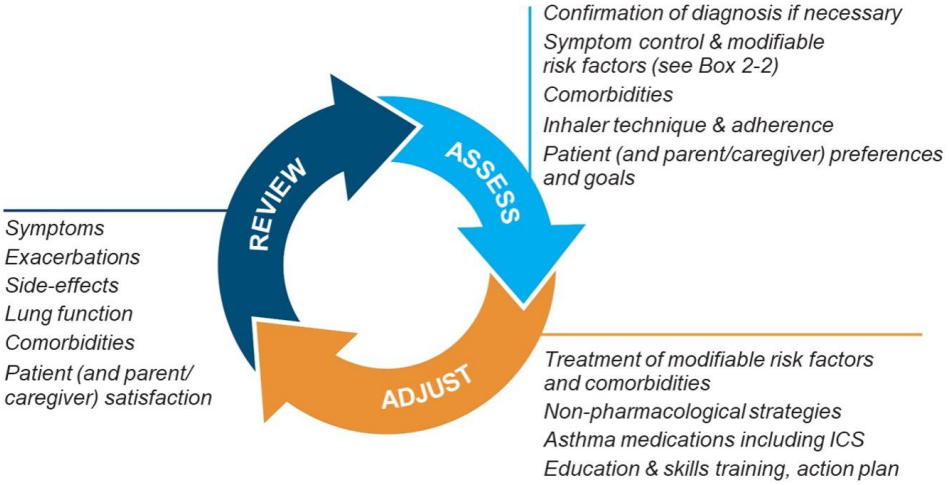
Asthma treatment is not 'set and forget', and not just medications



GINA 2024 Box 3-3 © Global Initiative for Asthma. www.ginasthma.org

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Focused Updates, Not Complete Revision of 2007 Guidelines

- Intended to improve asthma management and support informed, shared decision making between patients and their providers.
- Offer new guidance in **six key areas** of asthma diagnosis, management, and treatment, selected through a comprehensive literature review, consultation with experts, and soliciting comments from the public.
- Updates offer **19 recommendations** and include new features to help clinicians engage with patients.

NIH National Heart, Lung, and Blood Institute

2020 Focused Updates to the Asthma Management Guidelines
A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group
nhlbi.nih.gov/AsthmaGuidelines

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Topic Areas

1. Intermittent Inhaled Corticosteroids
2. Long-Acting Muscarinic Antagonists
3. Indoor Allergen Mitigation
4. Immunotherapy in the Treatment of Allergic Asthma
5. Fractional Exhaled Nitric Oxide Testing
6. Bronchial Thermoplasty

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nhlbi.nih.gov/AsthmaGuidelines

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Box 2-2. GINA assessment of asthma control in adults, adolescents and children 6–11 years

A. Asthma symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice/week?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
• Any night waking due to asthma?	Yes☐ No☐			
• SABA reliever for symptoms more than twice/week?*	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

Assessing Asthma Control

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Asthma Therapy Acronyms

SABA
- Short acting bronchodilator
  - e.g. albuterol
  - Quick onset ~<5 minutes
  - Short duration ~ 4 hrs

LABA
- Long acting bronchodilator
  - e.g. formoterol, salmeterol, vilanterol
  - All but salmeterol quick acting
  - Long duration: 12-24 hrs depending on LABA

LAMA
- Long acting muscarinic antagonist
  - e.g. tiotropium, umeclidinium

ICS
- Inhaled corticosteroid
  - e.g. budesonide, fluticasone, mometasone
  - Preventive therapy
  - Anti-inflammatory

MDI
- Metered dose inhaler

DPI
- Dry powder inhaler

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What Is SMART or MART Therapy?

- MART
  - Maintenance and reliever combined therapy
    - Maintenance: Inhaled Corticosteroids (ICS)
    - Reliever: Bronchodilator (in US this is a long-acting bronchodilator (LABA))
      - Preferred LABA is formoterol as rapid acting and can take **up to 12 puffs a day**
- SMART
  - Single maintenance and reliever therapy
    - Best studied is budesonide (ICS) and formoterol (LABA) a.k.a. Symbicort
  - One inhaler does it all!
- AIR
  - Anti-inflammatory Reliever

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Background to Changes in 2019 - the Risks of 'Mild' Asthma

- Patients with apparently mild asthma are at risk of serious adverse events
  - 15–20% of adults dying of asthma
- Inhaled SABA has been first-line treatment for asthma for 50 years
  - Patients commonly believe that "*My reliever gives me control over my asthma"*, so they often don't see the need for additional treatment

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Background to Changes in 2019 - the Risks of SABA-only Treatment

- Regular or frequent use of SABA is associated with adverse effects
- Higher use of SABA is associated with adverse clinical outcomes
  - Dispensing of ≥3 canisters per year is associated with higher risk of emergency department presentations *(Stanford, AAAI 2012)*
  - Dispensing of ≥12 canisters per year is associated with higher risk of death *(Suissa, AJRCCM 1994)*

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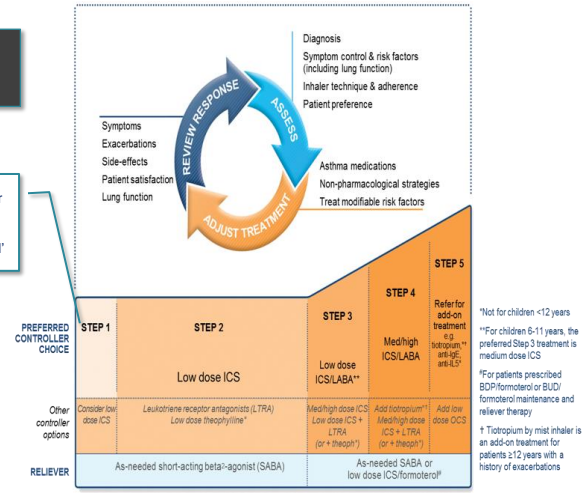
GINA 2018 – Main Treatment Figure

Step 1 treatment is for patients with symptoms <twice/month and no risk factors for exacerbations

Previously, no controller was recommended for Step 1, i.e. SABA-only treatment was 'preferred'



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GINA 2019 – Landmark Changes in Asthma Management

- For safety, GINA no longer recommends SABA-only treatment for Step 1
- GINA now recommends that all adults and adolescents with asthma should receive symptom-driven or regular low dose ICS-containing controller treatment, to reduce the risk of serious exacerbations

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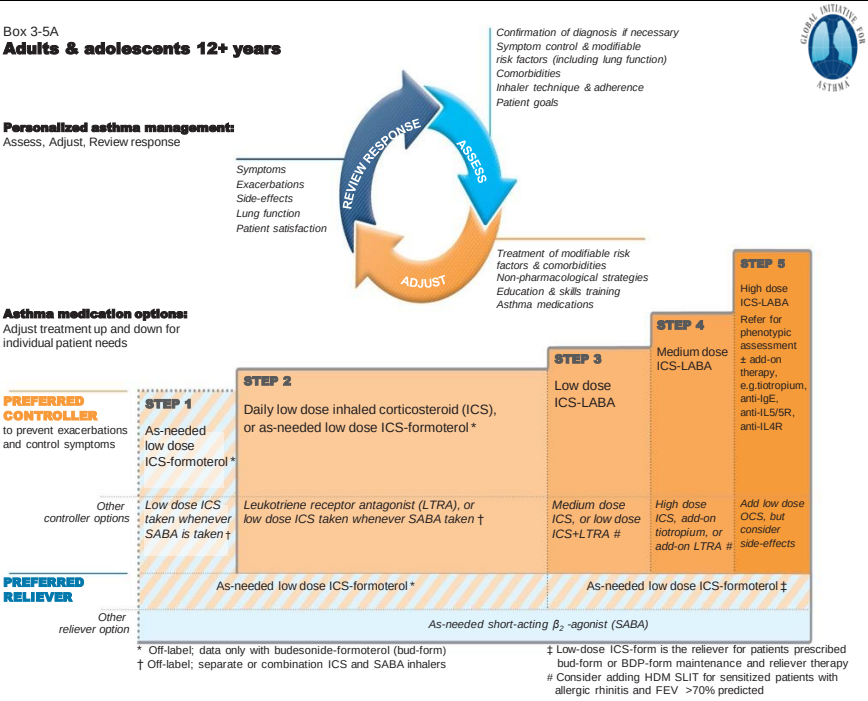
GINA 2019



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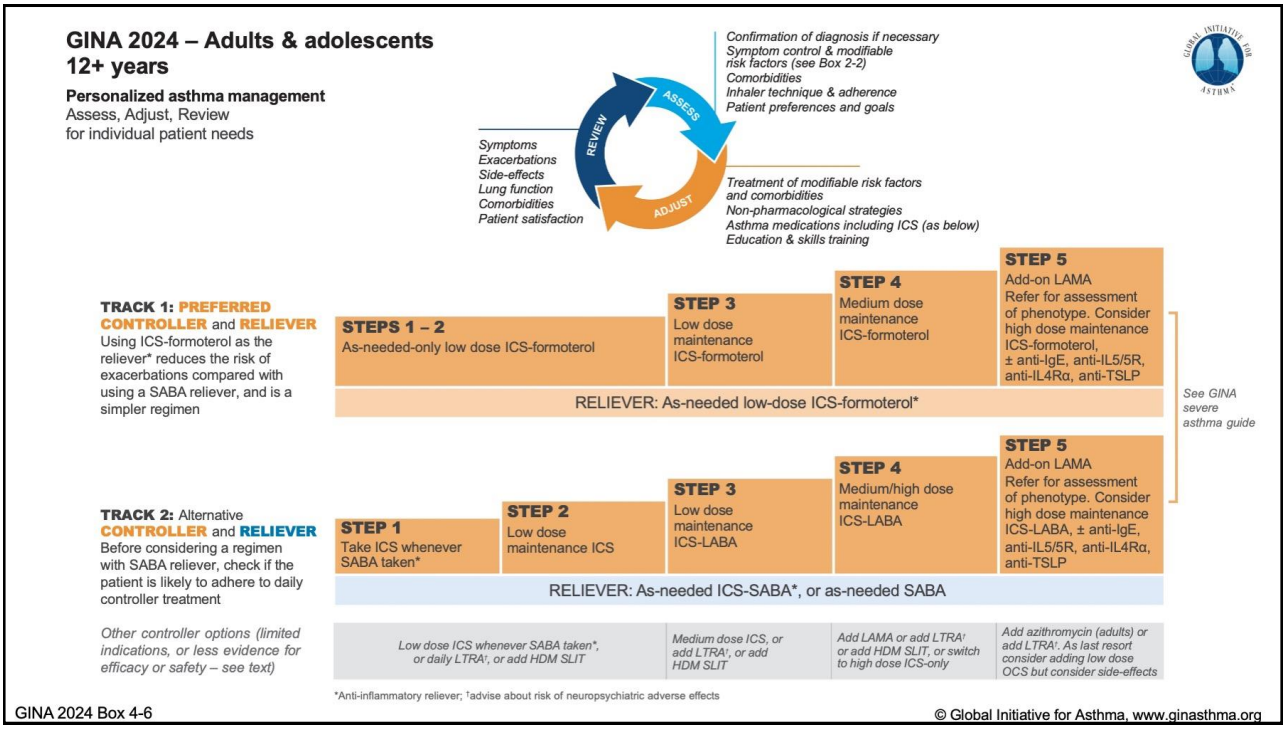

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TRACK 1, Steps 1–4: PREFERRED CONTROLLER and RELIEVER for adults and adolescents.

Using ICS-formoterol as an anti-inflammatory reliever (AIR), with or without maintenance ICS-formoterol, reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen, with a single medication across treatment steps.

For budesonide-formoterol 200/6 mcg [160/4.5] DPI or pMDI*, or beclometasone-formoterol 100/6 mcg DPI or pMDI

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed-only low dose ICS-formoterol reliever	Low dose maintenance and reliever therapy (MART) with ICS-formoterol	Medium dose maintenance and reliever therapy (MART) using low-dose ICS-formoterol	Refer for expert assessment, phenotyping, and add-on treatment for severe asthma
One inhaler, use as needed	Same inhaler, take 1 inhalation once or twice daily and 1 as needed	Same inhaler, take 2 inhalations twice daily and 1 as needed	

*In some countries, a budesonide-formoterol pMDI with 100/3 [80/2.25] mcg per actuation is available for AIR-only or MART. For this pMDI, the recommended number of inhalations is double those shown above above.

GINA 2024 Box 4-7

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NAEPP 2020 Update

Recommend SMART Therapy for Steps 3-4

Figure I.d: Stepwise Approach for Management of Asthma in Individuals Ages 12 Years and Older

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.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

J Allergy Clin Immunol. 2020;146(6):1217-70.

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What Is Maximum ICS-Formoterol?

Maximum total of budesonide-formoterol is 12 puffs/d

Most patients would never use this much

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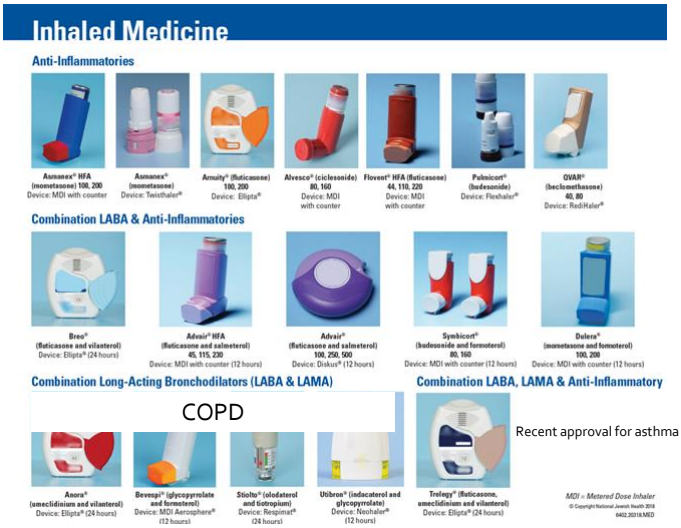

salmeterol can not be used for quick symptom relief

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Short-Acting Bronchodilators

ProAir® HFA (albuterol)
Device: MDI with counter

ProAir® (albuterol)
Device: RespiClick®

Proventil® HFA (albuterol)
Device: MDI

Ventolin® HFA (albuterol)
Device: MDI with counter

Xopenex® HFA (levalbuterol)
Device: MDI

Combivent® (ipratropium & albuterol)
Device: Respimat®

Long-Acting Bronchodilators (LAMA)

Incruse® (umeclidinium)
Device: Ellipta®
(24 hours)

Seebri® (glycopyrrolate)
Device: Neohaler®
(12 hours)

Spiriva® (tiotropium)
Device: HandiHaler®
(24 hours)

Spiriva® (tiotropium)
Device: Respimat®
(24 hours)

Tudorza® (aclidinium)
Device: Pressair®
(12 hours)

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Low, medium and high ICS doses: adults/adolescents

Adults and adolescents (12 years and older)			
Inhaled corticosteroid	Total daily ICS dose (mcg) Low	Medium	High
Beclometasone dipropionate (pMDI, standard particle, HFA)	200-500	>500-1000	>1000
Beclometasone dipropionate (pMDI, extrafine particle*, HFA)	100–200	>200–400	>400
Budesonide (DPI)	200–400	>400–800	>800
Ciclesonide (pMDI, extrafine particle*, HFA)	80–160	>160–320	>320
Fluticasone furoate (DPI)	100		200
Fluticasone propionate (DPI)	100–250	>250–500	>500
Fluticasone propionate (pMDI, standard particle, HFA)	100–250	>250–500	>500
Mometasone furoate (DPI)	200		400
Mometasone furoate (pMDI, standard particle, HFA)	200-400		>400

This is NOT a table of equivalence. These are suggested total daily doses for the 'low', 'medium' and 'high' dose treatment options with different ICS.

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler (non-CFC); * see product information

GINA 2020, Box 3-6A

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Adverse Effects of Inhaled GC

Systemic effects much less than with oral GC

- Growth suppression, osteoporosis effects vary by study
- Adrenal suppression
  - Rare at doses < 1000 mg/d
  - More common with fluticasone than other ICS

Local effects

- Oral candidiasis
- Dysphonia
  - Due to vocal cord myopathy

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Prednisone Bursts in Asthma

For adults, typically 40 mg/d prednisone is reasonable dose

Tapers not necessary if duration < 2 weeks

Duration is variable
- 3-14 days

Many patients can tell you how long it takes to get control

Prednisone bursts more than once a year indicates poor control

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Anti-Leukotriene Therapies

(LTRA) cysLT$_1$ receptor antagonists

- montelukast (Singulair)
- block actions of cysLTs
- Generally well tolerated
- Minimal effect in most patients
- association with neuropsychiatric problems (black box warning)

5-lipoxygenase inhibitor

- zileuton
- Rarely used

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Tiotropium (LAMA)

Several studies have found tiotropium to be beneficial when added to

- ICS alone
- ICS + LABA

FDA approved for asthma 2015

NHLBI update 2020 (LAMA + ICS/LABA)

- Small improvement in asthma symptoms and QOL
- No improvement in exacerbations

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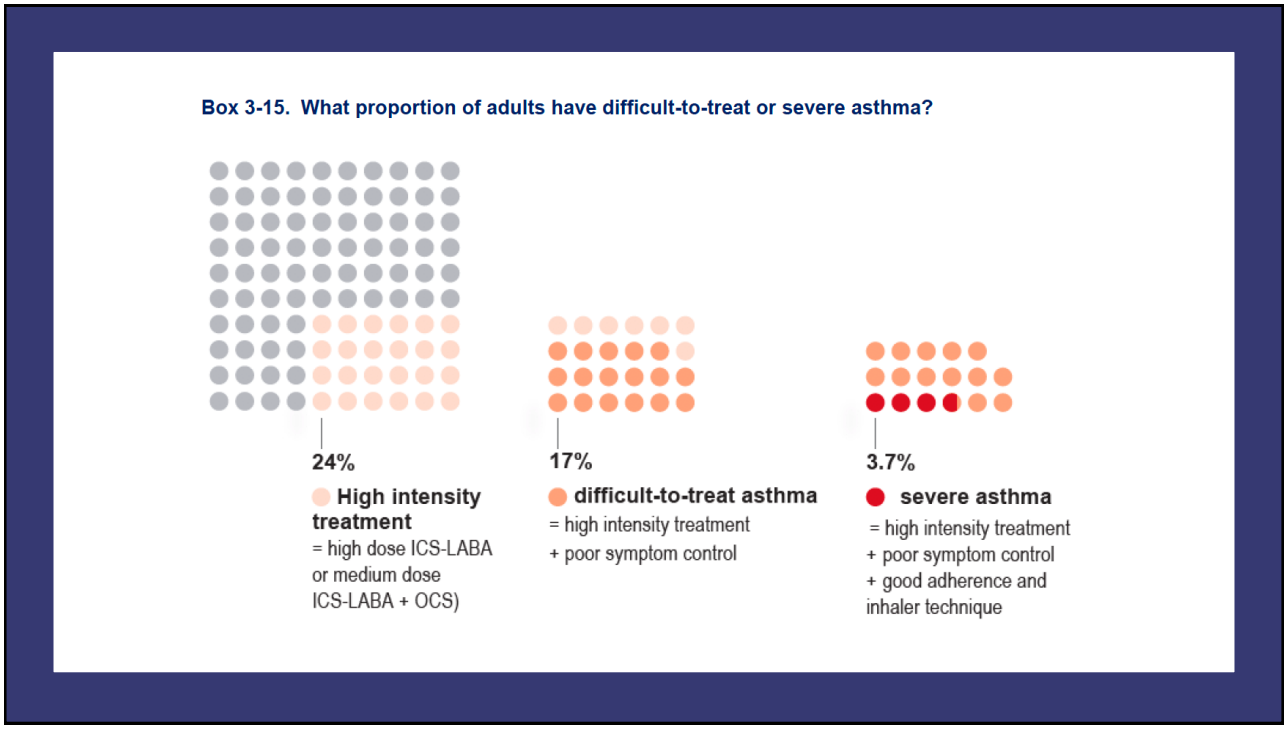

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Biologics in Asthma

- Omalizumab (anti-IgE) a.k.a. Xolair
- Mepolizumab (anti-IL-5) a.k.a. Nucala
- Reslizumab (anti-IL-5) a.k.a. Cinqair
- Benralizumab (anti-IL-5R) a.k.a. Fasenra
- Dupilumab (anti-IL-4Ra) a.k.a. Dupixent
- Tezepelumab (anti-TSLP) a.k.a. Tezspire

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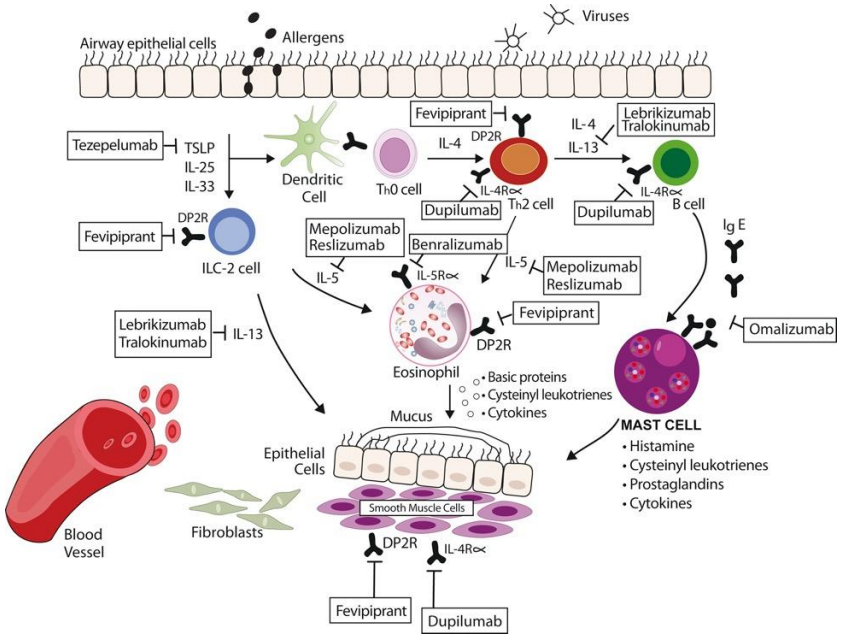

J Allergy Clin Immunol Pract 2019

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Biologics in Asthma

Careful phenotyping is essential for good results

- Allergic asthma with positive skin tests and elevated IgE: consider anti-IgE therapy (omalizumab)
- Asthma with elevated peripheral eosinophilia: consider anti-IL5 therapy (mepolizumab, reslizumab, benralizumab) or dupilumab

Biologics are expensive but do have oral steroid sparing effects

Usually reserved for severe asthma patients

- Frequent steroid bursts/year
- Frequent hospitalizations
- Steroid dependent

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Allergen Avoidance

- Very effective but hard to do
- Single allergen intervention does not appear to help
- Most dust mite avoidance strategies reduce mites but may not improve symptoms
- Most pet owners won't get rid of pets
- Outdoor allergens impossible to avoid

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2020 NAEPP Evidence on Allergen Mitigation

TABLE IIIB. Summary of certainty of evidence on allergen mitigation interventions

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	†	†

J Allergy Clin Immunol. 2020;146(6):1217-70.

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GINA

Box 3-10. Effectiveness of avoidance measures for indoor allergens

Measure	Evidence of effect on allergen levels	Evidence of clinical benefit
House dust mites		
Encase bedding in impermeable covers	Some (A)	Adults - none (A) Children - some (A)
Wash bedding on hot cycle (55–60°C)	Some (C)	None (D)
Replace carpets with hard flooring	Some (B)	None (D)
Acaricides and/or tannic acid	Weak (C)	None (D)
Minimize objects that accumulate dust	None (D)	None (D)
Vacuum cleaners with integral HEPA filter and double-thickness bags	Weak (C)	None (D)
Remove, hot wash, or freeze soft toys	None (D)	None
Pets		
Remove cat/dog from the home	Weak (C)	None (D)
Keep pet from the main living areas/bedrooms	Weak (C)	None (D)
HEPA-filter air cleaners	Some (B)	None (A)
Wash pet	Weak (C)	None (D)
Replace carpets with hard flooring	None (D)	None (D)
Vacuum cleaners with integral HEPA filter and double-thickness bags	None (D)	None (D)
Cockroaches		
Bait plus professional extermination of cockroaches	Minimal (D)	None (D)
Baits placed in households	Some (B)	Some (B)
Rodents		
Integrated pest management strategies	Some (B)	Some (B)
Fungi		
Remediation of dampness or mold in homes	A	A
Air filters, air conditioning	Some (B)	None (D)

This table is adapted from Custovic et al[354]

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Subcutaneous Immunotherapy for Asthma (SCIT)

- NAEPP 2020 Update
  - ≥5 yo with mild-moderate asthma conditionally recommends use of SCIT as adjunct to pharmacotherapy

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Sublingual Immunotherapy for Asthma (SLIT)

- NAEPP 2020 Update
  - Conditionally recommends AGAINST use of SLIT in asthma treatment

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Comorbidity	Clinical clues	Suggested evaluation	Recommended intervention	Anticipated asthma benefit
Allergic rhinitis	*Nasal symptoms*	*SPT or sIgE*	*INCS , oral/nasal antihistamines montelukast, nasal saline*	*Uncertain, possible fewer exacerbations*
CRSwNP	*Chronic congestion, sinus pressure, cough*	*Nasal examination, sinus CT, rhinoscopy;aspirin sensitivity In children: sweat test, ciliary bx/PCD genetics*	*Oral/intranasal steroids, antihistamines, nasal saline, antibiotics, sinus surgery; aspirin desensitization; anti-IgE, anti-IL5, anti-IL4R therapy*	*Improved symptoms, FEV1, exacerbations*
Obesity	*Elevated BMI*	*BMI, metabolic syndrome*	*Diet, exercise program; bariatric surgery (adult)*	*Improved QOL, asthma control, FEV1*
ILO	*Stridor, discrete episodes, hyperventilation*	*Laryngoscopy with provocation*	*Speech pathology, stimulus avoidance, inhaled anticholinergics*; psychopharmacologic therapy, if indicated*	*Improved symptoms*
Dysfunctional breathing	*Hyperventilation, sighing, asynchronous thoracoabdominal breathing*	*SEBQ/Nijmegen Questionnaire*	*Breathing retraining*	*Improved symptoms, QOL*
OSA	*Snoring, daytime somnolence*	*PSG*	*Adenotonsillectomy (children); CPAP*	*Improved exacerbations, symptoms, QOL*
GERD	*Heartburn, regurgitation, chest pain, cough*	*GI endoscopy, impedance/pH probe*	*Gastric acid suppression, fundoplication*	*Possible improved FEV1 and rescue medication use*
Anxiety/ depression	*Mood/behavioral cues*	*Screening tools (ie, GAD7, PHQ9, HADS);*	*psychology referral CBT, psychopharmacologic therapy*	*Possible improved symptoms, QOL*
Vitamin D deficiency		*25 OH vitamin D level (<30 ng/mL)*	*Vitamin D supplementation*	*Possible improved exacerbation rate in adults achieving normal vitamin D levels*
Smoking/SHS,	*History, observed odor of smoke History*	*urinary cotinine*	*Smoking cessation counseling, medical management*	*Symptoms, lung function, exacerbations*
COPD	*Dyspnea, chronic cough, sputum production history*	*pre- and post-spirometry*	*Smoking cessation; asthma pharmacotherapy; LAMA-LABA-ICS therapy*	*Symptoms, lung function, exacerbations*

Gaffin JM et al. J Allergy Clin Immunol Pract. 2022;10(2):397-408.

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Original Article

A Randomized, Double-Blind, Placebo-Controlled Trial of Escitalopram in Patients with Asthma and Major Depressive Disorder

E. Sherwood Brown, MD, PhD[a], Nasreen Sayed, MS[a], Erin Van Enkevort, PhD[a], Alexandra Kulikova, MS[a], Alyson Nakamura, MD[a], David A. Khan, MD[b], Elena I. Ivleva, MD, PhD[a], Prabha Sunderajan, MD[a], Bruce G. Bender, PhD[c], and Traci Holmes, BA[a] *Dallas, Texas; and Denver, Colo*

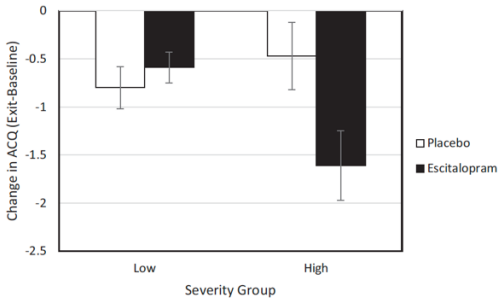

FIGURE 1. Change in the ACQ score in low- and high-severity groups.

Brown ES et al. J Allergy Clin Immunol Pract 2018;6:1604-12.

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Treating Childhood Asthma via Indirect Antidepressant Therapy

Original Article

The Impact of Caregiver Depression on Child Asthma Outcomes: Pathways and Mechanisms

E. Sherwood Brown, MD, PhD[a], Jayme M. Palka, PhD[a], Heather K. Lehman, MD[b], Alexandra Kulikova, MS[a], David A. Khan, MD[c], Josseline Lopez, BS[a], Anna Antony, MA[a], Donna Persaud, MD[d], Jasmine Tiro, PhD[a], Elena I. Ivleva, MD, PhD[a], Alyson Nakamura, MD[a], Zena Patel, PA-C[a], Traci Holmes, BS[a], Qurratulain Humayun, MBBS, MS, MD[f], Tressa Lloyd, MS[f], Karen Allen, MS[f], Savitoj Kaur, BS, BA[f], M. Seth Owitz, BS[f], Ray J. Pak, BS[f], Kevin G. Zablonski, BS[f], Michael S. Adragna, MD[f], Raymond Chankalal, MD[f], Beatrice L. Wood, PhD[f,+], and Bruce D. Miller, MD[f,+] *Dallas, Texas; and Buffalo, NY*

Improvement in caregiver depression positively influences child asthma outcomes partially through improvement in child depressive symptom severity

Caregiver depression screening and treatment might lead to improvement in child asthma outcomes

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When to Refer?

- Difficulty Confirming Diagnosis of Asthma
- Poorly controlled
- Suspected occupational asthma
- Patients with treatment related adverse effects
- Complex phenotypes of asthma
  - AERD, ABPA

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Summary

- Making a correct diagnosis of asthma is key
- Poorly controlled asthma
  - >2 albuterol inhalers /year
  - >1 prednisone bursts/year
- Check inhaler technique routinely
- For mild-moderate asthma, controllers (especially ICS/LABA) may be used as needed with good results
- Biologic therapies have been very helpful for severe asthma patients but one size does not fit all

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