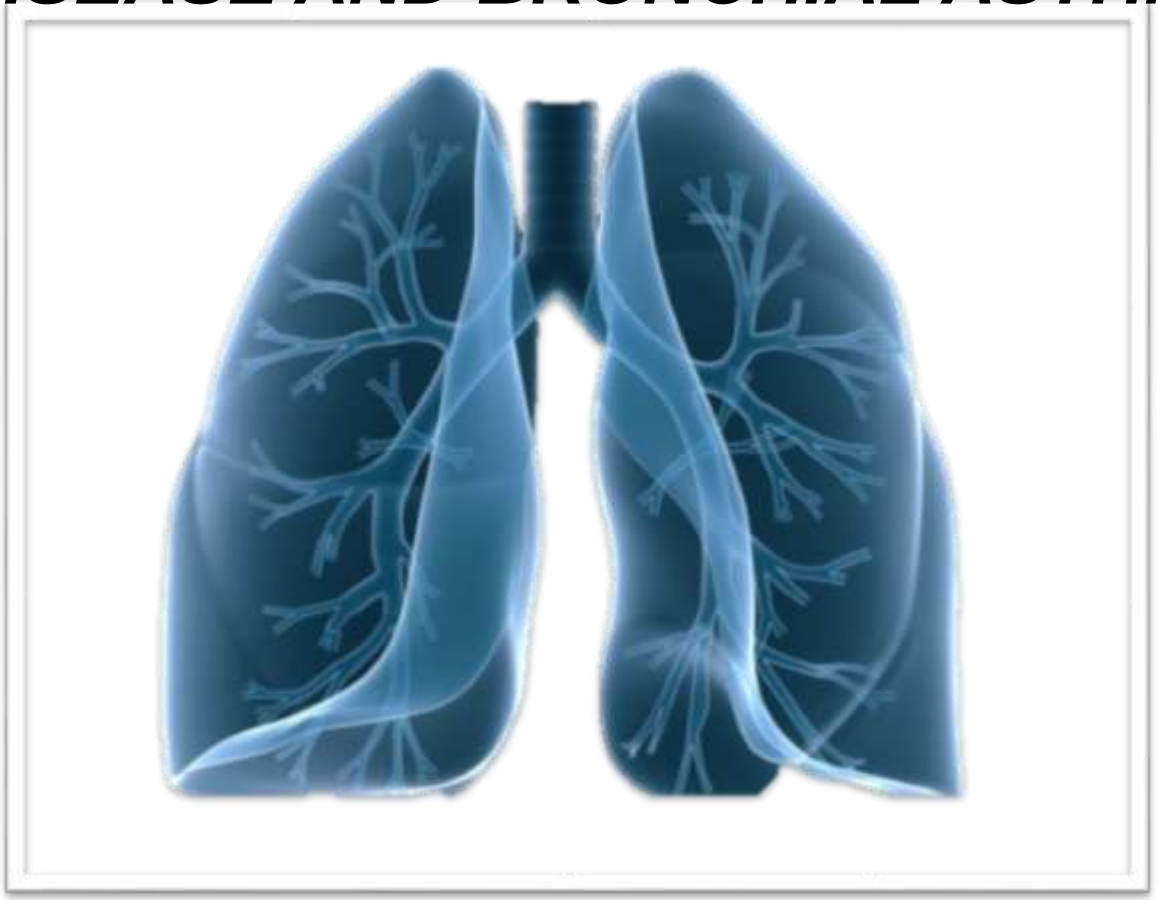
CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND BRONCHIAL ASTHMA



Lecturer: ass. professor Khyzhnyak O.V.

2024-2025

Definition of COPD

- COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases.

Mechanisms Underlying Airflow Limitation in COPD

Small Airways Disease

- Airway inflammation
- Airway fibrosis, luminal plugs
- Increased airway resistance

Parenchymal Destruction

- Loss of alveolar attachments
- Decrease of elastic recoil

AIRFLOW LIMITATION

2023

Proposed Taxonomy (Etiotypes) for COPD

Figure 1.2

Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	• Exposure to tobacco smoke, including *in utero* or via passive smoking • Vaping or e-cigarette use • Cannabis
Biomass and pollution exposure COPD (COPD-P)	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards
COPD due to infections (COPD-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD
COPD & asthma (COPD-A)	Particularly childhood asthma
COPD of unknown cause (COPD-U)	

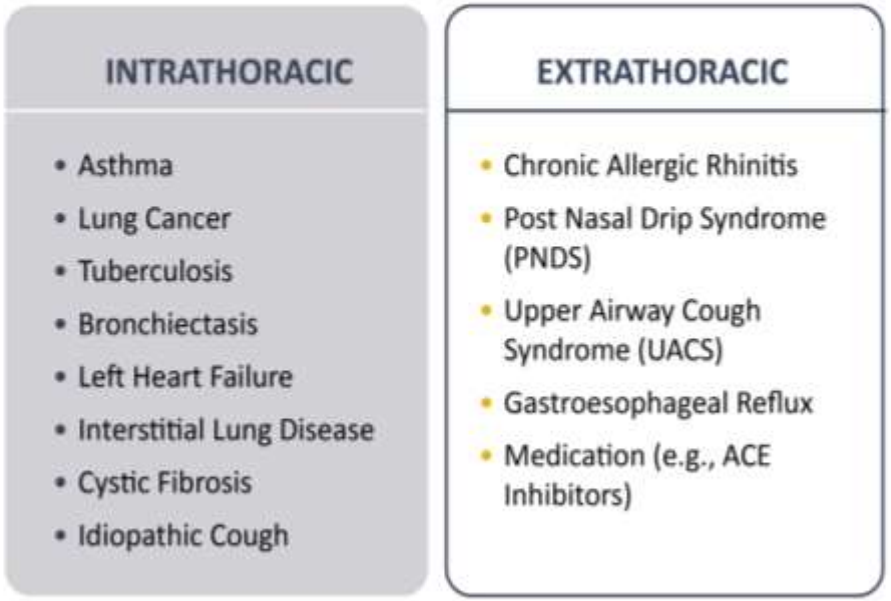
*Adapted from Celli et al. (2022) and Stolz et al. (2022)

Table 2.1. Key indicators for considering a diagnosis of COPD	
Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD. Spirometry is required to establish a diagnosis of COPD.	
Dyspnea that is:	Progressive over time. Characteristically worse with exercise. Persistent.
Chronic cough:	May be intermittent and may be unproductive. Recurrent wheeze.
Chronic sputum production:	Any pattern of chronic sputum production may indicate COPD.
Recurrent lower respiratory tract infections	
History of risk factors:	Host factors (such as genetic factors, congenital/developmental abnormalities etc.). Tobacco smoke (including popular local preparations). Smoke from home cooking and heating fuels. Occupational dusts, vapors, fumes, gases and other chemicals.
Family history of COPD and/or childhood factors:	For example low birthweight, childhood respiratory infections etc.

2023

Other Causes of Chronic Cough

Figure 2.2



© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Diagnosis of COPD

SYMPTOMS

cough

sputum

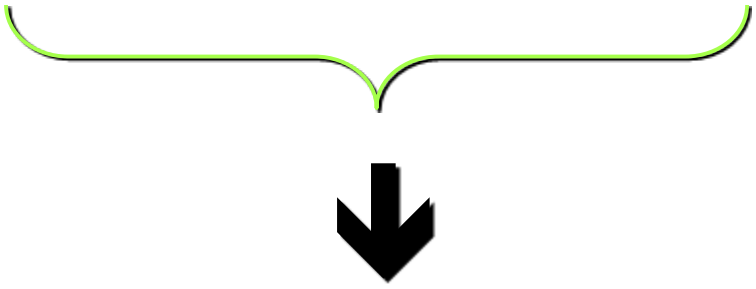
dyspnea

EXPOSURE TO RISK FACTORS

tobacco

occupation

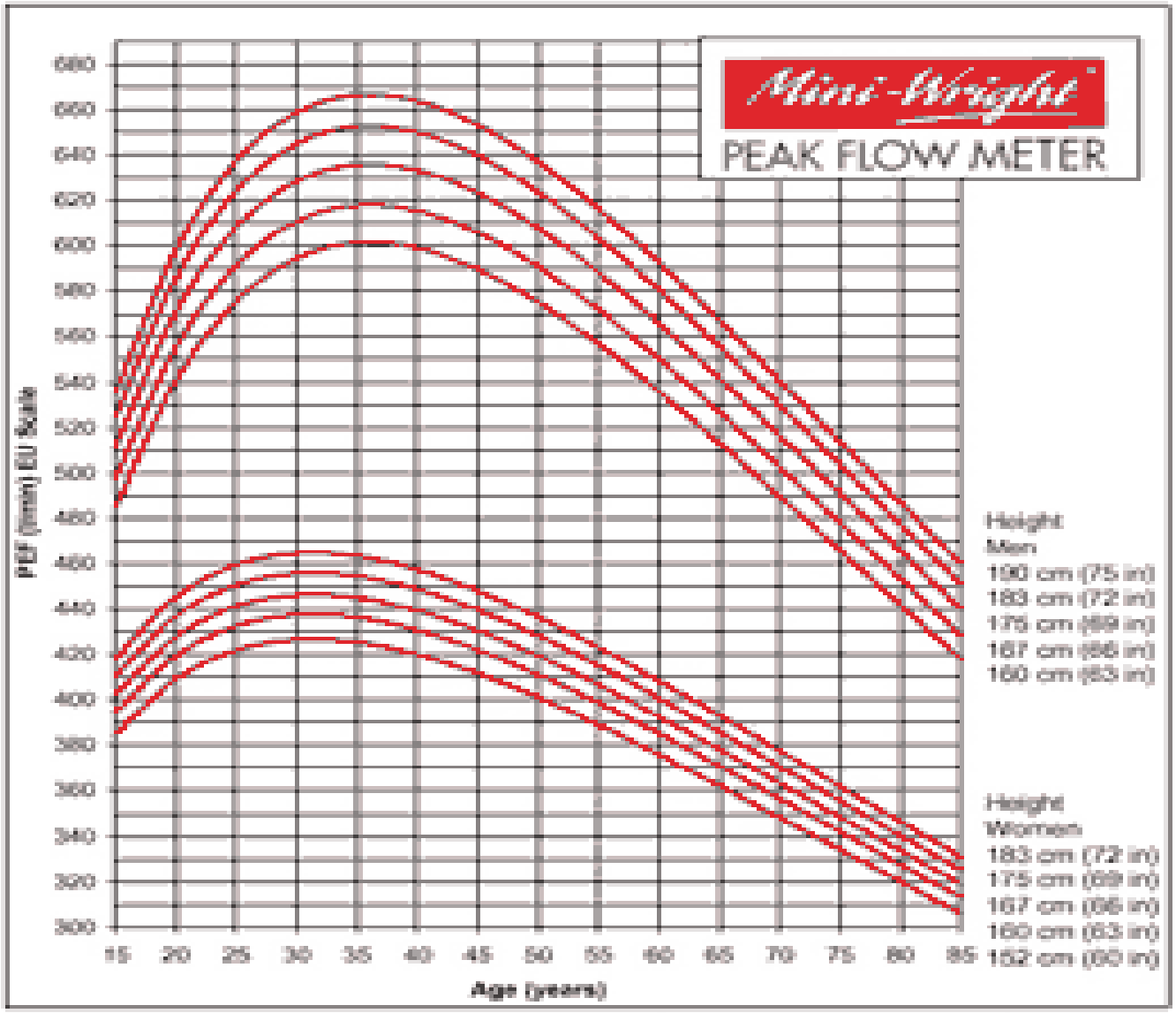
indoor/outdoor pollution



SPIROMETRY

PEAK EXPIRATORY FLOW RATE - NORMAL VALUES

For use with EU/EN13826 scale PEF meters only



Adapted by Clement Clarke for use with EN13826 / EU scale peak flow meters
from Nunn AJ Gregg I. Br Med J 1989;298;1068-70

410 ml FEV1 normal
310 ml
76% from predicted
<80%
320 ml
320-310/310 X 100%=3%
<12% - irreversible
>12% -reversible (+bronchodilatator test)

Figure 2.2A. Spirometry - Normal Trace

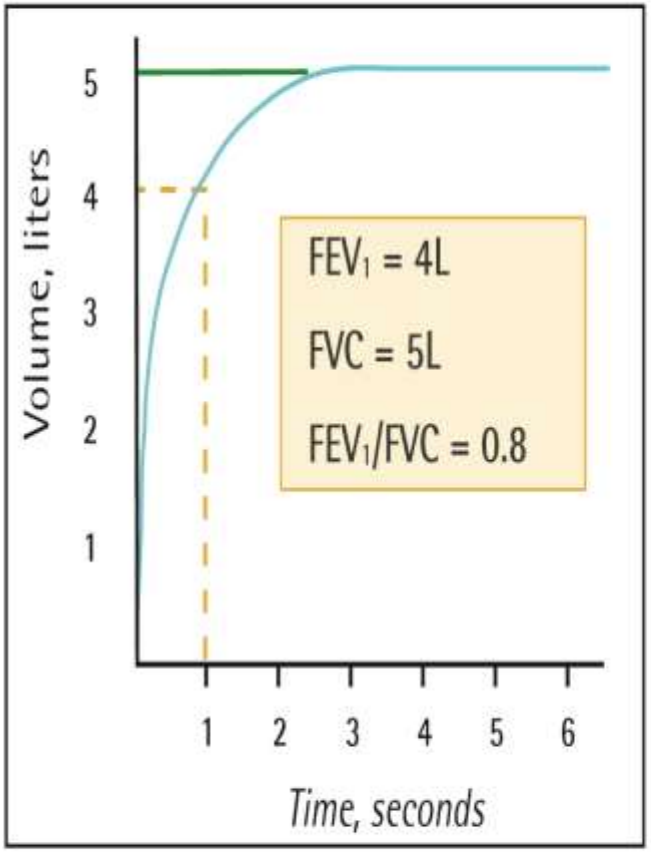
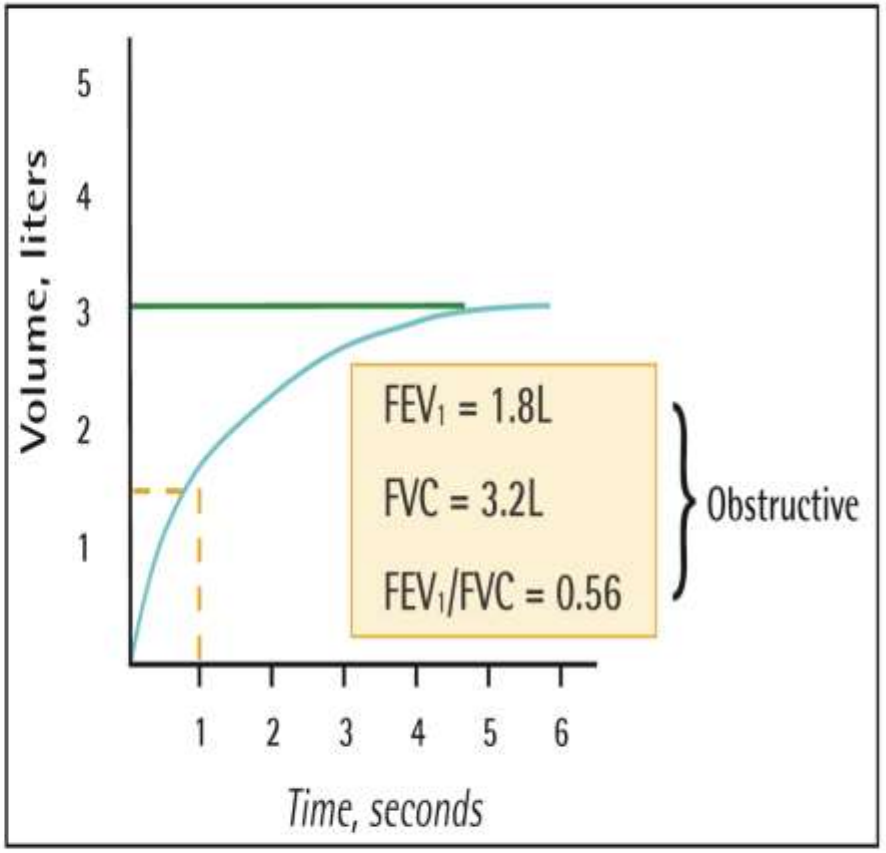


Figure 2.2B. Spirometry - Obstructive Disease



FVC =

FEV1 =

Diagnosis and Assessment: Key Points

- A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and a history of exposure to risk factors for the disease.
- Spirometry is *required* to make the diagnosis; the presence of a post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of persistent airflow limitation and thus of COPD.

Assessment of Airflow Limitation: Spirometry

- Spirometry should be performed after the administration of an adequate dose of a short-acting inhaled bronchodilator to minimize variability.
- A post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of airflow limitation.
- Where possible, values should be compared to age-related normal values to avoid overdiagnosis of COPD in the elderly.

revised GOLD classification

- Looks at 3 things:
- Symptoms
- FEV_1
- History of exacerbations

Assessment of COPD

- Assess symptoms

COPD Assessment Test (CAT)

or

Clinical COPD Questionnaire (CCQ)

or

mMRC Breathlessness scale

Assessment of Symptoms

COPD Assessment Test (CAT): An 8-item measure of health status impairment in COPD (http://catestonline.org).

Clinical COPD Questionnaire (CCQ): Self-administered questionnaire developed to measure clinical control in patients with COPD (http://www.ccq.nl).

CAT™ Assessment

Figure 2.9

2023

For each item below, place a mark (x) in the box that best describes you currently.
Be sure to only select one response for each question.

EXAMPLE: I am very happy	0 X 2 3 4 5	I am very sad	Score
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

TOTAL SCORE:

2023

Modified MRC Dyspnea Scale

Figure 2.8

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0	mMRC Grade 1	mMRC Grade 2	mMRC Grade 3	mMRC Grade 4
I only get breathless with strenuous exercise	I get short of breath when hurrying on the level or walking up a slight hill	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level	I stop for breath after walking about 100 meters or after a few minutes on the level	I am too breathless to leave the house or I am breathless when dressing or undressing
☐	☐	☐	☐	☐

Reference: ATS (1982) Am Rev Respir Dis. Nov;126(5):952-6.

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

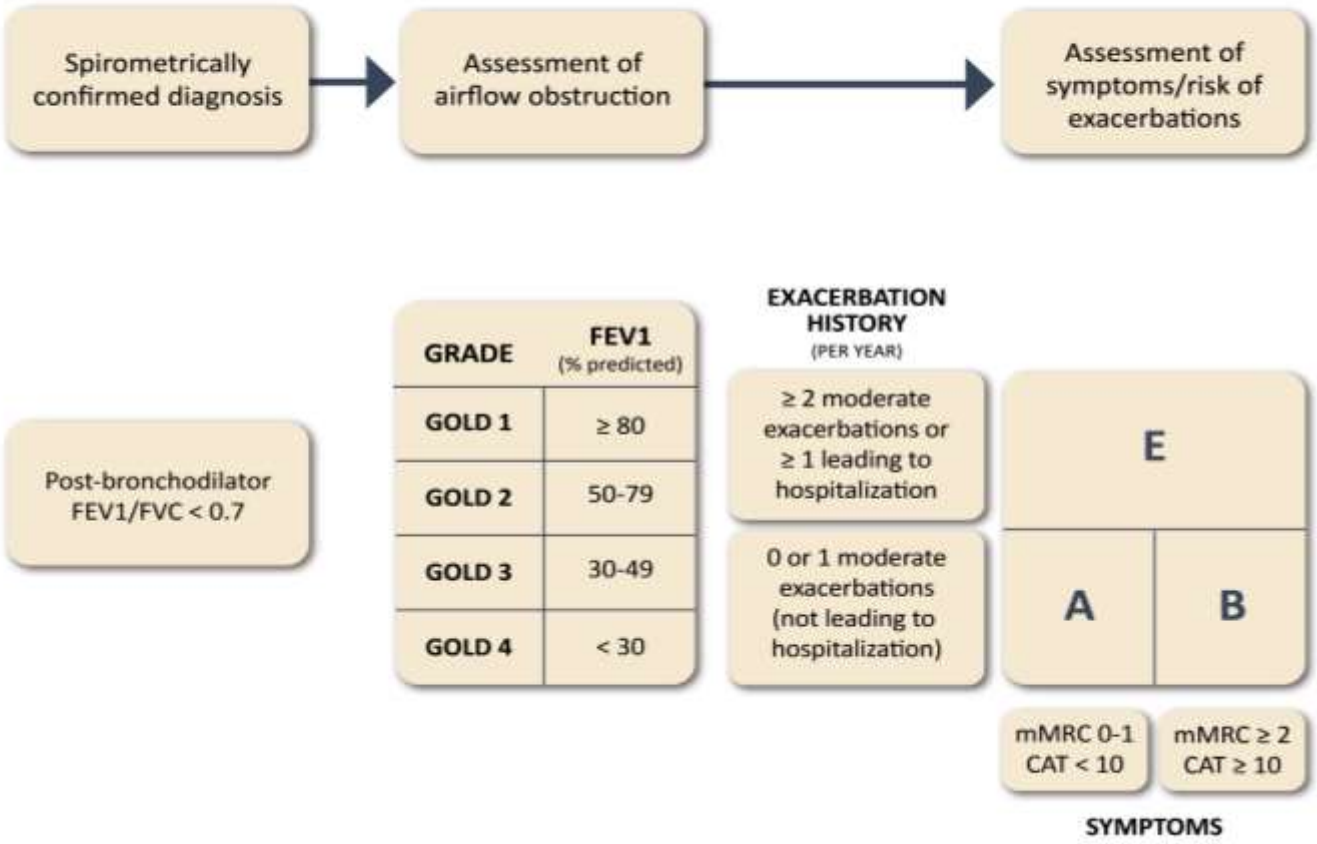
Grading severity of airflow

In patients with FEV_1/FVC <0.70		
GOLD 1	Mild	FEV_1>80%
GOLD 2	Moderate	50%<$FEV_{1<80\%}$
GOLD 3	Severe	30%<FEV_1<50%
GOLD 4	Very severe	FEV_1<30%

GOLD ABE Assessment Tool

Figure 2.10

2023



© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Revised 2017 ABCD Criteria

FEV_1	
GOLD 1	≥ 80%
GOLD 2	50-79%
GOLD 3	30-49%
GOLD 4	< 30%

Exacerbation History	mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10
≥ 2 or ≥ 1 requiring hospitalization	C	D
≤ 1 not requiring hospitalization	A	B

CASE

- 74 YO M with COPD p/w SOB x 2 days. At baseline he does not have any physical limitations. His last spirometry three years ago showed mild COPD. He was never given any inhalers besides a rescue inhaler that he seldom uses. He has never been intubated, but gets about 3 exacerbations per year. 2 days ago he required it around the clock after having URI symptoms. He has increased greenish sputum over the past couple of days. He called 911 after waking up SOB. He was given duonebs and placed on CPAP.
- What classification is he?

Grade 0 symptoms,
>2 exacerbations.

So class E

Assess COPD Comorbidities

COPD patients are at increased risk for:

- Cardiovascular diseases
- Osteoporosis
- Respiratory infections
- Anxiety and Depression
- Diabetes
- Lung cancer
- Bronchiectasis

These comorbid conditions may influence mortality and hospitalizations and should be looked for routinely, and treated appropriately.

Differential Diagnosis: COPD and Asthma

COPD

- Onset in mid-life
- Symptoms slowly progressive
- Long smoking history

ASTHMA

- Onset early in life (often childhood)
- Symptoms vary from day to day
- Symptoms worse at night/early morning
- Allergy, rhinitis, and/or eczema also present
- Family history of asthma

Additional Investigations

Chest X-ray: Seldom diagnostic but valuable to exclude alternative diagnoses and establish presence of significant comorbidities.

Lung Volumes and Diffusing Capacity: Help to characterize severity, but not essential to patient management.

Oximetry and Arterial Blood Gases: Pulse oximetry can be used to evaluate a patient's oxygen saturation and need for supplemental oxygen therapy.

Alpha-1 Antitrypsin Deficiency Screening: Perform when COPD develops in patients of Caucasian descent under 45 years or with a strong family history of COPD.

Use of CT in Stable COPD

Figure 2.11

2023

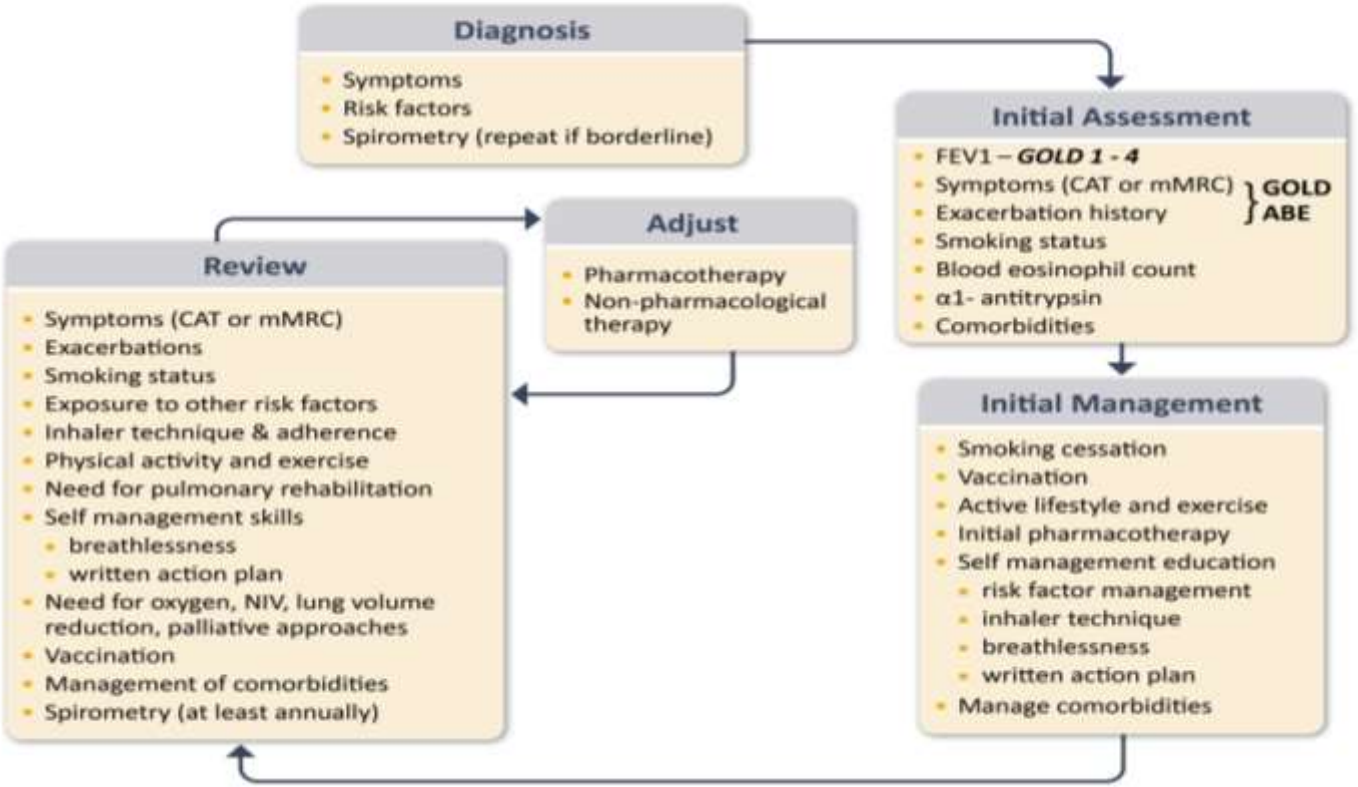
Differential Diagnosis	• Frequent exacerbations with excessive cough with sputum production, raising concern for bronchiectasis or atypical infection • Symptoms out of proportion to disease severity based on lung function testing
Lung Volume Reduction	• Endobronchial valve therapy may be a therapeutic option for patients if they demonstrate postbronchodilator FEV1 between 15% to 45% and evidence of hyperinflation • Lung volume reduction surgery may be a therapeutic option for patients with hyperinflation, severe upper lobe predominant emphysema and low exercise capacity after pulmonary rehabilitation
Lung Cancer Screening	• Annual low-dose CT scan is recommended for lung cancer screening in patients with COPD due to smoking according to recommendations for the general population

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Management of COPD

Figure 3.2

2023



© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Initial Pharmacological Treatment

Figure 3.7

*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

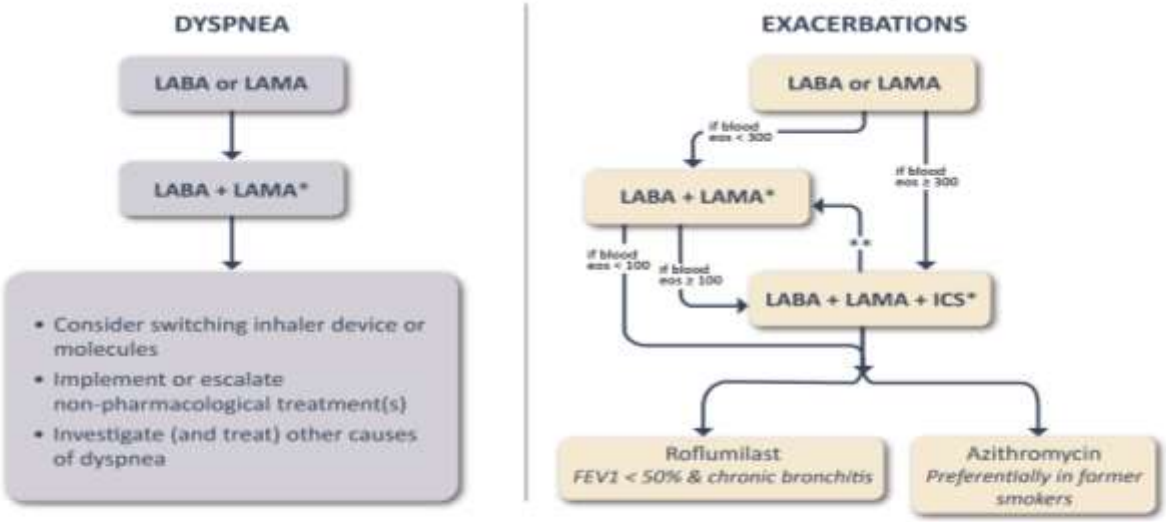
Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Follow-up Pharmacological Treatment

Figure 3.9

1. IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.
2. IF NOT:
   - Check adherence, inhaler technique and possible interfering comorbidities
   - Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - Place patient in box corresponding to current treatment & follow indications
   - Assess response, adjust and review
   - These recommendations do not depend on the ABE assessment at diagnosis



*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

**Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eos ≥ 300 cells/μl de-escalation is more likely to be associated with the development of exacerbations

Exacerbations refers to the number of exacerbations per year

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Table 1: Guide to addition of therapies*

Red boxes with crosses indicate classes of therapies that **should not be used together.*

SABA	• Salbutamol (Ventolin™, Airomir™, Asmol™) • Terbutaline (Bricanyl™)	
SAMA	• Ipratropium bromide (Atrovent™)	
LAMA	• Tiotropium bromide (Spiriva™) • Glycopyrronium bromide (Seebri™)	• Aclidinium bromide (Bretaris™) • Umeclidinium (Incruse™)
LABA	• Salmeterol (Serevent™) • Eformoterol (Oxis™, Foradile™)	• Indacaterol (Onbrez™)
LABA/ LAMA	• Indacaterol/Glycopyrronium bromide (Ultibro™)	• Umeclidinium/Vilanterol (Anoro™)
ICS/ LABA	• Fluticasone propionate/Salmeterol (Seretide™) • Budesonide/Eformoterol (Symbicort™)	• Fluticasone furoate/Vilanterol (Breo™)

Relievers

Spacers are recommended to be used with puffers

Ventolin® Inhaler

Asmol® Inhaler

Airomir™ Inhaler

Airomir™ Autohaler®

Bricanyl® Turbuhaler® (not used with spacer)

Atrovent® Metered Aerosol

Maintenance

ICS (For patients with COPD and Asthma)

Flixotide® Inhaler

Flixotide® Accuhaler®

QVAR® Inhaler

Pulmicort® Turbuhaler®

Alvesco® Inhaler

LAMA

Spiriva® HandiHaler®

Seebri® Breezhaler®

Bretaris® Genuair®

Incruse® Ellipta®

LAMA/LABA

Ultibro® Breezhaler®

Anoro® Ellipta®

LABA

Onbrez® Breezhaler®

Foradile® Aerolizer®

Oxis® Turbuhaler®

Serevent® Accuhaler®

ICS/LABA

Symbicort® Turbuhaler®

Symbicort® Rapihaler™

Seretide® Accuhaler®

Seretide® MDI

Breo® Ellipta®

Flare Up Medicines

1. Antibiotics
2. Oral steroids (Prednisone, Prednisolone)

Notes: • *Handihaler, Breezhaler and Aerolizer devices require a capsule to be loaded into the device. All other devices are preloaded.*
• *LABA monotherapy unsuitable for patients with Asthma or Asthma-COPD Overlap.*

Long-Acting Bronchodilators

• LAMAs

- Block acetylcholine-mediated bronchoconstriction (via M_3 receptors)
  - **Tiotropium**
  - **Aclidinium**
  - **Glycopyrronium (glycopyrrolate)**
  - **Umeclidinium**

• LABAs

- Direct relaxant activity on airway smooth muscle (via β_2 adrenoceptors)
  - **Formoterol**
  - **Salmeterol**
  - **Indacaterol**
  - **Oldaterol**
  - **Vilanterol**

LAMA inhalers for COPD

LAMA

DPI HandiHaler/ SMI Respimat		**Spiriva® (tiotropium)**
DPI Breezhaler		**Seebri® (glycopyrronium)**
DPI Genuair		**Eklira® (aclidinium)**
DPI Ellipta		**Incruse® (umeclidinium)**

LABA

DPI Diskus		**Serevent® (salmeterol)**
DPI Aerolizer		**Foradil® (formoterol)**
DPI Breezhaler		**Onbrez® (indacaterol)**
SMI Respimat		**Striverdi® (Olodaterol)**

Combination LABA/LAMA inhalers for COPD

Fixed-dose combination LABA/LAMA

DPI Ellipta  **Anoro®**
(vilanterol/umeclidinium)

DPI Breezhaler  **Ultibro®**
(indacaterol/glycopyrronium)

SMI Respimat  **Inspiolto®**
(olodaterol/tiotropium)

DPI Genuair  **Duaklir®**
(formoterol/aclidinium)

ICS/LABA

DPI Diskus

Advair®
(Fluticasone/salmeterol)

DPI Turbuhaler

Symbicort®
(Budesonide/formoterol)

DPI Ellipta

Relvar®
(Fluticasone/vilanterol)

Oxygen Therapy and Ventilatory Support in Stable COPD

Figure 3.14

2024 Teaching Slide Set

Oxygen Therapy	• The long-term administration of oxygen increases survival in patients with severe chronic resting arterial hypoxemia **(Evidence A)** • In patients with stable COPD and moderate resting or exercise-induced arterial desaturation, prescription of long-term oxygen does not lengthen time to death or first hospitalization or provide sustained benefit in health status, lung function and 6-minute walk distance **(Evidence A)** • Resting oxygenation at sea level does not exclude the development of severe hypoxemia when traveling by air **(Evidence C)**
Ventilatory Support	• NPPV may improve hospitalization-free survival in selected patients after recent hospitalization, particularly in those with pronounced daytime persistent hypercapnia ($PaCO_2$ > 53 mmHg) **(Evidence B)** • In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, long-term noninvasive ventilation may be considered **(Evidence B)**

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

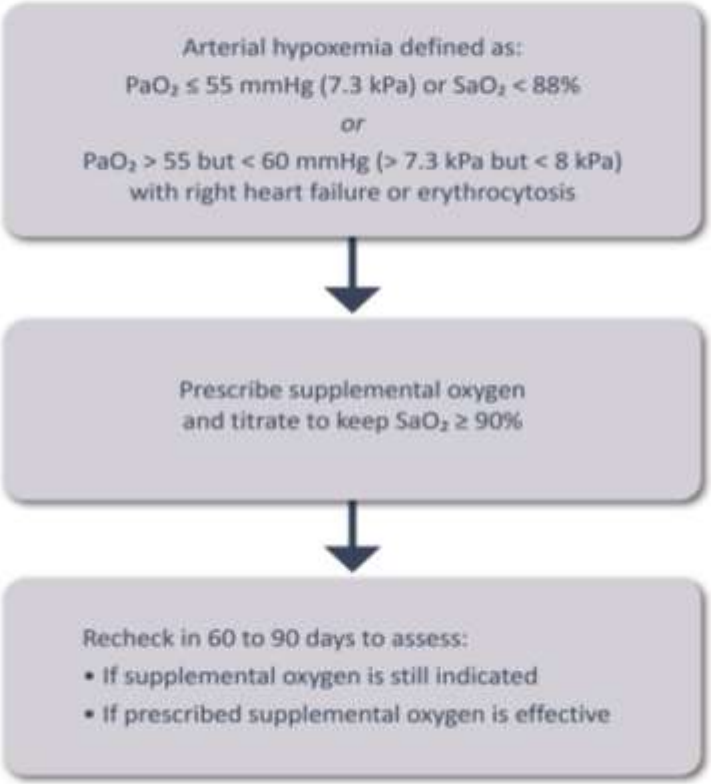
Therapeutic Options: Other Treatments

Oxygen Therapy: The long-term administration of oxygen (> 15 hours per day) to patients with chronic respiratory failure has been shown to increase survival in patients with severe, resting hypoxemia.

Ventilatory Support: Combination of noninvasive ventilation (NIV) with long-term oxygen therapy may be of some use in a selected subset of patients, particularly in those with pronounced daytime hypercapnia.

Prescription of Supplemental Oxygen to COPD Patients

Figure 3.15



2024
Teaching
Slide Set

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Factors to Consider when Initiating ICS Treatment

Figure 3.21

2024 Teaching Slide Set

Factors to consider when adding ICS to long-acting bronchodilators:

(note the scenario is different when considering ICS withdrawal)

STRONGLY FAVORS USE	History of hospitalization(s) for exacerbations of COPD[a]
	≥ 2 moderate exacerbations of COPD per year[a]
	Blood eosinophils ≥ 300 cells/μL
	History of, or concomitant asthma
FAVORS USE	1 moderate exacerbation of COPD per year[a]
	Blood eosinophils 100 to < 300 cells/μL
AGAINST USE	Repeated pneumonia events
	Blood eosinophils < 100 cells/μL
	History of mycobacterial infection

[a]despite appropriate long-acting bronchodilator maintenance therapy (see Figures 3.7 & 3.18 for recommendations); [b]note that blood eosinophils should be seen as a continuum; quoted values represent approximate cut-points; eosinophil counts are likely to fluctuate.

Adapted from & reproduced with permission of the © ERS 2019: *European Respiratory Journal 52 (6) 1801219; DOI: 10.1183/13993003.01219-2018 Published 13 December 2018*

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Anti-Inflammatory Therapy in Stable COPD

Figure 3.20

Inhaled Corticosteroids	• Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease **(Evidence A)** • An ICS combined with a LABA is more effective than the individual components in improving lung function and health status and reducing exacerbations in patients with exacerbations and moderate to very severe COPD **(Evidence A)** • We do not encourage the use of a LABA+ICS combination in COPD. If there is an indication for an ICS the combination LABA+LAMA+ICS has been shown to be superior to LABA+ICS and is therefore the preferred choice • Triple inhaled therapy of LABA+LAMA+ICS improves lung function, symptoms and health status, and reduces exacerbations, compared to LABA+ICS, LABA+LAMA or LAMA monotherapy **(Evidence A)**. Recent data suggesta beneficial effect of triple inhaled therapy versus fixed-dose LABA+LAMA combinations on mortality in symptomatic COPD patients with a history of frequent and/or severe exacerbations • If patients with COPD have features of asthma, treatment should always contain an ICS • Independent of ICS use, there is evidence that a blood eosinophil count < 2% increases the risk of pneumonia **(Evidence C)** • Combinations can be given as single or multiple inhaler therapy. Single inhaler therapy may be more convenient and effective than multiple inhalers
Oral Glucocorticoids	• Long-term use of oral glucocorticoids has numerous side effects **(Evidence A)** with no evidence of benefits **(Evidence C)**
PDE4 Inhibitors	• In patients with chronic bronchitis, severe to very severe COPD and a history of exacerbations: • Roflumilast improves lung function and reduces moderate and severe exacerbations **(Evidence A)**
Antibiotics	• Long-term azithromycin and erythromycin therapy reduces exacerbations over one year **(Evidence A)** • Preferentially, but not only in former smokers with exacerbations despite appropriate therapy, azithromycin can be considered **(Evidence B)** • Treatment with azithromycin is associated with an increased incidence of bacterial resistance **(Evidence A)** and hearing test impairments **(Evidence B)**
Mucoregulators and Antioxidant Agents	• Regular treatment with mucolytics such as erdosteine, carbocysteine and NAC reduces the risk of exacerbations in select populations **(Evidence B)** • Antioxidant mucolytics are recommended only in selected patients **(Evidence A)**
Other Anti-Inflammatory Agents	• Statin therapy is not recommended for prevention of exacerbations **(Evidence A)** • Simvastatin does not prevent exacerbations in COPD patients at increased risk of exacerbations and without indications for statin therapy **(Evidence A)**. However, observational studies suggest that statins may have positive effects on some outcomes in patients with COPD who receive them for cardiovascular and metabolic indications **(Evidence C)** • Leukotriene modifiers have not been tested adequately in COPD patients

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Other Pharmacological Treatments

Figure 3.22

Alpha-1 Antitrypsin Augmentation Therapy	• Intravenous augmentation therapy may slow down the progression of emphysema **(Evidence B)**
Antitussives	• There is no conclusive evidence of a beneficial role of antitussives in people with COPD **(Evidence C)**
Vasodilators	• Vasodilators do not improve outcomes and may worsen oxygenation **(Evidence B)**
Opioids	• Low-dose long acting oral and parenteral opioids may be considered for treating dyspnea in COPD patients with severe disease (**Evidence B**)
Pulmonary Hypertension Therapy	• Drugs approved for primary pulmonary hypertension are not recommended for patients with a pulmonary hypertension secondary to COPD (**Evidence B**)

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Overview of Current and Proposed Surgical and Bronchoscopic Interventions for People with COPD

Figure 3.24

Symptoms	Chronic Mucus Production	Exacerbations	Dyspnea
Disorders	• Chronic bronchitis	• Acute and chronic bronchitis • Bulla • Emphysema • Tracheobronchomalcia	• Bulla • Emphysema • Tracheobronchomalcia
Surgical and Bronchoscopic Interventions	• Nitrogen cryospray • Rheoplasty	• Targeted lung denervation	• Giant bullectomy • Large airway stenting • EBV • Coil • Thermal vapor ablation • Lung sealants • LVRS • Lung transplantation

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Manage Exacerbations

An exacerbation of COPD is:

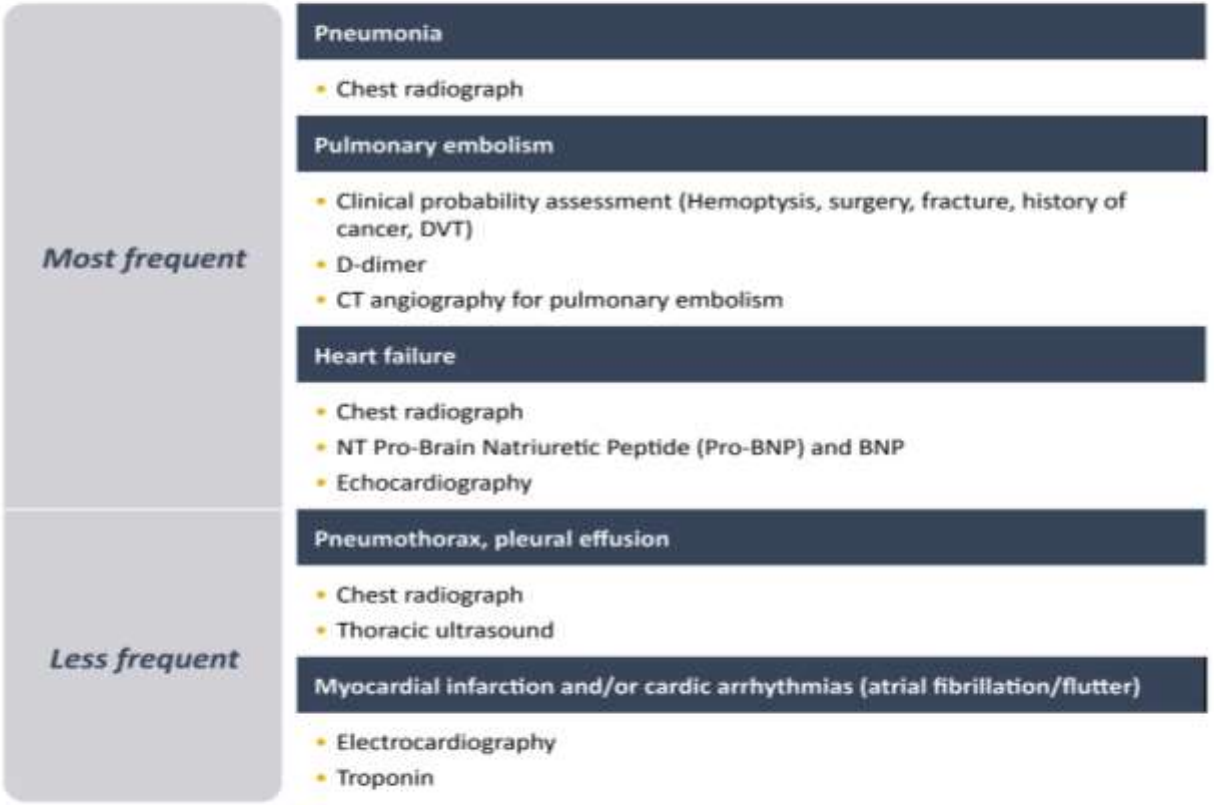
"*an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.*"

Manage Exacerbations: Assessments

Arterial blood gas measurements (in hospital): PaO_2 < 8.0 kPa with or without $PaCO_2$ > 6.7 kPa when breathing room air indicates respiratory failure.
Chest radiographs: useful to exclude alternative diagnoses.
ECG: may aid in the diagnosis of coexisting cardiac problems.
Whole blood count: identify polycythemia, anemia or bleeding.
Purulent sputum during an exacerbation: indication to begin empirical antibiotic treatment.
Biochemical tests: detect electrolyte disturbances, diabetes, and poor nutrition.
Spirometric tests: not recommended during an exacerbation.

Confounders or Contributors to be Considered in Patients Presenting with Suspected COPD Exacerbation

Figure 4.1



© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Diagnosis and Assessment

Figure 4.2

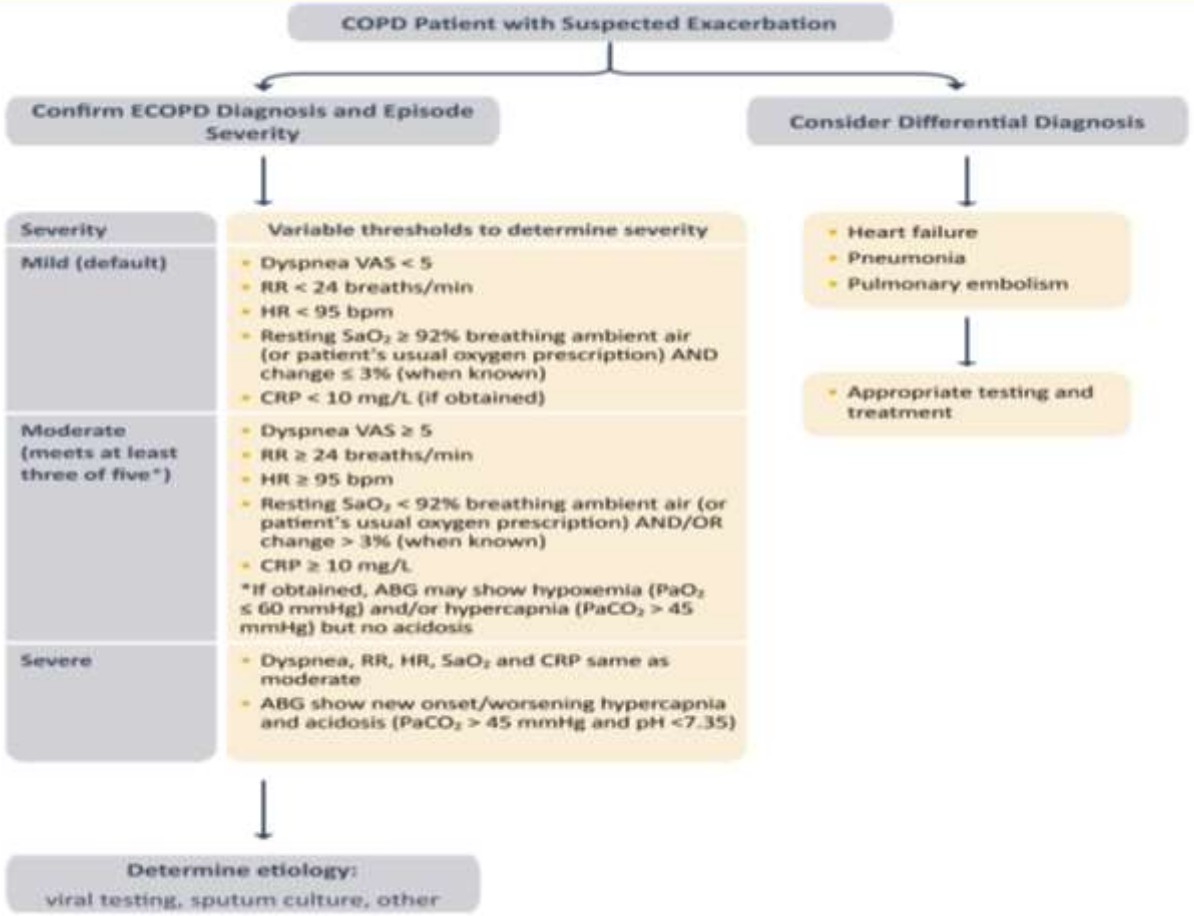
1.	Complete a thorough clinical assessment for evidence of COPD and potential respiratory and non-respiratory concomitant diseases, including consideration of alternative causes for the patient's symptoms and signs: primarily pneumonia, heart failure, and pulmonary embolism.
2.	**Assess:** a. Symptoms, severity of dyspnea that can be determined by using a VAS, and documentation of the presence of cough. b. Signs (tachypnea, tachycardia), sputum volume and color, and respiratory distress (accessory muscle use).
3.	Evaluate severity by using appropriate additional investigations such as pulse oximetry, laboratory assessment, CRP, arterial blood gases.
4.	Establish the cause of the event (viral, bacterial, environmental, other).

Abbreviations: COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; VAS = visual analog scale.

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Classification of the Severity of COPD Exacerbations

Figure 4.3



Adapted from: The ROME Proposal, Celli et al. (2021) Am J Respir Crit Care Med. 204(11): 1251-8.

Abbreviations: VAS visual analog dyspnea scale; RR respiratory rate; HR heart rate; SaO_2 oxygen saturation; CRP C-reactive protein; ABG arterial blood gases; PaO_2 Arterial pressure of oxygen.

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Potential Indications for Hospitalization Assessment*

Figure 4.4

- Severe symptoms such as sudden worsening of resting dyspnea, high respiratory rate, decreased oxygen saturation, confusion, drowsiness
- Acute respiratory failure
- Onset of new physical signs (e.g., cyanosis, peripheral edema)
- Failure of an exacerbation to respond to initial medical management
- Presence of serious comorbidities (e.g., heart failure, newly occurring arrhythmias, etc.)
- Insufficient home support

*Local resources need to be considered

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Indications for Respiratory or Medical Intensive Care Unit Admission*

Figure 4.7

- Severe dyspnea that responds inadequately to initial emergency therapy
- Changes in mental status (confusion, lethargy, coma)
- Persistent or worsening hypoxemia (PaO_2 < 5.3 kPa or < 40 mmHg) and/or severe/worsening respiratory acidosis (pH < 7.25) despite supplemental oxygen and noninvasive ventilation
- Need for invasive mechanical ventilation
- Hemodynamic instability - need for vasopressors

*Local resources need to be considered.

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Manage Exacerbations: Treatment Options

Oxygen: titrate to improve the patient's hypoxemia with a target saturation of 88-92%.

Bronchodilators: Short-acting inhaled beta$_2$-agonists with or without short-acting anticholinergics are preferred.

Systemic Corticosteroids: Shorten recovery time, improve lung function (FEV_1) and arterial hypoxemia (PaO_2), and reduce the risk of early relapse, treatment failure, and length of hospital stay. A dose of 40 mg prednisone per day for 5 days is recommended . Nebulized magnesium as an adjuvent to salbutamol treatment in the setting of acute exacerbations of COPD has no effect on FEV_1.

Interventions that Reduce the Frequency of COPD Exacerbations

Figure 4.11

Intervention Class	Intervention
Bronchodilators	LABAs LAMAs LABA + LAMA
Corticosteroid-containing regimens	LABA + ICS LABA + LAMA + ICS
Anti-inflammatory (non-steroid)	Roflumilast
Anti-infectives	Vaccines Long Term Macrolides
Mucoregulators	N-acetylcysteine Carbocysteine Erdosteine
Various others	Smoking Cessation Rehabilitation Lung Volume Reduction Vitamin D Shielding measures (e.g., mask wearing, minimizing social contact, frequent hand washing)

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Common Risk Factors for the Development of Lung Cancer

Figure 5.1

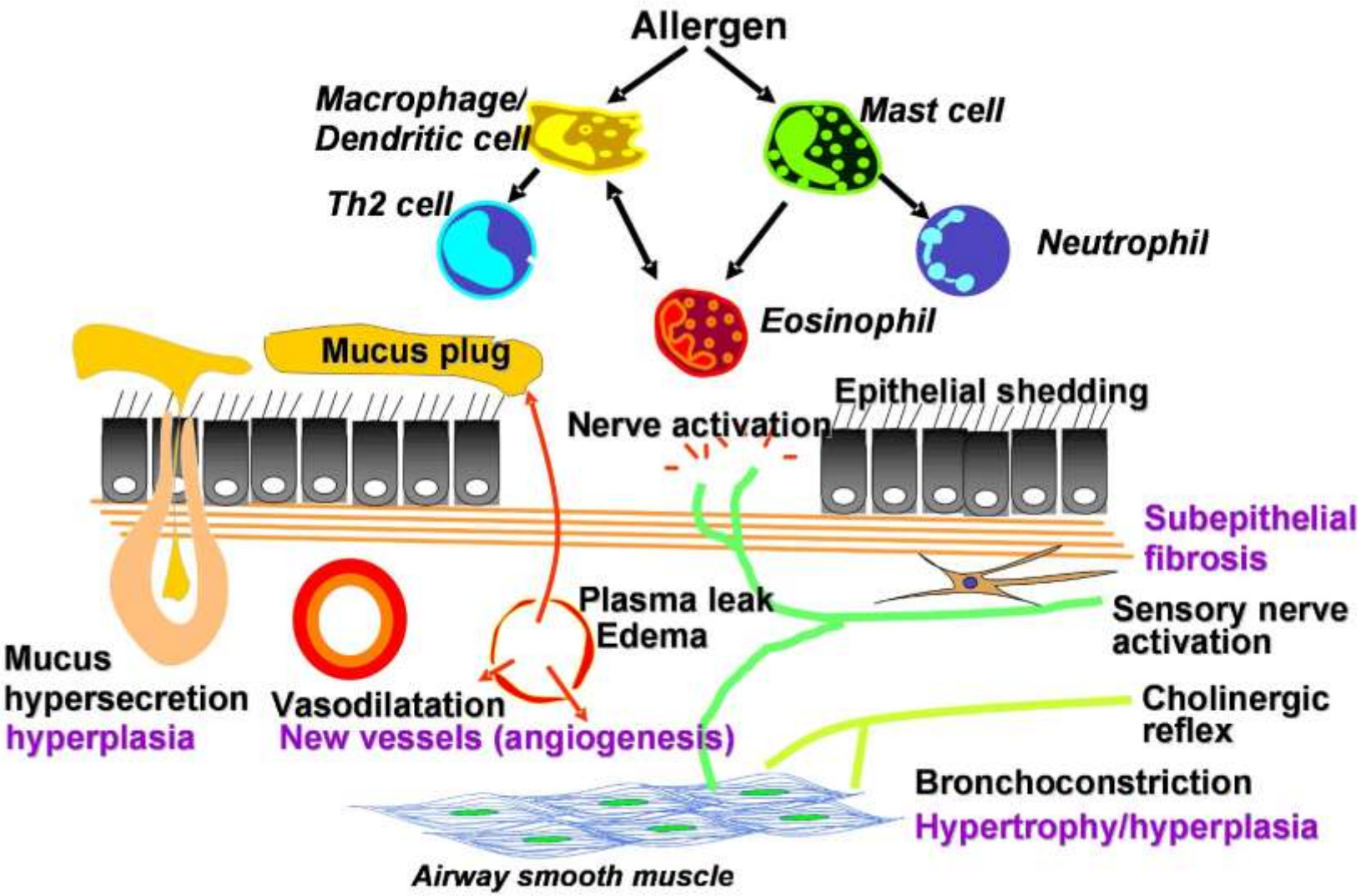
- Age > 55 years
- Smoking history > 30 pack years
- Presence of emphysema by CT scan
- Presence of airflow limitation FEV1/FVC < 0.7
- BMI < 25 kg/m^2
- Family history of lung cancer

© 2023, 2024 Global Initiative for Chronic Obstructive Lung Disease

Definition of Asthma

- *A chronic inflammatory disorder of the airways*
- *Many cells and cellular elements play a role*
- *Chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing*
- *Widespread, variable, and often reversible airflow limitation*

Fig. 1


Allergen
Macrophage/
Dendritic cell
Mast cell
Th2 cell
Neutrophil
Eosinophil
Mucus plug
Epithelial shedding
Nerve activation
Subepithelial
fibrosis
Plasma leak
Edema
Sensory nerve
activation
Mucus
hypersecretion
hyperplasia
Vasodilatation
New vessels (angiogenesis)
Cholinergic
reflex
Bronchoconstriction
Hypertrophy/hyperplasia
Airway smooth muscle

Factors that Influence Asthma Development and Expression

Host Factors

- Genetic
  - Atopy
  - Airway hyperresponsiveness
- Gender
- Obesity

Environmental Factors

- Indoor allergens
- Outdoor allergens
- Occupational sensitizers
- Tobacco smoke
- Air Pollution
- Respiratory Infections
- Diet

GINA 2011

Is it Asthma?

- Recurrent episodes of wheezing
- Troublesome cough at night
- Cough or wheeze after exercise
- Cough, wheeze or chest tightness after exposure to airborne allergens or pollutants
- Colds “go to the chest” or take more than 10 days to clear

GINA 2007: www.ginasthma.org

Classic triad of symptoms

1) Wheeze (high-pitched whistling sound, usually upon exhalation).

It is different from the monophasic wheezing of a local bronchial narrowing (eg, due to an aspirated foreign body or bronchogenic cancer), which has single pitch and repeatedly begins and ends at the same point in each respiratory cycle

- Transmission of expiratory noises from the upper airway (eg, larynx, pharynx) can mimic wheezing and is often described as wheezing by patients. However, these noises are typically loudest over the neck and greatly diminished over the chest.

2) Cough (typically worsening at night).

3) Shortness of breath or difficulty breathing.

All that wheezes is not asthma

- CHF
- Upper Airway Obstruction
- COPD
- Aspiration
- Bronchiectasis

The prior probability of asthma:

1) Episodic symptoms: come and go, with a time course of hours to days, resolving spontaneously with removal from the triggering stimulus or in response to anti-asthmatic medications**.**

2) Characteristic triggers: symptoms triggered by exercise, cold air, and exposure to allergens are suggestive of asthma.

3) Personal or family history of atopy: A strong family history of asthma and allergies or a personal history of atopic diseases (specifically, atopic dermatitis, seasonal allergic rhinitis and conjunctivitis, or hives) favors a diagnosis of asthma in a patient with suggestive symptoms.

4) History of asthmatic symptoms as a child:

As previously mentioned, recollection of childhood symptoms of chronic cough, nocturnal cough in the absence of respiratory infections, or a childhood diagnosis of "chronic bronchitis" or "wheezy bronchitis" favors asthma.

Adapted from GINA 2007: www.ginasthma.org

Typical Spirometric (FEV_1)

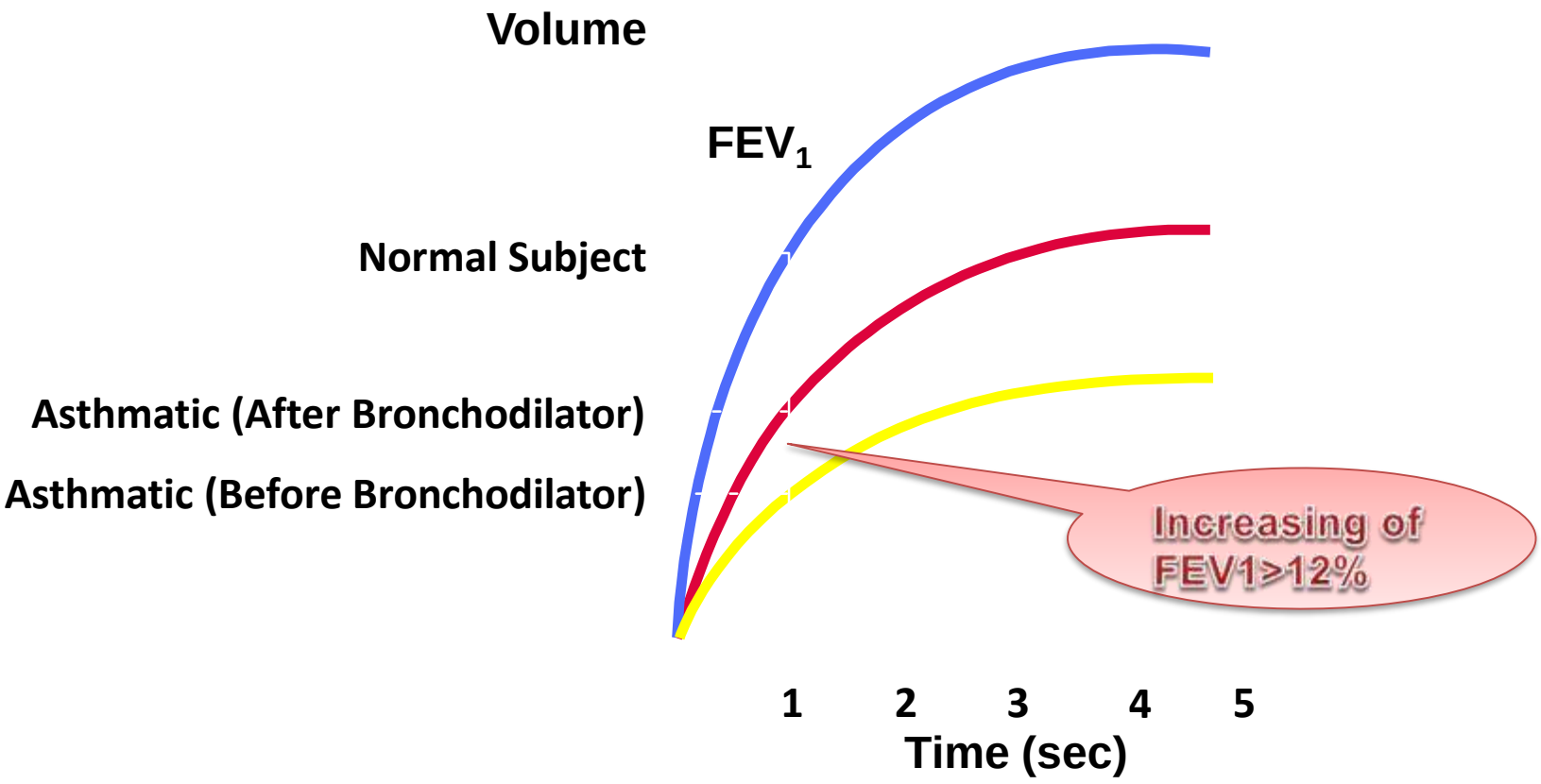


Table 2. Classifying Asthma Severity in Youths and Adults

- **Classifying severity for patients who are not currently taking long-term control medications.**

Components of Severity		Classification of Asthma Severity (Youths ≥12 years of age and adults)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8–19 yr 85% 20–39 yr 80% 40–59 yr 75% 60–80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 ≥80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. →			
		Relative annual risk of exacerbations may be related to FEV_1			

- Routine CXR is **not** indicated: Would be normal or would show hyperinflation Is indicated if there is suspicion of pneumonia, CHF, pneumothorax, or other medical concern
- Routine CBC is **not** indicated: Slight Leucocytosis sec. to β2 agonist or steroid use
- **ABG** is **not** indicated in most mild to moderate cases. It does not predict clinical outcome and should **not** supersede clinical findings to determine the need for intubation
- Theophylline levels
- ECG: May show RV Strain, non specific ST-T abnormalities
- Cardiac Monitoring for all elderly and/or cardiac patients

Clinical Control of Asthma

- Determine the initial level of control to implement treatment
- Maintain control once treatment has been implemented

Items	Controlled	Partly Controlled Over 1 item below during 1 week	Uncontrolled
Daytime symptom	None (or under 2 times/wk)	Over 3 times/wk	Over 3 items in partly controlled in any 1 week
Limitation of Activity	None	A few	
Nighttime symptom Sleep disturbance	None	A few	
Need resque medication	None (or under 2 times/wk)	Over 3 times/wk	
PFT(FEV1/PEFR)	Normal	Under 80% of Pred. or personal best value	
Attack	None	Over 1 time/yr	1 time in any 1 week

Goals of asthma treatment

- Few asthma symptoms
- No sleep disturbance
- No exercise limitation

} Symptom control (e.g. ACT, ACQ)

- Maintain normal lung function
- Prevent flare-ups (exacerbations)
- Prevent asthma deaths
- Minimize medication side-effects (including OCS)

} Risk reduction

- The patient's goals may be different
- Symptom control and risk may be discordant
  - Patients with few symptoms can still have severe exacerbations

ACQ: Asthma Control Questionnaire; ACT: Asthma Control Test; OCS: oral corticosteroids

© Global I

GINA 2023 – 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 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

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

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	STEP 3	STEP 4	STEP 5
As-needed-only 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-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	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-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 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*

*Anti-inflammatory reliever (AIR)

Box 3-12 © Global Initiative for Asthma, www.ginasthma.org

Equivalent dosage of ICS

Drug name	LOW, mcg	Moderate, mcg	High, mcg
Beclomethasone dipropionate CFC	200 - 500	500 – 1000	1000 - 2000
Budesonide	200 – 400	400 – 800	800 – 1600
Ciclesonide	80 – 160	160 -320	320 -1280
Flunisolide	500 – 1000	1000 – 2000	> 2000
Fluticasone propionate	100 – 250	250 – 500	500 - 1000
Mometasone furoate	200	≥ 400	≥ 800

GINA 2011; www.ginasthma.org Updated 2011

ANTILEUKOTRIENE DRUDS

Indications:

- **Treatment of aspirin-sensitive patients**
- **Prevention of bronchospasm due to physical overload**
- **smokers**
- **BA + allergic rhinitis**
- **Patients who can’t use inhalated drugs**

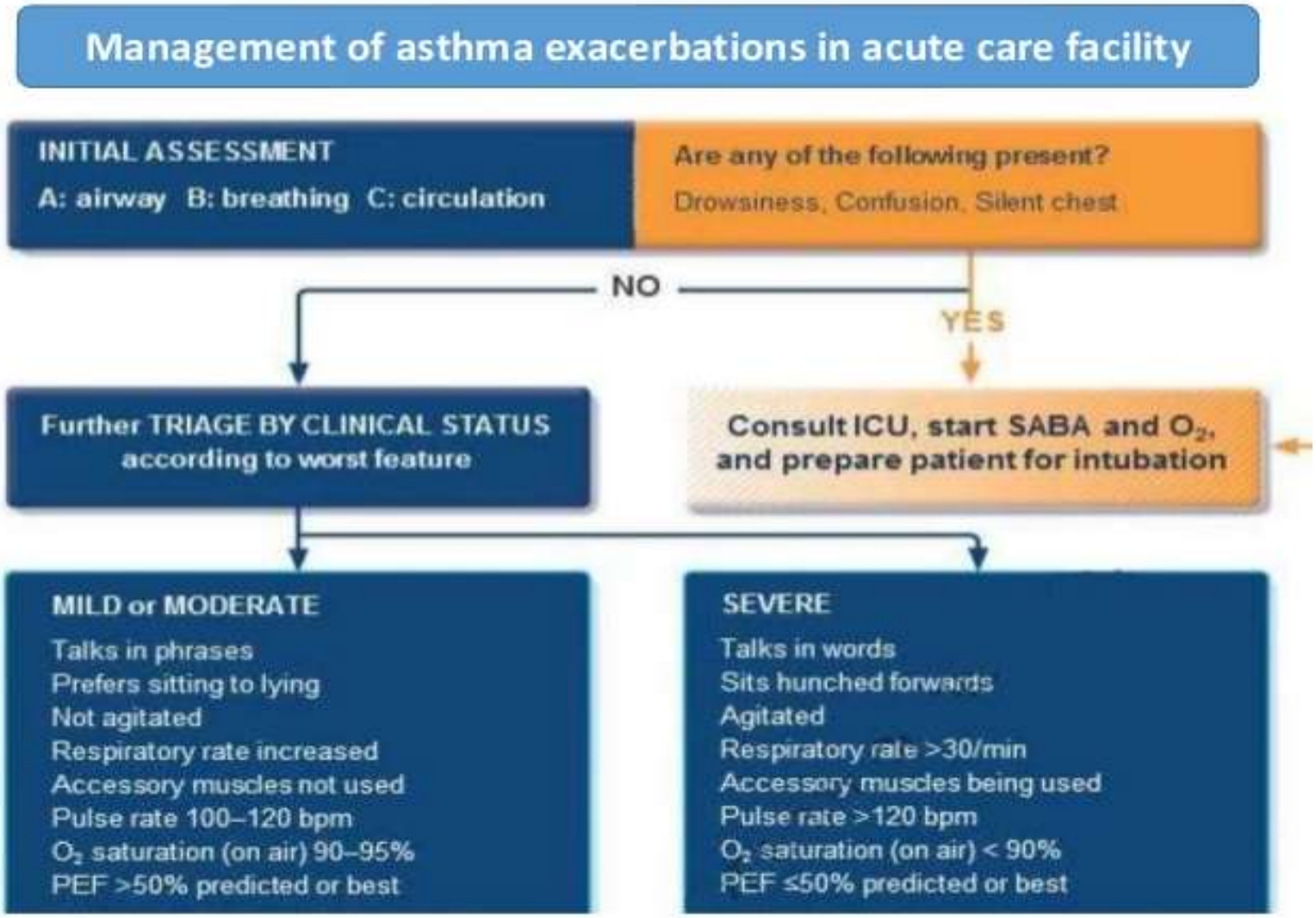
ZAFIRLUKAST – tab. 20 mg; 1 tab OD
MONTELUKAST – tab. 10 mg; 1 tab OD

Can be used as monotherapy at STEP 2 or as combination with ICS

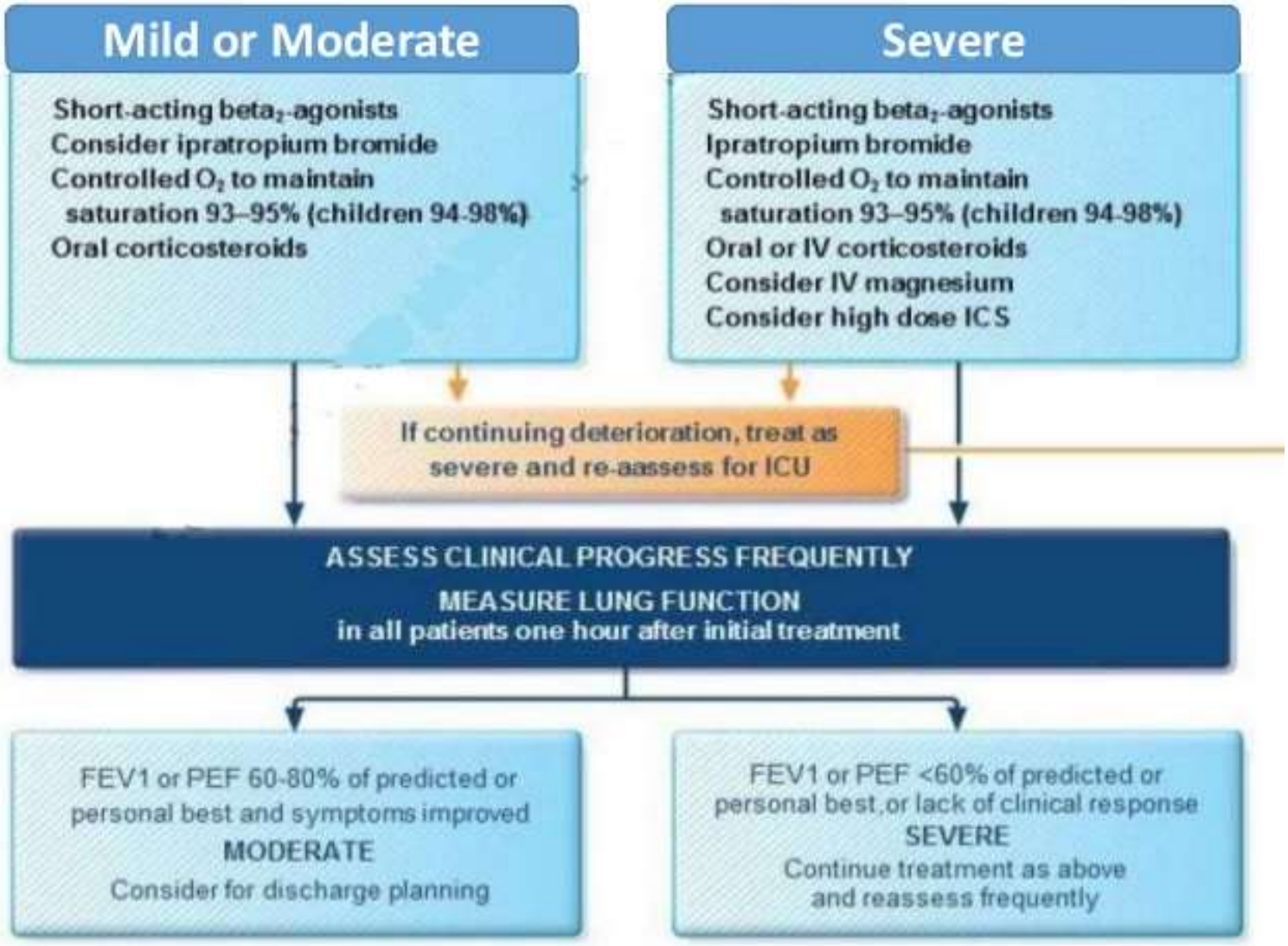
ANTIBODY TO IGE

- **OMALIZUMAB**

Dosage: 75 - 375 mg 1 time per 2 or 4 weeks s/c; is defined in accordance to body weight and baseline IgE level (before treatment)



GINA 2019; www.ginasthma.org



GINA 2019; www.ginasthma.org

Table 2

Classification of Asthma-Exacerbation Severity

Severity	PEF	Clinical Course
Mild	≥70% of predicted or personal best	Home care, use of SABA, and possible short course of oral corticosteroids
Moderate	40%-69% of predicted or personal best	Office or ED visit, frequent use of SABA, oral corticosteroids, and possible hospital admission
Severe	25%-39% of predicted or personal best	Hospitalization, frequent use of SABA, oral corticosteroids, and adjunct therapy
Life-threatening	<25% of predicted or personal best	Likely ICU admission, IV corticosteroids, and adjunct therapy

ED: emergency department; PEF: peak expiratory flow; SABA: short-acting beta agonist.
Source: Reference 17.

Adapted from GINA 2019: www.ginasthma.org

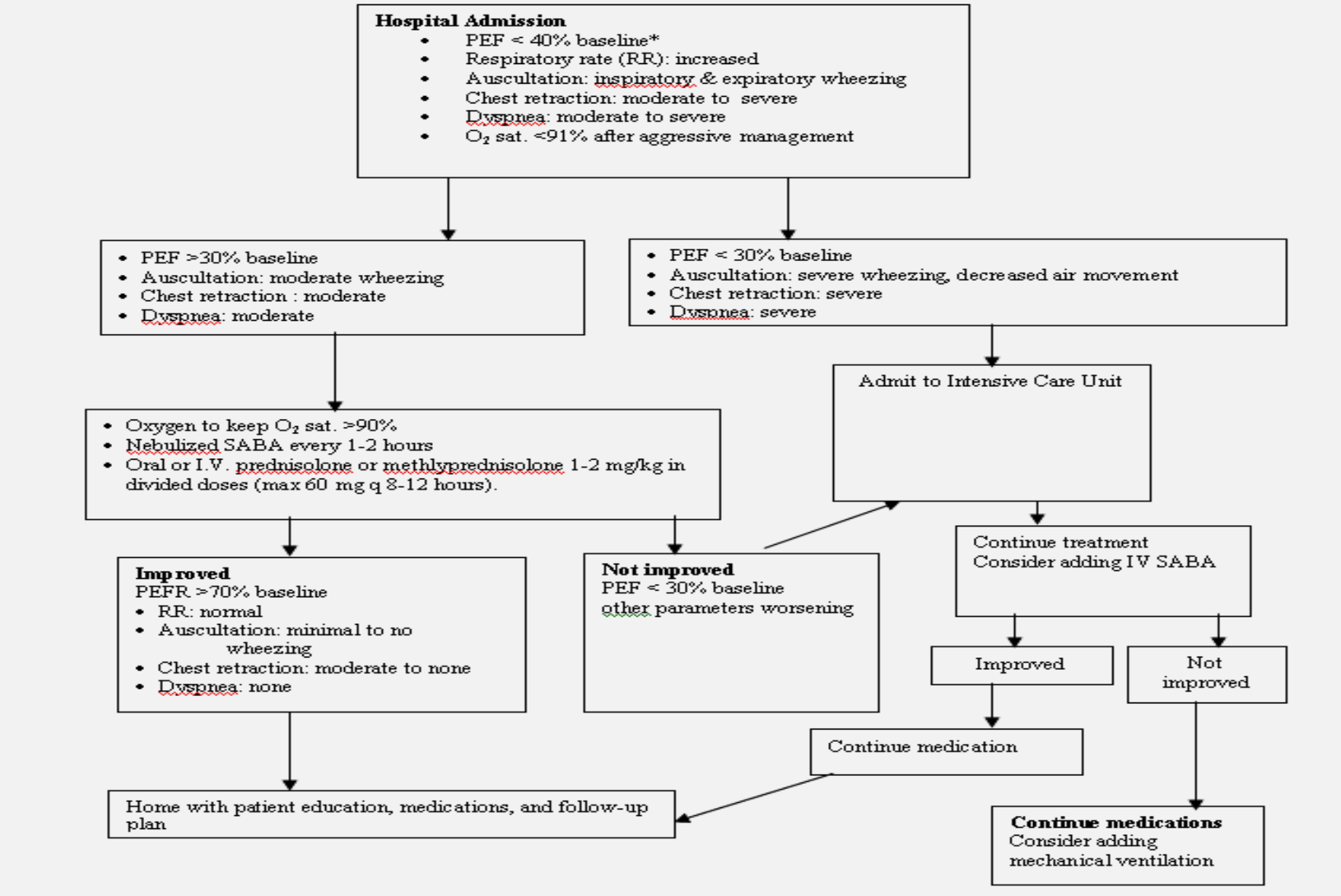
Component 4: Manage Asthma Exacerbations

Primary therapies for exacerbations:

- Repetitive administration of rapid-acting inhaled β_2-agonist
- Early introduction of systemic glucocorticosteroids
- Oxygen supplementation

Closely monitor response to treatment with serial measures of lung function

- The term ‘status asthmaticus’ was defined as asthma that had failed to resolve with therapy in 24 hours.
- Although this term is still used occasionally, it has been mainly discarded and replaced by ‘acute severe asthma’, i.e. severe asthma that has not been controlled by the patient’s use of medication.



Adapted from ATC 2016