

Disclosure

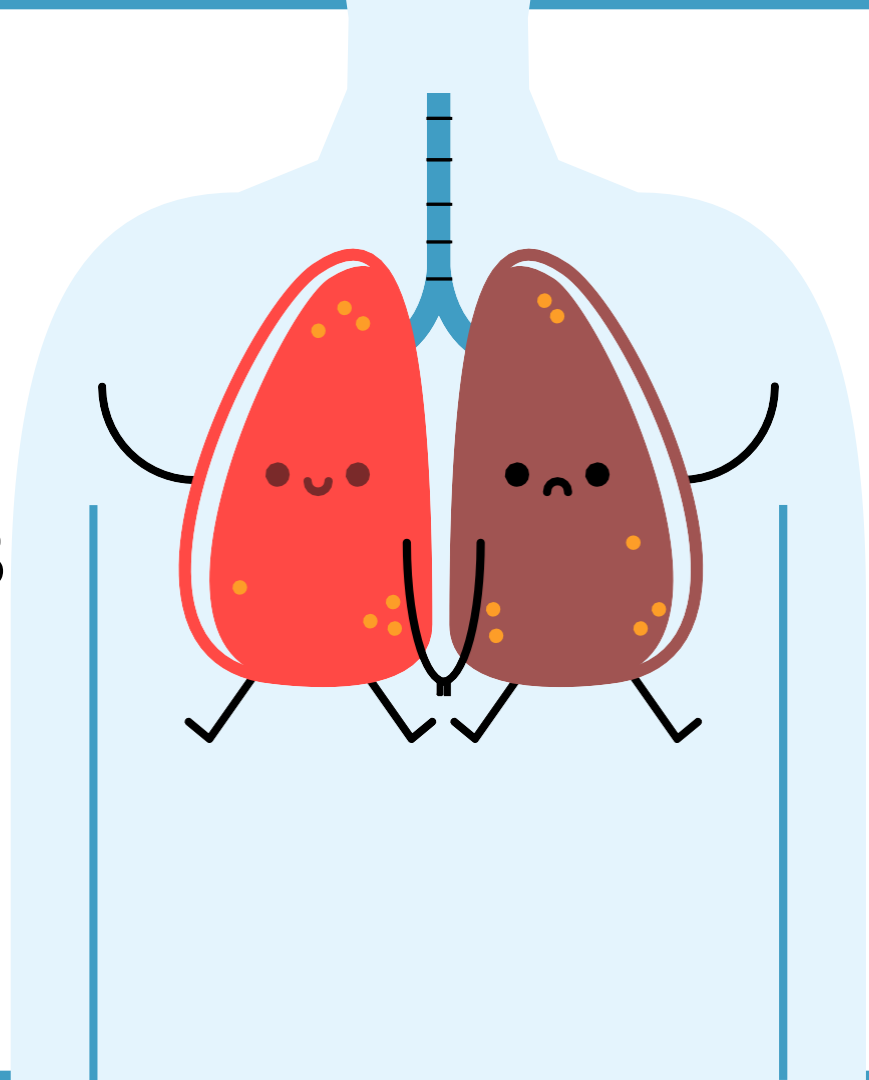
RELEVANT FINANCIAL RELATIONSHIPS

In compliance with continuing education requirements, ACPE, our planners, our presenters, and their spouses/partners wish to disclose we do not have relevant financial relationships with ineligible companies.

Update on COPD Management: The GOLD Guidelines

Prepared by: Sayel Rivera-García, PharmD, BCPS and
Wanda I Marrero, MSPh, PharmD

Presented by: Wanda I Marrero, MSPh, PharmD

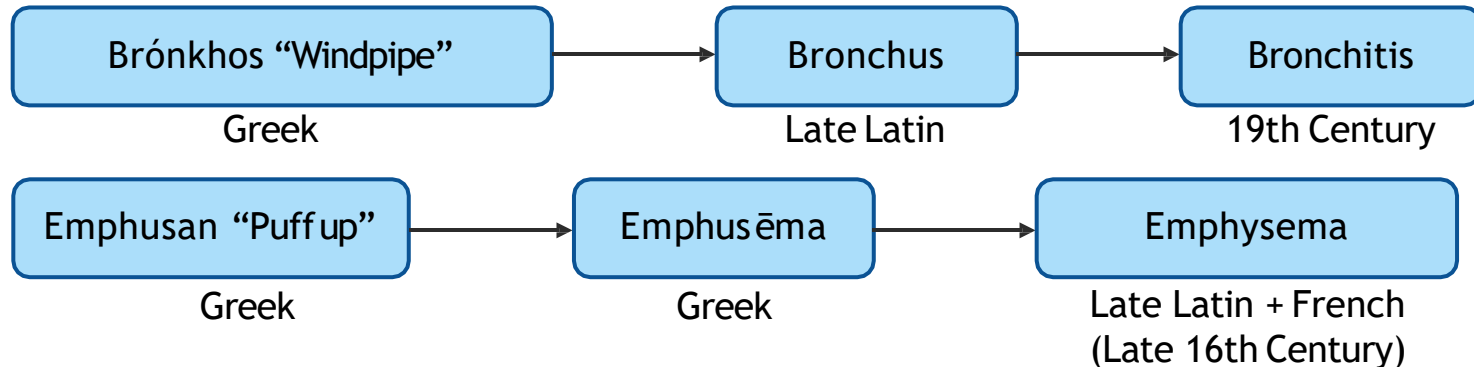


Objective

- Identify the challenges and barriers associated with chronic obstructive pulmonary disease (COPD) management, the disease's burden, and the need to improve patient outcomes.
- Discuss the 2023 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines updates and management recommendations.
- Describe non-pharmacological measures recommended for patients with COPD.
- List current and emerging treatments for COPD, including their safety, efficacy, place in therapy, and use in specific patient populations for optimal outcomes.
- Illustrate the role of the pharmacy team in optimizing the care of patients with COPD.

Introduction

- Chronic obstructive pulmonary disease is a relatively new term
- This term was first used by William Briscoe in late 20th century (1965)
- Before this term COPD has been described as a group of pulmonary diseases with fixed airflow limitation
 - Chronic bronchitis
 - Emphysema





Introduction

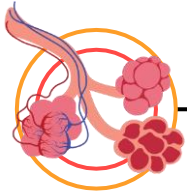
Modern definition:

- GOLD - “Chronic Obstructive Pulmonary Disease (COPD) is a **heterogeneous lung condition** characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that **cause persistent, often progressive, airflow obstruction**”.

Previous definition:

- GOLD - “Chronic Obstructive Pulmonary Disease (COPD) is a **common, preventable, and treatable disease** characterized by persistent respiratory symptoms and airflow limitation due to abnormalities of the airways and/or alveolar abnormalities **usually caused by significant exposure to noxious particles and gases and influenced by host factors including abnormal lung development**”.

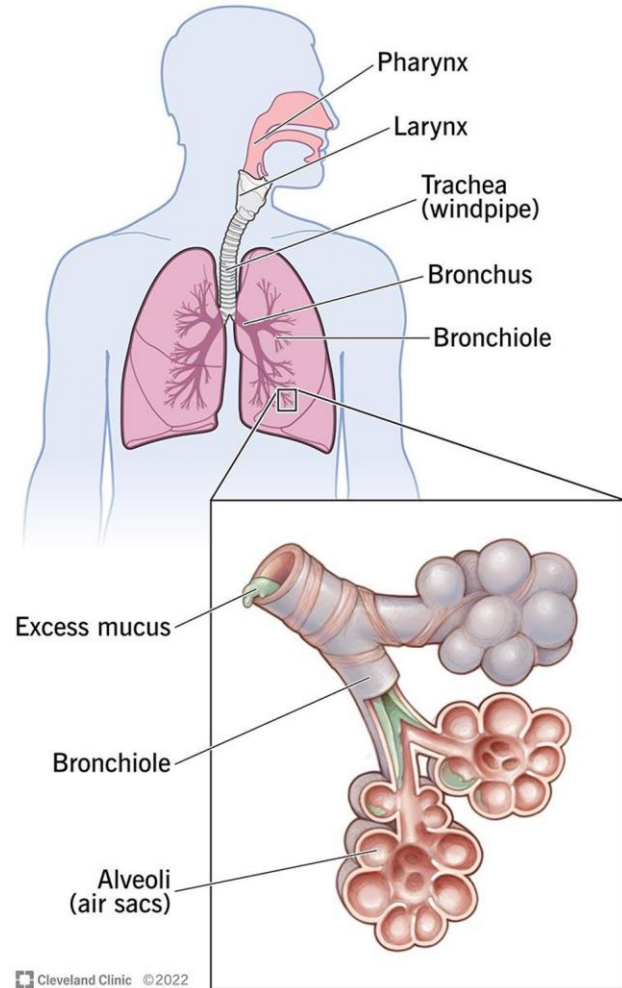
Introduction



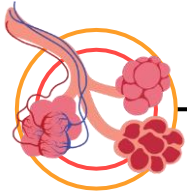
Chronic Bronchitis

- Defined as a **clinical term**
- Associated with:
 - Chronic or recurrent episodes of excessive mucus secretion into the bronchial tree
 - Cough present on most days for at least 3 months of the year for at least 2 consecutive years
 - In a patient in whom other causes of chronic cough have been excluded

Bronchitis

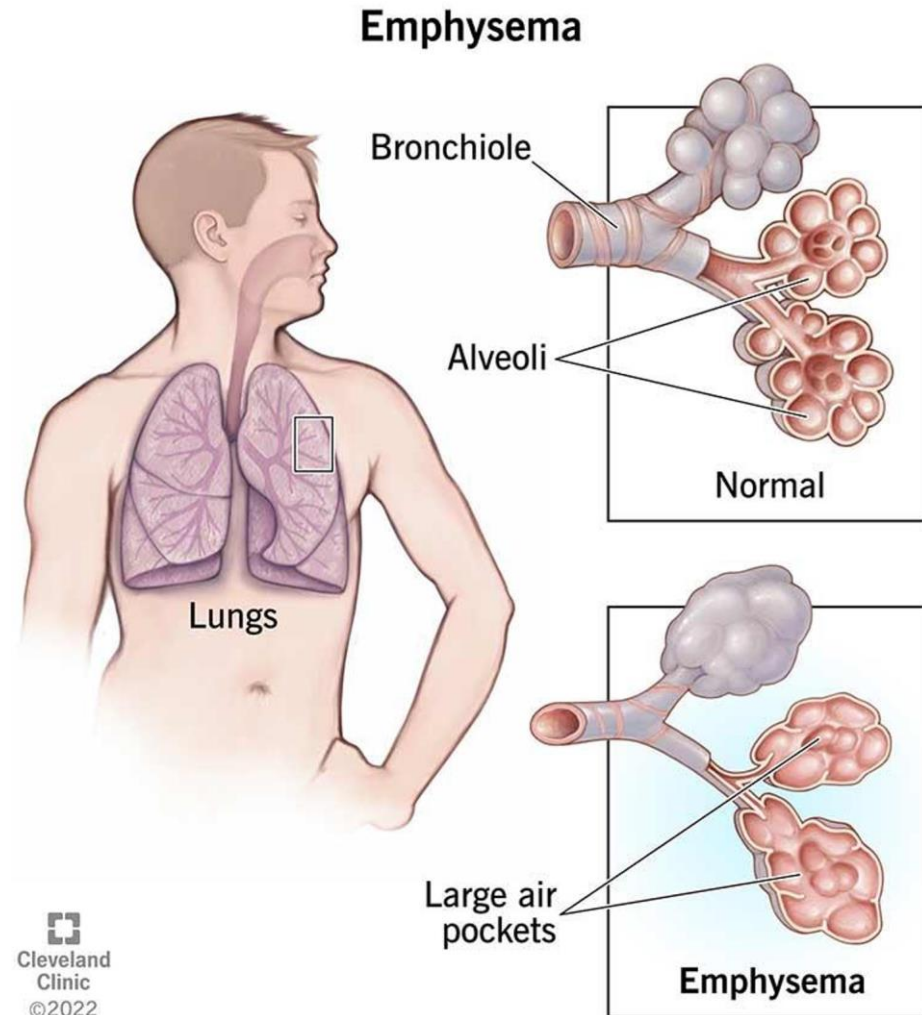


Introduction

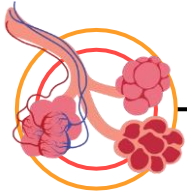


Emphysema

- Defined as an **anatomical pathology**
- Emphysema is characterized as an abnormal permanent enlargement of the airspaces distal to the terminal bronchioles accompanied by destruction of their walls without obvious fibrosis

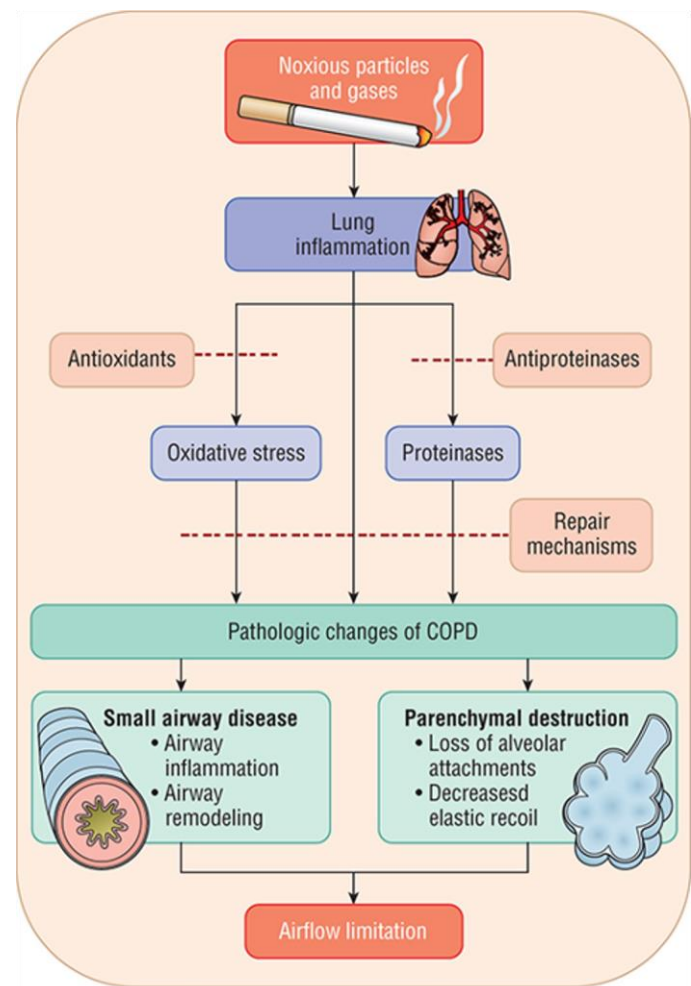


Introduction

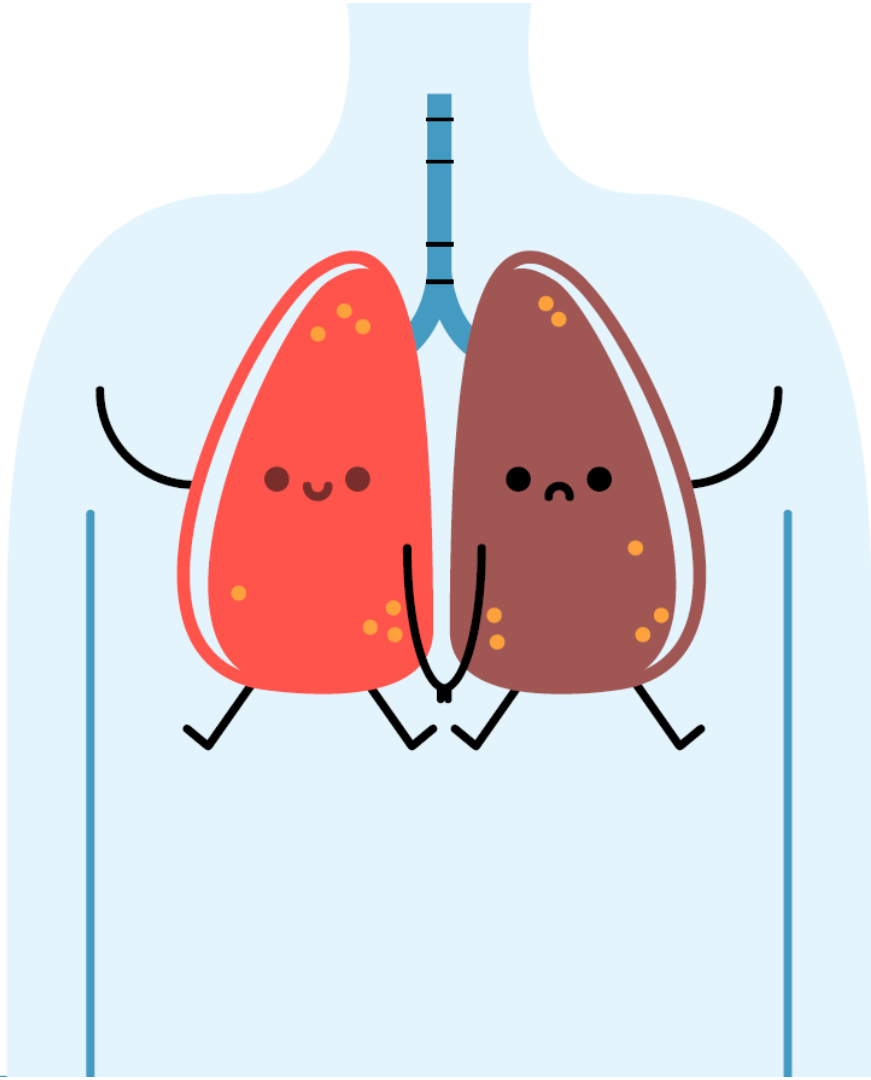


New Emphasis

- Differentiating COPD as either chronic bronchitis or emphysema as distinct subsets is no longer considered relevant
- Both are caused by a common risk factor
- Emphasis on pathophysiologic features of:
 - Small airway disease
 - Parenchymal destruction



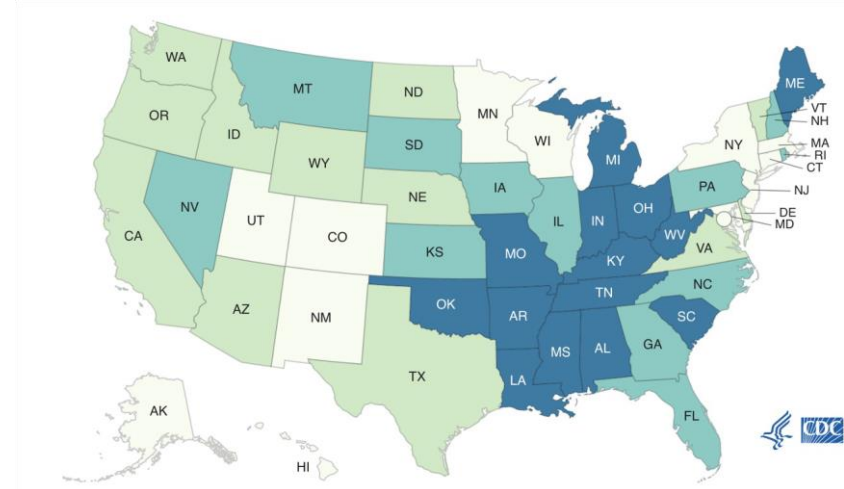
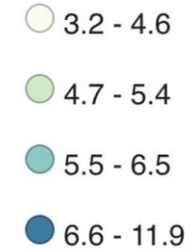
Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach*, 12e Copyright © McGraw Hill. All rights reserved.



Epidemiology

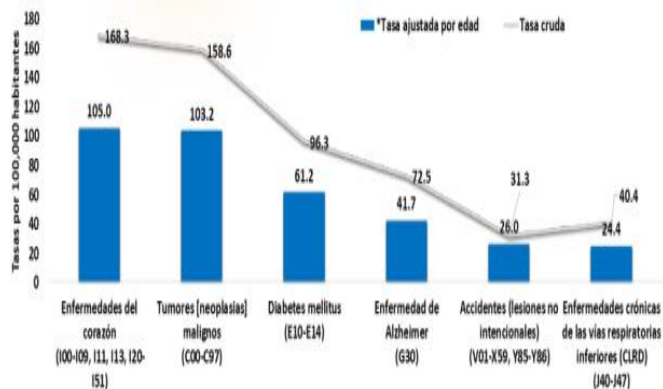
- Approximately 16 million americans are estimated to have COPD
- Cigarette smoking among adults in the United States has declined but prevalence of airflow obstruction and COPD is not expected to decrease in the future
 - Over the last 10 years the use of e-cigarettes has increased
- Historically considered a disease affecting white men but women are now more likely to have a diagnosis of COPD than men
- Prevalence is higher in southeastern states

Age-adjusted Prevalence (%)



PUERTO RICO

Primeras 6 causas de muertes totales en Puerto Rico, 2019

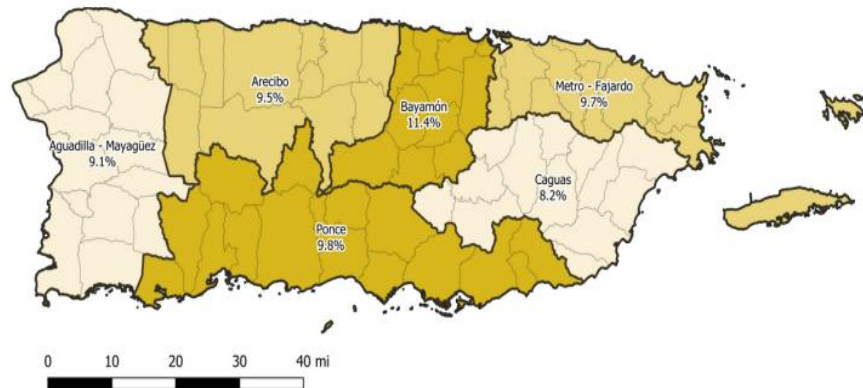


Tasas de mortalidad ajustada por edad (por cada 100,000 habitantes)

Fuente - Departamento de Salud, Registro Demográfico de Puerto Rico, Secretaría Auxiliar de Planificación y Desarrollo, División de Análisis Estadísticos, 2019

PREVALENCIA DE USO DE TABACO POR REGIÓN DE SALUD PARA EL AÑO-2019

04



Fuente: BRFSS 2019

Para el 2019, los residentes de las regiones de Bayamón (11.4%) y Ponce (9.8%) reportaron las prevalencias más altas de uso de tabaco.

Morbidity & Mortality



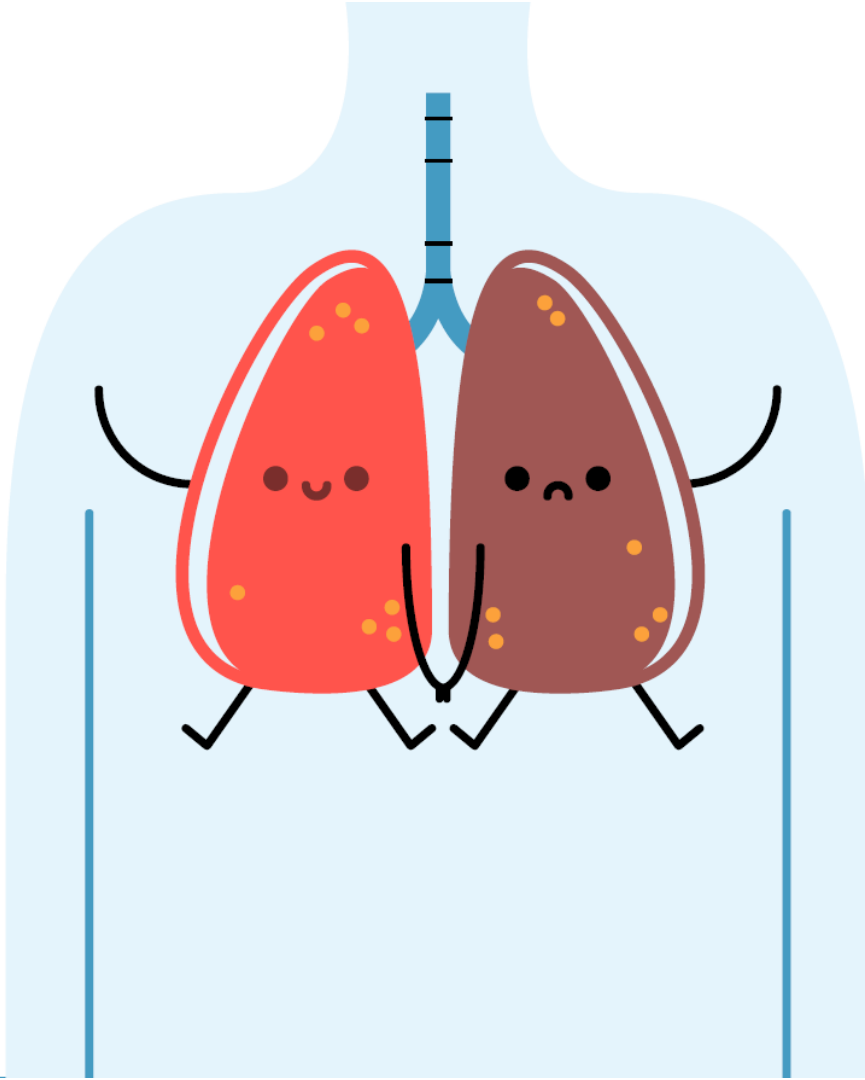
Morbidity

- Cost associated with the disease has significant impact on:
 - Patients & their families → Physical activity limitations and inability to work
 - Healthcare system → Annually, patients with COPD account for 700,000 hospitalizations
- An estimated \$32 billions was spent on services related to COPD in 2010
 - 2020 → \$49 billions

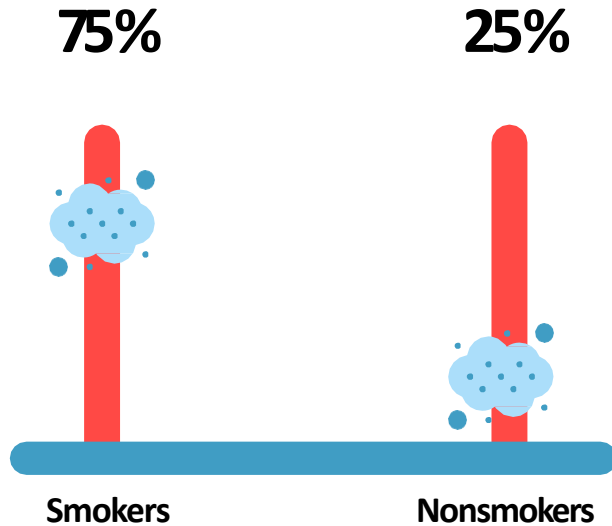


Mortality

- 4th leading cause of death
- Over 150,000 deaths are attributed to COPD annually
- Mortality rate has increased over the last 40 years



Etiology



Nonsmokers



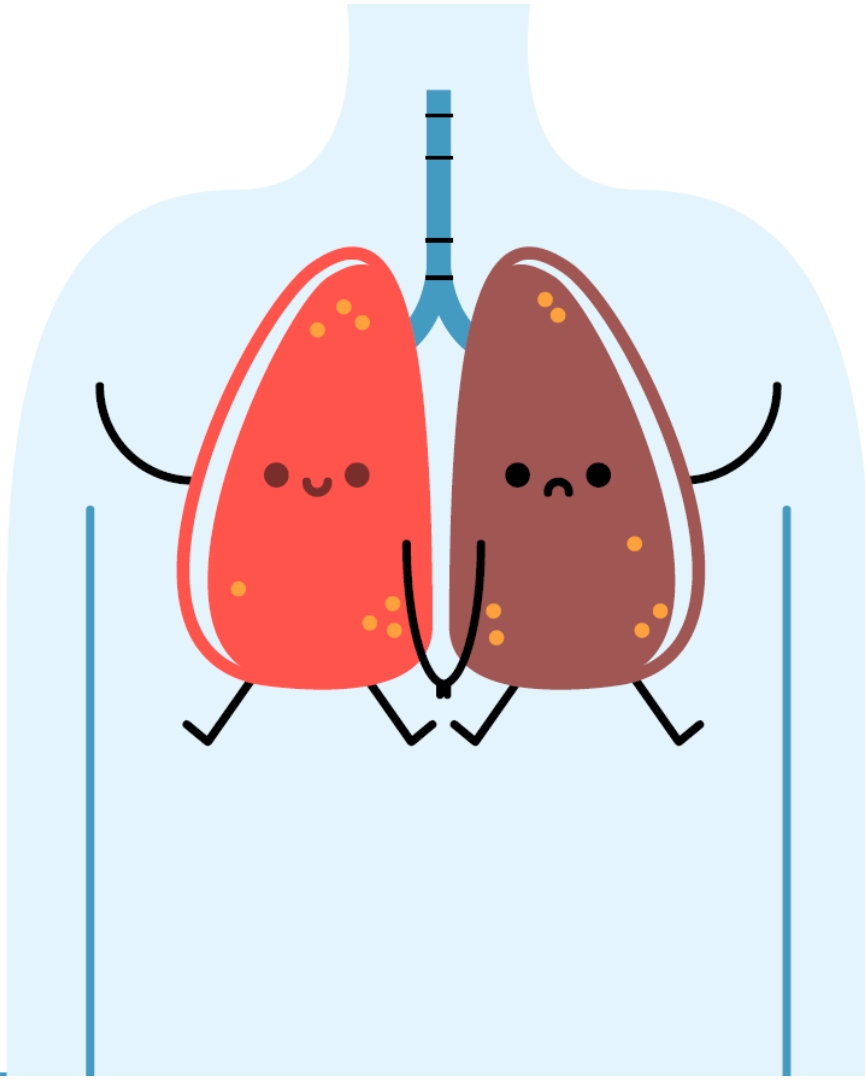
Exposure to environmental tobacco smoke



Secondhand smoking



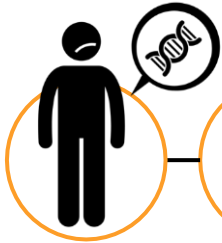
Occupational exposure



03

Risk Factors

Risk Factors



Host Factors

α_1 -antitrypsin (AAT) deficiency

Airway Hyperresponsiveness

Impaired lung growth



Environmental Factors

Environmental tobacco smoke

Occupational dust and chemicals

Air pollution

New Classification Taxonomy (Etiotypes)

Proposed Taxonomy (Etiotypes) for COPD

Table 1.1

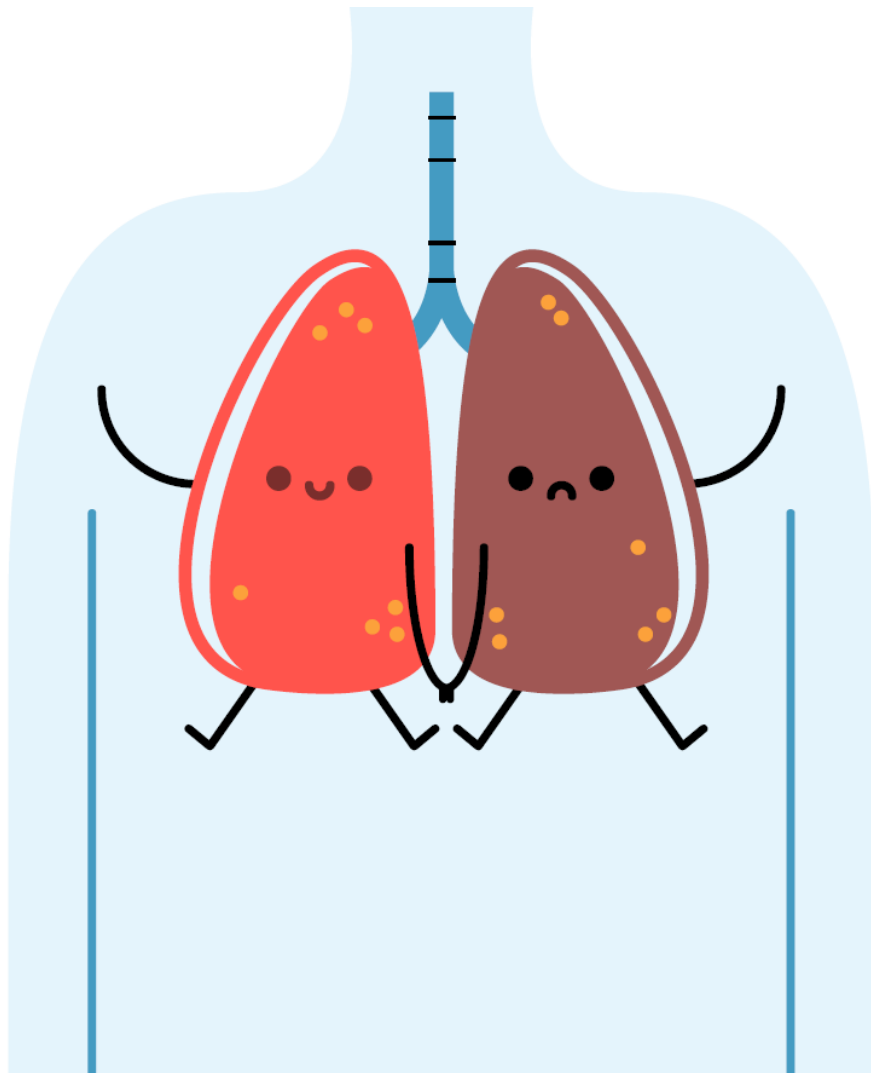
Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	<ul style="list-style-type: none">• Exposure to tobacco smoke, including <i>in utero</i> 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)

Test your knowledge

Which of the following risk factors is consider the first one cause of COPD:

- A. AAT
- B. Premature birth
- C. Pollution
- D. Cigarette Smoking
- E. Infections

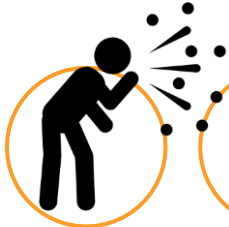


Symptoms

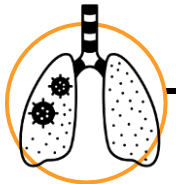


Chronic Cough

May be intermittent and unproductive



**Chronic Sputum
Production**



**Recurrent Respiratory
Infections**

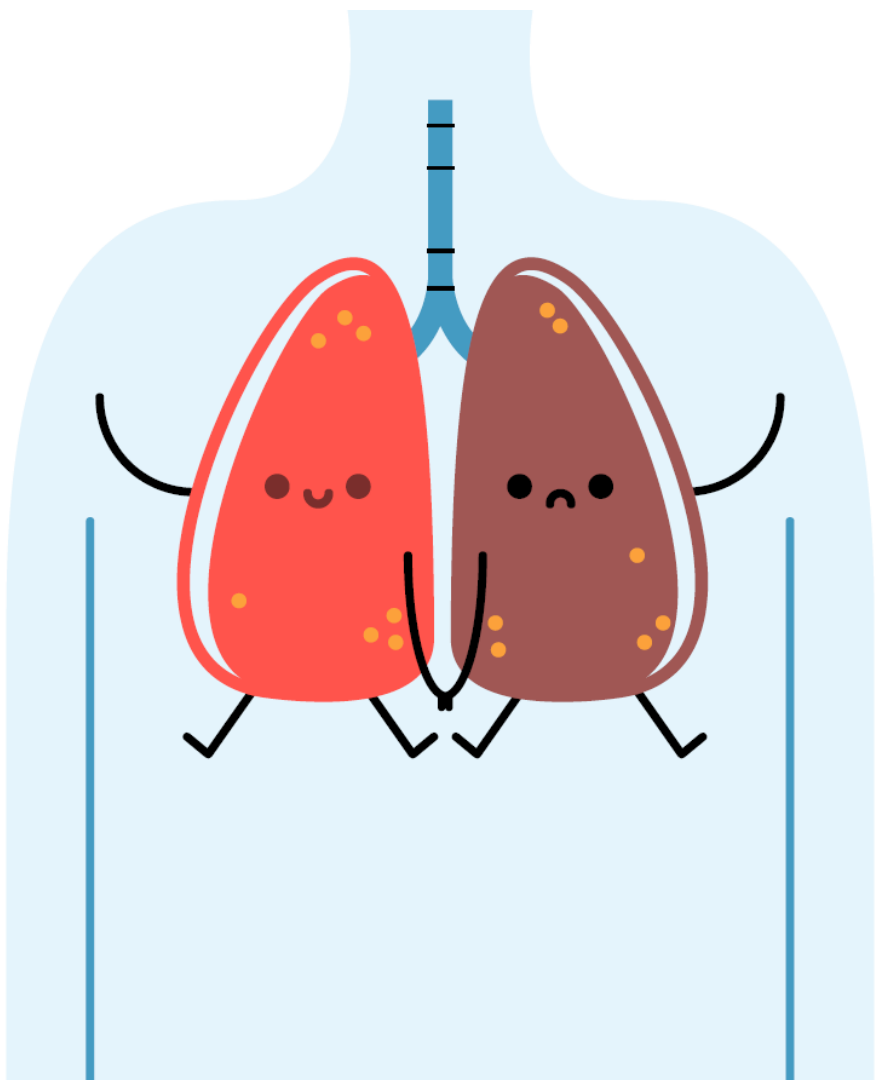


Dyspnea

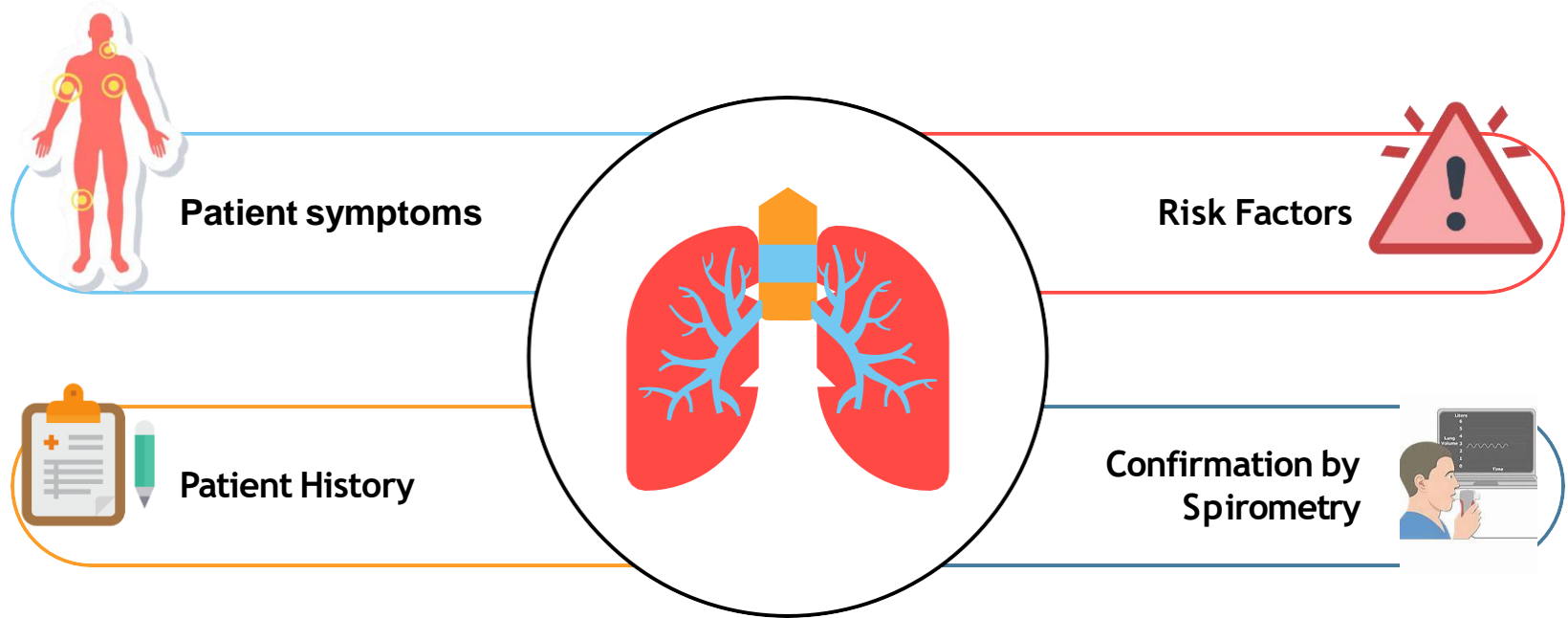
Worse with exercise and progressive overtime



Wheezing



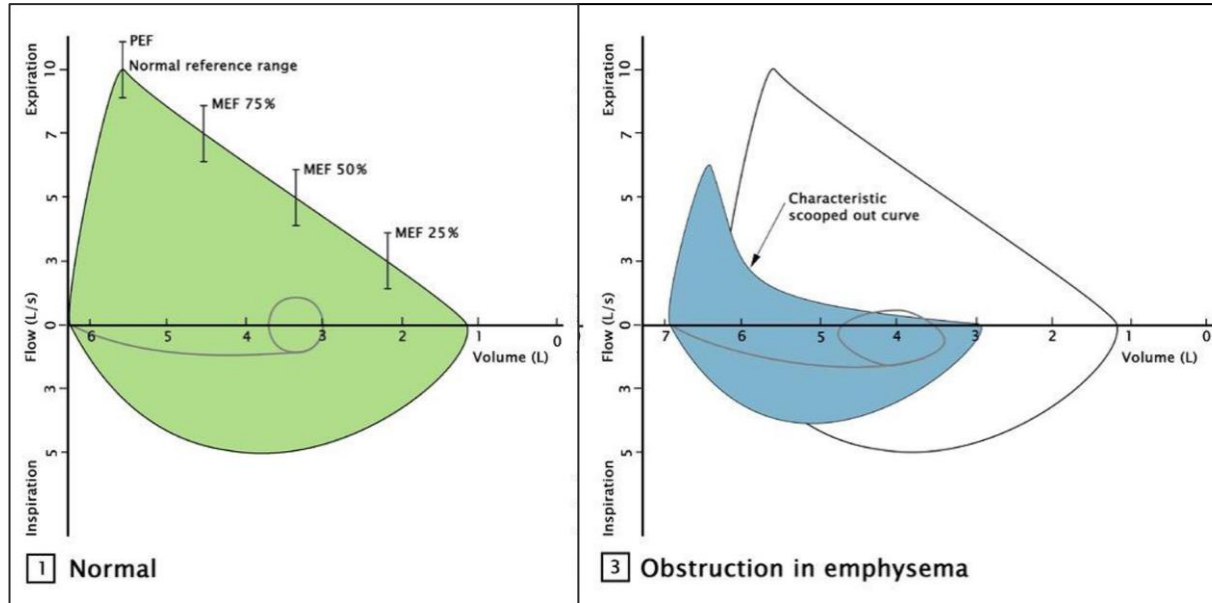
Diagnosis



Confirmation by Spirometry



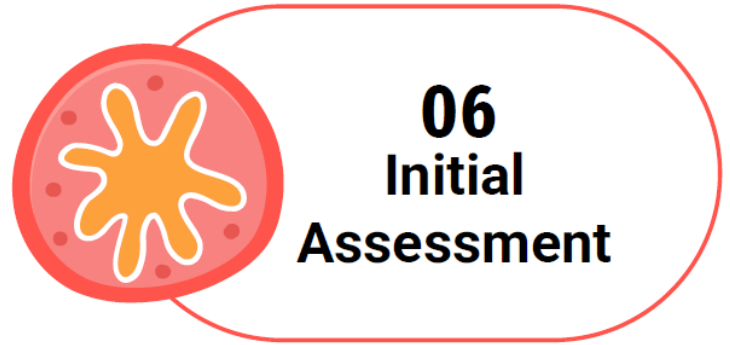
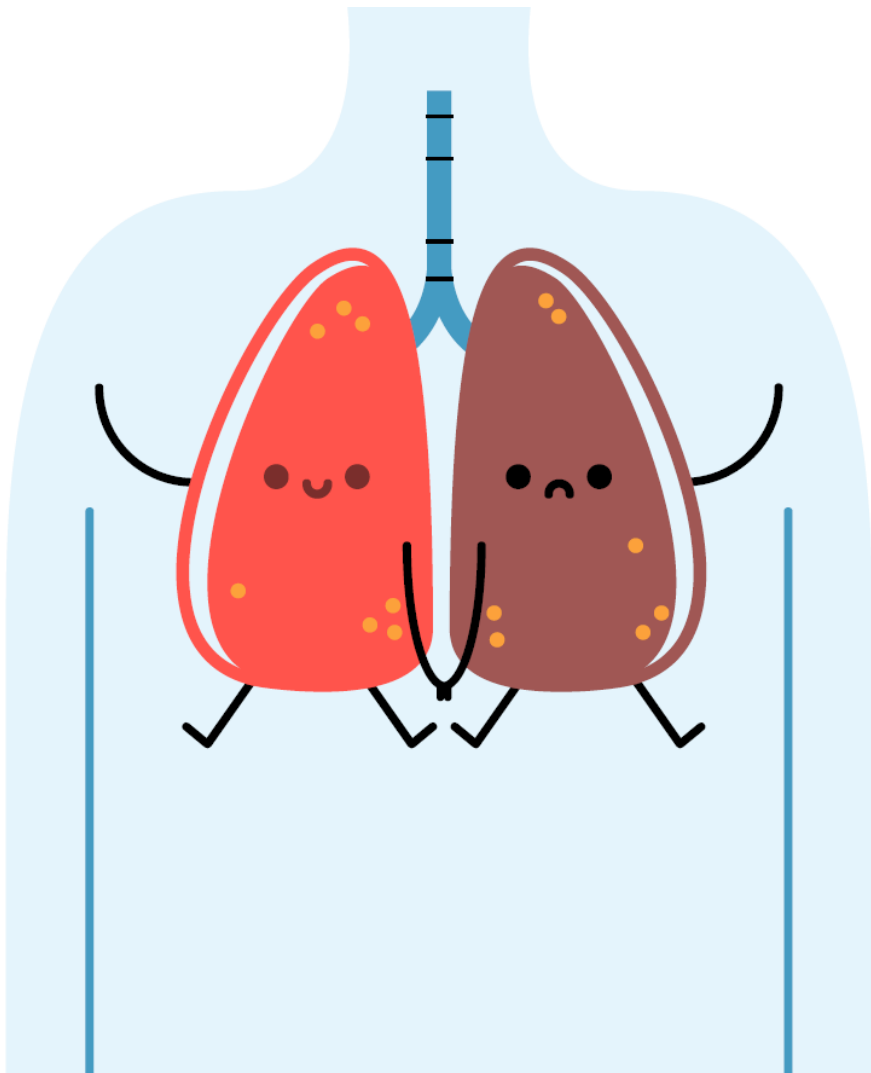
Flow-Volume Loop



Airflow limitation is confirmed by post-bronchodilator:

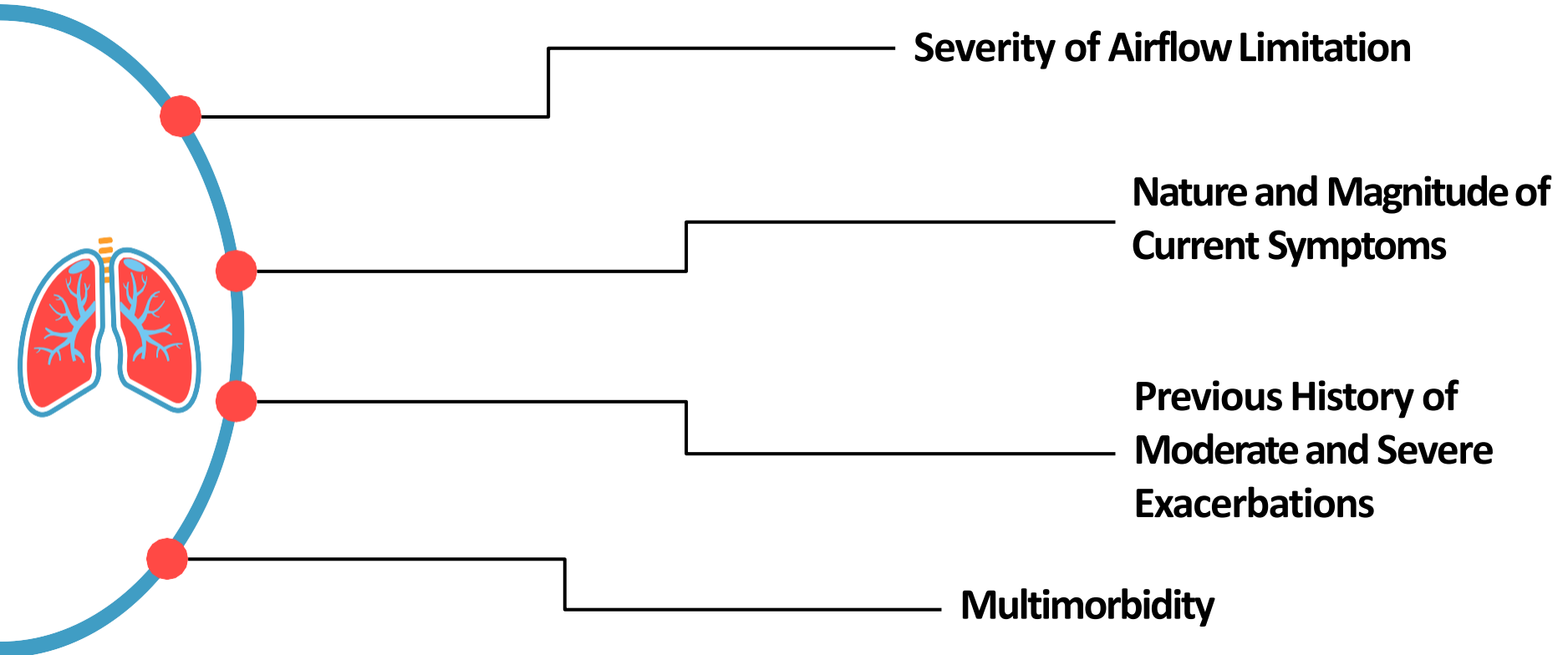
- $FEV_1/FVC < 70\%$

FEV_1 alone is no longer used to determine severity or therapy



06
Initial
Assessment

Initial Assessment



Severity of Airflow Limitation

GOLD Grades and Severity of Airflow Obstruction in COPD (based on post-bronchodilator FEV₁)

Table 2.6

In COPD patients (FEV₁/FVC < 0.7):

GOLD 1:

Mild

FEV₁ ≥ 80% predicted

GOLD 2:

Moderate

50% ≤ FEV₁ < 80% predicted

GOLD 3:

Severe

30% ≤ FEV₁ < 50% predicted

GOLD 4:

Very Severe

FEV₁ < 30% predicted

Nature and Magnitude of Symptoms

Modified MRC Dyspnea Scale

Table 2.7

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
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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

Nature and Magnitude of Symptoms

- 8 item dimensional measure of healthstatus impairment in COPD
- Score ranges from 0 to 40 with higher scores indicating increased impairment

CAT™ Assessment

Figure 2.2

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

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

TOTAL SCORE:

Exacerbations and Multimorbidity

Exacerbations (ECOPD)

Episodes of acute respiratory symptom worsening. ECOPD impacts significantly:

- The rate of lung function decline
- The prognosis of the patient
- Healthcare costs of COPD

The best predictor of having frequent exacerbations (**defined as two or more exacerbations per year**) is the previous history of exacerbations

Multimorbidity

Comorbid conditions should be looked for routinely, and treated appropriately if present, in any patient with COPD.

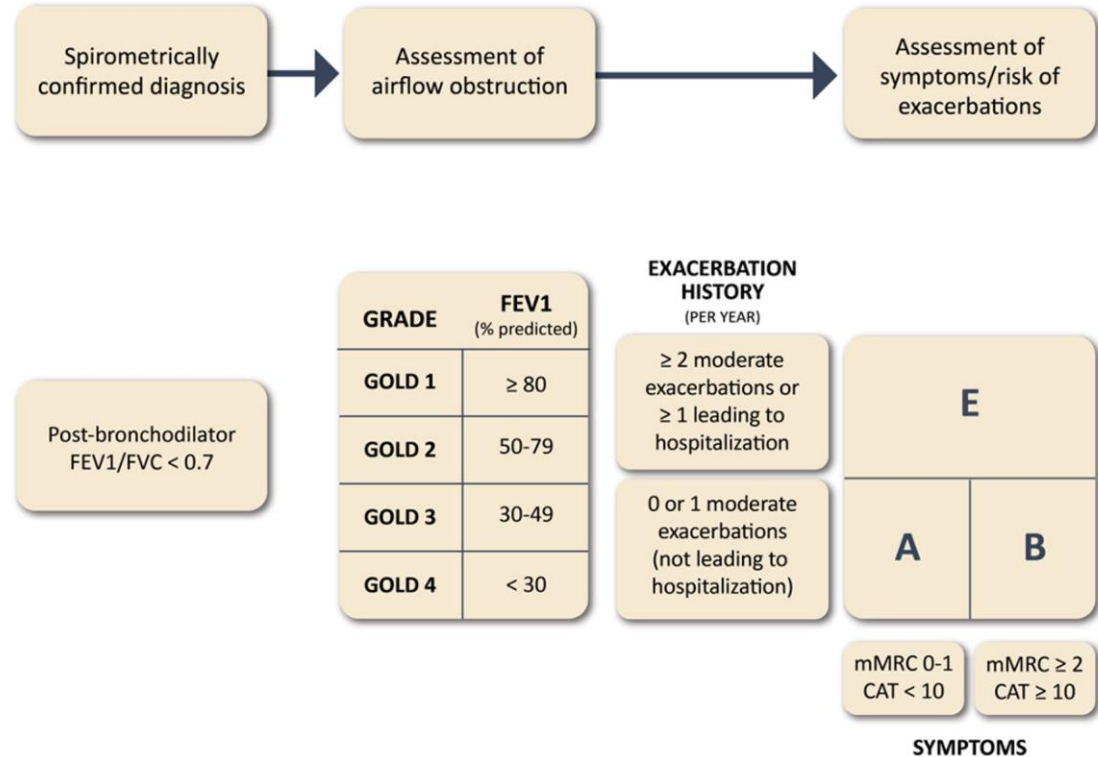
Frequent multimorbid diseases in COPD include:

- Cardiovascular disease
- Metabolic syndrome
- Osteoporosis
- Depression
- Anxiety
- Weight loss

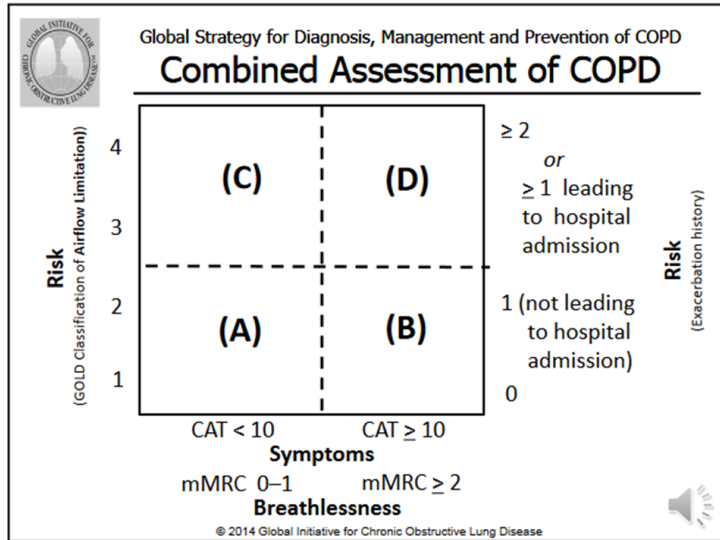
Combined Assessment of COPD

GOLD ABE Assessment Tool

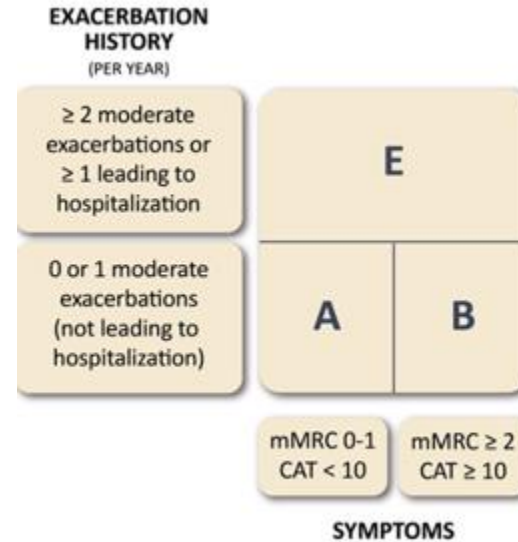
Figure 2.3



GOLD 2022 vs GOLD 2023



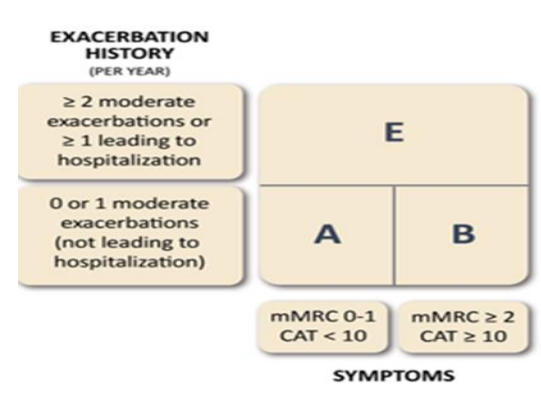
VS

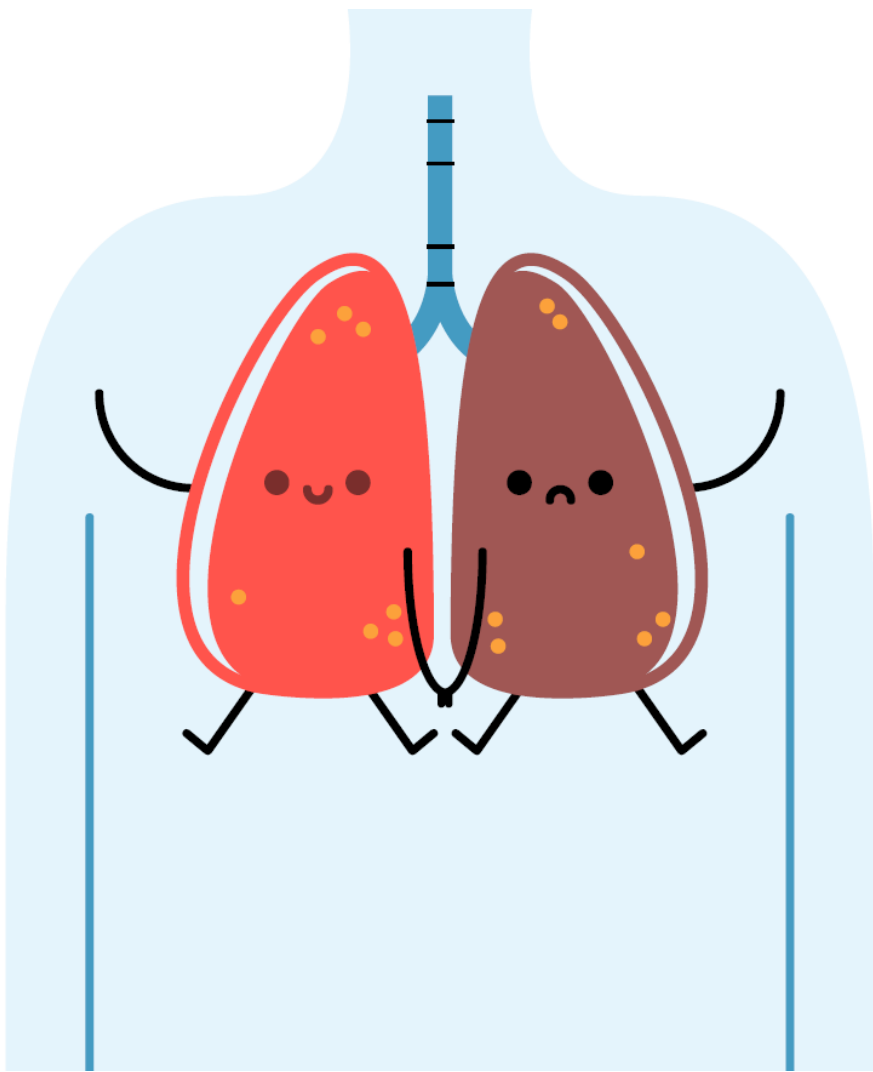


Test your knowledge

A 56 years hispanic woman diagnosed with COPD. She presented to the hospital with 1 exacerbation history **leading to the hospital**, Her mMRC questionnaire score is one, her CAT questionnaire score is 12. Based on the 2023 GOLD COPD classification, into what group would this patient fall?

- A. Category A
- B. Category B
- C. Category C
- D. Category D
- E. Category E





Complications of Progressive COPD



Pulmonary Hypertension (PH-COPD)

- May occur in up to 30% of patients
- Associated with increased mortality
- Therapy used in pulmonary hypertension provides conflictive results in PH-COPD
 - Endothelin receptor antagonist
 - Phosphodiesterase-5 Inhibitors
 - Prostacyclin analogues
 - Pulmonary vasodilators are not recommended in patients with PH-COPD



Cor Pulmonale

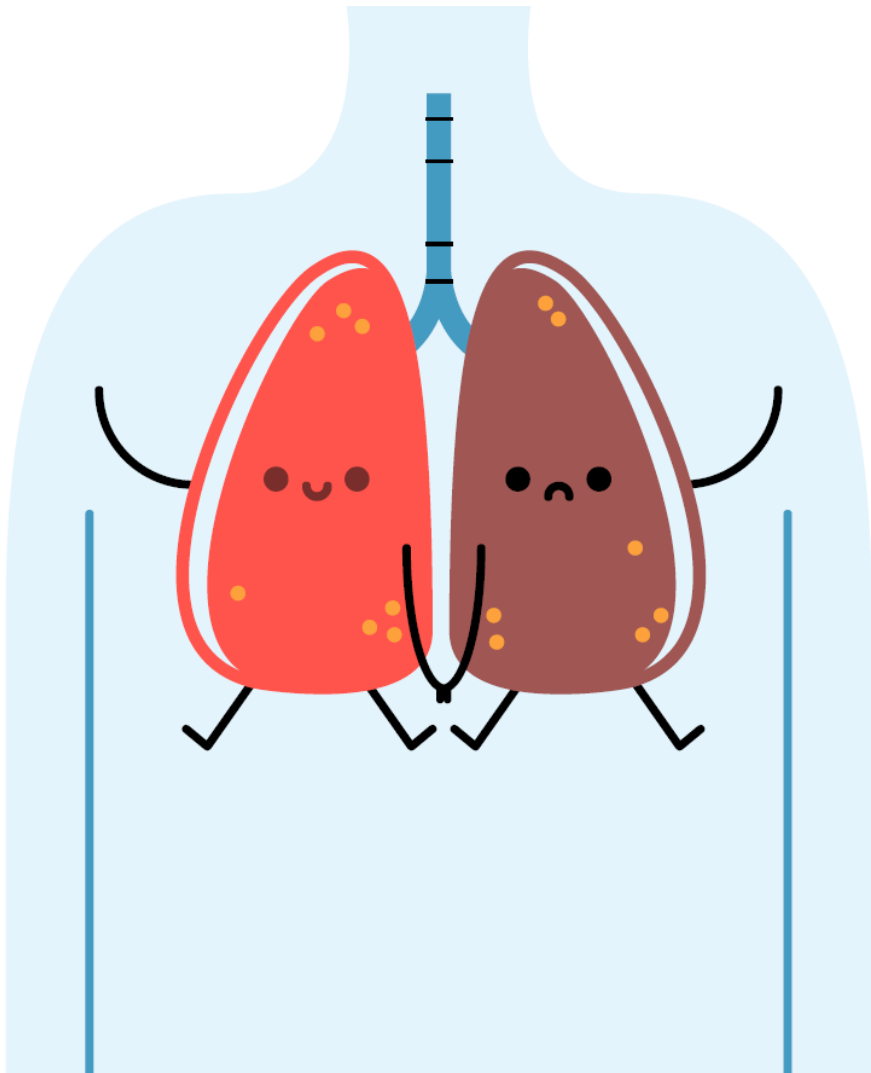
- Right-sided heart failure secondary to pulmonary hypertension
- Mainstay therapy is long-term oxygen and diuretics
- Cardiac glycosides have no role in cor pulmonale
- Beta blockers are indicated to treat systolic heart failure
 - Associated with improve overall survival

Complications of Progressive COPD



Polycythemia

- Secondary to chronic hypoxemia
- Can be improved by:
 - Continuous oxygen therapy
 - Periodic phlebotomy if oxygen therapy is not sufficient
 - Indicated if the hematocrit is above 55%-60% and patient is experiencing CNS effects



08
Desired
Outcomes

Desired Outcomes

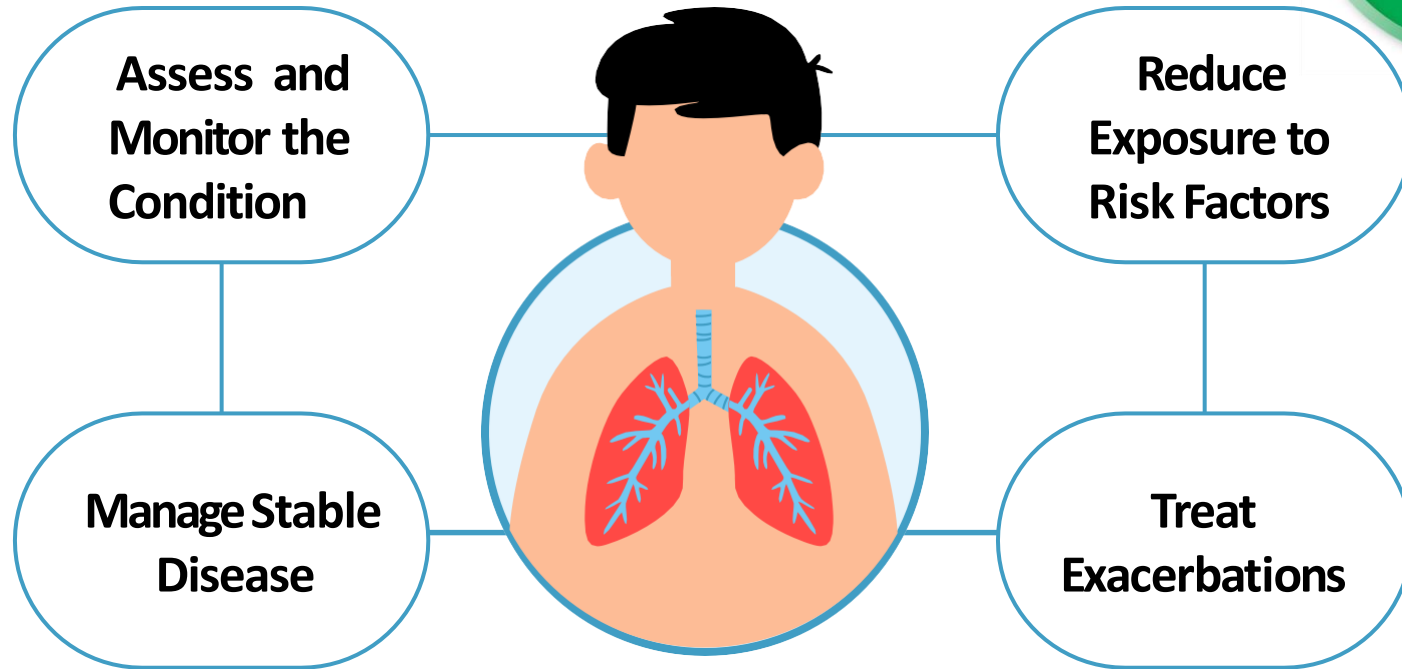
Prevention

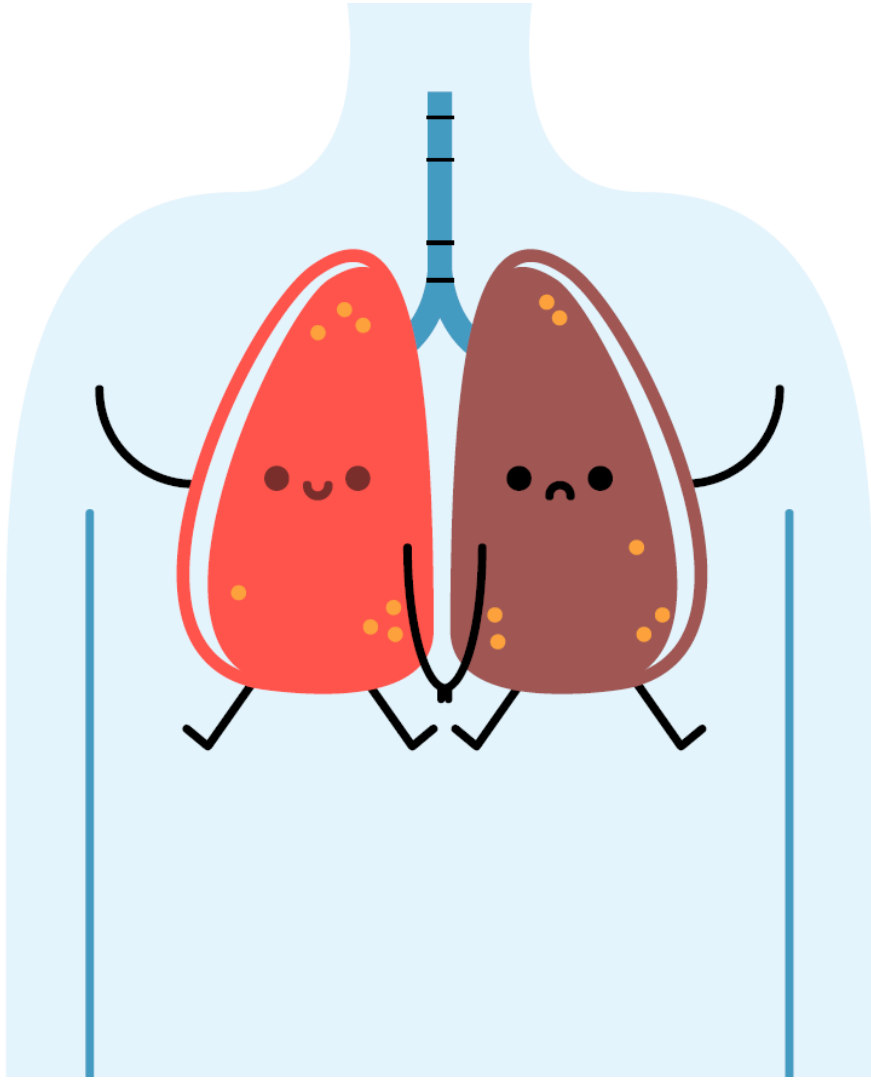
- Limiting or eliminating tobacco smoke
- Reduce environmental irritants

Management

- Prevent disease progression
- Relieve symptoms
- Improve exercise tolerance
- Improve overall health status
- Prevent and treat exacerbations
- Prevent and treat complications
- Reduce morbidity and mortality

General Approach to Treatment





09
Treatment:
Non-Pharmacologic

Non-Pharmacologic Therapy



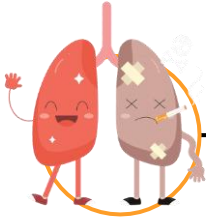
Smoking Cessation

- Single most important intervention in preventing development or progression of COPD
- Clinicians should be persistent in their motivational effort to determine the patient's readiness and support cessation attempts
- Leads to decreased symptomatology
- Slows rate of decline of pulmonary function

Five-step strategy for smoking cessation program (5 A's)

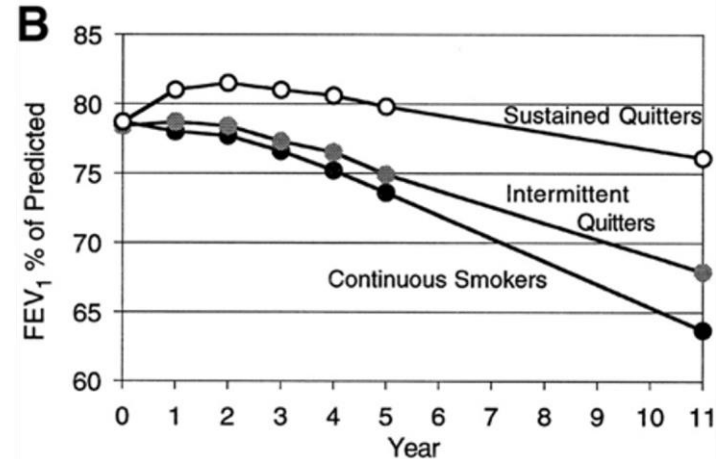
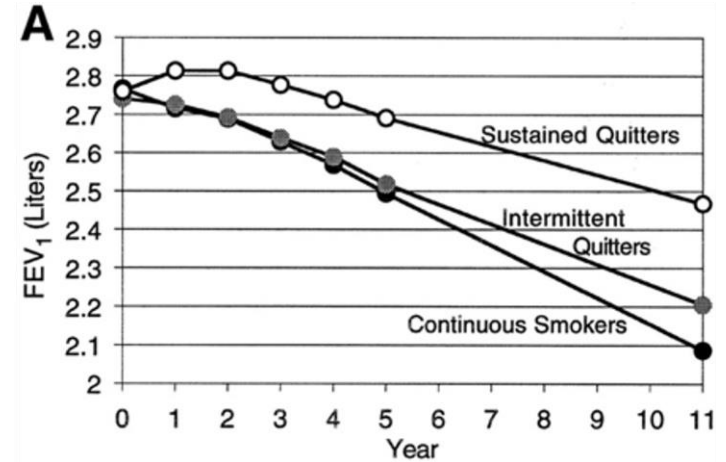
Ask	Identify all patients who use tobacco
Advice	Urge patients who use tobacco to quit
Assess	Determine willingness and motivation
Assist	Provide support for the patient to quit
Arrange	Follow-up and monitor abstinence

Non-Pharmacologic Therapy



Lung Health Study

- 5-year prospective trial
- Smokers with early COPD were randomly assigned to 3 groups:
 - Smoking cessation intervention+ inhaled ipratropium TID
 - Smoking cessation alone
 - No intervention
- 11-year follow-up revealed a rate of decline in FEV₁ in subject who continued to smoke was more than twice the rate of sustained quitters



Non-Pharmacologic Therapy



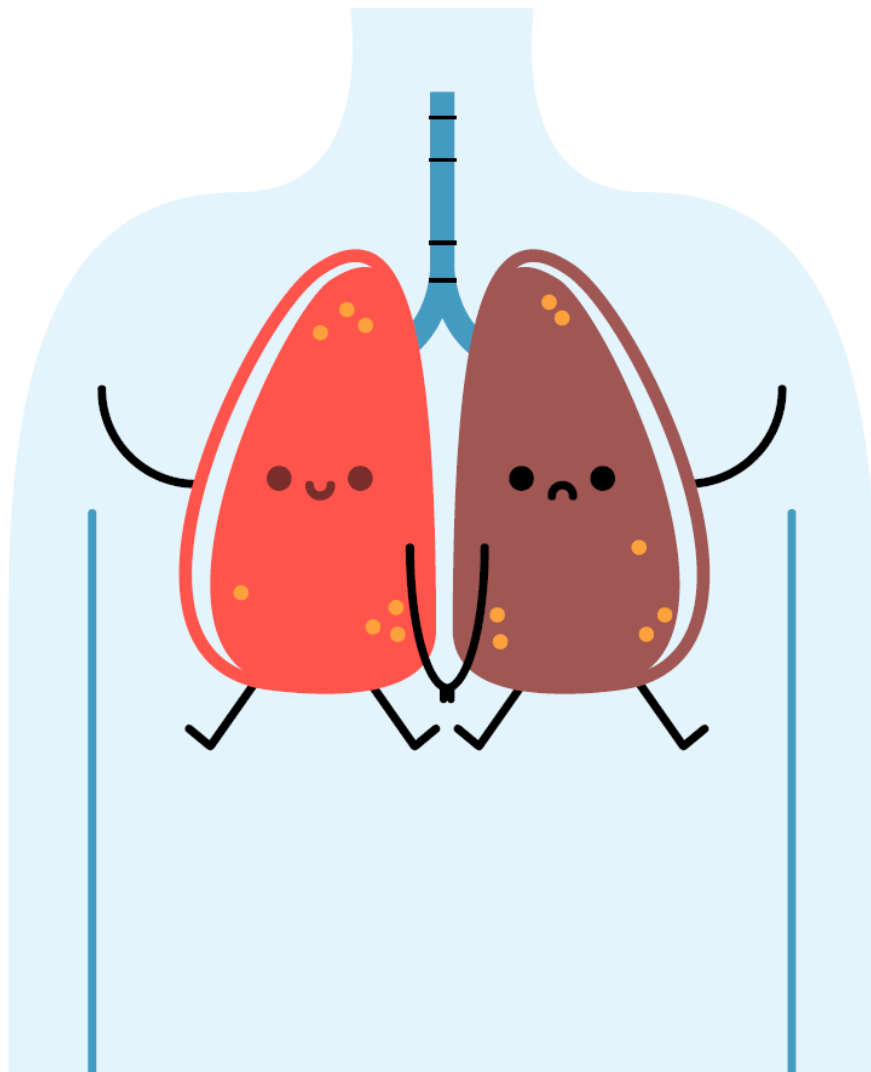
Long-Term Oxygen Therapy

- Supplemental oxygen increases survival in COPD patients with hypoxemia at rest
- Survival benefits are seen after 5 years of use
- Increased walking distance
- Improvement in neuropsychological conditions
- Reduced length of stay (LOS)



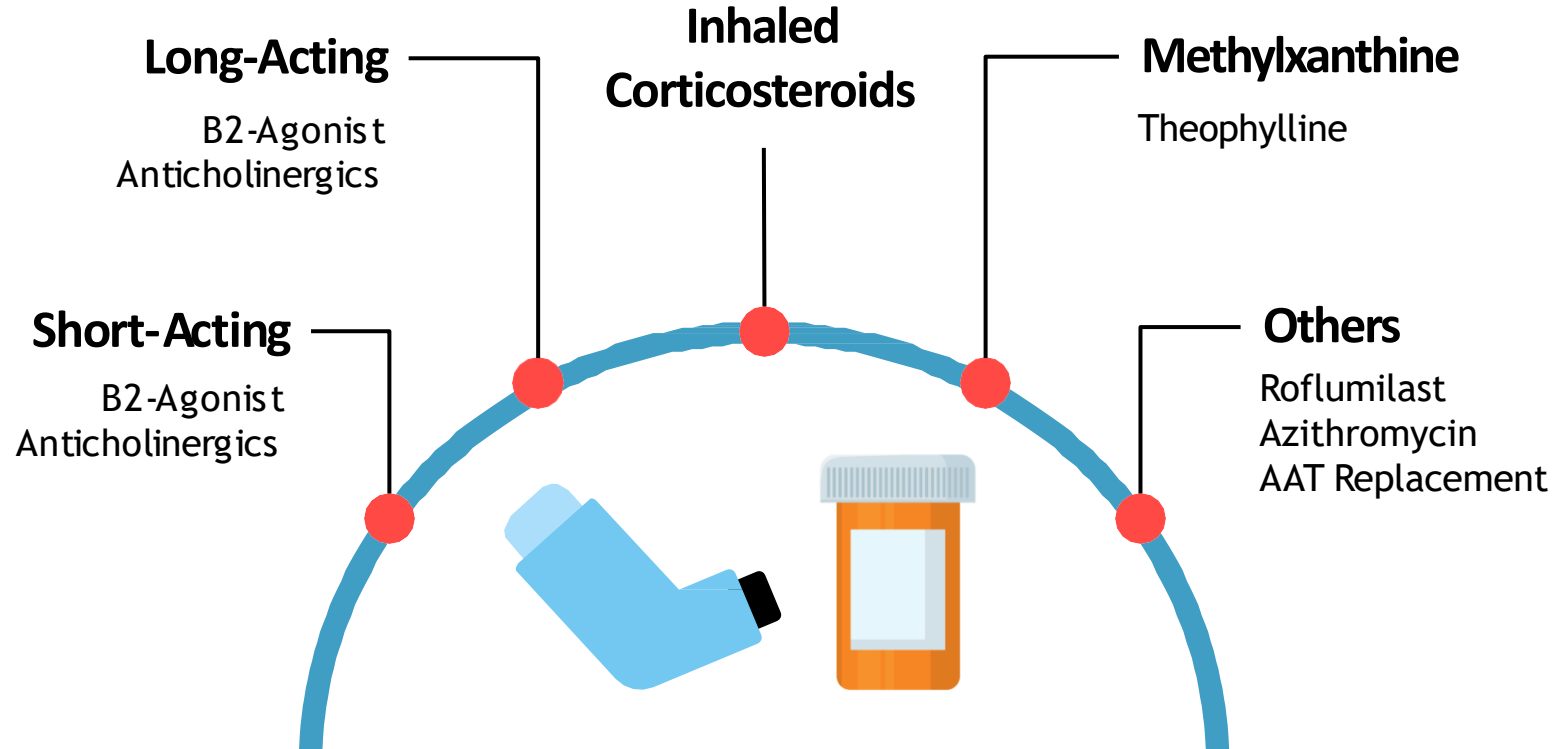
Vaccination

- Vaccines reduce the risk of respiratory infections that could lead to an exacerbation
 - Influenza
 - Pneumococcal infection
 - COVID-19
 - Tdap
 - Zoster



10
Treatment:
Pharmacologic

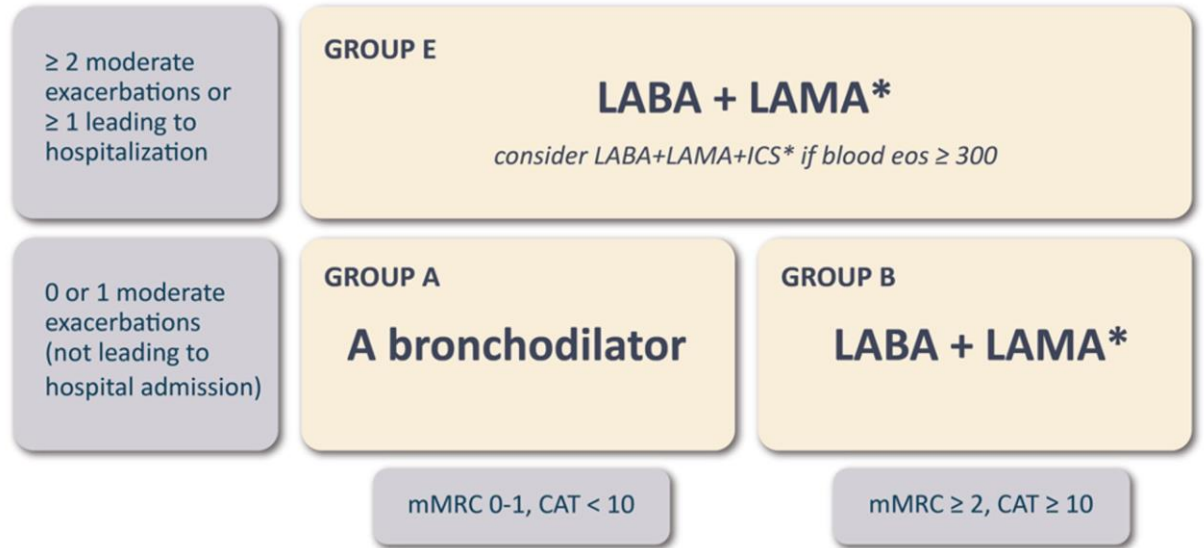
Efeito nos Brônquios



Pharmacologic Therapy

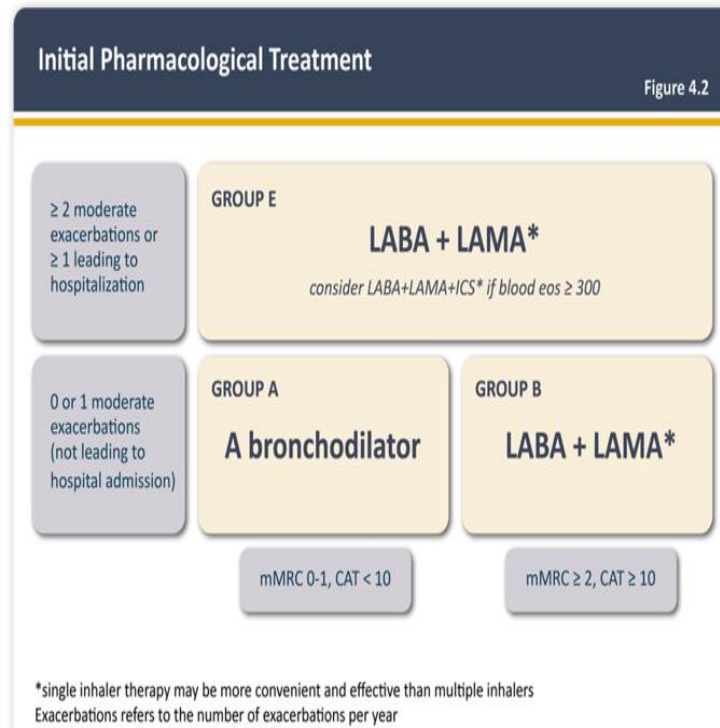
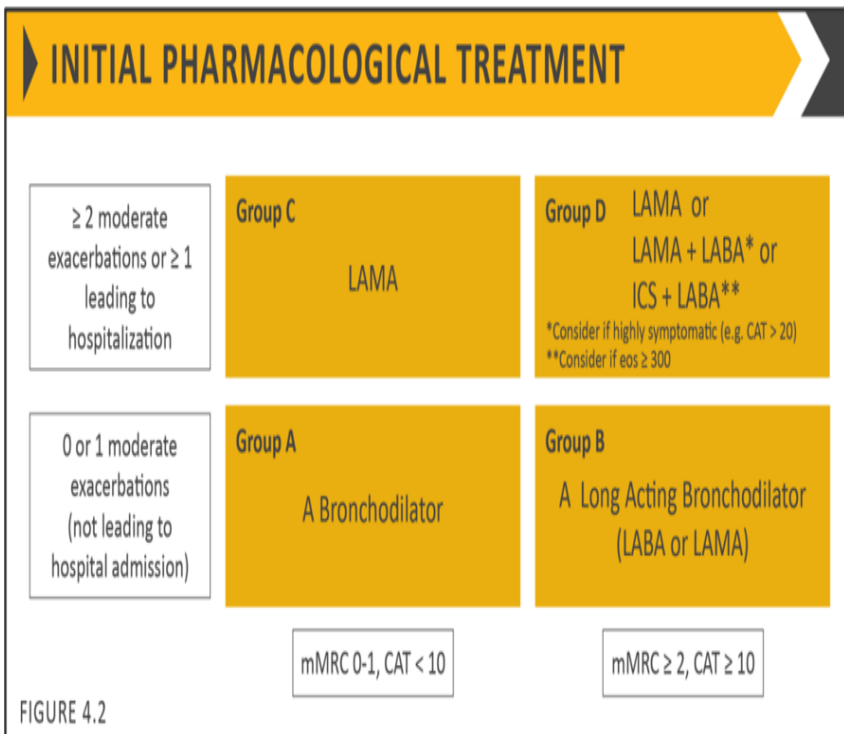
Initial Pharmacological Treatment

Figure 4.2



*single inhaler therapy may be more convenient and effective than multiple inhalers
Exacerbations refers to the number of exacerbations per year

GOLD 2022 vs GOLD 2023



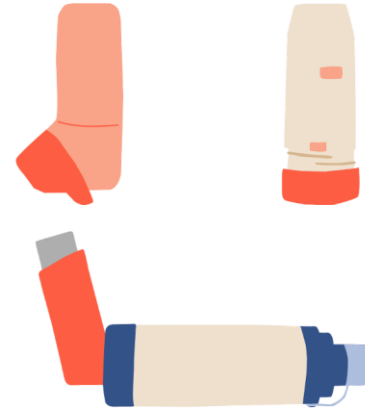
Pharmacologic Therapy



Inhaled Medications

- Requires patient knowledge and skill
- Various inhalation devices
- MDI, DPI, SMI and nebulizers
- There is no advantage of one delivery system over another
- Periodic and frequent observation by clinician is required to assess optimal use

“Pharmacist should assess patient’s administration inhaler technique before recommending a change in COPD therapy”



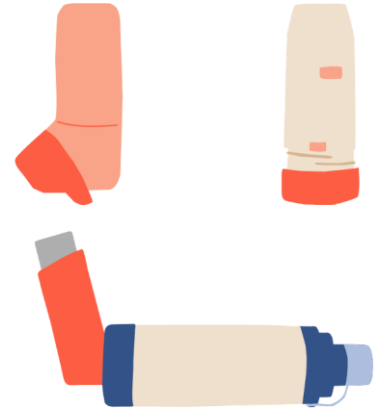
“Treatment of multiple inhalation devices adds complexity and may adversely impact adherence and disease management”

Pharmacologic Therapy



Inhaled Medications

- To increase adherence:
 - Share decision making, between the patient and the health professional, when selecting an inhaler.
 - Provide pick-up reminders.
 - Provide education of the disease, medication devices, techniques of inhalation, prevention factors.
 - Emphasized the importance of adherence.
 - Maintain good communication with the patient.



Pharmacologic Therapy - Bronchodilators

Short-Acting

- Initial recommended therapy for COPD patients who experience **occasional symptoms**
- Recommended for rescue or as-needed
- Choices include short-acting B₂-agonist and anticholinergic agents
- Combination of short-acting agents is reasonable for patients who do not achieve symptom control

Long-Acting

- For patients who experience **persistent symptoms** or in whom **short-acting therapies do not provide adequate relief**
- Are recommended as initial therapy in Group B and E
- Choices include LABA and LAMA
- LAMA appear to be more effective in preventing exacerbations but in regards of symptom control, both are equally effective

Pharmacologic Therapy - Short-Acting B_2 -Agonists

Pharmacological Effect

- Cause bronchodilation by increasing cyclic adenosine monophosphate (cAMP), which is responsible for relaxation of bronchial smooth muscle
- May also improve mucociliary clearance within the airways
- Improve respiratory symptoms and exercise tolerance

Adverse Effects

- Generally, well tolerated
- Older patients may be more predisposed to adverse effects



**Sinus Tachycardia and
Rhythm Disturbances**



Skeletal Muscle Tremors

Pharmacologic Therapy - Short-Acting B_2 -Agonists

Albuterol (Salbutamol)

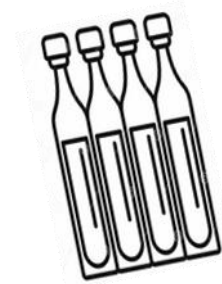
MDI, DPI, Pill, Syrup, ER Tablets,
Nebulizer, and Injection



Levalbuterol

MDI

Nebulizer



Pharmacologic Therapy - Short-Acting **Anticholinergics**

Pharmacological Effect

- Competitive inhibition of muscarinic receptor produces bronchodilation in bronchial smooth muscle and mucus glands
- Similar improvement in pulmonary function compared to B_2 -agonists
- Slow onset of action compared to B_2 -agonists

Adverse Effects

- Lack systemic absorption, which greatly diminishes anticholinergic adverse effects



Dry Mouth



Nausea

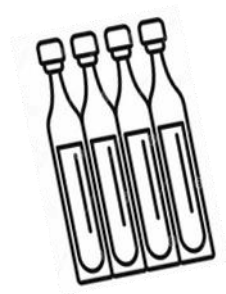
Pharmacologic Therapy - Short-Acting Anticholinergics

Ipratropium

MDI



Nebulizer



Pharmacologic Therapy - Long-Acting B_2 -Agonists

Benefits

- Compared to SABAs, LABAs provide superior improvement in:
 - Lung function
 - Symptoms
 - Exacerbation rate
- Better alternative when patient require short-acting B_2 -agonist on schedule basis
- LABA monotherapy in COPD is not associated with increased mortality as opposed to asthma

Available Agents

- Salmeterol
- Formoterol
- Vilanterol (Only available co-formulated)
- Olodaterol

**None are recommended
for acute relief of symptoms in COPD**

Pharmacologic Therapy - Long-Acting B_2 -Agonists

Salmeterol

MDI



DPI



Olodaterol

SMI(Soft Mist Inhaler)



Pharmacologic Therapy - Long-Acting **Anticholinergics**

Benefits

- More selective than ipratropium for M3 receptors
- They dissociate slowly from receptor, resulting in prolonged bronchodilation
- Once or twice daily dosing
- LAMA provide greater reduction in exacerbation frequency compared to LABAs (primarily tiotropium)
- Should be considered as first-line monotherapy for patients at high risk of exacerbation

Available Agents

- Tiotropium
- Glycopyrrolate
- Aclidinium
- Umeclidinium

**None are recommended
for acute relief of symptoms in COPD**

Pharmacologic Therapy - Long-Acting **Anticholinergics**

Tiotropium

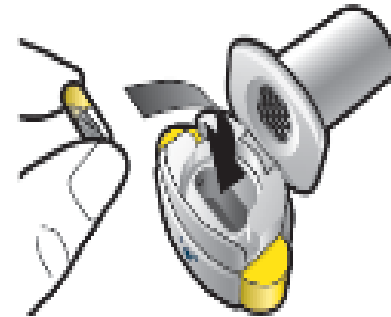
DPI

SMI



Glycopyrrolate

DPI



Pharmacologic Therapy - Long-Acting **Anticholinergics**

Aclidinium

DPI



Umeclidinium

DPI



Pharmacologic Therapy - Bronchodilators **Combinations**

Benefits

- Used in the treatment of COPD as symptoms worsen over time
- Bronchodilators with different mechanisms of action allows the lowest possible effective doses to be used and reduces potential adverse effects from individual agents

Short-Acting

- May preferred for patients experiencing persistent symptoms
 - Although step-up to long-acting bronchodilator monotherapy is usually preferred

Long-Acting

- Persistent symptoms
- Recurrent exacerbations on bronchodilator monotherapy

Pharmacologic Therapy - Short-Acting **Combinations**

SABA/SAMA: Albuterol/Ipratropium bromide

SMI



MDI



Pharmacologic Therapy - Long-Acting Combinations

Formoterol/Aclidinium

DPI



Formoterol/Glycopyrrolate

MDI



Pharmacologic Therapy - Long-Acting Combinations

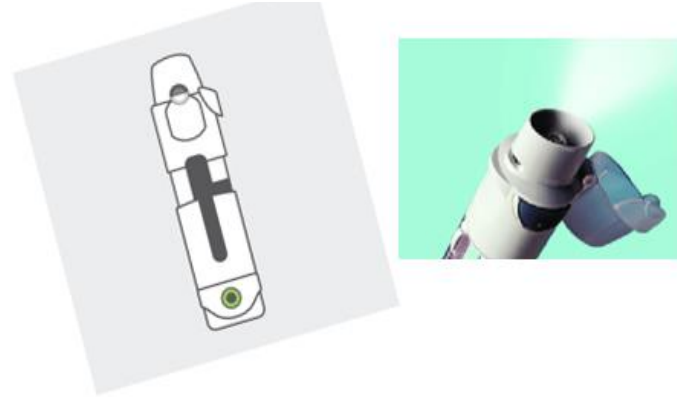
Vilanterol/Umeclidium

DPI



SMI: Olodaterol/Tiotropium

SMI



Pharmacologic Therapy - **Inhaled Corticosteroids**

Pharmacological Effect

- Anti-inflammatory mechanisms whereby corticosteroids exert their beneficial effect in COPD include:
 - Reduction in capillary permeability to decrease mucus
 - Inhibition of release of proteolytic enzymes from leukocytes
 - Inhibition of prostaglandins

Available Agents

- Beclomethasone
- Fluticasone
- Mometasone
- Budesonide

Systemic Corticosteroids should be avoided as chronic therapy in COPD

Pharmacologic Therapy - Inhaled Corticosteroids

Benefits

- Considered in patients with COPD with high risk of exacerbation (category E):
 - Decrease in exacerbation frequency
 - Time to first exacerbation
- **Recommended for:**
 - **Initial therapy** in patients at high risk of exacerbations with blood eosinophil count ≥ 300 cells/ μ L
 - **Escalation therapy** in patients with recurrent exacerbations despite optimal therapy

ICS Monotherapy is not recommended

Adverse effects



Risk of Pneumonia and Mycobacterial Infections

- Risk factors include:
 - Age >55 years
 - BMI $<$ than 25 kg/m^2
 - Current smoker
 - History of exacerbation or pneumonia (last 12 months)



Risk of Fractures

Pharmacologic Therapy - ICS/LABA Combinations

Fluticasone / Salmeterol

MDI



DPI



Fluticasone / Vilanterol

DPI



Pharmacologic Therapy - ICS/LABA Combinations

**Mometasone /
Formoterol**

MDI



Budesonide / Formoterol

MDI

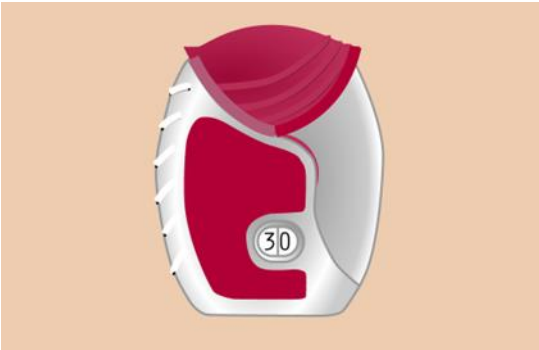


Pharmacologic Therapy - Triple Combinations

ICS + LABA + LAMA

Fluticasone / Vilanterol /
Umeclidinium

DPI



Budesonide / Formoterol /
Glycopyrrolate

MDI



Test your knowledge

Which of the following pharmacotherapy strategies is recommended for a patient newly diagnosed with Gold stage 1, category A COPD?

- A. Start an inhaled corticosteroid
- B. Start an inhaled bronchodilator
- C. Start an oral leukotriene modifier
- D. Start supplemental oxygen

Test your knowledge

Which of the following is a risk associated with inhaled corticosteroid use for the treatment of COPD?

- A. Increased mortality
- B. Leukopenia
- C. Lupus
- D. Pneumonia

Pharmacologic Therapy - Methylxanthines



Pharmacological Effect

- Methylxanthines produce bronchodilation through numerous mechanisms, including:
 - Inhibition of phosphodiesterase → increasing cAMP levels
 - Inhibition of calcium ion influx into smooth muscles
 - Prostaglandin antagonism
 - Stimulation of endogenous catecholamines
 - Adenosine receptor antagonism
 - Inhibition of release of mediators from mast cells and leukocytes



Available Agents

- Theophylline
- Sustained release preparations are the most appropriate for long term management

Pharmacologic Therapy - Methylxanthines

Current Use

- Chronic theophylline use for patients with COPD may offer improvements in lung function and gas exchange
 - Reduce dyspnea
 - Increase exercise tolerance
- Generally considered for patients who are intolerant or unable to use bronchodilators

Disadvantages

- It's a challenging medication to add in COPD therapy because:
 - Dosing challenges
 - Monitoring requirements
 - Interpatient variability in pharmacokinetics
 - Potential drug interactions
 - Risk of toxicities

Pharmacologic Therapy - **Phosphodiesterase 4 Inhibitors**

Pharmacological Effect

- Inhibition of PDE4 results in:
 - Relaxation of airway smooth muscle cells
 - Diminished inflammatory mediators such as TNF- α and IL-8

Available Agents

- Roflumilast

Clinical Use

- Recommended for patients with:
 - Recurrent exacerbations despite treatment with triple inhalation therapy
 - Recurrent exacerbation on dual long-acting bronchodilators (LABA/LAMA) who are not candidate for ICS

**Cannot be used
in combination with Theophylline**

Pharmacologic Therapy - **Phosphodiesterase 4 Inhibitors**

Adverse Effects

Bothersome adverse effects that may limit therapy



Diarrhea



Weight loss



Neuropsychiatric Effects

Interactions

- Metabolized by CYP3A4 and 1A2
- Coadministration with strong inducers of inhibitors cytochrome P450 is not recommended

Pharmacologic Therapy - Antibiotics

Azithromycin

- Has proven clinical benefit in certain pulmonary conditions due to their anti-inflammatory and antimicrobial properties
- Can be added to therapy for 12 months for patients with recurrent exacerbations despite optimal therapy and who are not active smokers

Active smokers are not candidates for chronic azithromycin treatment

Adverse Effects

Colonization with macrolide-resistant bacteria



Hearing deficits



QT Prolongation



- Increases the risk of cardiac events

Pharmacologic Therapy - α_1 -Antitrypsin Replacement

Clinical Use

- For patients with inherited AAT deficiency (AATD)-associated emphysema
- Referred as augmentation therapy
 - Weekly infusions of pooled human AAT
- Treatment also focuses on:
 - Reducing risk factors such as smoking
 - Symptom management with bronchodilators

**Augmentation Therapy
can cost over \$50,000 annually**

Pharmacologic Therapy – New Product in the Future ...

IL-5 medications

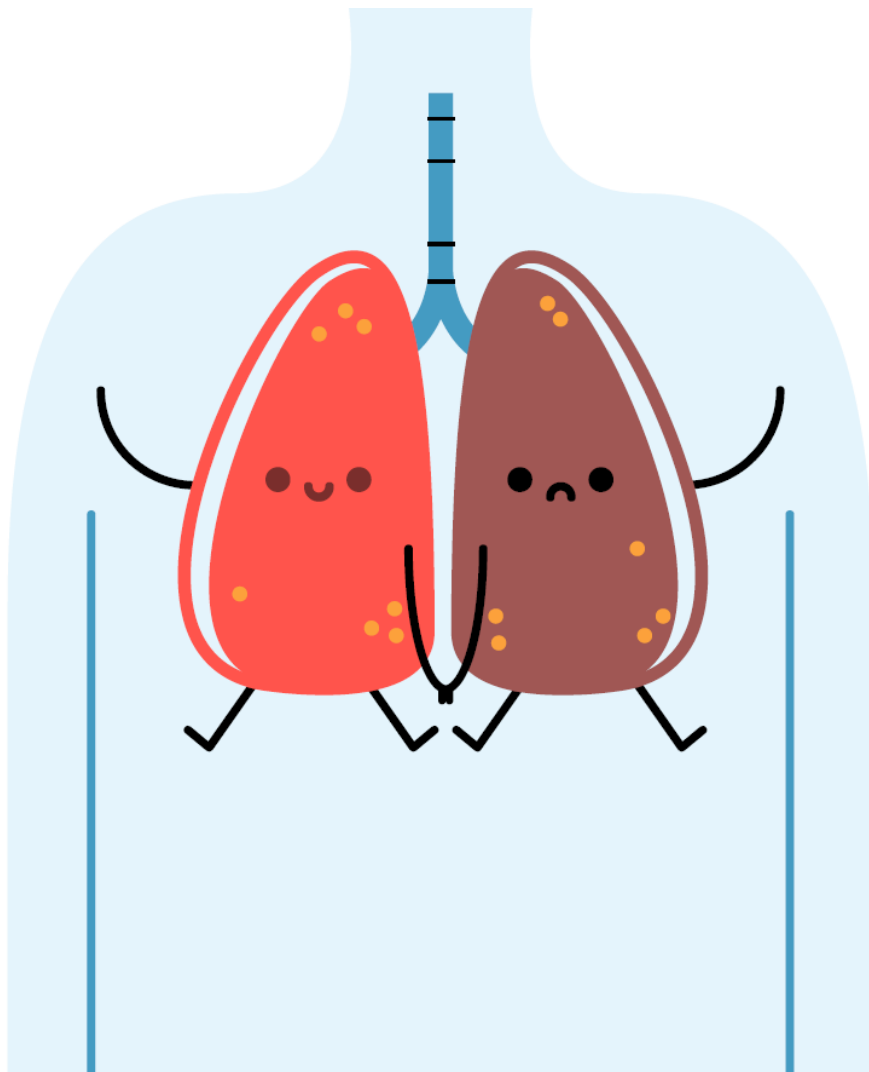
COPD can result from several different mechanisms. Newer treatments aim to target those specific causes in order to eliminate them and stop inflammation.

For example, some people with COPD have many eosinophils, a specific type of white blood cell. A drug called anti-interleukin-5 (IL-5) targets airway inflammation caused by eosinophils. But more research is needed.

Stem cell therapy

Clinical trials are also evaluating the use of stem cell therapy for the treatment of COPD. Stem cells are undifferentiated cells that are fed into the body.

Once they're injected, they then become specialized to a specific need – in this case, regenerating lung tissue and reversing lung damage (could be used to create new alveolar cells)



11

Acute Exacerbation

Exacerbation of Chronic Obstructive Pulmonary Disease (ECOPD)

- GOLD - An exacerbation of chronic obstructive pulmonary disease is defined as an **event** characterized by **increased dyspnea** and/or **cough** and **sputum** that **worsens in < 14 days** which may be accompanied by tachypnea and/or tachycardia and is often associated with increased local and systemic inflammation caused by infection, pollution, or other insult to the airways
- Exacerbations have a significant impact on the natural course of COPD and occur more frequently in patients with
 - Advanced age
 - Significant airflow limitation
 - Comorbid conditions



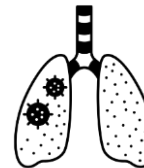
Signs and Symptoms of ECOPD

Signs

- Fever
- Wheezing

Symptoms

- Increased sputum volume
 - May be purulent
- Acutely worsening dyspnea
- Chest tightness
- Malaise, fatigue

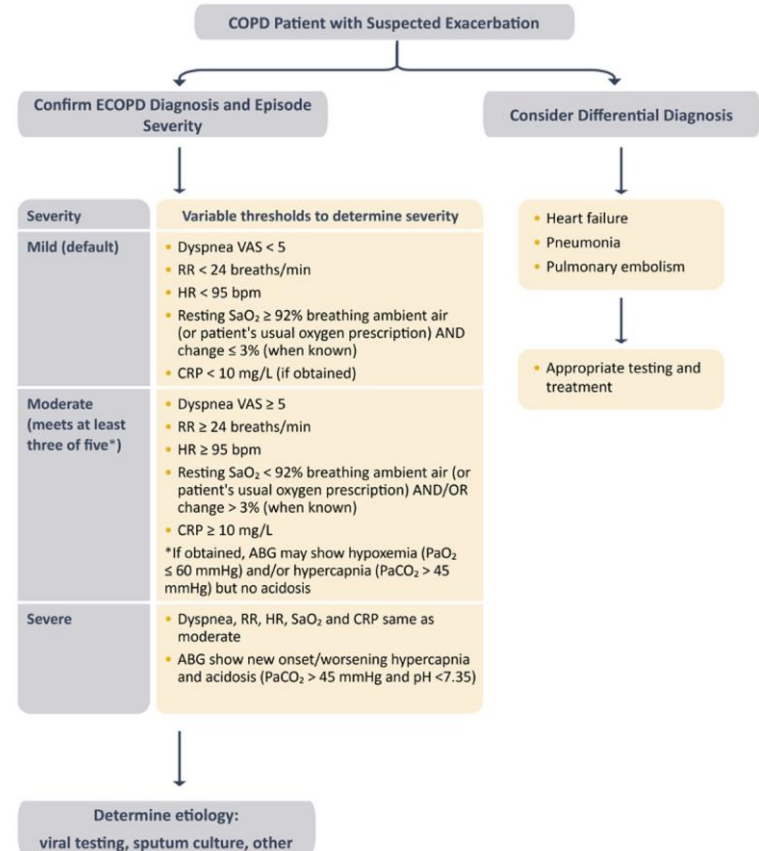


Diagnosis

- Patients with COPD are at increased risk of other acute events that may also mimic or aggravate ECOPD, particularly:
 - Decompensated heart failure
 - Pneumonia
 - Pulmonary embolism
- Severity of symptoms should be established using visual analogue dyspnea scale (VAS)
- Establishing the cause of exacerbation will help guide further treatment
 - Viral
 - Bacterial
 - Environmental

Classification of the Severity of COPD Exacerbations

Figure 5.1



Complications

Acute Respiratory Failure

- ABG usually is obtained to assess the severity of an exacerbation
- The diagnosis of acute respiratory failure in COPD is made based on an acute change in the ABGs
- Clinical manifestations of respiratory failure include:
 - Confusion
 - Tachycardia
 - Cyanosis
 - Hypotension
 - Irregular breathing
 - Unconsciousness

Severity

Mild (default)

Moderate
(meets at least
three of five*)

Severe

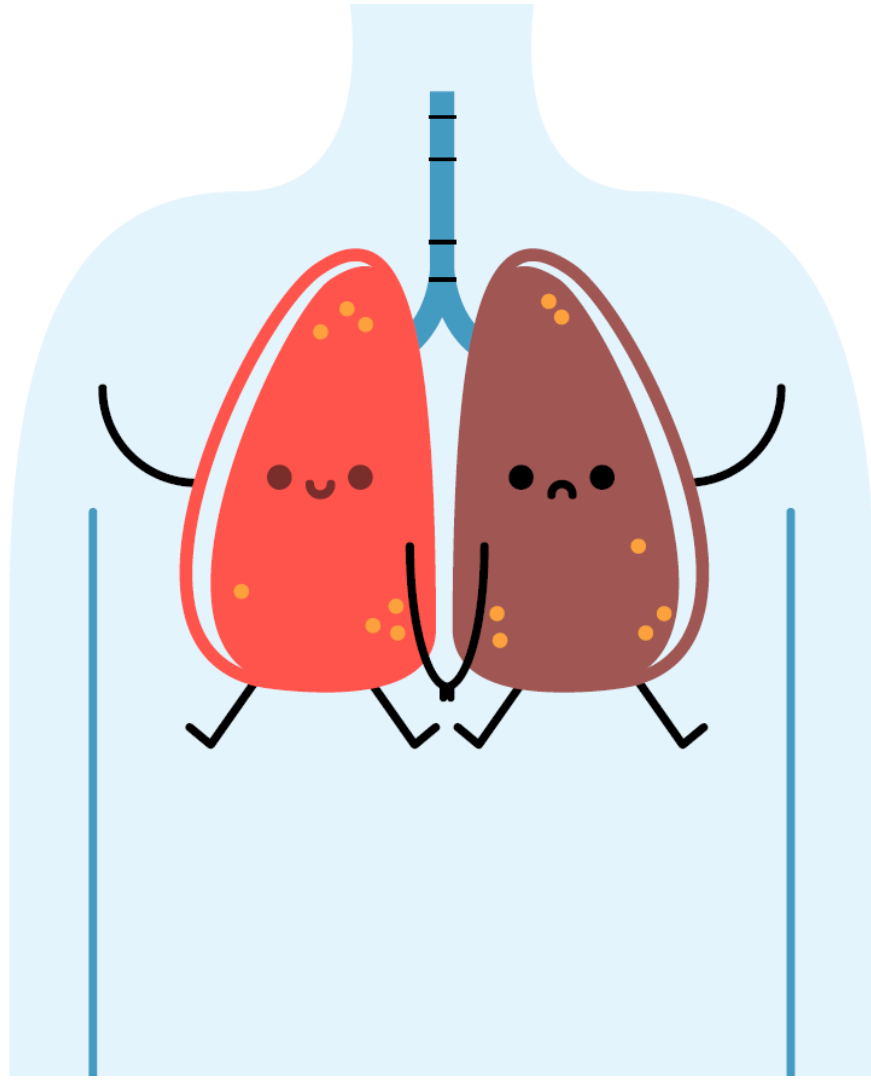
No Respiratory Failure

**Non-Life-Threatening
Respiratory Failure**

**Life-Threatening
Respiratory Failure**

Prognosis

- Mortality rates are higher for patients admitted to the hospital
 - Higher rates among those admitted to ICU
 - COPD exacerbations contribute to in-hospital mortality, deaths after discharge, and the decline of lung function
- Many patients do not return to their baseline status for several weeks after an ECOPD
- 50% of patients hospitalized for an exacerbation are readmitted within 6 months
 - Risk factors for readmission include:
 - FEV1 less than 50% of predicted
 - The severity of exacerbation
 - Previous exacerbation frequency
 - Presence of comorbidities
 - Inadequate antibiotic therapy



12
Treatment:
ECOPD

Desired Outcomes

Minimize Negative Consequences of ECOPD

- Reduce symptoms
- Prevent hospitalization
- Shorten hospital stay
- Prevent acute respiratory failure
- Prevent death

Prevent Future Exacerbations

Treatment - Non-pharmacologic

Noninvasive positive-pressure ventilation

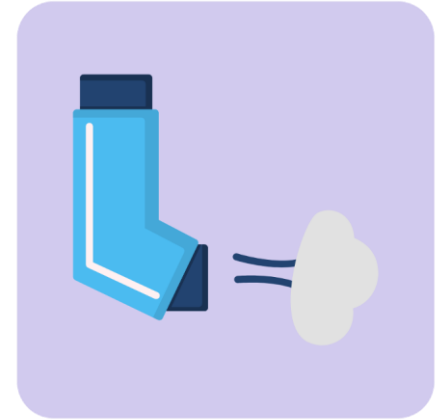
- NPPV provides ventilatory support with oxygen and pressurized airflow using a face or nasal mask with a tight seal **but without endotracheal intubation**
- NPPV has been associated with
 - Lower mortality
 - Lower intubation rates
 - Shorter hospital stays for COPD exacerbations
- Patients with severe acidosis ($\text{pH} < 7.25$) or respiratory arrest **should not be considered for NPPV**
- Patients who fail a trial of NPPV should be considered for intubation and mechanical ventilation



Treatment - Pharmacologic

Bronchodilators

- SABAs are preferred for their rapid onset
 - Doses and frequency are increased to achieve symptomatic relief
- Anticholinergics are added if SABA does not achieve sufficient symptomatic relief
- There is no difference in FEV₁ between MDI or Nebulization
 - Nebulization is preferred in most cases based given it's ease of delivery
- Theophylline should be avoided due to concern of adverse effects



**Baseline treatment must
not be discontinued
during Exacerbation**

Treatment - Pharmacologic

Antibiotics

- Bacterial infections cause most ECOPD
- Their use remain controversial

Indicated in 3 Scenarios

Patients with 3 cardinal symptoms

- Dyspnea, sputum volume, and sputum purulence

Patients with 2 cardinal symptoms

- One of them has to be increases purulent sputum

Patients requiring mechanical ventilation

- Invasive or noninvasive

Days of Therapy

- Therapy with antibiotics generally should be continued for at least 5 to 7 days

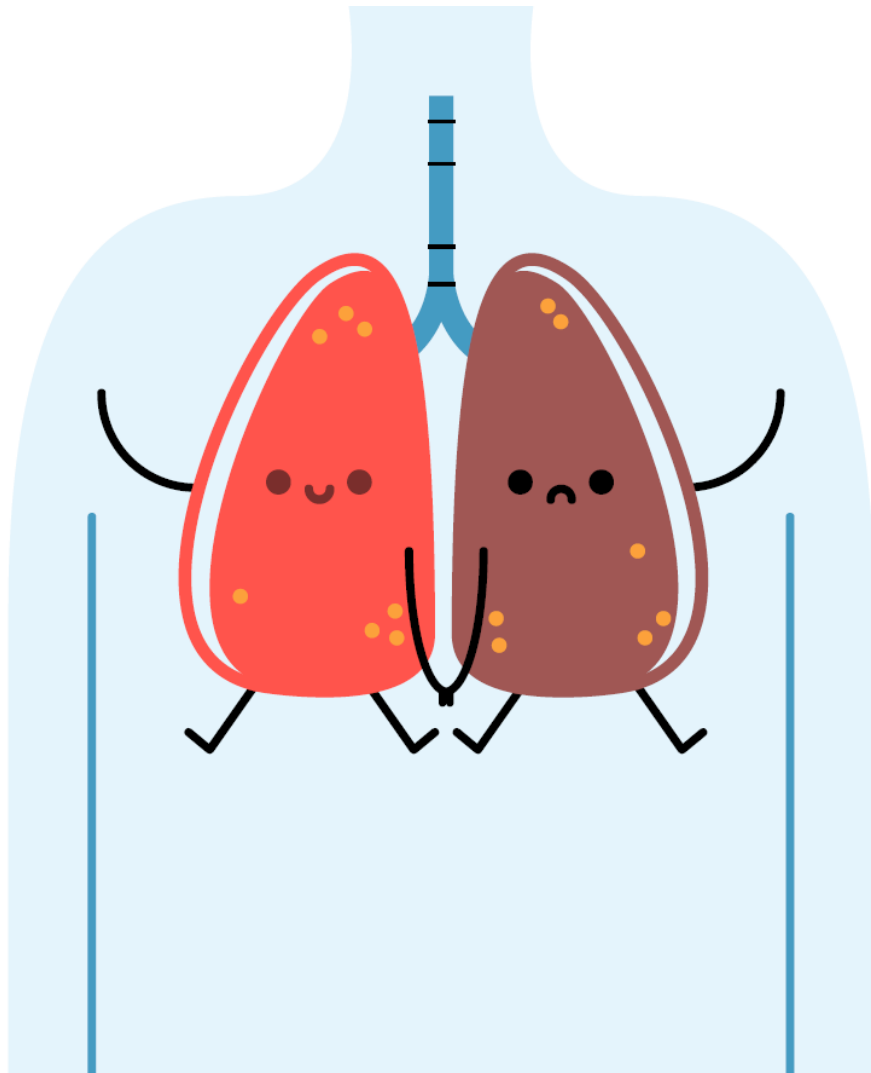


Patient Characteristic	Likely pathogens	Recommended Therapy
Uncomplicated exacerbations: <ul style="list-style-type: none"> • <4 exacerbations per year • No comorbid illness 	H. influenzae M. catarrhalis S. pneumoniae H. parainfluenzae	Azithromycin Second- and third-generation cephalosporins Doxycycline
Complicated exacerbations: <ul style="list-style-type: none"> • Age ≥ 65 and >4 exacerbations per year • Presence of comorbid illness 	Above pathogens plus: Penicillin-resistant S. pneumoniae β -lactamase producing H. influenzae β -lactamase producing M. catarrhalis	Amoxicillin/Clavulanate Respiratory fluoroquinolones
Risk factors for multidrug-resistant pathogens <ul style="list-style-type: none"> • Chronic corticosteroid therapy • Recent hospitalization (90 days) • Recent antibiotic treatment (90 days) • Resident of long-term care facility 	Above pathogens plus: Some enteric gram negative bacteria and P. aeruginosa	IV therapy may be required: Levofloxacin Piperacillin-Tazobactam Ceftazidime Cefepime

Test your knowledge

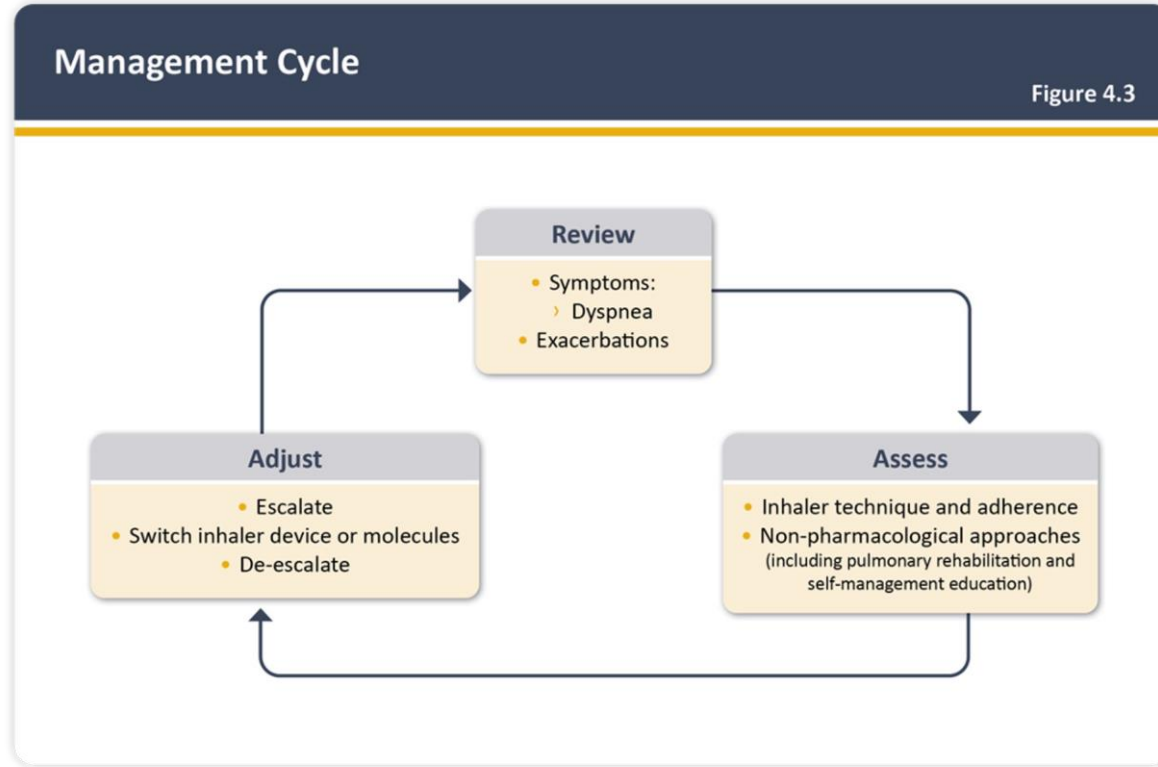
Which of the following medication classes is utilized in the treatment of an acute exacerbation of COPD?

- A. Short-acting beta-agonists
- B. Long-acting beta-agonists
- C. Inhaled corticosteroids
- D. Long-acting muscarinic antagonists



13
Follow-up

Follow-Up



Follow-Up

Dyspnea

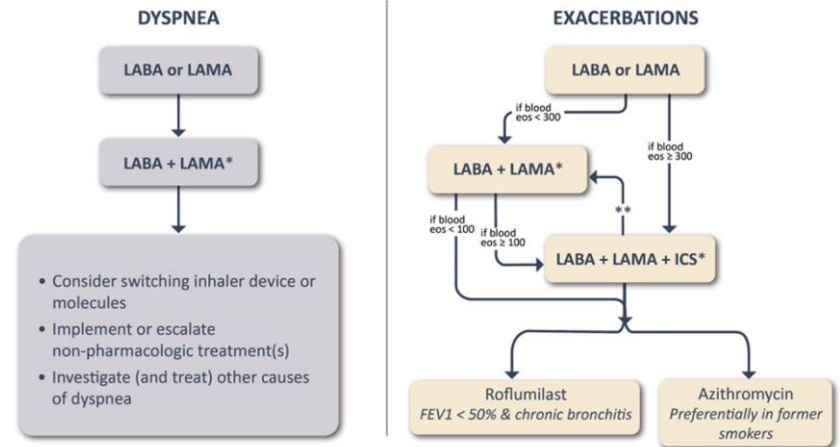
- Follow up can be applied to any patient who is in maintenance treatment irrespective of their GOLD group allocation
- Patients experiencing persistent breathlessness on bronchodilator monotherapy should be switched to two long-acting bronchodilators
 - If second agent provides not improvement a change of inhaler or molecule may be warranted

Follow-up Pharmacological Treatment

Figure 4.4

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

**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

Follow-Up

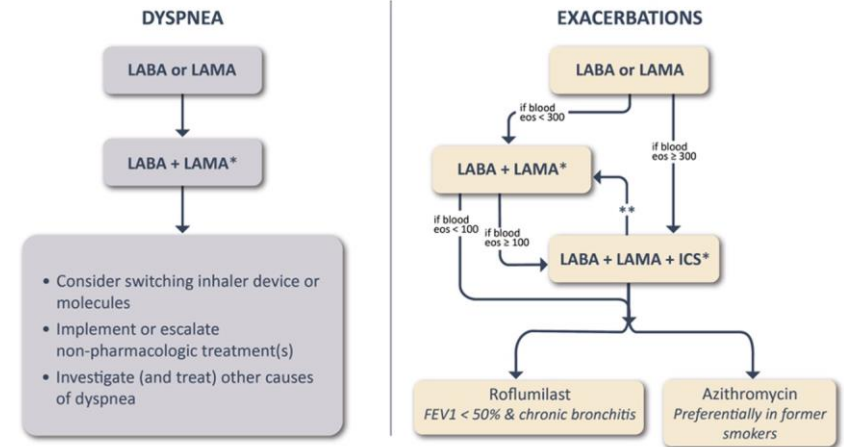
Exacerbations

- Patient should receive an education of new treatment or current treatment before discharge
- Post-discharge follow-up should be made to reinforce patient education and adherence
- Follow-up in 1-4 weeks have been associated reduction in readmission due to ECOPD
 - Lack of discharge follow-up increases 90-day mortality

Follow-up Pharmacological Treatment

Figure 4.4

- 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

**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

Follow up - Inhaled Corticosteroids

Withdrawing ICS Therapy

- Recently clinicians have advocated for withdrawing ICS therapy in selected patients
- ICS may be withdrawn from therapy if there is concern for respiratory infections or adverse effects



Recommend ICS Withdrawal

1	Patients with no clear guideline-based indication
2	Patients experiencing adverse effects with ICS therapy and limited therapeutic benefit
3	Patients experiencing no perceived therapeutic benefit with ICS
4	Blood eosinophils less than 100 cells/ μ L

Test your knowledge

Which of the following genetic factors is a risk for developing COPD?

- A. Poor metabolizer status for cytochrome 3A4
- B. G6PD enzyme deficiency
- C. Atopic phenotype
- D. Alpha-1 antitrypsin deficiency

Test your knowledge

Which of the following is recommended for a patient who continues to experience symptoms of COPD despite treatment with a single long-acting bronchodilator therapy?

- A. Add a scheduled short-acting bronchodilator agent
- B. Add an inhaled corticosteroid
- C. Add another long-acting bronchodilator
- D. Add a chronic anti-inflammatory such as azithromycin



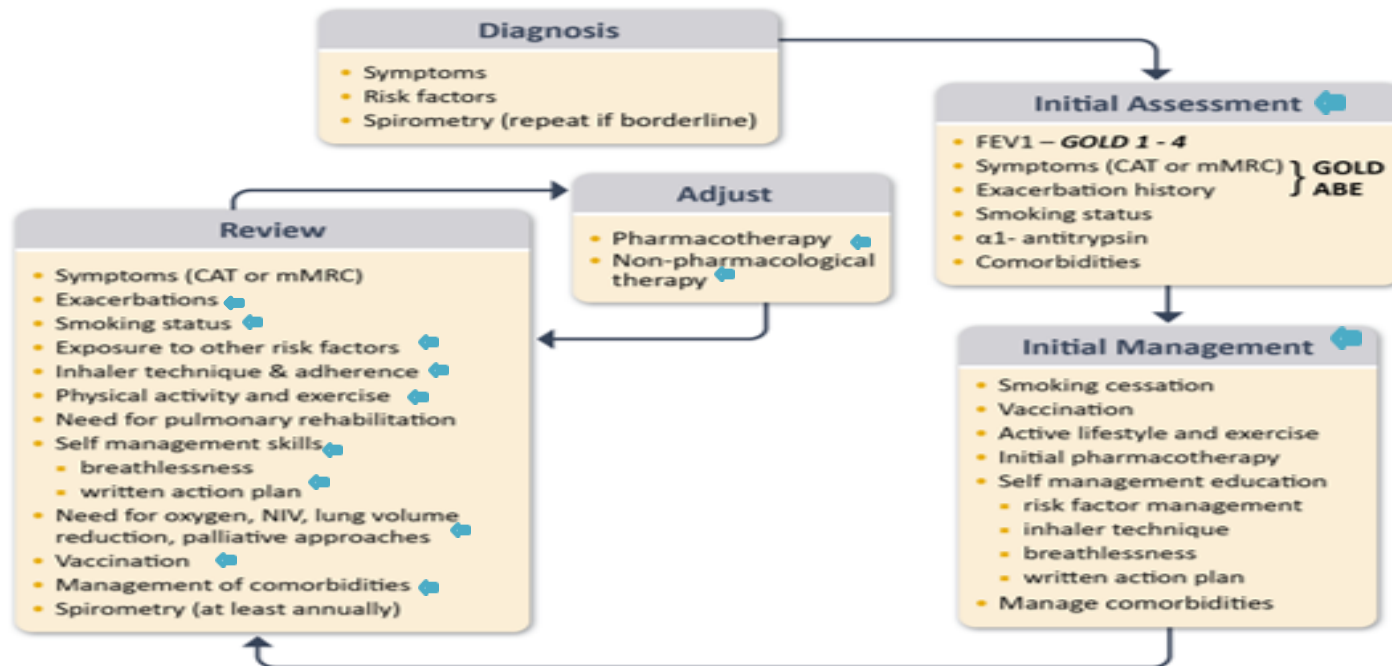
Pharmacist Role

Senior Care Pharmacists are well-suited to provide assessment, treatment, and patient education related to COPD and smoking cessation. Early and frequent interventions can decrease symptom burden, reduce costs, and improve the lives of those with COPD.

*By Jessica R Merlo and
Danielle Backus*

Management of COPD

Figure 4.1



References

Venkatesan P. GOLD COPD report: 2023 update. *Lancet Respir Med*. 2023;11(1):18. doi:10.1016/S2213-2600(22)00494-5

Anthonisen NR, Connett JE, Murray RP. Smoking and lung function of Lung Health Study participants after 11 years. *Am J Respir Crit Care Med*. 2002;166(5):675-679. doi:10.1164/rccm.2112096

Bourdet SV, Williams DM. Chronic Obstructive Pulmonary Disease. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey L. eds. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition*. McGraw Hill; 2023. Accessed April 20, 2023. <https://accesspharmacy.mhmedical.com/content.aspx?bookid=3097§ionid=267239611>

Leuppi JD, Schuetz P, Bingisser R, et al. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. *JAMA*. 2013;309(21):2223-2231. doi:10.1001/jama.2013.5023

Strnad P, McElvaney NG, Lomas DA. Alpha₁-Antitrypsin Deficiency. *N Engl J Med*. 2020;382(15):1443-1455. doi:10.1056/NEJMra1910234

References

Jia X, Zhou S, Luo D, et al. Effect of pharmacist-led interventions on medication adherence and inhalation technique in adult patients with asthma or COPD: A systematic review and meta-analysis. J Clin Pharm Ther. 2020;00:1-14.

Schnipper JL., Kirwin JL, Cotugno MC, et al. Role of Pharmacist Counseling in Preventing Adverse Drug Events After Hospitalization. ARCH INTERN MED/VOL 166, MAR 13, 2006.

(2021, October 4). New and Current Treatments for COPD. Healthline. Retrieved June 22, 2023, from <https://www.healthline.com/health/copd/new-treatments-copd>

Thanks!

Do you have any questions?

sayel.rivera@upr.edu

wanda.marrero1@upr.edu

