Asthma

Definition

Asthma is an inflammatory disorder of the airways characterized by cough, wheezing, chest tightness, dyspnea, and variable airflow obstruction.

Pathogenesis

The pathophysiologic mechanisms of asthma include:

- Chronic airway inflammation
- Airway narrowing due to edema
- Subepithelial fibrosis
- Smooth muscle hypertrophy,
- Mucus hypersecretion
- Airway smooth muscle constriction causing bronchial hyperreactivity in response to various stimuli.

Risk Factors

Risk factors for asthma include both **host** and **environmental** factors.

Host factors: genes predisposing to atopy; bronchial hyperreactivity; and airway inflammation have been identified.

Environmental factors:

- Exposure to indoor allergens (mites, furred animals, cockroaches, molds)
- Outdoor allergens (pollens, molds)
- Tobacco smoke
- Occupational sensitizers and allergens,
- Viral respiratory infections
- Air pollution.
- Obesity

Symptoms and Clinical Evaluation

Symptoms are :

- Intermittent and occur in response to various potential stimuli include: allergens, infections, dusts, fumes, and exercise.
- Have a diurnal variation, worsening in the evening and early morning.
- Variability of symptoms (both improvement and worsening of symptoms over time) is a key diagnostic feature of asthma.
- Symptoms often occur with or worsen with viral infection.

Common symptoms :

- Cough
- Wheezing
- Chest tightness
- Shortness of breath

Physical examination

- Wheezing
- Reduced airflow
- Prolonged expiratory phase
- Patients may also have a completely **normal** respiratory exam, particularly when they are symptom-free.

History taking should include also :

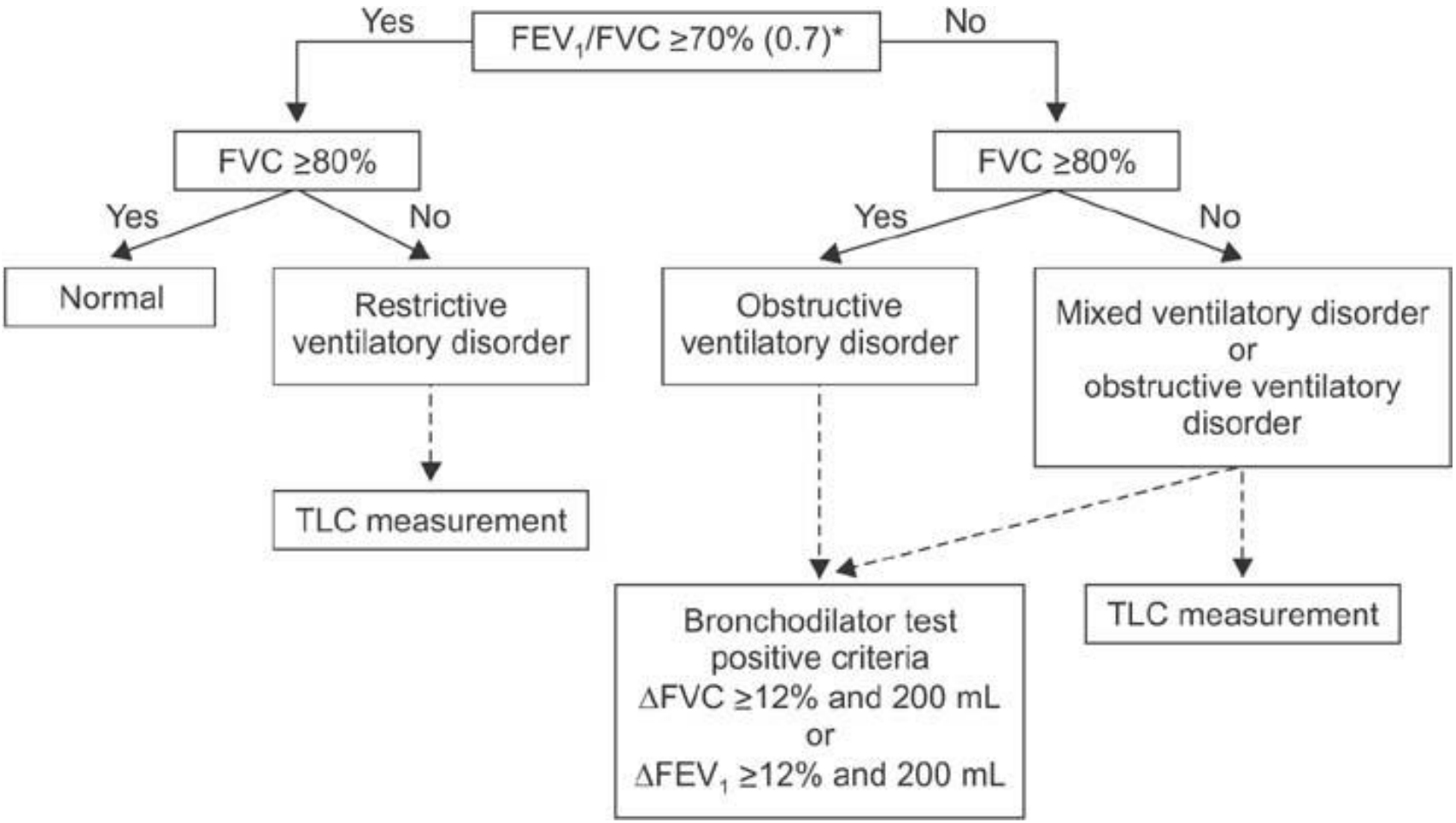
- Smoking history
- Pets exposure
- Work place exposure to dust, fumes, or particulate matter known to cause bronchial hyperreactivity.
- Personal or family history of atopy or allergic sinus disease.
- Presence of nasal polyps, sensitivity to aspirin, and wheezing is known as the "asthmatic triad“

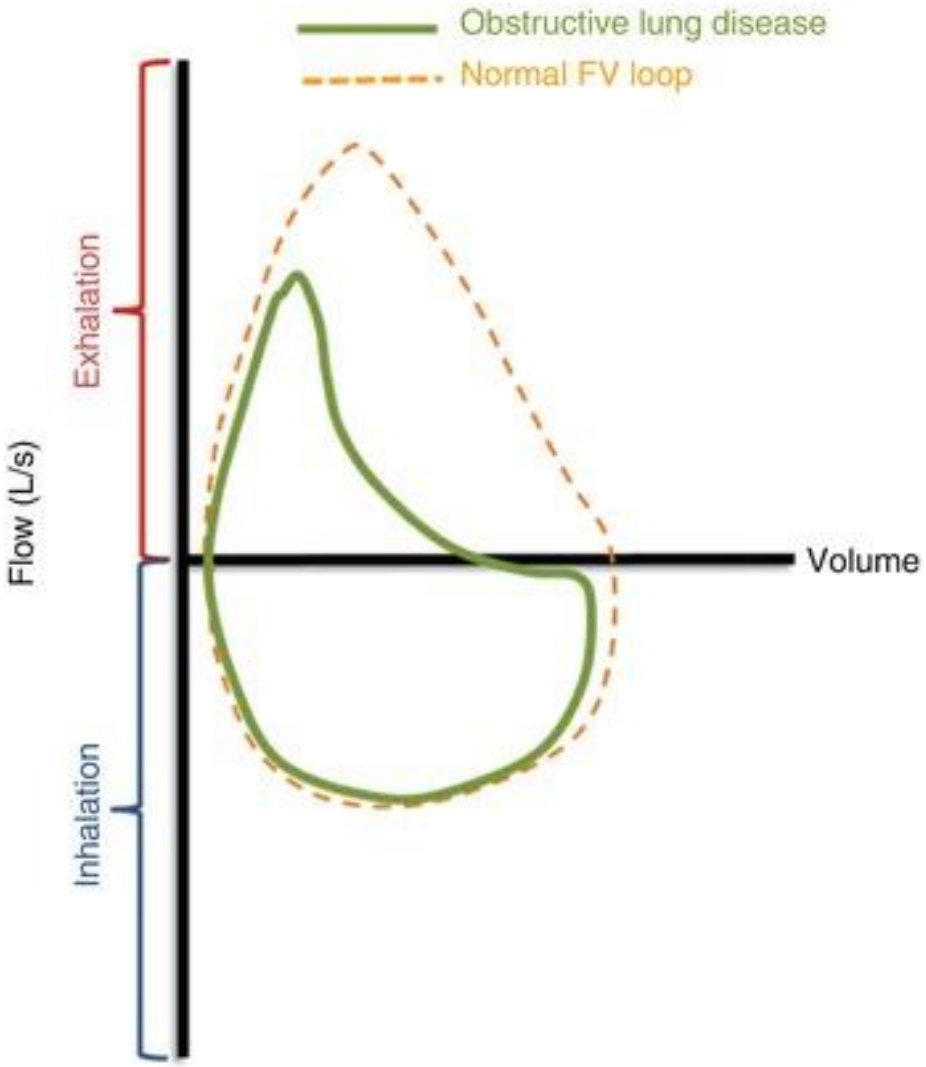
Diagnosis

Confirmation of reversible airflow obstruction with bronchodilators is a cornerstone of asthma diagnosis and can be assessed by spirometry or by serial measurement of peak expiratory flow rates.

Diagnosis of asthma in low- and middle-income countries

- Asthma is often under-diagnosed
  - Differential diagnosis often includes other endemic respiratory disease, e.g. tuberculosis, HIV/AIDS-associated lung disease, parasitic or fungal lung diseases
  - A syndromic approach is often used for diagnosis
- GINA recommends confirmation of asthma diagnosis with lung function testing, whenever possible, before commencing long-term treatment
  - **Spirometry-based testing if available**
  - **Peak expiratory flow (PEF)**
    - **>20% increase in PEF, 15 minutes after 2 puffs of salbutamol = asthma likely (WHO-PEN)**
    - **Improvement of symptoms and PEF after 4 weeks ICS treatment**
- Access to affordable diagnostic equipment and skills training needs to be substantially scaled up in low- and middle-income countries


FEV1/FVC ≥70% (0.7)*
Yes
No
FVC ≥80%
FVC ≥80%
Yes
No
Yes
No
Normal
Restrictive ventilatory disorder
Obstructive ventilatory disorder
Mixed ventilatory disorder or obstructive ventilatory disorder
TLC measurement
Bronchodilator test positive criteria
ΔFVC ≥12% and 200 mL
or
ΔFEV1 ≥12% and 200 mL
TLC measurement


Obstructive lung disease
Normal FV loop
Exhalation
Flow (L/s)
Volume
Inhalation

Bronchodilator reversibility :

Significant bronchodilator reversibility is defined by: FEV1 increases by > 200 mL **AND** >12% of the baseline value.

It is assessed by the administration of a short acting beta 2 agonist and repeating spirometry after around 10 minutes

Bronchial challenge test

- This is usually performed with inhaled methacholine, although other stimuli (exercise, mannitol) have been validated.
- Positive test : if there is 20% decrease in FEV1 from the baseline
- A negative test excludes asthma
- A positive test requires clinical correlation and may require additional testing.

Asthma Syndromes

1) Allergic Asthma
2) Cough-Variant Asthma
3) Exercise-Induced Bronchospasm
4) Occupational Asthma
5) Reactive Airways Dysfunction Syndrome
6) Aspirin-Exacerbated Respiratory Disease
7) Allergic Bronchopulmonary Aspergillosis

Common Comorbidities

Comorbidities in asthma are common and should be considered and actively managed to reduce symptoms and potentially improve asthma control.

- Gastroesophageal Reflux Disease
- Sinus Disease
- Obstructive Sleep Apnea
- Vocal Cord Dysfunction
- Obesity

Management of Chronic Asthma

The goals of longitudinal asthma management are :

1) Control chronic asthma symptoms
2) Prevent acute exacerbations
3) Minimize risks of developing fixed airway obstruction

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☐			

B. Risk factors for poor asthma outcomes

Assess risk factors at diagnosis and periodically, particularly for patients experiencing exacerbations.

Measure FEV_1 at start of treatment, after 3–6 months of controller treatment to record the patient's personal best lung function, then periodically for ongoing risk assessment.

Having uncontrolled asthma symptoms is an important risk factor for exacerbations.[86]

Additional **potentially modifiable risk factors for flare-ups (exacerbations)**, even in patients with few symptoms† include:

- ***Medications***: high SABA use (associated with increased risk of exacerbations[123,87] and mortality particularly if ≥1 x 200-dose canister per month[88,89]); inadequate ICS: not prescribed ICS; poor adherence;[90] incorrect inhaler technique[91]
- ***Other medical conditions***: obesity;[92,93] chronic rhinosinusitis;[93] GERD;[93] confirmed food allergy;[94] pregnancy[95]
- ***Exposures***: smoking;[96] allergen exposure if sensitized;[96] air pollution[97-99]
- ***Context***: major psychological or socioeconomic problems[100]
- ***Lung function***: low FEV_1, especially <60% predicted[96,101]; high BD reversibility[93,102,103]
- ***Other tests*** in patients with Type 2 inflammation: blood eosinophils;[93,104,105] elevated FeNO (in adults with allergic asthma taking ICS)[106]

Having any of these risk factors increases the patient's risk of exacerbations *even if they have few asthma symptoms*

Other major independent risk factors for flare-ups (exacerbations)

- Ever intubated or in intensive care unit for asthma[107]
- ≥1 severe exacerbation in last 12 months[108,109]

Risk factors for developing persistent airflow limitation

- History: preterm birth, low birth weight and greater infant weight gain;[110] chronic mucus hypersecretion[111,112]
- Medications: lack of ICS treatment in patients who had a severe exacerbation[113]
- Exposures: tobacco smoke;[111] noxious chemicals; occupational exposures[40]
- Investigations: low initial FEV_1;[112] sputum or blood eosinophilia[112]

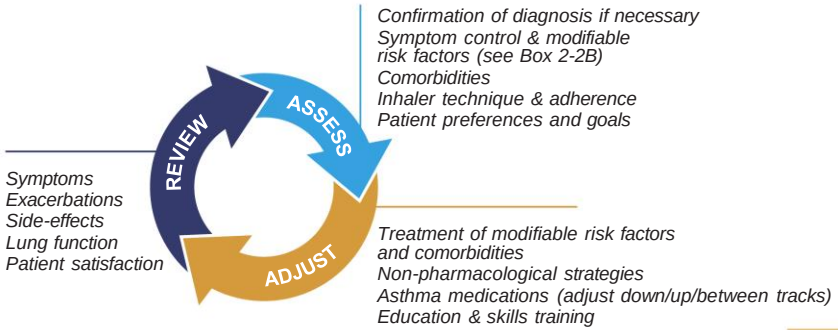
Risk factors for medication side-effects

- Systemic: frequent OCS; long-term, high dose and/or potent ICS; also taking P450 inhibitors[114]
- Local: high dose or potent ICS;[114,115] poor inhaler technique[116]

BD: bronchodilator; FEV_1: forced expiratory volume in 1 second; ICS: inhaled corticosteroid; OCS: oral corticosteroid; P450 inhibitors: cytochrome P450 inhibitors such as ritonavir, ketoconazole, itraconazole; SABA: short-acting beta$_2$-agonist. *Based on SABA (as-needed ICS-formoterol reliever not included); excludes reliever taken before exercise. For children 6–11 years, also refer to Box 2-3, p.37. See Box 3-8, p.74 for specific risk reduction strategies. †'Independent' risk factors are those that are significant after adjustment for the level of symptom control.

Adults & adolescents 12+ years

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



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	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP
RELIEVER: As-needed low-dose ICS-formoterol			

See GINA severe asthma guide

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	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP
RELIEVER: As-needed short-acting beta$_2$-agonist				

Other controller options for either track (limited indications, or less evidence for efficacy or safety)	*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*

GINA 2022, Box 3-5A

Adults & adolescents 12+ years

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Assess, Adjust, Review
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RELIEVER: As-needed low-dose ICS-formoterol

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RELIEVER: As-needed short-acting beta$_2$-agonist

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GINA 2022, Box 3-5A, 2/4

Adults & adolescents 12+ years

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

Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2B)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks)
Education & skills training

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	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: As-needed short-acting beta$_2$-agonist

Other controller options for either track (limited indications, or less evidence for efficacy or safety)

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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

GINA 2022, Box 3-5A, 3/4

Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
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RELIEVER: As-needed low-dose ICS-formoterol

See GINA severe asthma guide

CONTROLLER and **ALTERNATIVE RELIEVER**

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
	Low dose	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE,

Other controller options for either track (limited indications, or less evidence for efficacy or safety)		*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*


Symbicort
budesonide/
formoterol
Turbuhaler
160/4.5 µg/dose
120 doses
Inhalation powder
160 4.5
AstraZeneca
Symbicort
budesonide/
formoterol
160 4.5

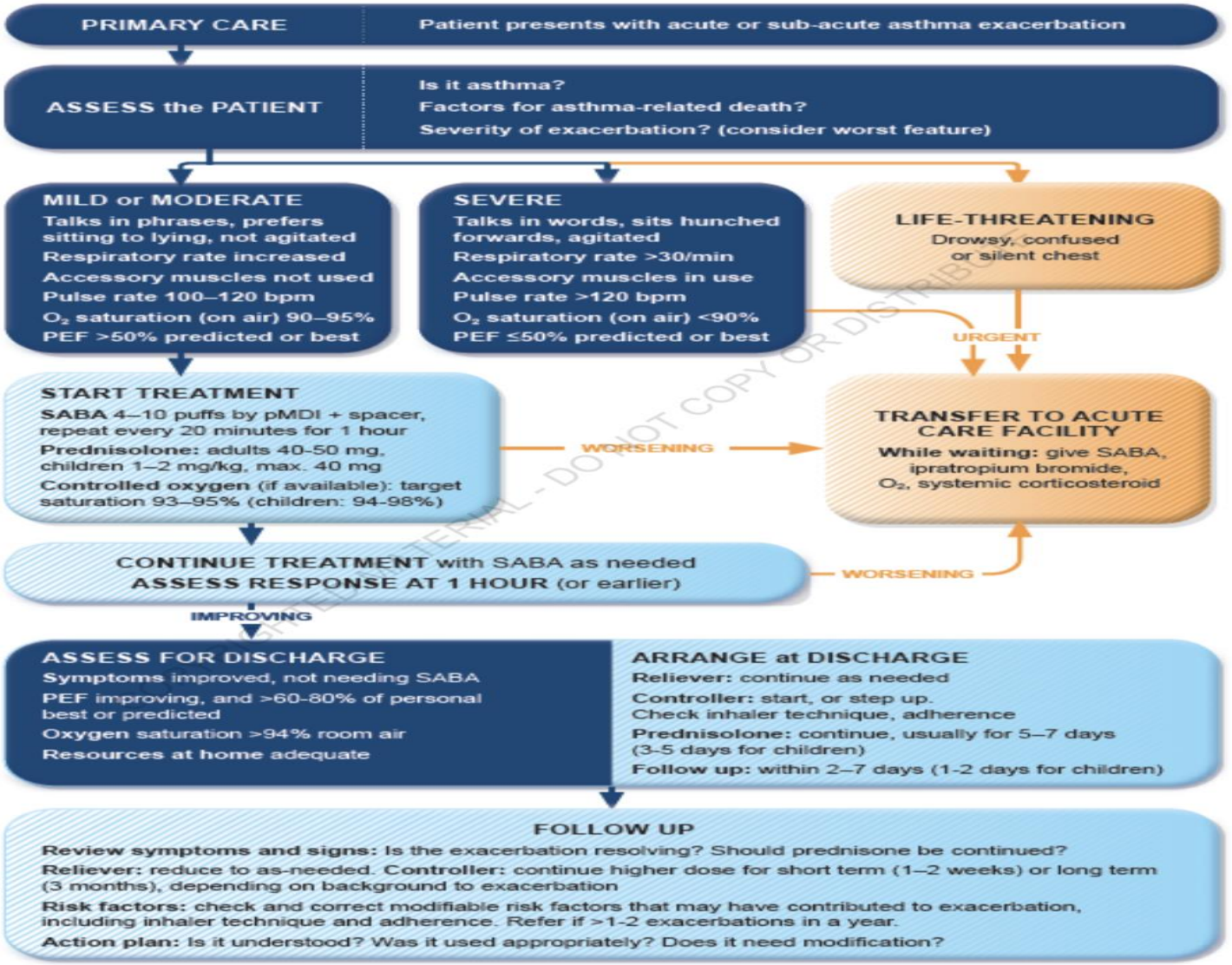
Management of Asthma Exacerbations

- Asthma exacerbation refers to an acute worsening in symptoms or lung function from baseline that necessitates a step-up in therapy.

- All asthma patients should have a written asthma management plan that helps them to recognize the symptoms of an exacerbation and begin self-treatment.

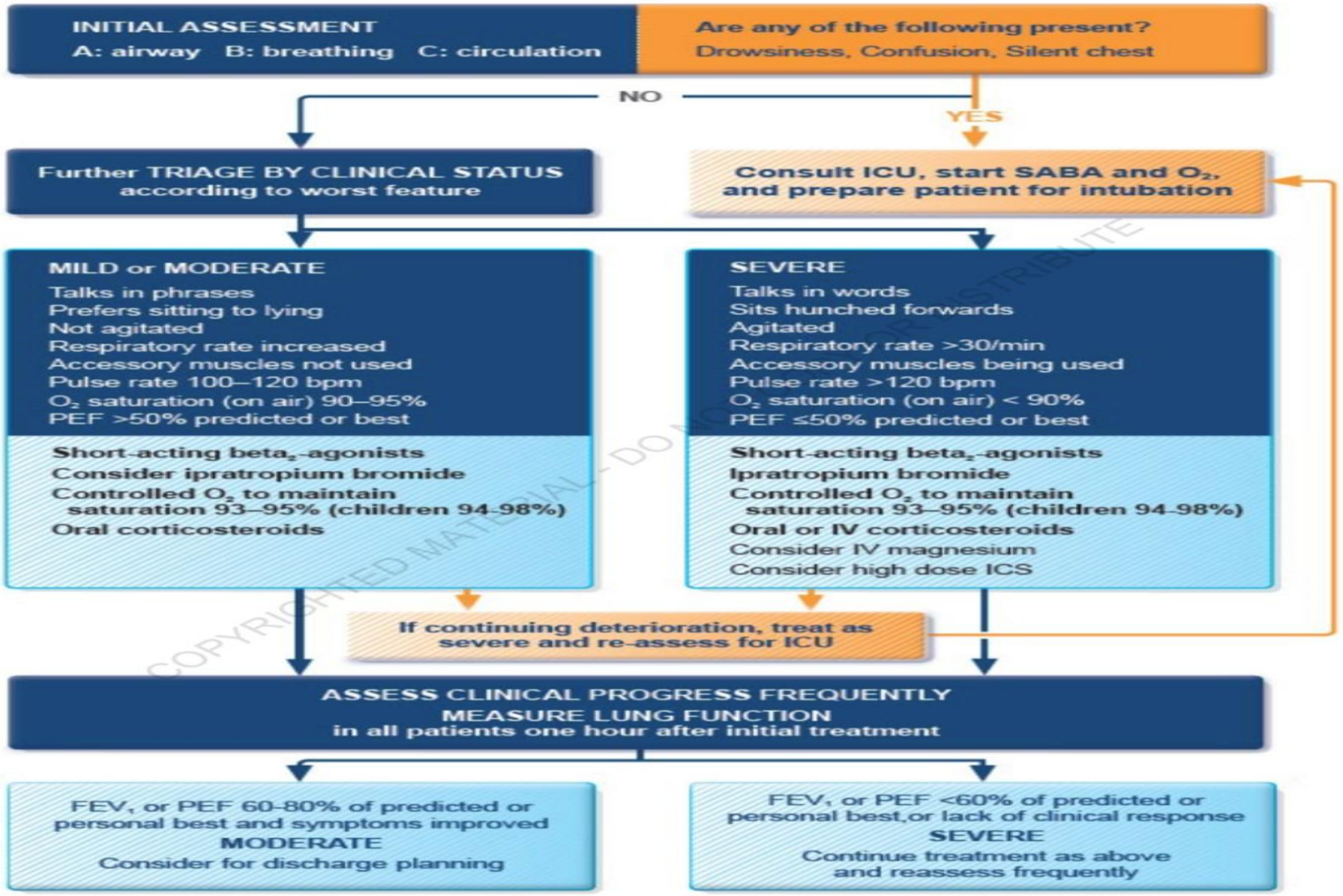
- Clinicians should screen for patient factors that contribute to an increased risk of death from asthma and counsel patients appropriately.

Box 4-3. Management of asthma exacerbations in primary care (adults, adolescents, children 6–11 y



O_2: oxygen; PEF: peak expiratory flow; SABA: short-acting beta$_2$-agonist (doses are for salbutamol).

ox 4-4. Management of asthma exacerbations in acute care facility, e.g. emergency department



: inhaled corticosteroids; ICU: intensive care unit; IV: intravenous; O_2: oxygen; PEF: peak expiratory flow; FEV_1: forced expiratory volume in

anagement of worsening asthma and exacerbations

Box 4-1. Factors that increase the risk of asthma-related death

- A history of near-fatal asthma requiring intubation and mechanical ventilation[557]
- Hospitalization[557,558] or emergency care visit for asthma in the past year
- Currently using or having recently stopped using oral corticosteroids (a marker of event severity)[557]
- Not currently using inhaled corticosteroids[90,557]
- Over-use of SABAs, especially use of more than one canister of salbutamol (or equivalent) monthly[89,107,559]
- Poor adherence with ICS-containing medications and/or poor adherence with (or lack of) a written asthma action plan[100]
- A history of psychiatric disease or psychosocial problems[100]
- Food allergy in a patient with asthma[452,560]
- Several comorbidities including pneumonia, diabetes and arrhythmias were independently associated with an increased risk of death after hospitalization for an asthma exacerbation.[[558]

Asthma in Pregnancy

- Pregnant patients should be advised that the advantages of treatment are significantly greater than the potential risk to the fetus from asthma therapies or exacerbations.

- Pregnancy can affect asthma control, leading to either worsening or improvement, and patients should be closely monitored for signs of exacerbation, which occurs most frequently during the second trimester.

- Inhaled glucocorticoids, oral glucocorticoids, SABAs, leukotriene-receptor antagonists (montelukast, zafirlukast), and LABAs have **ALL** been used extensively during pregnancy without data to suggest fetal harm.

THANK YOU!