COPD Pathophysiology and Management Considerations & GOLD 2024 Report

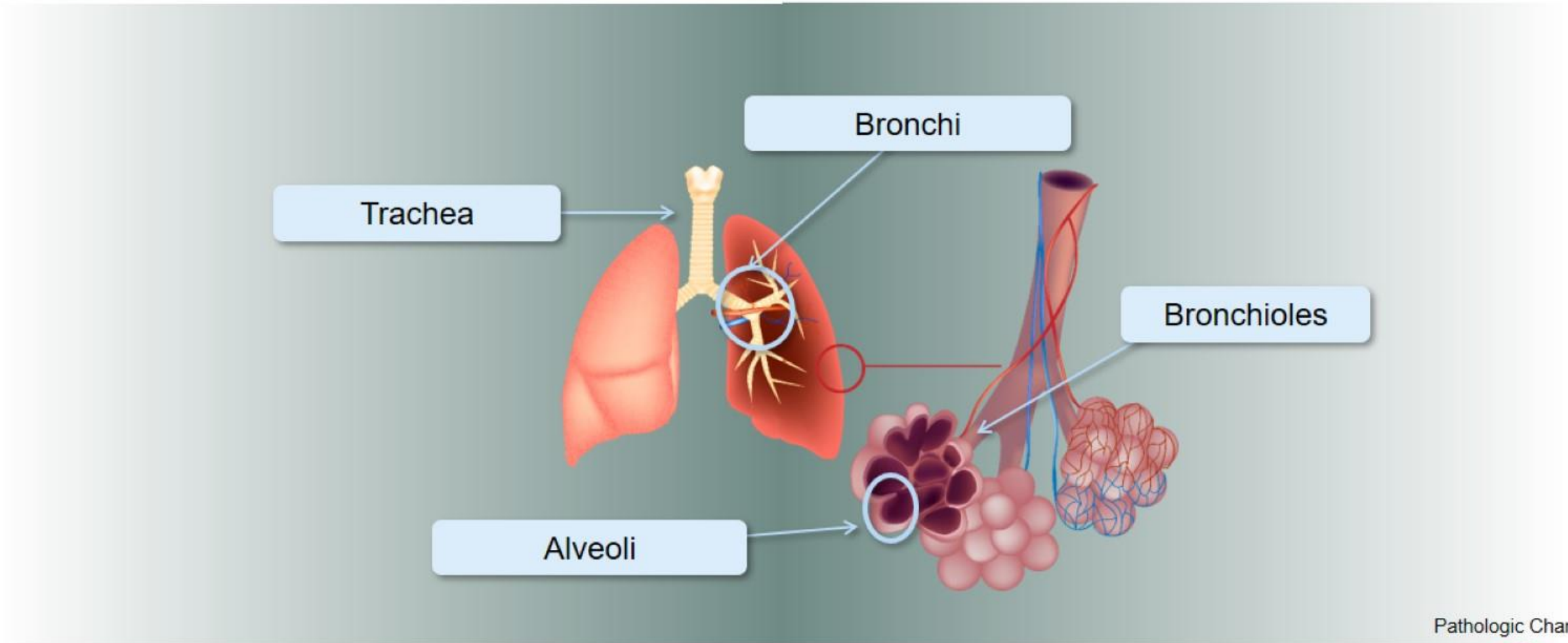
US-82492 Approved 11/23

Pathophysiology

GOLD 2024 Report

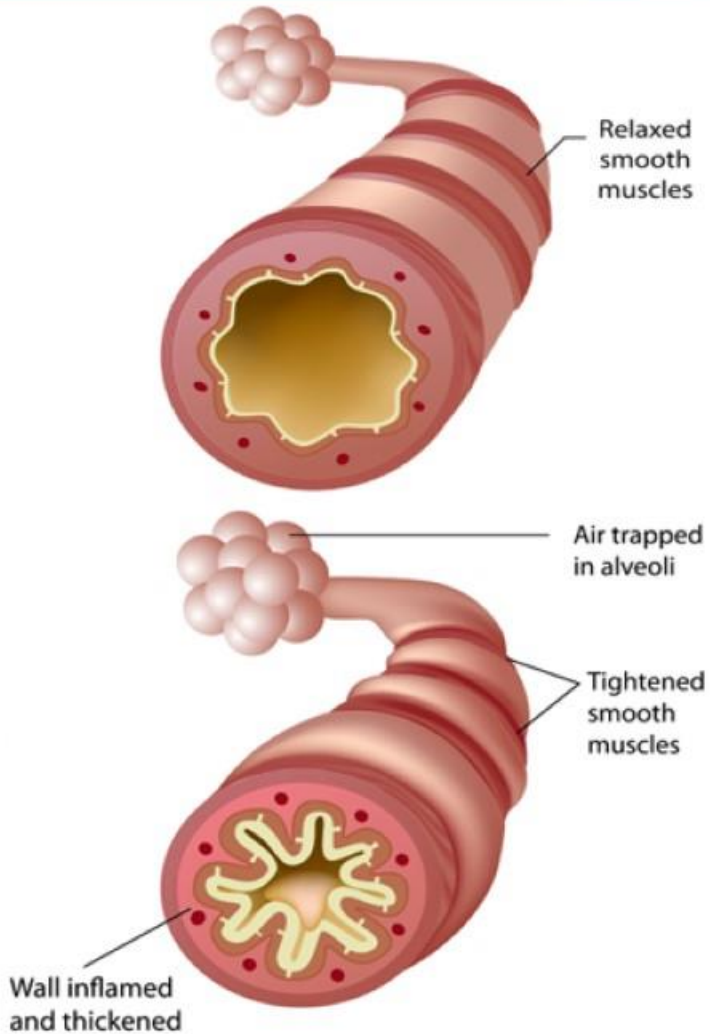
Pathophysiology

Respiratory Anatomy

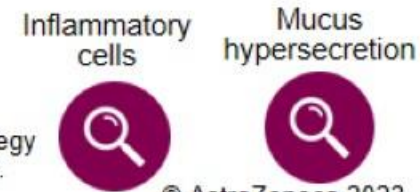


Pathologic Changes

Chronic Bronchitis and Airway Inflammation

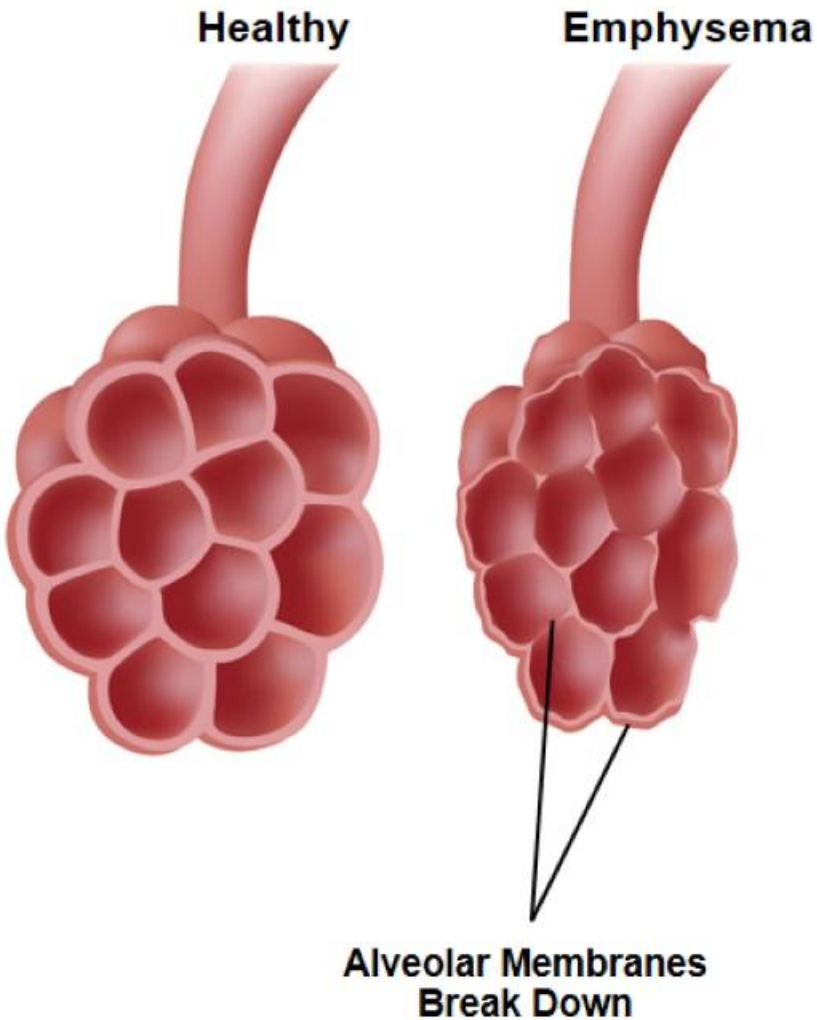


- In healthy lungs, the airways are elastic and flexible[1] and lung health depends upon effective mucus clearance[2]
- In disease states, thick and viscoid mucus can lead to airway inflammation and infection[2]
- Mucus hypersecretion results in a chronic productive cough[3]
- Chronic bronchitis is defined by the presence of cough with expectorated sputum on a regular basis over a defined period[2]
- Airways may become partially obstructed, making it harder to get air out of the lung. The resulting hyperinflation also makes inspiration difficult[1]



1. NIH. National Heart, Lung, and Blood Institute. A quick guide on COPD. NIH.gov website. Accessed November 22, 2023. https://www.nhlbi.nih.gov/sites/default/files/publications/A-QuickGuide-on-COPD-2022_0.pdf; 2. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD (2024 report). GOLD website. Accessed November 22, 2023. https://goldcopd.org/2024-gold-report/; 3. MacNee W. *BMJ*. 2006;332:1202-1204.

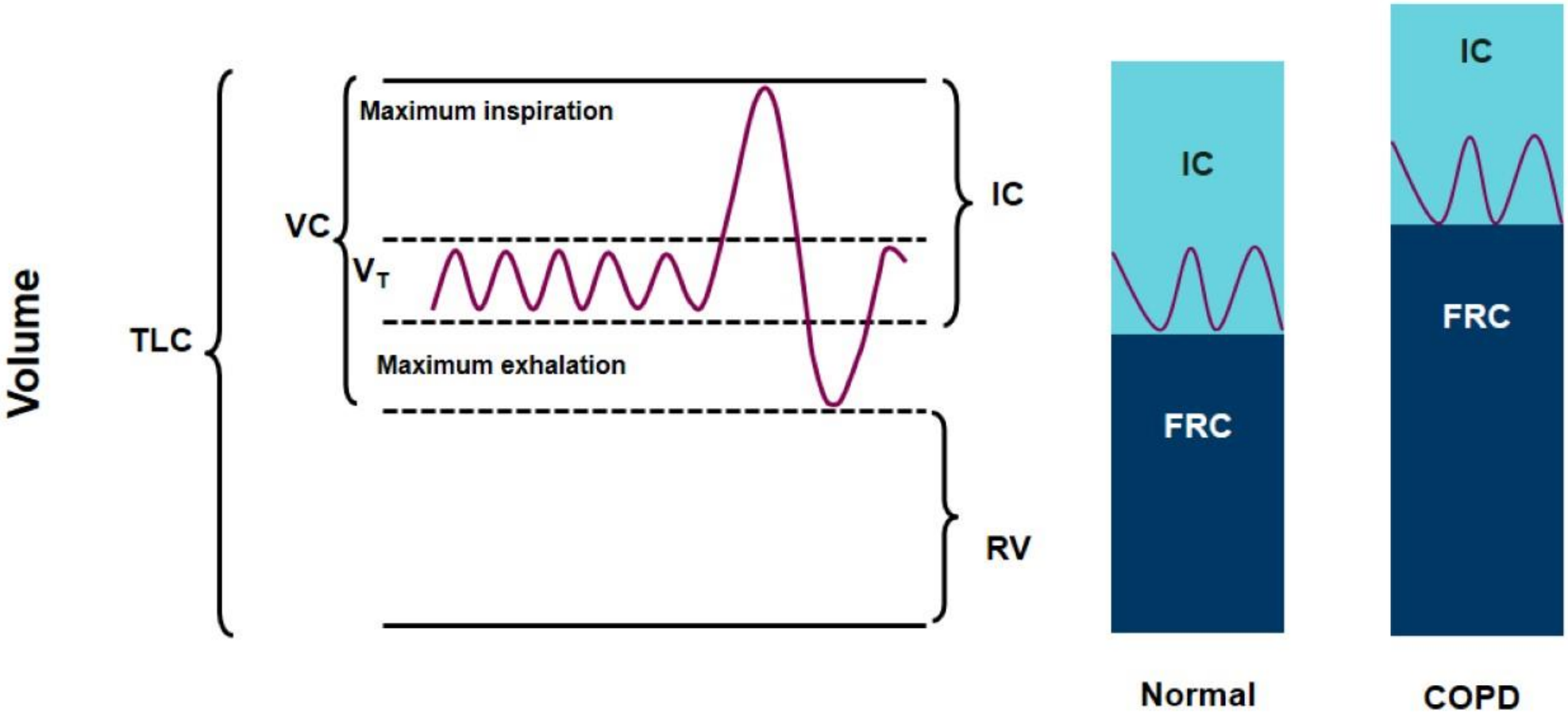
Emphysema Is Caused by Damage to the Alveoli Walls



- Healthy alveoli are elastic and capable of springing back to their original size after active inspiration
- Emphysema involves damage to the walls of the alveoli
- In emphysema, alveoli lose their elasticity, which impairs natural passive exhalation, resulting in trapping of air and hyperinflation

American Thoracic Society (ATS) Patient education information series. Chronic obstructive pulmonary disease (COPD). ATS website. Accessed November 22, 2023. https://www.thoracic.org/patients/patient-resources/resources/copd-intro.pdf

Understanding Lung Volume Measurements in Patients With COPD[1,2]



Hyperinflation

1. Ferguson GT. *Proc Am Thorac Soc*. 2006;3:176-179. 2. Sutherland ER et al. *N Engl J Med*. 2004;350:2689-2697.

The GOLD Report 2024

- Definition and Overview of COPD
- Diagnosis and Disease Assessment in COPD
- Key Updates in GOLD 2024
- Management of Stable COPD

Definition and Overview of COPD

What Is COPD?

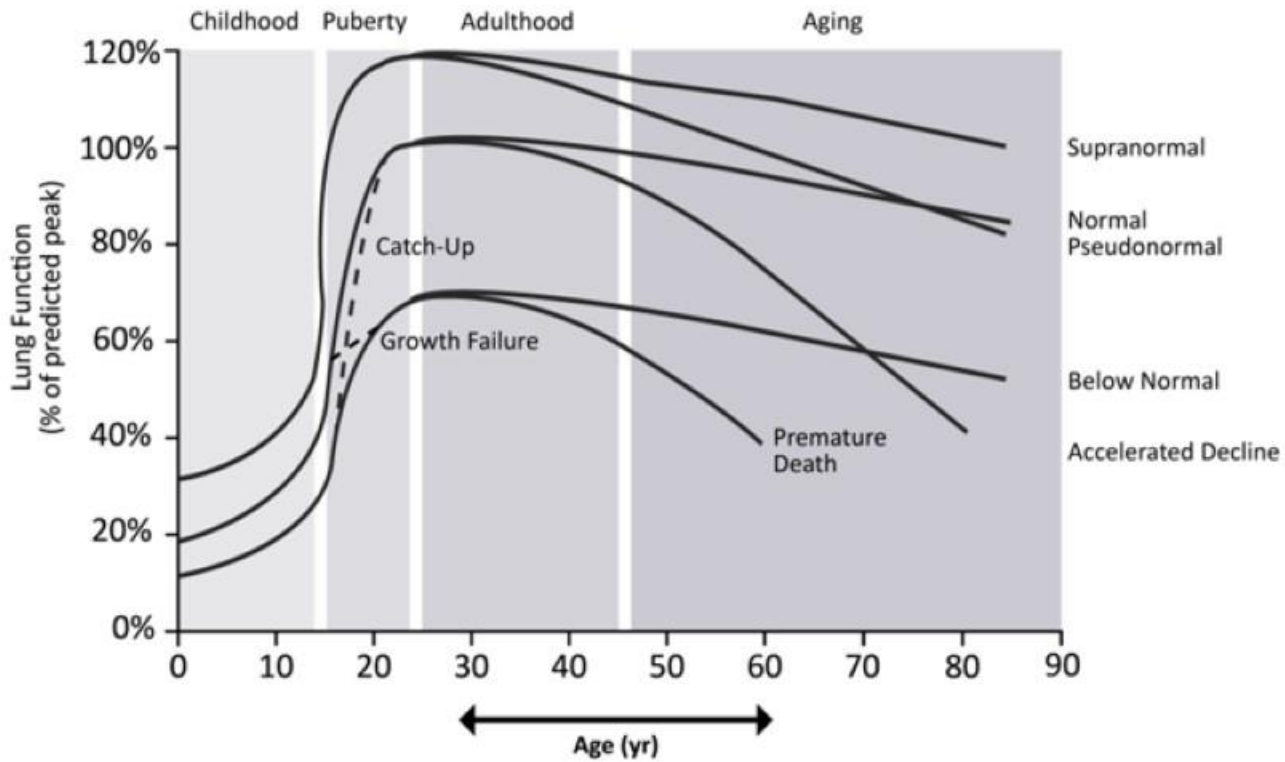
COPD is...

- **A heterogeneous lung condition**
- Associated with significant **concomitant chronic diseases** which increase its **morbidity and mortality**
- Characterized by **chronic respiratory symptoms (dyspnea, cough, sputum production, exacerbations)**
  - due to **airway (bronchitis, bronchiolitis)** and/or **alveolar (emphysema) abnormalities**
  - that cause **persistent**, often **progressive, airflow obstruction**

Statistics

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD (2024 report). GOLD website. Accessed November 22, 2023. https://goldcopd.org/2024-gold-report/

FEV_1 Trajectories Over the Life Course



Modified from: Agusti A, Hogg JC. Update on the Pathogenesis of Chronic Obstructive Pulmonary Disease. *N Engl J Med.* 2019;381:1248-56.

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD (2024 report). GOLD website. Accessed November 22, 2023. https://goldcopd.org/2024-gold-report/

COPD Detection

Diagnosis and Disease Assessment in COPD

Key Indicators for Considering a Diagnosis of COPD

Symptoms and Past Medical History

- Dyspnea
- Chronic cough
- Sputum production
- Wheezing and chest tightness
- Fatigue
- Recurrent lower respiratory tract infections

History of Risk Factors

- Host factors (genetic factors, developmental abnormalities, low birthweight, prematurity, childhood respiratory infections)
- Tobacco smoke
- Smoke from home cooking/heating fuels
- Occupational dusts, vapors, fumes, gases, or other chemicals

Family History of COPD and/or Childhood Factors

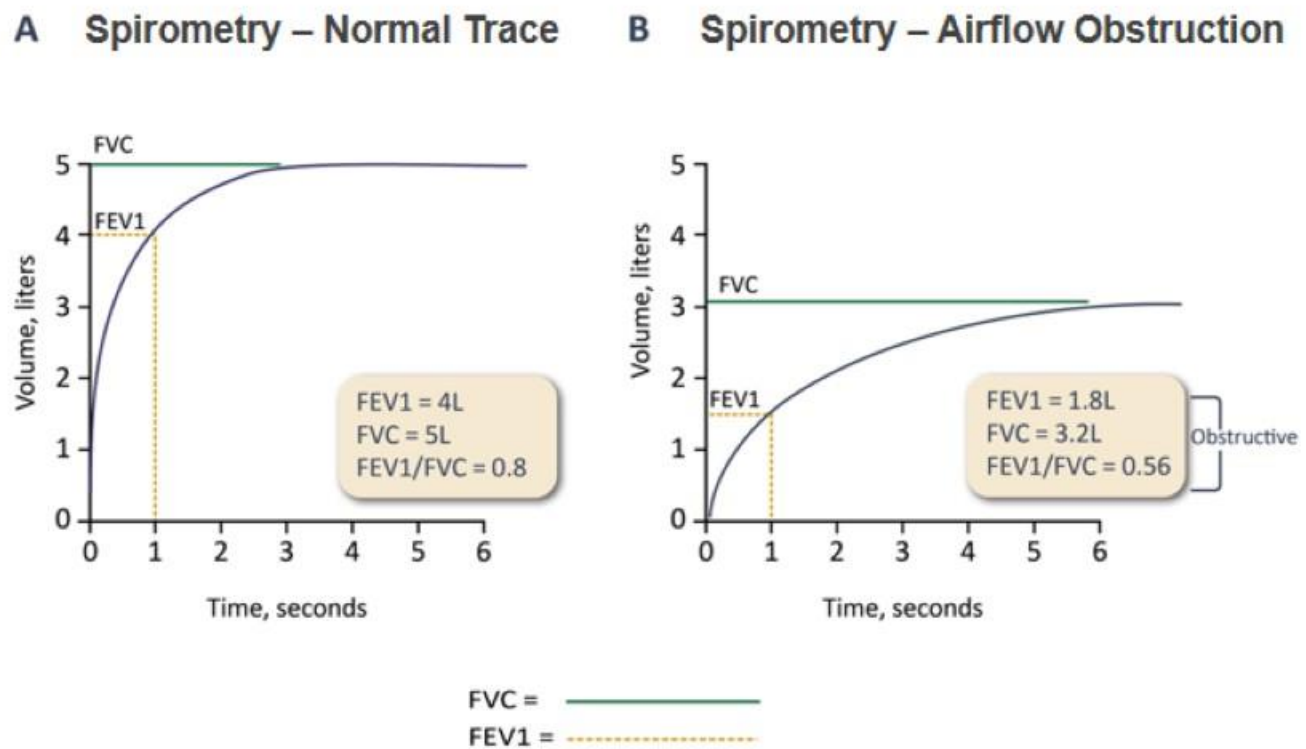
GOLD advocates active case finding, performing spirometry in patients with symptoms and/or risk factors, but not screening spirometry

Comorbidities

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD (2024 report). GOLD website. Accessed November 22, 2023. https://goldcopd.org/2024-gold-report/

Spirometry Is Required to Establish a COPD Diagnosis[1]

Post-bronchodilator FEV_1/FVC <0.7 confirms the presence of non-fully reversible airflow obstruction



FEV_1: Amount of air exhaled in the first second during the FVC maneuver[2]

FVC: Total amount of air a person can forcibly exhale after maximum inhalation[2]

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD (2024 report). GOLD website. Accessed November 22, 2023. https://goldcopd.org/2024-gold-report/; 2. Miller MR, et al. *Eur Respir J*. 2005;26:319-338.

Asthma and COPD Emphasized as Different Disorders

GOLD no longer refers to asthma and COPD overlap (ACO)

Instead, it emphasizes that asthma and COPD are different disorders

Asthma and COPD may share some common treatable traits and clinical features

Such as eosinophilia and some degree of reversibility

Asthma and COPD can coexist in an individual patient

If a concurrent diagnosis of asthma is suspected, pharmacotherapy should primarily follow asthma treatment guidelines, but pharmacological and nonpharmacological approaches may also be needed to treat COPD

GOLD includes 'COPD & asthma' in the proposed taxonomy for COPD

COPD & Asthma (COPD-A) is included in the proposed taxonomy (etiotypes) for COPD. The proposal highlights the need to explore current and future therapies for different etiotypes of COPD, including COPD-A.

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD (2024 report). GOLD website. Accessed November 22, 2023. https://goldcopd.org/2024-gold-report/

Key Updates in GOLD 2024

Overview of Changes in the GOLD 2024 Report

- Expanded Managing Inhaled Therapy section; includes information on the patient's ability to use the delivery system correctly and the choice of inhaler device
- Focus on early diagnosis and intervention by leveraging screening programs and endorsing pre-bronchodilator spirometry; highlights the risks of PRISm (preserved ratio impaired spirometry)
- Blood eosinophil count added to the Initial Assessment section
- In patients without features of asthma who have further exacerbations on ICS/LABA, triple therapy is recommended in those with a blood eosinophil count ≥100 cells/µL
- Dupilumab added to the Overview of the Evidence: Pharmacotherapy section
- New section on hyperinflation

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD (2024 report). GOLD website. Accessed November 22, 2023. https://goldcopd.org/2024-gold-report/

Additional Changes in the GOLD 2024 Report

Chapters 3 and 4 have been consolidated into one chapter along with the consolidation of some tables to reduce repetitive information

Smoking cessation section revised: vaping/E-cigarettes not recommended for smoking cessation based on available evidence and lack of knowledge on the long-term effects in patients with COPD

Vaccine recommendations updated to include the RSV vaccine for patients ≥60 years and/or at risk of severe RSV illness in line with the CDC and the European Commission

Interstitial lung abnormalities added within the Imaging section

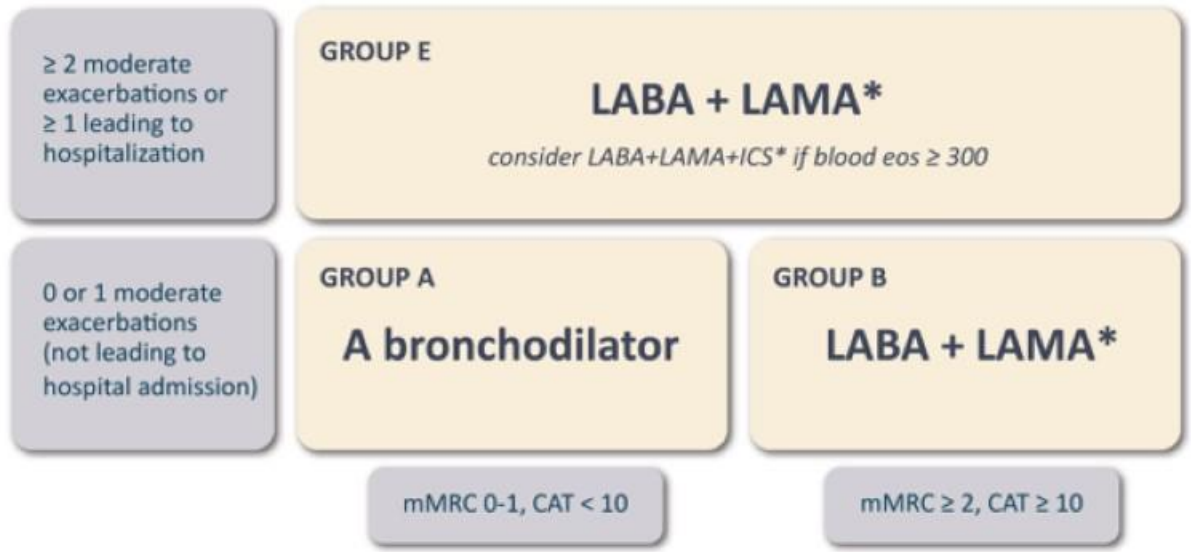
Information about PRISm expanded to include updated values on prevalence and information on the transition to obstructed spirometry over time

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD (2024 report). GOLD website. Accessed November 22, 2023. https://goldcopd.org/2024-gold-report/

Managing Inhaled Therapy & Pharmacological Treatment of COPD

2024

- 'Single inhalers improve adherence to treatment' added in the subtext of treatment algorithms
- It is crucial to check regularly that patients continue to use their device correctly:
  - Suboptimal peak inspiratory flow and inhalation technique errors were associated with higher COPD-related healthcare utilization and costs in patients on DPI maintenance therapy
  - The proper use of an inhaler has a positive environmental impact through the reduction of exacerbations and their CO_2 footprint (especially when hospitalization is required)



*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™.

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Focus on Early Diagnosis and Intervention

2024

Screening for COPD in Targeted Populations

- There is missed opportunity to perform spirometry in lung cancer screening
- Underdiagnosis of COPD in lung cancer screening can approach 90% in some reports
- Leveraging incidental lung imaging abnormalities allows for identification of individuals at increased risk of COPD via detection of emphysema and other abnormalities

Performing Pre-bronchodilator Spirometry to Simplify Diagnosis

- Post-bronchodilator spirometry is time consuming and may deter clinicians from performing spirometry
- GOLD states that pre-bronchodilator spirometry can be used as an initial test to investigate whether symptomatic patients have airflow obstruction
- If pre-bronchodilator spirometry does not show obstruction, post-bronchodilator spirometry is not necessary unless there is a very high clinical suspicion of COPD

Encouraging the Treatment of Patients With PRISm

- PRISm[a] is associated with an increased risk of cardiopulmonary disease, all-cause and cardiovascular mortality, hospitalization, and development of airways obstruction
- Predictors of transition to COPD include lower baseline FEV_1% and FEV_1/FVC, higher age, current smoker status, and female sex

[a]PRISm (preserved ratio impaired spirometry) describes individuals with preserved ratio (FEV_1/FVC ≥0.7) but impaired spirometry (FEV_1 <80%) after bronchodilation and is present in up to 11% of former/current smokers.

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of COPD (2024 report). GOLD website. Accessed November 22, 2023. https://goldcopd.org/2024-gold-report/

In Patients Without Features of Asthma Who Have Further Exacerbations on ICS/LABA, Triple Therapy is Recommended in Those With a Blood Eosinophil Count of ≥100 cells/µL

2024

Patients under treatment with ICS/LABA

- If a patient with COPD and no features of asthma has been treated with ICS/LABA and is well controlled in terms of symptoms and exacerbations, continuation with ICS/LABA is an option.
- However, if the patient has:
  - Further exacerbations: treatment should be escalated to ICS/LAMA/LABA if the blood eosinophil count is ≥100 cells/µL or switched to LAMA/LABA if it is <100 cells/µL
  - Major symptoms: switching to LAMA/LABA should be considered

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New Section on Hyperinflation

2024

- Hyperinflation is clinically relevant to patients with COPD and contributes to dyspnea, impaired exercise tolerance, hospitalization, respiratory failure, and increased mortality
- Hyperinflation occurs when gas volume in the lungs is increased compared to normal values at the end of spontaneous expiration
  - Static hyperinflation at rest is caused by the loss of elastic lung recoil as a consequence of emphysema
  - Dynamic hyperinflation during exercise is caused by airflow obstruction as ventilatory demands increase and expiratory times reduce
  - Hyperinflation can be found in patients with even mild obstruction at rest and even more so during exercise
- Lung volume measurements to assess the presence or degree of hyperinflation can be determined by body plethysmography or gas dilution techniques. Measurement of inspiratory capacity at rest and during exercise is an indirect measurement of increased end-expiratory lung volumes. Hyperinflation can also be detected by chest imaging, but standardization is lacking

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Dupilumab has been Added to the Overview of the Evidence: Pharmacotherapy Section

2024

- A RCT showed that treatment with the humanized anti-IL-4 receptor alpha monoclonal antibody dupilumab reduced exacerbations and improved FEV_1 as well as symptoms and health-related quality of life in patients with COPD, chronic bronchitis, a baseline blood eosinophil count ≥300 cells/μL, and a relevant exacerbation history
- These findings are potentially important and clinical practice changing but require confirmation in further studies

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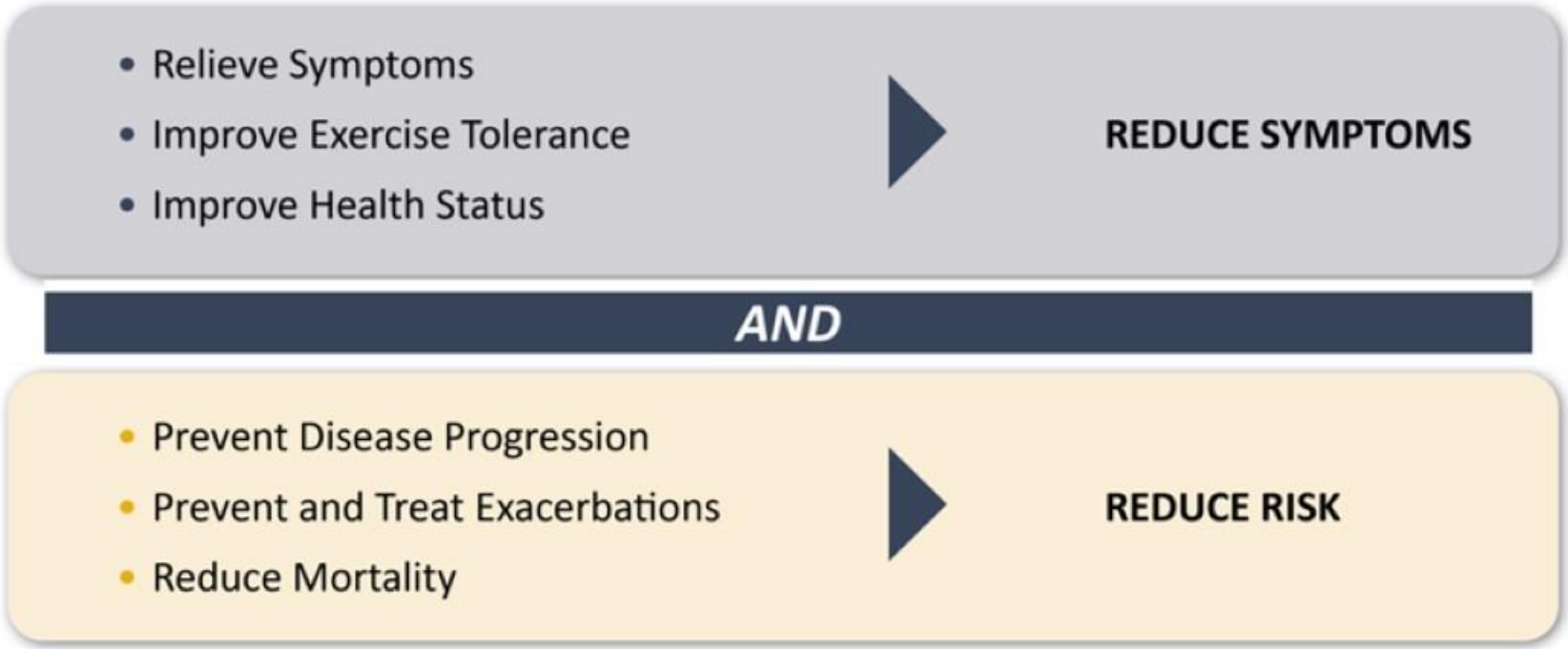
Management of Stable COPD

Goals for Treatment of Stable COPD



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Individualized Treatment Approaches for COPD

Pharmacologic

Pharmacologic treatment for COPD should be individualized, matching the patients' therapy to their needs, guided by:

- Severity of symptoms and risk of exacerbations
- Side effects and comorbidities
- Drug availability and cost
- Patient response, preference and ability to use drug-delivery device

Non-Pharmacologic

Non-pharmacological intervention such as pulmonary rehabilitation should also be individualized to maximize personal functional gains

Integrative Care

Integrated care needs to be individualized to the stage of the person's illness and health literacy

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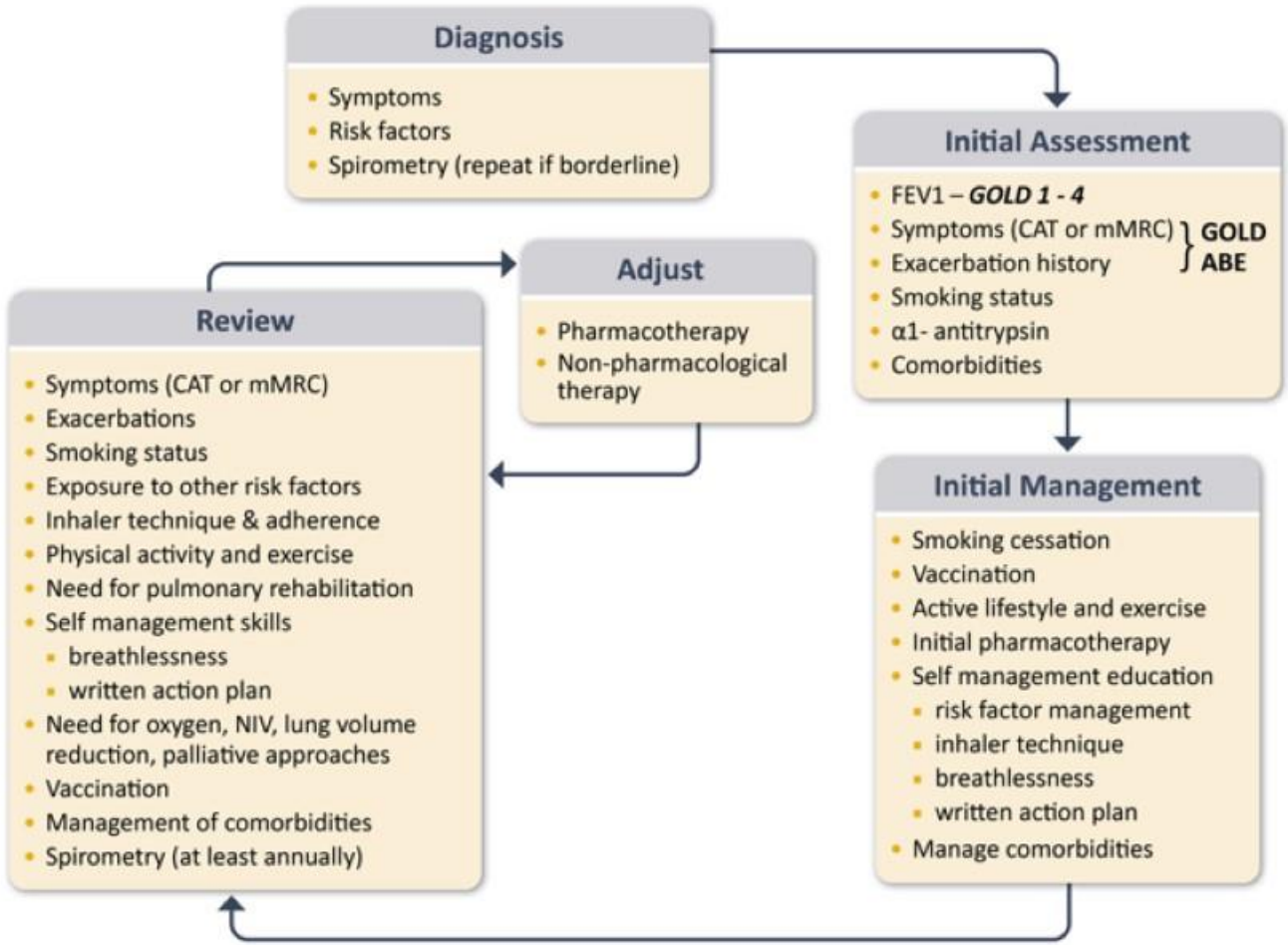
Management of COPD



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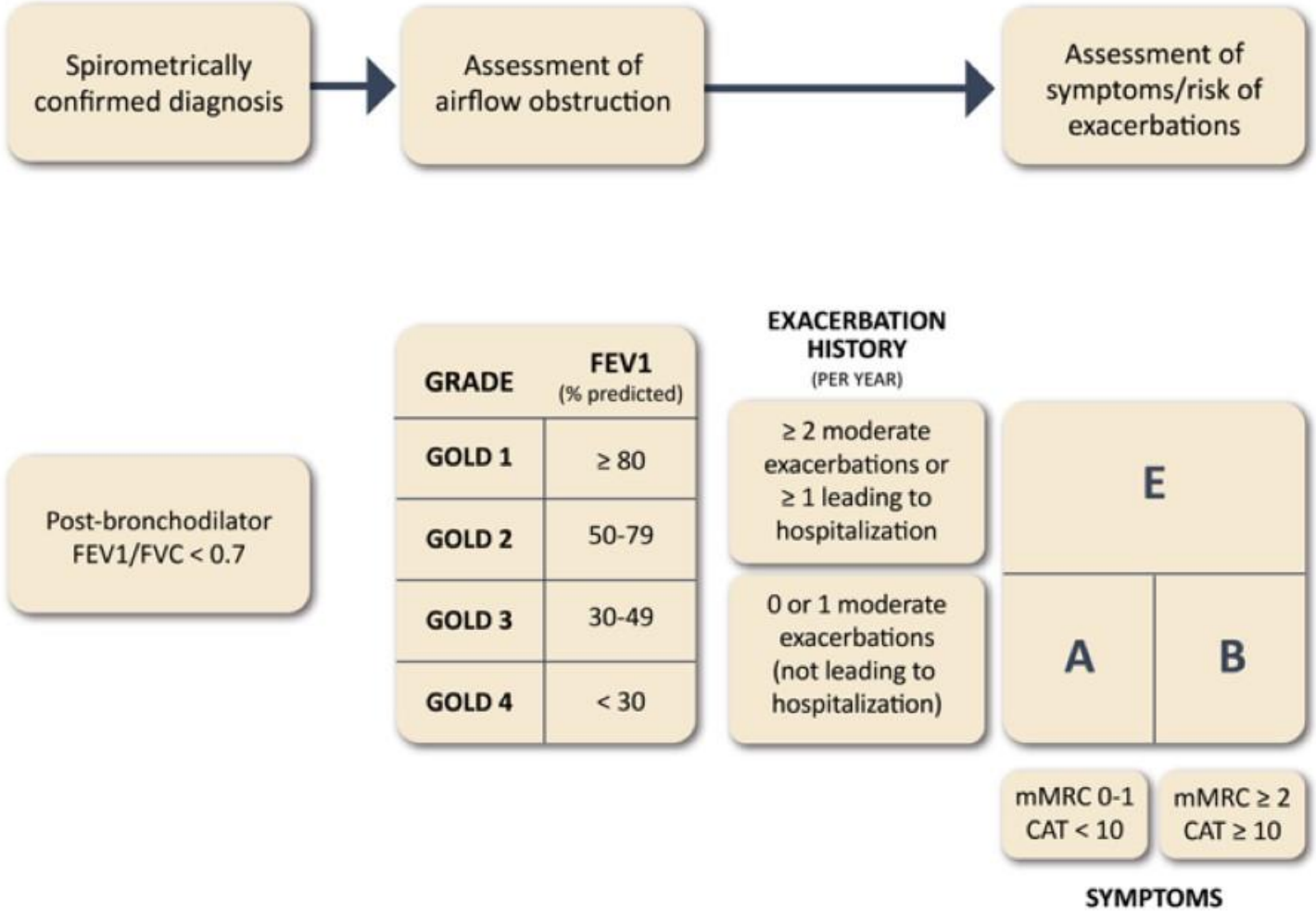
GOLD ABE Assessment Tool



Exacerbation Risk Factors and Impact

Symptom Tests

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Treatment of Stable COPD

Initial Pharmacological Treatment

*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™.

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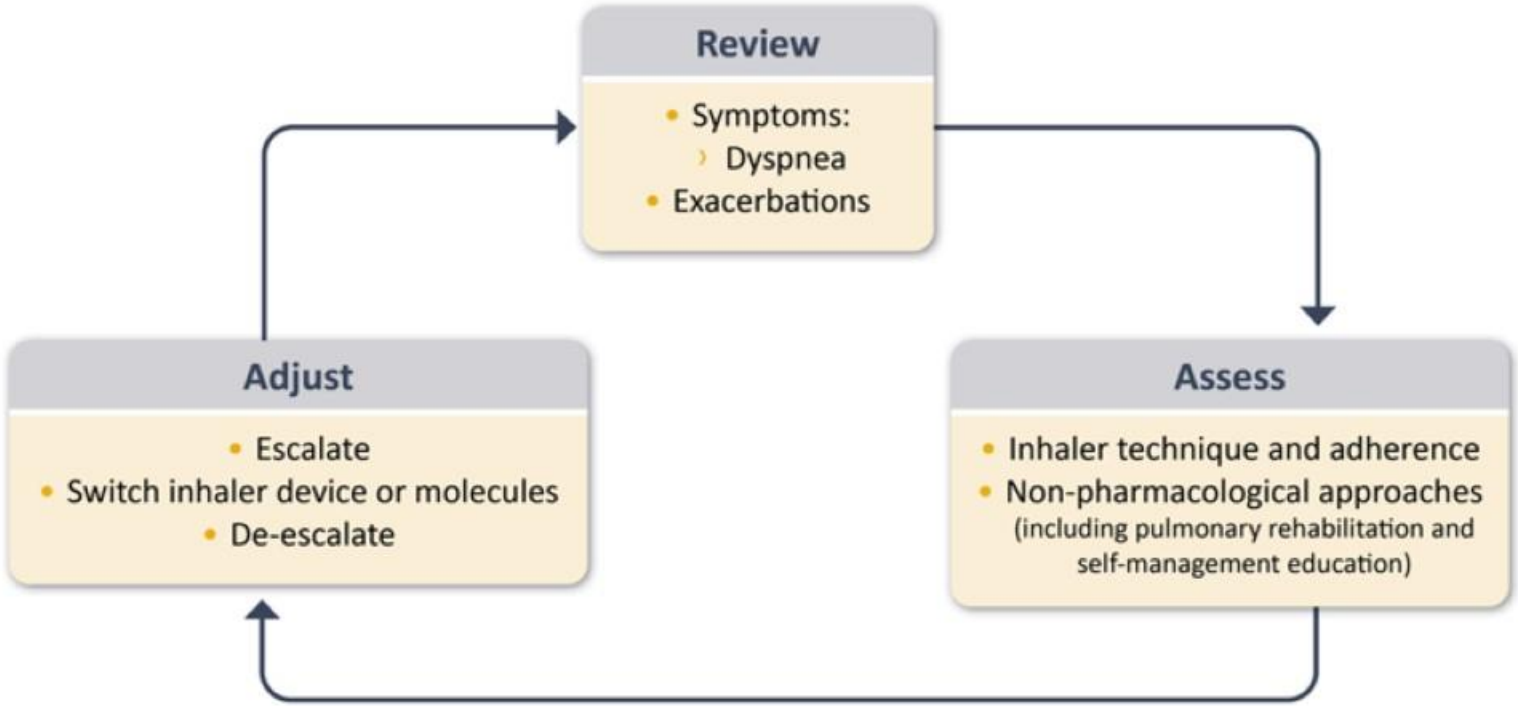
Treatment of Stable COPD
Management Cycle



Patients, in whom treatment modification is considered, in particular de-escalation, should be undertaken under close medical supervision.

Inhaled Delivery

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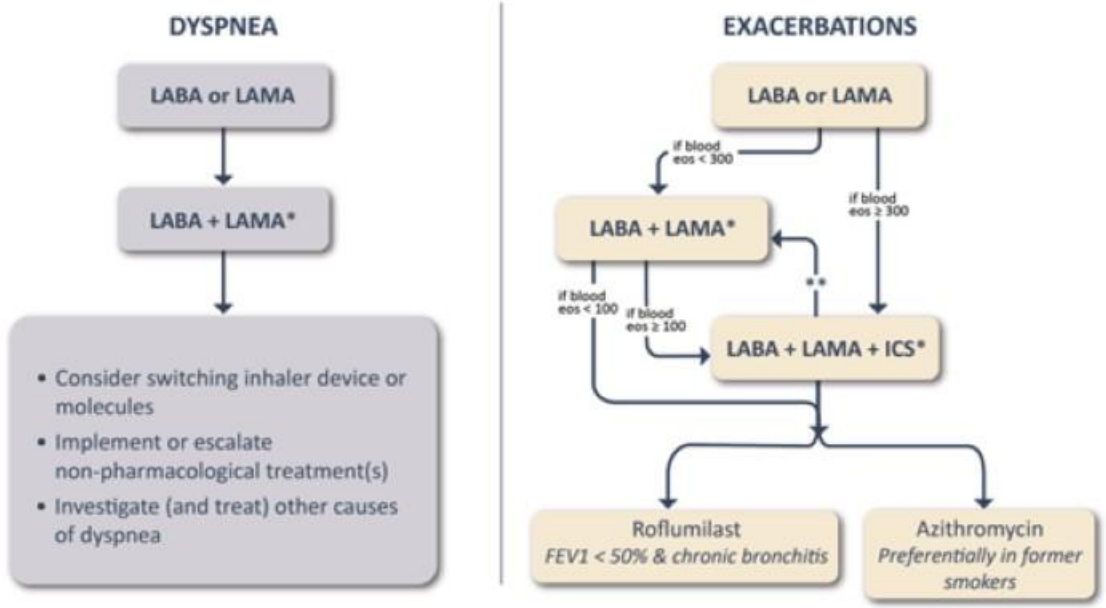
Treatment of Stable COPD

Follow-up Pharmacological Treatment

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

Other Options

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Non-Pharmacologic Management of COPD[a]

Personalized Strategies

Activity

[a]Not all options are appropriate for each patient.

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