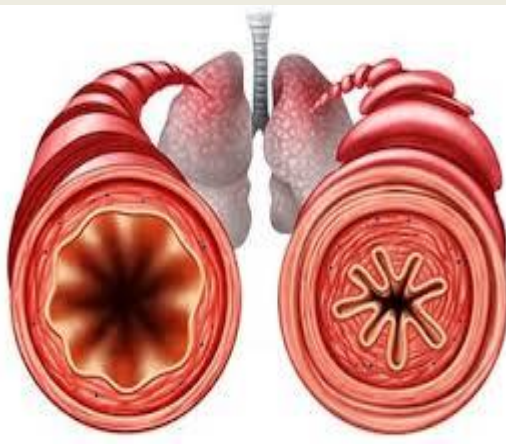


Asthma Management



Dr. M. Hadi Alakkad

Asthma Diagnosis

Box 1-2. Criteria for initial diagnosis of asthma in adults, adolescents, and children 6–11 years

1. HISTORY OF TYPICAL VARIABLE RESPIRATORY SYMPTOMS

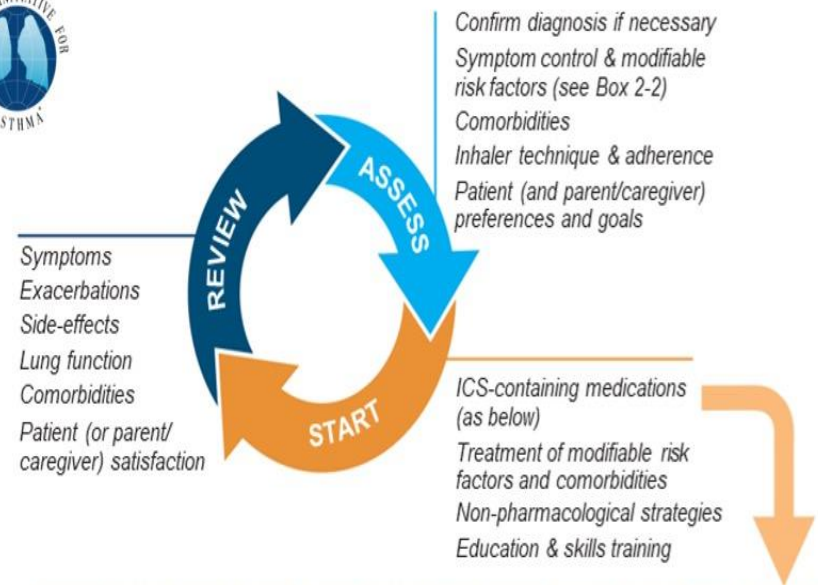
<i>Feature</i>	<i>Symptoms or features that support the diagnosis of asthma</i>
Wheeze, shortness of breath, chest tightness and/or cough (Descriptors may vary between cultures and by age)	<ul style="list-style-type: none">• Symptoms occur variably over time and vary in intensity• Symptoms are often worse at night or on waking• Symptoms are often triggered by exercise, laughter, allergens, cold air• Symptoms often appear or worsen with viral infections

2. CONFIRMED VARIABLE EXPIRATORY AIRFLOW LIMITATION

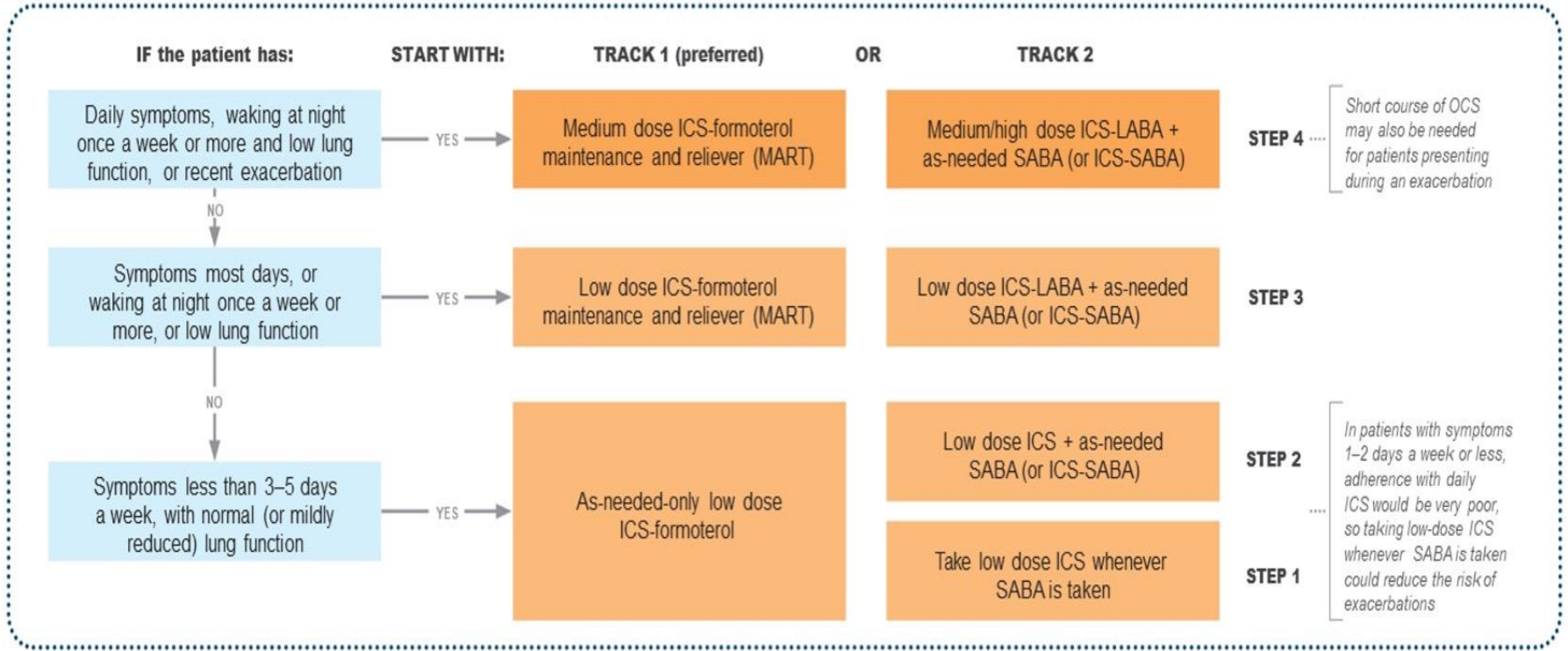
<i>Feature</i>	<i>Considerations, definitions, criteria</i>
Excessive variability in expiratory lung function (one or more of the following):	The greater the variations, or the more occasions excess variation is seen, the more confident the diagnosis of asthma. If initially negative, tests can be repeated during symptoms or in the early morning. If spirometry is not possible, PEF [†] may be used, but it is less reliable.

Positive bronchodilator (BD) responsiveness (reversibility) test with spirometry (or PEF [†])	<p>Adults: increase from baseline in FEV₁ or FVC of ≥12% and ≥200 mL, with greater confidence if the increase is ≥15% and ≥400 mL; or increase in PEF[†] ≥20% if spirometry is not available.</p> <p>Children: increase from baseline in FEV₁ of ≥12% predicted (or in PEF[†] of ≥15%).</p> <p>Measure change 10–15 minutes after 200–400 mcg salbutamol (albuterol) or equivalent, compared with pre-BD readings. Positive test more likely if BD withheld before test: SABA ≥4 hours, long-acting bronchodilators 24–48 hours (see below).</p>
Excessive variability in twice-daily PEF over 2 weeks*	<p>Adults: average daily diurnal PEF variability >10%*</p> <p>Children: average daily diurnal PEF variability >13%*</p>
Increase in lung function after 4 weeks of treatment	<p>Adults: increase from baseline in FEV₁ by ≥12% and ≥200 mL (or PEF[†] by ≥20%) after 4 weeks of daily ICS-containing treatment</p> <p>Children: increase from baseline in FEV₁ of ≥12% predicted (or in PEF[†] of ≥15%).</p>
Positive bronchial challenge test	<p>Adults: Fall from baseline in FEV₁ of ≥20% with standard doses of methacholine, or ≥15% with standardized hyperventilation, hypertonic saline or mannitol challenge, or >10% and >200 mL with standardized exercise challenge.</p> <p>Children: fall from baseline in FEV₁ of >12% predicted (or fall in PEF[†] >15%) with standardized exercise challenge.</p> <p>If FEV₁ decreases during a challenge test, check that FEV₁/FVC ratio has also decreased, since incomplete inhalation, e.g., due to inducible laryngeal obstruction or poor effort, can result in a false reduction in FEV₁.</p>
Excessive variation in lung function between visits (good specificity but poor sensitivity)	<p>Adults: variation in FEV₁ of ≥12% and ≥200 mL (or in PEF[†] of ≥20%) between visits.</p> <p>Children: variation in FEV₁ of ≥12% (or ≥15% in PEF[†]) between visits</p>

Stable Asthmatic Patient Approach



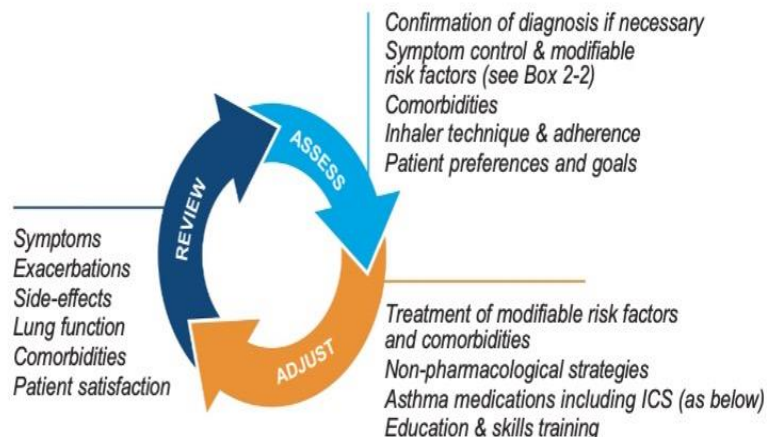
These recommendations are based on the (little) available evidence and consensus



GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management

Assess, Adjust, Review
for individual patient needs



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

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-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

See GINA severe asthma guide

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

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-IL4Rα, anti-TSLP

RELIEVER: As-needed ICS-SABA*, or as-needed SABA

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

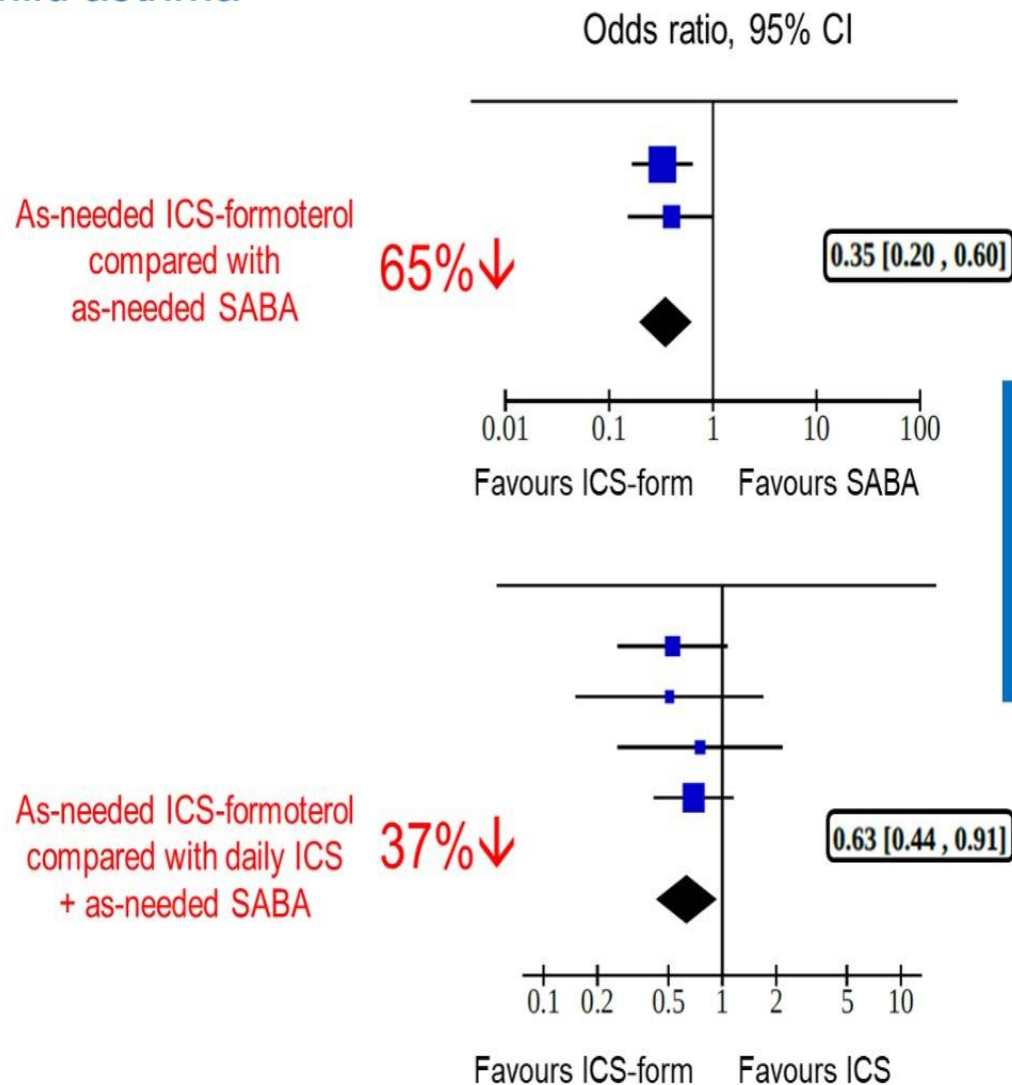
Medium dose ICS, or add LTRA†, or add HDM SLIT

Add LAMA or add LTRA† or add HDM SLIT, or switch to high dose ICS-only

Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

As-needed-only ICS-formoterol reduces emergency visits and hospitalisations in patients with mild asthma



Approved by regulators
in ~50 countries
Recommended in
asthma guidelines
of ~32 countries

From Crossingham et al,
Cochrane Database Syst Rev
2021 (n=9565)

Assessment of asthma control

Ideally, patients should be seen **1-3 months** after starting treatment and every **3-12 months** thereafter

Asthma symptoms control tools for adults

Simple screening tools

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 <input type="checkbox"/> No <input type="checkbox"/>	None of these	1–2 of these	3–4 of these
• Any night waking due to asthma?	Yes <input type="checkbox"/> No <input type="checkbox"/>			
• SABA reliever for symptoms more than twice/week?*	Yes <input type="checkbox"/> No <input type="checkbox"/>			
• Any activity limitation due to asthma?	Yes <input type="checkbox"/> No <input type="checkbox"/>			

Asthma symptoms control tools for adults

Asthma Control Test (ACT)

Asthma Control Test™

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
0	0	0	0	0
1	2	3	4	5

2. During the past 4 weeks, how often have you had shortness of breath?

More than Once a day	Once a day	3 to 6 times a week	Once or twice a week	Not at all
0	0	0	0	0
1	2	3	4	5

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a week	2 to 3 nights a week	Once a week	Once or twice	Not at all
0	0	0	0	0
1	2	3	4	5

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

3 or more times per day	1 or 2 times per day	2 or 3 times per week	Once a week or less	Not at all
0	0	0	0	0
1	2	3	4	5

5. How would you rate your asthma control during the past 4 weeks?

Not Controlled at All	Poorly Controlled	Somewhat Controlled	Well Controlled	Completely Controlled
0	0	0	0	0
1	2	3	4	5

Asthma symptoms control tools for adults

The asthma control test (ACT) is a validated, commonly used numeric tool to distinguish different levels of asthma symptom control. Possible scores range from **5 to 25**, with a higher score indicating better symptom control.

Asthma symptoms control tools for adults

ACT scores are classified as follows:

20-25, well-controlled asthma

16-19, not well-controlled

5-15, very poorly controlled

Role of lung function in assessing asthma control

Role of lung function in assessing asthma control

Lung function **does not correlate** strongly with asthma symptoms

Role of lung function in assessing asthma control

Lung function at individual visits is of **limited use for guiding treatment** because of its large (up to 20%) **visit-to-visit variation**

Role of lung function in assessing asthma control

Low FEV₁ is a **strong independent** predictor of **risk of exacerbations** even after adjustment for symptom frequency

A low FEV₁ percent predicted:

- Identifies patients at risk of asthma exacerbations, independent of symptom levels, especially if FEV₁ is <60% predicted^{[96](#),[105](#),[162](#),[163](#)}
- Is a risk factor for lung function decline, independent of symptom levels^{[116](#)}
- If symptoms are few, suggests limitation of lifestyle, or poor perception of airflow limitation,^{[164](#)} which may be due to untreated airway inflammation.^{[152](#)}

Normal FEV₁: A 'normal' or near-normal FEV₁ in a patient with frequent respiratory symptoms (especially when symptomatic) prompts consideration of alternative causes for the symptoms (e.g., cardiac disease, or cough due to post-nasal drip or gastroesophageal reflux disease;

Persistent bronchodilator responsiveness: Finding significant bronchodilator responsiveness (increase in FEV₁ >12% and >200 mL from baseline)³⁵ in a patient taking ICS-containing treatment, or who has taken a SABA within 4 hours, or a LABA within 12 hours (or 24 hours for a once-daily LABA), suggests uncontrolled asthma, particularly poor adherence and/or incorrect technique.

Role of lung function in assessing asthma control

Lung function should be assessed

- At diagnosis or start of treatment**
- After 3-6 months of ICS- containing treatment** to assess the patient's personal best **FEV₁** and

Role of lung function in assessing asthma control

Lung function should be assessed

- **Periodically** thereafter (*e.g.* at least once **every 1–2 years**; **more often in at-risk patients** and those with **severe asthma**) to identify progressive **decline**.

a. Risk factors for exacerbations

Uncontrolled asthma symptoms: Having uncontrolled symptoms is an important risk factor for exacerbations.⁸⁵

Factors that increase the risk of exacerbations even if the patient has few asthma symptoms[†]

SABA over-use: High SABA use ($\geq 3 \times 200$ -dose canisters/year associated with increased risk of exacerbations, increased mortality particularly if ≥ 1 canister per month)⁸⁶⁻⁸⁹

Inadequate ICS: not prescribed ICS, poor adherence,⁹⁰ or incorrect inhaler technique⁹¹

Other medical conditions: Obesity,^{92,93} chronic rhinosinusitis,⁹³ GERD,⁹³ confirmed food allergy,⁹⁴ pregnancy⁹⁵

Exposures: Smoking,⁹⁶ e-cigarettes,⁹⁷ allergen exposure if sensitized,^{96,98} air pollution⁹⁹⁻¹⁰²

Psychosocial: Major psychological or socioeconomic problems^{103,104}

Lung function: Low FEV₁ (especially $< 60\%$ predicted),^{96,105} high bronchodilator responsiveness^{93,106,107}

Type 2 inflammatory markers: Higher blood eosinophils,^{93,108,109} high FeNO (adults with allergic asthma on ICS)¹¹⁰

Exacerbation history: Ever intubated or in intensive care unit for asthma;¹¹¹ ≥ 1 severe exacerbation in last year^{112,113}

Stepping up

Short- term step up (for 1-2 weeks)

A **short term increase** in maintenance ICS dose for **1-2 weeks** may be necessary (during viral infection or seasonal allergen).

This increase may be **initiated by the patient** according to their **written asthma action plan**

Sustained step up (for at least 2-3 months)

Some patients whose asthma is uncontrolled or partially controlled may benefit **from increasing the maintenance dose.**

Sustained step up (for at least 2-3 months)

A **step up** in treatment may be recommended after **confirming** that the symptoms are

- **Due to asthma,**
- **Inhaler technique**
- **Adherence** are satisfactory
- **Modifiable risk factor** such as smoking have been addressed

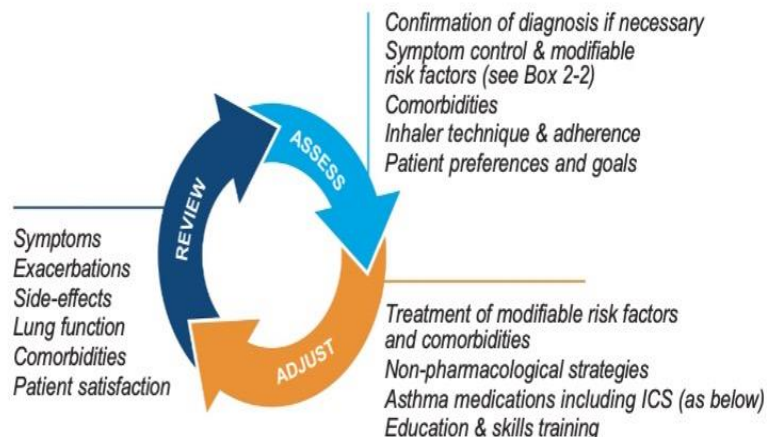
Stepping Down

Once good **asthma control** has been achieved and maintained for **2-3 months** and lung function has reached a plateau, treatment can often be reduced, without loss of asthma control.

GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management

Assess, Adjust, Review
for individual patient needs



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

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-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

See GINA severe asthma guide

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

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-IL4Rα, anti-TSLP

RELIEVER: As-needed ICS-SABA*, or as-needed SABA

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 add LTRA† or add HDM SLIT, or switch to high dose ICS-only

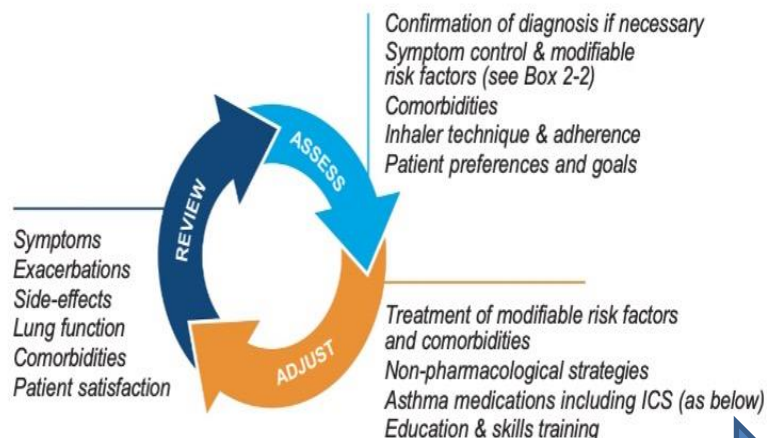
Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management

Assess, Adjust, Review
for individual patient needs



TRACK 1: PREFERRED CONTROLLER and RELIEVER

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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-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

See GINA severe asthma guide

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

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-IL4Rα, anti-TSLP

RELIEVER: As-needed ICS-SABA*, or as-needed SABA

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 add LTRA† or add HDM SLIT, or switch to high dose ICS-only

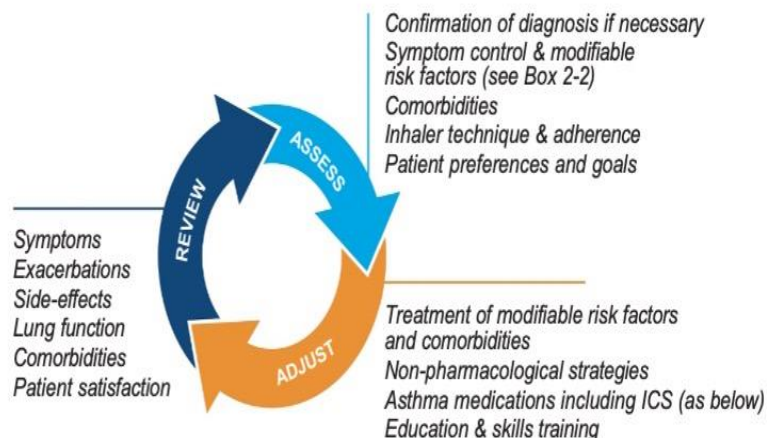
Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management

Assess, Adjust, Review
for individual patient needs



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

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-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

See GINA severe asthma guide

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

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-IL4Rα, anti-TSLP

RELIEVER: As-needed ICS-SABA*, or as-needed SABA

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 add LTRA† or add HDM SLIT, or switch to high dose ICS-only

Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

Assessing Asthma Severity

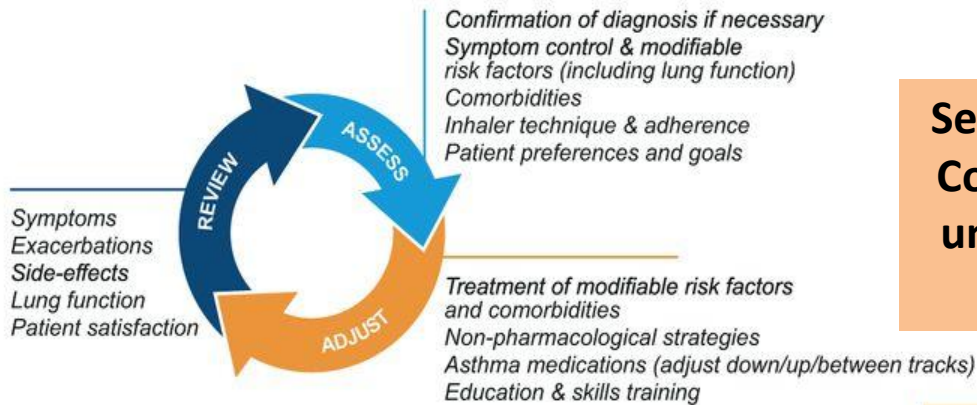
Assessing Asthma Severity

Sever Asthma is defined that remains **uncontrolled** despite optimized treatment with **high dose ICS-LABA**, or that requires high dose ICS-LABA to **prevent it from becoming uncontrolled**

Adults & adolescents
12+ years

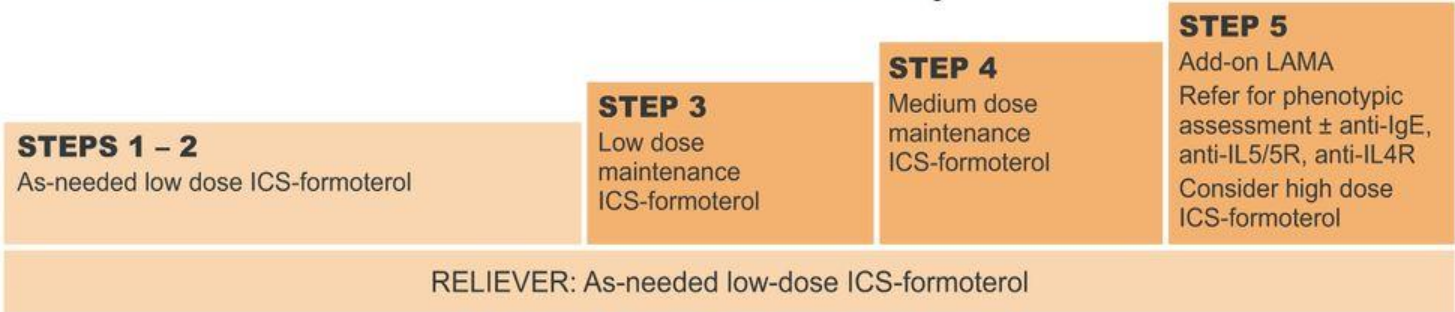
Personalized asthma management

Assess, Adjust, Review
for individual patient needs

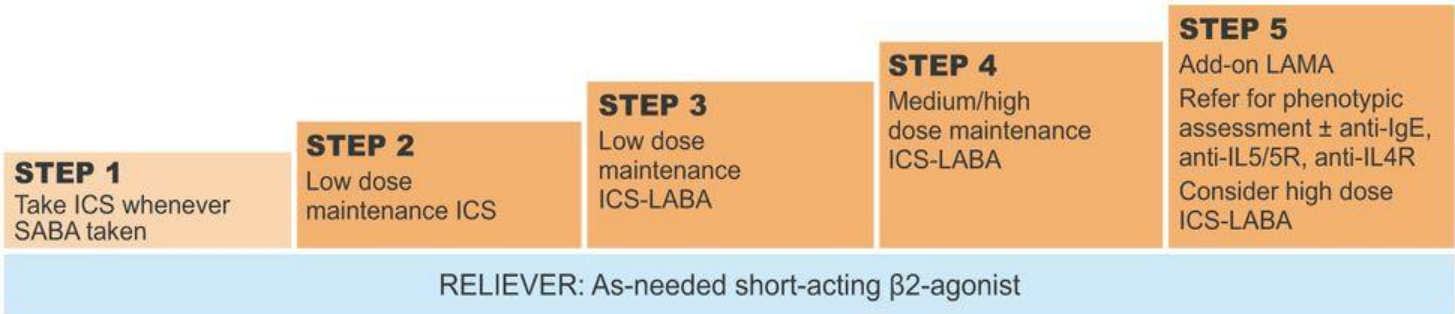


Sever Asthma
Controlled or
uncontrolled
step 5

CONTROLLER and **PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever



CONTROLLER and **ALTERNATIVE RELIEVER**
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller



Other controller options
for either track

	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; add low dose OCS but consider side-effects
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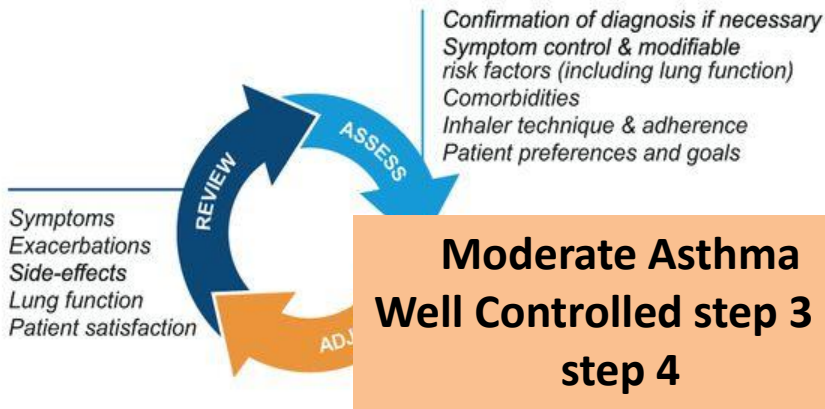
Assessing Asthma Severity

Moderate Asthma is currently defined as asthma that is **well controlled with step 3 or step 4 treatment**

Adults & adolescents
12+ years

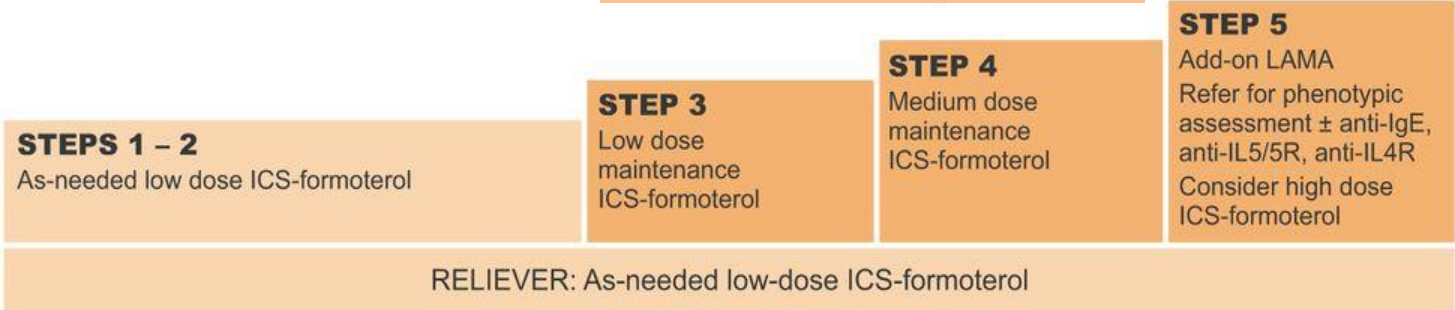
Personalized asthma management

Assess, Adjust, Review
for individual patient needs

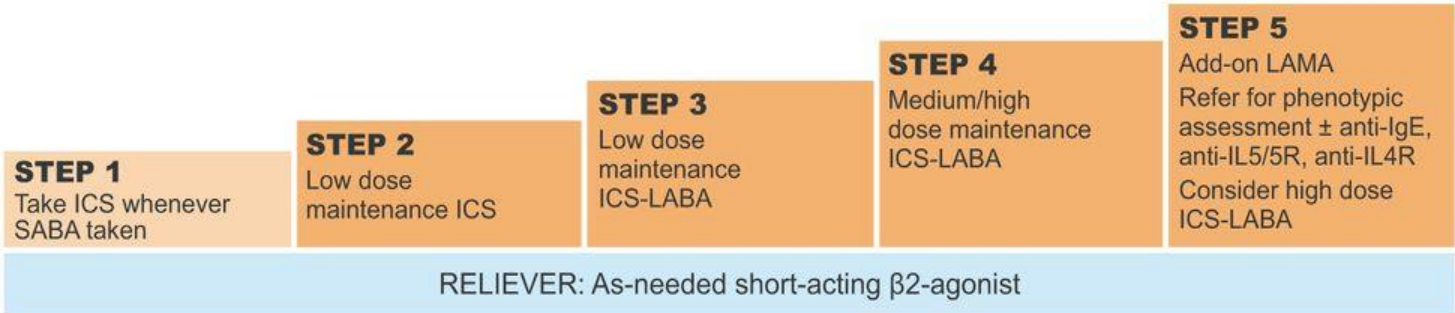


Sever Asthma
Controlled or uncontrolled
step 5

CONTROLLER and **PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever



CONTROLLER and **ALTERNATIVE RELIEVER**
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller



Other controller options
for either track

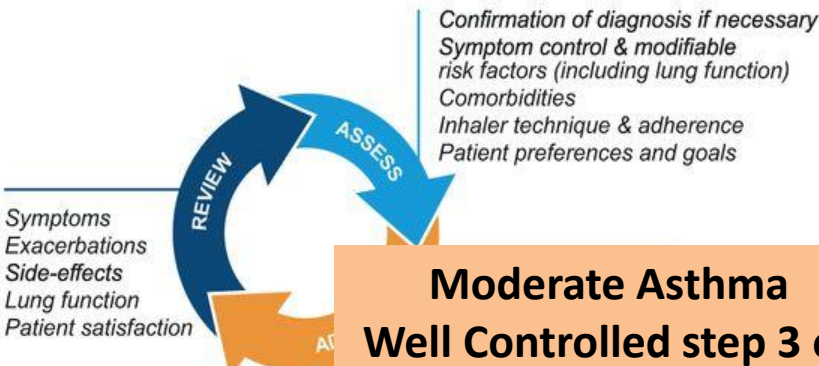
	Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	Medium dose ICS, or add LTRA, or add HDM SLIT	Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS	Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects
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Assessing Asthma Severity

Mild Asthma is currently defined as asthma that is **well controlled with as needed ICS-Formoterol**, or with **low dose ICS plus as needed SABA**

Adults & adolescents
12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Sever Asthma
Controlled or
uncontrolled
step 5

Moderate Asthma
Well Controlled step 3 or
step 4

Mild Asthma well
Controlled step 1 or step 2

CONTROLLER and
PREFERRED RELIEVER
(Track 1). Using ICS-formoterol
as reliever reduces the risk of
exacerbations compared with
using a SABA reliever

STEPS 1 – 2
As-needed 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 phenotypic
assessment ± anti-IgE,
anti-IL5/5R, anti-IL4R
Consider high dose
ICS-formoterol

RELIEVER: As-needed low-dose ICS-formoterol

CONTROLLER and
ALTERNATIVE RELIEVER
(Track 2). Before considering a
regimen with SABA reliever,
check if the patient is likely to be
adherent with daily controller

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 phenotypic
assessment ± anti-IgE,
anti-IL5/5R, anti-IL4R
Consider high dose
ICS-LABA

RELIEVER: As-needed short-acting β2-agonist

Other controller options
for either track

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; add low dose OCS
but consider side-effects

Assessing Asthma Severity

By this retrospective definition, **asthma severity** can only be assessed **after good asthma control** has been achieved and treatment stepped down to find the patient's minimum effective dose, or if **asthma remains uncontrolled** despite at least several months of **optimized maximal therapy**

STEP 5

Add-on LAMA

Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, \pm anti-IgE, anti-IL5/5R, anti-IL4R α , anti-TSLP

STEP 5

Add-on LAMA

Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, \pm anti-IgE, anti-IL5/5R, anti-IL4R α , anti-TSLP

Add azithromycin (adults) or add LTRA[†]. As last resort consider adding low dose OCS but consider side-effects

SEVERE ASTHMA PHENOTYPES

Clinical Phenotypes

Well-established severe asthma **clinical phenotypes** are based on a combination of clinical characteristics that have been validated in clustering analyses of patients. These include

Clinical Phenotypes

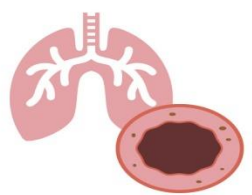
- The **timing** of asthma **onset** (early vs late)
- **Atopy status** (allergic vs nonallergic),
- **Lung function** (persistence of airflow limitation),
- **Treatment response** (OCS resistance)

Clinical Phenotypes

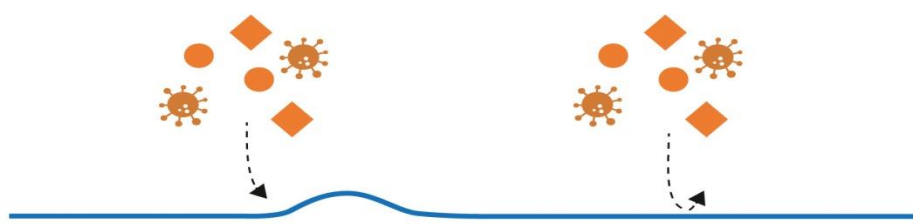
- Other **comorbidities** (eg, **obesity**, chronic - **rhinosinusitis** with or without **nasal polyps**, gastroesophageal reflux disease, atopic dermatitis, urticaria, eosinophilic esophagitis, and **aspirin-exacerbated respiratory disease**).
- **Lung biopsy** Asthmatic granulomatosis

PHENOTYPING BASED ON BIOMARKERS OF INFLAMMATION

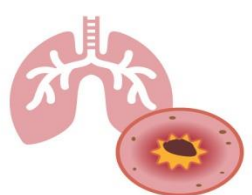
 **Viruses**
 **Allergens**
 **Pollutants**



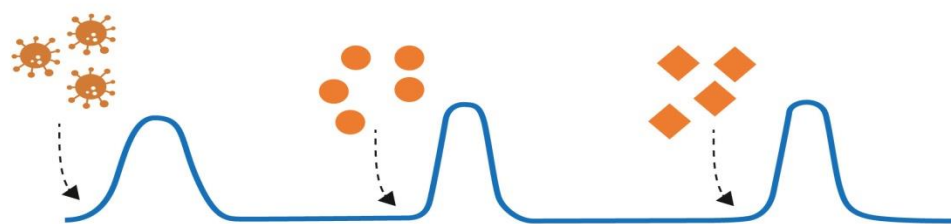
Stable asthma



Triggers cause little inflammation and no exacerbations

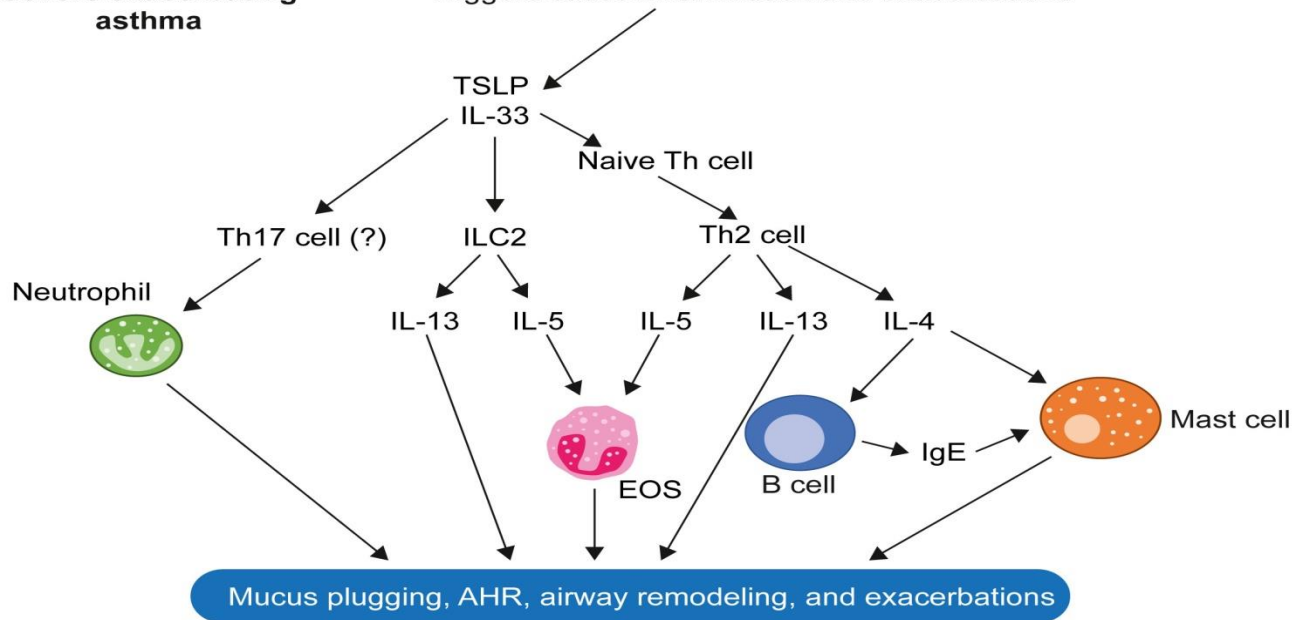


Severe exacerbating asthma



Triggers cause inflammation and exacerbations

Exacerbating asthma:
increased airway
immunoreactivity
to exacerbation triggers



Asthma phenotypes are categorized into 2 main overarching inflammatory phenotypes defined by the predominant immunological pathways driving the disease pathology:

- **Eosinophilic (type 2 high asthma)**
- **Noneosinophilic (type 2 low asthma)**

Type 2/eosinophilic asthma

Approximately **70 percent of severe asthma** is associated with persistent elevation in markers of Type 2 inflammation (**blood eosinophils** and fraction of exhaled nitric oxide [FeNO])

Type 2/eosinophilic asthma

data from clinical trials suggest that blood levels of **eosinophils 150 /micro L** or **FeNO levels above 24 ppb** support an underlying active **Type 2 immune process**, which will respond to Type 2 specific therapy.

Neutrophilic asthma

The existence of a neutrophilic asthma phenotype (eg, **40 to 60 percent neutrophils in induced sputum**) is **controversial**

Neutrophilic asthma

The specificity of neutrophilic inflammation for a particular subtype of asthma is **complicated** by the many confounding factors that can contribute to neutrophilia in sputum,

Neutrophilic asthma

- the use of inhaled glucocorticoids,
- air pollution,
- respiratory infection,
- sensitization to aspergillus,
- gastroesophageal disease

Severe asthma and T2 inflammation

Phenotyping

- High BECs
- High FeNO levels
- High IgE levels (?)

- Low BECs
- Low FeNO levels

Unmasking of T2 biomarkers
(likely underlying T2-high
asthma)

- Repeated phenotyping to rule out T2-high asthma while tapering ICS/OCS*
- Consider alternative diagnosis
- Reconfirm diagnosis of asthma
- Assess sputum/tissue eosinophils

Persistently low T2 biomarkers (T2-low asthma)

T2-high asthma

- High BECs
- High FeNO levels

Clinical characteristics

- Early-onset allergic
- Late-onset eosinophilic
- Responsive to CS (mild, moderate-to-severe), refractory to ICS (severe)

Biologic treatment

- Anti-IgE
- Anti-IL-5
- Anti-IL-4/IL-13
- Anti-TSLP

T2-low asthma

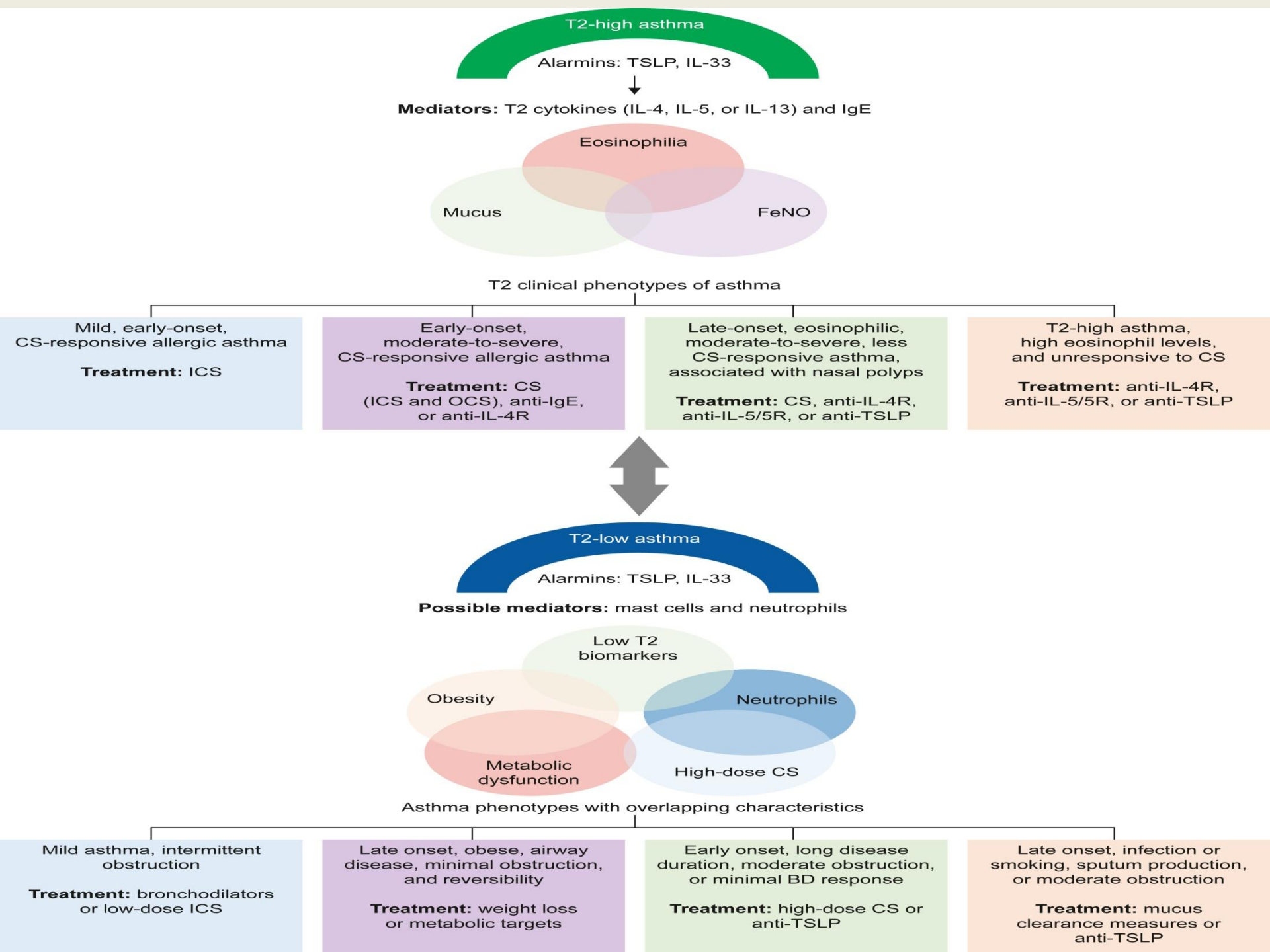
- Noneosinophilic, neutrophilic or paucigranulocytic

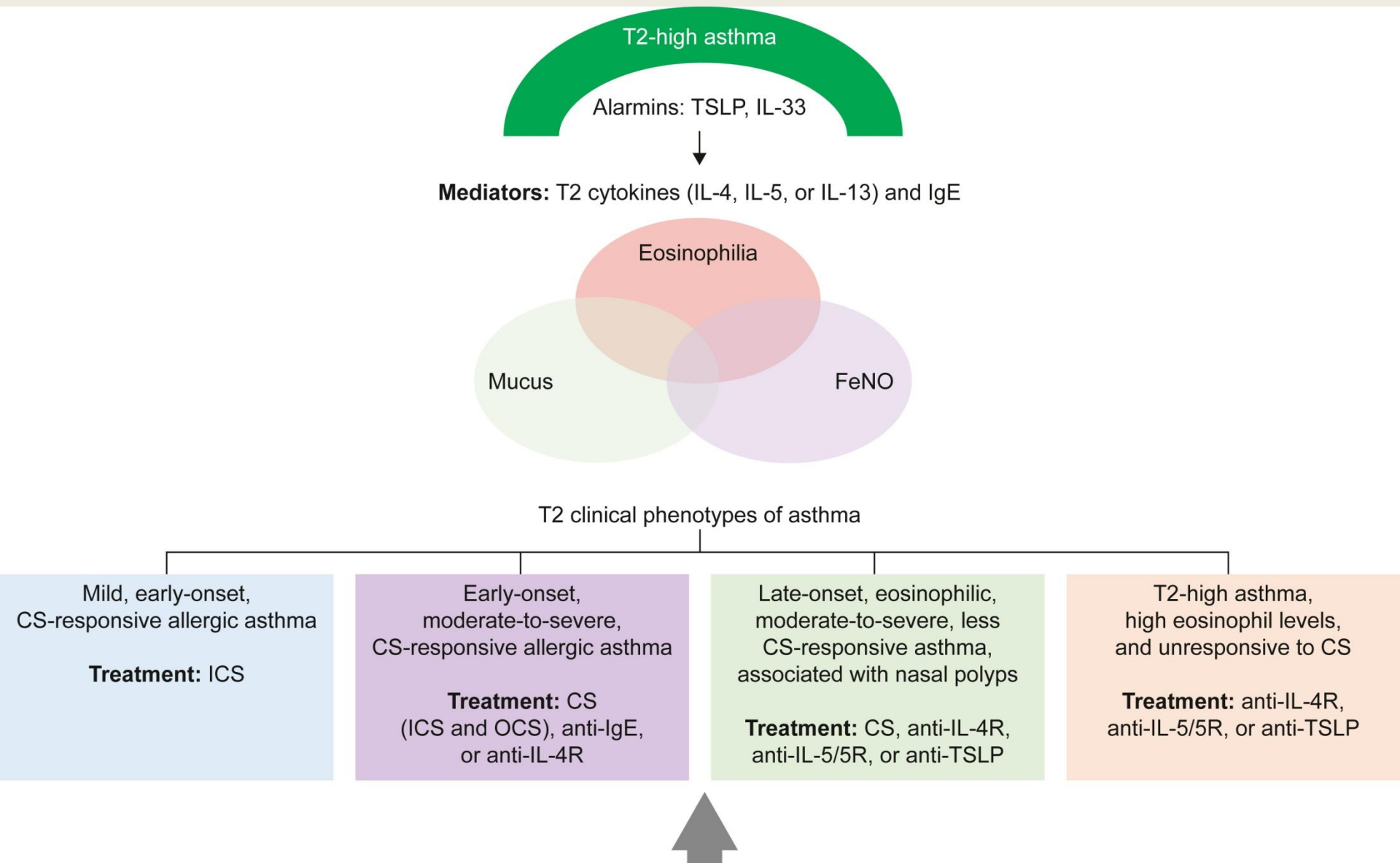
Clinical characteristics

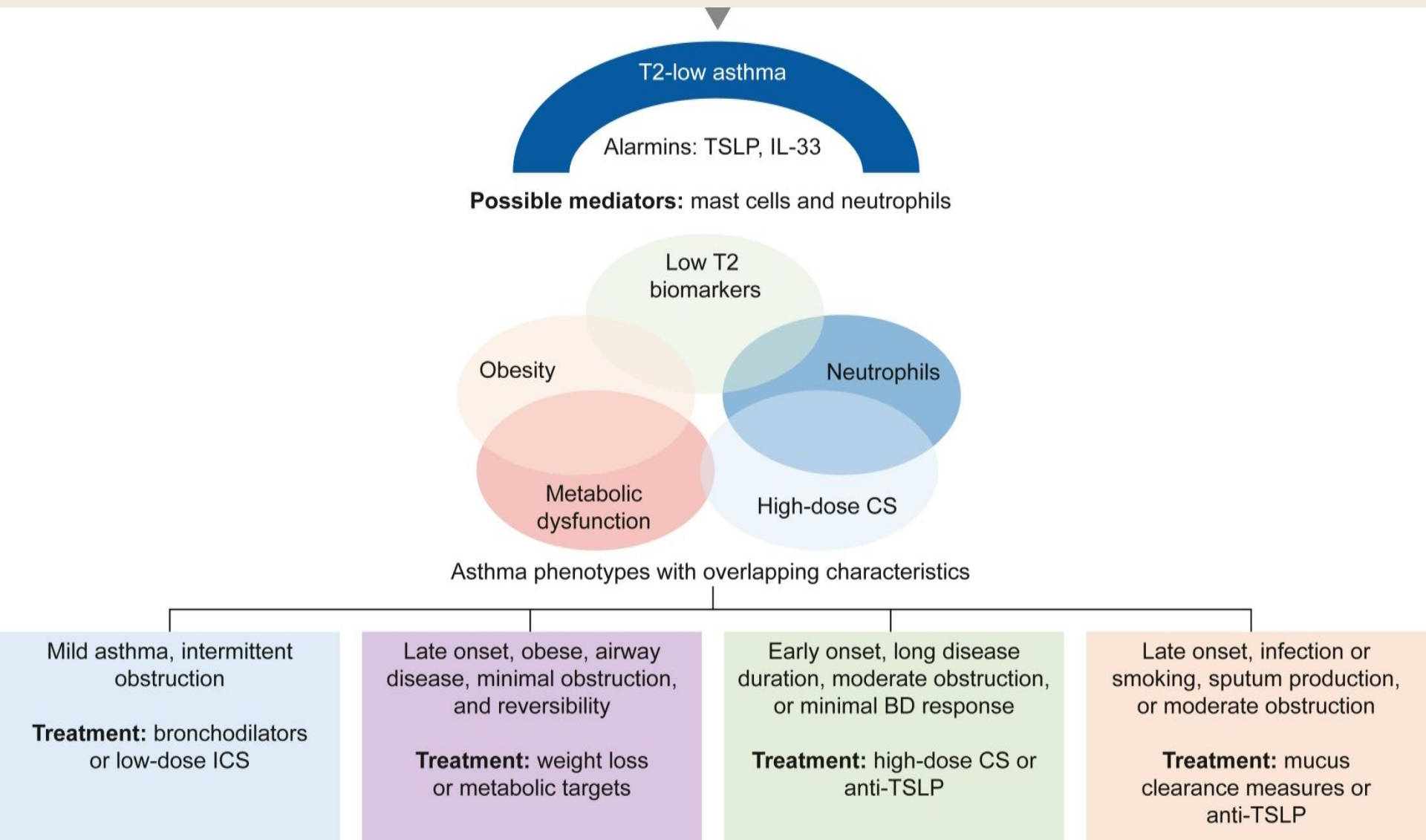
- Very late onset
- Obesity
- Smoking
- Lower risk of asthma exacerbations
- Poorly responsive to CS

Treatment

- Anti-IL-17R α (?)
- Anti-TSLP
- Azithromycin (if evidence of infection)
- Treatments for other traits (obesity, inducible laryngeal obstruction, dysfunctional breathing)







Anti-IgE therapy (omalizumab)

The anti-IgE agent omalizumab is approved for use in patients age **six years and above** with

- With **moderate to severe persistent asthma eosinophilic phenotype** with **incomplete symptom control** with **inhaled glucocorticoid** treatment
- an **IgE level of 30 to 700** international units/mL,
- **positive allergen-skin** or **allergen-specific IgE** tests to a perennial allergen, and

Anti-IL-5 therapy

Interleukin (IL)-5 is a **pro-eosinophilic cytokine** that is a potent mediator of eosinophil hematopoiesis and contributes to eosinophilic inflammation in the airways.

Mepolizumab and reslizumab are anti-IL-5 monoclonal antibodies [83];

benralizumab is an **anti-IL-5 receptor alpha** antibody

Anti-IL-5 therapy

is used for **add-on**, maintenance treatment of **uncontrolled severe asthma** in patients who have an **eosinophilic phenotype**

Anti-IL-5 therapy

Clinical trial data suggest that efficacy requires an absolute blood **eosinophil count ≥ 150 micro/L**, but this threshold is **less clear** in patients on daily **systemic glucocorticoids**.

Mepolizumab

is used for **add-on**, maintenance treatment of severe asthma in patients who are age **six years or older**

Mepolizumab

Mepolizumab is also approved for treatment of **chronic rhinosinusitis** and **nasal polyposis**

Reslizumab

add-on, maintenance therapy of severe asthma in patients who are **age 18 years or older**

Benralizumab

Benralizumab is a **monoclonal antibody directed against IL-5 receptor alpha** that is approved by the FDA as **add-on** therapy in patients (**≥ 12 years**)

It appears to be **more effective than anti-IL-5 antibodies** in **reducing eosinophil numbers**.

Anti-IL-4 receptor alpha subunit antibody (dupilumab)

Dupilumab is a fully **human monoclonal** antibody that binds to the alpha subunit of the IL-4 receptor. Through blockade of this receptor, dupilumab **inhibits** the activity of both **IL-4 and IL-13**, Type 2 cytokines that play a key role in allergy and asthma.

Anti-IL-4 receptor alpha subunit antibody (dupilumab)

Dupilumab is approved by the FDA for the treatment of **moderate-to-severe, eosinophilic** asthma in patients **age six years and older**

Anti-thymic stromal lymphopoietin (tezepelumab)

Thymic stromal lymphopoietin (TSLP) is an **epithelial cell-derived cytokine** that participates in **asthma inflammation**.

Tezepelumab is approved by the FDA **for add-on maintenance therapy** in patients with **severe asthma (both phenotypes)** who are **≥12 years of age**

Thank You