

Pediatric Asthma Potpourri

at Nebraska Society Respiratory Care Annual Meeting - 2023

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Topics for Today

- **Nebraska Asthma Coalition**
- **Diagnosing Asthma in Children**
- **Pediatric Asthma Phenotypes**
- **Pulmonary Function in Children**
- **Picking Asthma Therapy in Children**
- **SMART Therapy**
- **Biologics for Moderate to Severe Asthma in Children**
- **Asthma in Children during COVID**

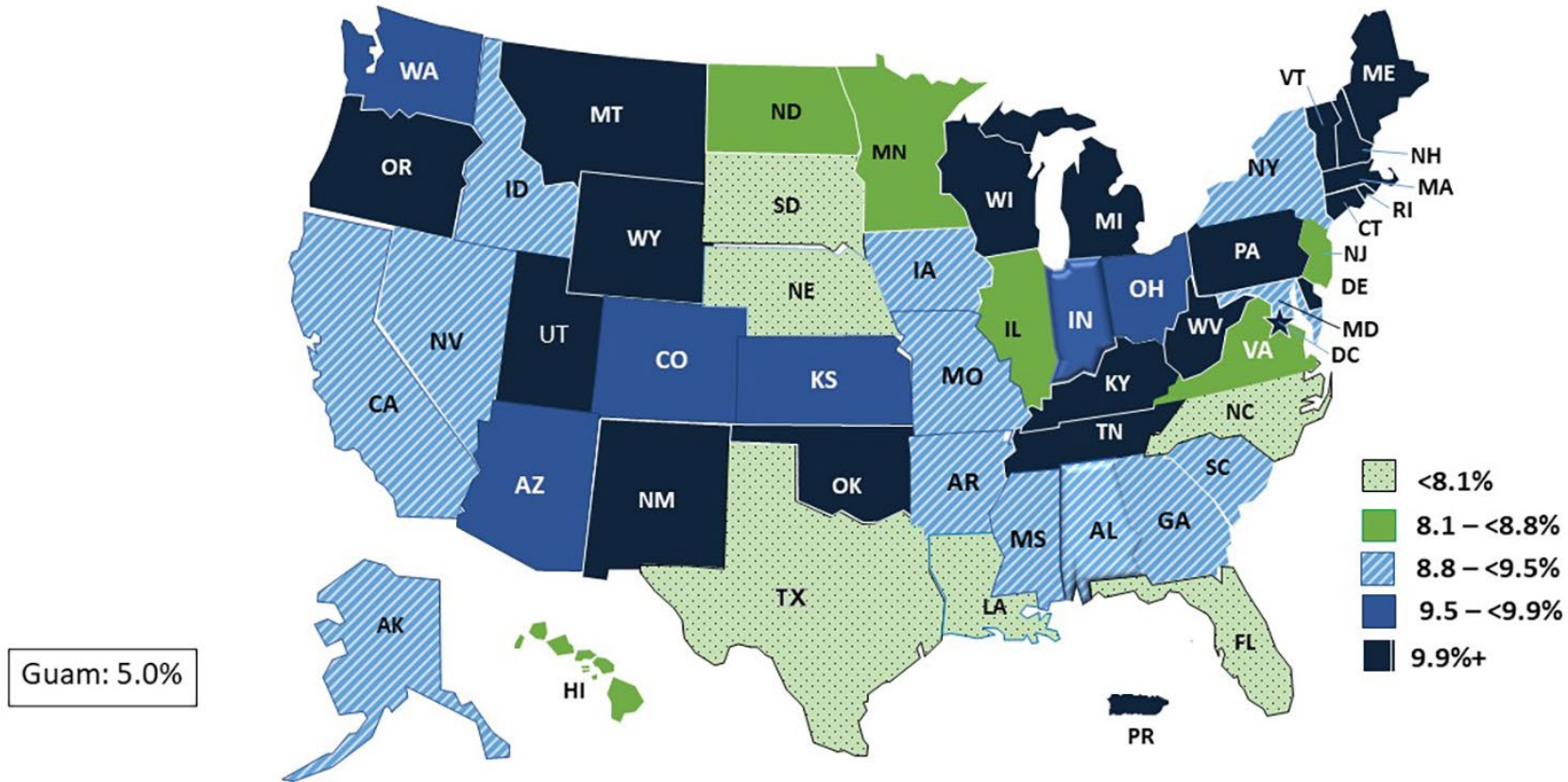


Nebraska Asthma Coalition



- <https://nebraskaasthmacoalition.org/>
- The Nebraska Asthma Coalition strives to improve health outcomes and quality of life for individuals affected by asthma in our state. We work to accomplish our mission through our core values of collaboration, inclusivity, data-driven decision making and a commitment to addressing health disparities.
- Grass Roots organization of health care professionals across the state
- Data driven
- mcardona@childrensomaha.org

Adult^a Current Asthma^b Prevalence, BRFSS 2020



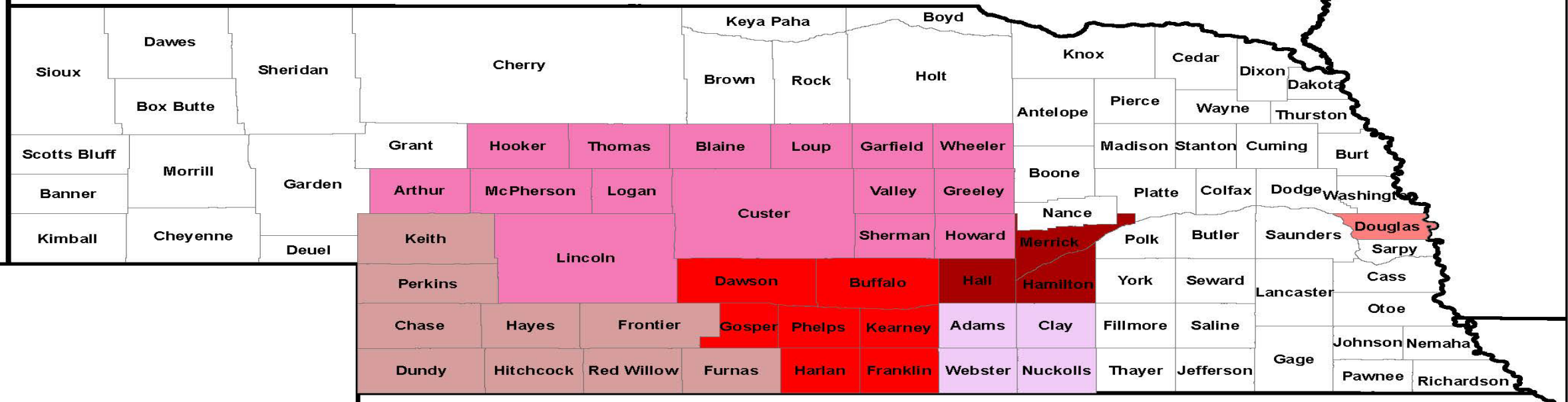
^aAged 18+ years

^bCurrent asthma question: "Do you still have asthma?"

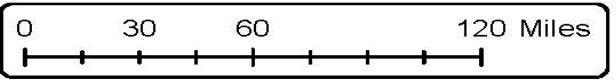
Legend: percentiles of the overall current asthma prevalence estimates from year 2011 data: 0%, 20%, 40%, 60%, 80%, 100%

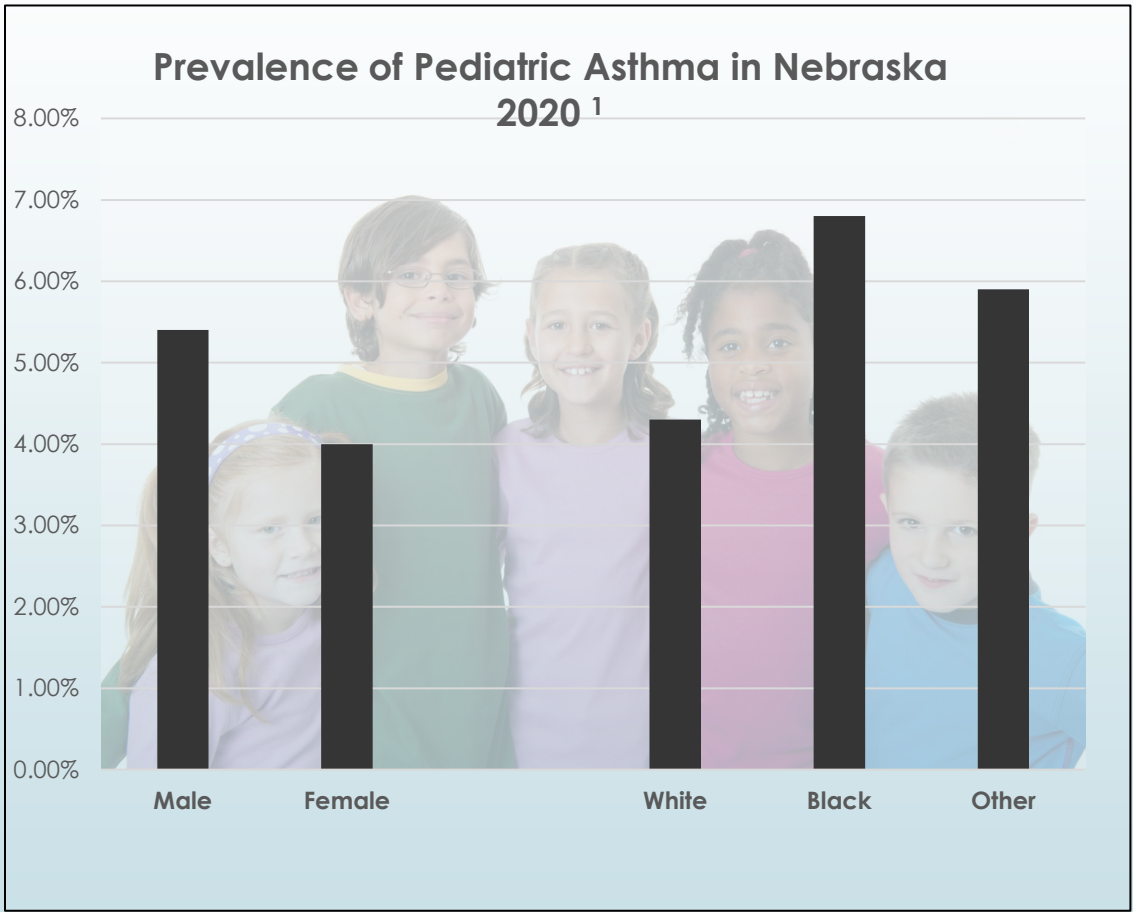
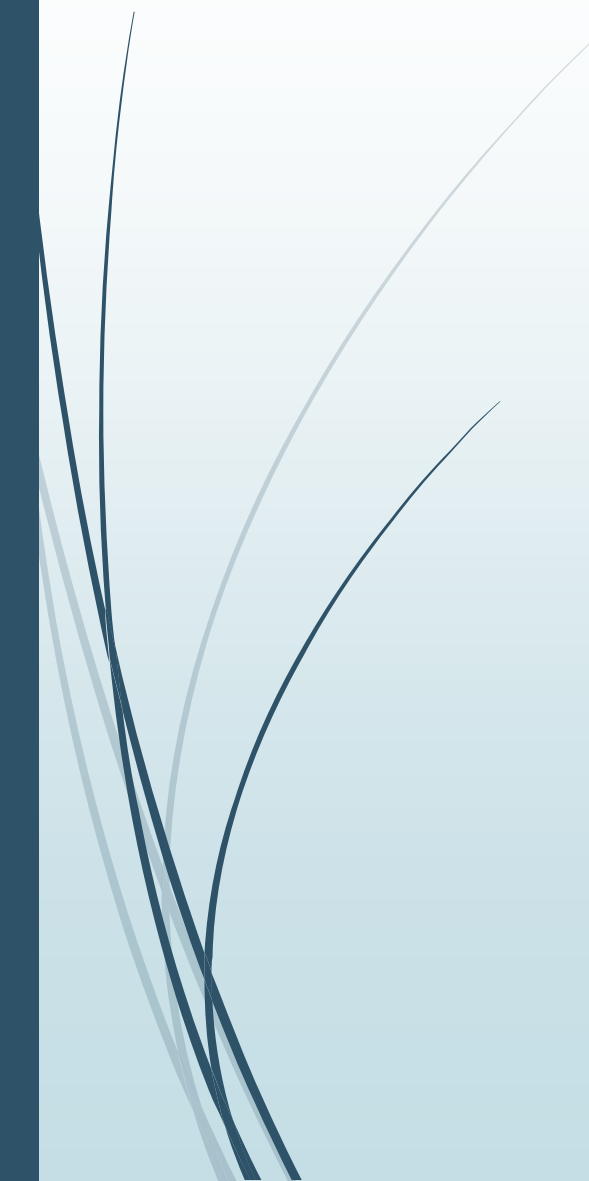
Asthma and Community Health Branch, National Center for Environmental Health
Centers for Disease Control and Prevention

Top Health Districts for Asthma Admissions 2020



Central District Health Dept.
 Two Rivers Public Health Dept.
 Douglas County Health Dept.
 Southwest NE Public Health Dept.
 West Central District Health Dept.
 Loup Basin Public Health Dept.
 South Heartland District Health Dept.
 State Line
 dtl_cnty









Asthma Diagnosis

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Young Asthmatics

- ▶ Any age 0-6 (roughly)
- ▶ Clinical diagnosis (mostly)
- ▶ Cough, wheeze, dyspnea, mostly with viral illnesses (Rhinovirus)
- ▶ What factors would provide co-evidence?
- ▶ Pediatric asthma phenotypes

Likely has asthma if:

A young child wheezes frequently and has:

- ▶ Parent with asthma
- ▶ Atopic dermatitis
- ▶ Allergic on skin test
- ▶ Multiple wheezing triggers

- ▶ Food allergy
- ▶ Eosinophilia on CBC
- ▶ Allergic rhinitis

Not normal to wheeze



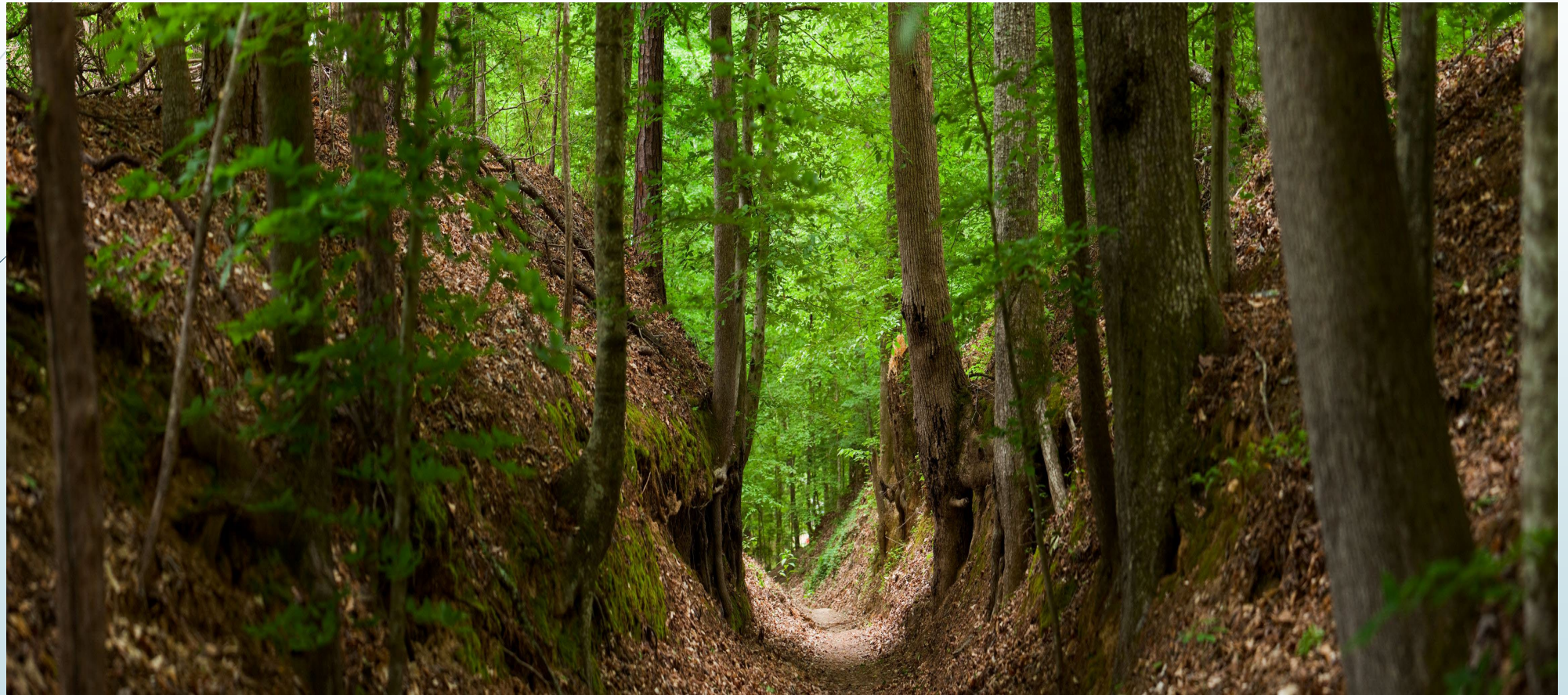
Next step/historical information

- ▶ **Historical information or next step**
 - Past Asthma therapy response?
 - Future asthma therapy response
- ▶ **CXR (looks like asthma changes)**
- ▶ **Attempt PFT (IOS)**
- ▶ **IOS testing available at Children's. Ages 2-6 is applicable**



Risk factors for asthma in school age children

- Maternal asthma for both genders
- Paternal asthma for boys
- Presence of allergies -- food or environmental
- Family history of asthma or allergies
- Exposure to tobacco smoke before or after birth
- Presence of eczema
- Being male (before age 10)
- Being black
- ???????? Perinatal factors??????????





Pediatric Asthma Phenotypes

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Asthma Types in Children

- High Type 2 Phenotype
- Low Type 2 Phenotype

- ?? Other vs Acts like Asthma
- Protracted bacterial bronchitis in toddlers
- Post- Severe **early** RSV

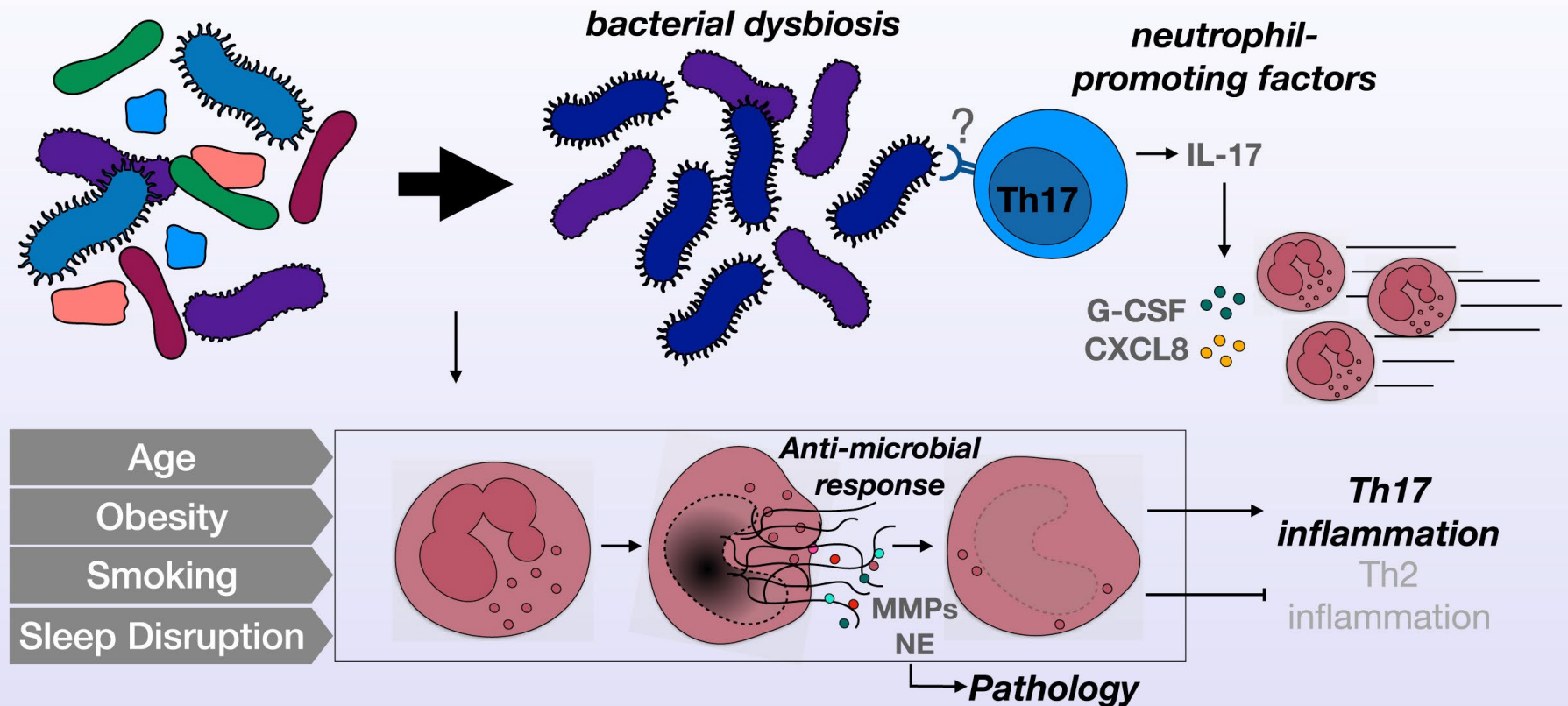


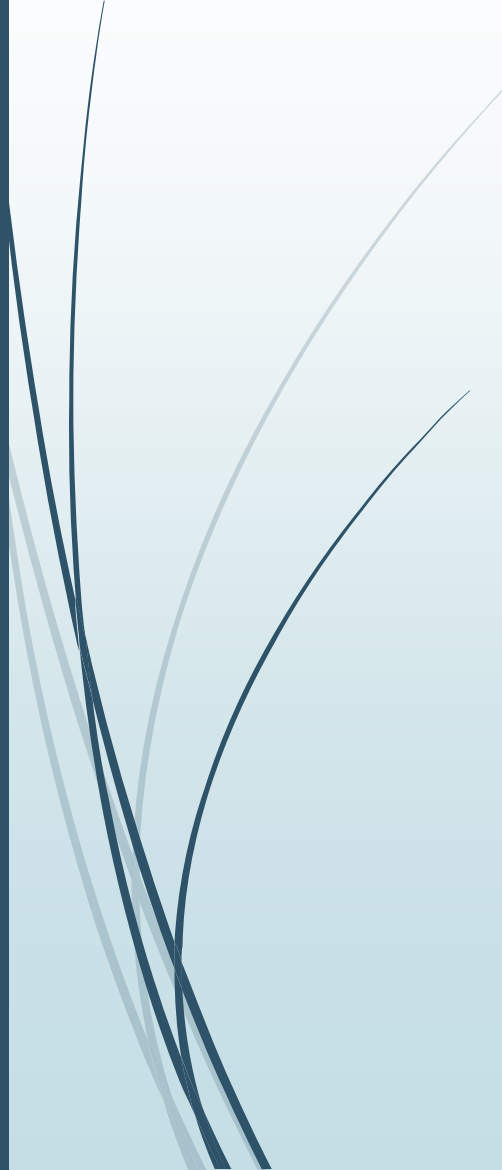
RSV

- ▶ Did child have first wheeze in RSV season?
- ▶ Was a RSV test done?
- ▶ Is the child **only** re-wheezing with a new viral infection?
- ▶ Is the child still young
- ▶ **Epidemiological evidence that RSV infection can make “asthma “ happen, or it’s post-RSV wheeze**
- ▶ May be “non-atopic wheezers”- “asthmatics”
- ▶ Need a RSV vaccine to solve this puzzle!
- ▶ RSV vaccine released for adults > 60

Pediatric Neutrophilic Asthma (Protracted bronchitis of childhood)

Model of neutrophilic asthma







The Asthma Test

Genetic test for Asthma?



God Calling





Pulmonary Function in Children

- ▶ **Graham BL et al Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement.** Am J Respir Crit Care Med. 2019 Oct 15;200(8):e70-e88. doi: 10.1164/rccm.201908-1590ST. PMID: 31613151; PMCID: PMC6794117.
- ▶ GLI standards
- ▶ Expiratory time (minimum of one second plateau)
- ▶ FEV1 % predicted improvement: 10%
- ▶ Z-scores (< 5% or % 95%)

BDR after albuterol

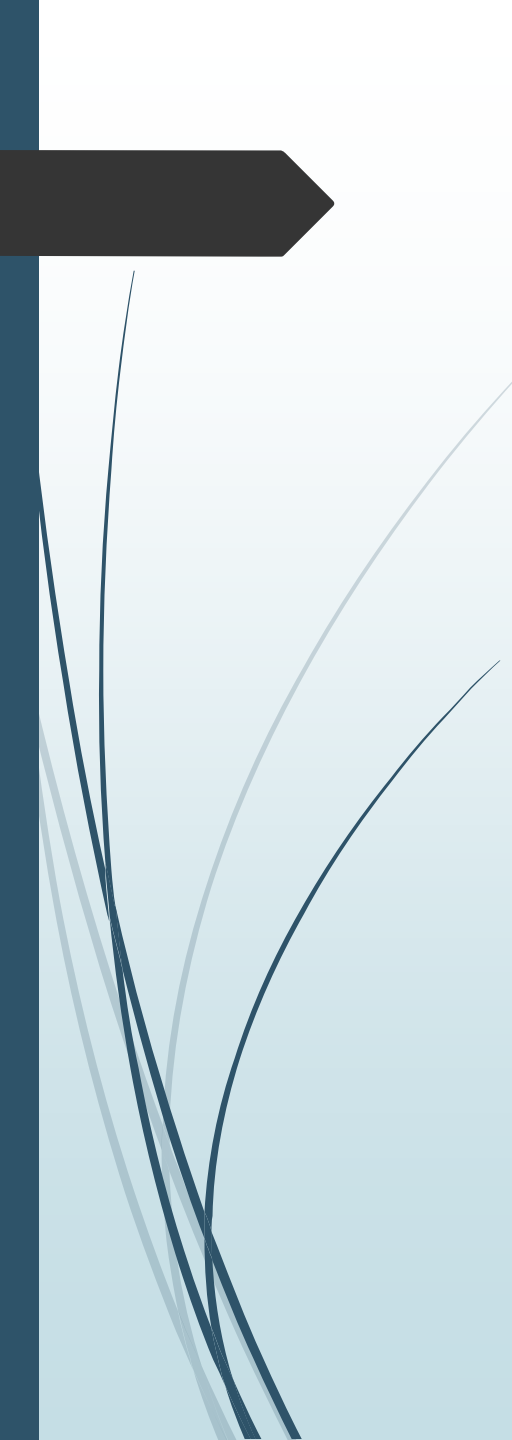
A change of >10% is considered a significant bronchodilator response. #: predicted value should be determined using the appropriate Global Lung Function Initiative (GLI) spirometry equation.

It is recommended that BDR be classified as a change of >10% relative to the predicted value for FEV₁

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).

$$\text{BDR} = (2.4 - 2.0) * 100 / 3.32 = 12.1\% \text{ improvement}$$

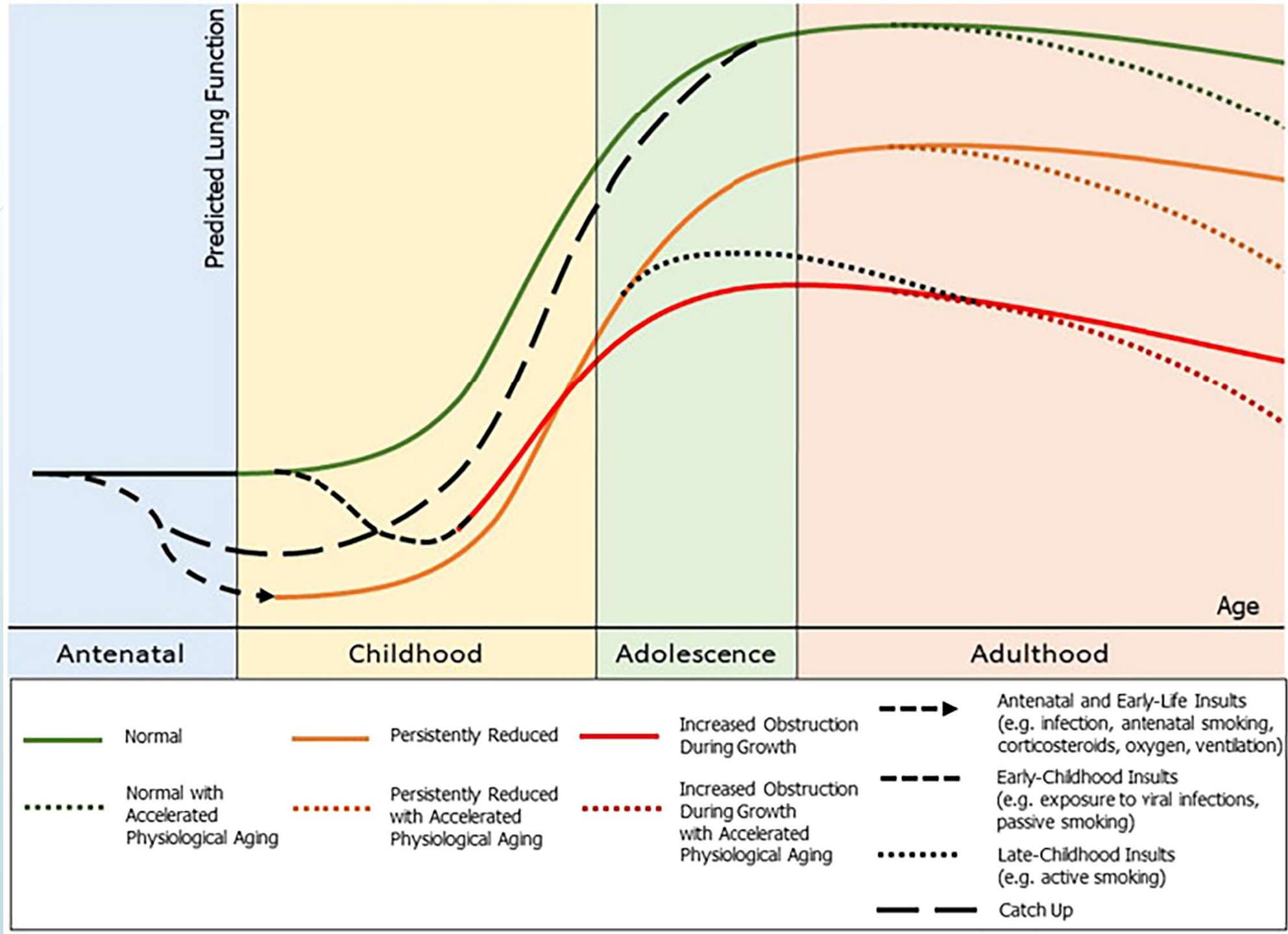
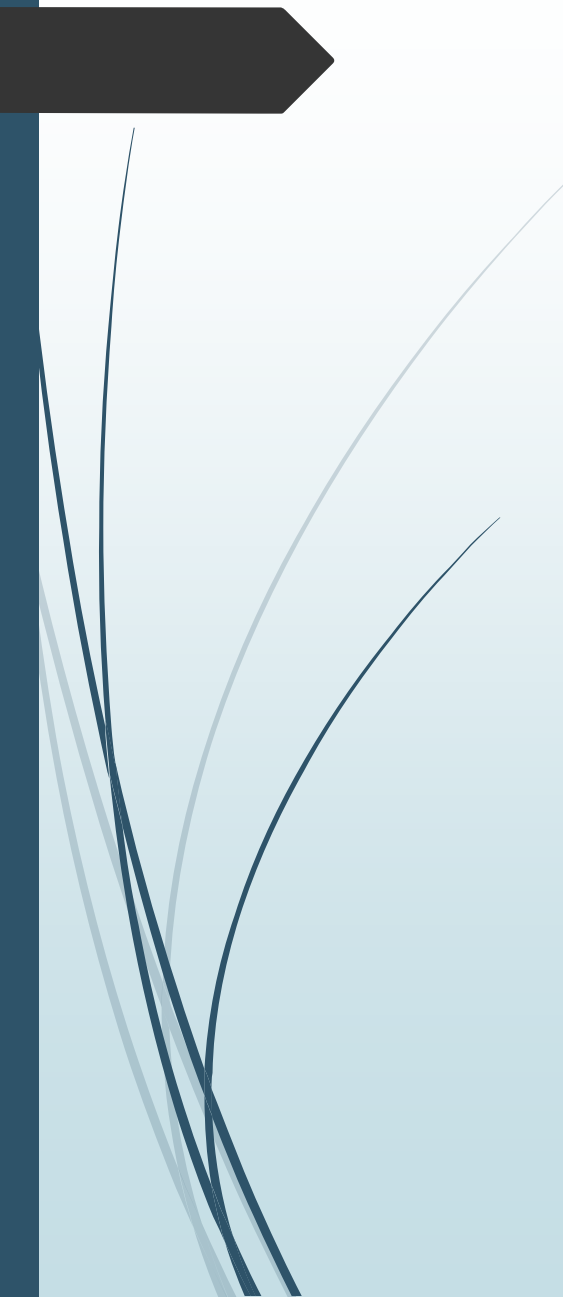
$$\text{BDR} = 2.4 / 2.0 = 12\% \text{ improvement}$$



Race and Ethnicity in Pulmonary Function Test Interpretation: An Official American Thoracic Society Statement

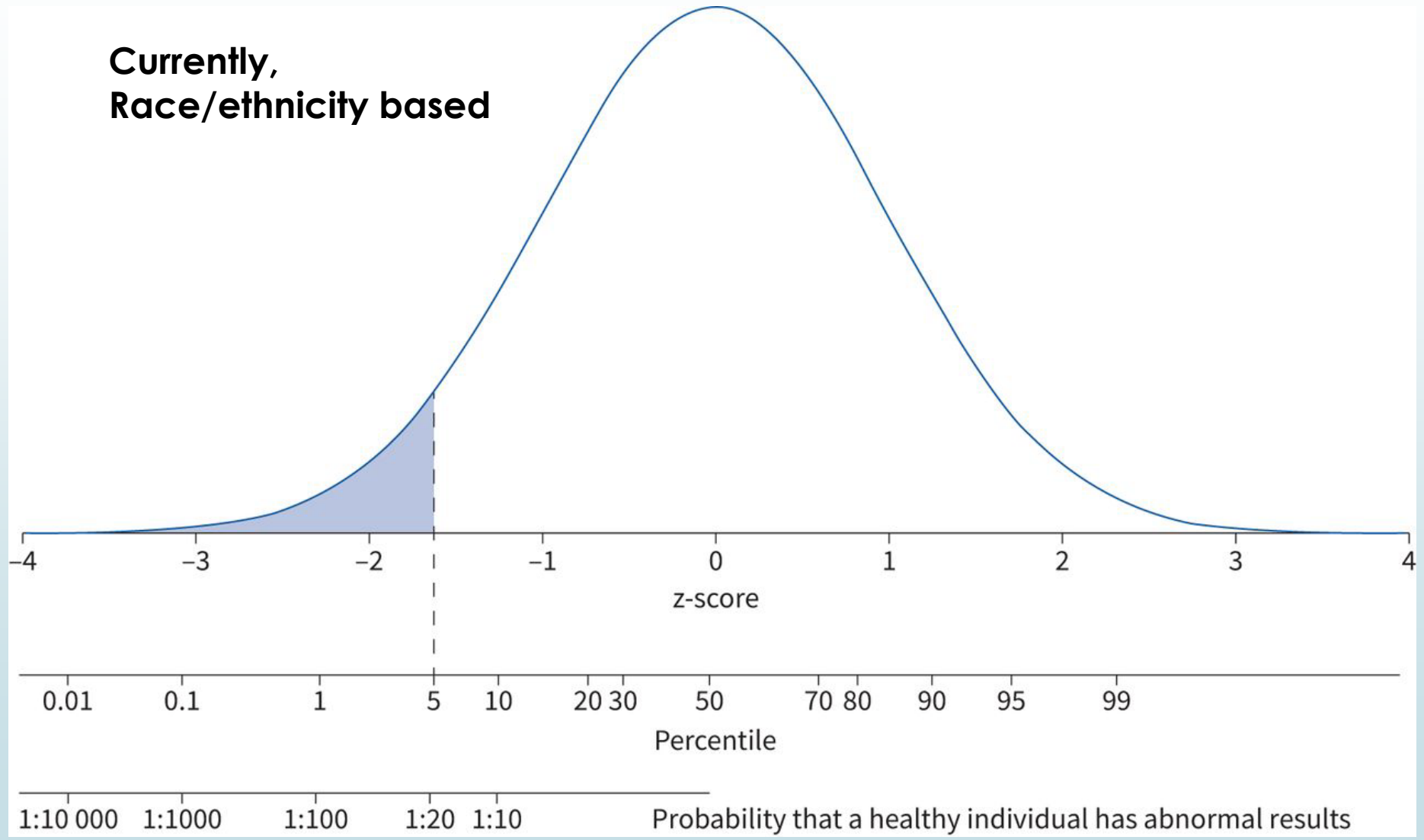
Nirav R. Bhakta. April 2023

- PFT laboratories should adopt a race-neutral approach to PFT interpretation by reporting and interpreting results using average reference equations.
- The Global Lung Function Initiative (GLI) average equation, published as GLI Global, is a recommended race-neutral average reference equation. There are important limitations and considerations to an implementation of GLI Global that we expect ongoing research to address.
- <https://doi.org/10.1164/rccm.202302-0310ST>



Z-scores

Currently,
Race/ethnicity based



Nitric Oxide



Exhaled Nitric Oxide (eNO) testing is a quick and easy way to measure inflammation (swelling) in the bronchial tubes of the lungs. The test may be done to HELP diagnose asthma, to evaluate a chronic cough or to see how well inhaled corticosteroid treatment is working in a child who has already been diagnosed with asthma.





Picking Asthma Therapy in Children

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Asthma Therapy

- ▶ **Correct Diagnosis**
- ▶ **Severity Determination**
- ▶ **Base Rescue Therapy for all children**
- ▶ **Maintenance therapy**
- ▶ **Follow-up plan**
- ▶ **School action Plan**



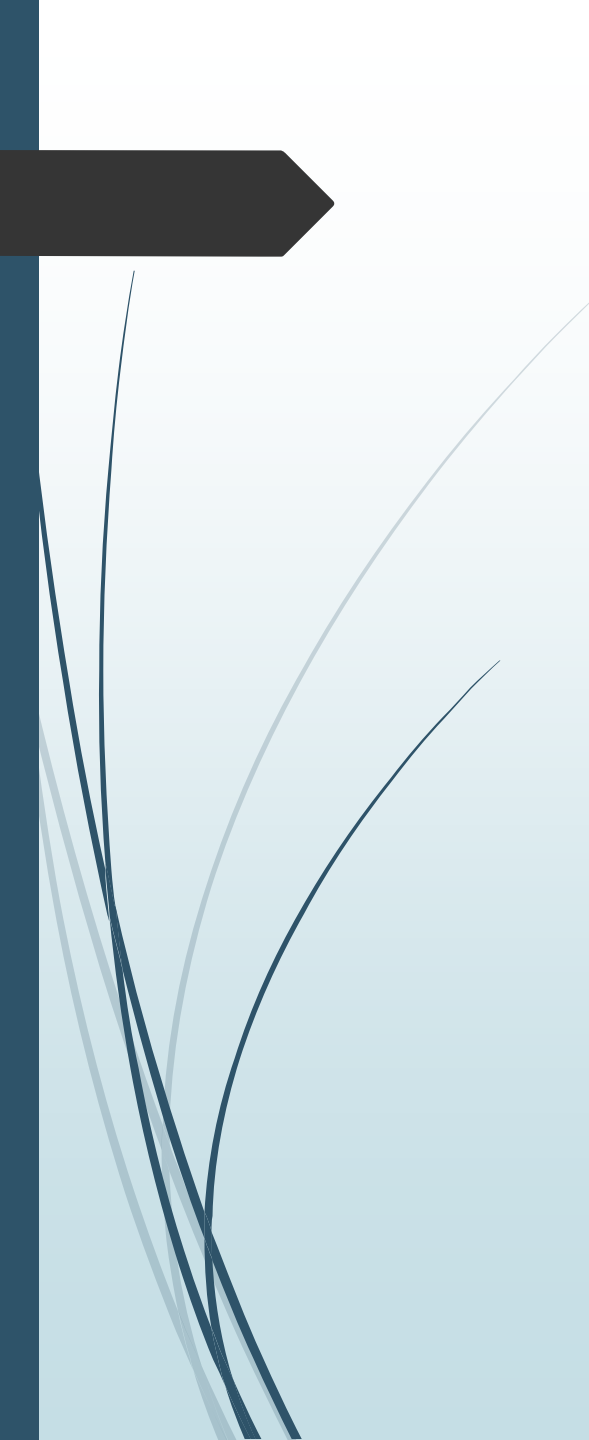
Severity: *Intermittent, mild persistent, moderate persistent, severe persistent*

Additive for severity: asthma symptoms, nocturnal awakening, use of albuterol (if already prescribed), ability to do exercise or activities.

Severity: Exacerbations having required oral corticosteroids: ≥ 2 in 12 months is persistent

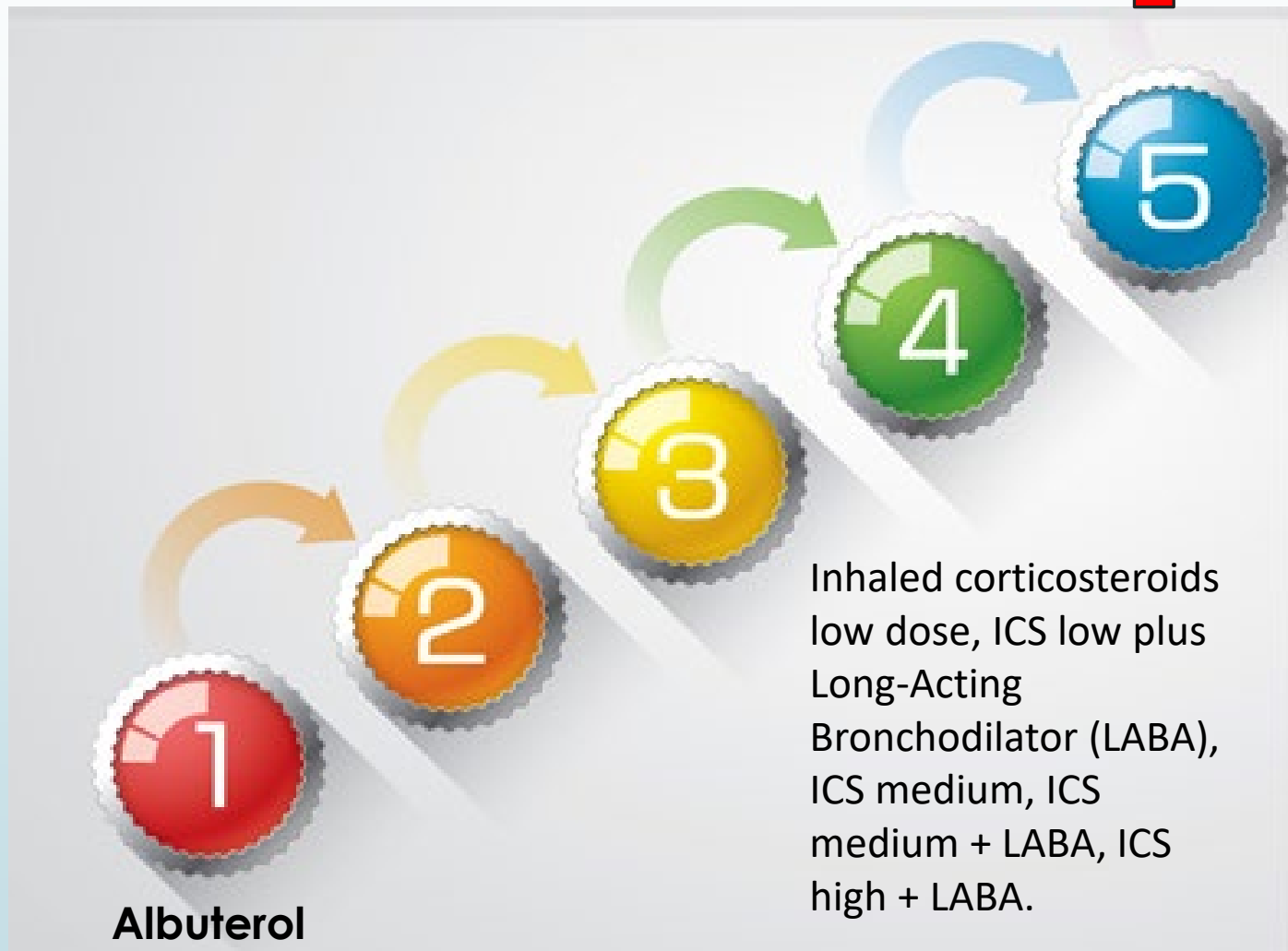
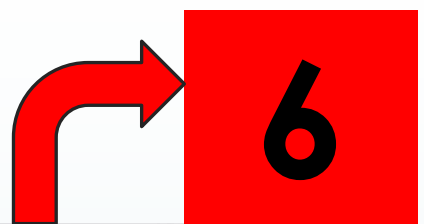
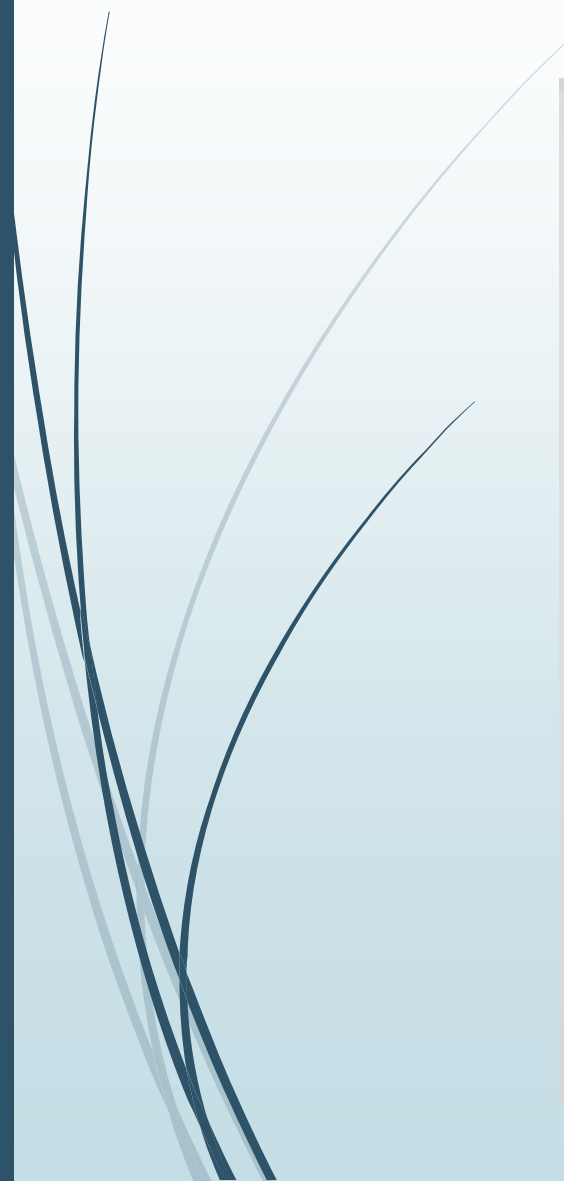
Severity: Pulmonary function test for all patients capable of performing. Forced Expiratory Volume at 1 second (FEV₁) and FEV₁/FVC (Forced Vital Capacity) are the critical components: Age range and levels in guidelines: $> 80\%$ FEV₁; 60-80% FERV₁, and $< 60\%$ FEV₁ are critical levels for persistent.

The EPR-3 guidelines are available at: <https://www.nhlbi.nih.gov/health-topics/guidelines-for-diagnosis-management-of-asthma>



Medications: Rank Scale for Persistent : Inhaled corticosteroids low dose, ICS low plus Long-Acting Bronchodilator (LABA), ICS medium, ICS medium + LABA, ICS high + LABA.

Medications: Leukotriene modifiers (LM), Theophylline, short or long-acting muscarinic antagonists. Biologics are add-on therapies based on severity and/or allergies.



Albuterol

Inhaled corticosteroids low dose, ICS low plus Long-Acting Bronchodilator (LABA), ICS medium, ICS medium + LABA, ICS high + LABA.

Leukotriene modifiers (LM), Theophylline, short or long-acting muscarinic antagonists.

Biologics are therapy based on severity and/or allergies.





SMART Therapy



SMART Therapy

Standard treatments for asthma have been aimed at treating symptoms rather than preventing them, with options relying on inhaled corticosteroids (ICS) and short-acting beta agonist (SABA) or bronchodilators. Updated guidelines now support Single Maintenance and Reliever Therapy (SMART).

What is SMART Therapy?

In 2020, the **National Asthma Education and Prevention Program** supports Single Maintenance and Reliever Therapy (SMART) for people with moderate to severe asthma. SMART is:

- The use of a single combination inhaler with an ICS and a long-acting beta agonist (specifically formoterol) as the preferred daily controller and as-needed rescue therapy option.
- Similar to albuterol in that bronchodilation happens within 5 minutes; however, research shows the effects are longer lasting
- Proven to be more effective in reducing ED visits and hospitalizations without an increase in side effects.

Prescribing SMART to Patients

SMART guidelines are aligned with those of the **Global Initiative for Asthma** and their preference is to use a low dose inhaled ICS-formoterol inhaler as a rescuer and daily controller treatment for asthma management. This regimen reduces the risk of severe exacerbations compared with using a SABA as the rescuer. To make it easier to prescribe SMART for their patients, MO HealthNet has the following preferred products available without a prior authorization for both maintenance and rescue use:

DRUG	STRENGTH	PDL STATUS
Dulera (mometasone/formoterol)	100mcg/5mcg 200mcg/5mcg	Preferred - Open Access
Symbicort (budesonide/formoterol)	80-4.5mcg 160-4.5mcg	Preferred - Open Access

Our Goal for Asthma Patients

In Missouri, 69.6% Medicaid adults and 64.8% Medicaid children were dispensed the appropriate asthma controller medications. While this percentage is encouraging, MO HealthNet aims to increase this measure. In fiscal year 2021, MO HealthNet paid for 333,252 inhalers for 85,692 participants with almost 2,000 participants experiencing an asthma exacerbation related ED visit or inpatient stay. While albuterol inhalers will continue to be available, MO HealthNet hopes as SMART is implemented more widely, albuterol inhaler prescriptions will decrease as Dulera and Symbicort prescriptions increase and that we will see a decrease in asthma-related ED visits and hospitalizations.

(Example of action plan template for budesonide/formoterol.

A similar action plan could be constructed for other ICS/formoterol formulations, e.g. mometasone/formoterol)

My Asthma Action Plan

For Single Inhaler Maintenance and Reliever Therapy (SMART) with budesonide/formoterol

Name: _____ Action plan provided by: _____

Date: _____ Doctor: _____

Usual best PEF: _____ L/min Doctor's phone: _____
(if used)

Normal mode

My SMART Asthma Treatment is:

- budesonide/formoterol 160/4.5 (12 years or over)
- budesonide/formoterol 80/4.5 (4-11 years)

My Regular Treatment Every Day:

(Write in or circle the number of doses prescribed for this patient)

Take [1, 2] inhalation(s) in the morning

and [0, 1, 2] inhalation(s) in the evening, every day

Reliever

Use 1 inhalation of budesonide/formoterol whenever needed for relief of my asthma symptoms

I should always carry my budesonide/formoterol inhaler

My asthma is stable if:

- I can take part in normal physical activity without asthma symptoms

AND

- I do not wake up at night or in the morning because of asthma

Other Instructions

Asthma Flare-up

If over a Period of 2-3 Days:

- My asthma symptoms are getting worse **OR NOT** improving **OR**
- I am using more than 6 budesonide/formoterol reliever inhalations a day (if aged 12 years and older) or more than 4 inhalations a day (if 4-11 years)

I should:

- Continue to use my regular everyday treatment **PLUS** 1 inhalation budesonide/formoterol whenever needed to relieve symptoms
- Start a course of prednisolone
- Contact my doctor

Course of Prednisolone Tablets:

Take _____ mg prednisolone tablets per day for _____ days **OR**

- If I need more than **12 budesonide/formoterol inhalations (total)** in any day, (or more than 8 inhalations for children 4-11 years) I **MUST** see my doctor or go to the hospital the same day

Asthma Emergency

Signs of an Asthma Emergency:

- Symptoms getting worse quickly
- Extreme difficulty breathing or speaking
- Little or no improvement from my budesonide/formoterol reliever inhalations.

If I have any of the above danger signs, I should dial _____ for an ambulance and say I am having a severe asthma attack.

While I am waiting for the ambulance start my asthma first aid plan:

- Sit upright and stay calm
- Take 1 inhalation of budesonide/formoterol. Wait 1-3 minutes. If there is no improvement take another inhalation of budesonide/formoterol (up to a maximum of 6 inhalations on a single occasion)
- If only albuterol is available, take 4 puffs as often as needed until help arrives
- Start a course of prednisolone tablets (as directed) while waiting for the ambulance
- Even if my symptoms appear to settle quickly, I should see my doctor immediately after a serious attack



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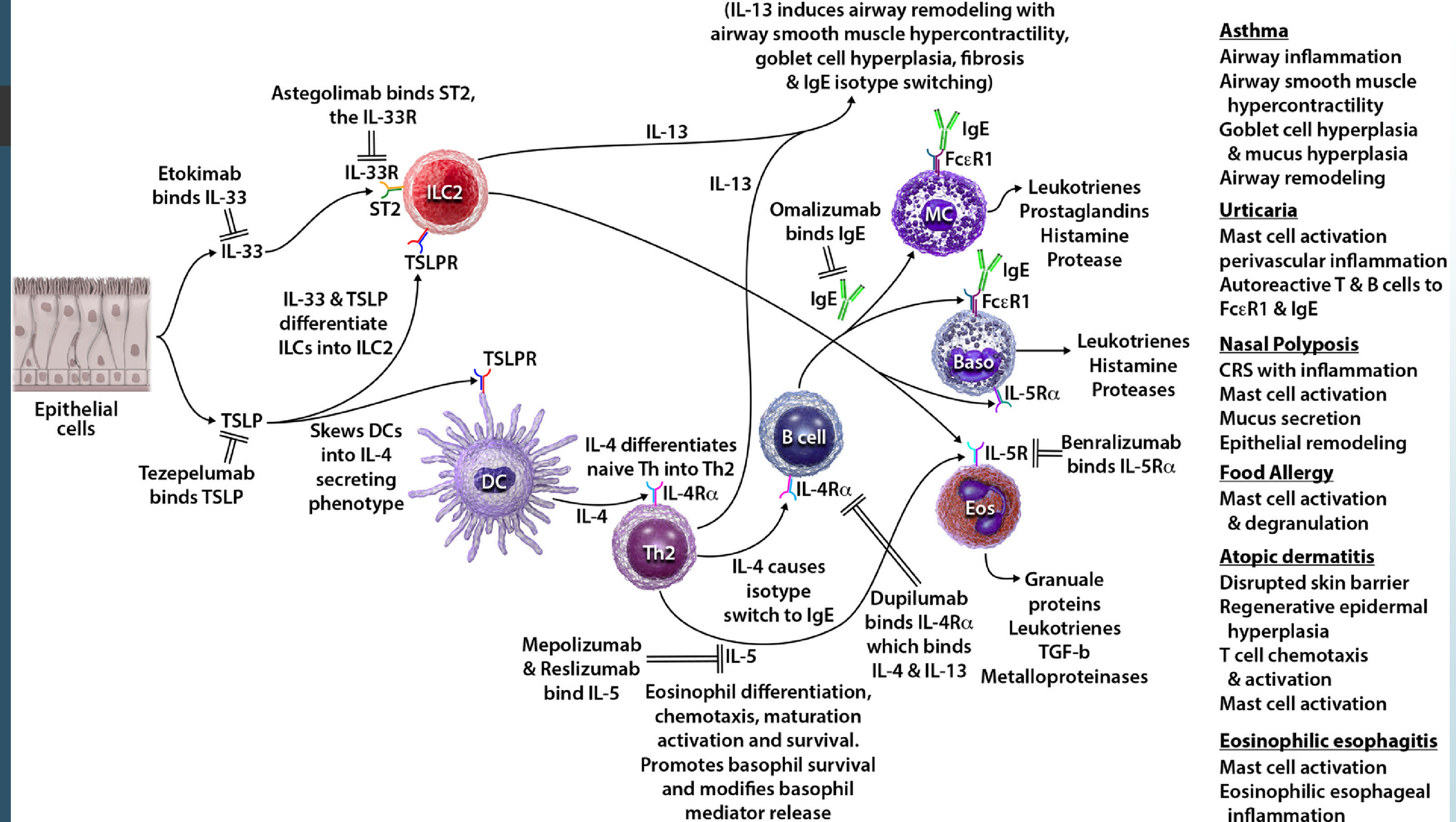
Biologics in Pediatric Asthma


- ▶ **Age < 18 years of age**
- ▶ **Xolair**
- ▶ **Dupilamab (Dupixent)**



In whom shall I consider a Biologic?

- ▶ A biologic is used for patients who continue to have symptoms despite use of standard daily controller medications. Symptoms of poorly controlled asthma include frequent coughing, wheezing, or shortness of breath; waking up at night with difficulty breathing; requiring a fast-acting reliever medication, such as albuterol, several times a day or week; and recurrent hospital admissions, emergency room visits, or need for oral steroids for exacerbations.

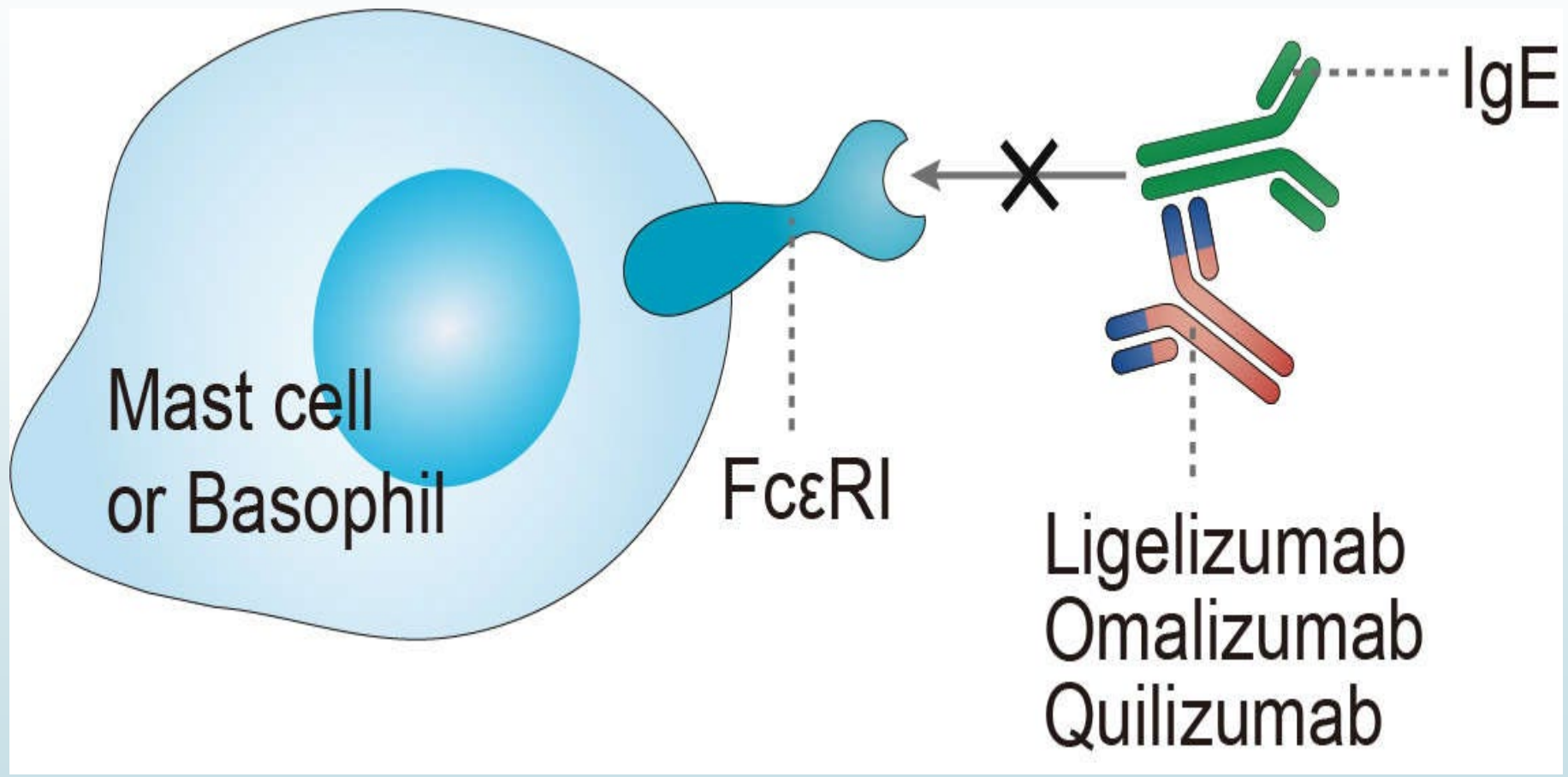




Six and counting

The FDA has approved six biologics as treatments for severe asthma and more approvals are expected.

Biologic	Approved by the FDA for severe asthma	
Cinquair (reslizumab)	2016	≥ 18
Dupixient (dupilumab)	2018	≥ 6
Fasenra (benralizumab)	2017	≥ 12
Nucala (mepolizumab)	2015	≥ 6
Tezspire (tezepelumab)	2021	> 12
Xolair (omalizumab)	2003	≥ 6



Mast cell
or Basophil

FcεRI

IgE

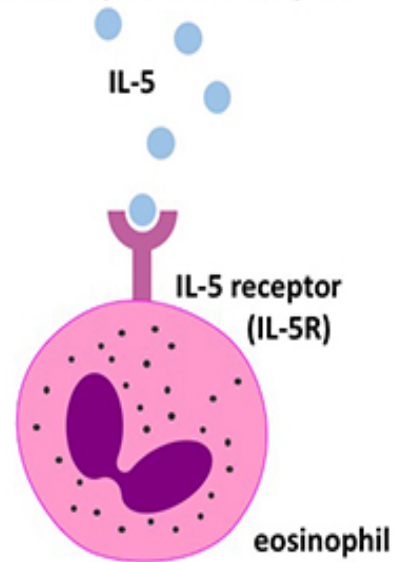
Ligelizumab
Omalizumab
Quilizumab

How do the IL-5 inhibitors Cinqair, Fasenra, and Nucala work?

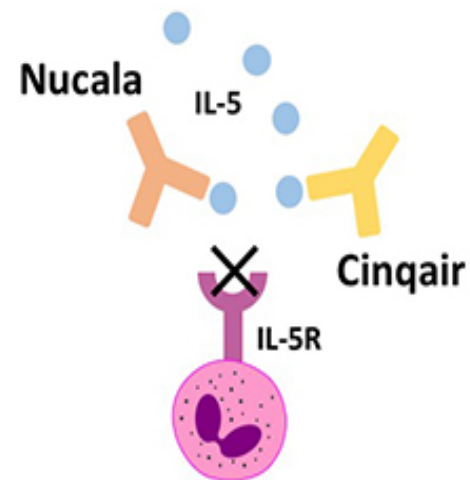
IL-5 inhibitors block IL-5 from binding to the IL-5 receptor on eosinophils

normal IL-5 signaling

IL-5 molecules bind to the IL-5 receptor on eosinophils

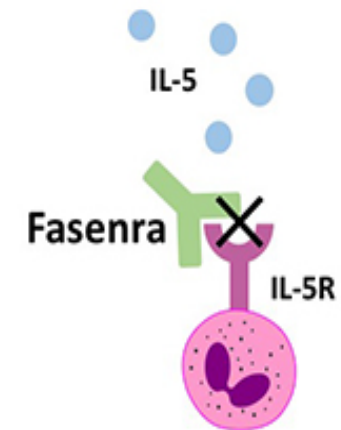


IL-5 molecules are blocked



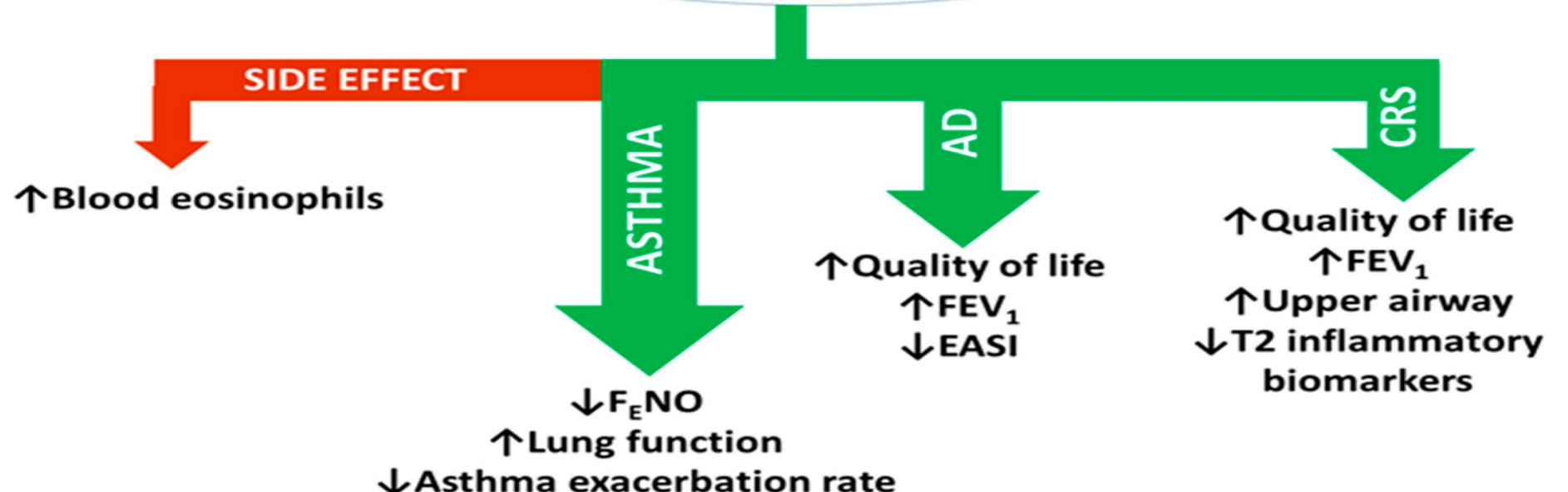
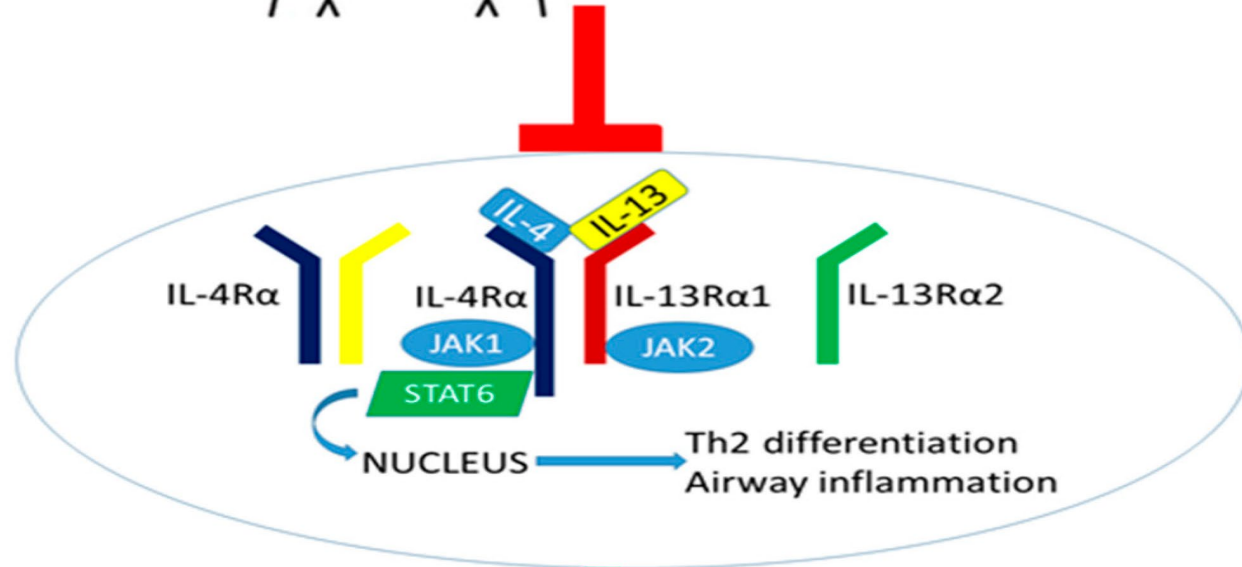
Nucala (mepolizumab) and Cinqair (reslizumab) bind directly to IL-5 and stop IL-5 from binding to its receptor

IL-5 receptor is blocked



Fasenra (benralizumab) binds to the IL-5 receptor and stops IL-5 from binding

www.vasculitides.com



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Lung Function after Biologics Started

- ➡ Increase (Children ?)
- ➡ Prevent more rapid decline (Adults ?)

Allergic asthma if evidence of sensitization to ≥ 1 perennial aeroallergen and total IgE 30-1300 IU/mL (6-11 years) or 30-700 IU/mL (12+ years)

Nonallergic asthma if NO evidence of sensitization to ≥ 1 perennial aeroallergen, or total IgE <30, or >1300 IU/mL (6-11 years) or >700 IU/mL (12+ years)

*** Consider coexisting disorders**

- OMA – chronic idiopathic urticaria
- MEPO – HES, CRSwNP, EGPA
- DUPI – atopic dermatitis, CRSwNP, EoE

Difficult to control asthma

Confirm diagnosis, adherence, inhaler technique, environmental exposures, comorbidities

Nonbiologic step-ups

Severe uncontrolled asthma



Phenotyping – blood EOS, $F_{E}NO$, tIgE & sIgE/skin test, lung function

Blood EOS <150 cells/ μ L

Blood EOS 150-1500 cells/ μ L

Blood EOS > 1500 cells/ μ L

$F_{E}NO$ < 20 ppb

$F_{E}NO \geq 20$ ppb

$F_{E}NO$ < 20 ppb

$F_{E}NO \geq 20$ ppb

Rule out other causes of eosinophilia

Allergic asthma

Nonallergic asthma

Allergic asthma

Nonallergic asthma

Allergic asthma

Nonallergic asthma

Allergic asthma

Nonallergic asthma

Allergic asthma

Nonallergic asthma

6-11 years

OMA*

NONE

DUPI*, or OMA*

DUPI*

DUPI*, MEPO*, or OMA*

DUPI* or MEPO*

DUPI*, MEPO*, or OMA*

DUPI* or MEPO*

OMA* or MEPO*

MEPO*

12+ years

OMA* or TEZ

TEZ

DUPI*, OMA*, or TEZ

DUPI* or TEZ

BENRA[†], DUPI*, MEPO*, OMA*, or TEZ

BENRA[†], DUPI*, MEPO*, or TEZ

BENRA[†], DUPI*, MEPO*, OMA*, or TEZ

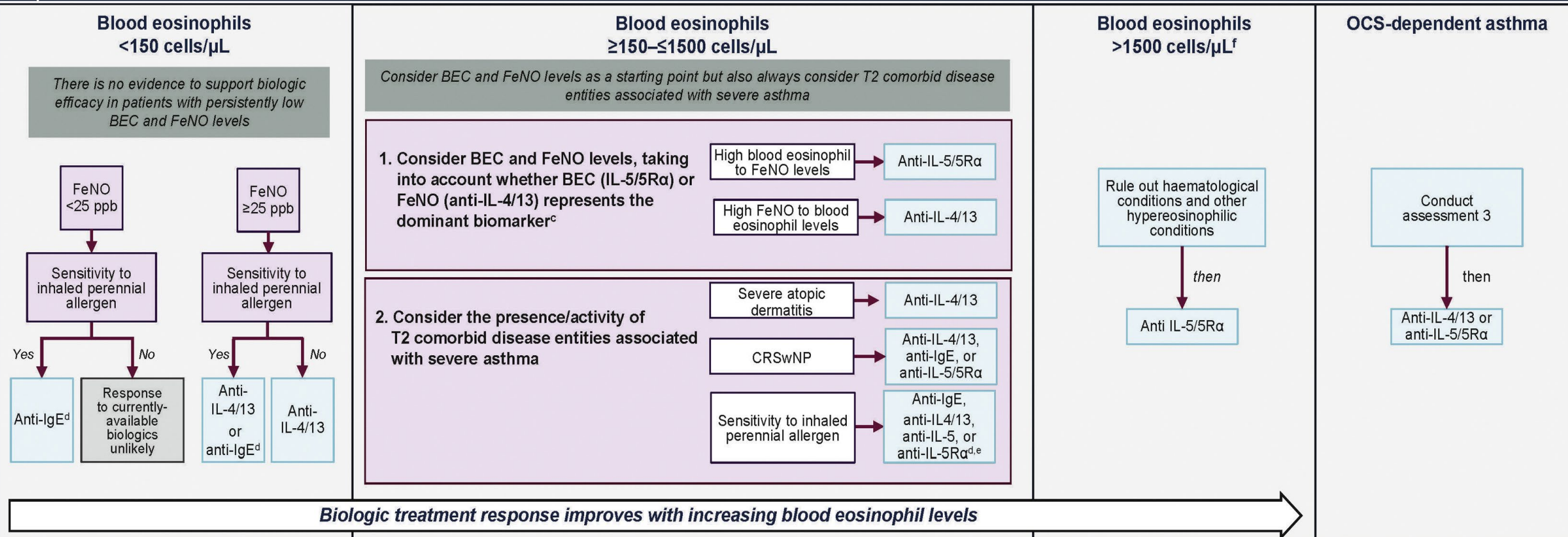
BENRA[†], DUPI*, MEPO*, or TEZ

BENRA, MEPO*, OMA*, or TEZ

BENRA, MEPO*, or TEZ

Baseline assessment

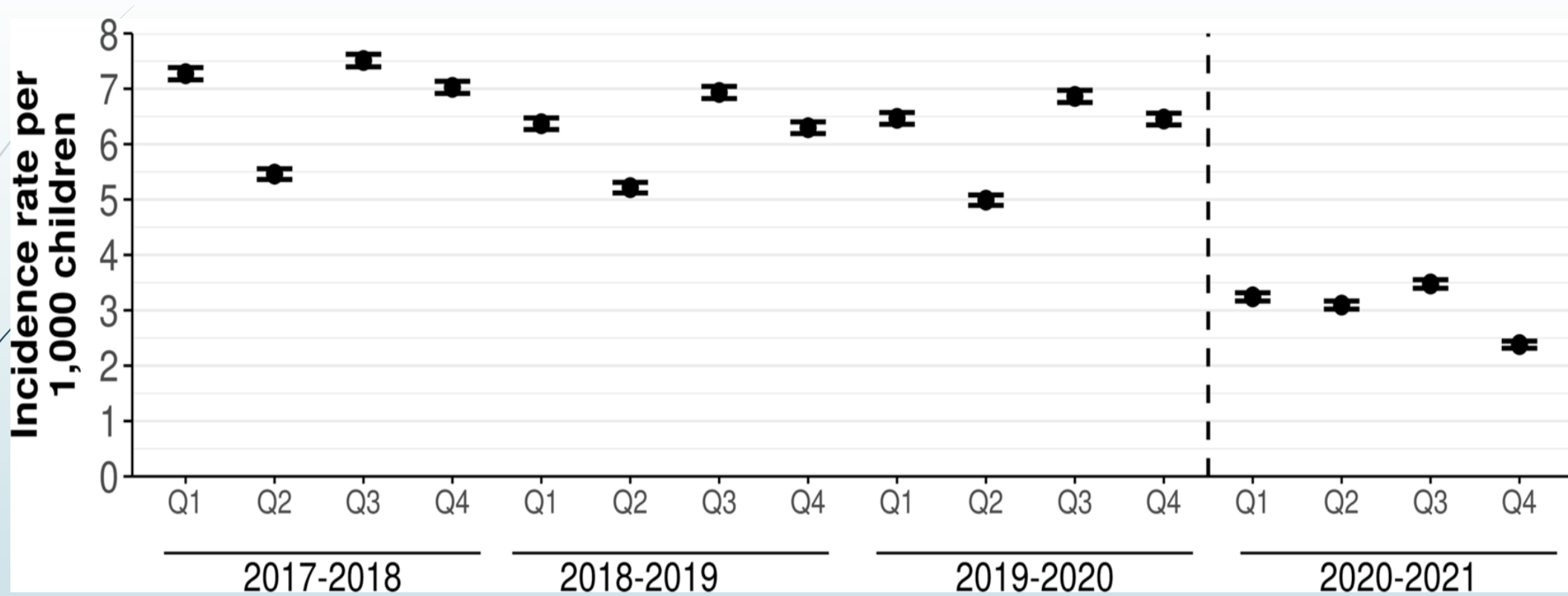
- 1 Confirm presence of severe asthma, according to the GINA report [12], and T2 inflammation (OCS dependency or exacerbations ≥ 2 per year). Identify and address adherence to ICS and other controller medication treatment, comorbidities, and potential exposure to risk factors and complicating factors^a
- 2 Establish blood eosinophil levels and FeNO levels^b
- 3 Validate eosinophil levels by reviewing historic blood eosinophil counts, performing repeat measures, and confirming the presence/activity of T2 asthma and comorbid disease entities associated with severe asthma.
If historic eosinophil counts are not available, consider an OCS-tapering approach in asymptomatic patients receiving daily or frequent OCS treatment to assess for elevated eosinophil levels
- 4 Biomarkers and comorbid disease entities associated with severe asthma should be considered in combination and in context. Consider T2 comorbid disease entities associated with severe asthma (e.g., severe atopic dermatitis, CRSwNP, perennial allergy, EGPA, eosinophilic pneumonia, and hypereosinophilic syndrome), their severity relative to asthma, and whether they are a predictor of response to biologics or a treatment target — address the greatest clinical need for the patient



Additional considerations influencing biologic selection: pregnancy, BMI, patient preference, treatment compliance, frailty, dexterity, and age.^g Consider switching to a different treatment option if a suboptimal response to first-line therapy is observed.



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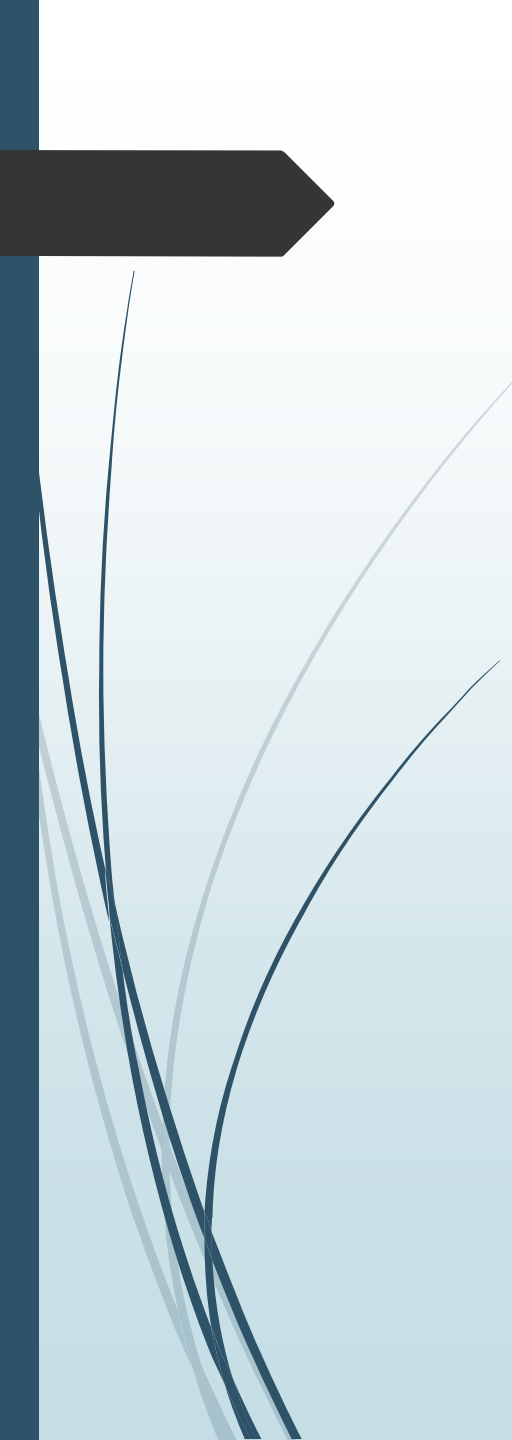




Admission rate for asthma in Nebraska 2019 and 2021

- The COVID year 2020 had a 40% reduction in asthma admissions across Nebraska. These findings are also reflected nationally.



- 
- In general, the goals of asthma treatment are: Preventing long-term (chronic) symptoms that interfere with daily living, such as coughing or shortness of breath during the night or after exercise. Maintaining lung function near the personal best measurement