Global Initiative for Chronic Obstructive Lung Disease

2027 POCKET GUIDE



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POCKET GUIDE TO COPD DIAGNOSIS, MANAGEMENT, AND PREVENTION

A Guide for Health Care Professionals

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE

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2027 EDITION

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INTRODUCTION

COPD is now one of the top three causes of death worldwide and nearly 90% of these deaths occur in LMICs.[1,2] More than 3 million people died of COPD in 2021 accounting for 5% of all deaths globally.[3] COPD represents an important public health challenge that is both preventable and treatable. COPD is a major cause of chronic morbidity and mortality throughout the world; many people suffer from this disease for years and die prematurely from it or its complications. Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population.[4]

This Pocket Guide has been developed from the Global Strategy for the Diagnosis, Management, and Prevention of COPD (**GOLD 2027 Report**), which aims to provide a non-biased review of the current evidence for the assessment, diagnosis and treatment of patients with COPD that can aid the clinician. Discussions of COPD and COPD management, evidence levels, and specific citations from the scientific literature are included in the source document.

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DEFINITION AND OVERVIEW

KEY POINTS:

Definition

- 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.

Causes and risk factors

- COPD results from gene(G)-environment(E) interactions occurring over the lifetime(T) of the individual (GETomics) that can damage the lungs and/or alter their normal development/aging processes.
- The main environmental exposures leading to COPD are tobacco smoking and the inhalation of toxic particles and gases from household and outdoor air pollution, but other environmental and host factors (including abnormal lung development and accelerated lung aging) can also contribute.

Diagnostic criteria

- In the appropriate clinical context (see 'Definition' & 'Causes and Risk Factors' above), the presence of non-fully reversible airflow obstruction (i.e., FEV1/FVC < 0.7 post-bronchodilation) measured by spirometry confirms the diagnosis of COPD.

Clinical presentation

- Patients with COPD typically complain of dyspnea, activity limitation and/or cough with or without sputum production, and may experience acute respiratory events characterized by increased respiratory symptoms called exacerbations that require specific preventive and therapeutic measures.
- Patients with COPD frequently harbor other comorbid diseases that influence their clinical condition and prognosis and require specific treatment. These comorbid conditions can mimic and/or aggravate an acute exacerbation.

New opportunities

- COPD is a common, preventable, and treatable disease, but extensive under-diagnosis and misdiagnosis leads to patients receiving no treatment or incorrect treatment. Appropriate and earlier diagnosis of COPD can have a very significant public-health impact.
- The realization that environmental factors other than tobacco smoking can contribute to COPD, that it can start early in life and affect young individuals, and that there are precursor conditions (pre-COPD, PRISm), opens new windows of opportunity for its prevention, early diagnosis, and prompt and appropriate therapeutic intervention.

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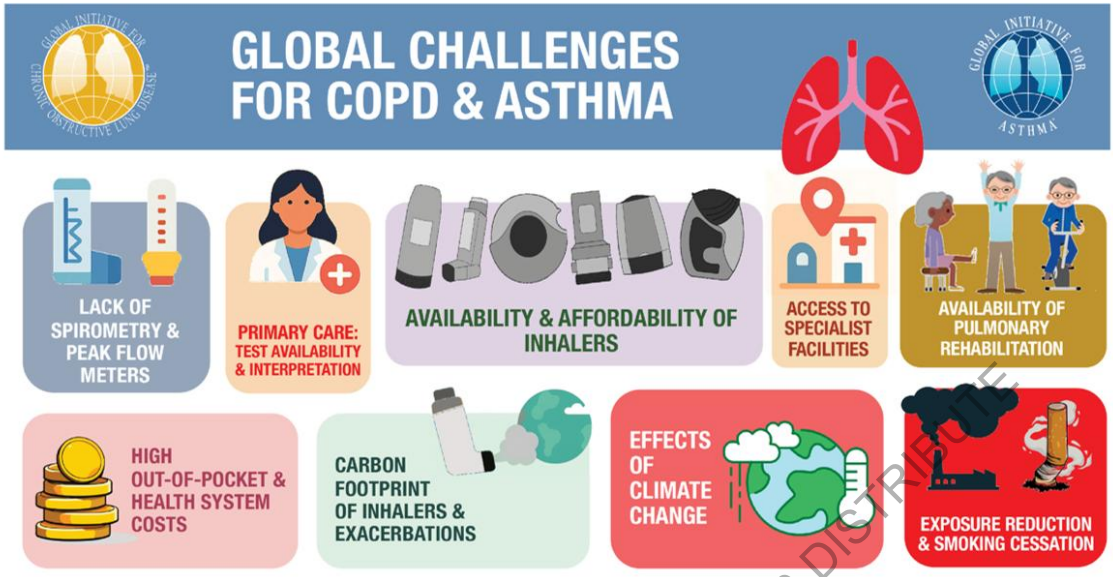
Global Challenges for COPD & Asthma

Figure A



Reproduced with permission of the American Thoracic Society (ATS).

Reference: Halpin et al. American Journal of Respiratory and Critical Care Medicine, February 2026, 212, 2, 97–302, https://doi.org/10.1164/rccm.202508-1894PP.

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Description of Levels of Evidence

Figure B

Evidence Category	Sources of Evidence	Definition
A	Randomized controlled trials (RCTs)	Evidence is from endpoints of well-designed RCTs that provide consistent findings in the population for which the recommendation is made without any important limitations.
	Rich body of high quality evidence without any significant limitation or bias	Requires high quality evidence from ≥ 2 clinical trials involving a substantial number of subjects, or a single high quality RCT involving substantial numbers of patient without any bias.
B	Randomized controlled trials (RCTs) with important limitations	Evidence is from RCTs that include only a limited number of patients, *post hoc* or subgroup analyses of RCTs or meta-analyses of RCTs.
	Limited body of evidence	Also pertains when few RCTs exist, or important limitations are evident (methodological flaws, small numbers, short duration, undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent).
C	Non-randomized trials Observational studies	Evidence is from outcomes of uncontrolled or non-randomized trials or from observational studies.
D	Panel consensus judgment	Provision of guidance is deemed valuable but clinical literature addressing the subject is insufficient. Panel consensus is based on clinical experience or knowledge that does not meet the above stated criteria.

Estimated COPD Prevalence According to Different Sources

Figure 1.1

	GBD 2019[a]	GBD 2021[b]	Population-based study 2019[c]	Other sources 2020[d]
Prevalence (%)	2.6	2.5	10.3	10.6
Number of cases (million)	212	213	392	479

References: [a]Safiri et al. BMJ 2022;378:e069679; [b]Wang et al. Respir Res 2025;26:2; [c]Adeloye et al. Lancet Respir Med 2022;10:447–458; [d]Boers et al. JAMA Netw Open 2023;6:E2346598.

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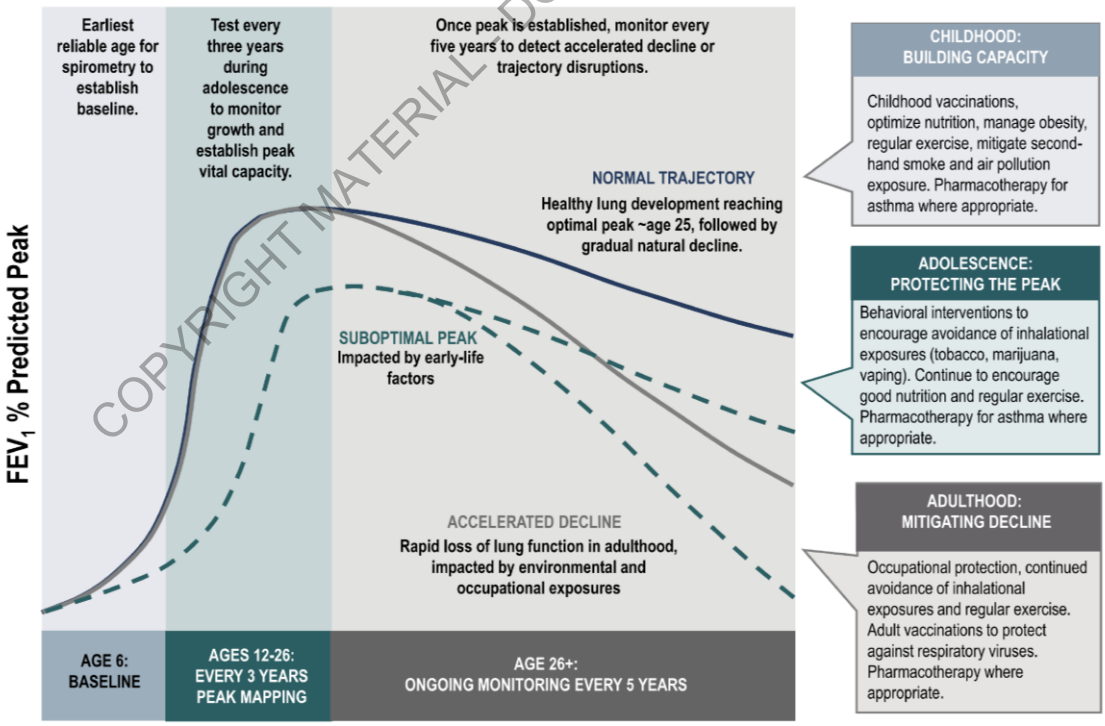
FEV1 Trajectories (TR) Over the Life Course

Figure 1.2

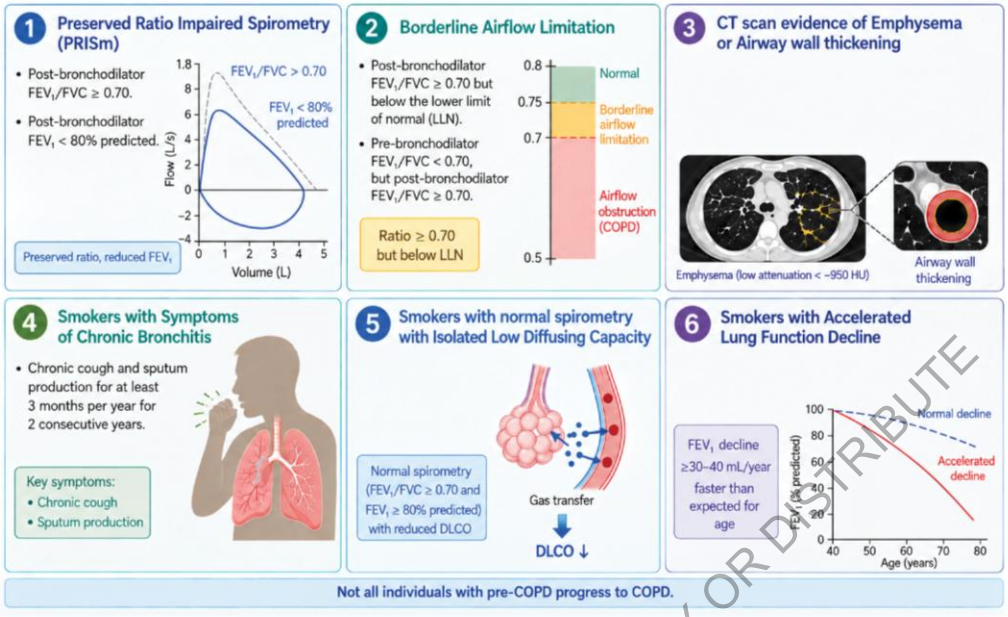


References: Agusti A, Hogg JC. N Engl J Med. 2019;381:1248-56; Han, MK et al. AJRCCM 2026, aamag432.

Groups that can be Categorized as Having Pre-COPD

Figure 1.3

These individuals may, but do not necessarily, develop persistent airflow obstruction (i.e., COPD) over time.



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Proposed Taxonomy (Etiotypes) for COPD

Figure 1.4

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

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

DIAGNOSIS, ASSESSMENT AND MONITORING

KEY POINTS:

Diagnosis

- A diagnosis of COPD should be **considered** in any patient who has dyspnea, chronic cough or sputum production, a history of recurrent lower respiratory tract infections and/or a history of exposure to risk factors; **spirometry** with post-bronchodilator FEV1/FVC < 0.7 is **mandatory** to establish the diagnosis of COPD.
- Pre-bronchodilator spirometry can be used to exclude a diagnosis of COPD.

Initial assessment

- The goals of the initial COPD assessment are to determine the severity of airflow obstruction, assess the impact of current symptoms on the patient, and their risk of future events (such as exacerbations, hospital admissions, or death), to guide therapy.

Monitoring and follow-up

- Routine follow-up of lung function, symptoms and exacerbations is essential to determine when to modify management and to identify any complications and/or comorbidities.
- Virtual and hybrid virtual/in-person care models may offer improved healthcare access, outcomes, and affordability, but use should be based on evidence.

Additional investigations

- Additional clinical assessment, including the measurement of lung volumes, diffusion capacity, exercise testing and/or lung imaging may be considered in patients with COPD who have a marked discordance between the level of airflow obstruction and the perceived symptoms.
- Concomitant chronic diseases (multimorbidity) occur frequently in patients with COPD, including cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression, anxiety, and lung cancer. These comorbidities should be actively sought, and treated appropriately when present, because they influence health status, hospitalizations and mortality independently of the severity of airflow obstruction due to COPD.

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Clinical Indicators for Considering a Diagnosis of COPD

Figure 2.1

Consider the diagnosis of COPD, and perform spirometry, if any of these clinical indicators are present:
(these indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of the presence of COPD; in any case, spirometry is required to establish a diagnosis of COPD)

Dyspnea that is	Progressive over time Worse with exercise Persistent
Recurrent wheeze	
Chronic cough	May be intermittent and may be non-productive
Recurrent lower respiratory tract infections	
History of risk factors	Tobacco smoke (including popular local preparations) Smoke from home cooking and heating fuels Occupational dusts, vapors, fumes, gases and other chemicals Host factors (e.g., genetic factors, developmental abnormalities, low birthweight, prematurity, childhood respiratory infections etc.)

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Other Causes of Chronic Cough

Figure 2.2

INTRATHORACIC	EXTRATHORACIC
• Asthma • Lung Cancer • Tuberculosis • Bronchiectasis • Left Heart Failure • Interstitial Lung Disease • Cystic Fibrosis • Idiopathic Cough	• Chronic Allergic Rhinitis • Post Nasal Drip Syndrome • Upper Airway Cough Syndrome • Gastroesophageal Reflux • Medication (e.g., ACE Inhibitors)

Differential Diagnosis of COPD

Figure 2.3

Diagnosis	Suggestive Features
COPD	Symptoms slowly progressive History of tobacco smoking or other risk factors
Asthma	Variable airflow obstruction Symptoms vary widely from day to day Symptoms worse at night/early morning Allergy, rhinitis, and/or eczema also present Often occurs in children Family history of asthma
Congestive heart failure	Chest X-ray shows dilated heart, pulmonary edema Pulmonary function tests indicate volume restriction, not airflow obstruction
Bronchiectasis	Large volumes of purulent sputum Commonly associated with bacterial infection Chest X-ray/HRCT shows bronchial dilation
Tuberculosis	Onset at all ages Chest X-ray shows lung infiltrate Microbiological confirmation High local prevalence of tuberculosis
Obliterative bronchiolitis	Can occur in children Seen after lung or bone marrow transplantation HRCT on expiration shows hypodense areas
Diffuse panbronchiolitis	Predominantly seen in patients of Asian descent Most patients are male and nonsmokers Almost all have chronic sinusitis Chest X-ray & HRCT show diffuse small centrilobular nodular opacities & hyperinflation

These features tend to be characteristic of the respective diseases, but are not mandatory. For example, a person who has never smoked may develop COPD (especially in LMICs where other risk factors may be more important than cigarette smoking).

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Considerations in Performing Spirometry

Figure 2.4

PREPARATION	• Spirometers should produce hard copy or have a digital display of the expiratory curve to permit detection of technical errors or have an automatic prompt to identify an unsatisfactory test and the reason for it • The supervisor of the test needs training in optimal technique and quality performance • Maximal patient effort in performing the test is required to avoid underestimation of values and hence errors in diagnosis and management
PERFORMANCE	• Spirometry should be performed following national and/or international recommendations[a] • The expiratory volume/time traces should be smooth and free from irregularities • The pause between inspiration and expiration should be less than one second • The recording should go on long enough for a volume plateau to be reached, which may take more than 15 seconds in severe disease • Both FVC and FEV1 should be the largest value obtained from any of three technically satisfactory curves and the FVC and FEV1 values in these three curves should vary by no more than 5% or 150 mL, whichever is greater • The FEV1/FVC ratio should be calculated using the largest FVC and the largest FEV1 even though they may not come from the same maneuver
BRONCHODILATION	• Possible dosage protocols are 400 mcg short-acting beta$_2$-agonist, 160 mcg short-acting anticholinergic, or the two combined[b]; FEV1 should be measured 10-15 minutes after a short-acting beta$_2$-agonist is given, or 30-45 minutes after a short-acting anticholinergic or a combination of both classes of drugs • Patients already on bronchodilator treatment, in whom spirometry is requested for monitoring purposes do not need to stop their regular treatment for spirometry
EVALUATION	• Spirometry measurements are evaluated by comparison of the results with appropriate reference values based on age, height and sex • The presence of a post-bronchodilator FEV1/FVC < 0.7 confirms the presence of non-fully reversible airflow obstruction

[a]Miller et al. Eur Respir J 2005; **26**(2): 319-38;
[b]Pellegrino et al. Eur Respir J 2005; **26**(5): 948-68.

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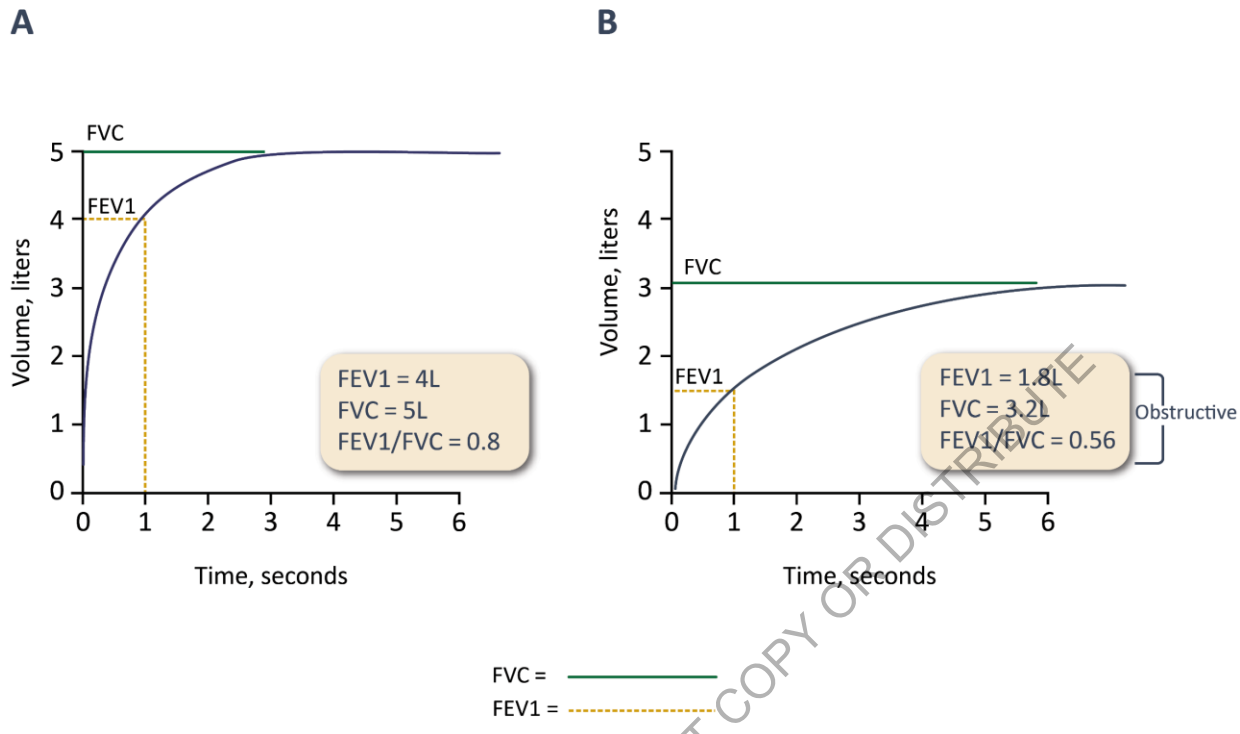
A. Spirometry - Normal Trace B. Spirometry - Airflow Obstruction

Figure 2.5



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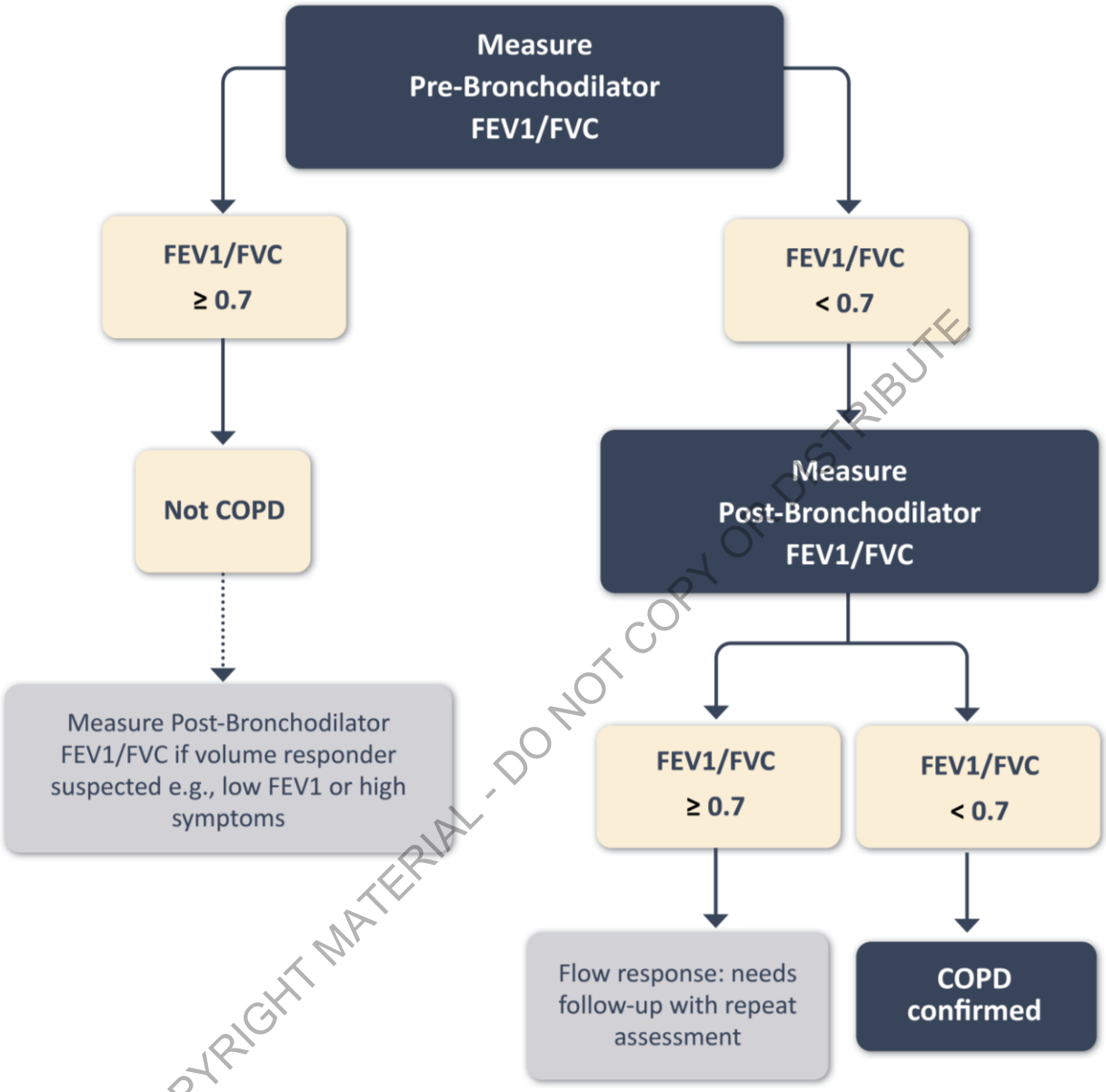
Spirometry to Confirm a COPD Diagnosis

Figure 2.6



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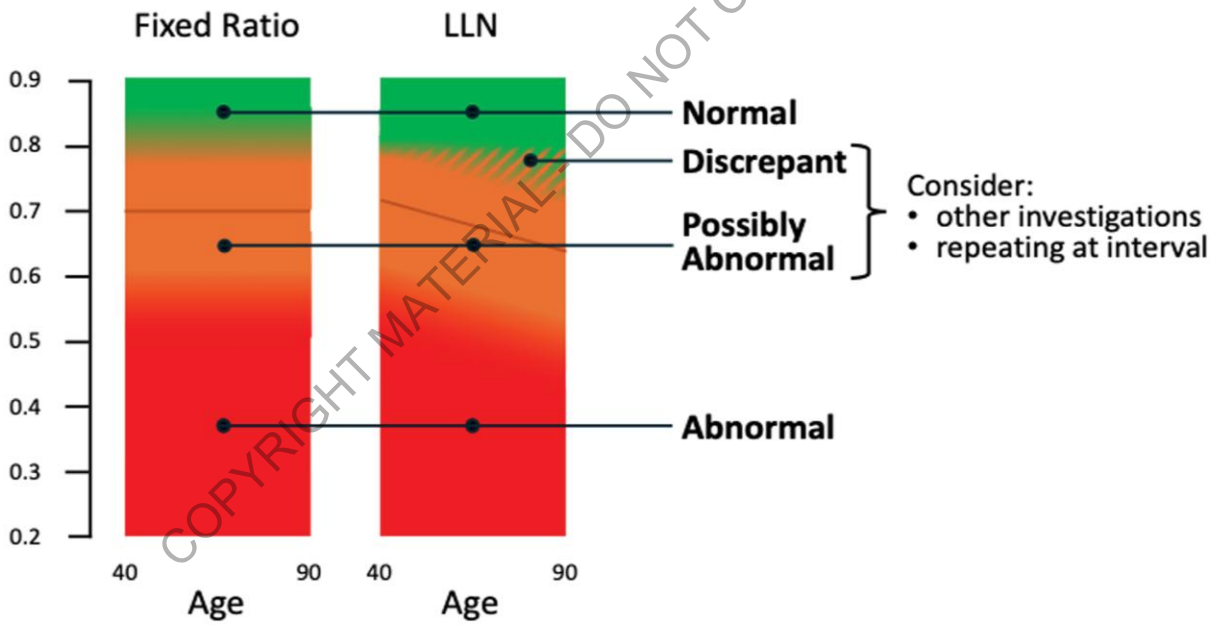
Role of Spirometry in COPD

Figure 2.7

- **Diagnosis**
- **Assessment of severity of airflow obstruction (for prognosis)**
- **Follow-up assessment**
  - Therapeutic decisions
    - Pharmacological in selected circumstances (e.g., discrepancy between spirometry and level of symptoms)
    - Consider alternative diagnoses when symptoms are disproportionate to degree of airflow obstruction
    - Non-pharmacological (e.g., interventional procedures)
  - Identification of rapid decline

Interpretation of FEV1/FVC Ratio in a Person with Suspected COPD

Figure 2.8



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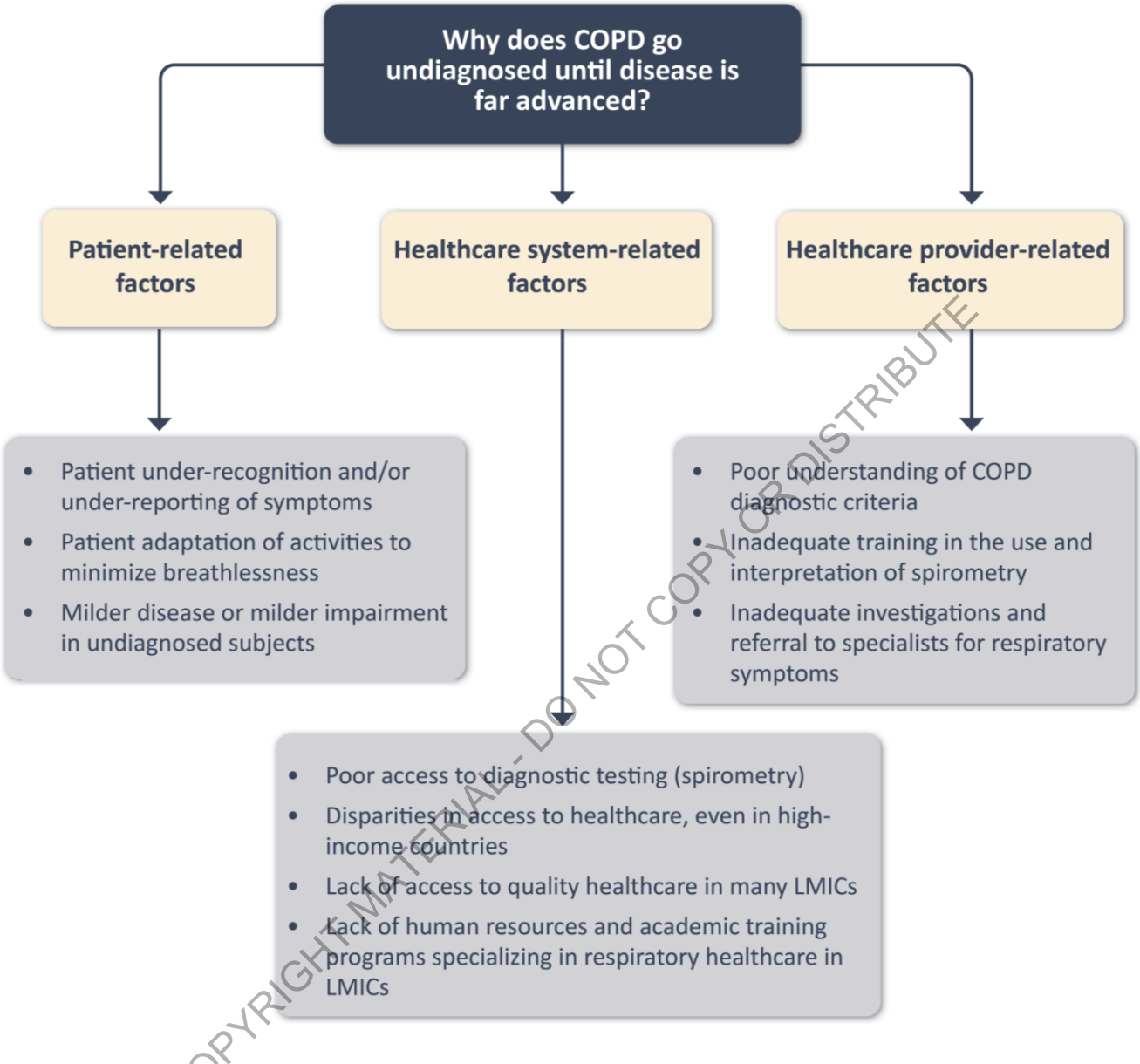
Factors that May Be Associated with COPD Underdiagnosis

Figure 2.9



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

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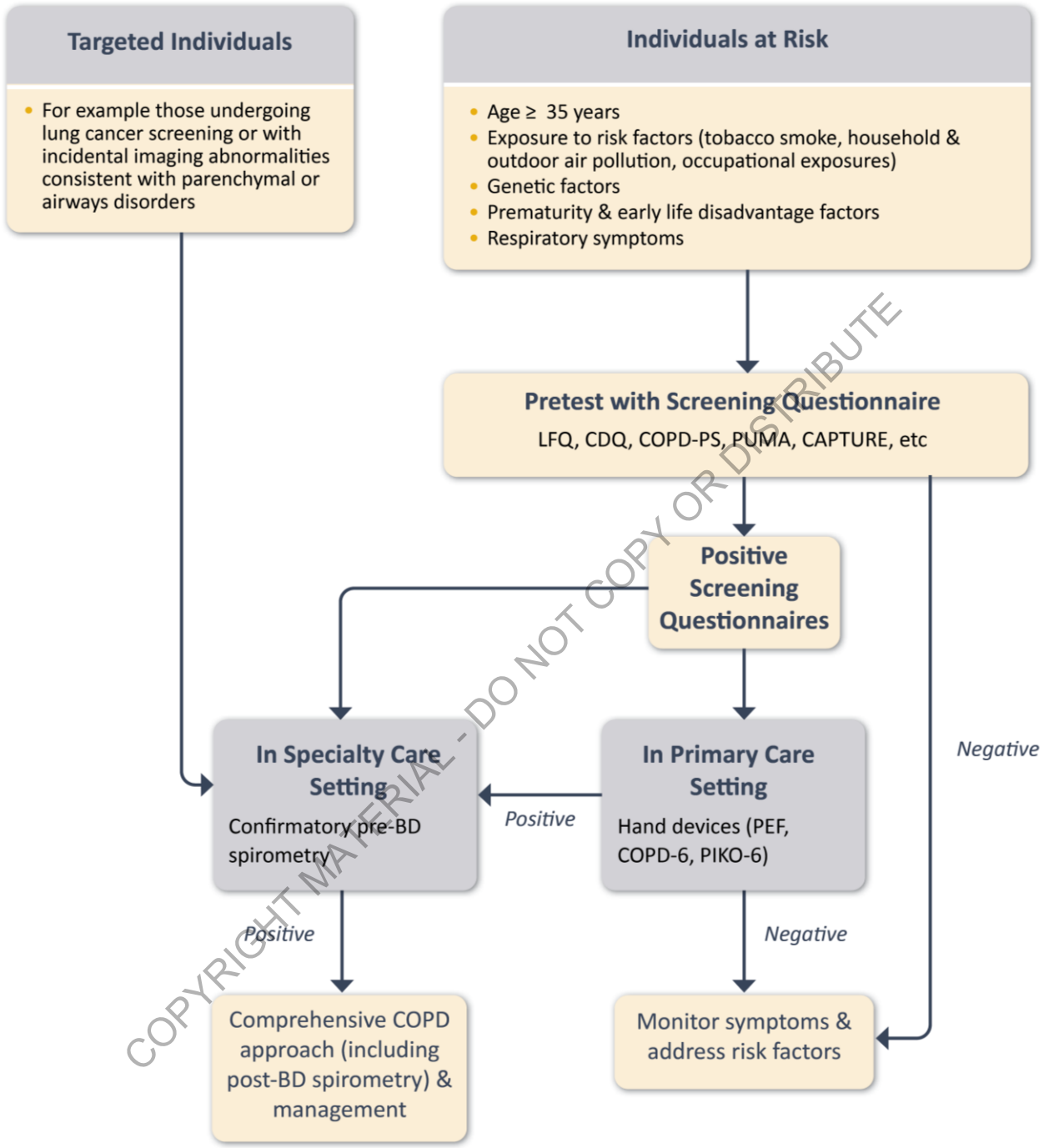
An Algorithm for COPD Case-finding

Figure 2.10



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

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

Figure 2.11

In patients with COPD (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

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Modified MRC Dyspnea Scale

Figure 2.12

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.

CAAT™ Assessment

Figure 2.13

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.

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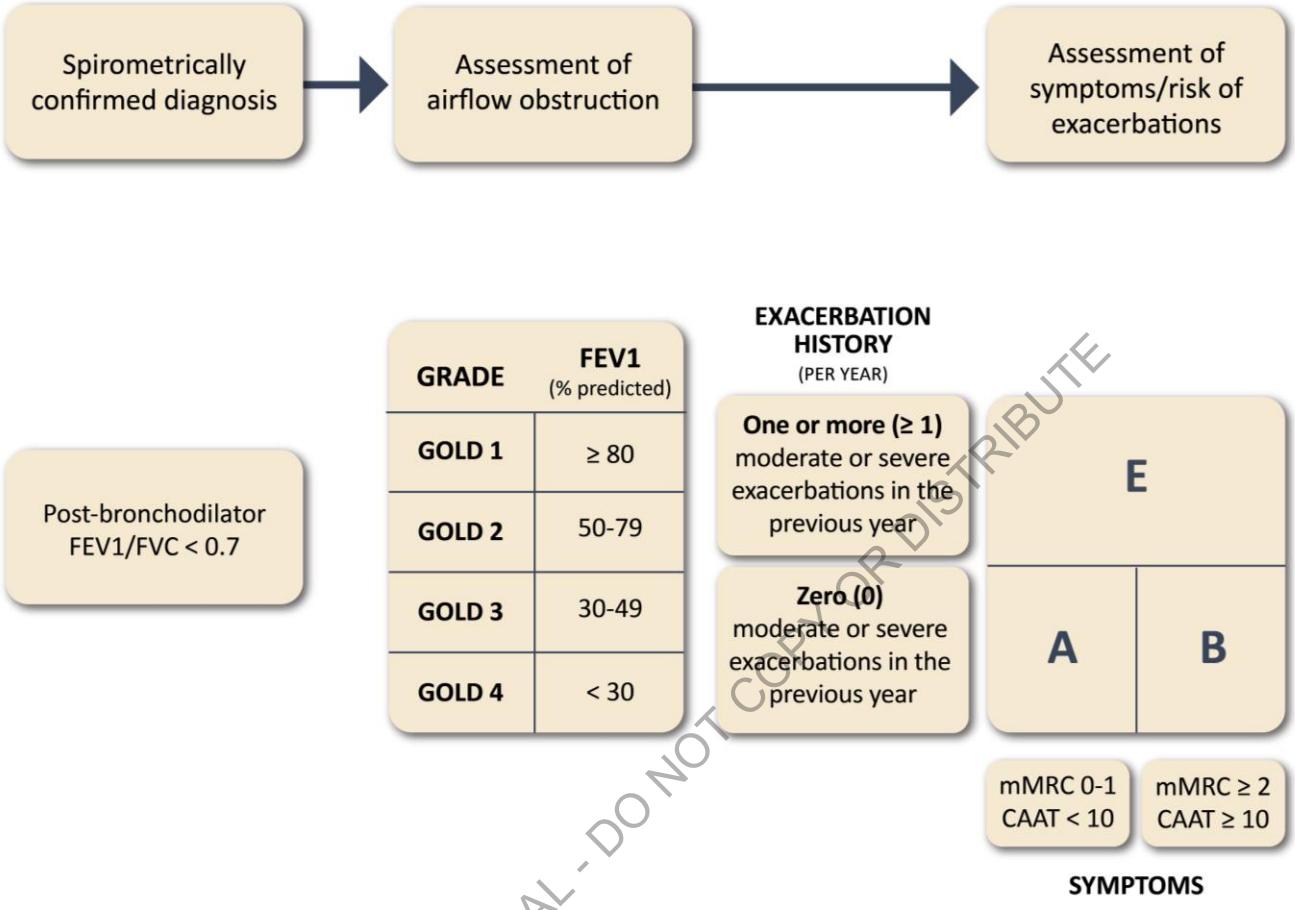
GOLD ABE Assessment Tool

Figure 2.14



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Exercise Tests in COPD Assessment

Figure 2.15

Test	Setting & Equipment	Main Outcome	Minimal Important Difference (MID)
EXERCISE CAPACITY			
Incremental maximal cardiopulmonary exercise test[1,2]	Laboratory: cardiorespiratory and metabolic responses to incremental exercise on ergometer	Peak oxygen consumption and peak work rate	No robust data (approx. 5 watts severe COPD)
6-minute walking test (6MWT)[3,4]	Field (30 m corridor)	Maximal distance walked in 6 minutes (functional walking test)	25-30 m
Incremental shuttle walking test (ISWT)[3,4,5]	Field (10 m track)	Maximal distance covered with incremental pace (functional, incremental walking speed)	35-48 m
1-minute sit-to-stand test[6]	Field/home/primary care	Maximal number of rises in 1 min from chair (functional sit-stand transition)	3 repetitions
EXERCISE ENDURANCE (in submaximal tests)			
Constant work rate cycling test[7]	Cycle at high fraction (75% to 80%) of peak work rate	Bicycle endurance time	Approx. 60 sec
Endurance shuttle walking test[3]	Constant work rate at high fraction of ISWT speed	Walking endurance time	159 sec

References: 1. Puente-Maestu et al. Eur Respir J. 2016 Feb;47(2):429-60; **2.** Radtke et al. Eur Respir Rev. 2019 Dec 18;28(154):180101; **3.** Daynes et al. Eur Respir Rev. 2025 May 28;34(176):240198; **4.** Holland et al. Eur Respir J. 2014 Dec;44(6):1428-46; **5.** Evans RA, Singh SJ. Thorax. 2019 Oct;74(10):994-995; **6.** Spence et al. NPJ Prim Care Respir Med. 2023 Mar 15;33(1):11; **7.** Casaburi et al. Ann Am Thorac Soc. 2024 May;21(5):727-739.

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Use of CT in COPD

Figure 2.16

Chest CT (non-contrast) with inspiratory and expiratory images should be considered as part of the initial evaluation for all patients with COPD at least once, where available, and is additionally recommended for patients with persistent symptoms or exacerbations, for lung volume reduction evaluation, and lung cancer screening.

Initial Evaluation	• **Characterize emphysema:** assess its extent and distribution. • **Assess airway disease:** identify bronchiectasis, mucus plugging, and airway wall thickening. • **Identify interstitial abnormalities:** assess for interstitial lung abnormalities and coexisting pulmonary fibrosis. • **Assess comorbidities:** identify coronary artery calcification, pulmonary artery enlargement, low bone density or vertebral fractures, and low muscle mass.
Frequent Exacerbations	• **Identify potential contributors to exacerbations:** evaluate for bronchiectasis, mucus plugging, or findings suggestive of atypical infection, including nontuberculous mycobacterial infection, particularly in patients with purulent sputum or before initiating long-term macrolide therapy.
Persistent Symptoms Despite Optimized Treatment	• **Evaluate structural abnormalities and alternative or coexisting causes of symptoms,** particularly when symptoms are disproportionate to the degree of airflow limitation.
Lung Volume Reduction Evaluation	• **Assess suitability for bronchoscopic or surgical lung volume reduction based on emphysema severity and distribution.** • **Endobronchial valve therapy** may be a therapeutic option for patients if they demonstrate postbronchodilator FEV1 15% to 45% and evidence of hyperinflation. • **Lung volume reduction surgery** may be a therapeutic option for patients with hyperinflation, severe upper lobe predominant emphysema and low exercise capacity after pulmonary rehabilitation.
Lung Cancer Screening	• **Detect lung cancer:** perform repeated low-dose CT in patients who meet lung cancer screening eligibility criteria, according to recommendations for the general population.

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KEY POINTS:

Risk reduction, lifestyle and patient education

- All individuals who smoke should be strongly encouraged and supported to quit. Nicotine replacement and pharmacotherapy reliably increase long-term smoking abstinence rates. Legislative smoking bans and counseling, delivered by healthcare professionals, improve quit rates. There is no evidence to support the effectiveness and safety of e-cigarettes as a smoking cessation aid at present.
- People with COPD should receive all recommended vaccinations in line with the relevant local guidelines.
- COVID-19 vaccines are highly effective against SARS-CoV-2 infection and people with COPD should have the COVID-19 vaccination in line with local recommendations.
- Influenza, pneumococcal and RSV vaccines have been shown to decrease the incidence of lower respiratory tract infections.
- The immunization committees recommend Tdap vaccination (dTaP/dTPa; pertussis, tetanus and diptheria) for people with COPD who were not vaccinated in adolescence; and routine use of herpes zoster (shingles) vaccine.

Pharmacological maintenance treatment of COPD

- Initial pharmacological treatment of COPD should be individualized and guided by the severity of symptoms, risk of exacerbations, side-effects, comorbidities, drug availability and cost, and the patient's preference, and ability to use various drug delivery devices.
- Patients should be reviewed after a suitable interval (shorter in patients with more severe disease, and longer in patients with less severe disease) and reassessed for attainment of treatment goals and identification of any barriers for successful treatment.
- Inhaler technique and adherence need to be assessed regularly.

Non-pharmacological treatment of COPD

- Non-pharmacological treatment of COPD is complementary to pharmacological maintenance treatment and should form part of comprehensive management as it addresses lifestyle modifications, disease-specific self-management, and psychological interventions targeting daily symptoms, which cannot be resolved by medication alone.
- Pulmonary rehabilitation, including exercise training combined with disease-specific education, and interventions addressing other treatable traits, improves patient function (physical and mental), exercise capacity, symptoms, and quality of life across all grades of COPD severity. Physical activity coaching can be added for patients with low physical activity levels.
- LTOT should not be prescribed routinely for patients with stable COPD and resting or exercise-induced moderate desaturation, but it may improve survival in patients with severe resting chronic hypoxemia ($PaO_2 \leq 55$ mmHg or < 60 mmHg if there is *cor pulmonale* or secondary polycythemia).
- Long-term NIV may be of some use in a selected group of patients, particularly those with pronounced daytime hypercapnia and recent hospitalization.

Palliative, interventional and surgical therapies

- In select patients with advanced emphysema refractory to optimized medical care, surgical or bronchoscopic interventional treatments may be beneficial.
- Palliative approaches are effective in controlling symptoms in advanced COPD.

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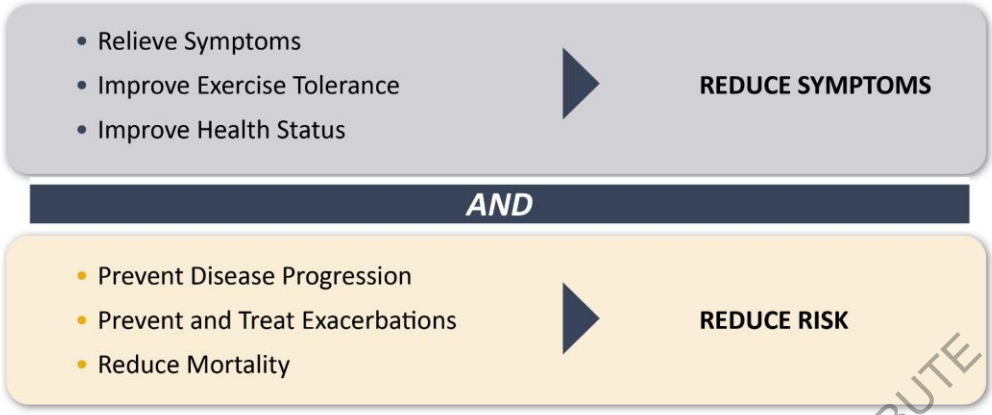
Goals for Treatment of Stable COPD

Figure 3.1



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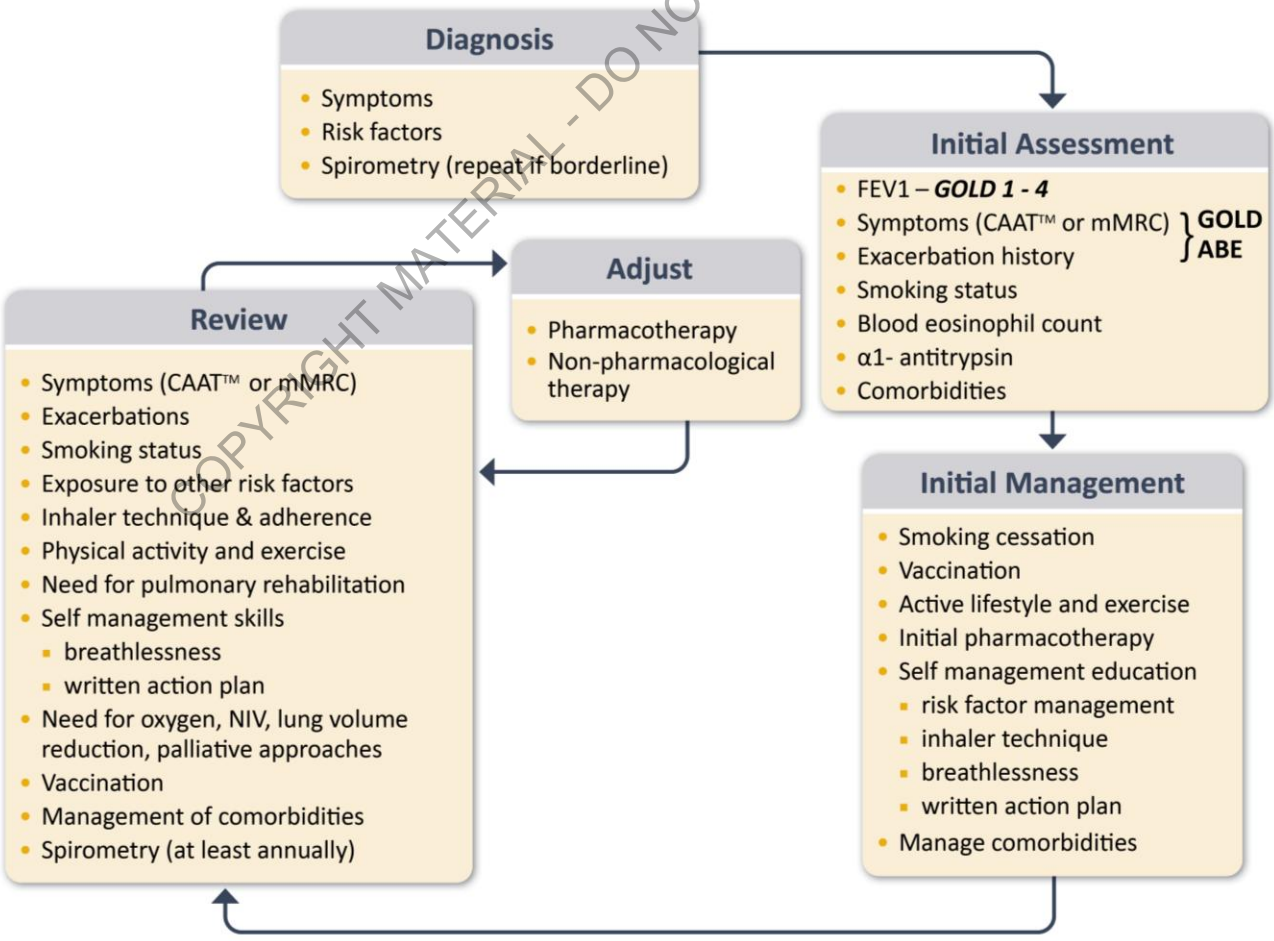
Management of COPD

Figure 3.2



Identify & Reduce Risk Factor Exposure

Figure 3.3

- Smoking cessation interventions should be actively pursued in all people with COPD **(Evidence A)**
- Efficient ventilation, non-polluting cooking stoves and similar interventions should be recommended **(Evidence B)**
- Clinicians should advise patients to avoid continued exposures to potential irritants and occupational dust, if possible **(Evidence D)**

Brief Strategies to Help the Patient Willing to Quit

Figure 3.4

ASK	Systematically identify all tobacco users at every visit *Implement an office-wide system that ensures that, for EVERY patient at EVERY clinic visit, tobacco-use status is queried and documented*
ADVISE	Strongly urge all tobacco users to quit *In a clear, strong, and personalized manner, urge every tobacco user to quit*
ASSESS	Determine willingness and rationale of patient's desire to make a quit attempt. *Ask every tobacco user if he or she is willing to make a quit attempt at this time (e.g., within the next 30 days)*
ASSIST	Aid the patient in quitting *Help the patient with a quit plan; provide practical counseling; provide intra-treatment social support; help the patient obtain extra-treatment social support; recommend use of approved pharmacotherapy except in special circumstances; provide supplementary materials*
ARRANGE	Schedule follow-up contact *Schedule follow-up contact, either in person or via telephone*

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Treating Tobacco Use and Dependence

Figure 3.5

Major Findings & Recommendations from the Tobacco Use & Dependence Clinical Practice Guideline Panel:

- Tobacco dependence is a chronic condition that warrants repeated treatment until long-term or permanent abstinence is achieved
- Effective treatments for tobacco dependence exist and all tobacco users should be offered these treatments
- Clinicians and health care delivery systems must operationalize the consistent identification, documentation, and treatment of every tobacco user at every visit
- Brief smoking cessation counseling is effective and every tobacco user should be offered such advice at every contact with health care providers
- There is a strong dose-response relation between the intensity of tobacco dependence counseling and its effectiveness
- Three types of counseling have been found to be especially effective: practical counseling, social support of family and friends as part of treatment, and social support arranged outside of treatment
- First-line pharmacotherapies for tobacco dependence — varenicline, nortriptyline, bupropion sustained release, nicotine gum, nicotine inhaler, nicotine nasal spray, and nicotine patch— are effective and at least one of these medications should be prescribed in the absence of contraindications
- Financial incentive programs for smoking cessation may facilitate smoking cessation
- Tobacco dependence treatments are cost effective interventions

Reference: The Tobacco Use and Dependence Clinical Practice Guideline Panel. *JAMA* 2000; **283**(24): 3244-54

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Vaccination for People with COPD

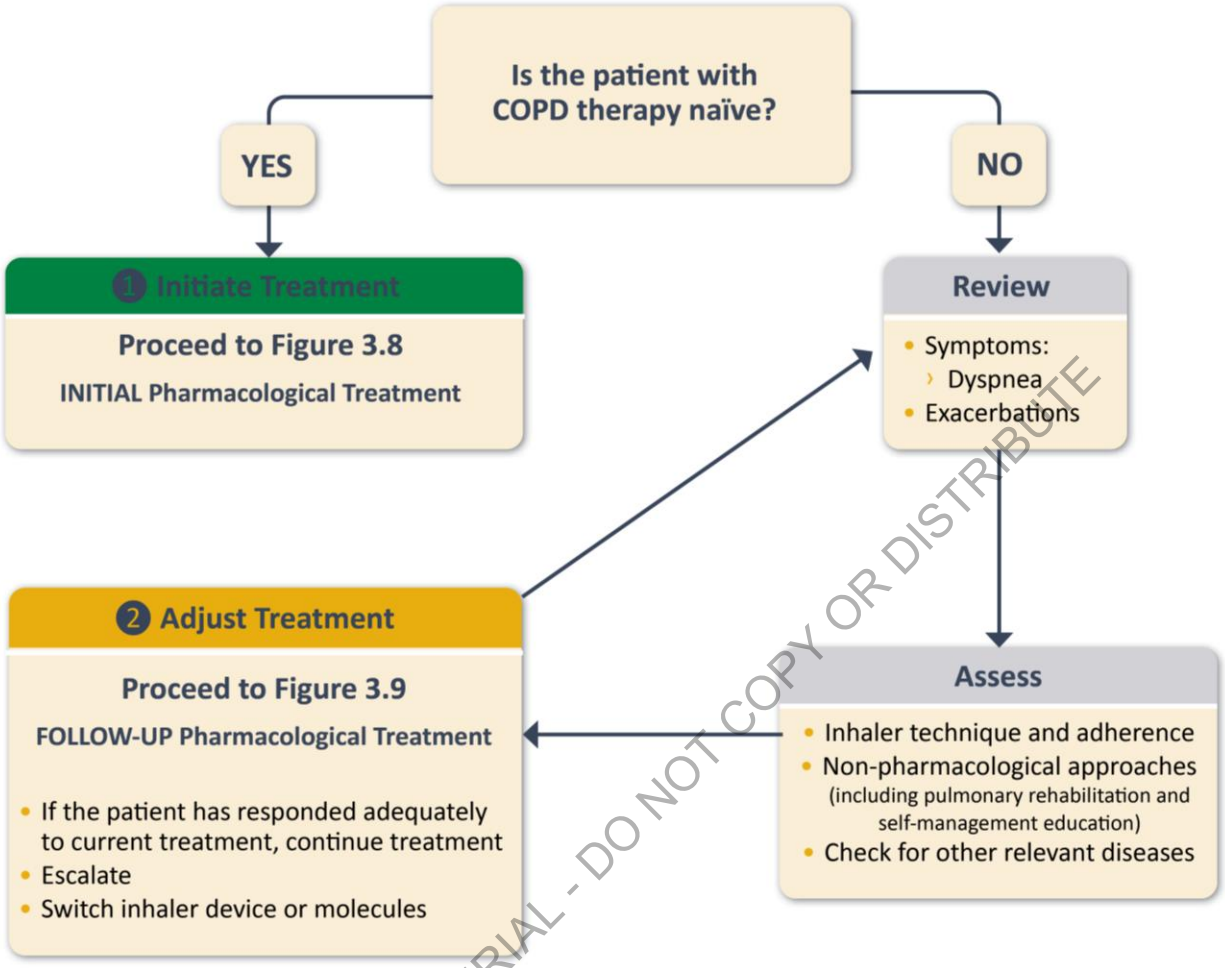
Figure 3.6

People with COPD should receive all recommended vaccinations in line with the relevant local guidelines:

- Yearly influenza vaccination **(Evidence B)**
- SARS-CoV-2 (COVID-19) vaccination based on WHO and CDC updated recommendations **(Evidence B)**
- We recommend either one dose of 21-valent pneumococcal conjugate vaccine (PCV21) or one dose of PCV20 **(Evidence B)**. Pneumococcal vaccination has been shown to reduce the incidence of community-acquired pneumonia and exacerbations for people with COPD **(Evidence B)**
- Respiratory syncytial virus (RSV) vaccination for individuals aged ≥ 50 years and/or with chronic heart or lung disease, as recommended by the CDC **(Evidence A)**
- Tdap (dTaP/dTPa) vaccination to protect against pertussis (whooping cough), in addition to tetanus and diphtheria, for people with COPD that were not vaccinated in adolescence, as recommended by the CDC **(Evidence B)**
- Zoster vaccine to protect against herpes zoster (shingles) for people with COPD aged > 50 years, as recommended by the CDC **(Evidence B)**

Diagnosis and Management Cycle

Figure 3.7



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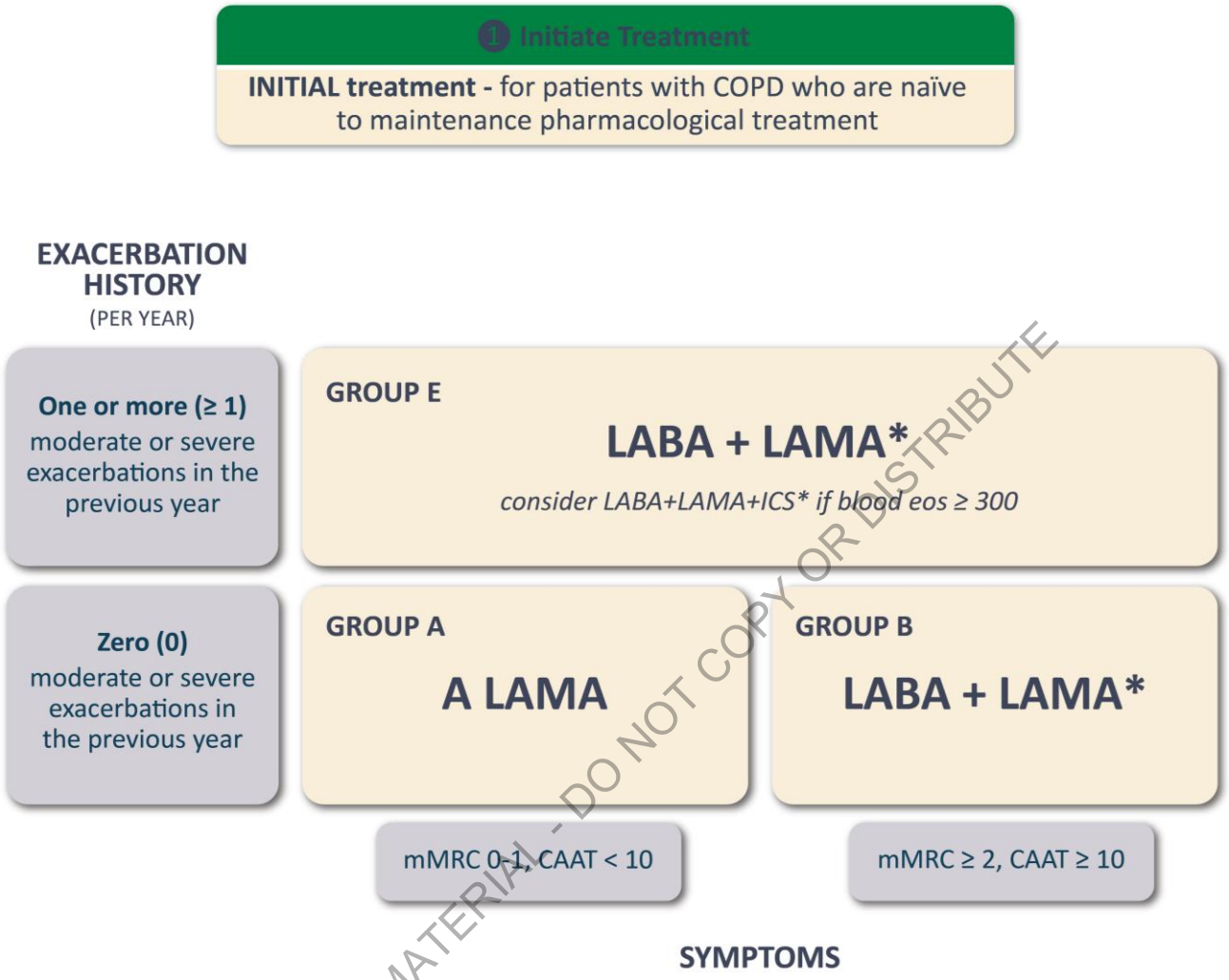
Initial Pharmacological Treatment

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™.

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Follow-up Pharmacological Treatment

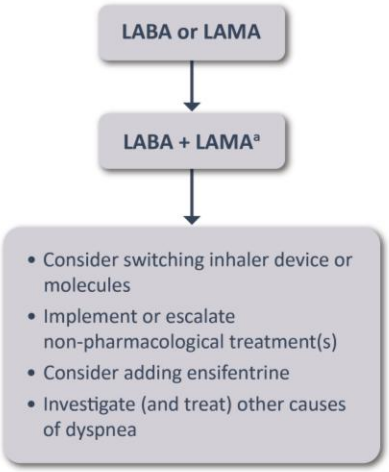
Figure 3.9

2 Adjust Treatment

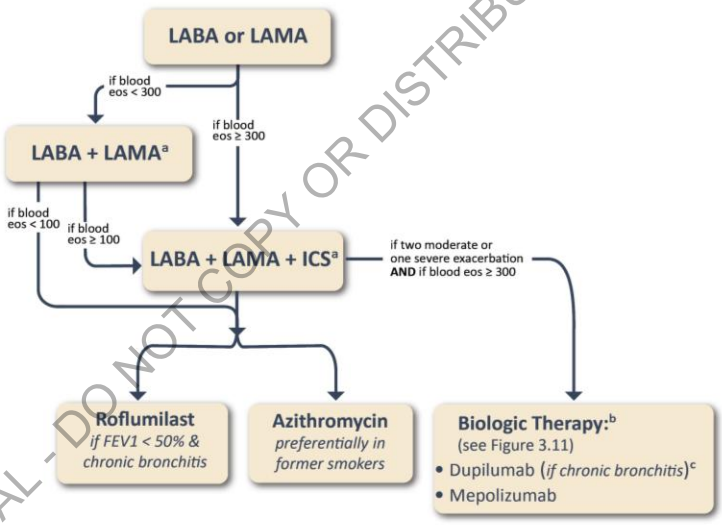
CONTINUE CURRENT TREATMENT

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.

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Factors to Consider when Initiating ICS Treatment

Figure 3.10

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

(note the scenario is different when considering ICS withdrawal)

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

[#]despite appropriate long-acting bronchodilator maintenance therapy (see Figures 3.8 & A5.1 for recommendations); *note that blood eosinophils should be seen as a continuum; quoted values represent approximate cut-points; eosinophil counts are likely to fluctuate.

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Evidence Supporting Use of Biologics Registered for the Treatment of COPD

Figure 3.11

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 (95% CI: 0.58, 0.86)	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 (95% CI: 0.54, 0.82)	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 (100 mg); NS RR 0.86 (300 mg); 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 (95% CI: 0.68, 0.98)	-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 (95% CI: 0.66, 0.94)	-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; .

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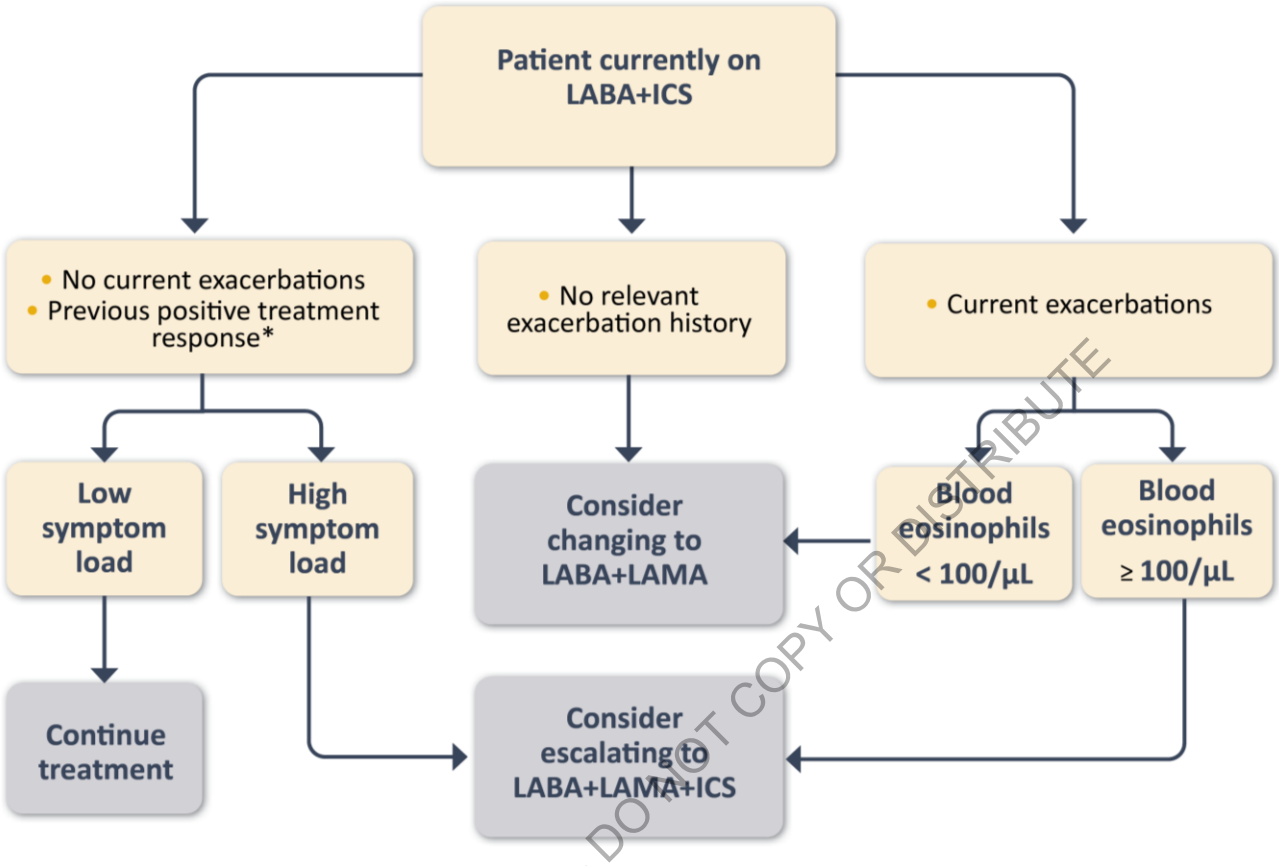
Management of Patients Currently on LABA+ICS

Figure 3.12



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

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Key Points for Inhalation of Drugs

Figure 3.13

- When a treatment is given by the inhaled route, the importance of education and training in inhaler device technique cannot be over-emphasized
- 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
- It is essential to provide instructions and to demonstrate the proper inhalation technique when prescribing a device, to ensure that inhaler technique is adequate and to re-check at each visit that patients continue to use their inhaler correctly
- Inhaler technique (and adherence to therapy) should be assessed before concluding that the current therapy is insufficient

Basic Principles for Appropriate Inhalation Device Choice

Figure 3.14

- Availability of the drug in the device.
- Patients' beliefs, satisfaction with current and previous devices and preferences need to be assessed and considered.
- The number of different device types should be minimized for each patient.
- Device type should not be switched in the absence of clinical justification nor without proper information, education and medical follow-up.
- Shared decision-making is the most appropriate strategy for inhalation device choice.
- Patient's cognition, dexterity and strength must be taken into account.
- Patient's ability to perform the correct specific inhalation maneuver for the device must be assessed:
  - Dry powder inhalers are appropriate only if the patient can make a forceful and deep inhalation. Check visually that the patient can inhale forcefully through the device - if there is doubt assess objectively or choose alternative device.
  - Metered-dose inhalers and, to a lesser extent, soft mist inhalers require coordination between device triggering and inhalation and patients need to be able to perform a slow and deep inhalation. Check visually that the patient can inhale slowly and deeply from the device - if there is doubt consider adding a spacer/VHC or choose an alternative device.
  - For patients unable to use an MDI (with or without spacer/VHC), SMI or DPI a nebulizer should be considered.
- Other factors to consider include size, portability, cost.
- Smart inhalers may be useful if there are issues with adherence/persistence or inhalation technique (for devices that can check it).
- Physicians should prescribe only devices they (and the other members of the caring team) know how to use.

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Non-Pharmacological Management of COPD*

Figure 3.15

Patient Group	Essential	Recommended	
A	• Smoking cessation (can include pharmacological treatment)	• Physical activity • Education, self-management personalized on patient needs	• Influenza vaccination • COVID-19 vaccination • Pneumococcal vaccination • Pertussis vaccination • Zoster (shingles) vaccination • RSV vaccination
B and E	• Smoking cessation (can include pharmacological treatment) • Pulmonary rehabilitation	• Physical activity • Education, self-management personalized on patient needs	• Influenza vaccination • COVID-19 vaccination • Pneumococcal vaccination • Pertussis vaccination • Zoster (shingles) vaccination • RSV vaccination

*Can include pharmacological treatment

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Follow-up of Non-Pharmacological Treatment

Figure 3.16

1. If response to initial treatment is appropriate, maintain it and offer:

- Influenza vaccination every year and other recommended vaccinations according to guidelines
- Self-management education
- Assessment of behavioral risk factors such as smoking cessation (if applicable) and environmental exposures

Ensure

- Maintenance of exercise program and physical activity
- Adequate sleep and a healthy diet

2. If not, consider the predominant treatable trait to target

DYSPNEA

- Self-management education (written action plan) with integrated self-management regarding:
  - Breathlessness, energy conservation techniques, and stress management strategies
- Pulmonary rehabilitation (PR) program and/or maintenance exercise program post PR

EXACERBATIONS

- Self-management education (written action plan) that is personalized with respect to:
  - Avoidance of aggravating factors
  - How to monitor/manage worsening of symptoms
  - Contact information in the event of an exacerbation
- Pulmonary rehabilitation (PR) program and/or maintenance exercise program post PR

All patients with advanced COPD should be considered for end of life and palliative care support to optimize symptom control and allow patients and their families to make informed choices about future management.

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Non-pharmacological Programs in COPD

Figure 3.17

Program	Components	Setting	Anticipated effect
Physical activity coaching	Counseling, telemonitoring using wearables	In-person or tele-coaching	Improved physical activity
Exercise training*	Whole body exercise training (endurance/interval) Resistance training	Monitored exercise training (in-person or tele-supervised; synchronous or asynchronous)	Improved exercise tolerance, skeletal muscle function, nutritional status (FFM), symptoms and health-related quality of life
Pulmonary rehabilitation	Exercise training (aerobic & resistance) is the cornerstone plus education/ self-management plus multidisciplinary support: dietitians & nutritionists, nursing professionals, occupational therapists, physiotherapists, psychologists, social work and counselling professionals and specialist medical practitioners/physical & rehabilitation medicine physicians	Center-based (outpatient or inpatient), community-based, home-based. In-person or tele-rehabilitation (supervised remotely)	Improved exercise tolerance, health-related quality of life, respiratory and non-respiratory symptoms, utilization of healthcare resources, self-efficacy, physical activity

*Exercise training can be culturally adapted to include exercise modalities that are appropriate in specific populations. Examples are yoga, Tai Chi, dancing and water-based exercises.[1,2] The frequency, intensity, and duration (time) and type of exercise needs to be appropriate, progressed, and is best monitored.

References: 1. Sánchez Romero et al. NPJ Prim Care Respir Med. 2026 Apr 11;36(1):52; **2.** Zhang et al. Thorax. 2023 Jan;78(1):69-75.

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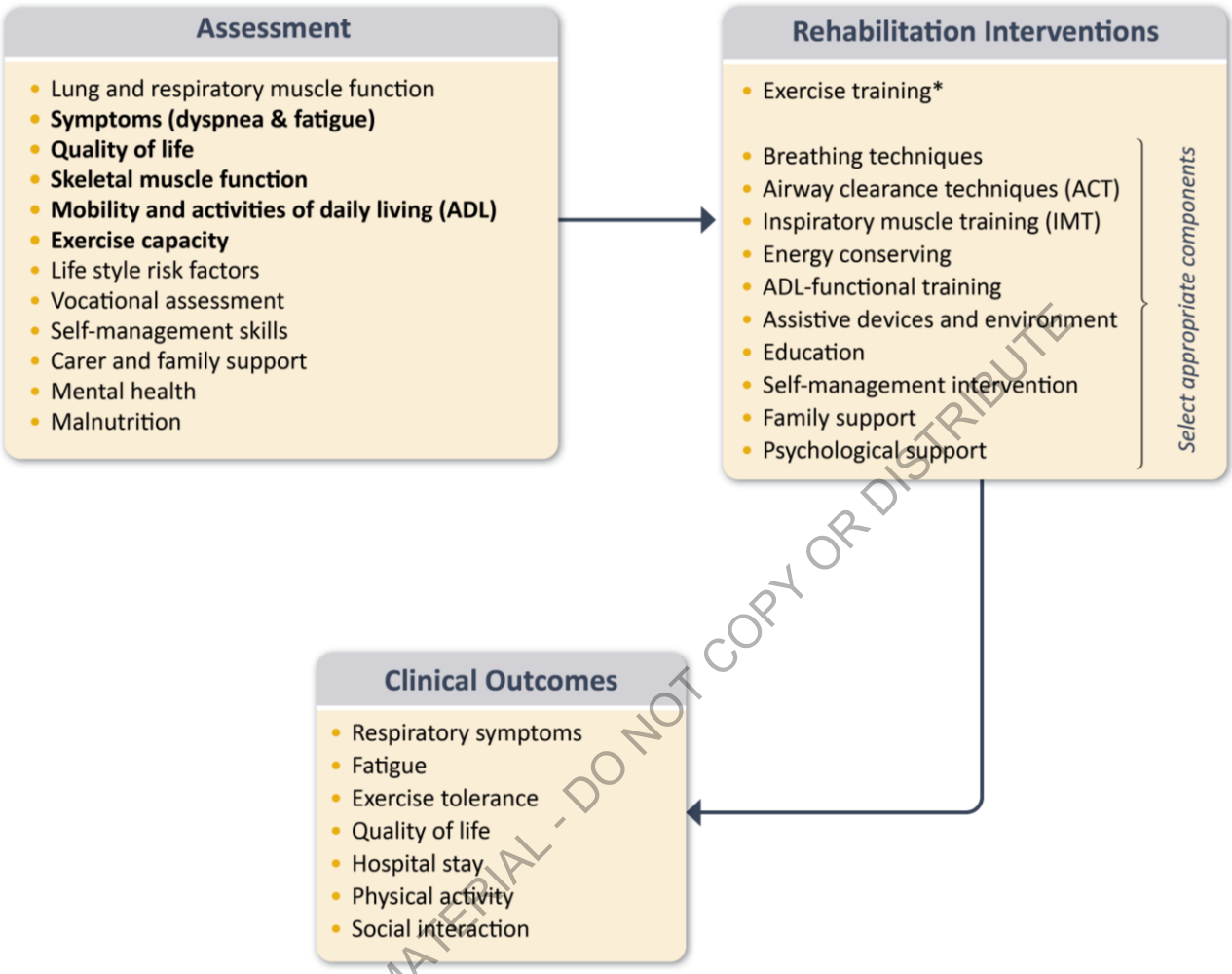
Assessment and Rehabilitation Interventions

Figure 3.18



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*Default component; assessment allows for proper prescription (frequency, intensity, type and time). The assessment items in bold type are also outcomes identified in the domains of a 'Core Outcome Set' for pulmonary rehabilitation according to Souto-Miranda et al. Thorax. 2023 Dec;78(12):1240-1247.

Adapted from the WHO Package of Interventions for Rehabilitation Module 4: Cardiopulmonary Conditions.

Pulmonary Rehabilitation Outcomes in COPD

Figure 3.19

Outcome	Evidence in COPD Pulmonary Rehabilitation	Effect Estimate	Clinical Interpretation
Exercise capacity (6MWD)[1]	Improves walking	44 m increase (95% CI: 33, 55)	MCID 25 m to 30 m
ISWT[1]	Improves walking	40 m increase (95% CI: 22, 57)	MCID 35 m to 48 m
SGRQ[1]	Improves respiratory quality of life	6.89 unit decrease (95% CI: -9.26, -4.52)	MCID -4 points
Physical activity[2]	Improves physical activity	CBRP increase of 680 steps per day (95% CI: 12, 1,348) CBRP + coaching increase of 1,376 steps per day (95% CI: 608, 2,144)	MCID 600 to 1,000 steps per day
Dyspnea (CRQ)[1]	Improves dyspnea	0.79 unit increase (95% CI: 0.56, 1.03)	MCID 0.5 units
Depression/ anxiety[3]	Improves symptoms of anxiety & depression	Depression SMD -0.35 (95% CI: -0.58, -0.12) Anxiety SMD -0.27 (95% CI: -0.53, -0.01)	Clinically relevant
Hospital admissions[4]	Reduces hospital admissions/ readmissions	RR 0.60 (95% CI: 0.32, 0.95)	Significant reduction
Mortality[5]	Not conclusive	OR 0.68 (95% CI: 0.28, 1.67) Non-randomized US-based VA cohort study suggests HR 0.74 (95% CI: 0.65, 0.84)	Prospective trials cannot be conducted

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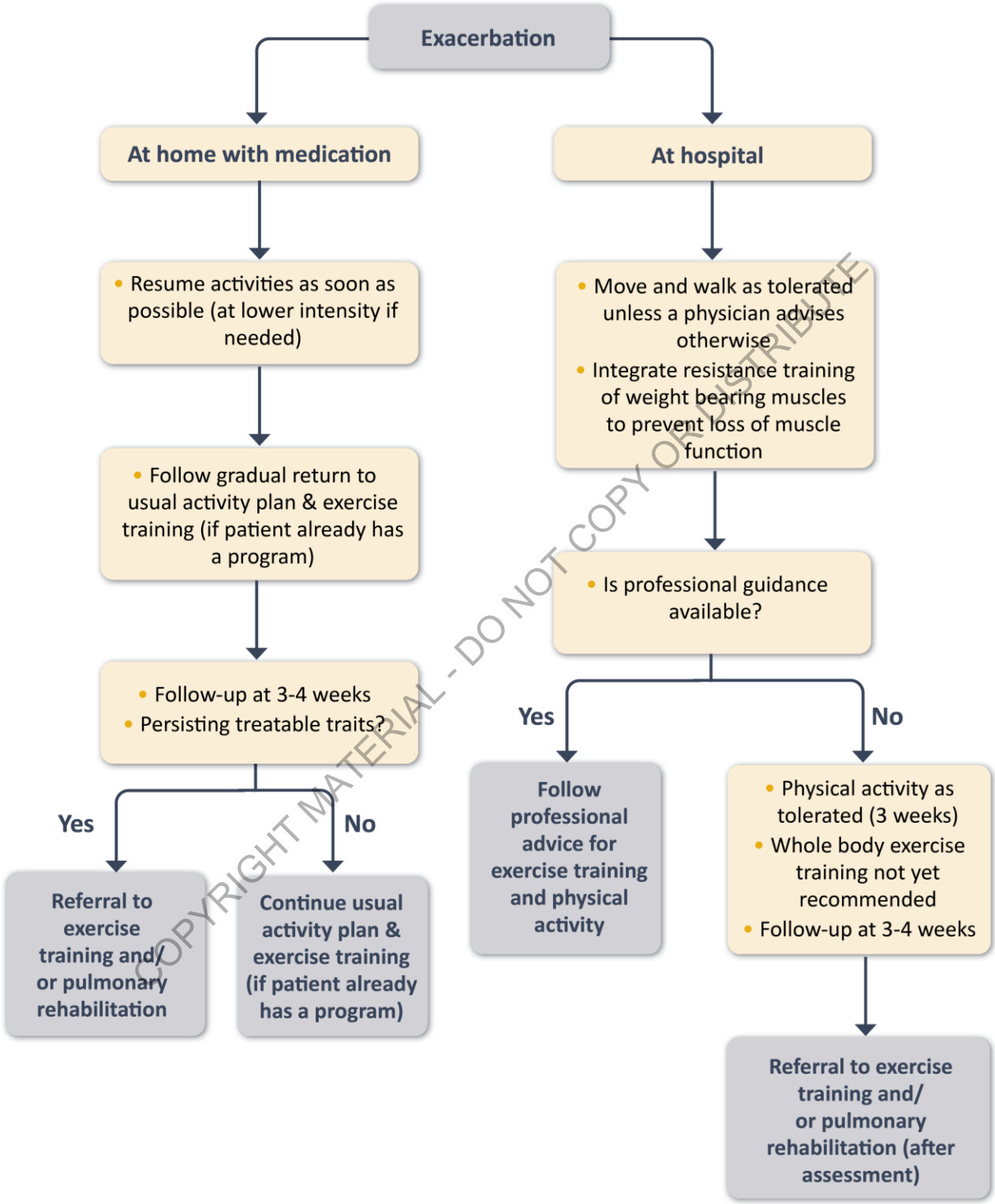
Abbreviations: CRQ: chronic respiratory disease questionnaire; MCID: mean clinically important difference; 6MWD: 6-minute walking distance; ISWT: incremental shuttle walk test; PR: pulmonary rehabilitation; RR: relative risk; SGRQ: St George's Respiratory Questionnaire; SMD: symptoms of major depressive disorder scale.

References: 1. McCarthy et al. Cochrane Database Syst Rev. 2015 Feb 23;2015(2):CD003793; **2.** Manifield et al. Eur Respir Rev. 2024 Apr 10;33(172):230225; **3.** Chen et al. Int J Chron Obstruct Pulmon Dis. 2026 May 6;21:578054; **4.** Jia et al. BMC Med. 2026 Mar 16;24(1):260; **5.** Robinson et al. Am J Respir Crit Care Med. 2026 Jun 1;212(6):1227-1236.

Physical Activity and Exercise Training After COPD Exacerbation

Figure 3.20



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Oxygen Therapy and Ventilatory Support in Stable COPD

Figure 3.21

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

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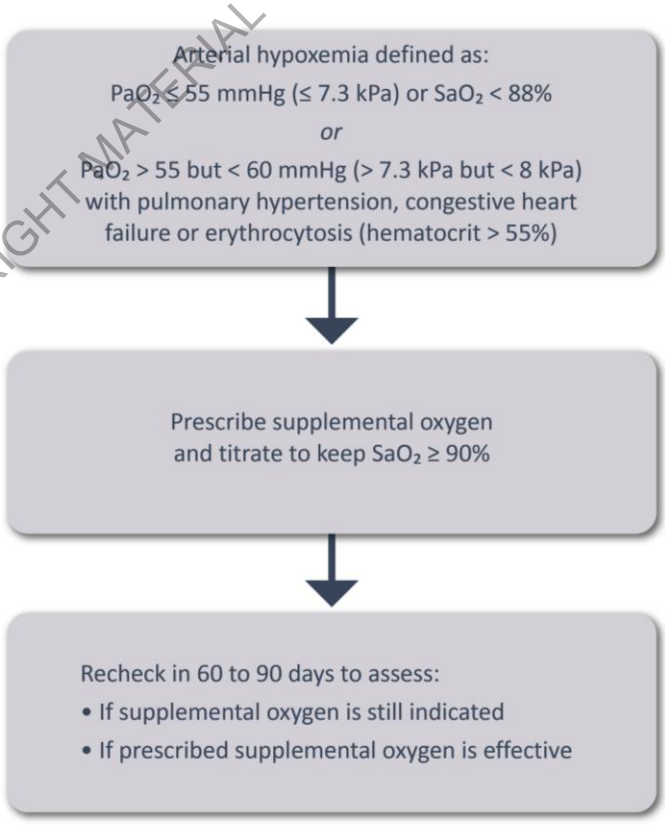
Prescription of Supplemental Oxygen to Patients with COPD

Figure 3.22



Evidence Supporting a Reduction in Mortality with Pharmacotherapy and Non-pharmacotherapy in COPD Patients

Figure 3.23

Therapy	RCT*	Treatment effect on mortality	Patient characteristics
Pharmacotherapy			
LABA+LAMA+ICS[1]	Yes	Single inhaler triple therapy compared to dual LABD therapy relative risk reduction: IMPACT: HR 0.72 (95% CI: 0.53, 0.99)[1a] ETHOS: HR 0.51 (95% CI: 0.33, 0.80)[1b]	Symptomatic people with a history of frequent and/or severe exacerbations
Non-pharmacological Therapy			
Smoking cessation[2]	Yes	HR for usual care group compared to intervention group (smoking cessation) HR 1.18 (95% CI: 1.02, 1.37)[2]	Asymptomatic or mildly symptomatic
Pulmonary rehabilitation[3#]	Yes	Old trials: RR 0.28 (95% CI 0.10, 0.84)[3a] New trials: RR 0.68 (95% CI 0.28, 1.67)[3b]	Hospitalized for exacerbations of COPD (during or ≤ 4 weeks after discharge)
Long-term oxygen therapy[4]	Yes	NOTT: ≥ 19 hours of continuous oxygen vs ≤ 13 hours: 50% reduction[4a] MRC: ≥ 15 hours vs no oxygen: 50% reduction[4b]	PaO_2 ≤ 55 mmHg or < 60 mmHg with *cor pulmonale* or secondary polycythemia
Noninvasive positive pressure ventilation[5]	Yes	12% in NPPV (high IPAP level) and 33% in control HR 0.24 (95% CI 0.11, 0.49)[5]	Stable COPD with marked hypercapnia
Lung volume reduction surgery[6]	Yes	0.07 deaths/person-year (LVRS) vs 0.15 deaths/person-year (UC) RR for death 0.47 (p = 0.005)[6]	Upper lobe emphysema and low exercise capacity

*RCT with pre-specified analysis of the mortality outcome (primary or secondary outcome); #Inconclusive results likely due to differences in pulmonary rehabilitation across a wide range of participants and settings.

1. a) IMPACT trial (Lipson et al. 2020) and b) ETHOS trials (Martinez et al. 2021); 2.Lung Health Study (Anthonisen et al. 2005); 3. a) Puhan et al. (2011) and b) Puhan et al. 2016; 4. a) NOTT (NOTT, 1980) and b) MRC (MRC, 1981); 5. Kohlein trial (Kohlein et al. 2014); 6. NETT trial (Fishman et al. 2003).

ICS: inhaled corticosteroid; IPAP: inspiratory positive airway pressure; LABA: long-acting beta$_2$-agonist; LABD: long-acting bronchodilator; LAMA: long-acting muscarinic antagonist; LTOT: long-term oxygen therapy; NPPV: noninvasive positive pressure ventilation; LVRS: lung volume reduction surgery; UC: usual treatment control group.

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Palliative Care, End of Life and Hospice Care in COPD

Figure 3.24

- All clinicians managing patients with COPD should be aware of the effectiveness of palliative approaches to symptom control and use these in their practice **(Evidence D)**
- End of life care should include discussions with patients and their families about their views on resuscitation, advance directives and place of death preferences **(Evidence D)**
- Opiates, neuromuscular electrical stimulation (NMES), oxygen and fans blowing air onto the face can relieve breathlessness **(Evidence C)**
- Nutritional supplementation should be considered in malnourished patients with COPD (**Evidence B**) as it may improve respiratory muscle strength and overall health status **(Evidence B)**
- Fatigue can be improved by self-management education, pulmonary rehabilitation, nutritional support and mind-body interventions **(Evidence B)**

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

Figure 3.25

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

Interventional Therapy in Stable COPD

Figure 3.26

Lung Volume Reduction Surgery	• Lung volume reduction surgery improves survival in patients with severe emphysema who have an upper-lobe and low post-rehabilitation exercise capacity **(Evidence A)**
Bullectomy	• In selected patients, bullectomy is associated with decreased dyspnea, improved lung function and exercise tolerance **(Evidence C)**
Transplantation	• In appropriately selected patients with very severe COPD, lung transplantation has been shown to improve quality of life and functional capacity **(Evidence C)** • In patients with very severe COPD (progressive disease, BODE score of 7 to 10, and not candidates for lung volume reduction) lung transplantation may be considered for referral with at least one of the following: (1) history of hospitalization for exacerbation associated with acute hypercapnia ($PaCO_2$ > 50 mmHg); (2) pulmonary hypertension and/or cor pulmonale, despite oxygen therapy; or (3) FEV1 < 20% and either DLco < 20% or homogenous distribution of emphysema **(Evidence C)**
Bronchoscopic Interventions	• In select patients with advanced emphysema, bronchoscopic interventions reduce end-expiratory lung volume and improve exercise tolerance, health status and lung function at 6-12 months following treatment. Endobronchial valves **(Evidence A)**; Lung coils **(Evidence B)**; Vapor ablation **(Evidence B)**
Bronchoscopic Interventions Under Study	• Phase 3 trials are currently being conducted to determine the efficacy of treatments for patients with chronic bronchitis

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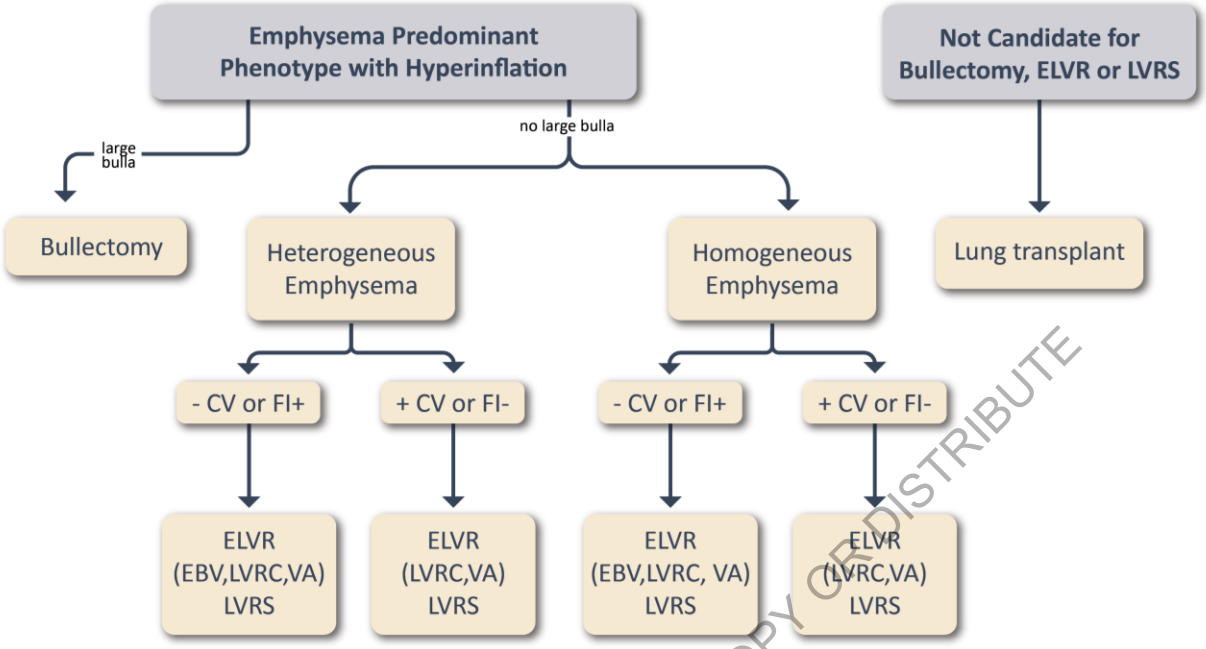
Surgical and Interventional Therapies in Advanced Emphysema

Figure 3.27



Note: not all therapies are clinically available in all countries. Long term ELVR outcomes or direct comparisons to LVRS are unknown.

Definition of abbreviations: CV, collateral ventilation measure by Chartis; FI + fissure integrity > 90% by HRCT; FI-, fissure integrity < 90% by HRCT; ELVR, Endoscopic Lung Volume Reduction, EBV, Endobronchial Valve; VA, Vapor Ablation; LVRC, Lung Volume Reduction Coil; LVRS, Lung Volume Reduction Surgery. Modified from Vogelmeier, AJRCCM, 2017.

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MANAGEMENT OF EXACERBATIONS

KEY POINTS:

- An exacerbation of COPD is an acute event with 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. Exacerbations are often associated with increased local and systemic inflammation caused by airway infection, pollution, or other insults to the lungs.
- Although COPD exacerbations are most frequently caused by infections (viral, bacteria) or environmental pollutants, other conditions can mimic or worsen exacerbation-like symptoms. These include pneumonia, pulmonary embolism, acute heart failure, and pneumothorax. In many patients the exact cause of an exacerbation is unknown.
- Exacerbation severity is classified as mild, moderate or severe based on the clinical characteristics of the patient, according to the Rome proposal.
- Pharmacological therapy should be started as soon as possible to prevent both complications and subsequent events. It includes:
    - SABAs, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat moderate/severe exacerbations.
    - Systemic corticosteroids are recommended for up to 5 days in patients with moderate/severe exacerbations.
    - Antibiotics are recommended for a total of 5 days in patients with purulent sputum, prior history of lung infections, etc.
    - Methylxanthines are not recommended due to increased side effect profiles.
- High flow oxygen systems and mechanical NIV are indicated for patients with COPD and acute respiratory failure because they improve gas exchange, reduce work of breathing and the need for intubation. They also decrease hospitalization duration and improve survival.
- Maintenance therapy with LABDs should be initiated as soon as possible. In patients with ≥ 1 moderate or severe exacerbation and elevated blood eosinophil levels, the addition of ICSs to a dual bronchodilator regimen should be considered at discharge.
- Exacerbation recovery time varies, taking up to 4-6 weeks, with some patients failing to return to their pre-exacerbation functional state.
- Following an exacerbation (of any severity) there is an increased risk of severe cardiovascular events.
- Following an exacerbation, the management of COPD and its comorbidities should be reviewed and appropriate measures for exacerbation prevention should be implemented (see **Chapter 3**).

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Exacerbations: Diagnosis and Assessment

Figure 4.1

1.	Complete a thorough clinical assessment for evidence of COPD and potential respiratory and non-respiratory conditions, including patient's symptoms, and signs of pneumonia, cardiovascular conditions, and pulmonary embolism.
2.	**Assess:** a. Symptoms, severity of dyspnea that can be determined by using a VAS, and documentation of the presence of cough. b. Signs (tachypnea, tachycardia), sputum volume and color, and respiratory distress (accessory muscle use).
3.	Perform additional investigations, if needed and available, to evaluate severity such as pulse oximetry, laboratory assessments such as blood eosinophils, CRP, viral and bacterial studies, and arterial blood gases.
4.	Evaluate for underlying conditions such as viral or bacterial infections, environmental or cardiovascular events that mimic the exacerbation.
5.	Consider appropriate place of care.

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

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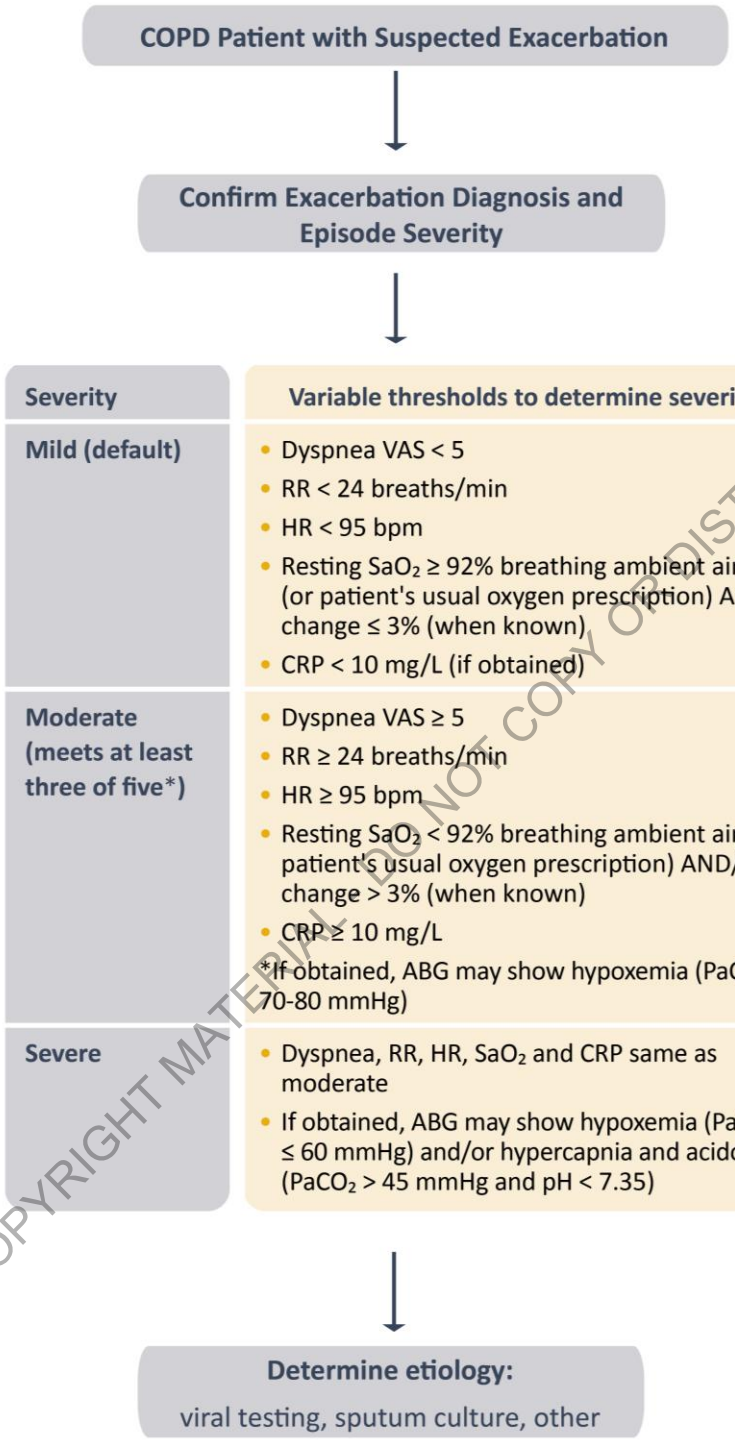
Classification of the Severity of COPD Exacerbations

Figure 4.2



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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.

Conditions That May Mimic or Worsen Exacerbation-like Symptoms

Figure 4.3

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 (echocardiogram)
	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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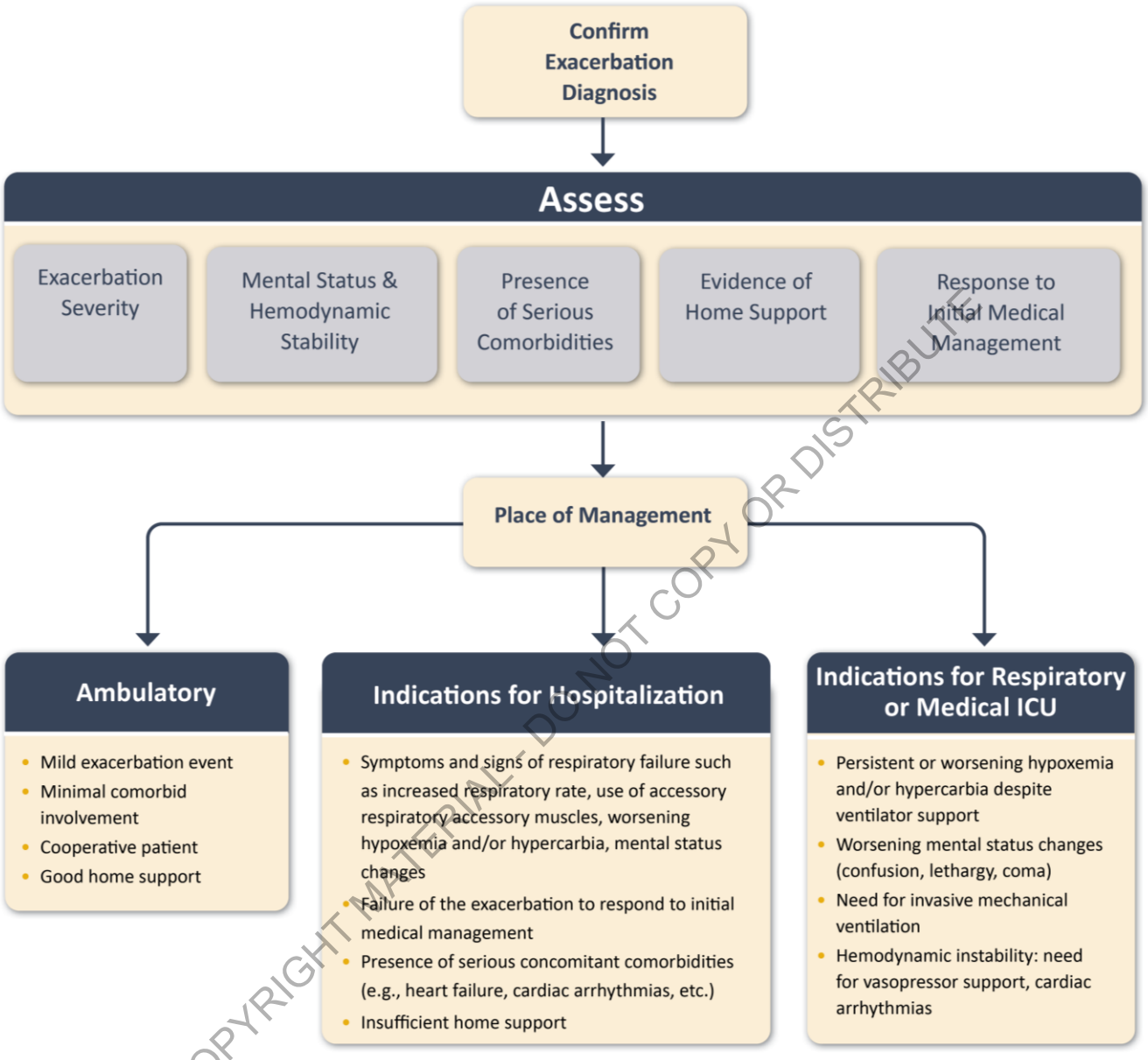
Assessing the Appropriate Place of Management During COPD Exacerbation

Figure 4.4



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Risk of Severe Cardiovascular Event or All-Cause Death following COPD Exacerbation of any Severity

Figure 4.5

Exposure (days after exacerbation)	Pooled Hazard Ratio*
1-7 days	10.22 (95% CI: 5.34, 19.57)
8-14 days	4.00 (95% CI: 2.58, 6.18)
15-30 days	2.93 (95% CI: 2.13, 4.02)
31-180 days	1.70 (95% CI: 1.45, 2.00)
181-365 days	1.24 (95% CI: 1.08, 1.40)
> 365 days	1.18 (95% CI: 0.93, 1.50)

*Random effects meta-analysis of adjusted hazard ratio; HR: hazard ratio; CI: confidence interval; adapted from Nordon et al.ERJ Open Res. 2025 Jun 16;11(3):01091-2024.

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Management of Severe but not Life-threatening Exacerbations*

Figure 4.6

Assess severity of symptoms, blood gases, chest radiograph

Bronchodilators:

- Increase doses and/or frequency of short-acting bronchodilators
- Combine short-acting beta$_2$-agonists and anticholinergics
- Consider use of long-acting bronchodilators when patient becomes stable
- Use spacers or air-driven nebulizers when appropriate

Consider oral corticosteroids

Consider antibiotics (oral) in patients with purulent oral secretions, prior positive sputum bacteria culture or requiring mechanical ventilation (invasive or noninvasive)

Consider high flow oxygen (HFNT) or noninvasive ventilation (NIV), obtain serial blood gas, venous blood gas and pulse oximetry measurements

At all times:

- Monitor fluid balance
- Consider subcutaneous heparin or low molecular weight heparin for thromboembolism prophylaxis
- Identify and treat associated conditions (e.g., heart failure, arrhythmias, pulmonary embolism etc.)

*Local resources need to be considered

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Key Points for the Management of Exacerbations

Figure 4.7

- Short-acting inhaled beta$_2$-agonists, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat an acute exacerbation **(Evidence C)**
- Systemic corticosteroids can improve lung function (FEV1), oxygenation and shorten recovery time and hospitalization duration. Duration of therapy 5 days **(Evidence A)**
- Antibiotics are indicated in patients with purulent sputum, prior positive sputum bacteria culture, or requiring mechanical ventilation (invasive or noninvasive) **(Evidence A)**
- Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy 5 days **(Evidence B)**
- High flow oxygen (HFNT) is the first mode of ventilation used in COPD patients with acute hypoxemic respiratory failure. For patients with hypercarbic respiratory failure or those who do not respond to HFNT, use non-invasive mechanical ventilation (NIV) unless absolutely contraindicated. NIV has been shown to: improve gas exchange, reduce breathing work and need for intubation, decrease hospitalization duration and improve survival **(Evidence A)**

Indications for High Flow Oxygen Therapy (HFNT)*

Figure 4.8

At least one of the following:

- Persistent hypoxemia
- Unable to tolerate noninvasive ventilation (NIV)
- Contraintidaction for NIV
- Weaning patient off supplemental oxygen following NIV
- Preventing reintubation in patients requiring intubation and positive pressure ventilation
- Treatment of patients with stable COPD at risk of exacerbations

*Local resources need to be considered.

Indications for Noninvasive Mechanical Ventilation (NIV)

Figure 4.9

At least one of the following:

- Respiratory acidosis ($PaCO_2 \geq 6.0$ kPa or 45 mmHg and arterial pH ≤ 7.35)
- Severe dyspnea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as use of respiratory accessory muscles, paradoxical motion of the abdomen, or retraction of the intercostal spaces
- Persistent hypoxemia despite supplemental oxygen therapy

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Indications for Invasive Mechanical Ventilation

Figure 4.10

- Persistent life-threatening hypoxemia despite high flow oxygen (HFNT) or NIV
- Unable to tolerate HFNT and/or NIV
- Status post-respiratory or cardiac arrest
- Diminished consciousness, psychomotor agitation inadequately controlled by sedation
- Massive aspiration or persistent vomiting
- Persistent inability to remove respiratory secretions
- Severe hemodynamic instability without response to fluids and vasoactive drugs
- Severe ventricular or supraventricular arrhythmias

Discharge Criteria and Recommendations for Follow-up

Figure 4.11

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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Interventions that Reduce the Frequency of COPD Exacerbations

Figure 4.12

Intervention Class	Intervention
Bronchodilators	LABAs LAMAs LABA + LAMA
Corticosteroid-containing regimens	LABA + LAMA + ICS
Anti-inflammatory (non-steroid)	Roflumilast Dupilumab Mepolizumab
Anti-infectives	Vaccines Long term macrolides
Mucoregulators	N-acetylcysteine Carbocysteine Erdosteine
Various others	Smoking cessation Rehabilitation Lung volume reduction Vitamin D Shielding measures (e.g., mask wearing, minimizing social contact, frequent hand washing) Exposure avoidance (e.g., avoiding exposure to outdoor air pollution)

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COPD AND MULTIMORBIDITY

KEY POINTS:

- Patients with COPD often have other chronic conditions (multimorbidity) that increase the risk of poor outcomes.
- Multimorbidity is often underdiagnosed and undertreated, and should be actively searched for in each patient with COPD.
- The presence of those morbidities should not alter COPD treatment; comorbid disease should be treated as per usual standards, despite the presence of COPD.
- CVDs, particularly hypertension, ischemic heart disease, heart failure and atrial fibrillation, are common in COPD. The risk of a major cardiovascular event is significantly increased during and up to one year after a moderate or severe exacerbation.
- Lung cancer is a major cause of death in patients with COPD. An annual LDCT scan is recommended for lung cancer screening in patients with a smoking history, similar to recommendations for the general population. Screening for lung cancer in patients with COPD not associated with tobacco smoking is not recommended due to lack of evidence.
- Bronchiectasis is frequently present in patients with COPD, and when associated with infections impacts disease progression, exacerbations and risk of death.
- Depression/anxiety are frequent and important morbidities in COPD. They are often under-diagnosed and under-treated and are associated with poor health status and increased risk of death.
- In COPD, low BMI (< 21 kg/m^2) is associated with increased risk of death. Obesity (> 30 kg/m^2) is associated with metabolic syndrome and OSA. If OSA is present, CPAP treatment decreases risk of death.
- GERD is associated with an increased risk of exacerbations and poor health status.
- Multiple organ loss of tissue (MOLT) manifested by osteoporosis, sarcopenia, anemia and emphysema is associated with poor outcomes. Adequate nutrition, pulmonary rehabilitation and management of MOLT can improve outcomes.
- When COPD is part of a multimorbidity care plan, a goal should be simplicity of treatment, minimizing polypharmacy.

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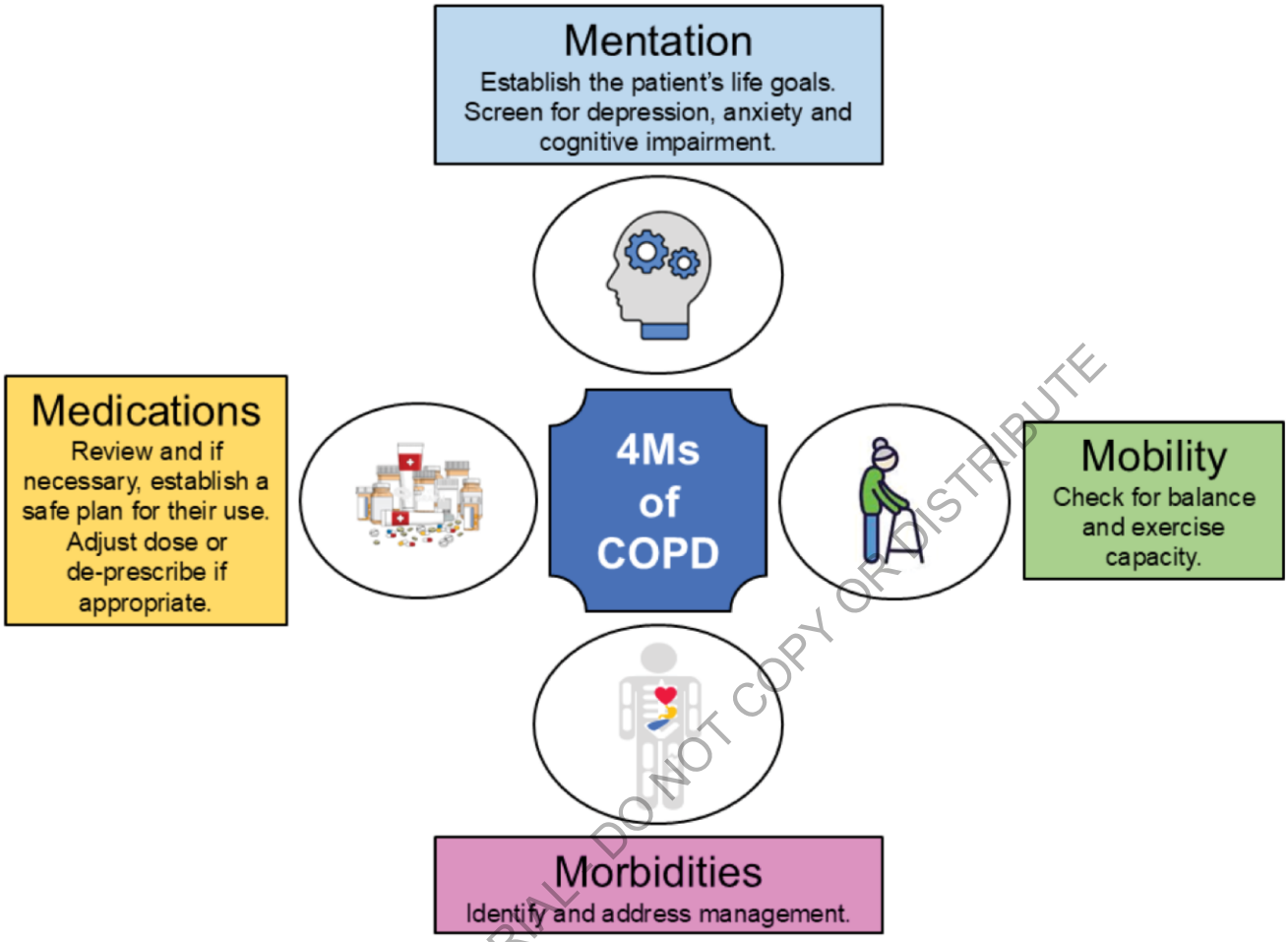
Summary of the Modified 4Ms Person-centered Approach to Multimorbid Patients with COPD

Figure 5.1



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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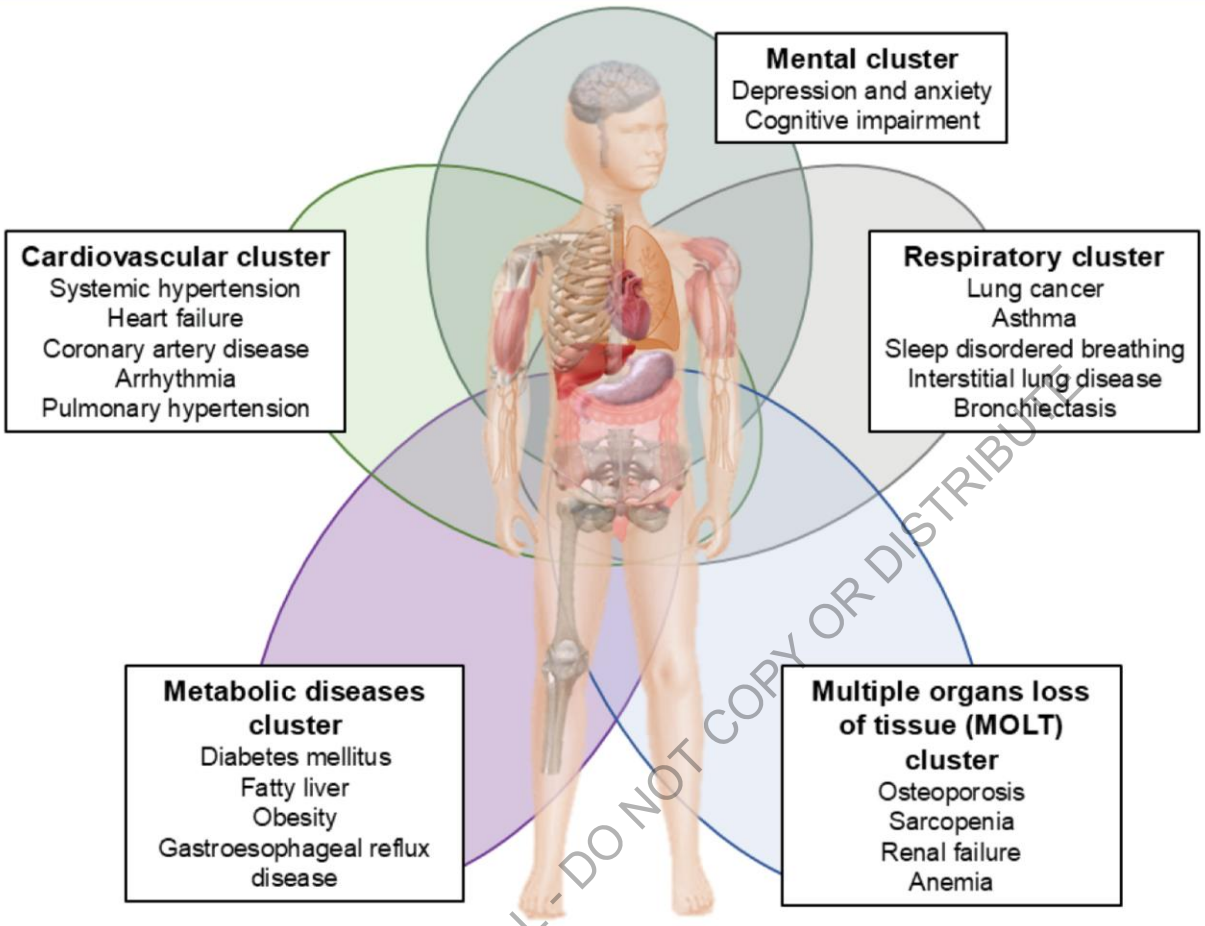
Morbidity Clusters Frequently Present in Patients with COPD that Independently Impact Outcomes

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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Cardiovascular Diseases in COPD: Burden & Management

Figure 5.3

Systemic Hypertension	• Approximately 50% of people with COPD have systemic hypertension • Systemic hypertension increases the risk of heart failure, myocardial infarction and stroke • Blood pressure (BP) should be recorded at every medical evaluation • BP over 130/80 is abnormal and warrants treatment
Heart Failure	• Approximately 30% of people with COPD have heart failure • Overlapping symptoms can make the diagnosis of heart failure challenging • Evaluate natriuretic peptide (NTproBNP) levels in all cases of suspected heart failure • Cardioselective beta-blockers are recommended and safe in COPD • SGLT2 inhibitors are indicated in all heart failure types • Treatment with ACEi/ARB/ARNI plus BB+MRA+SGLT2i is indicated in heart failure with reduced ejection fraction • Continue heart failure therapies during a COPD exacerbation
Coronary Artery Disease	• Approximately 20% of people with COPD have coronary artery disease • Cardiovascular risk for primary prevention of CVD can be estimated using calculators, but these underestimate risk in COPD • The use of troponins should be reserved for cases of suspected acute coronary syndrome • Treatment of coronary artery disease should follow standard cardiovascular guidelines irrespective of COPD • Beta-blockers should not be withheld in COPD when indicated for coronary artery disease
Arrhythmias	• Common in people with COPD • COPD should not preclude guideline-directed arrhythmia management • For atrial fibrillation, there is no contraindication to any specific rate or rhythm control medication or strategy in patients with COPD, including beta-blockers • For supraventricular and ventricular arrhythmias, follow guideline recommendations, with caution regarding bronchoconstriction risk and use of atrioventricular nodal agents
Valvular Heart Disease	• Up to 50% of people with COPD have valvular heart disease • Diagnostic evaluation of valvular heart disease is similar in patients with and without COPD • Additional imaging, including CT coronary angiography and cardiac magnetic resonance, may be necessary to assess valve anatomy, function, and suitability for transcatheter interventions

Abbreviations: ACEi (ACE inhibitor); ARB (Angiotensin Receptor Blocker); ARNI (Angiotensin Receptor-Neprilysin Inhibitor); BB (Beta-Blocker); MRA (Mineralocorticoid Receptor Antagonist); NTproBNP (N-terminal prohormone of brain natriuretic peptide test); SGLT2i (Sodium-Glucose Co-transporter 2 Inhibitor).

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Treatable Traits in Pulmonary Hypertension-COPD (PH-COPD) & Suggested Management

Figure 5.4

COPD and PAH (Group 1 PH)	• Treat as PAH according to 2026 ERS PAH treatment guidelines update
COPD and severe PH associated with lung diseases and/or hypoxia (Group 3 PH)	• Individualized treatment approach in PH center with experience in respiratory diseases
COPD and CTEPH (Group 4 PH)	• Treat as CTEPH according to 2022 ESC/ERS PH guidelines

Abbreviations: PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; ESC/ERS, European Society of Cardiology/European Respiratory Society; CTEPH, chronic thromboembolic PH.

Reference: Kovacs et al. European Respiratory Society clinical practice guidelines update for the treatment of pulmonary arterial hypertension. Eur Respir J. 2026 Sep 7:2601178.

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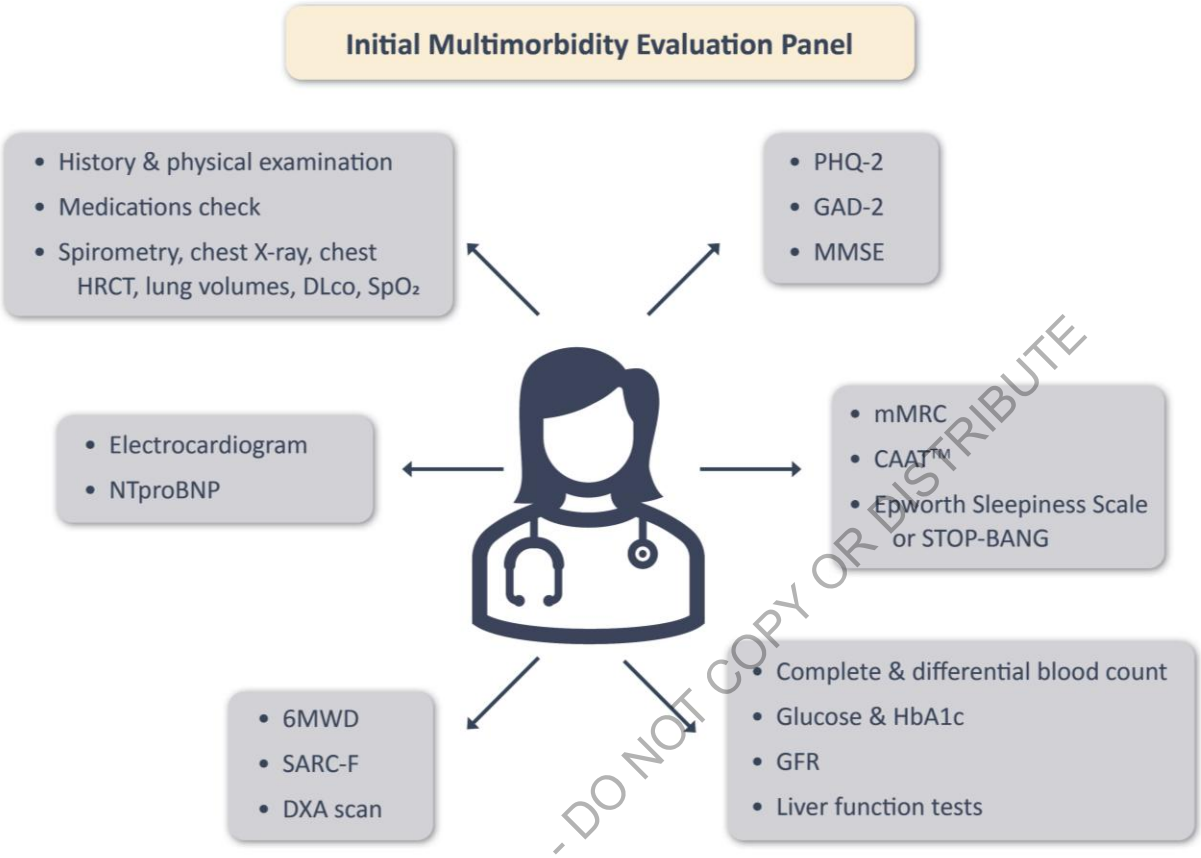
Common Risk Factors for the Development of Lung Cancer

Figure 5.5

- Age > 55 years
- Smoking history > 30 pack years
- Presence of emphysema by CT scan
- Presence of airflow limitation FEV1/FVC < 0.7
- BMI < 25 kg/m²
- Family history of lung cancer

Potential Complementary Approach for the Detection of Frequent Morbidities in all Patients with COPD – Initial Evaluation

Figure 5.6



Abbreviations: HRCT, high-resolution computerized tomography; DLco, diffusing capacity for carbon monoxide; SpO_2, oxygen saturation; SARC-F, Strength, Assistance walking, Rising from chair, Climbing stairs and Falls; DXA, dual energy X-ray absorptiometry; mMRC, modified Medical Research Council dyspnea scale; CAAT™, Chronic Airways Assessment Test; GFR, glomerular filtration rate; NTproBNP, N-terminal prohormone of brain natriuretic peptide; 6MWD, 6-minute walking distance test; HbA1c, glycated hemoglobin A1c test; PHQ-2, Patient Health Questionnaire-2; GAD-2, Generalized Anxiety Disorder-2; MMSE, Mini Mental State Examination.

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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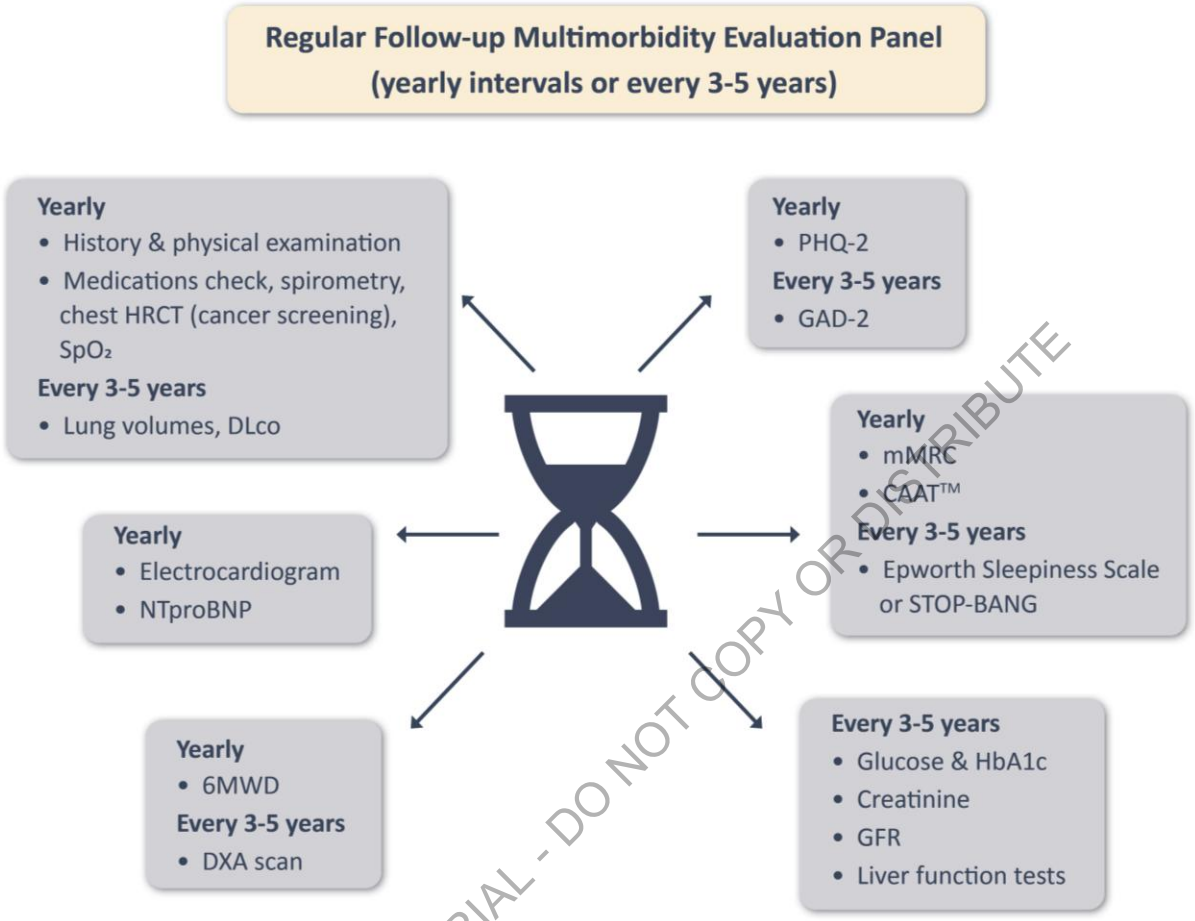
Potential Complementary Approach for the Detection of Frequent Morbidities in all Patients with COPD – Regular Follow-up

Figure 5.7



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Abbreviations: HRCT, high-resolution computerized tomography; DLco, diffusing capacity for carbon monoxide; SpO_2, oxygen saturation; SARC-F, Strength, Assistance walking, Rising from chair, Climbing stairs and Falls; DXA, dual energy X-ray absorptiometry; mMRC, modified Medical Research Council dyspnea scale; CAAT™, Chronic Airways Assessment Test; GFR, glomerular filtration rate; NTproBNP, N-terminal prohormone of brain natriuretic peptide; 6MWD, 6-minute walking distance test; HbA1c, glycated hemoglobin A1c test; Patient Health Questionnaire-2; GAD-2, Generalized Anxiety Disorder-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.

ARTIFICIAL INTELLIGENCE AND EMERGING TECHNOLOGIES IN COPD

KEY POINTS:

- Artificial intelligence can help in the diagnosis, assessment, clinical management, and prediction of prognosis of COPD.
- Yet, AI comes with risks and limitations that need careful consideration before deployment in clinical practice.
- Telehealth includes virtual, hybrid virtual and in-person care models.
- Telehealth may offer improved healthcare access, outcomes, and affordability.
- Pulmonary rehabilitation and self-management may be delivered virtually.
- Evidence is still emerging regarding the effectiveness of virtual compared to in-person delivery.

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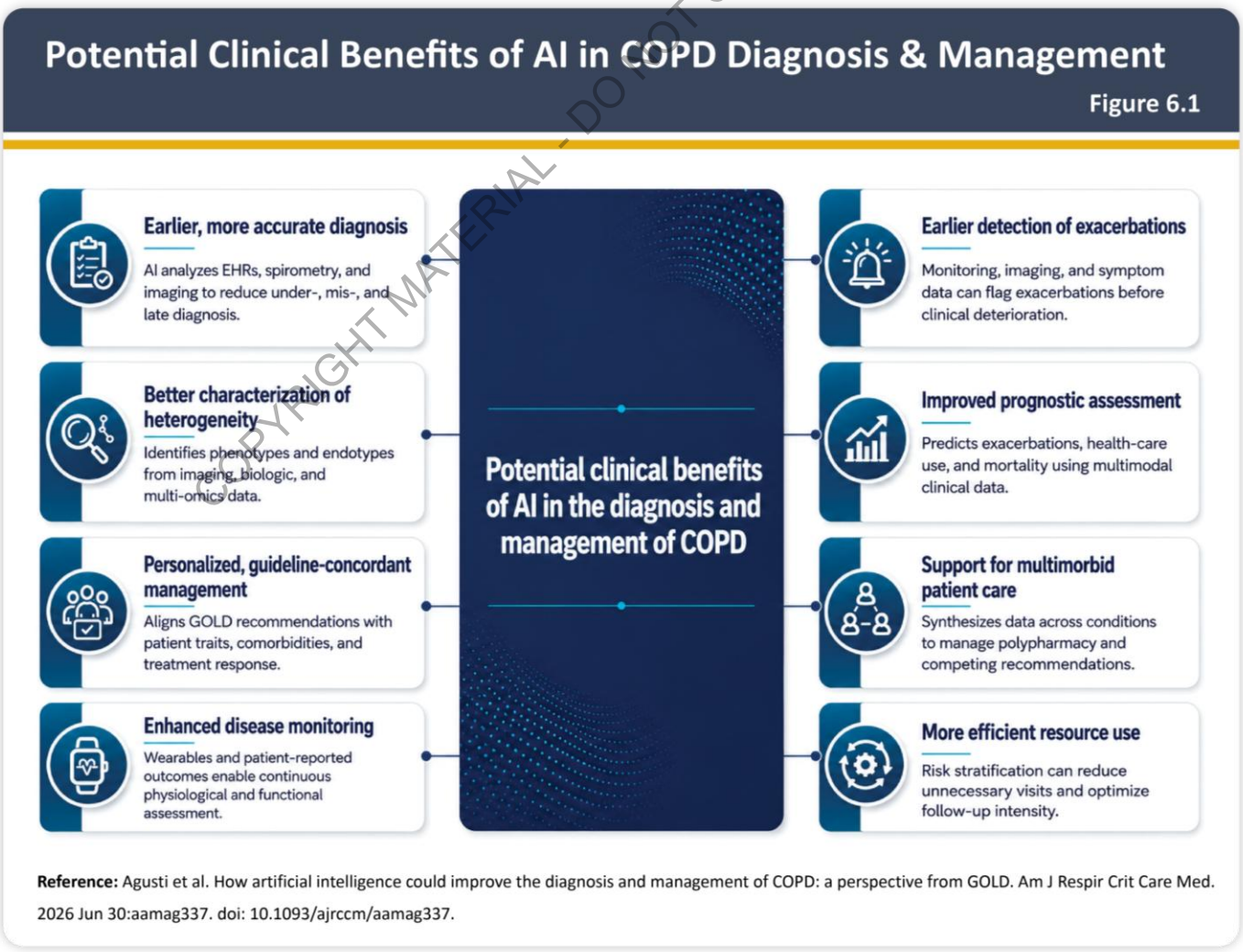

Reference: Agusti et al. How artificial intelligence could improve the diagnosis and management of COPD: a perspective from GOLD. Am J Respir Crit Care Med. 2026 Jun 30:aamag337. doi: 10.1093/ajrccm/aamag337.

Potential Risks and Mitigation Strategies of AI in Medicine

Figure 6.2

	Potential Risks	Mitigation Strategies
Clinical Risks	• Misdiagnosis, overreliance on AI, biased outcomes	• Rigorous validation, human oversight, bias testing
Data-Related Risks	• Poor data quality, biased training data, privacy breaches	• Data cleaning, diverse datasets, strong security protocols
Technical Limitations	• Black-box models, poor generalizability, data drift	• Use interpretable models, retraining, external validation
Ethical & Legal Risks	• Unclear accountability, informed consent issues, inequity	• Clear liability frameworks, transparent patient communication, equitable access
Operational Challenges	• Workflow integration problems, regulatory complexity, high maintenance costs	• User-centered design, regulatory alignment, ongoing monitoring and funding

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PHARMACOLOGICAL THERAPY CHECKLIST

Patient Name: _____
Date: _____
Clinician: _____

Inhaler Treatment Summary Checklist

☐ **Inhaler prescribed:** Medication name and device type documented
☐ **Purpose of inhaler:** Controller/preventer or reliever/rescue confirmed
☐ **Dose and schedule:** Dose, frequency, and timing reviewed
☐ **Adherence:** Regular use and missed doses assessed
☐ **Inhaler technique:** Patient demonstrates correct use
☐ **Spacer use:** Assessed and technique reviewed (if applicable)
☐ **Mouth rinsing:** Reviewed after inhaled corticosteroids (if applicable)
☐ **Device care:** Cleaning, storage, and dose counter checked
☐ **Symptom control:** Effectiveness of treatment assessed
☐ **Reliever use:** Frequency of rescue inhaler use reviewed
☐ **Side effects:** Assessed and documented
☐ **Patient education:** Technique and treatment plan reinforced
☐ **Follow-up:** Need for reassessment or treatment adjustment identified

Overall inhaler treatment assessment:
☐ Effective and well tolerated
☐ Technique requires correction
☐ Adherence support required
☐ Treatment review/change recommended

Follow-Up Plan

Identified barriers:

_____

Interventions planned:

_____

Next review date: _____

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NON-PHARMACOLOGICAL THERAPY CHECKLIST

Patient Name: _____
Date: _____
Clinician: _____

1. Engagement with Prescribed Non-Pharmacological Interventions

☐ Patient has been referred to non-pharmacological interventions
☐ Patient has participated in recommended interventions
☐ Patient has not participated in recommended interventions

If not engaged, reasons identified:
☐ Lack of awareness/understanding
☐ Lack of motivation or confidence
☐ Symptom limitations (dyspnea, fatigue, pain)
☐ Access barriers (transportation, cost, availability)
☐ Other: _____

Interventions completed:
☐ Pulmonary rehabilitation
☐ Exercise training program
☐ Patient education/self-management program
☐ Smoking cessation support
☐ Nutritional counseling
☐ Other: _____

---

2. Pulmonary Rehabilitation and Maintenance Exercise Program

Has the patient completed pulmonary rehabilitation?
☐ Yes
☐ No
☐ Currently participating

If completed:

☐ Patient continues maintenance exercise program
☐ Patient follows recommended exercise frequency
☐ Patient follows recommended exercise intensity/duration
☐ Patient monitors symptoms during exercise
☐ Patient understands strategies to manage breathlessness during exercise

Adherence barriers identified:
☐ Increased symptoms

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☐ Lack of motivation
☐ Lack of support
☐ Time constraints
☐ Other: _____

Maintenance exercise plan reviewed:
☐ Yes
☐ No

---

3. Physical Activity Assessment and Promotion

Patient awareness of current physical activity level:
☐ Aware
☐ Partially aware
☐ Not aware

Physical activity assessment completed:
☐ Daily activity level reviewed
☐ Sedentary behavior assessed
☐ Activity goals discussed
☐ Exercise recommendations reviewed

Patient currently engages in:
☐ Walking
☐ Strength training
☐ Breathing exercises
☐ Other: _____

Physical activity goals:

---

4. Self-Management Skills Integration

Breathing Control Techniques
☐ Patient understands breathing control strategies
☐ Patient demonstrates appropriate technique
☐ Patient uses breathing control technique
☐ Techniques reviewed/reinforced

Examples:
☐ Pursed-lip breathing
☐ Pacing techniques
☐ Diaphragmatic breathing

Stress and Anxiety Management

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☐ Patient identifies stress/anxiety triggers
☐ Patient uses coping strategies
☐ Relaxation techniques discussed
☐ Referral/support offered if needed

Exacerbation Prevention and Management

☐ Patient recognizes early warning signs of exacerbation
☐ Patient understands when to seek medical advice
☐ Written action plan reviewed
☐ Patient demonstrates appropriate use of action plan

Written action plan available:

☐ Yes
☐ No
☐ Needs updating

Follow-Up Plan

Identified barriers:

_____

Interventions planned:

_____

Next review date: _____

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COPD FOLLOW-UP CHECKLIST

In-person follow-up □ **Phone follow-up** □ **Virtual/online follow-up** □

Date: YYYY / MM / DD	**Diagnosis:**

1. BASELINE SYMPTOMS – Breathlessness on a regular day: mMRC /4

Daily sputum production: □ no □ yes, color: Regular cough □ no □ yes

Recent change in symptoms □ no □ yes If yes, since when: □ Sputum color: □ Sputum volume ↑ = ↓ □ Dyspnea ↑ = ↓ □ Fatigue ↑ = ↓ □ Cough ↑ = ↓ □ Other □ Signs of hypercapnia **CAAT™: /40**	*Maintenance medication and adherence*: □ SABA □ LABA+LAMA □ LABA □ LABA+ICS □ LAMA □ LABA+LAMA+ICS □Other: *Non pharmacological Rx*: O2: CPAP: BIPAP :

2. AIRBORNE VIRUS – If patient is feeling unwell, check other symptoms: □ Fever____ □ Sore throat □ Anosmia □ Others_____

Contact with someone positive for airborne virus? □ no □ yes Tested for airborne virus? □ no □ yes If yes □ positive □ negative

3. WRITTEN ACTION PLAN – no □ yes □

Instruction and any additional treatment: _____

Last time it has been used (date):

4. RECENT ADMISSIONS AND EMERGENCY VISITS

Hospital/ED	Where	Date	Length	Reason (Dx)

Comments:

5. COPD Self-management (healthy behaviors) – Integrated (patient has used it in their daily life)?

Smoke-free environment	yes	no	cannot tell
Medication adherence	yes	no	cannot tell
Prevention/management of exacerbations	yes	no	cannot tell
Breathing control	yes	no	cannot tell
Stress management	yes	no	cannot tell
Physical activity and exercise	yes	no	cannot tell
Other _____	yes	no	

Comments and what patient should prioritize based on his/her needs:

6. MAIN ISSUES

1.	*2.*	*3.*

7. SUMMARY, INTERVENTIONS & PLAN

(healthcare professional name & signature)

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Instructions for using the COPD follow-up checklist

1. **Introduction**
    a. Identify dates, Dx and whether this follow-up is being done in-person, by phone or remotely.
2. **Section 1 – Baseline symptoms**
    a. Go over the patient symptoms and whether there have been changes in dyspnea, cough, sputum volume and color (from least to most purulent: mucus; mucopurulent; purulent).
    b. Identify maintenance pharmacological and non-pharmacological treatment and whether the patient is observing treatment as prescribed.
3. **Section 2 – Airborne virus**
    a. Assess whether the patient has any symptoms of airborne virus infection and would need to be tested. Have at hand local numbers where the patient can be referred to for testing and treatment.
    b. If the patient has already been tested identify when the results will be obtained, or whether the result was positive or negative. If positive, is there a follow-up test planned, and dates.
    c. Verify patient is practicing precautions (face masks, hand washing, social distancing, or shielding if necessary).
4. **Section 3 – Action plan**
    a. Describe if the patient already has a written action plan. See example of an action plan from the Living well with COPD program.[821] Describe if the education for this action plan has already been done. Describe if the written action plan includes a prescription to be self-administered at home or whether the patient need to call his contact person / physician to obtain the prescription. Describe when it was used the last time and if used appropriately.
5. **Section 4 – Recent admissions and ED visits**
    a. Write down recent admissions and ED visits, dates and where they took place.
6. **Section 5 – COPD self-management behaviors**
    a. Go over each of the self-management behaviors described in the list. You should cover what is pertinent to the patient treatable traits (dyspnea and/or exacerbation). Describe whether the patient has integrated these strategies in their daily life (yes), not at all (e.g., it has not been discussed or not applicable), and whether the patient is unsure “cannot tell”.
7. **Section 6 – Main issues**
    a. Identify with the patient the main issues of the call. Up to a maximum of 3 items that can be covered for the duration of the call. Avoid covering too many issues in one visit.
8. **Section 7 – Summary, intervention and plan**
    a. Finalize by describing the interventions done during the remote visit, the ones to be put in place, and agreed by the patient, the plan, including whether the patient needs to be referred to other services, healthcare professionals, etc. and when the next follow-up will take place (describe whether will it be in-person or remote).

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OVERVIEW OF THE EVIDENCE: PHARMACOTHERAPY

Maintenance Medications Registered for the Treatment of COPD*

Figure A5.1

Generic Drug Name	Inhaler Type	Nebulizer	Oral/Injectable Delivery	Duration of Action
$BETA_2$-Agonists				
Short-acting (SABA)				
Fenoterol	MDI	✓	tablet, solution	variable
Levalbuterol	MDI	✓		variable
Salbutamol (albuterol)	MDI, DPI	✓	syrup, tablet	variable
Terbutaline	DPI		tablet	variable
Long-acting (LABA)				
Arformoterol		✓		12 hours
Formoterol	DPI	✓		12 hours
Indacaterol	DPI			24 hours
Olodaterol	SMI			24 hours
Salmeterol	MDI, DPI			12 hours
Anticholinergics				
Short-acting (SAMA)				
Ipratropium bromide	MDI	✓		6-8 hours
Oxitropium bromide	MDI	✓		7-9 hours
Long-acting (LAMA)				
Aclidinium bromide	DPI			12 hours
Glycopyrronium bromide	DPI	✓	solution	variable
Tiotropium	DPI, SMI, MDI			24 hours
Umeclidinium	DPI			24 hours
Revefenacin		✓		24 hours
Combination Short-Acting $Beta_2$-Agonist Plus Anticholinergic in One Device (SABA+SAMA)				
Fenoterol/ipratropium	SMI	✓		6-8 hours
Salbutamol/ipratropium	SMI, MDI	✓		variable
Combination Long-Acting $Beta_2$-Agonist Plus Anticholinergic in One Device (LABA+LAMA)				
Formoterol/aclidinium	DPI			12 hours
Formoterol/glycopyrronium	MDI			12 hours
Indacaterol/glycopyrronium	DPI			12-24 hours
Vilanterol/umeclidinium	DPI			24 hours
Olodaterol/tiotropium	SMI			24 hours
Methylxanthines				
Aminophylline			solution, injectable	variable
Theophylline (SR)			tablet, capsule, elixir, solution, injectable	variable
Combination of Long-Acting $Beta_2$-Agonist Plus Corticosteroid in One Device (LABA+ICS)				
Formoterol/beclometasone	MDI, DPI			12 hours
Formoterol/budesonide	MDI, DPI			12 hours
Formoterol/mometasone	MDI			12 hours
Salmeterol/fluticasone propionate	MDI, DPI			12 hours
Vilanterol/fluticasone furoate	DPI			24 hours
Triple Combination in One Device (LABA+LAMA+ICS)				
Fluticasone/umeclidinium/vilanterol	DPI			24 hours
Beclometasone/formoterol/glycopyrronium	MDI, DPI			12 hours
Budesonide/formoterol/glycopyrrolate	MDI			12 hours
Phosphodiesterase-3 and/or -4 Inhibitors				
Roflumilast			tablet	24 hours
Ensifentrine		✓		12 hours
Mucolytic Agents				
Erdosteine			capsule, suspension	12 hours
Carbocysteine†			capsule, packet, solution, syrup	6-8 hours
N-acetylcysteine†		✓	solution, tablet	2-6 hours
Biologics				
Dupilumab			injectable	2 weeks
Mepolizumab			injectable	4 weeks

*This list is not exhaustive. Not all formulations are available in all countries. In some countries other formulations and dosages may be available. †Dosing regimens are under discussion. MDI = metered dose inhaler; DPI = dry powder inhaler; SMI = soft mist inhaler. Note that glycopyrrolate & glycopyrronium are the same compound.

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Bronchodilators in Stable COPD

Figure A5.2

- Inhaled bronchodilators in COPD are central to symptom management and commonly given on a regular basis to prevent or reduce symptoms **(Evidence A)**
- Inhaled bronchodilators are recommended over oral bronchodilators (**Evidence A**)
- Regular and as-needed use of SABA or SAMA improves FEV1 and symptoms **(Evidence A)**
- Combinations of SABA and SAMA are superior compared to either medication alone in improving FEV1 and symptoms **(Evidence A)**
- LABAs and LAMAs are preferred over short-acting agents except for patients with only occasional dyspnea (**Evidence A**), and for immediate relief of symptoms in patients already on long-acting bronchodilators for maintenance therapy
- LABAs and LAMAs significantly improve lung function, dyspnea, health status, and reduce exacerbation rates **(Evidence A)**
- LAMAs have a greater effect on exacerbation reduction compared with LABAs **(Evidence A)** and decrease hospitalizations **(Evidence B)**
- When initiating treatment with long acting bronchodilators the preferred choice is a combination of a LABA and a LAMA. In patients with persistent dyspnea on a single long-acting bronchodilator treatment should be escalated to two (**Evidence A**).
- Combination treatment with a LABA and a LAMA increases FEV1 and reduces symptoms compared to monotherapy **(Evidence A)**
- Combination treatment with a LABA+LAMA reduces exacerbations compared to monotherapy **(Evidence B)**
- Combinations can be given as single inhaler or multiple inhaler treatment. Single inhaler therapy may be more convenient and effective than multiple inhalers
- Ensifentrine significantly improves lung function **(Evidence A)**, dyspnea **(Evidence A)** and health status **(Evidence B)**
- Theophylline exerts a small bronchodilator effect in stable COPD **(Evidence A)** and that is associated with modest symptomatic benefits **(Evidence B)**

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Anti-Inflammatory Maintenance Therapy Registered for the Treatment of COPD

Figure A5.3

Inhaled Corticosteroids	• Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease **(Evidence A)** • An ICS combined with a LABA is more effective than the individual components in improving lung function and health status and reducing exacerbations in patients with exacerbations and moderate to very severe COPD **(Evidence A)** • We do not encourage the use of a LABA+ICS combination in COPD. If there is an indication for an ICS the combination LABA+LAMA+ICS has been shown to be superior to LABA+ICS and is therefore the preferred choice • Triple inhaled therapy of LABA+LAMA+ICS improves lung function, symptoms and health status, and reduces exacerbations, compared to LABA+ICS, LABA+LAMA or LAMA monotherapy **(Evidence A)**. Recent data suggesta beneficial effect of triple inhaled therapy versus fixed-dose LABA+LAMA combinations on mortality in symptomatic COPD patients with a history of frequent and/or severe exacerbations • If patients with COPD have features of asthma, treatment should always contain an ICS • Independent of ICS use, there is evidence that a blood eosinophil count < 2% increases the risk of pneumonia **(Evidence C)** • Combinations can be given as single or multiple inhaler therapy. Single inhaler therapy may be more convenient and effective than multiple inhalers
Oral Glucocorticoids	• Long-term use of oral glucocorticoids has numerous side effects **(Evidence A)** with no evidence of benefits **(Evidence C)**
PDE Inhibitors	• In patients with chronic bronchitis, severe to very severe COPD and a history of exacerbations: ▪ Roflumilast improves lung function and reduces moderate and severe exacerbations **(Evidence A)** • Ensifentrine improves lung function **(Evidence A)** but an effect on exacerbations has not been evaluated in patients at increased exacerbation risk
Antibiotics	• Long-term azithromycin and erythromycin therapy reduces exacerbations over one year **(Evidence A)** • Preferentially, but not only in former smokers with exacerbations despite appropriate therapy, azithromycin can be considered (**Evidence B**) • Treatment with azithromycin is associated with an increased incidence of bacterial resistance **(Evidence A)** and hearing test impairments **(Evidence B)**
Mucoregulators & Antioxidant Agents	• Regular treatment with mucolytics such as erdosteine, carbocysteine and N-acetylcysteine reduces the risk of exacerbations in select populations **(Evidence B)** • Antioxidant mucolytics are recommended only in selected patients **(Evidence A)**

Biologics	• In patients with moderate to severe COPD with a history of exacerbations despite triple therapy and higher blood eosinophils (≥ 300 cells/µL):
	  ▪ Dupilumab reduces exacerbations, improves lung function and quality of life in patients with chronic bronchitis **(Evidence A)**
	  ▪ Mepolizumab reduces exacerbations in patients with and without chronic bronchitis **(Evidence A)**

Other Anti-Inflammatory Agents	• Statin therapy is not recommended for prevention of exacerbations (**Evidence A**) • Simvastatin does not prevent exacerbations in COPD patients at increased risk of exacerbations and without indications for statin therapy **(Evidence A)**. However, observational studies suggest that statins may have positive effects on some outcomes in patients with COPD who receive them for cardiovascular and metabolic indications **(Evidence C)** • Leukotriene modifiers have not been tested adequately in COPD patients

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Other Pharmacological Treatments

Figure A5.4

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

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OVERVIEW OF THE EVIDENCE: NON-PHARMACOLOGICAL THERAPY

Education, Self-Management, Physical Activity, Pulmonary Rehabilitation & Integrated Care in COPD

Figure A6.1

Education & Self-Management	• Education is needed to change patient's knowledge but there is no evidence that used alone it will change patient behavior **(Evidence C)** • Self-management intervention with communication with a health care professional improves health status and decreases hospitalizations and emergency department visits **(Evidence B)**
Physical Activity	• Physical activity is a strong predictor of mortality **(Evidence A)**. People with COPD should be encouraged to increase their level of physical activity. Programs that use effective behavioral change techniques, including the use of step counters, have been shown to increase physical activity in the short term.
Pulmonary Rehabilitation	• Rehabilitation is indicated in all patients with relevant symptoms and/or a high risk for exacerbation **(Evidence A)** • Pulmonary rehabilitation improves dyspnea, health status and exercise tolerance in stable patients **(Evidence A)** • Pulmonary rehabilitation reduces hospitalization among patients who have had a recent exacerbation (≤ 4 weeks from prior hospitalization) **(Evidence B)** • Pulmonary rehabilitation leads to a reduction in symptoms of anxiety and depression **(Evidence A)** • Pulmonary rehabilitation leads to an improvement in sleep quality **(Evidence C)**
Integrated Care Programs	• Integrative care and telehealth have no demonstrated benefit at this time **(Evidence B)**

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ABBREVIATIONS

6MWD, 6-minute walking distance
6MWT, 6-minute walking test
AATD, α-1 antitrypsin deficiency
ABG, arterial blood gas
ACE, angiotensin converting enzyme
ACEi, angiotensin converting enzyme inhibitor
ACS, acute coronary syndrome
ACT, airway clearance technique(s)
ADL, activities of daily living
AF, atrial fibrillation
AI, artificial intelligence
ARB, angiotensin receptor blocker
ARNI, angiotensin receptor-neprilysin inhibitor
ATS, American Thoracic Society
BAI, breath-actuated metered-dose inhaler
BB, beta-blocker
BD, bronchodilator
BMI, body mass index
BODE, Body mass index, Obstruction, Dyspnea, and Exercise
BOLD, Burden of Obstructive Lung Diseases
CAT™, COPD Assessment Test
CAAT™, Chronic Airways Assessment Test
CAC, coronary artery calcium
CAD, coronary artery disease
CAPTURE, COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk
CCQ©, Clinical COPD Questionnaire
CDC, US Centers for Disease Control
CDQ, COPD Diagnostic Questionnaire
CI, confidence interval
CISNET, Cancer Intervention and Surveillance Modeling Network
COPD, chronic obstructive pulmonary disease
COPD-PS, COPD Population Screener
COS, core outcome set
COVID-19, coronavirus disease 2019
CPAP, continuous positive airway pressure
CRP, C-reactive protein
CRQ, Chronic Respiratory Questionnaire
CT, computed tomography
CVD, cardiovascular disease
CVRS, cardiovascular risk score
DALY, disability-adjusted life years
DLco, carbon monoxide diffusing capacity of the lungs
DM, diabetes mellitus
DNA, deoxyribonucleic acid
DPI, dry powder inhaler
ED, emergency department
EBV, endobronchial one-way valves
ECG, electrocardiogram
EHR, electronic health record
ELVR, endoscopic lung volume reduction
ERS, European Respiratory Society
ESC, European Society of Cardiology
EU, European Union
EVALI, e-cigarette or vaping product use-associated lung injury
FDA, US Food and Drug Administration
FEV1, forced expiratory volume in 1 second
FFM, fat free mass
FiO_2, fraction of inspired oxygen
FVC, forced vital capacity
GBD, Global Burden of Disease
GERD, gastroesophageal reflux disease
GETomics, gene(G)-environment(E) interactions occurring over the lifetime(T) of the individual
GFR, glomerular filtration rate
GLI, Global Lung Initiative
GOLD, Global Initiative for Chronic Obstructive Lung Disease
HADS, Hospital Anxiety and Depression Scale
HFNT, high-flow nasal therapy
HFpEF, heart failure with preserved ejection fraction
HFrEF, heart failure with reduced ejection fraction
HICs, high-income countries
HIV, human immunodeficiency virus
HMICs, high- and middle-income countries
HRCT, high-resolution computed tomography
hs troponin, high sensitivity troponin
ICD, International Statistical Classification of Diseases and Related Health Problems
ICS, inhaled corticosteroid
ICU, intensive care unit
ILA, interstitial lung abnormalities
ILD, interstitial lung disease
Ig, immunoglobulin
IL, interleukin
IMP, inspiratory muscle training
IPAP, inspiratory positive airway pressure
IRR, incidence rate ratio
ISWT, incremental shuttle walking test
LABA, long-acting $beta_2$-agonist
LABD, long-acting bronchodilator
LAMA, long-acting muscarinic antagonist
LAS, lung allocation severity
LDCT, low-dose computed tomography
LFQ, Lung Function Questionnaire
LICs, low-income countries
LLN, lower limit of normal
LMICs, low- and middle-income countries
LTOT, long-term oxygen therapy

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LVRS, lung volume reduction surgery
MCID, mean clinically important difference
mmHG, millimeters of mercury
mMRC scale, modified Medical Research Council dyspnea scale
MOLT, multiple organ loss of tissue
mPAP, mean pulmonary arterial pressure
MRA, mineralocorticoid receptor antagonist
NAFLD, non-alcoholic fatty liver disease
NETT, National Emphysema Treatment Trial
NHLBI, National Heart, Lung, and Blood Institute
NIH, National Institutes of Health
NIV, noninvasive ventilation
NPPV, noninvasive positive pressure ventilation
NS, not statistically significant
NTproBNP, N-terminal prohormone of brain natriuretic peptide test
OSA, obstructive sleep apnea
$PaCO_2$ partial pressure of carbon dioxide
PAD, peripheral artery disease
PAH, pulmonary arterial hypertension
PaO_2 partial pressure of oxygen
PCV, pneumococcal conjugate vaccine
PDE, phosphodiesterase
PEF, peak expiratory flow
PH, pulmonary hypertension
PLATINO, Project for the Investigation of Obstructive Lung Disease
PM2.5 or PM10, particulate matter of 2.5 or 10 µm or less in diameter
pMDI, pressurized metered-dose inhaler
PPSV, pneumococcal polysaccharide vaccine
PR, pulmonary rehabilitation
PRIME-MD, Primary Care Evaluation of Mental Disorders
PRISm, preserved ratio impaired spirometry
PROs, patient reported outcomes
PUMA, PUMA COPD questionnaire
RCT, randomized controlled trial
RPM, remote patient monitoring
RSV, respiratory syncytial virus
SABA, short-acting $beta_2$-agonist
SABD, short acting bronchodilator
SaO_2, oxygen saturation of arterial blood
SARS-CoV-2, severe acute respiratory syndrome coronavirus 2
SE, standard error
SGLT2i, sodium-glucose co-transporter 2 inhibitor
SGRQ, St. George's Respiratory Questionnaire
SMI, soft mist inhaler
T2, type 2 (referring to inflammation)
TB, pulmonary tuberculosis
TDI, Translational Dyspnea Index
UC, Usual treatment control group
UK, United Kingdom
USPSTF, United States Preventative Service Task Force
US, United States of America
VAS, visual analog scale
V_A/Q, ventilation-perfusion
VHC, valved holding chamber
VHD, valvular heart disease
WHO, World Health Organization

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