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COPD Pathophysiology and Management Considerations – GOLD 2026 Report

Document Number: US-108790

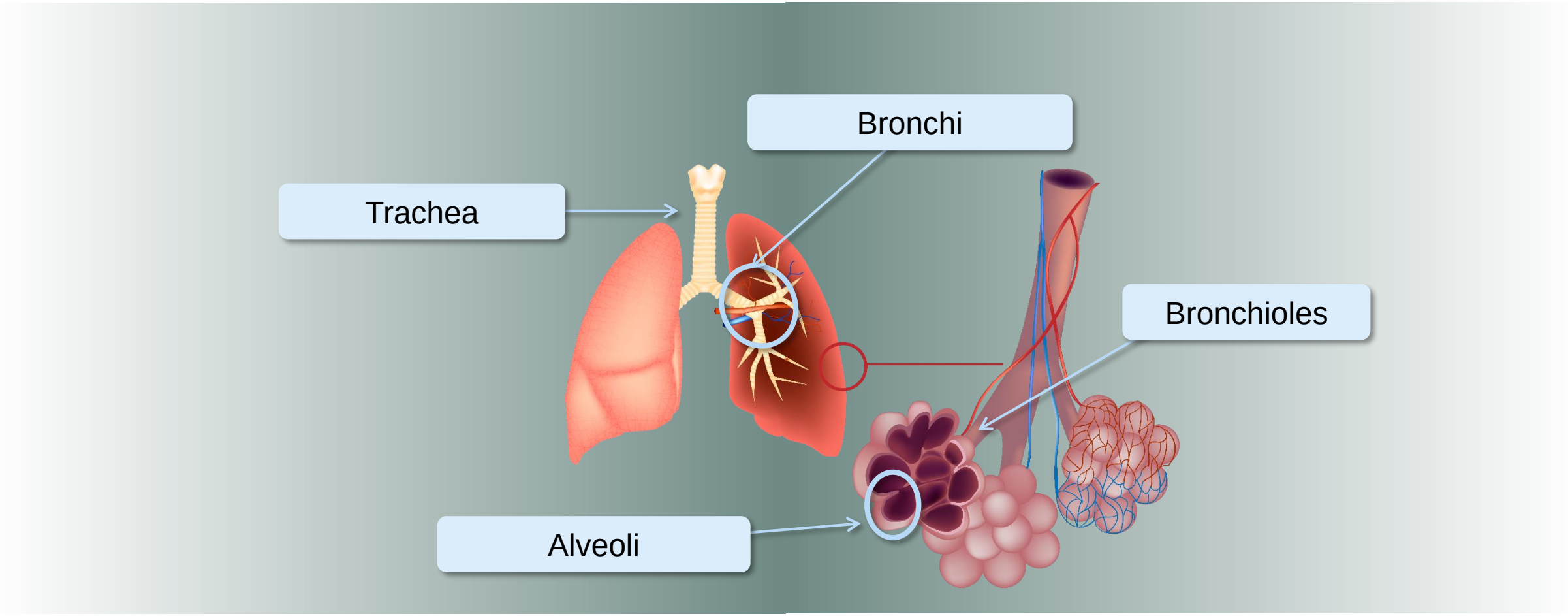
Approval Date: 2/26

Pathophysiology

GOLD 2026 Report

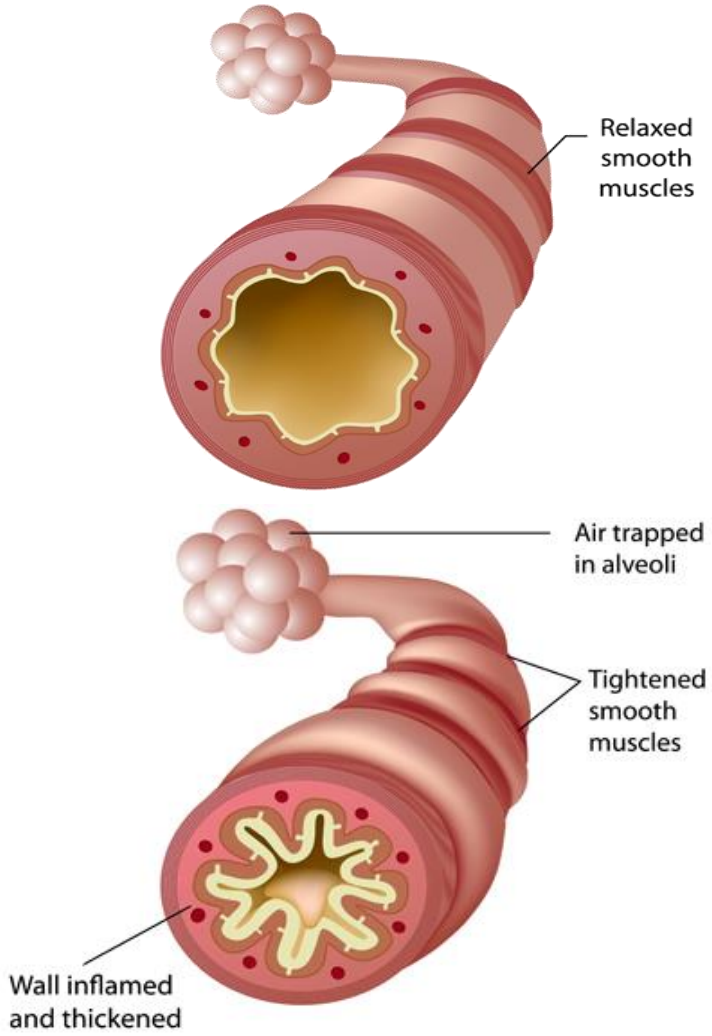
Pathophysiology

Respiratory Anatomy



Pathologic Changes

Chronic Bronchitis and Airway Inflammation



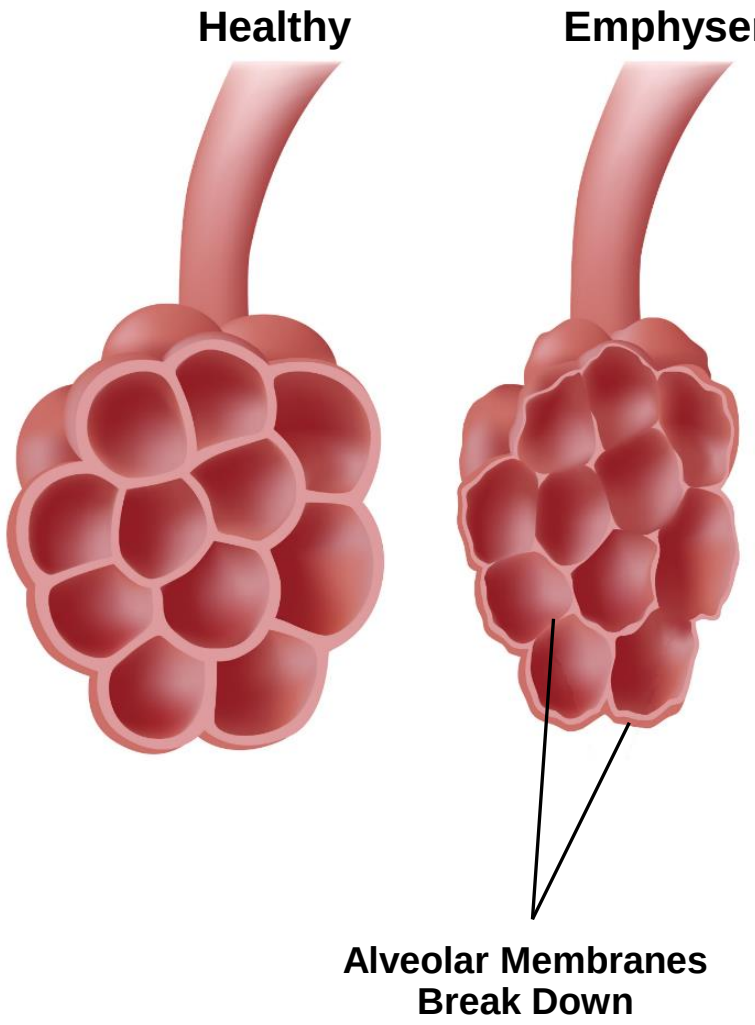
- In healthy lungs, the airways are elastic[1] and lung health depends upon effective mucus clearance[2]
- In disease states, thick and viscous mucus can lead to airway inflammation and infection[2]
- Mucus hypersecretion results in a chronic productive cough[3]
- Chronic bronchitis is defined by the presence of cough with expectorated sputum on a regular basis over a defined period[2]
- This condition results from constant irritation and inflammation of the airway lining, leading to thickening of the lining and the production of thick mucus, which makes breathing difficult.[1]

Inflammatory cells

Mucus hypersecretion

1. National Heart, Lung, and Blood Institute. A quick guide on COPD. March 2022. https://www.nhlbi.nih.gov/sites/default/files/publications/A-QuickGuide-on-COPD-2022_0.pdf; 2. GOLD. Global strategy for prevention, diagnosis and management of COPD: 2026 Report. GOLD website. https://goldcopd.org/2026-gold-report-and-pocket-guide/; 3. MacNee W. *BMJ*. 2006;332:1202-1204.

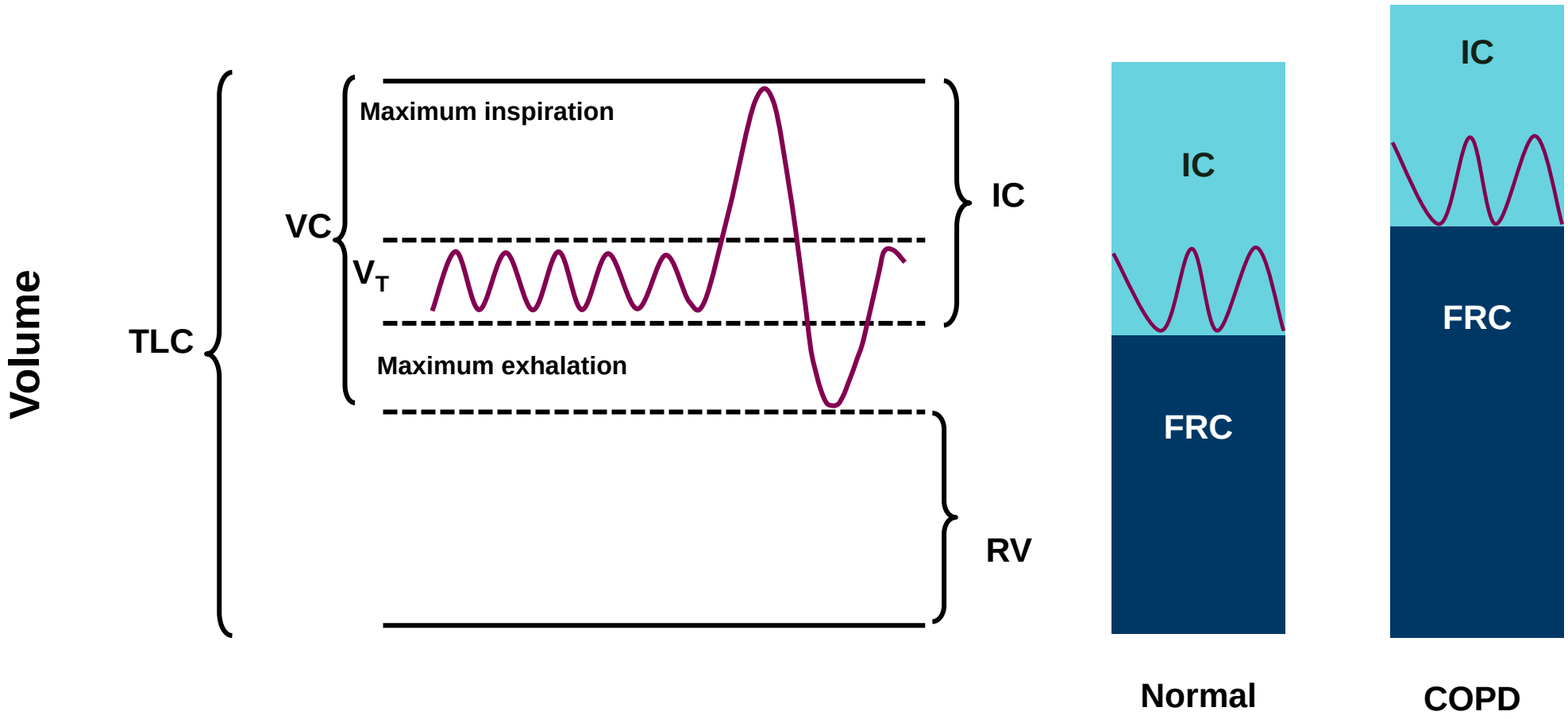
Emphysema Is Caused by Damage to the Alveoli Walls



- 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. Patient education information series. Chronic obstructive pulmonary disease (COPD). October 2021. https://www.thoracic.org/patients/patient-resources/resources/copd-intro.pdf

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



Definitions
Hyper-inflation

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 2026

- Definition and Overview of COPD
- Key Updates in GOLD 2026
- Diagnosis and Disease Assessment in COPD
- Management of Stable COPD

Definition and Overview of COPD

What Is COPD?

COPD is...

- A **heterogeneous** lung condition
- 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**
- Associated with significant **concomitant chronic diseases** which increase its **morbidity and mortality**

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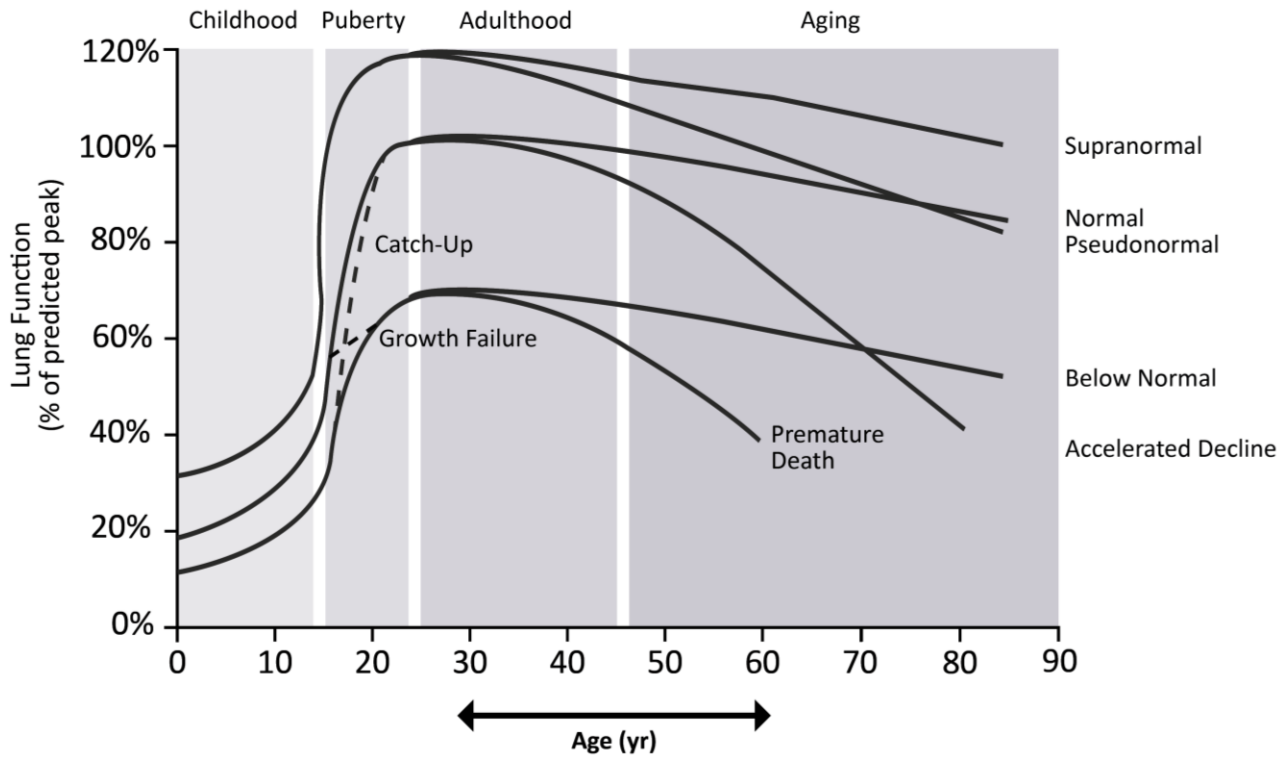
Figure 1.2

FEV_1 Trajectories Over the Life Course



Modified from: Agusti A, Hogg JC. N Engl J Med. 2019;381:1248-56.

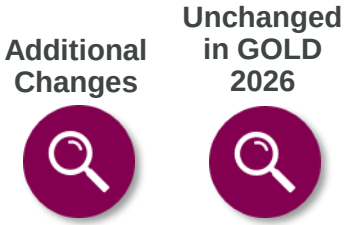
GOLD. Global strategy for prevention, diagnosis and management of COPD: 2026 Report. GOLD website. https://goldcopd.org/2026-gold-report-and-pocket-guide/

COPD Detection

Key Updates in GOLD 2026

Overview of Key Changes in The GOLD 2026 Report

- **Group E** is now defined as patients with **≥1 moderate or severe exacerbation** in the past year, which increases the number of patients eligible for triple therapy as initial treatment; **Groups A** and **B** are now defined as patients with **0 exacerbations** in past year. **Follow-up** treatment expanded to include patients with **≥1 moderate or severe exacerbation**
- Discharge recommendations now include the **prescription of triple therapy to reduce subsequent exacerbation risk** and comorbidity follow up
- **Exacerbation severity** should now be determined based on the patient's clinical characteristics **using the Rome classification**, rather than HCRU and treatment implemented
- [New] recommendations for **active and opportunistic case-finding** to ensure earlier diagnosis
- **Mepolizumab** now included but is only for **patients continuing to have exacerbations on triple therapy with blood eosinophils ≥300 cells/µL**
- **'COPD and Multimorbidity'** chapter revisions: additional focus on **CVD** and its impact on COPD. [New] information included on other 'morbidity clusters' (respiratory, mental, multi-organ loss of tissue, and metabolic diseases)
- [New] concepts of **'disease stability'** and **'disease control'**
- **Mass switching** of devices is **not recommended**: devices should only be changed with clinical justification. Switching for cost or supply reasons driven by payors, or perceived impact on the environment, is not advised



GOLD. Global strategy for prevention, diagnosis and management of COPD: 2026 Report. GOLD website. https://goldcopd.org/2026-gold-report-and-pocket-guide/

Group E Now Has a Lower Threshold of ≥1 Moderate or Severe Exacerbation

- **Revised guidance for groups A, B, and E**
  - **Lowered threshold for Group E** to **≥1 moderate or severe exacerbation** in 2026[d]
    - **Initial LABA + LAMA + ICS** treatment should be considered for **Group E** if **eos ≥300 cells/µL**
  - **Groups A and B** apply to individuals with **0** moderate or severe exacerbations in the previous year[e]
- Revisions to the initial pharmacological treatment and follow-up pharmacological treatment algorithms to reflect this **(Figures 3.8 and 3.9)**
  - **Follow-up** treatment for the exacerbation pathway expanded from “exacerbations” to **≥1 moderate or severe exacerbation**

Figure 3.8. Initial Pharmacological Treatment

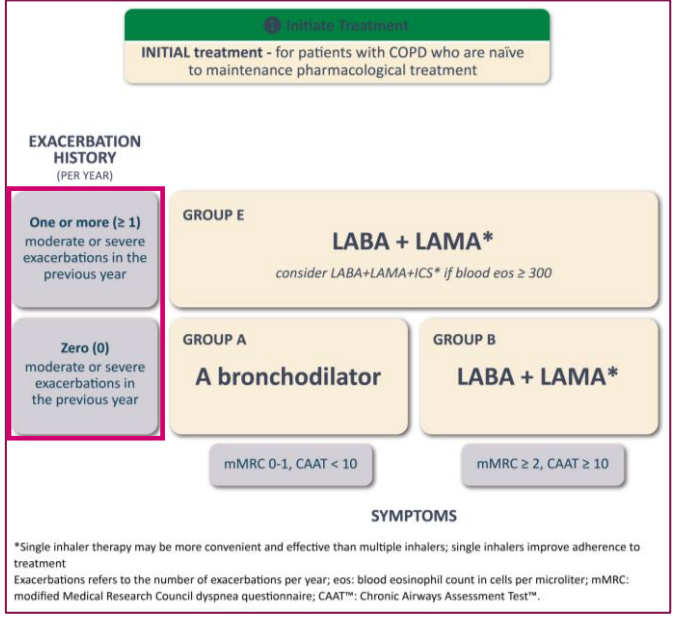
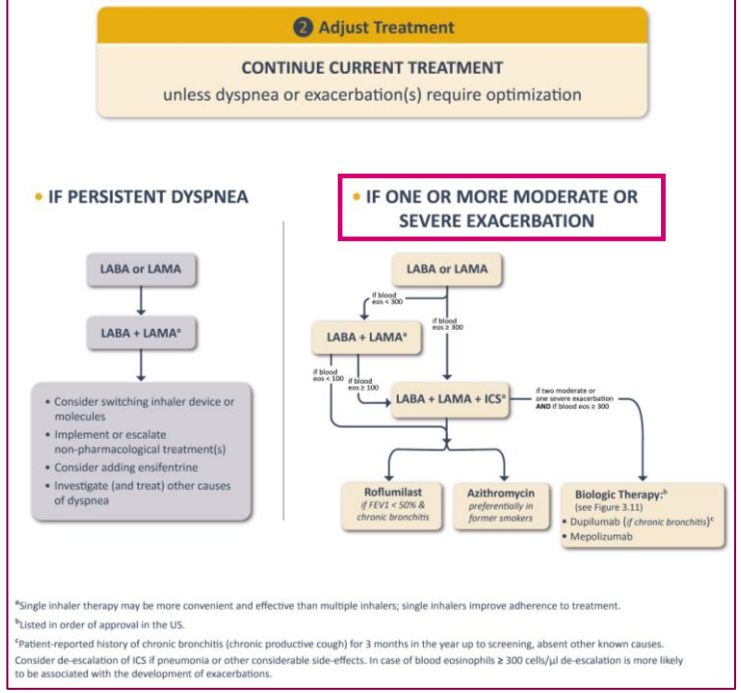


Figure 3.9. Follow-up Pharmacological Treatment



The COPD Assessment Test CAT™ was designed to assess the impact of COPD on a person’s health status. To facilitate its use in other chronic airway diseases, CAT™ has been renamed as the Chronic Airways Assessment Test CAAT™. CAT™ and CAAT™ are equivalent, and the scores are interchangeable.

In the GOLD 2025 Report, [d]Group E exacerbation history was defined as ≥2 moderate or ≥1 exacerbation leading to hospitalization in the previous year and [e]Groups A and B exacerbation history was defined as 0 or 1 moderate or severe exacerbations in the previous year.

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Discharge Recommendations Now Include the Prescription of Triple Therapy to Reduce Exacerbation Risk

- GOLD recommends continuation of long-acting bronchodilators or triple therapy during an exacerbation, or to start these medications as soon as possible before hospital discharge
  - Observational studies analyzing retrospective claims **(including the EROS study)** have demonstrated that **LABA + LAMA + ICS following first exacerbation reduced the first moderate or severe exacerbation and rehospitalization rates**
  - GOLD has included the US observational study findings showing that **most patients were discharged on inappropriate therapy**
- Readmissions occur in 30–50% of patients within 30 days of discharge after an exacerbation, and are associated with increased mortality
- **Prevention of readmission, treatment optimization,** stabilization of health status, **prevention of comorbidity-related events,** and **prolongation of survival** are major goals of post-discharge care
  - Reaching these goals requires planning discharge properly, including timing, follow-up, and implementation of **appropriate long-term pharmacological and non-pharmacological therapy**
- **Figure 4.10 has been updated to include recommendations to provide a management plan and follow-up comorbidities, such as CVD**

Figure 4.10. Discharge Criteria And Recommendations For Follow-up

1. Full review of all clinical and laboratory data
2. Check maintenance therapy (see **Figure 3.9**, patients with elevated blood eosinophils should be discharged on LABA+LAMA+ICS)
3. Reassess inhaler technique
4. Ensure understanding of withdrawal of acute medications (steroids and/or antibiotics)
5. Assess need for continuing supplemental oxygen
6. Provide management plan
7. Follow-up comorbidities such as cardiovascular disease
8. Ensure follow-up arrangements: early follow-up < 4 weeks, and late follow-up > 12 weeks as indicated

1 – 4 Weeks Follow-up

- Evaluate ability to cope in his/her usual environment
- Review understanding of treatment regimen
- Reassessment of inhaler techniques
- Reassess need for long-term oxygen
- Document the capacity to do physical activity and consider patient eligibility to be enrolled in pulmonary rehabilitation
- Document symptoms: CAAT™ or mMRC
- Determine status of comorbidities

12 – 16 Weeks Follow-up

- Evaluate ability to cope in his/her usual environment
- Review understanding of treatment regimen
- Reassessment of inhaler techniques
- Reassess need for long-term oxygen
- Document the capacity to do physical activity and activities of daily living
- Measure spirometry: FEV1
- Document symptoms: CAAT™ or mMRC
- Determine status of comorbidities

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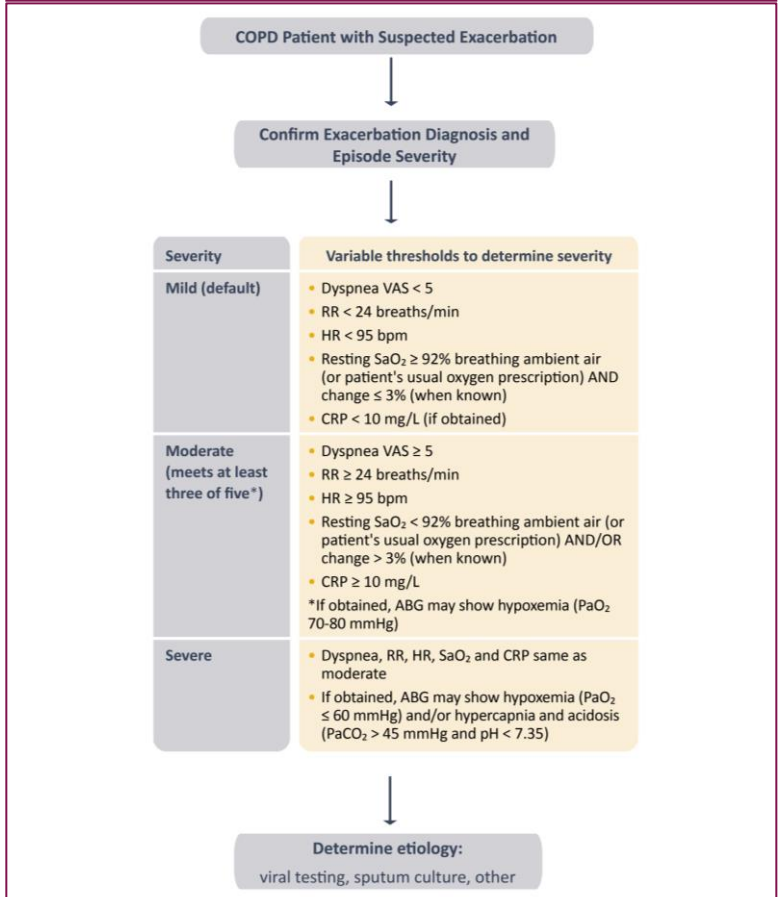
Exacerbation Severity is Now Determined by the Clinical Characteristics of the Patient

- Exacerbation severity has previously been classified ***post hoc*** based on HCRU and the treatment implemented, which **is not useful to guide treatment**
- Now, exacerbation severity, as well as treatment and place of care, should be determined based on the **clinical characteristics of the patient using the Rome classification (Figure 4.2)**
  - Data suggest that **fewer exacerbations will be classified as severe** when using the Rome classification compared with classification using healthcare resource use
  - The previous classification of severity based on treatment interventions and HCRU is still acceptable in clinical trials
- The laboratory variables included in the Rome classification are routinely available in hospital settings, but this may not be the case for primary care. In these settings, the exacerbation severity can be determined by quantification of dyspnea intensity using a VAS dyspnea scale, respiratory rate, heart rate, and SaO_2
- Some of the **variable thresholds** to determine the severity of an exacerbation have changed:
  - **Hypoxemia (PaO_2) values used to classify moderate and severe exacerbations** have been updated
  - **Hypercapnia and acidosis are criteria for severe exacerbations only,** not moderate cases

Figure 4.2. Classification of the Severity of COPD Exacerbations



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; $PaCO_2$ arterial pressure of carbon dioxide.

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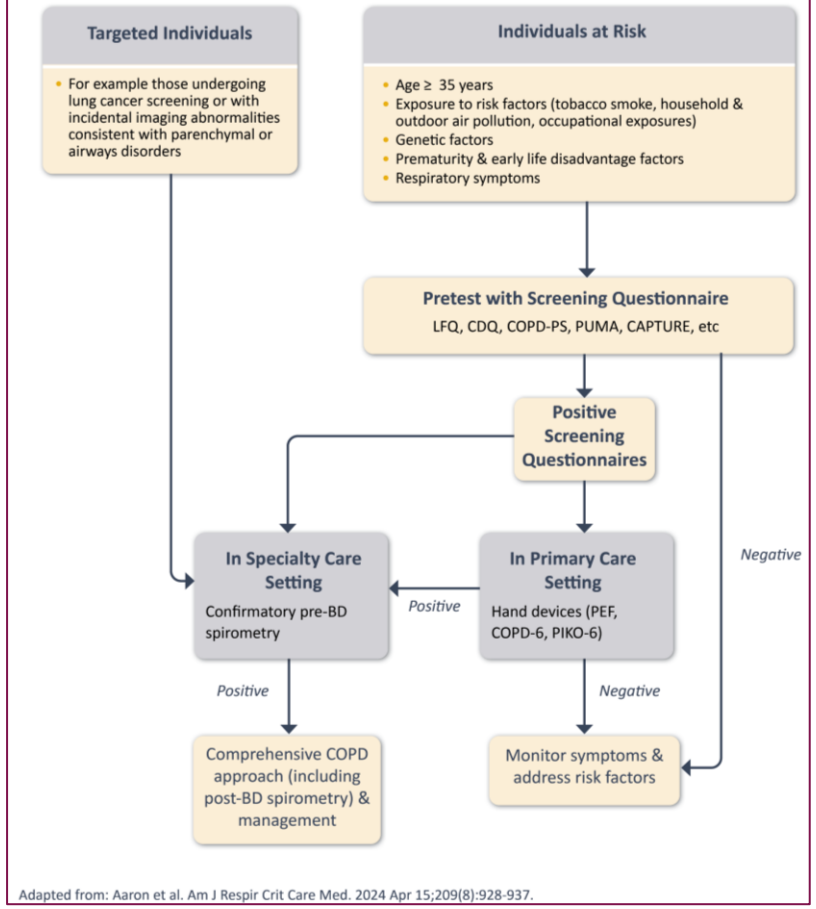
[New] Recommendations for Active and Opportunistic Case-finding to Ensure Earlier Diagnosis

- Explores the **negative impact of undiagnosed COPD** on quality of life and exacerbations
- **Factors associated with COPD underdiagnosis** (eg patient under-recognition, poor access to diagnostic testing, and inadequate training) **are summarized in a figure (Figure 2.8, not shown)**
- Advocates for **active case-finding** in preference to screening
- **[New] algorithm for COPD case-finding (Figure 2.9)** in targeted individuals and individuals at risk in specialty and primary care settings
- **Spirometry continues to be considered a marker of an individual's global health**
  - GOLD now also includes the case for universal spirometry, mapping individual trajectories from childhood through to adult, citing increasing evidence of variability in pulmonary function over time and across the patient's life
  - GOLD continues to recommend diagnostic criteria based on spirometry rather than other assessments (eg CT scans) owing to lack of availability and accessibility in many countries

Figure 2.9. An Algorithm for COPD Case-finding



Adapted from: Aaron et al. Am J Respir Crit Care Med. 2024 Apr 15;209(8):928-937.

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Mepolizumab is Now Included But is Only for Patients Continuing to Have Exacerbations on Triple Therapy With Eos ≥300 cells/µL

- **Mepolizumab is now an option** (in addition to dupilumab) but only for patients with **eos ≥300 cells/µL** who continue to have exacerbation despite LABA + LAMA + ICS
  - This differs from the FDA approval of eos ≥150 cells/µL (see Figure 3.9 on slide 22) from the meta-analysis of METREX and METREO data **(Figure A)**
  - Mepolizumab does not have the restriction of chronic bronchitis phenotype, which is included for dupilumab
- The algorithm refers to the **new Figure 3.11** stating key inclusion criteria and results from the main dupilumab and mepolizumab randomized clinical controlled trials

Figure A: Moderate or Severe Exacerbations According to Blood Eosinophil Count Category at Screening

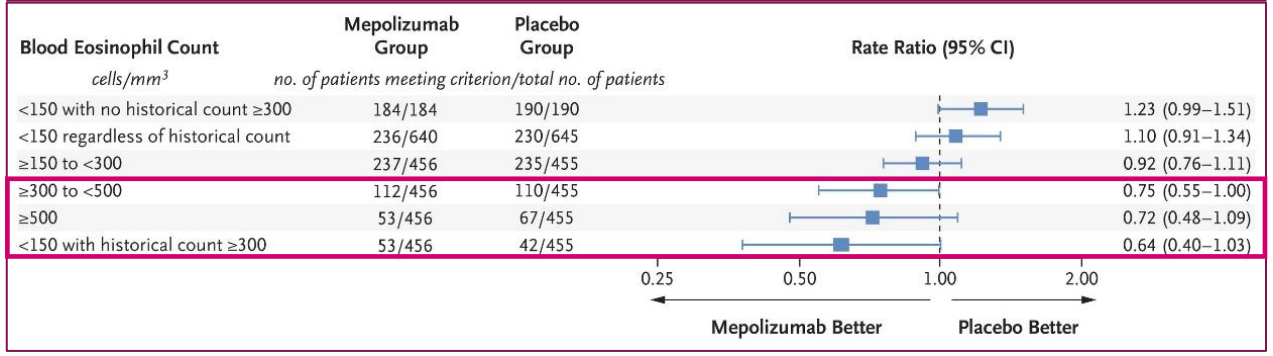


Figure from Pavord ID et al. *N Engl J Med.* 2017; 377(17):1613-1629.

Figure 3.11. Evidence Supporting Use of Biologics in the Treatment of COPD

Molecule/RCT*	Key inclusion criteria[a]	Annualized rate of moderate/severe exacerbations	Lung function improvement (pre-BD FEV1)[d]	Quality of life improvement (SGRQ)
Dupilumab (300 mg/2 weeks)				
BOREAS[1] (n=939)	FEV1 post-BD 30-70% chronic bronchitis[b] eos ≥ 300 (screen)	RR 0.70; P < 0.001	83mL; P < 0.001 (95% CI: 42, 125)	-3.4; P = 0.002 (95% CI: -5.5, -1.3)
NOTUS[2] (n=935)	FEV1 post-BD 30-70% chronic bronchitis[b] eos ≥ 300 (screen)	RR 0.66; P < 0.001	62mL; P = 0.02 (95% CI: 11, 113)	-3.4[e] (95% CI: -5.8, -0.9)
Mepolizumab (100 mg/4 weeks)				
METREO[3] (n=674)	FEV1 post-BD 20-80% eos ≥ 150 (screen) or eos ≥ 300 (previous year)	RR 0.80; NS	19mL; NS (95% CI: -29, 67)	-1.8; NS (95% CI: -4.5, 0.8)
METREX[3] (n=836)	FEV1 post-BD 20-80% eos ≥ 150 (screen) or eos ≥ 300 (previous year)[c]	RR 0.82; P = 0.04	-10mL; NS (95% CI: -54, 33)	0.2; NS (95% CI: -2.8, 3.2)
MATINEE[4] (n=804)	FEV1 post-BD 20-80% eos ≥ 300 (screen) and eos ≥ 150 (previous year)	RR 0.79; P = 0.01	-9.0mL; NS (95% CI: -60.1, 42.1)	-2.3; NS (95% CI: -4.6, 0.1)

*Molecules are listed in order of approval in the US.

These results cannot be directly compared across trials as there were different patient populations included.

a: all studies recruited patients with exacerbations in the previous year while receiving inhaled triple therapy
b: patient-reported history of chronic bronchitis (chronic productive cough) for 3 months in the year up to screening, absent other known causes
c: pre-defined eosinophilic population
d: at 52 weeks
e: significance not tested according to hierarchical testing procedure

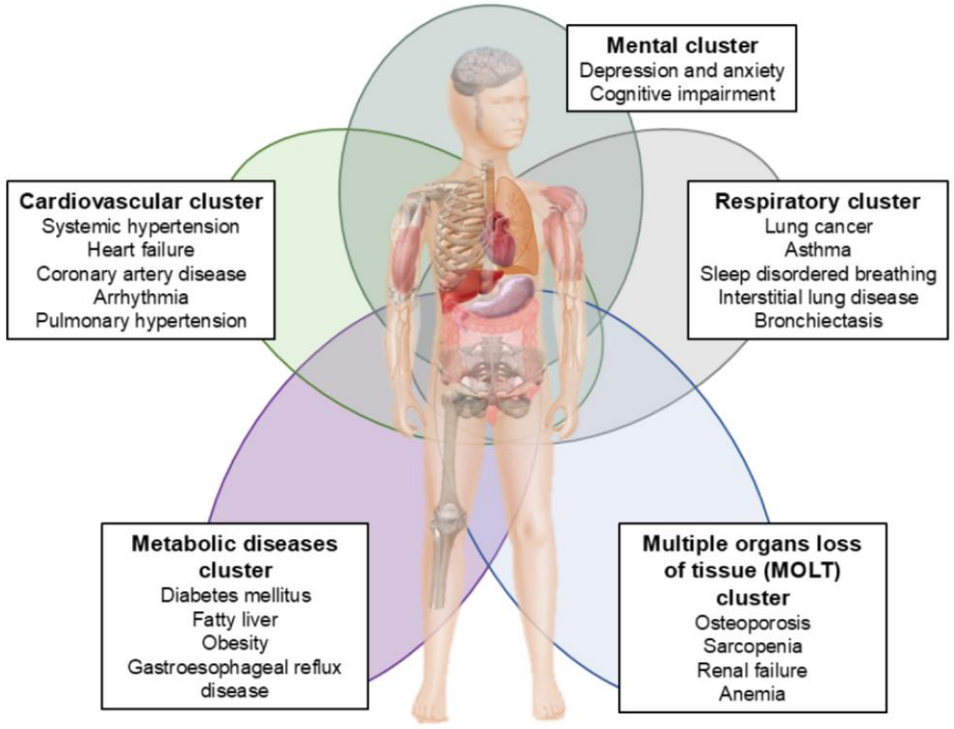
NS: not statistically significant; eos: blood eosinophils (cells/µL); SGRQ: St George's Respiratory Questionnaire; BD: bronchodilator; RR: risk ratio.

References: [1]Bhatt et al. N Engl J Med 2023;389:205-214; [2]Bhatt et al. N Engl J Med 2024;390:2274-2283; [3]Pavord et al. N Engl J Med 2017;377:1613-1629; [4]Sciurba et al. N Engl J Med 2025;392:1710-1720; .

‘COPD and Multimorbidity’ Chapter Revisions: Additional Focus on CVD and Its Impact on COPD

- **Renamed chapter to ‘COPD and Multimorbidity’**,[a] which includes a new section on CVD with further information on:
  - Common CVD in patients with COPD
  - **Increased risk of cardiovascular events** during, and for **at least 1 year after an acute COPD exacerbation**
    - New cardiovascular event risk data supplement the ‘Cardiovascular risk in COPD’ subsection in Chapter 2
- **[New] section on COPD, frailty, and multimorbidity**, which includes a **new Figure 5.2** depicting morbidity clusters frequently present in patients with COPD that independently impact outcomes
- **Expanded diagnosis and management guidance** for each of the **five morbidity clusters:** cardiovascular, mental, respiratory, MOLT, and metabolic disease
- GOLD recognizes the importance of **integrative care in COPD management**, particularly given the prevalence of multimorbidity
- Addition of guidance for **detection of frequent morbidities in all patients with COPD at initial assessment and follow up (yearly or every 3–5 years)**
- Although COPD is negatively impacted by multiple comorbidities, **COPD is one of the most important conditions that adversely affects outcomes of other disorders**

Figure 5.2. Morbidity Clusters Frequently Present in Patients With COPD that Independently Impact Outcomes



Adapted from: Celli BR, Fabbri LM, Yohannes AM, Hawkins NM, Criner GJ, Bon J, Humbert M, Jenkins CR, Pantoni L, Papi A, Quint JK, Sethi S, Stolz D, Agusti A, Sin DD. A person-centred clinical approach to the multimorbid patient with COPD. Eur J Intern Med. 2025 Aug 12:106424. doi: 10.1016/j.ejim.2025.07.020.

[a]Previously “COPD and Comorbidities.”

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Introduction of the Concepts of ‘Disease Stability’ and ‘Disease Control’

- Achieving **low disease activity is a treatment target in COPD** with the aim to prevent any exacerbations over both the short and long term
- **[New] definitions** proposed to describe the clinical state achieved when considering symptom and treatment outcomes over time:[a]
  - **Disease stability:** a low disease activity state with no exacerbations, no worsening of symptoms, and no accelerated loss of lung function
  - **Disease control:** a state of low disease activity, defined by no exacerbations and no worsening of symptoms, plus low impact on the patient defined as symptoms below a threshold value
- **Aiming for control** is more ambitious than stability and **is unachievable for individuals with extensive end-organ damage**. However, **reduction of disease activity may be achieved** with a combination of pharmacological and non-pharmacological interventions
- **Early targeting of disease activity has the potential to minimize disease progression** and associated structural damage, and **emphasizes the importance of earlier diagnosis, disease activity evaluation using biomarkers, and therapy that suppresses disease activity**

[a]At present, these definitions do not feature in any diagnostic, management, or treatment algorithms within the GOLD Report.

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Additional Key Changes

Inhaler Device

- Once a device has been selected, it **should not be changed without clinical justification**
- **Mass switching** of devices for cost or supply reasons driven by payors, or **perceived impact on the environment**, has led to **increased prednisolone use and higher healthcare utilization**

[New] Chapter on AI and Emerging Technologies

- **[New] chapter on AI** in COPD, which discusses how AI can potentially help in the diagnosis, assessment, clinical management, and prediction of prognosis in COPD. Yet, there are risks and limitations, which need careful consideration before application in clinical practice
- **Inclusion of alternatives to spirometry**, which highlights analysis of **voice features and oscillometry (FOT, IOS, AOS)** as techniques being explored and requiring validation in larger cohorts

Recognition of Additional Causes and Risk Factors of COPD

- **COPD prevalence estimates likely reflect widespread under-recognition and underdiagnosis**
  - **Underdiagnosis is universally high**, one study estimated that **81.4% of COPD cases** are undiagnosed
- Smoking and outdoor and household air pollution are the largest global contributors to the mortality of patients with COPD
- COPD DALY estimates have been updated and now reflect the expected rise to the **fourth leading cause of years lost worldwide by 2050**
  - **China is cited as a positive example** through the implementation of strategies aimed at reducing smoking rates, promoting clean energy sources, and improving access to quality healthcare to mitigate the COPD burden

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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 and opportunistic case-finding, performing spirometry in patients with symptoms and/or risk factors, but not screening spirometry in asymptomatic individuals without any significant exposures to tobacco or other risk factors

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Figure 2.8

Factors That May Be Associated With COPD Underdiagnosis

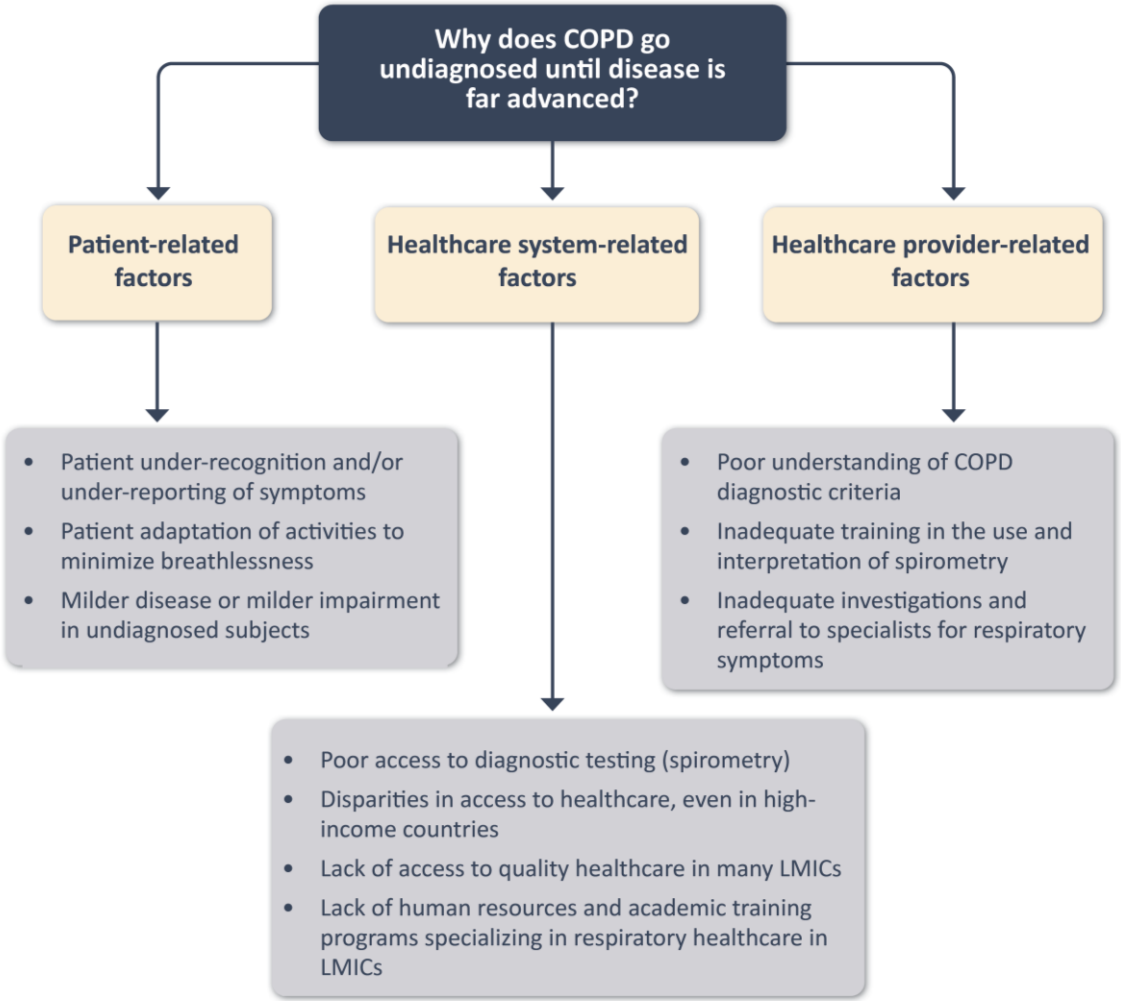

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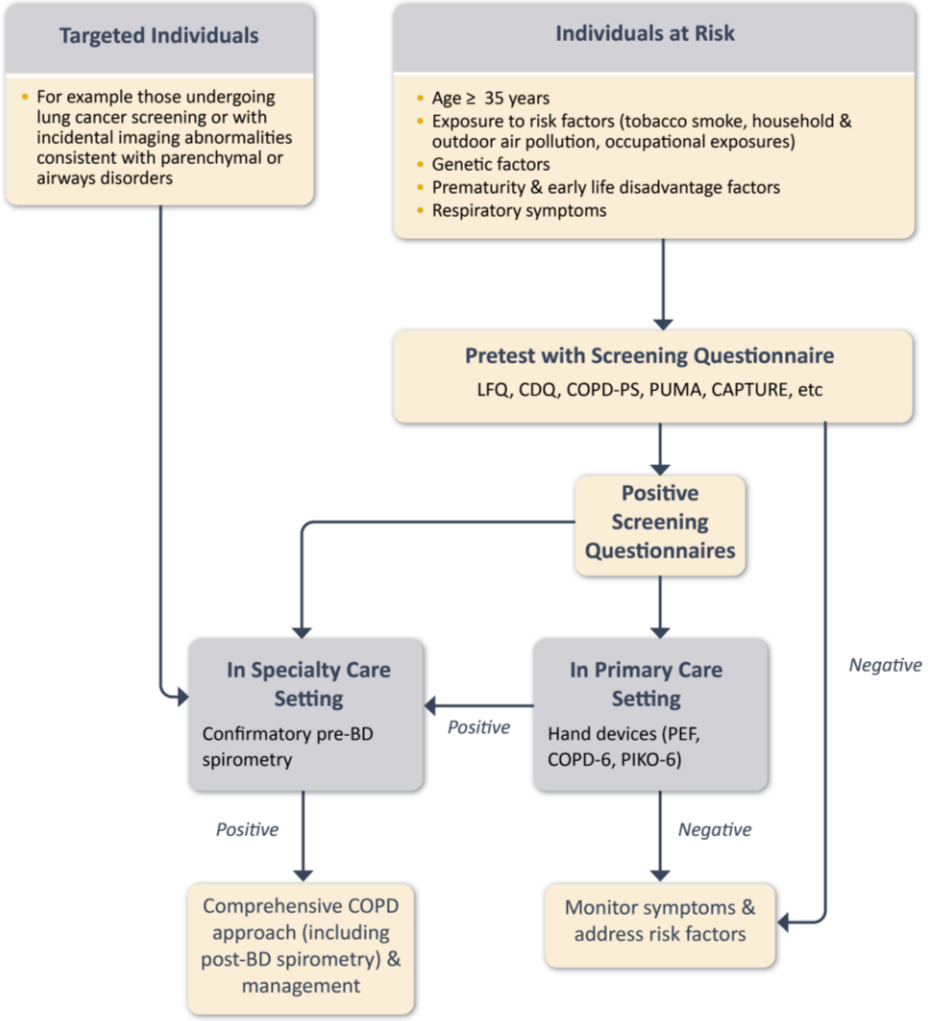
Figure 2.9

Algorithm for COPD Case-finding



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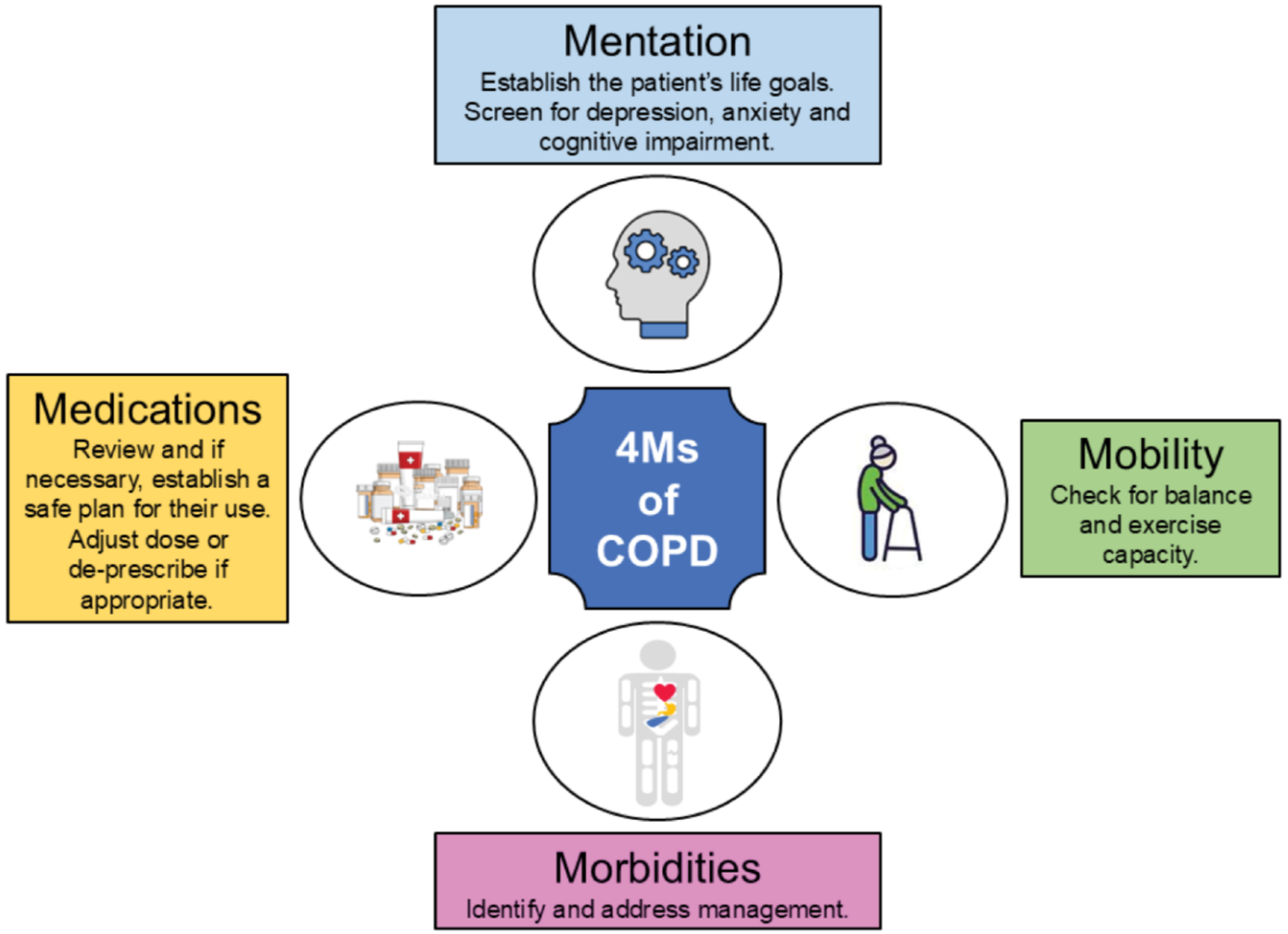
Summary of the Modified 4Ms Person-centered Approach to Multimorbid Patients With COPD

Figure 5.1



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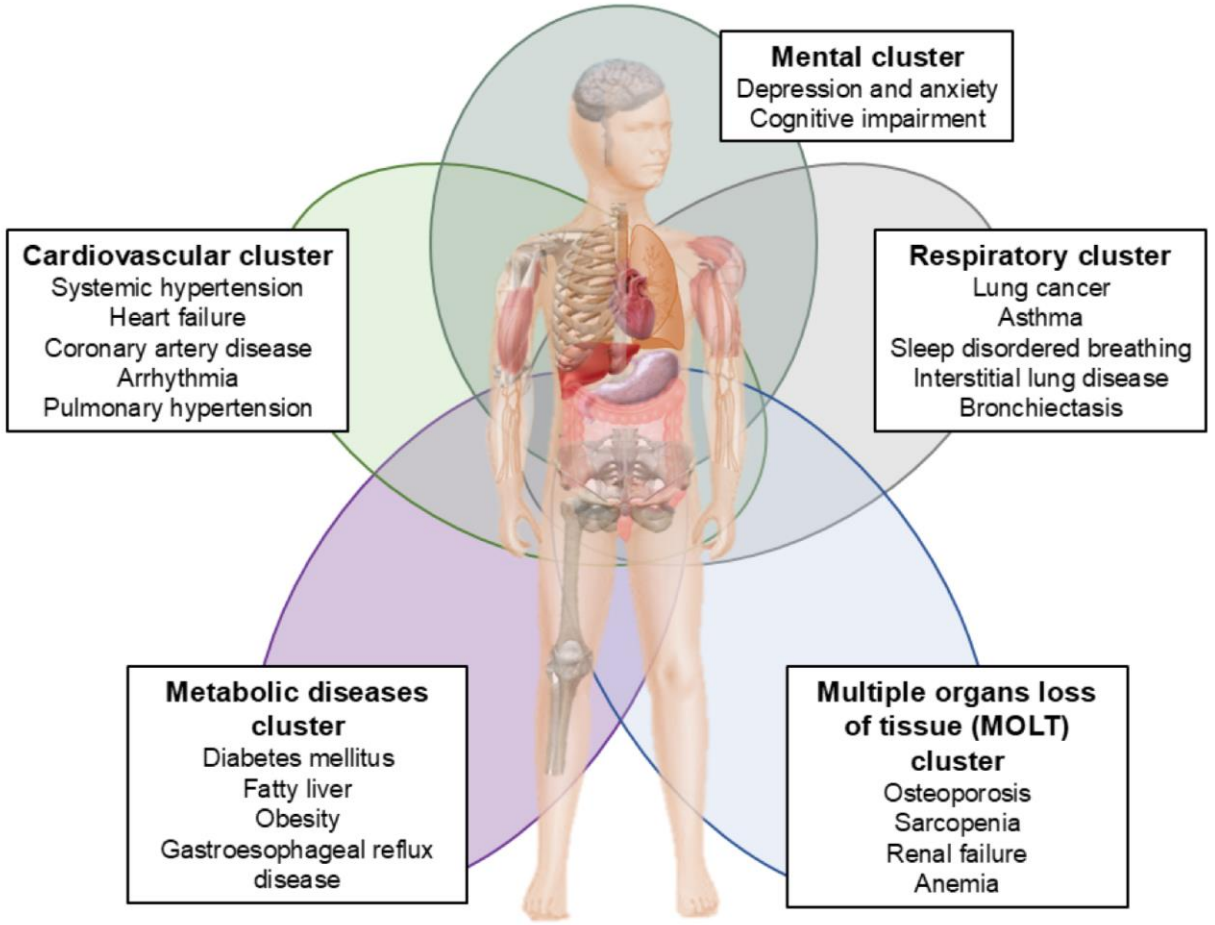
Morbidity Clusters Frequently Present in Patients With COPD That Independently Impact Outcomes

Figure 5.2



Adapted from: Celli BR, Fabbri LM, Yohannes AM, Hawkins NM, Criner GJ, Bon J, Humbert M, Jenkins CR, Pantoni L, Papi A, Quint JK, Sethi S, Stolz D, Agusti A, Sin DD. A person-centred clinical approach to the multimorbid patient with COPD. Eur J Intern Med. 2025 Aug 12:106424. doi: 10.1016/j.ejim.2025.07.020.

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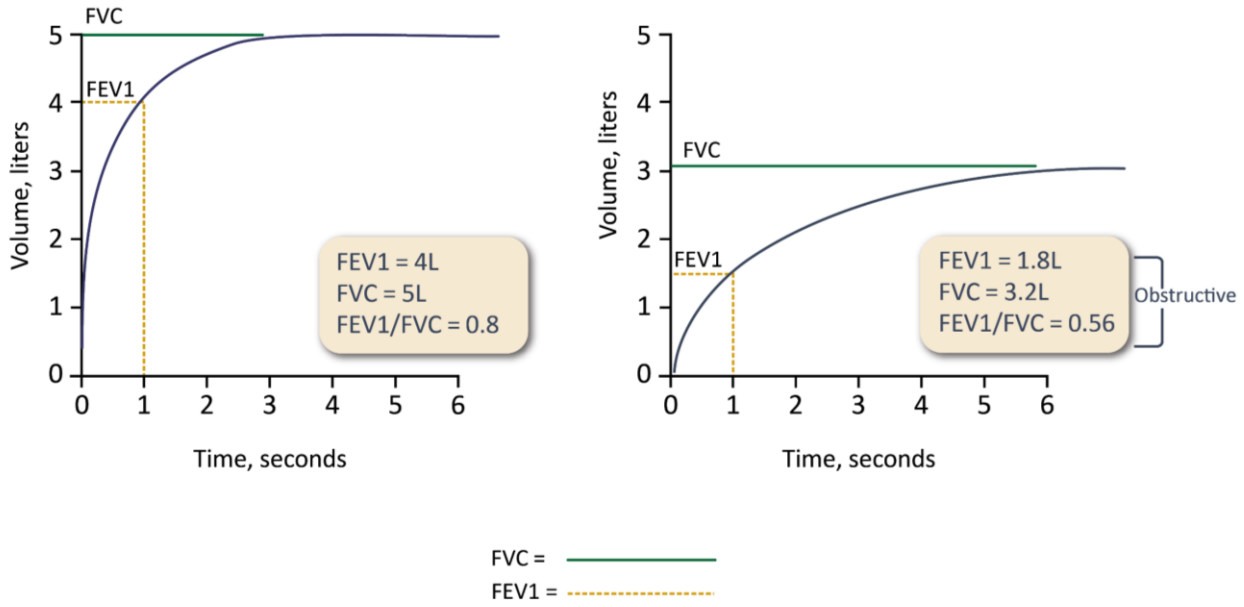
Figure 2.5

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. GOLD. Global strategy for prevention, diagnosis and management of COPD: 2026 Report. GOLD website. https://goldcopd.org/2026-gold-report-and-pocket-guide/; 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 included '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

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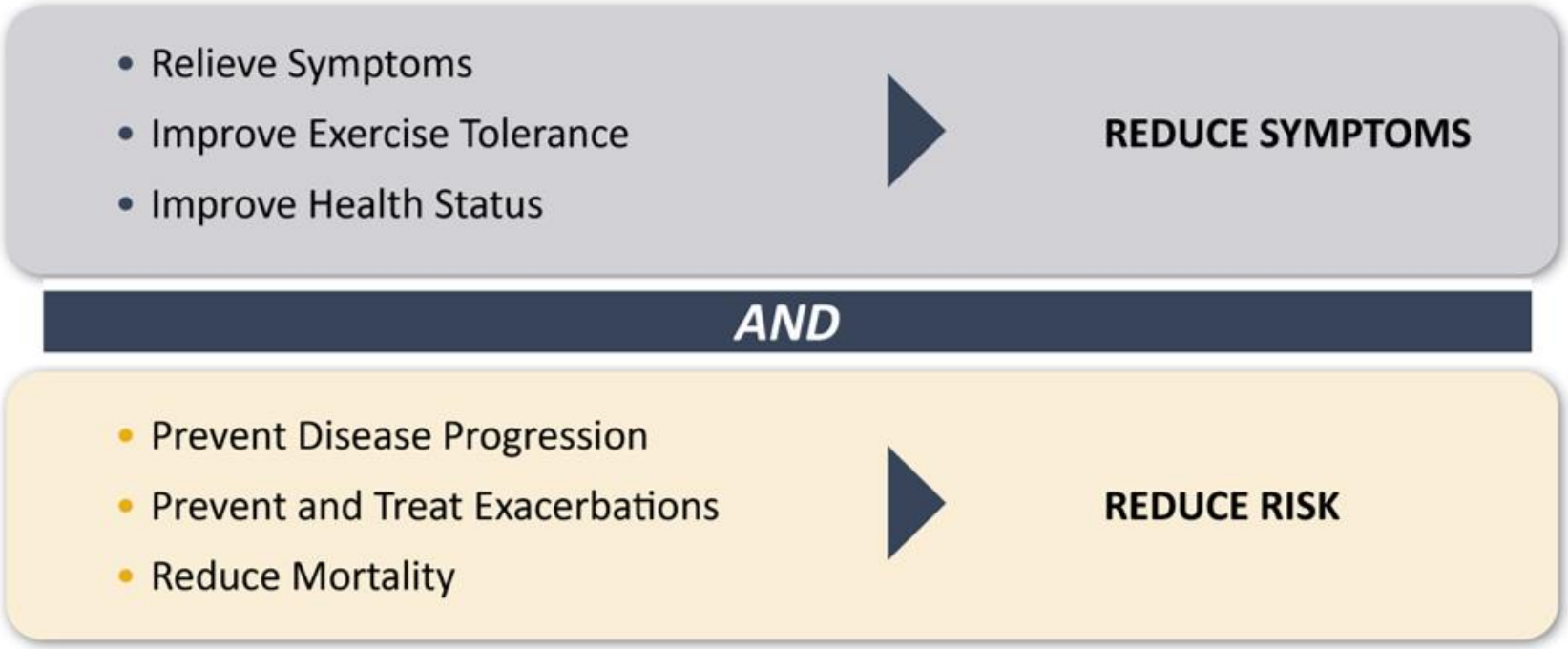
Management of Stable COPD

Figure 3.1

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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Figure 3.2

Management of COPD

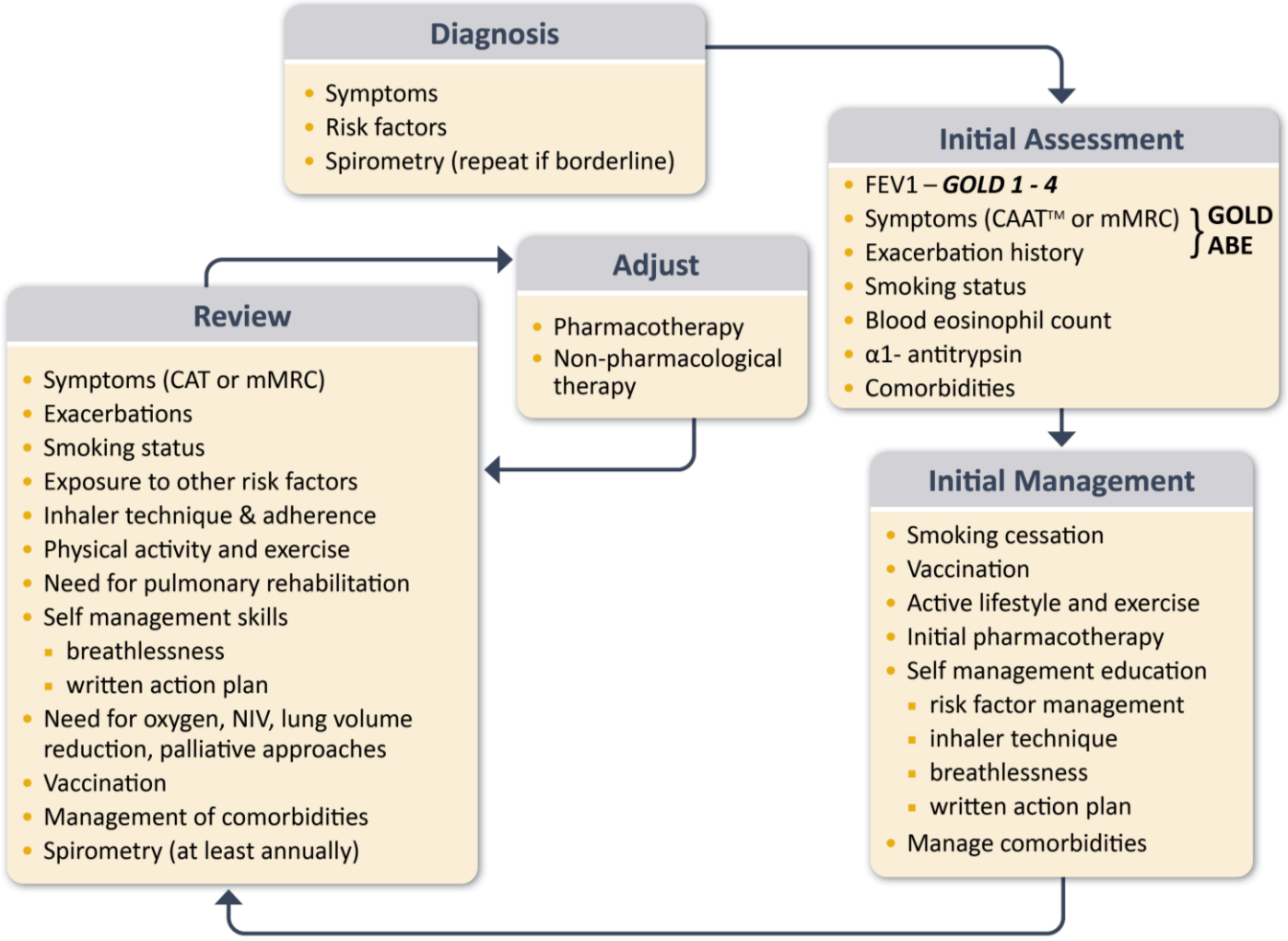

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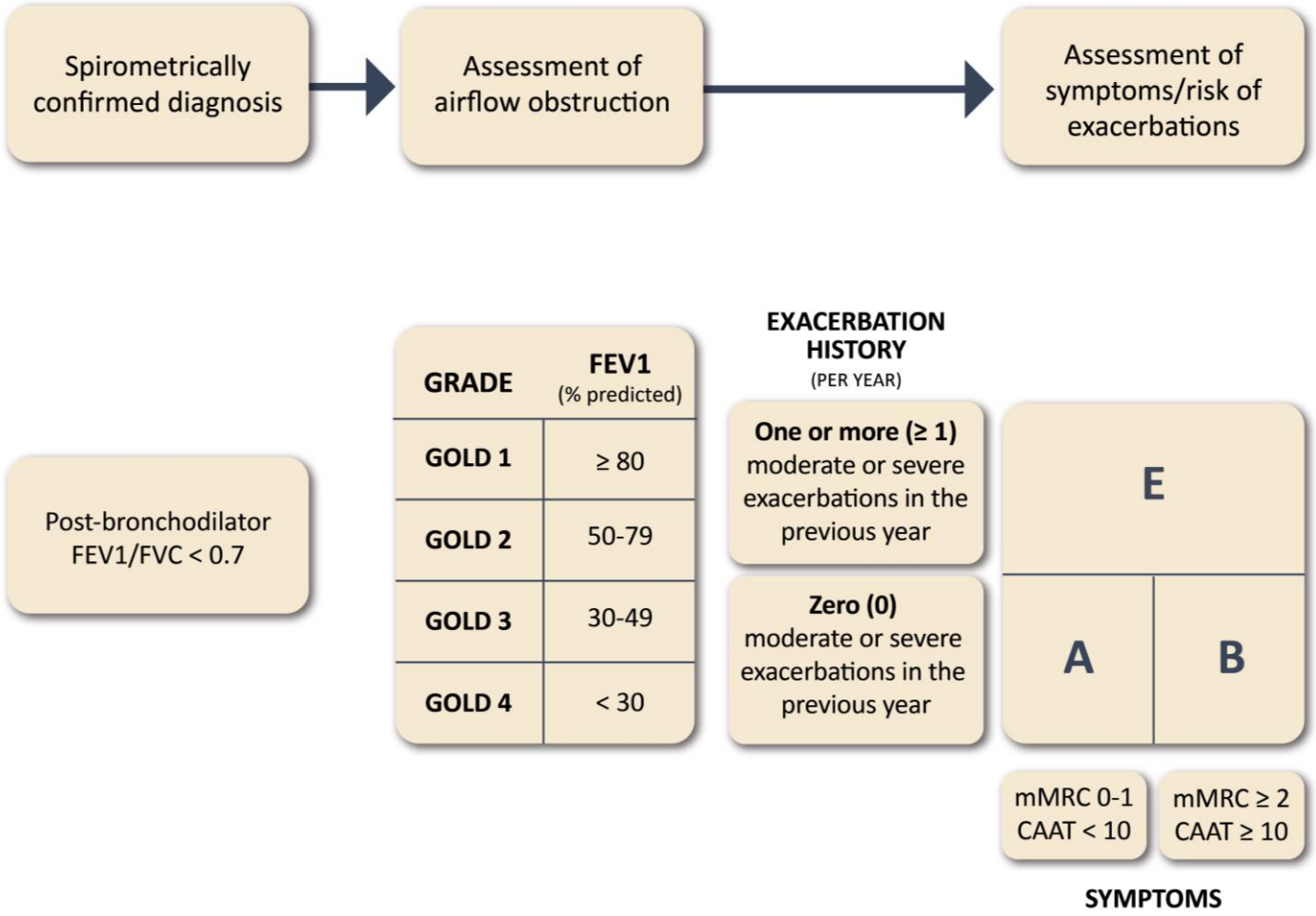
Figure 2.13

GOLD ABE Assessment Tool



Exacerbation Risk Factors and Impact

Symptom Tests

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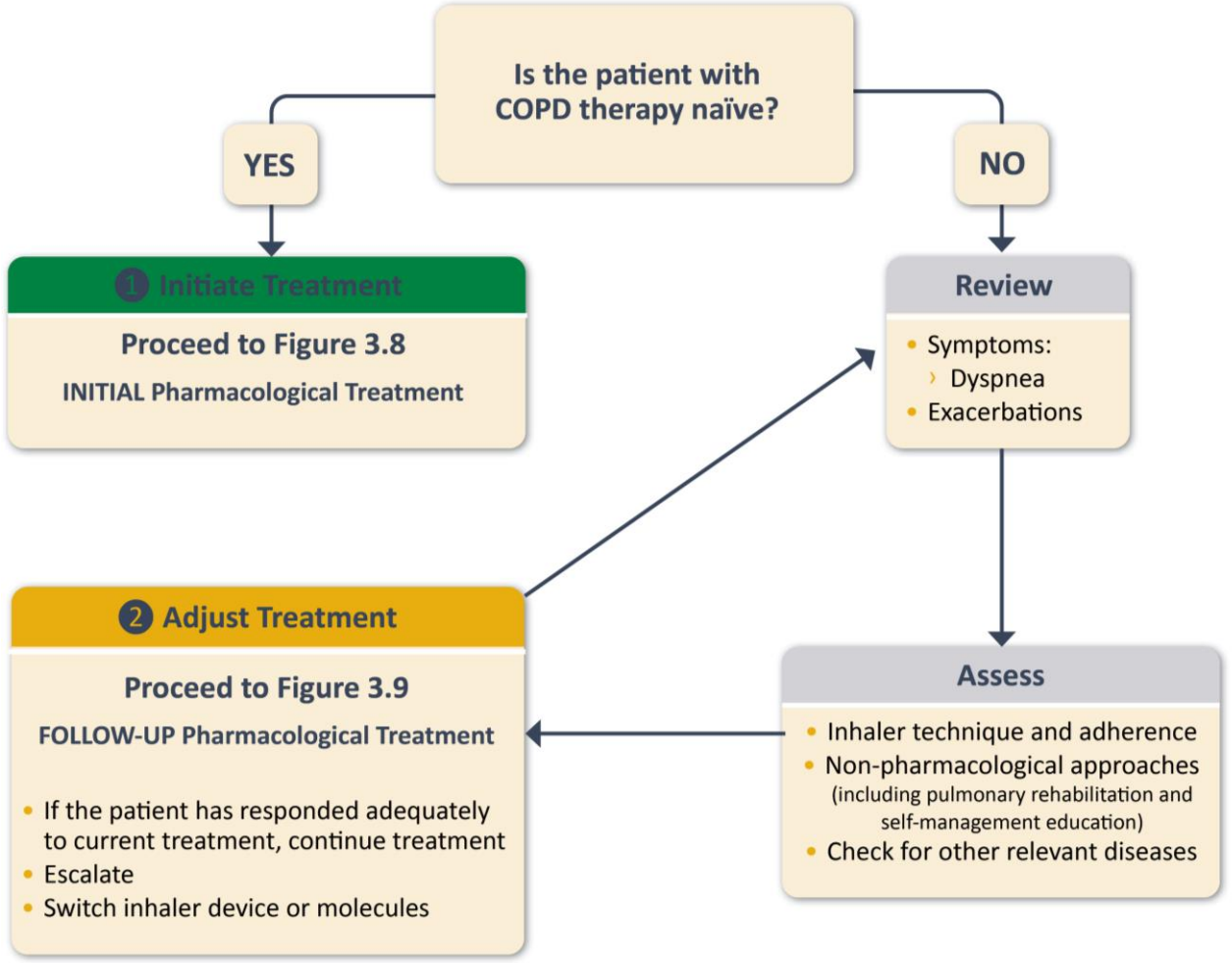
Treatment of Stable COPD

Diagnosis and Management Cycle

Figure 3.7



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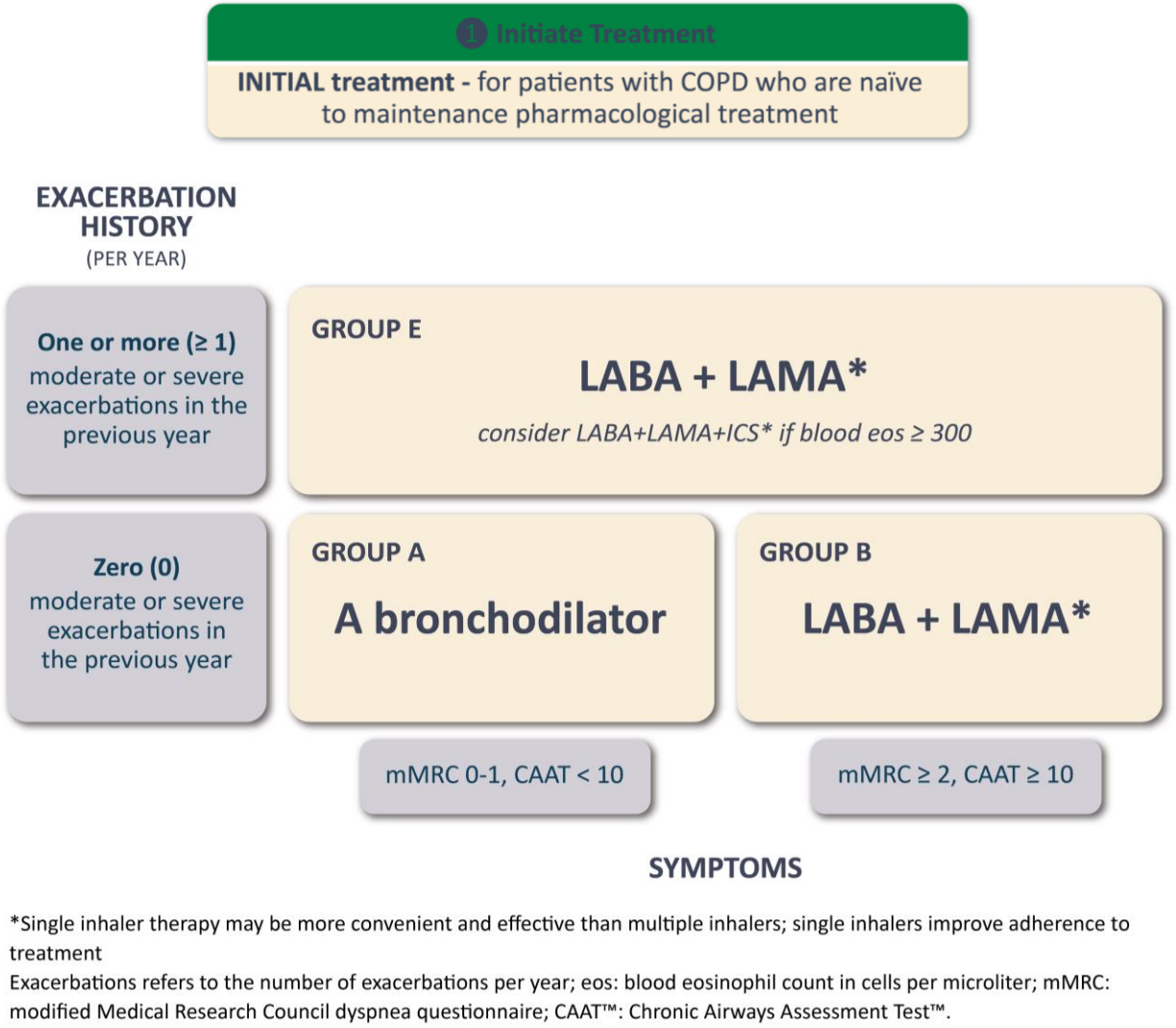
Treatment of Stable COPD

Initial Pharmacological Treatment

Figure 3.8



*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; CAAT™: Chronic Airways Assessment Test™.

Inhaled Delivery

COPD Exacerbations Confounders

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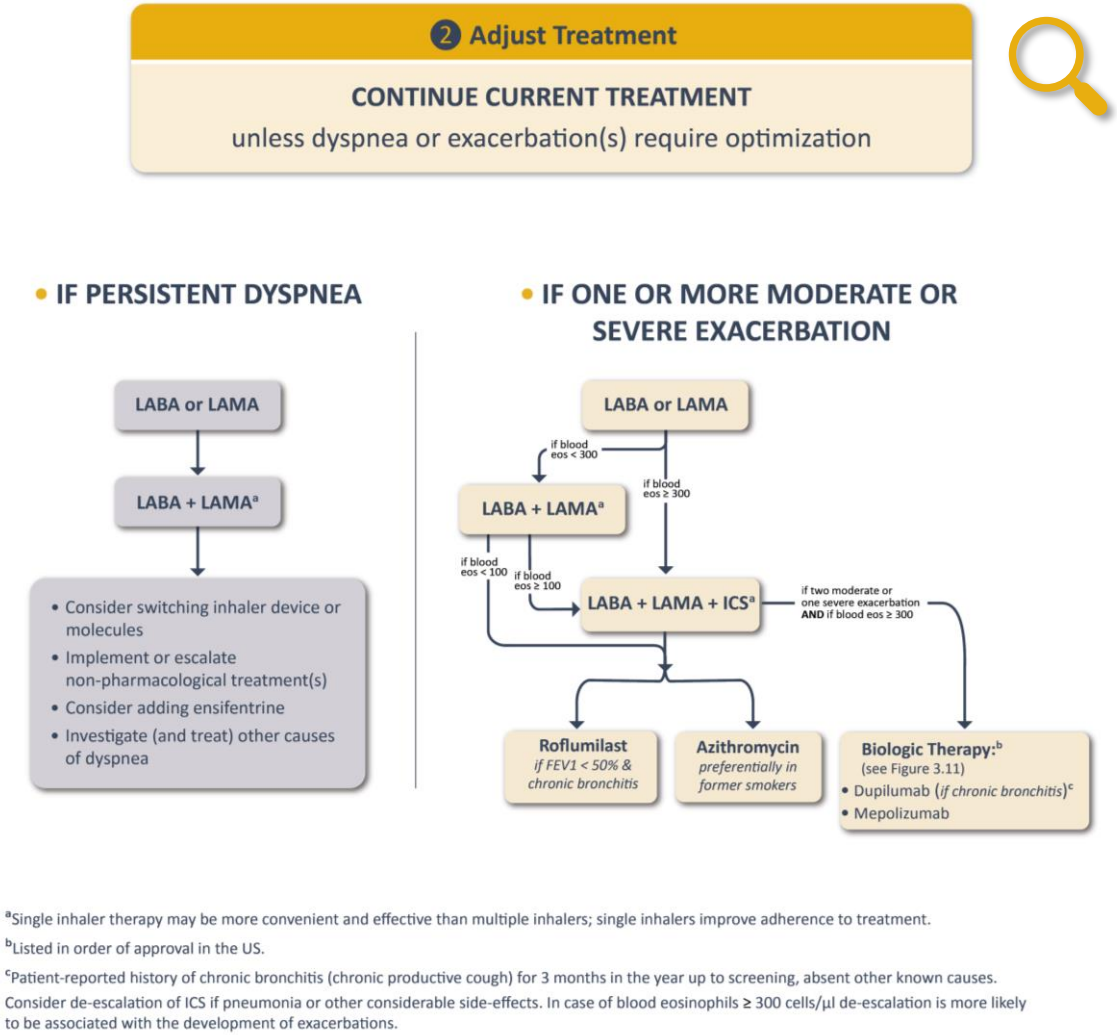
Treatment of Stable COPD

Follow-up Pharmacological Treatment

Figure 3.9



[a]Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment.

[b]Listed in order of approval in the US.

[c]Patient-reported history of chronic bronchitis (chronic productive cough) for 3 months in the year up to screening, absent other known causes.

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

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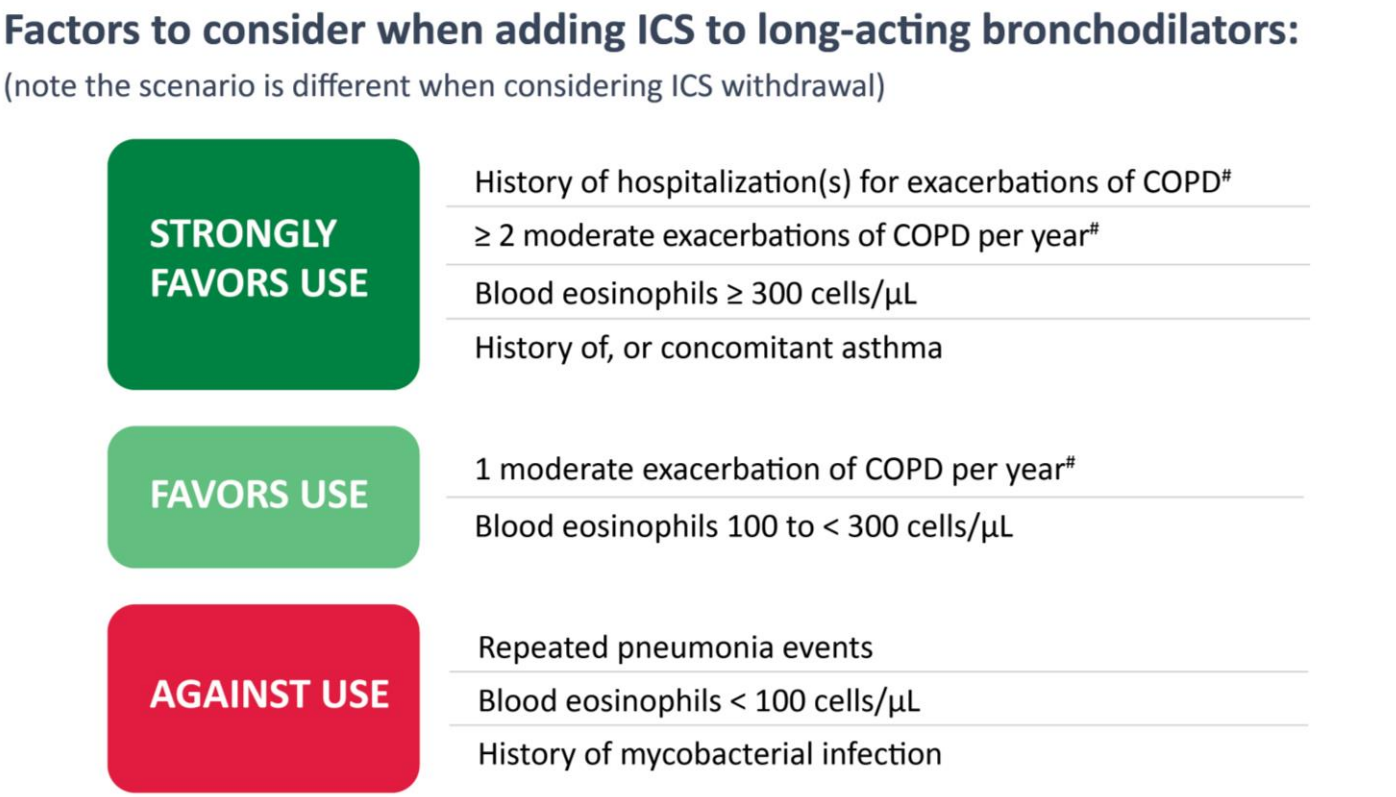
Figure 3.10

Factors to Consider When Initiating ICS Treatment



#despite appropriate long-acting bronchodilator maintenance therapy (see Figures 3.8 & A3.1 for recommendations); *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*

Other Pharmacologic Options

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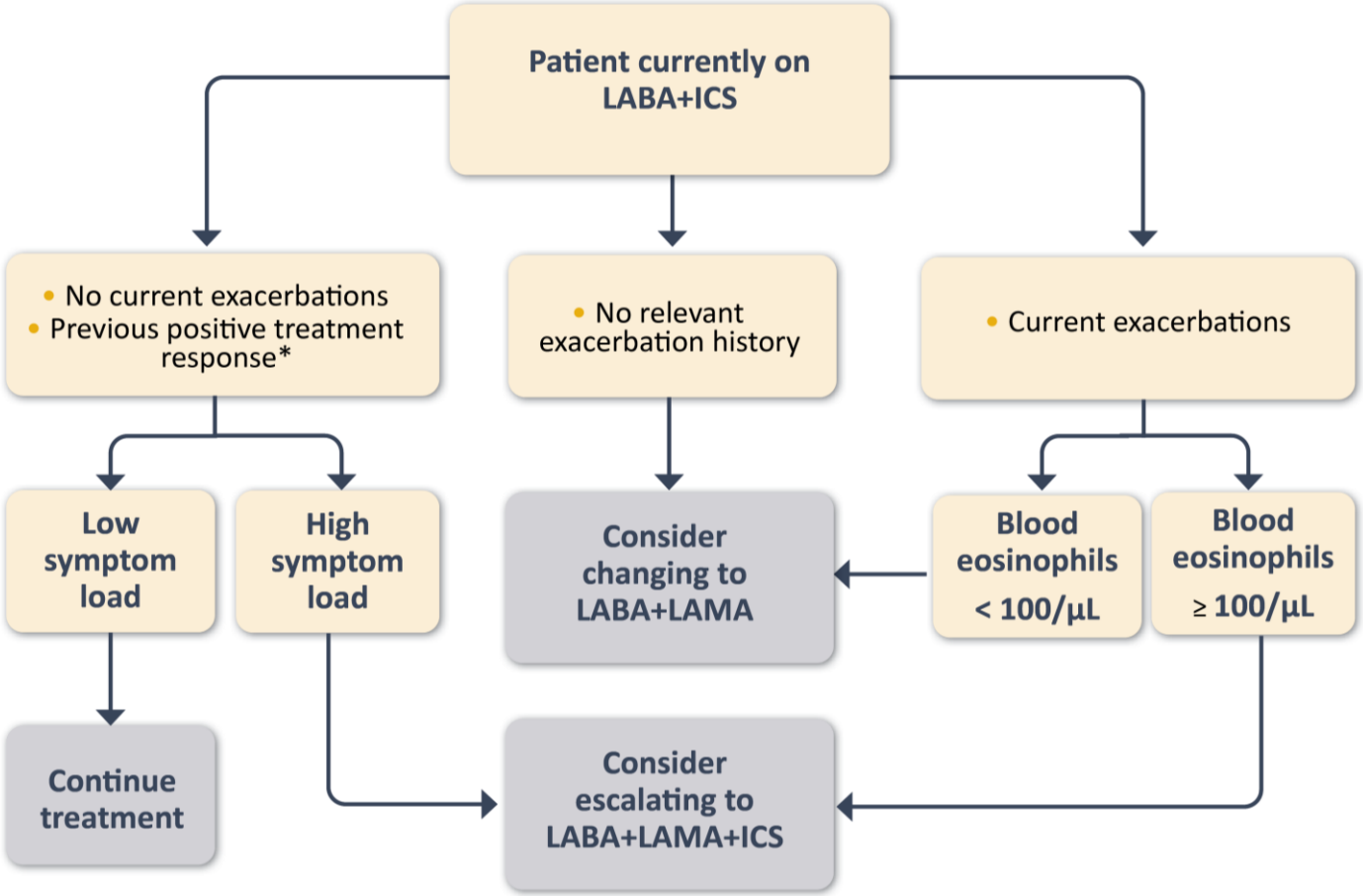
Figure 3.12

Management of Patients Currently on ICS/LABA



*Patient previously had exacerbations and responded to LABA+ICS treatment

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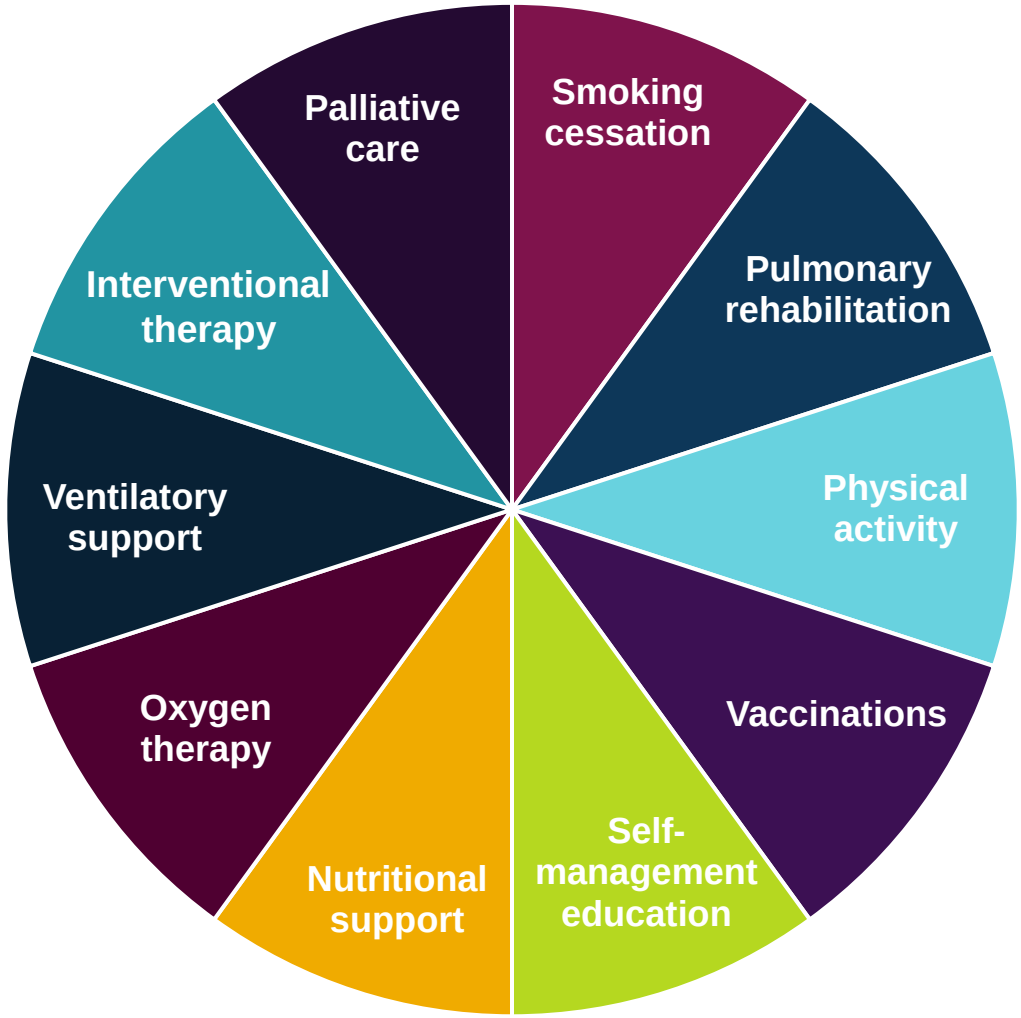
Non-Pharmacologic Management of COPD[a]



Personalized Strategies

Activity

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

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Appendix

Principles of Disease: Pathologic Changes in Airways

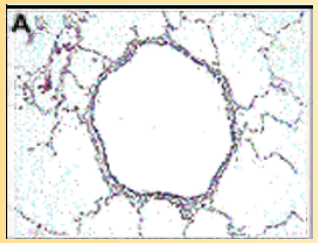
Proximal cartilaginous airways (>2 mm in diameter)[1]

- Increased numbers of macrophages and CD8 T lymphocytes
- Submucosal bronchial gland enlargement and goblet cell metaplasia
- Neutrophil and lymphocyte infiltrate in bronchial glands
- Airway epithelial squamous metaplasia
- Ciliary dysfunction
- Hypertrophy of smooth muscle and connective tissue

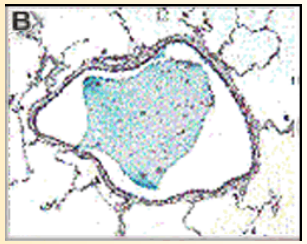
Peripheral noncartilaginous airways (<2 mm in diameter)[1]

- Increased numbers of macrophages and T lymphocytes (CD8 > CD4)
- Increased number of B lymphocytes, lymphoid follicles, and fibroblasts
- Luminal and inflammatory exudates
- Extension of goblet cells and squamous metaplasia into peripheral airways
- Peribronchial fibrosis and airway narrowing

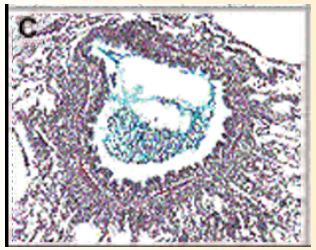
Histologic Changes Associated With Cigarette Smoking[2]



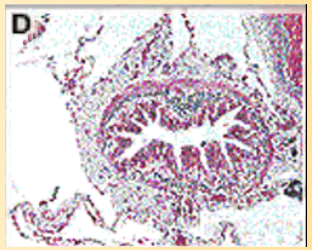
Normal airway



Plug of mucoid exudate



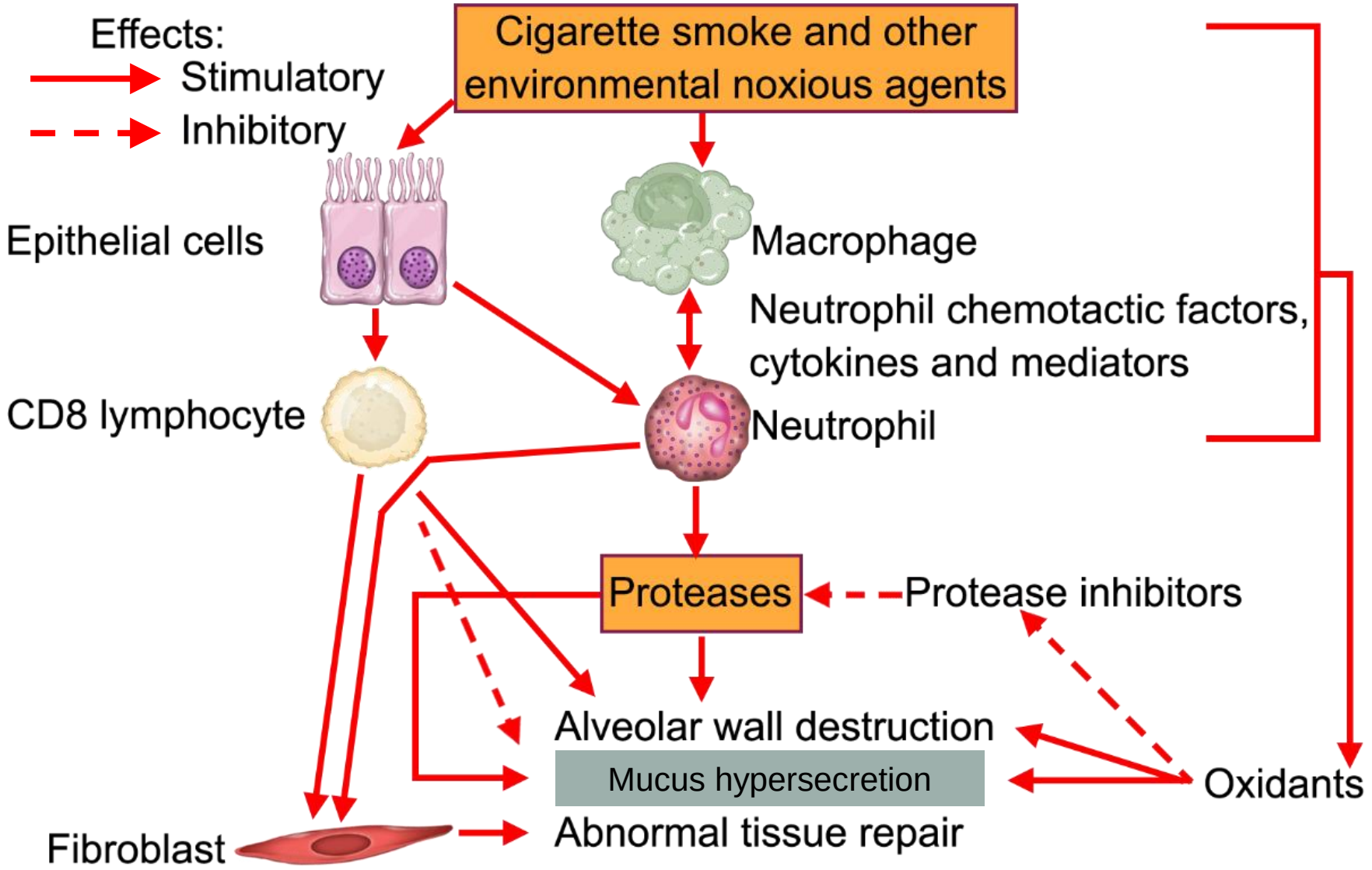
Inflammatory exudate in the wall and lumen of airway



Airways with reduced lumen, increased smooth muscle and deposition of peribronchial connective tissue

1. MacNee W. *BMJ*. 2006;332:1202-1204; 2. Adapted from: Hogg JC et al. *N Engl J Med*. 2004;350:2645-2653.

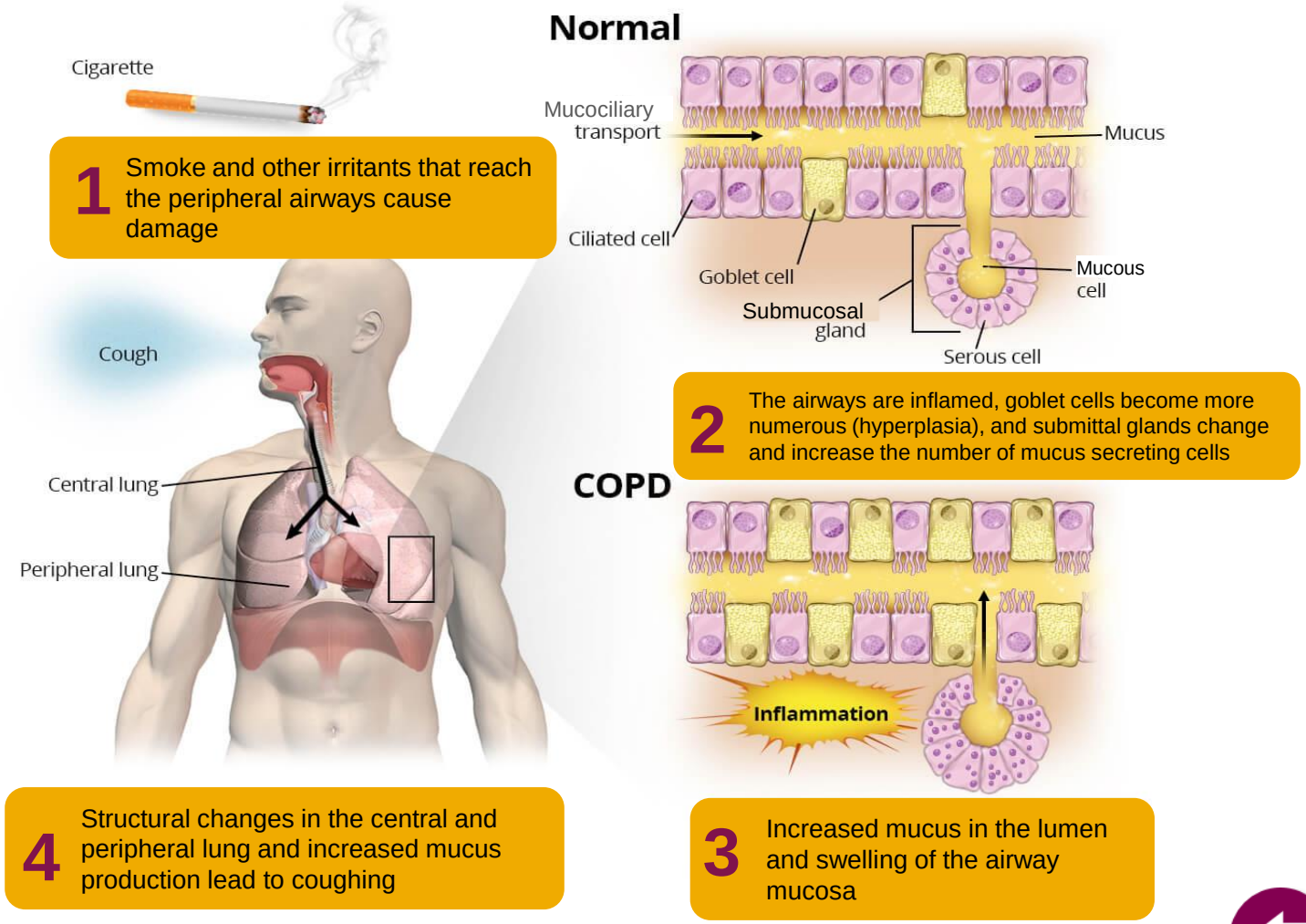
Principles of Disease: Role of Inflammatory Cells



Adapted from MacNee W. *BMJ*. 2006;332:1202-1204.

Principles of Disease: Mucus Hypersecretions and Ciliary Dysfunction

- Mucus hypersecretion results in a chronic productive cough
- Characteristic of chronic bronchitis, but not necessarily airflow obstruction
- Due to squamous metaplasia of epithelial cells, increased numbers of goblet cells and increased size of bronchial submucosal glands
  - Abnormal mucociliary clearance
  - Difficult to expectorate



MacNee W. *BMJ*. 2006;332:1202-1204.

Definitions: Lung Volumes and Capacities

Lung Volumes[1]
(amount of air for a specific function)

Tidal volume (V_T)
- Amount of air breathed in or out during a normal breath

Inspiratory reserve volume (IRV)
- Additional amount of air that can be inhaled after a normal inhalation

Expiratory reserve volume (ERV)
- Additional amount of air that can be exhaled after a normal exhalation

Residual volume (RV)
- Amount of air that remains in the lung following forced maximum expiration

Lung Capacities[1]
(sum of 2 or more volumes)

Inspiratory capacity (IC) = V_T + IRV
- Amount of air that can be inhaled after the end of a normal expiration

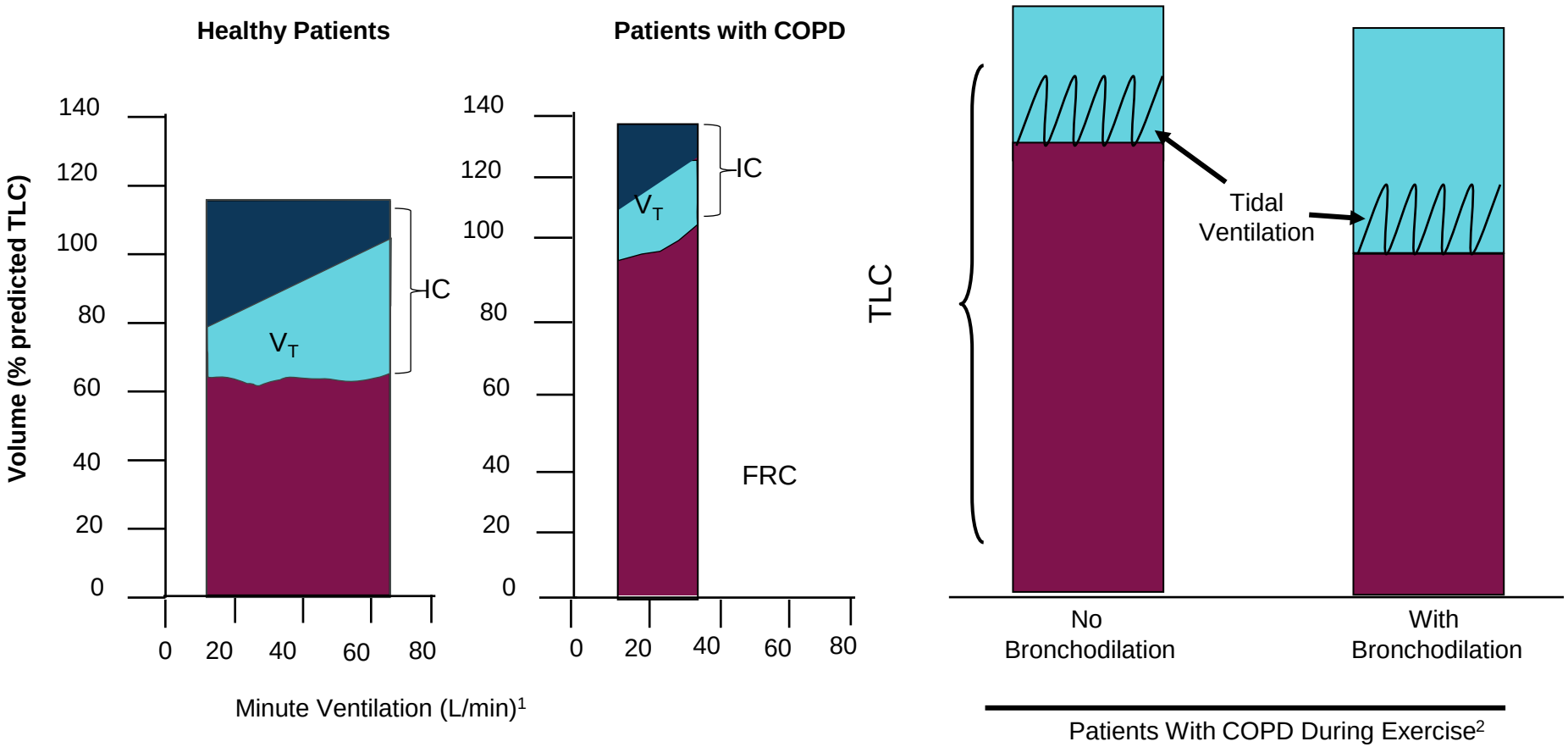
Functional residual capacity (FRC) = ERV + RV
- Volume of air present in the lungs at the end of normal exhalation[2]

Vital capacity (VC) = ERV + V_T + IRV
- The maximum amount of air that can be inhaled or exhaled during a respiratory cycle

Total lung capacity (TLC) = RV + ERV + V_T + IRV
- Measurement of the total amount of air that the lung can hold

1. LibreTexts™ Biology. Gas exchange across respiratory surfaces - lung volumes and capacities; 2. Wanger J, et al. *Eur Respir J*. 2005;26:511-522.

Principles of Disease: Hyperinflation Is a Hallmark of COPD



- Increases FRC (EELV)
- Decreases IC
- Increases volume at which tidal breathing occurs
- Worsens with exercise and reduces exercise tolerance (dynamic hyperinflation)

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

The Importance of COPD Detection

Early Identification

- Studies from across the world suggest that up to 70% of adults with COPD remain undiagnosed.
- Individuals with undiagnosed COPD are afflicted by poor quality of life and suffer exacerbations like those seen in diagnosed disease.
- Extensive under-diagnosis and misdiagnosis in COPD can lead to patients receiving no or incorrect treatment.
- Appropriate and earlier diagnosis of COPD can have a very significant public health impact.

Exacerbations

- Exacerbations of COPD are episodes of acute respiratory symptoms worsening over a few days (up to 14 days) and characterized by increased dyspnea and/or cough and sputum that may be accompanied by tachypnea and/or tachycardia.
- They are often associated with increased local and systemic inflammation caused by airway infection, pollution, or other insults to the lungs.
- Exacerbations of COPD have negative impact on health status, worsening airflow obstruction, disease progression, rates of hospitalization and readmission, and risk of death.
- CV risk during and after such episodes increases significantly. The risk remains high during the first few weeks after hospital discharge for an exacerbation and can remain significantly increased one year later.

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Additional Changes in the GOLD 2026 Report

- [New] guidance for assessing where the **most appropriate place of management is for a patient with COPD during an exacerbation (Figure 4.4)**
- **Updated vaccine** recommendations to include **tetanus** and **diphtheria** vaccination for those **not previously immunized**, and now also recommends **RSV** vaccination for adults aged ≥50 years and/or with chronic heart or lung disease
- Acknowledgment that **mucus plugging** is associated with **elevated blood eosinophils**, suggesting association with **Type 2 inflammation**; however, plugging may also be associated with other phenotypes
- Recognition of ongoing studies on **oscillometry and vocal biomarkers**; however, no recommendations have been provided at this time as further validation in larger cohorts is required
- **[New] Chapter 6** acknowledges the valuable role of **AI in COPD diagnosis**, addressing disease heterogeneity and driving practice change, while also recognizing the associated risks and emphasizing the need for validation

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Content Unchanged in GOLD 2026

Determination of the risk of future events (such as exacerbations, hospital admissions, or death) to guide therapy is a **goal of initial COPD assessment**

Main **treatment goals** are to reduce symptoms and **future risk of exacerbations**

Acknowledgment of evidence supporting a reduction in mortality with pharmacotherapy;[a] fixed-dose **inhaled triple therapies reduce all-cause mortality** vs LABA + LAMA in symptomatic patients[b] with a history of frequent and/or severe exacerbations[c]

Use of ICS + LABA in COPD is not encouraged; if there is an indication for an ICS, **triple therapy is preferred as it has been shown to be superior to ICS + LABA**

Recognition of key pathobiological and **pathophysiological mechanisms of COPD**, including hyperinflation, pulmonary gas exchange abnormalities (resulting in hypoxemia), inflammation, and exacerbations

Proper use of an inhaler has a positive environmental impact through reduction of exacerbations and their CO_2 footprint, especially when hospitalization is required

[a]Supported by evidence from IMPACT and ETHOS; [b]Symptomatic is defined as CAAT™ ≥10; [c]Patients with history of exacerbation in the past year.

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COPD Exacerbations: Risk Factors and Impact

Risk factors

- Frequent past exacerbations
- Severity of FEV_1 impairment
- Chronic bronchial mucus hypersecretion
- Daily cough and wheeze
- Increased age
- Persistent symptoms of chronic bronchitis
- Comorbid conditions, mainly cardiovascular disease

Impact

- More rapid decline of FEV_1
- Increased dyspnea
- Greater decline in health status
- Increased mortality

Anzueto A. *Eur Respir Rev*. 2010;19(116):113–118.

Symptom Tests

mMRC

The **mMRC** is a measure of breathlessness that comprises a **5-grade scale** (0 to 4). It relates well to other multidimensional **health status** measures and predicts future mortality risk

CAAT™

The **CAAT™/CAT™** is an **8-item questionnaire** that assesses health status in patients with COPD, which provides a **score ranging from 0-40**. It correlates closely with the **SGRQ** and is extensively documented in numerous publications

The COPD Assessment Test CAT™ was designed to assess the impact of COPD on a person's health status. To facilitate its use in other chronic airway diseases, CAT™ has been renamed as the Chronic Airways Assessment Test CAAT™. CAT™ and CAAT™ are equivalent, and the scores are interchangeable.

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Figure 2.11

Modified MRC Dyspnea Scale[1,2]

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: American Thoracic Society. Am Rev Respir Dis 1982;126(5):952-6.

1. GOLD. Global strategy for prevention, diagnosis and management of COPD: 2026 Report. GOLD website. https://goldcopd.org/2026-gold-report-and-pocket-guide/; 2. American Thoracic Society. *Am Rev Respir Dis.* 1982;126(5):952-956.

Figure 2.12

CAAT™ Assessment[1,2]

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 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: ☐

CAT™ has been renamed as the Chronic Airways Assessment Test CAAT™; CAT™ and CAAT™ are equivalent and the scores are interchangeable.

1. GOLD. Global strategy for prevention, diagnosis and management of COPD: 2026 Report. GOLD website. https://goldcopd.org/2026-gold-report-and-pocket-guide/; 2. Jones PW et al. *Eur Respir J*. 2009;34:648-654.

The GOLD Report Addresses Inhaled Drug Delivery

When treatment is given via inhalation, proper education, and training must be emphasized

- Provide instruction and demonstrate proper inhaler technique when prescribing a device, to ensure the patient has adequate technique
- Re-check the patient's inhaler technique at each visit

The choice of inhaler device has to be individually tailored and will depend on access, cost, prescriber, and most importantly, patient's ability and preference

Inhaler technique (and adherence) should be assessed prior to deciding if the current therapy is insufficient

Device Selection

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Assessing the Patient to Assist in Device Selection

Critical to consider[1]

1. **Is the patient capable of conscious inhalation?**
2. **Is the patient likely to reliably generate and control sufficient inspiratory flow?**
3. **Is the patient capable of hand–inhalation coordination?**

Assess patient capabilities

- Conscious inhalation[1]
- Peak inspiratory flow[1]
- Hand strength[2]
- Physical ability to load, prime, and actuate[2]
- Manual dexterity to ensure hand–inhalation coordination[2]
- Cognitive competency[2]

1. Dekhuijzen PN, et al. *Patient Prefer Adherence.* 2016;10:1561-1572; 2. Barrons R, et al. *Patient Intell*. 2015;7:53-65.

Figure 4.3

Conditions That May Mimic or Worsen Exacerbation-like Symptoms

Tools available to address potential confounders:

Most frequent	**Acute viral or bacterial bronchitis** • Viral and bacterial microbiological assessment • Chest X-ray
	Heart failure • Chest X-ray or chest CT scan • NT pro-brain natriuretic peptide (NT proBNP) and BNP • Cardiac ultrasound
	Myocardial infarction and/or cardiac arrhythmias (atrial flutter/fibrillation) • Electrocardiography • Troponin
	Pulmonary embolism • Clinical probability assessment (hemoptysis, deep vein thrombosis, history of cancer, surgery, bone fracture) • D-dimer • CT angiography for pulmonary embolism
	Pneumonia • Viral and bacterial microbiological assessment • Chest X-ray or chest CT scan • Lung ultrasound
Less frequent	**Pneumothorax** • Chest X-ray or chest CT scan • Thoracic ultrasound

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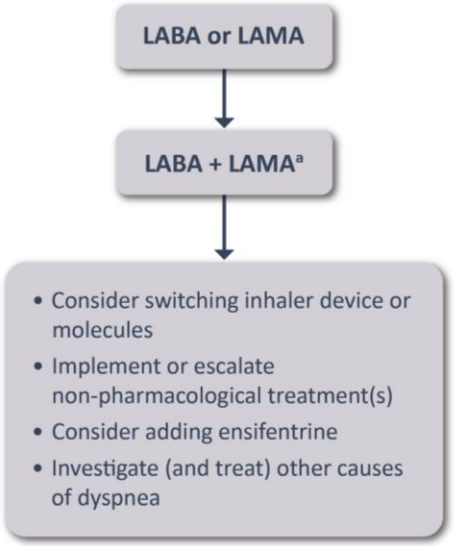
Figure 3.9

2 Adjust Treatment

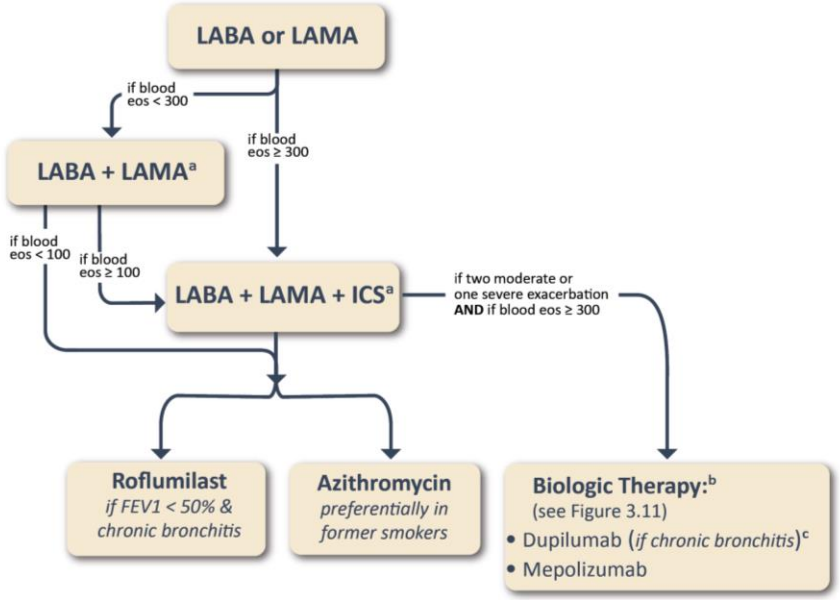
CONTINUE CURRENT TREATMENT

unless dyspnea or exacerbation(s) require optimization

• IF PERSISTENT DYSPNEA



• IF ONE OR MORE MODERATE OR SEVERE EXACERBATION



[a]Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment.

[b]Listed in order of approval in the US.

[c]Patient-reported history of chronic bronchitis (chronic productive cough) for 3 months in the year up to screening, absent other known causes.

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

Considerations Regarding Other Pharmacologic Options in Stable COPD

Oral glucocorticoids

- *Oral glucocorticoid use has numerous side effects (Evidence A) with no evidence of benefits (Evidence C)*

Mucolytics and antioxidants

- *Regular use of erdosteine, carbocysteine, and N-acetylcysteine may reduce risk of exacerbations in select populations (Evidence B)*

Antitussives

- *No conclusive evidence of a beneficial role in patients with COPD (Evidence C)*

Vasodilators

- *Do not improve outcomes and may worsen oxygenation (Evidence B)*

GOLD. Global strategy for prevention, diagnosis and management of COPD: 2026 Report. GOLD website. https://goldcopd.org/2026-gold-report-and-pocket-guide/

Figure 3.15

Additional Personalized Non-Pharmacological Strategies[a]

Patient Group	Essential	Recommended	Depending on Local Guidelines
A	Smoking cessation (can include pharmacological treatment)	Physical activity	Influenza vaccination COVID-19 vaccinations Pneumococcal vaccination Pertussis vaccination Shingles vaccination RSV vaccination
B and E	Smoking cessation (can include pharmacological treatment) Pulmonary rehabilitation	Physical activity	Influenza vaccination COVID-19 vaccinations Pneumococcal vaccination Pertussis vaccination Shingles vaccination RSV vaccination

[a]Can include pharmacological treatment.

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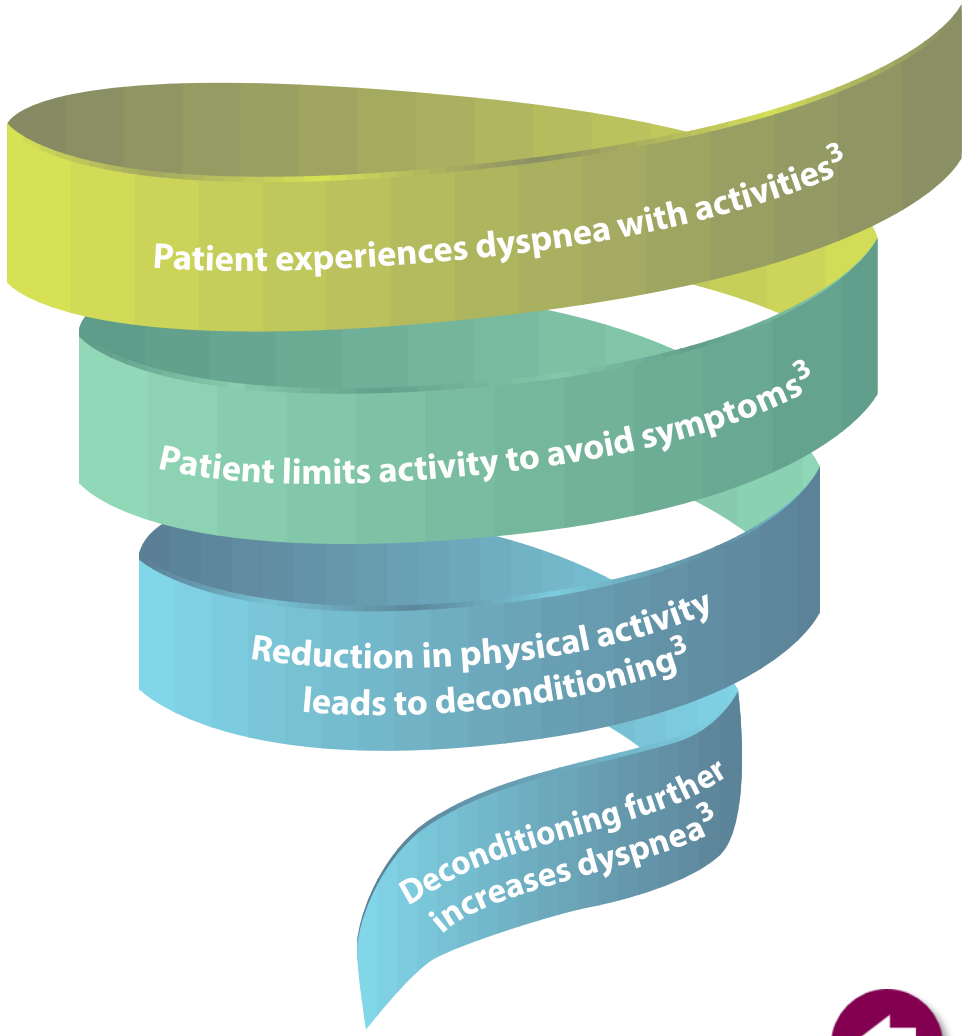
Recognizing the Impact of Activity on COPD Outcomes

- Even patients with mild to moderate COPD may limit and avoid certain activities[1,2]
- The deconditioning and muscle weakness may result in increased unwillingness to attempt activity in the future[4]

Objectively measured physical activity appears to be an independent predictor of all-cause mortality for patients with COPD[5]



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