



Improving People's Lives Through Innovations in Personalized Health Care

Updates in Asthma Care: What's New in 2024

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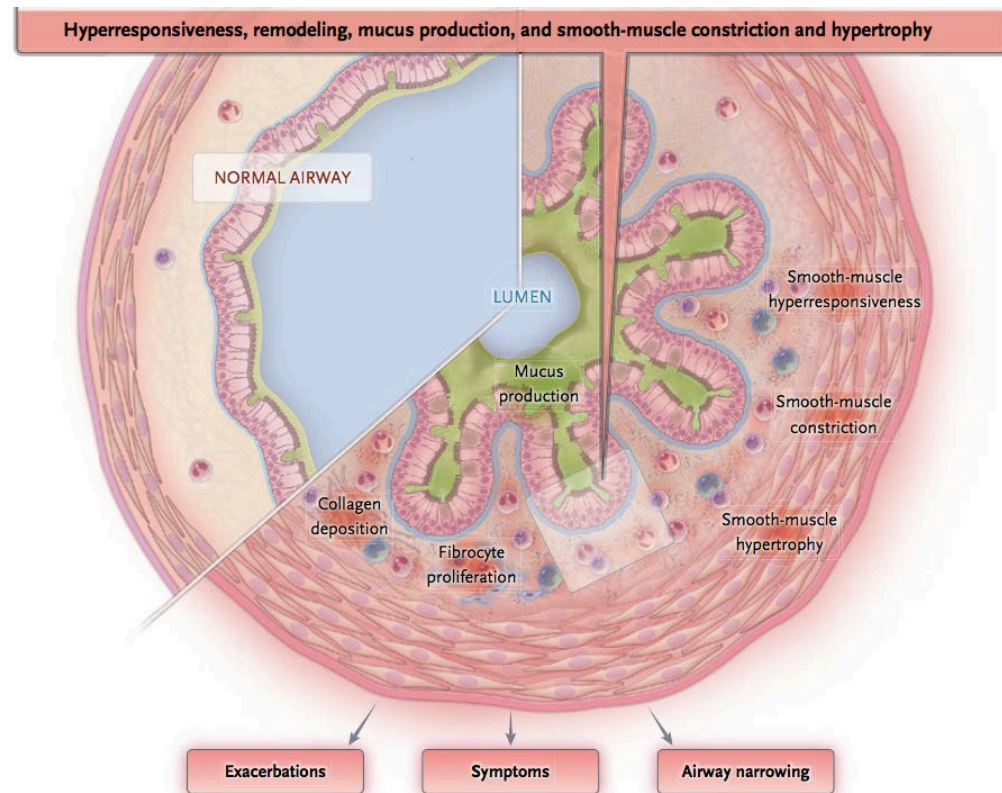
WEXNER MEDICAL CENTER

Outline

- Review asthma pathology and definition
- Practice classifying of asthma
- Discuss recent guideline changes for mild asthma
- Compare difficult-to-treat v. severe asthma
- Introduce biologic therapies for T2 asthma

Asthma: What it Is

- Inflammatory disorder of the airways
 - Chronic airway inflammation
 - Airway narrowing
 - Smooth muscle hypertrophy
 - Mucus hypersecretion
 - Bronchial hyper-reactivity



Asthma: Why We Care

- Affects 20 million Americans or 1 in 12 adults
- 8 million adults have asthma attacks a year
- \$89 in estimated lost costs
- 14.2 lost workdays per adult each year



Case 1

- 40 yo woman presents to your office with shortness of breath
 - DOE with walking up a flight of stairs
 - Waking up 1x/week coughing/SOB
 - Using albuterol inhaler 3x/week - +improvement with this
 - No recent ED visits
- Physical Exam
 - NAD
 - Lungs clear
 - Heart RRR; No JVD; No edema
- What else do you want to know?

Asthma: History

- Triggers
 - Exertion, air, pet dander, fumes/smoke, seasons, infection, certain environment
- Allergies
 - ASA
- Personal, family history
 - Atopy
 - Eczema
 - Nasal polyps

Case 1: Spirometry

- 40 yo woman presents to your office with shortness of breath

	Pre-Bronchodilator					Post-Bronchodilator		
	Pred(L)	LLN	ULN	Actual (L)	% predicted	Actual	%Pred	%Change
FVC	3.28	2.74	3.82	2.95	90	3.30	100	+11
FEV1	2.7	2.25	3.14	2.06	76	2.47	91	+19
FEV1/FVC	83	70	97	70	83	75	89	+7
FEF25-75	2.95	2.47	3.44	1.31	44	2.39	80	+82

Does she have asthma?

- Yes?
- No?

Case 1

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- +Obstruction

Bronchodilator Reversibility

- +Bronchodilator reversibility
 - 10%!

BOX 1 Determination of a bronchodilator response

$$\text{Bronchodilator response} = \frac{(\text{post-bronchodilator value (L)} - \text{pre-bronchodilator value (L)}) \times 100}{\text{predicted value (L)}^\#}$$

A change of >10% is considered a significant bronchodilator response.

[#]: predicted value should be determined using the appropriate Global Lung Function Initiative (GLI) spirometry equation.

For example, a 50-year-old male, height 170 cm, has a pre-bronchodilator forced expiratory volume in 1 s (FEV₁) of 2.0 L and a post-bronchodilator FEV₁ of 2.4 L. The predicted FEV₁ is 3.32 L (GLI 2012 “other” equation).

$$\text{Bronchodilator response} = \frac{(2.4 - 2.0) \times 100}{3.32} = 12.1\%$$

Therefore, their bronchodilator response is reported as an increase of 12.1% of their predicted FEV₁ and classified as a significant response.

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 - No recent ED visits
- Physical Exam
 - NAD
 - Lungs clear
 - Heart RRR; No JVD; No edema
- How severe is her asthma?

How would you characterize this patient's asthma?

- Mild intermittent
- Mild persistent
- Moderate persistent
- Severe persistent
- Not enough information to characterize

How would you characterize this patient's asthma?

- Mild intermittent
- Mild persistent
- **Moderate persistent**
- Severe persistent
- Not enough information to characterize

What If Spirometry was Normal?

- What test could be ordered for further evaluation?
 - Exhaled nitric oxide
 - Methacholine challenge testing
 - CT chest
 - TTE

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Fractional Exhaled Nitric Oxide

- eNO
 - <25ppb: Inconsistent with T2 inflammation; suggest alternative diagnosis
 - 25-50ppb: Inconclusive
 - > 50ppb: Suggest T2 inflammation; disease would likely be responsive to steroids

Methacholine Challenge Testing

- Used to “rule out” asthma
- Several false positives

TABLE 5
CATEGORIZATION OF BRONCHIAL RESPONSIVENESS

PC_{20} (mg/ml)	Interpretation*
> 16	Normal bronchial responsiveness
4.0–16	Borderline BHR
1.0–4.0	Mild BHR (positive test)
< 1.0	Moderate to severe BHR

* Before applying this interpretation scheme, the following must be true: (1) baseline airway obstruction is absent; (2) spirometry quality is good; (3) there is substantial postchallenge FEV_1 recovery.

Methacholine Challenge Testing

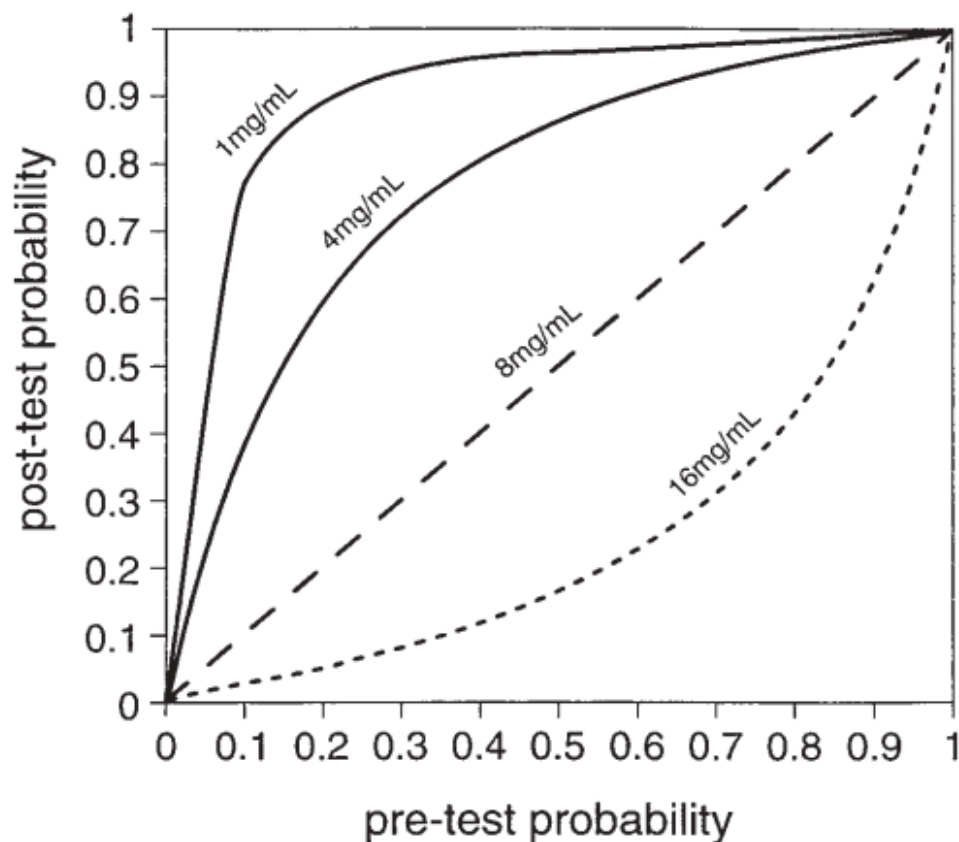


Figure 3. Curves illustrating pretest and posttest probability of asthma after a methacholine challenge test with four PC_{20} values. The curves represent a compilation of information from several sources (10, 152, 153). They are approximations presented to illustrate the relationships and principles of decision analysis. They are not intended to calculate precise posttest probabilities in patients.

Case 2

- 24 yo man with a history of asthma
- Previously managed by a pediatric pulmonologist
- Today:
 - Denies any difficulty breathing at rest or with exertion.
 - He wakes up at night ~3x/month coughing or feeling short of breath.
 - He is running ~4x/week for 30 min and is using his albuterol inhaler 10-15 min before each run.
 - No recent hospitalizations or exacerbations requiring a steroid burst within the past year.

Asthma Control

A. Assessment of symptom control

In the past 4 weeks, has the patient had:

Daytime symptoms more than twice/week? Yes No

Any night waking due to asthma? Yes No

SABA reliever needed more than twice/week? Yes No

Any activity limitation due to asthma? Yes No

Level of asthma symptom control

Well controlled

None
of these

Partly controlled

1–2
of these

Uncontrolled

3–4
of these

DISPENSATE

Case 2

- What action would you take next?
 - A. Add scheduled ICS with prn ICS/SABA
 - B. Add prn ICS-formoterol
 - C. Add scheduled ICS-LABA
 - D. Add scheduled ICS-LABA and montelukast
 - E. A or B
 - F. No additional therapy needed

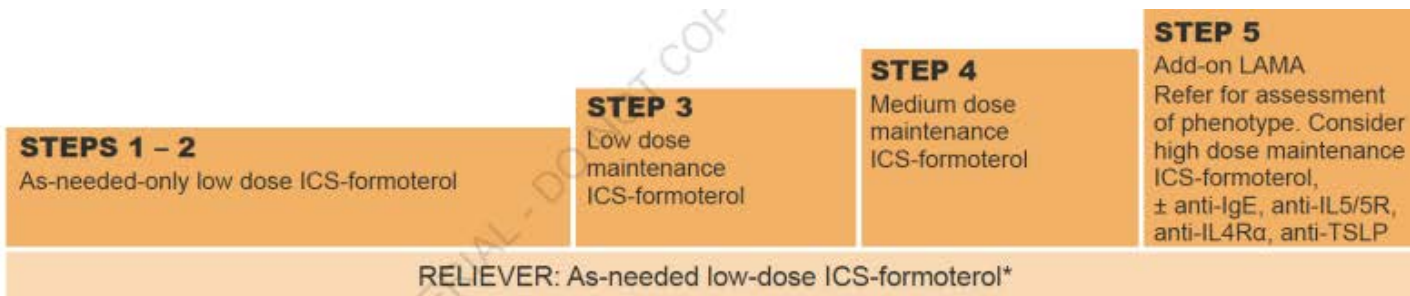
Case 2

- What action would you take next?
 - A. Add scheduled ICS with prn ICS/SABA
 - B. **Add prn ICS-formoterol**
 - C. Add scheduled ICS-LABA
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 - E. **A or B**
 - F. No additional therapy needed

GINA 2023 Updates

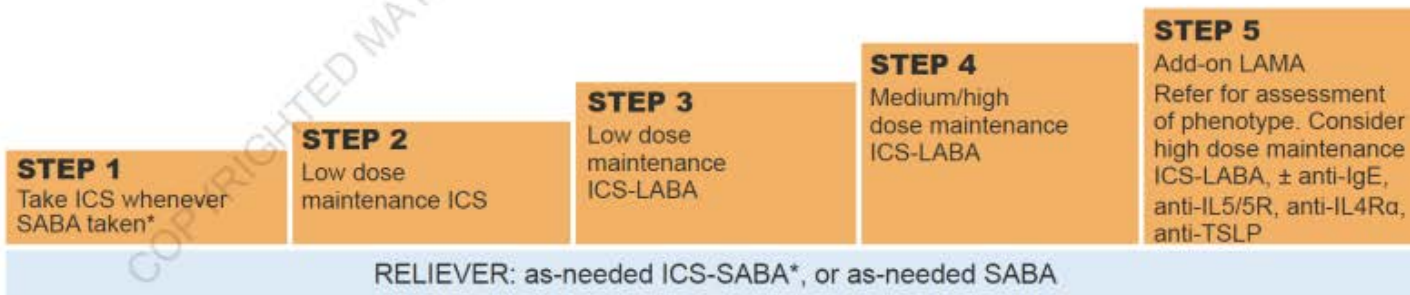
TRACK 1: PREFERRED CONTROLLER and RELIEVER

Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen



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)

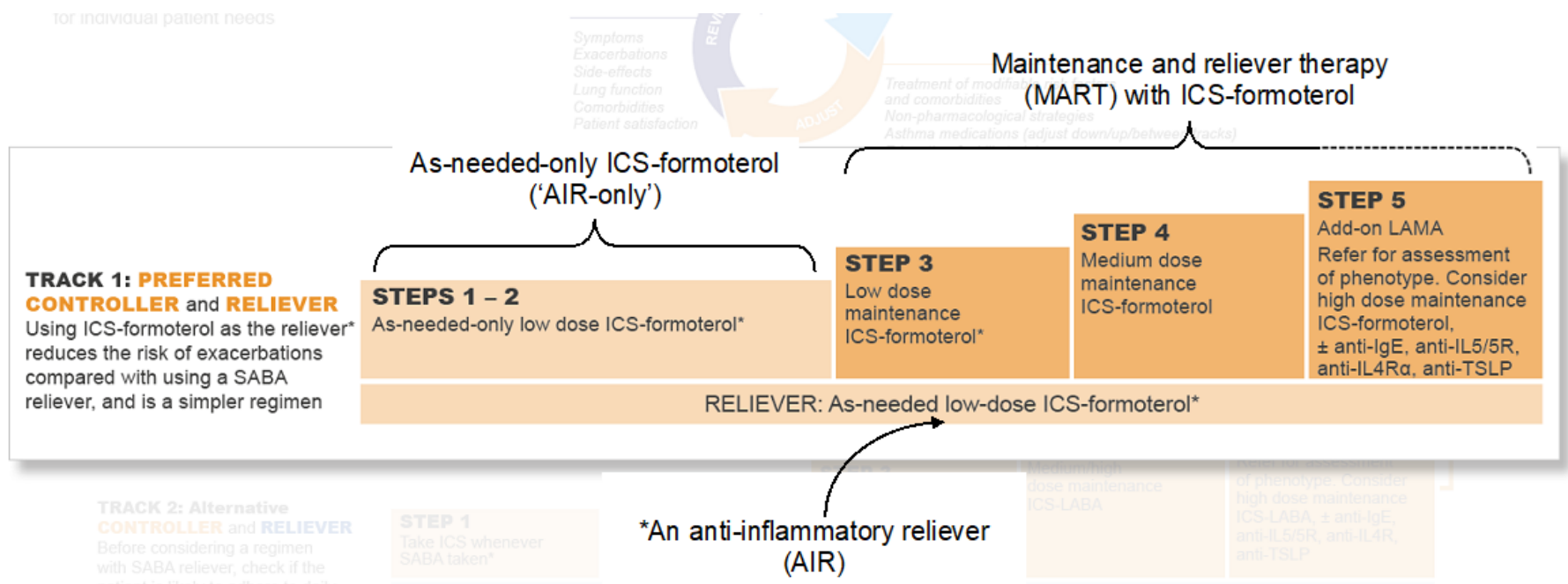
	Low dose ICS whenever SABA taken*, or daily LTRA, or add HDM SLIT	Medium dose ICS, or add LTRA, or add HDM SLIT	Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS	Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects
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ICS-Formoterol ≠ ICS-LABA

- Formoterol is a fast-acting LABA and can be used up to 6x/day
- This is not true of all LABA
- Recommendations for prn ICS-formoterol are SPECIFIC to formoterol
 - Cannot mix prn ICS-formoterol with a different scheduled ICS-LABA

New in 2023!

- Clarification regarding terminology when ICS-LABA is ONLY prn (“AIR-only”) v. scheduled and prn (“MART”)



Remember this:

- **ICS are the most effective class in treating asthma**
- These are now part of initial therapy (either alone or in combination with ICS-formoterol)

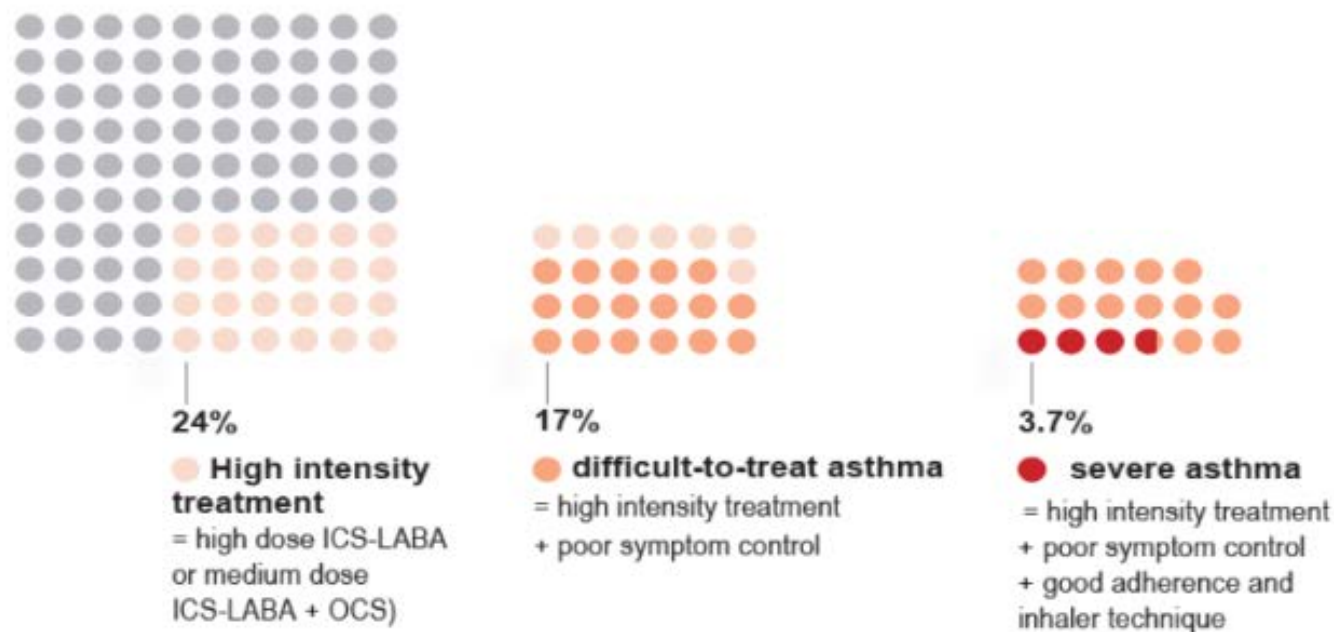
Case 3

- 64 yo woman with a reported history of asthma, HTN, GERD, chronic sinus complaints, and seasonal allergies who presents to establish care.
- Currently managed on high dose fluticasone-salmeterol (advair), montelukast (singulair), and prn albuterol.
- Feeling more limited - short of breath with walking on flat surfaces, using her albuterol inhaler daily, waking up at night coughing several times a week.



Difficult-to-treat v. Severe v. Uncontrolled Asthma

- Severe asthma: asthma that remains uncontrolled despite optimized treatment with high dose ICS-LABA or requires high dose ICS-LABA to prevent it from becoming uncontrolled



Data from Hekking et al, JACI 2015

Improper Inhaler Technique

- N = 100 (asthma and COPD)



86%



71%

Inhaler Teaching

- 24% felt comfortable prior to the training
- 98% felt comfortable post-training

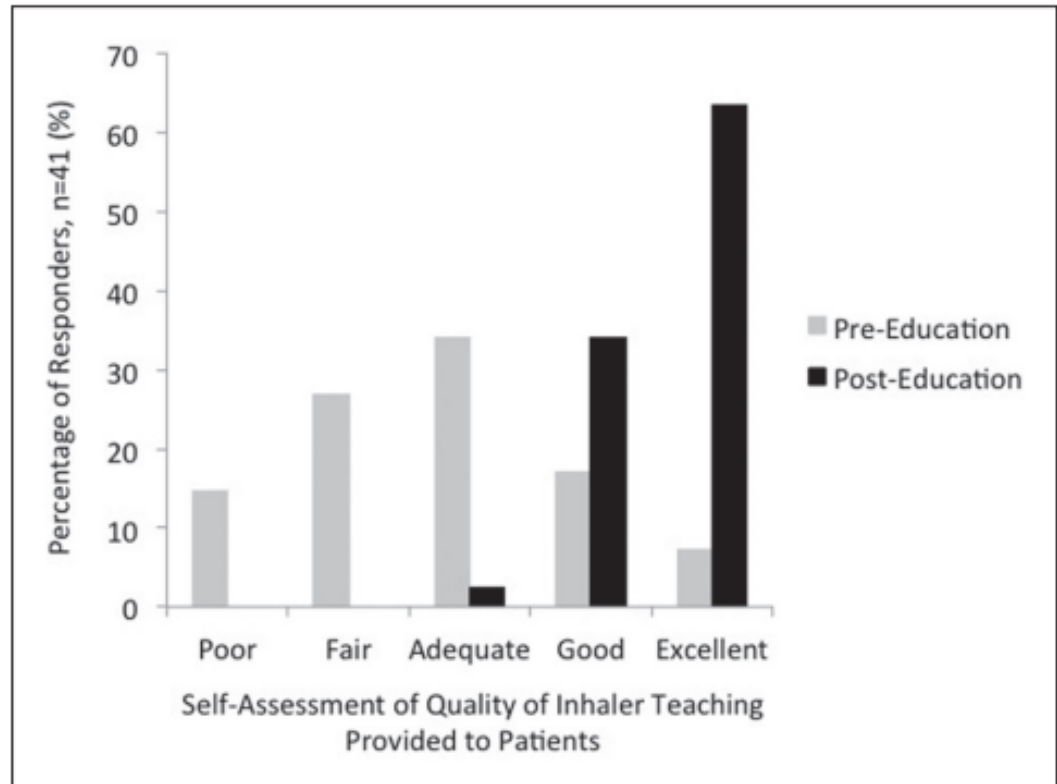
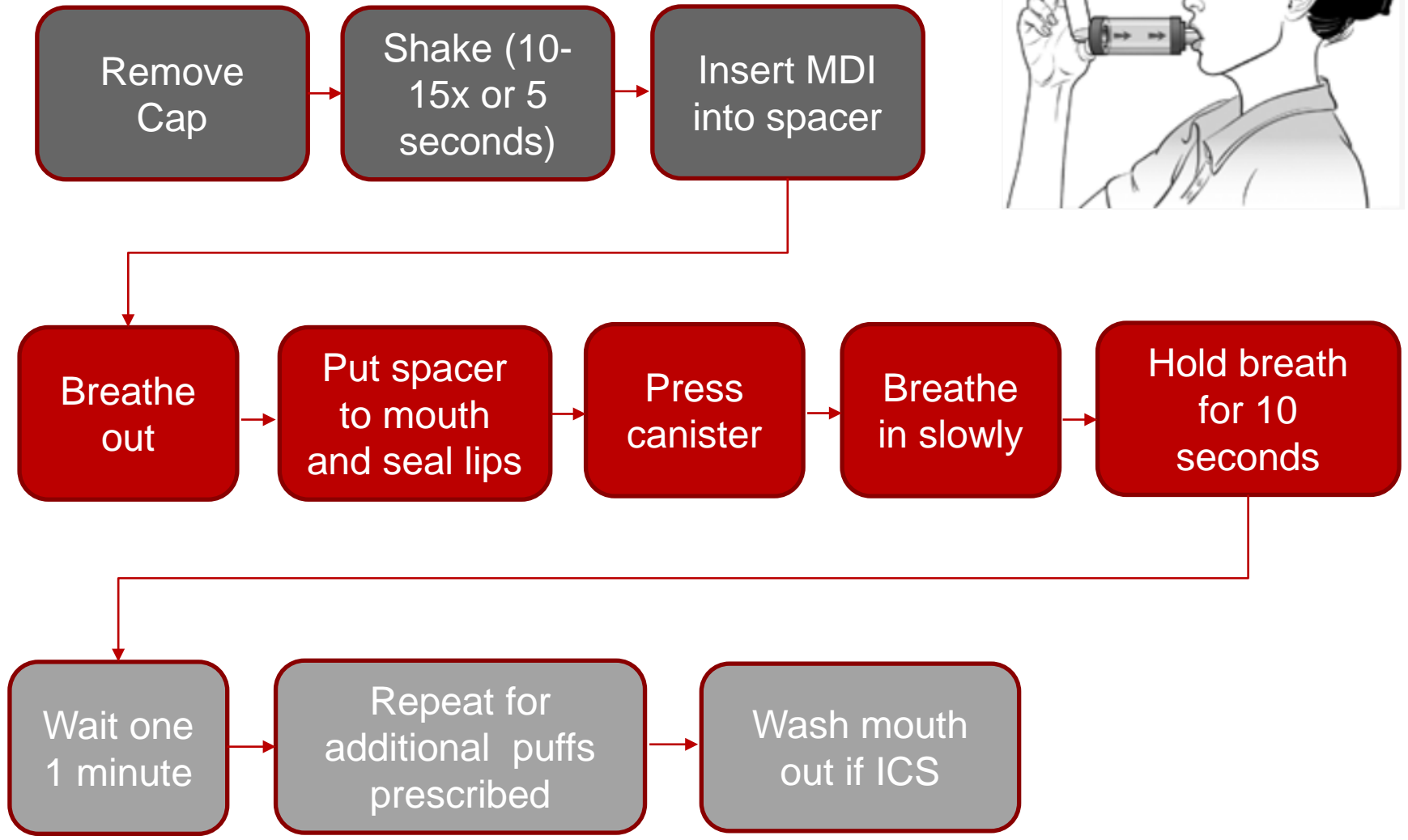
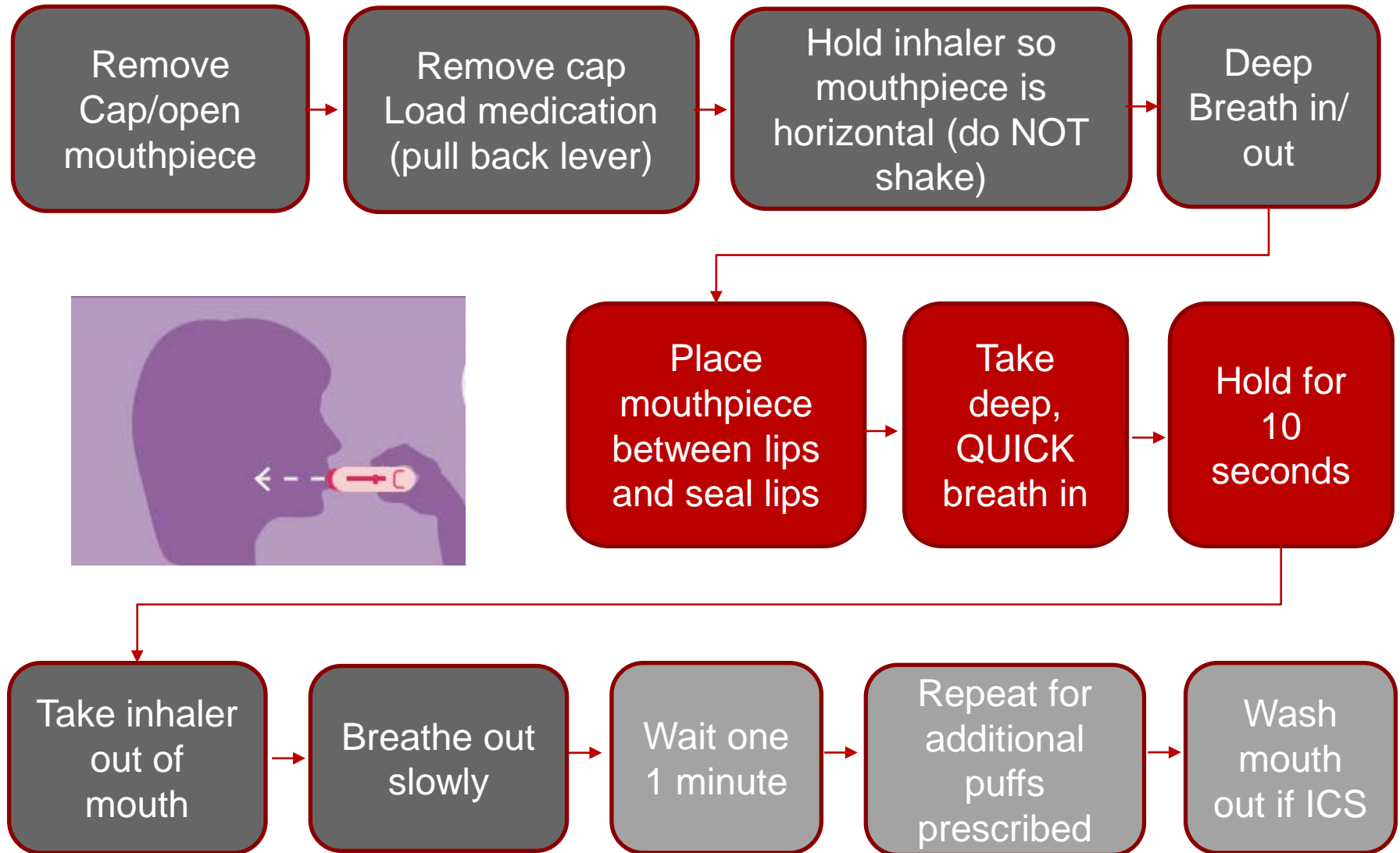


Figure 1) The quality of inhaler teaching provided to patients as self-assessed by physicians before (grey bars) and after (black bars) the inhaler education program. The percentage of responders reporting good to excellent quality of inhaler teaching increased following completion of the inhaler education program

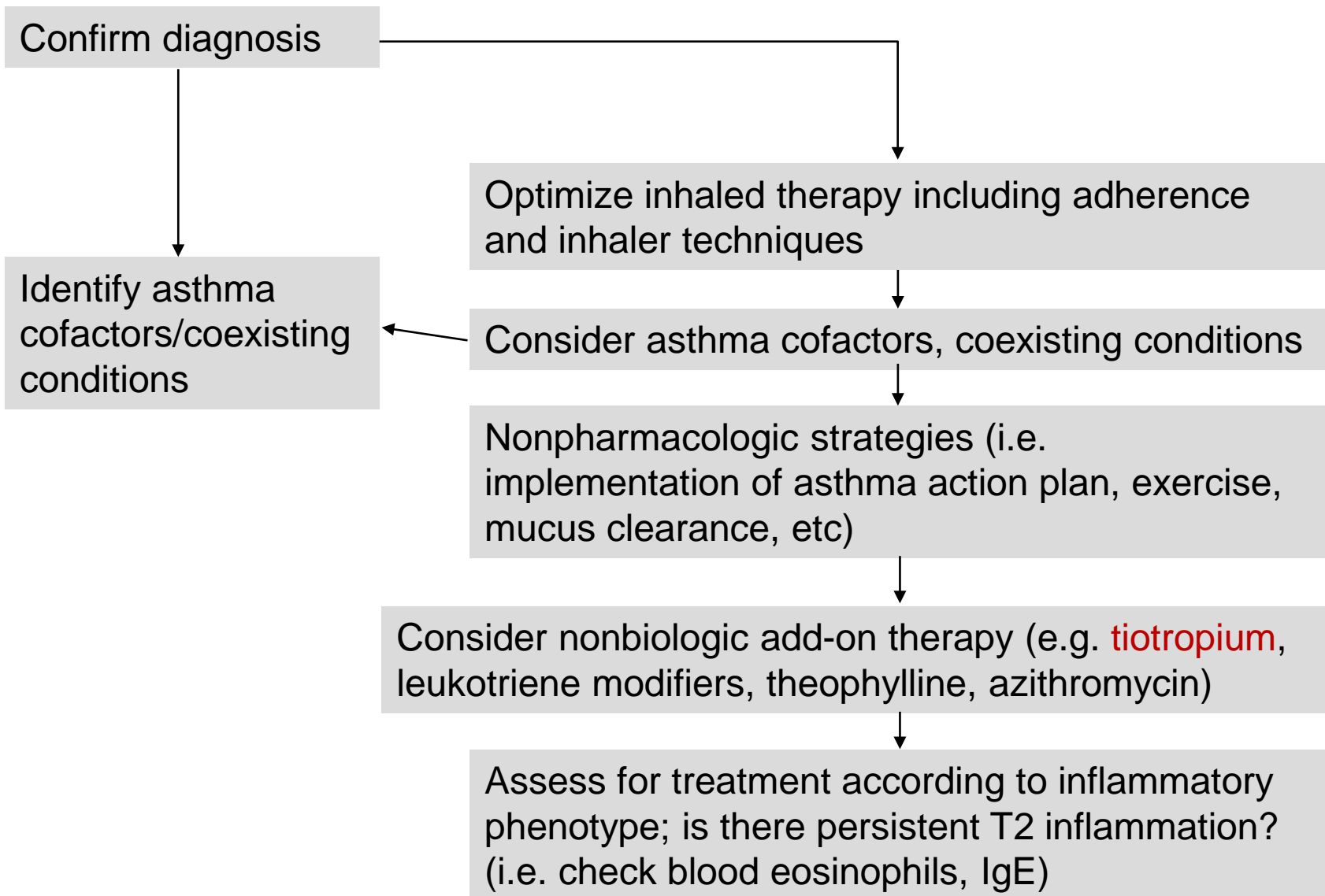
Inhaler Technique - MDI



Inhaler Technique - DPI



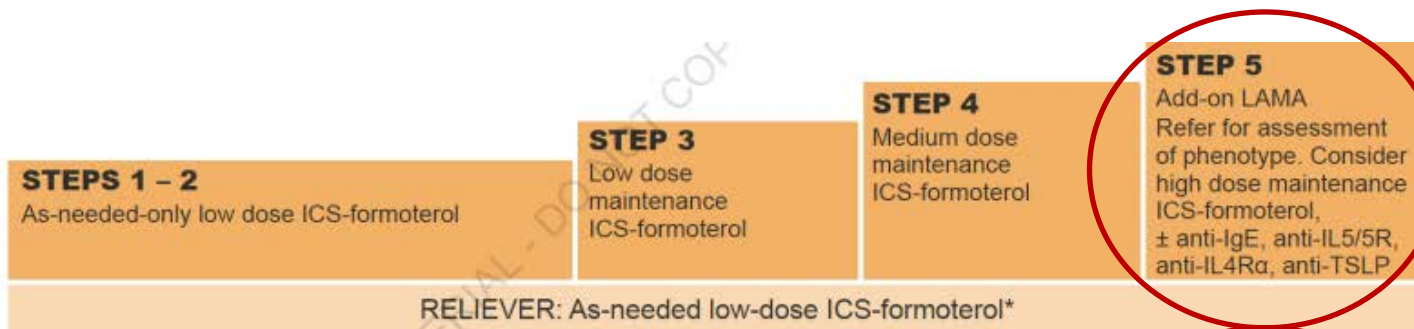
Treatment of Severe Asthma



Inhaled LAMA

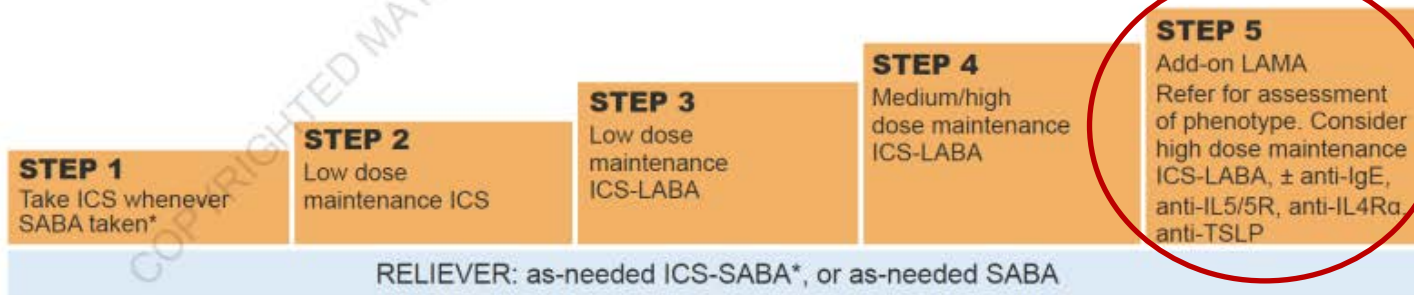
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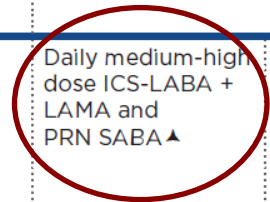
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Inhaled tiotropium

Figure 1.d: Stepwise Approach for Management of Asthma in Individuals Ages 12 Years and Older

	Intermittent Asthma		Management of Persistent Asthma in Individuals Ages 12+ Years			
Treatment	STEP 1	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)**	





Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline

1. Consider anti-IL-5/anti-IL-5 receptor alpha for severe uncontrolled, eosinophilic asthma
2. Use eosinophil count $\geq 150\mu\text{L}$ for initiation of therapy
3. Consider using eosinophil count $\geq 260\mu\text{L}$ and eNO $\geq 19.5\text{ppb}$ to identify individuals most likely to respond to IgE therapy
4. **Use inhaled tiotropium with severe uncontrolled asthma**
5. Trial chronic macrolide to reduce asthma exacerbations
6. Use anti-IL-4/13 for adult patients with severe eosinophilic asthma and/or severe corticosteroid dependent asthma

Case 4

- 55 yo woman with a history of severe persistent asthma
- Currently managed on high-dose Advair (ICS/LABA), Singulair (leukotriene modifier), and tiotropium (LAMA) but continues to have frequent exacerbations
- CBC with differential reveals a peripheral eosinophilia; IgE is within normal limits

Case 4

- What biologic therapy would NOT be appropriate?
 - Omalizumab (Xolair)
 - Mepolizumab (Nucala)
 - Benralizumab (Fasenra)
 - Dupilumab (Dupixent)
 - I don't know, I'd place an ambulatory referral to pulmonary

Case 4

- What biologic therapy would NOT be appropriate?
 - **Omalizumab (Xolair)**
 - Mepolizumab (Nucala)
 - Benralizumab (Fasenra)
 - Dupilumab (Dupixent)
 - **I don't know, I'd place an ambulatory referral to pulmonary**

Is it time to consider a biologic?

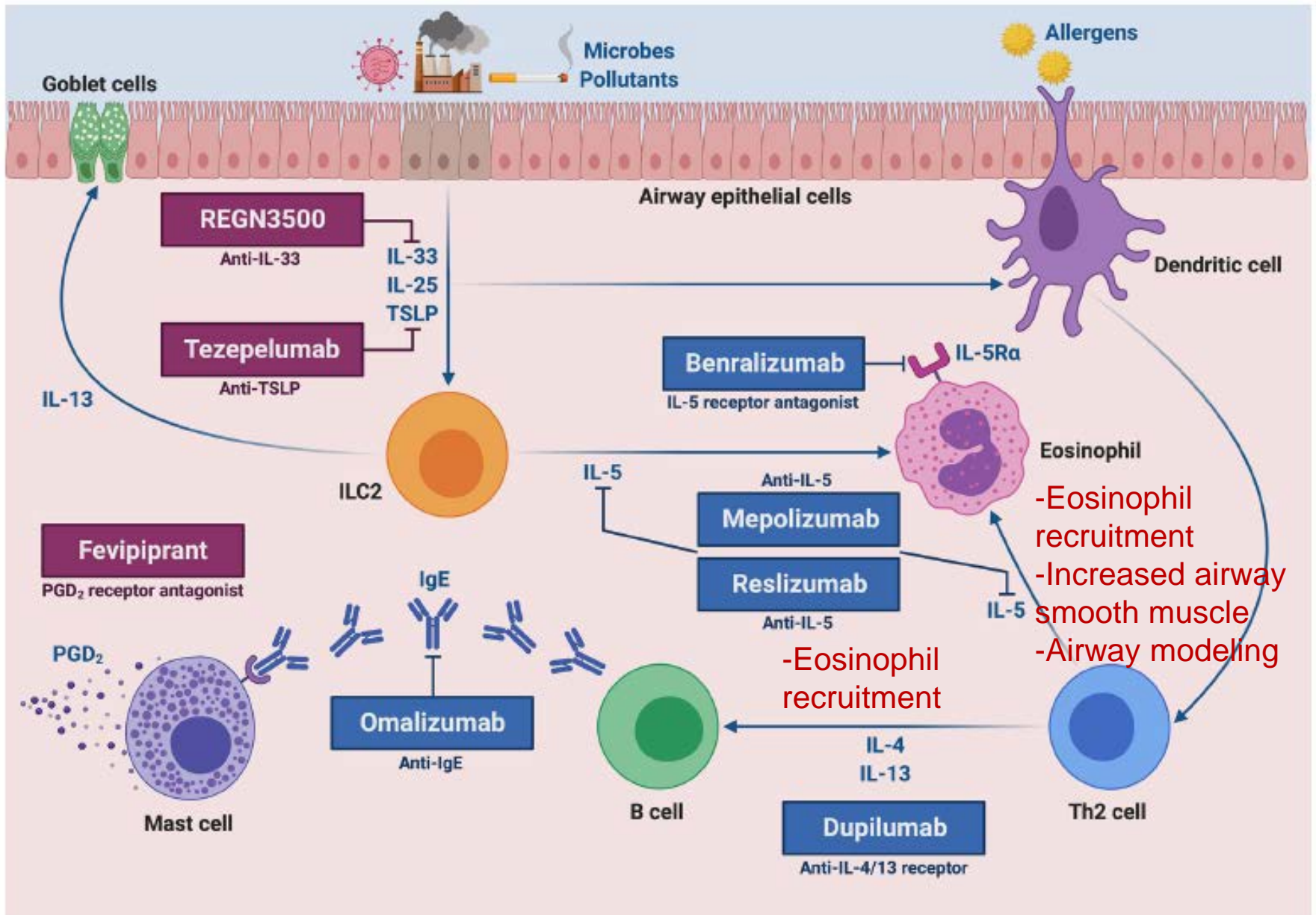
- Moderate-high dose ICS/LABA?
- Uncontrolled?

Labs

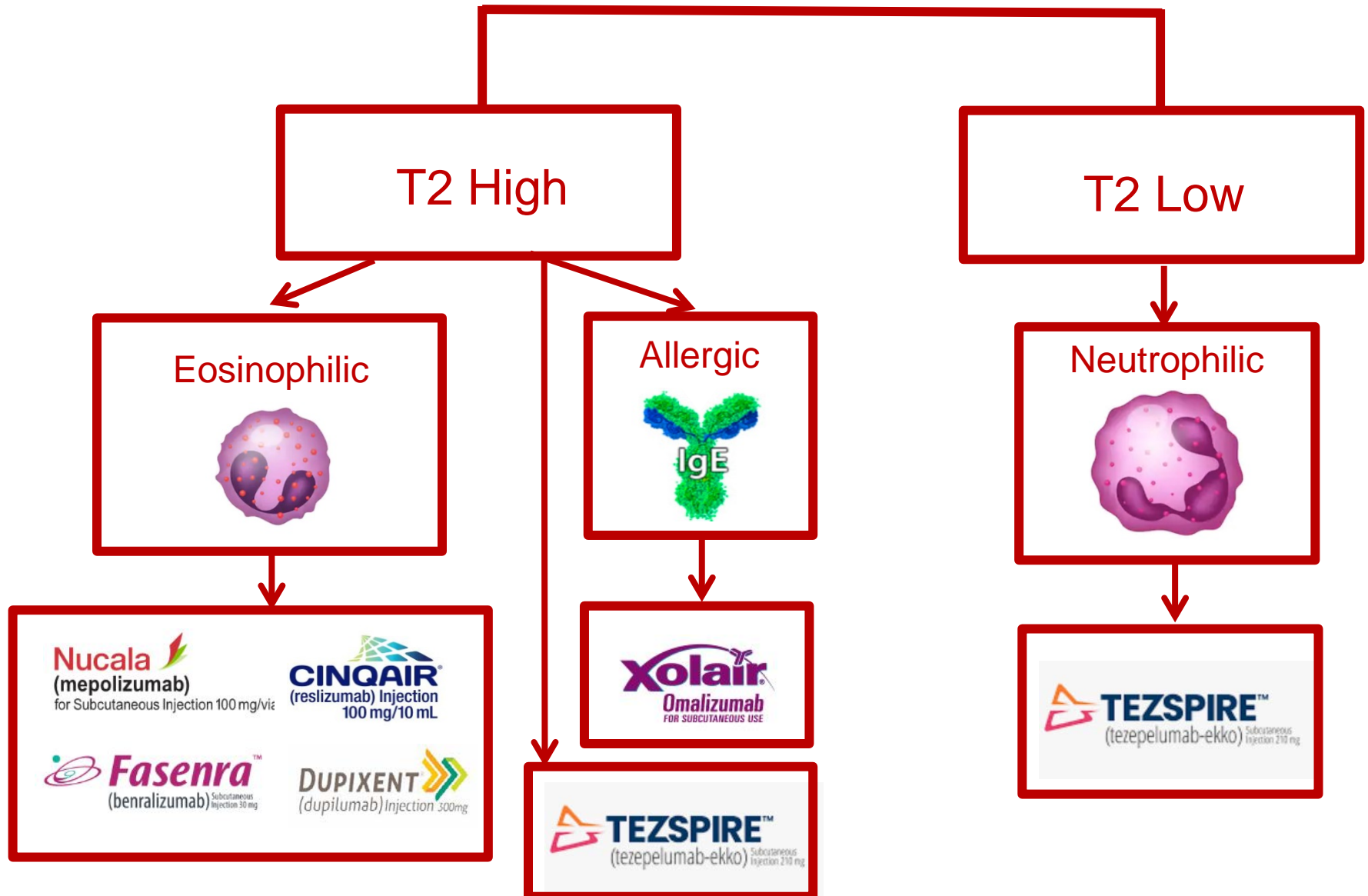
TABLE 3] Biomarkers of Type-2 Airway Inflammation

Biomarker	Cutoffs	Association With Treatment Response	Comments
IgE	Variable	Anti-IgE	IgE levels do not consistently predict clinical outcomes nor treatment responsiveness
Blood eosinophil count	$\geq 0.15 \times 10^9$ per L	Corticosteroids Anti-IL-5/5R Anti-IL4R α Anti-IgE Anti-TSLP	Generally available, cheap, directly relates to asthma control and risk of asthma attacks
Sputum eosinophils	$\geq 2\%$	Corticosteroids Anti-IL-5 Anti-IL4R α	Not routinely available, tissue-specific, time-consuming
FENO	≥ 25 ppb	ICS Anti-IL-4R α Anti-TSLP	Quick, cheap, noninvasive, associated with increased risk of asthma attacks; increases probability of ICS responsiveness

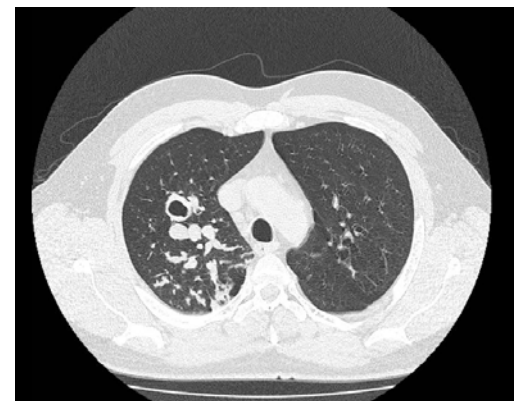
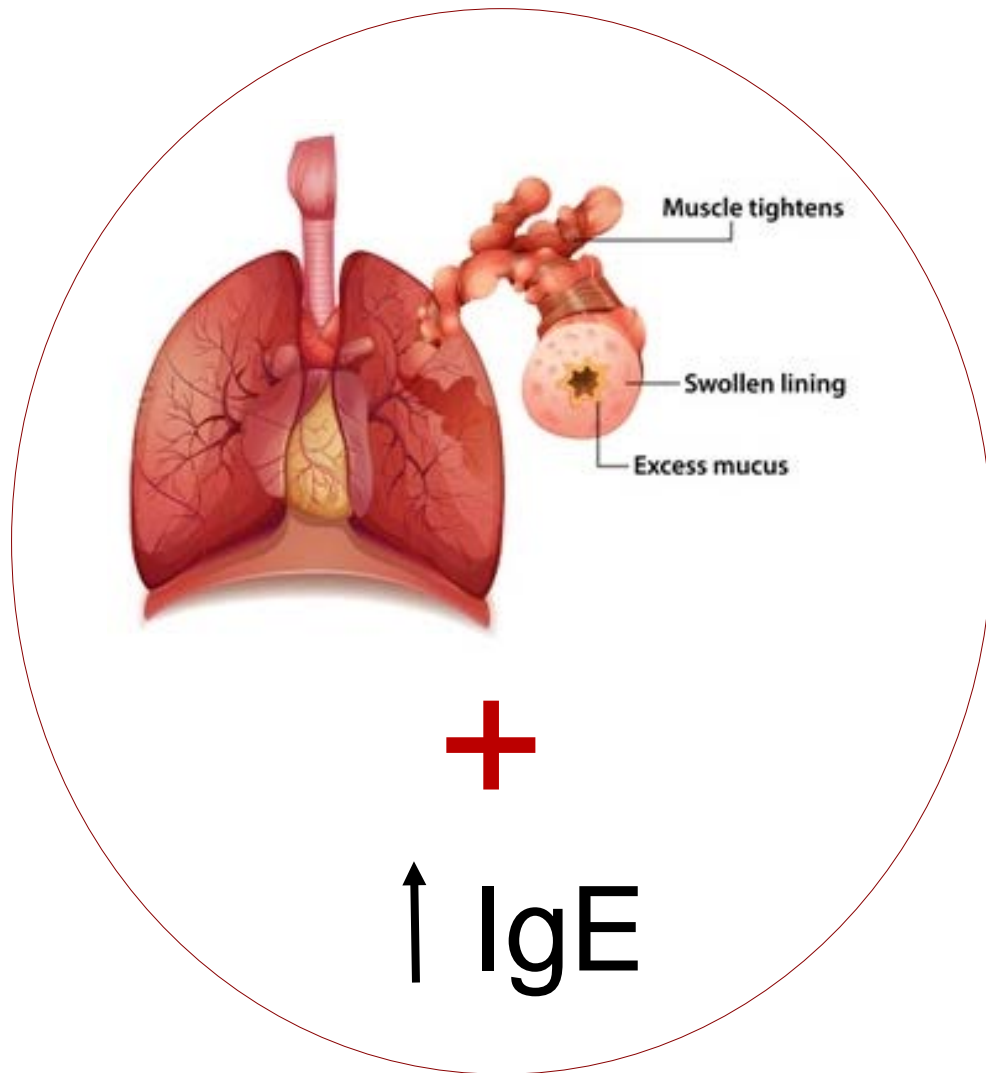
- RAST
- Consider ANCA, Strongyloides ab, sputum (?chronic infection), CT chest



Immunology of Asthma Inflammation



Omalizumab (xolair)



Omalizumab (xolair)

- Mechanism: Anti-IgE
- IgE: 30-700 IU/mL (US) (30-1500 IU/mL in Europe)

In trials:

- Decreased rate of exacerbations
- Improvement in quality of life

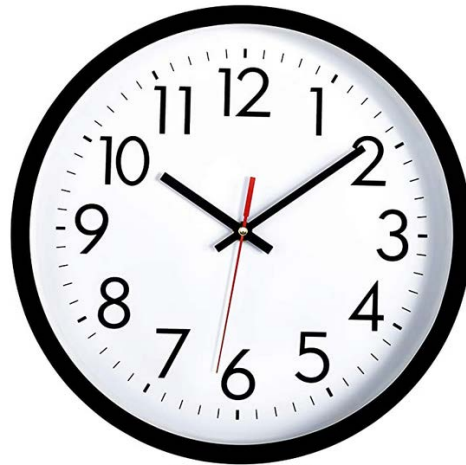
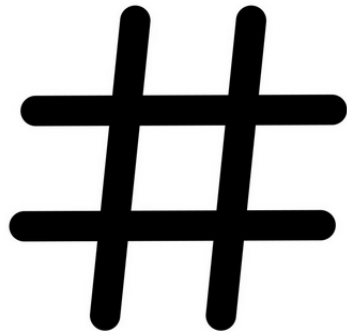
- High eos (> 260microL) and high eNO (> 20ppb) associated with longer time to exacerbation and decreased rate of exacerbation

Eosinophilic Asthma

- Mepolizumab (nucala)
- Reslizumab (cinqair)
- Benralizumab (fasenra)
- Duplimab (dupixent)

- AND...
- Tezepelumab (tezspire)

Which Biologic?



Assess Response

- Wait four-six months to assess treatment response
- If poor response:
 - Consider adherence (if home autoinjector)
 - Ensure coexisting conditions are addressed
 - Reassess biomarkers (eos, FeNO, IgE)
 - Consider changing therapy

Summary

- Though it's important to characterize severity of asthma initially, future assessments should focus on control
- ICS are the most important class of medications in treating asthma (and should now be used in “step 1”)
- Biologics can aid with improving control in T2 asthma
- When asthma is severe/difficult-to-control, don't hesitate to refer!

Questions?

