Current Approach to Asthma Evaluation and Management

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Disclosures

Dr. Margaret Johnson, faculty for this educational activity, has no relevant financial relationships with ineligible companies* to disclose, and has indicated that the presentations or discussions will include off-label or unapproved product usage.

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

PRN use of ICS/LABA

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Learning Objectives

Understand	Appreciate	Identify	Review
Understand the importance of accurately establishing/refuting the diagnosis of asthma	Appreciate the changing paradigms of asthma therapy • Set v. prn inhaled steroid use • Choice for rescue medication use	Identify role of biologic therapy in patients with asthma	Review interplay between asthma and obesity and potentil role of GLP-1 inhibitors

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What is Asthma?

Heterogenous disease

- Reversible expiratory airflow obstruction

Respiratory symptoms that vary over time and in intensity

Airway hyperresponsiveness

Chronic airway inflammation

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Improving Diagnostic Accuracy

Clues from history

- Early AM awakenings
- Worsening with cold
- Marked improvement with steroids

Objective testing

- Spirometry with bronchodilator
- Bronchoprovocation testing
- Peak flow variability
- ?eNO (>41 ppb)

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Limitations of eNO for diagnosis

- Lack of specificity
- Not elevated in non-eosinophilic asthma
- Variability
  - Lower in active smokers, early phase of allergic response, during bronchoconstriction
  - May be increased or decreased in acute viral infections

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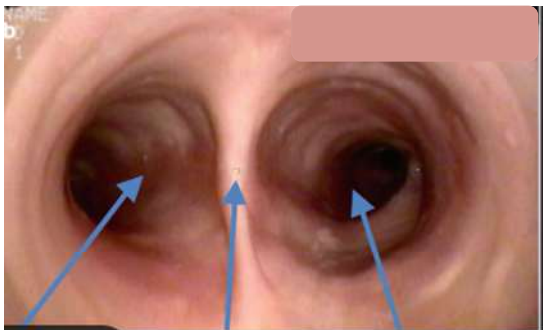
ECAC



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Review
- Symptoms
- Exacerbations
- Side Effects
- Lung function
- Side effects
- Com-morbidities

Assess
- Confirmation of diagnosis
- Modifiable risk factors
- Inhaler technique
- Com-morbidities
- Patient preferences and values

Adjust
- Treat modifiable risk factors
- Nonpharmacological strategies
- Education

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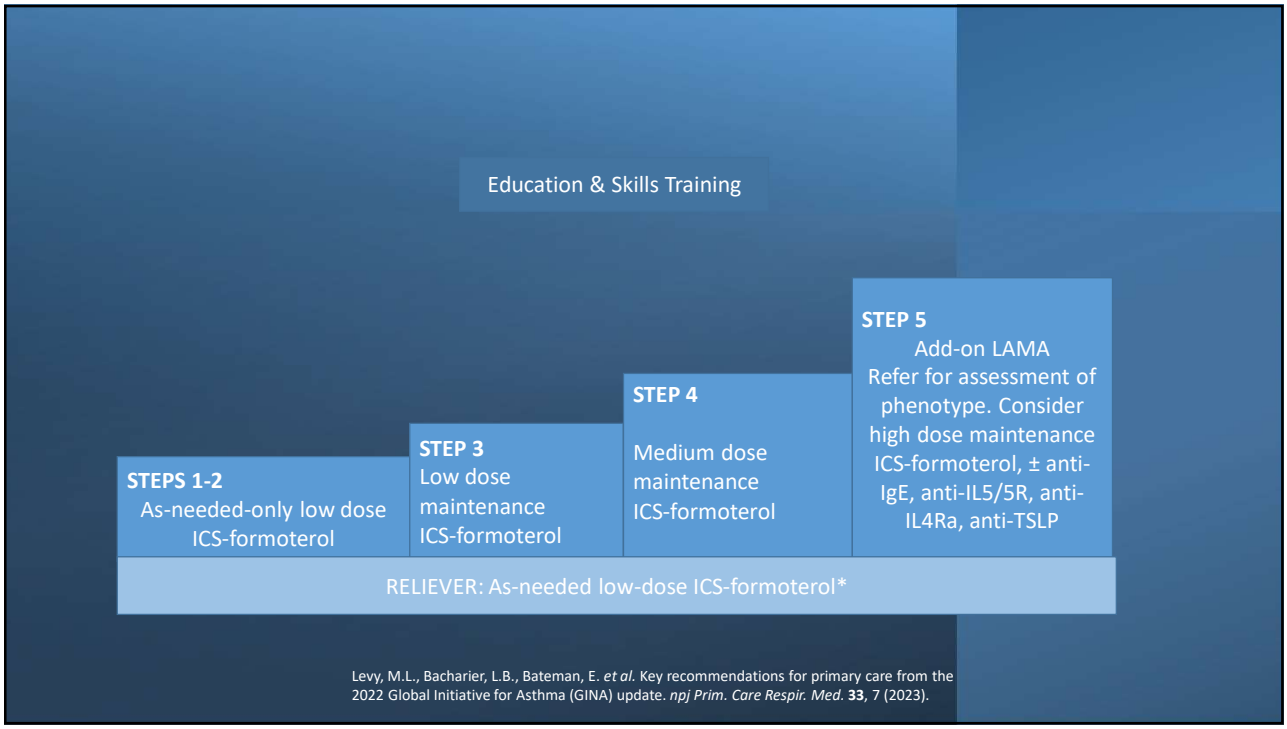
Education & Skills Training
STEPS 1-2
As-needed-only low dose ICS-formoterol
STEP 3
Low dose maintenance ICS-formoterol
STEP 4
Medium dose maintenance ICS-formoterol
STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Ra, anti-TSLP
RELIEVER: As-needed low-dose ICS-formoterol*
Levy, M.L., Bacharier, L.B., Bateman, E. et al. Key recommendations for primary care from the 2022 Global Initiative for Asthma (GINA) update. npj Prim. Care Respir. Med. 33, 7 (2023).

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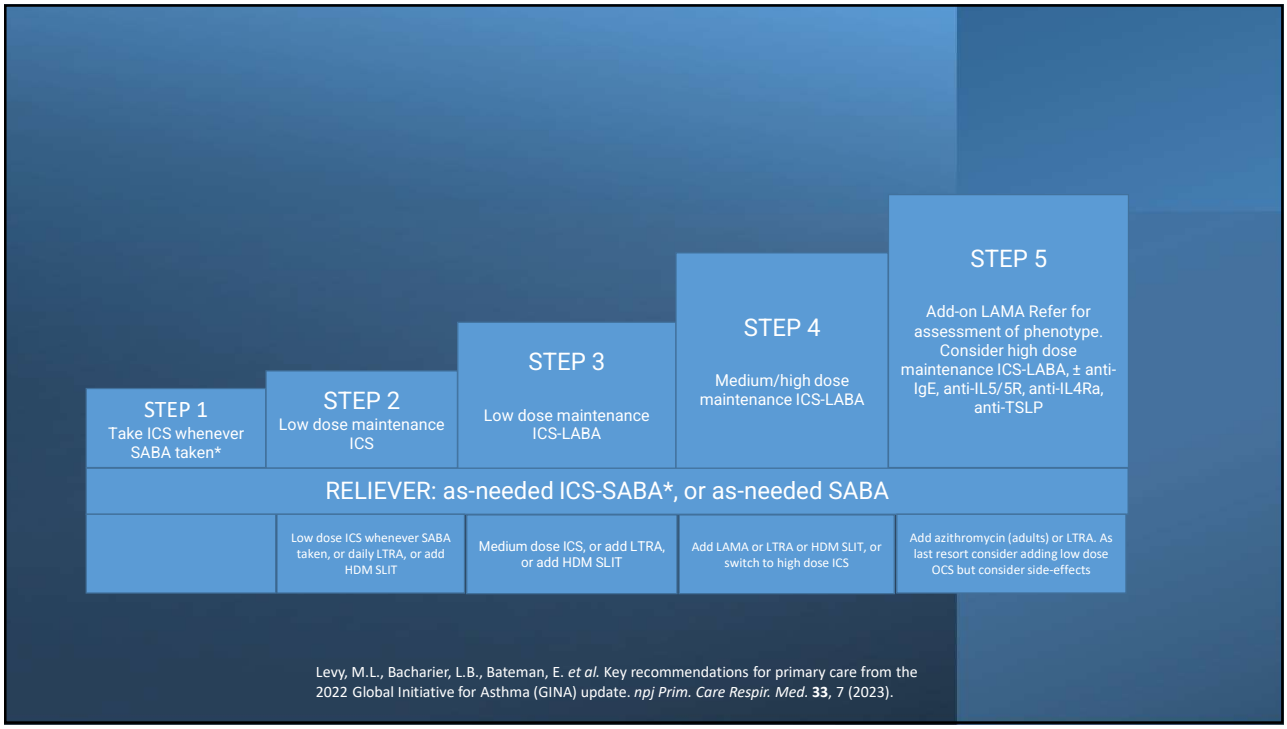
STEP 1
Take ICS whenever SABA taken*
STEP 2
Low dose maintenance ICS
STEP 3
Low dose maintenance ICS-LABA
STEP 4
Medium/high dose maintenance ICS-LABA
STEP 5
Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Ra, anti-TSLP
RELIEVER: as-needed ICS-SABA*, or as-needed SABA
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. As last resort consider adding low dose OCS but consider side-effects
Levy, M.L., Bacharier, L.B., Bateman, E. et al. Key recommendations for primary care from the 2022 Global Initiative for Asthma (GINA) update. npj Prim. Care Respir. Med. 33, 7 (2023).

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Albuterol-Budesonide Fixed dose Rescue therapy

- Hypothesis: Use of ICS/SABA for rescue would reduce severe exacerbations compared with SABA rescue
- Moderate to severe asthma (n = 3132)
- At least one severe exacerbation prior year
- On ICS or ICS-LABA
- Three arms-two puffs for rescue
  - Albuterol alone
  - Low dose budesonide (40 ug/puff) + albuterol
  - High dose budesonide (90 ug/puff) + albuterol

Papi A. N Engl J Med 2022;386:2071-83.

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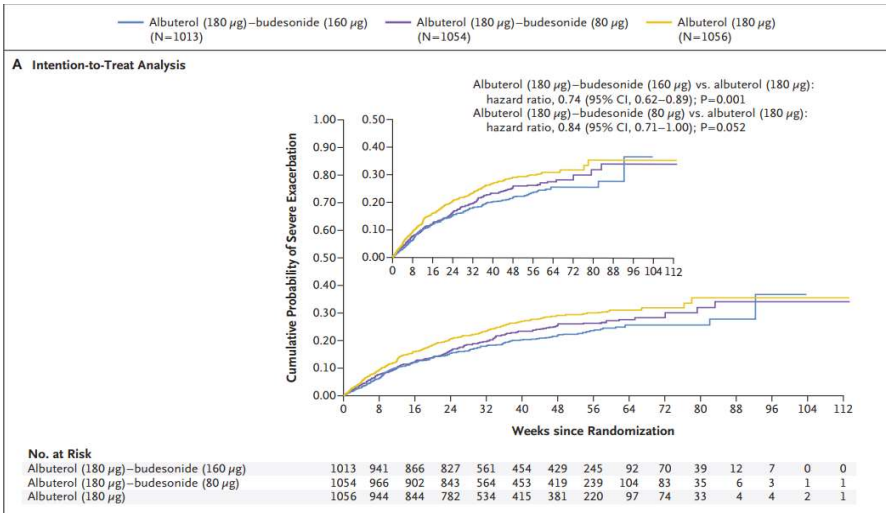

- Papi A. N Engl J Med 2022;386:2071-83.

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Inflammatory Patterns

Type 2 High	Type 2 Low
Mediated by Il 5, Il-4, Il -13	Neutrophilic airway inflammation
Eosinophilic airway inflammation and peripheral eosinophilia	Paucigranulocytic inflammation
Elevated eNO	

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Biologics for asthma: Decision making

Indicated?

Diagnosis confirmed?

Control inadequate?

Contributors to inadequate control mitigated?

Which one

Phenotype
Administration
- Home or facility
- Sq or IV

Co-existing conditions
- Atopic dermatitis
- Nasal polyposis

Insurance
Patient preference

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Overview of Biologics

Anti-IgE	Il-5/IL-5R	Il-4	Epithelial cytokines (TSLP)
• Omalizumab	• Mepolizumab • Reslizumab • Benralizumab (Il-5R)	• Dupilimab	• Tezepelumab • Itepekimab

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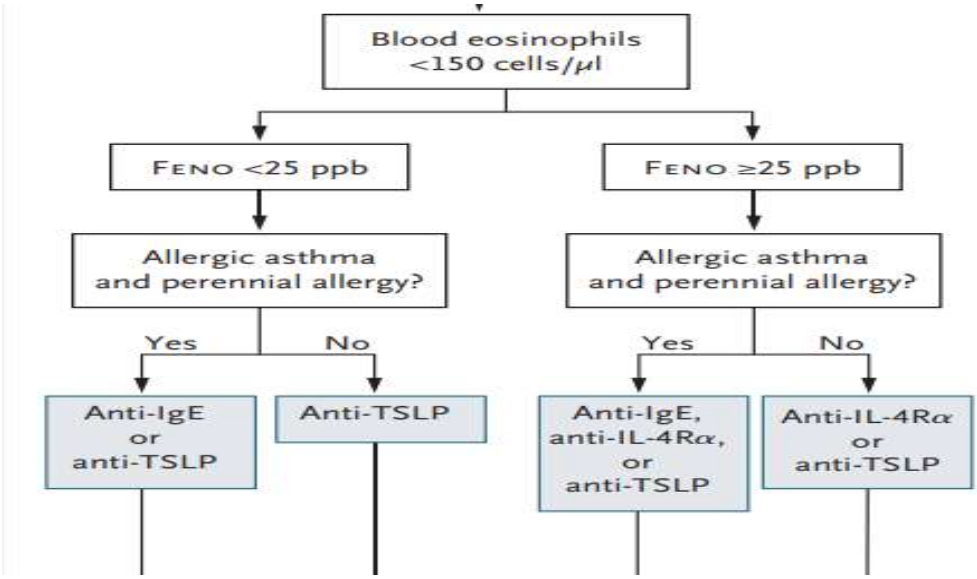

- Taichman, DB N Engl J Med 2022;386:157-71

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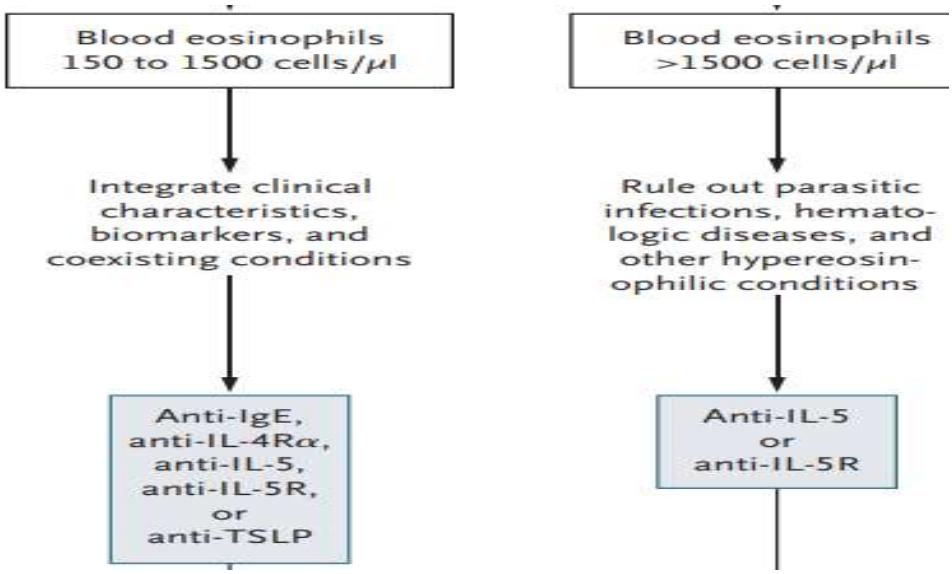

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Table 2. Choice of Monoclonal Antibody Treatment of Severe Asthma According to Patient Characteristics.*

Characteristic	Anti-IgE Antibody	Anti–Interleukin-4R Antibody	Anti–Interleukin-5 or Anti–Interleukin-5R Antibody
Indication	Severe allergic asthma	Severe type 2 asthma	Severe eosinophilic asthma
Age group	Children, adolescents, and young adults	Children, adolescents, and adults	Adults
Onset	Childhood	Childhood or adulthood	Adulthood
Allergy	Prerequisite: IgE sensitization to perennial allergen	Irrespective of allergy	Irrespective of allergy
Dominant biomarker	Serum total IgE (for dosing)	Increased FENO	Increased blood eosinophil count
Serum total IgE	Serum total IgE and weight within dose range, according to local eligibility criteria	Irrespective of total IgE	Irrespective of total IgE
Blood eosinophil count†	Slightly better response with increased count	>150 to <1500/μl†	Prerequisite: increased counts (according to local eligibility criteria), >150 to 300/μl†
FENO†	Slightly better response if increased FENO	Better response if FENO >25 ppb	Irrespective of FENO
Coexisting conditions	Allergic rhinitis, CRS with nasal polyposis, chronic urticaria	Atopic dermatitis, CRS with nasal polyposis	CRS with nasal polyposis
Exacerbations in previous yr	According to local criteria	According to local criteria	High frequency (≥2), as specified by local criteria

- Taichman, DB N Engl J Med 2022;386:157-71

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Montelukast

- Black box warning
- Mental health related side effects
  - Depression
  - Agitation
  - Suicidal thoughts

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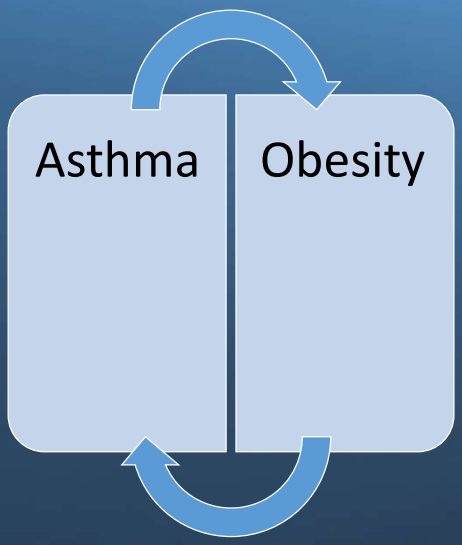
Asthma co-existent with obesity



Asthma as a consequence of obesity

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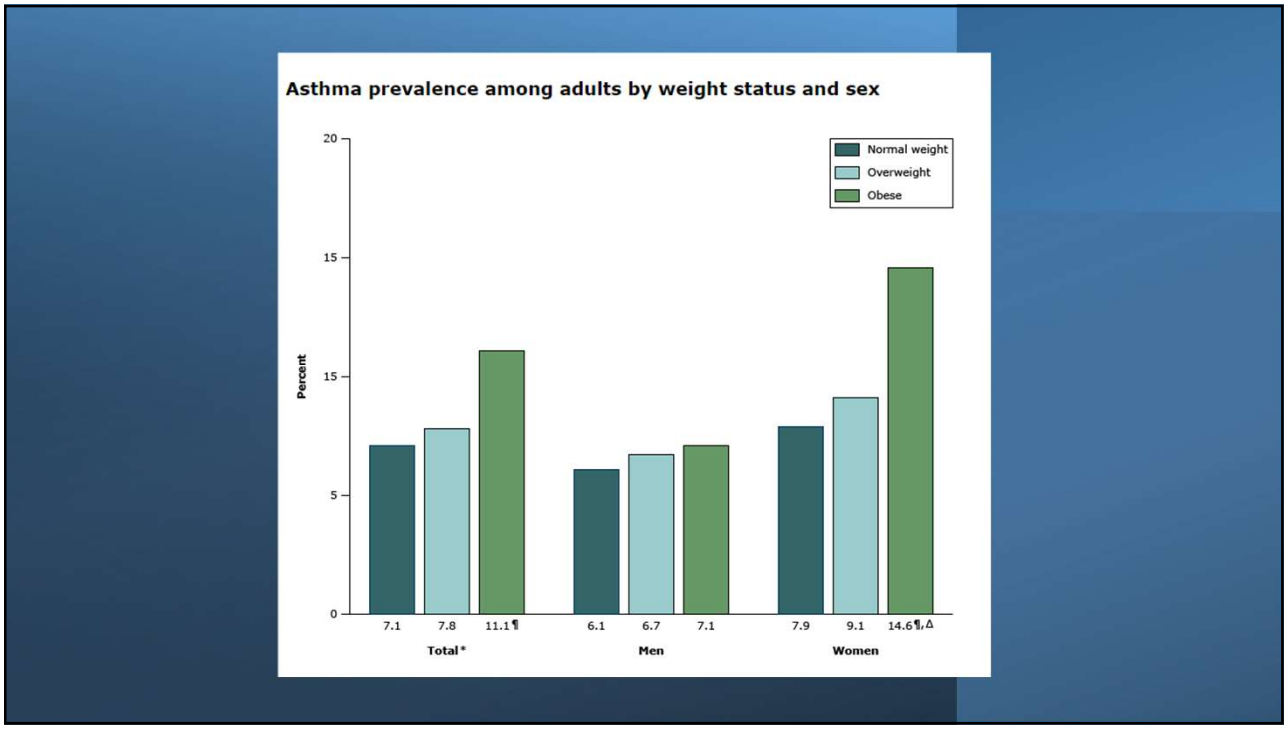
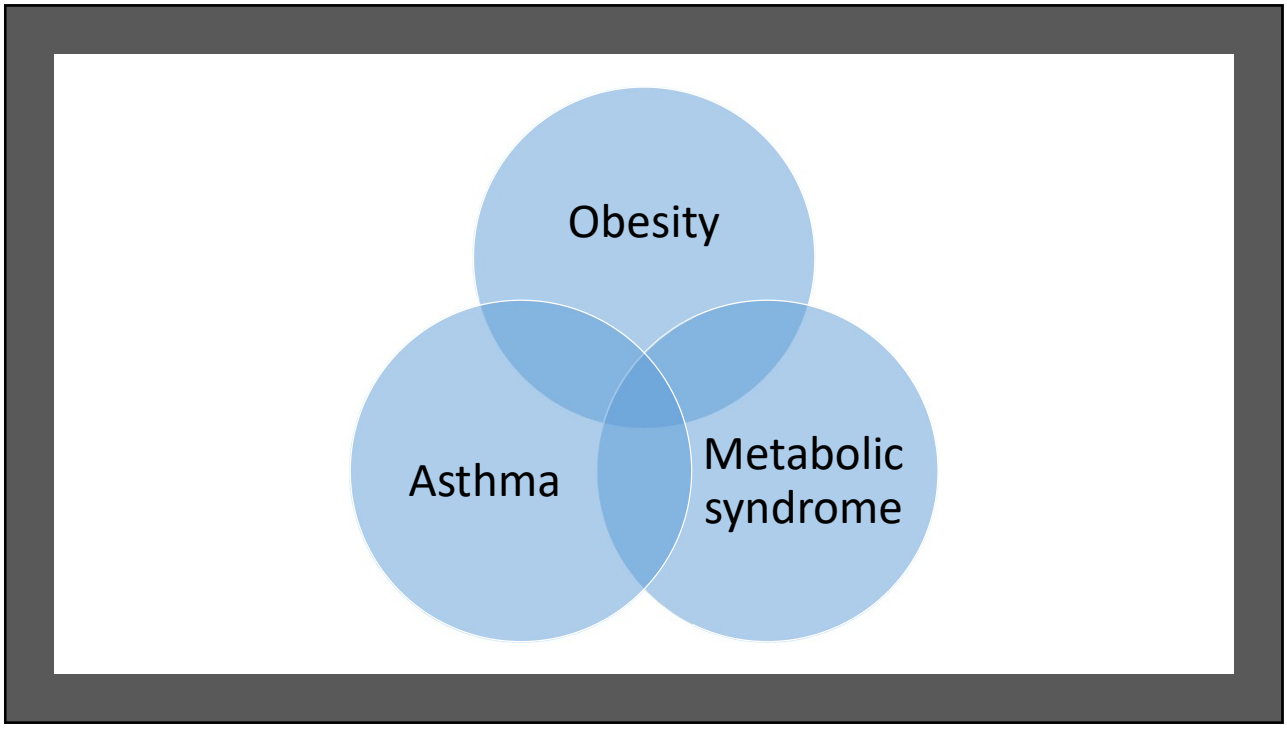

Asthma prevalence among adults by weight status and sex
Normal weight
Overweight
Obese
Percent
20
15
15
5
0
7.1
7.8
11.1¶
6.1
6.7
7.1
7.9
9.1
14.6¶,Δ
Total*
Men
Women

21


Obesity
Asthma
Metabolic syndrome

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GLP-1: Potential mechanism of benefit in asthma

- GLP-1 receptors are abundant in the lung and might stimulate vasodilation, surfactant production, and bronchodilation.
- In murine model, liraglutide, decreased airway inflammation, mucus secretion, and production of proinflammatory cytokines
- Studies using human tissue to mimic asthmatic conditions ex vivo showed that GLP-1R stimulation improved bronchial hyperresponsiveness and inflammatory changes

- Nguyen DV, et al Obesity-related, metabolic asthma: a new role for glucagon-like peptide 1 agonists.
- Lancet Respir Med. 2017 Mar;5(3):162-164.

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Take Home Messages

- Overdiagnosis and underdiagnosis are not uncommon and are deleterious
- Pharmacologic therapy is predicated on controller and reliever therapy
- Use of non-pharmacologic strategies and treatment of co-morbid disease is critical
- Biologic therapy is indicated in selected patients
- The intersection of asthma and obesity is common, incompletely understood, and pharmacologic therapy for obesity may improve asthma outcomes

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References

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Lancet Respir Med. 2017 Mar;5(3):162-164.

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