Global Initiative for Chronic Obstructive Lung Disease

2025 POCKET GUIDE

POCKET GUIDE TO COPD DIAGNOSIS, MANAGEMENT, AND PREVENTION

A Guide for Health Care Professionals

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GOLD is a member of The Global Alliance against Chronic Respiratory Diseases (GARD)

*Disclosure forms for GOLD Committees are posted on the GOLD Website, www.goldcopd.org

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is now one of the top three causes of death worldwide and 90% of these deaths occur in low- and middle-income countries (LMICs).[1,2] More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally. 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.[3]

This Pocket Guide has been developed from the Global Strategy for the Diagnosis, Management, and Prevention of COPD (**GOLD 2025 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 that source document.

TABLE OF FIGURES

DEFINITION & OVERVIEW

KEY POINTS:

Definition

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

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.
- The most relevant (albeit rare) genetic risk factor for COPD identified to date are mutations in the SERPINA1 gene that lead to α-1 antitrypsin deficiency. A number of other genetic variants have also been associated with reduced lung function and risk of COPD, but their individual effect size is small.

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.
- Some individuals can have respiratory symptoms and/or structural lung lesions (e.g., emphysema) and/or physiological abnormalities (including low FEV1, gas trapping, hyperinflation, reduced lung diffusing capacity and/or rapid FEV1 decline) without airflow obstruction (FEV1/FVC ≥ 0.7 post-bronchodilation). These subjects are labeled 'Pre-COPD'. The term 'PRISm' (Preserved Ratio Impaired Spirometry) has been proposed to identify those with normal ratio but abnormal spirometry. Subjects with Pre-COPD or PRISm are at risk of developing airflow obstruction over time, but not all of them do.

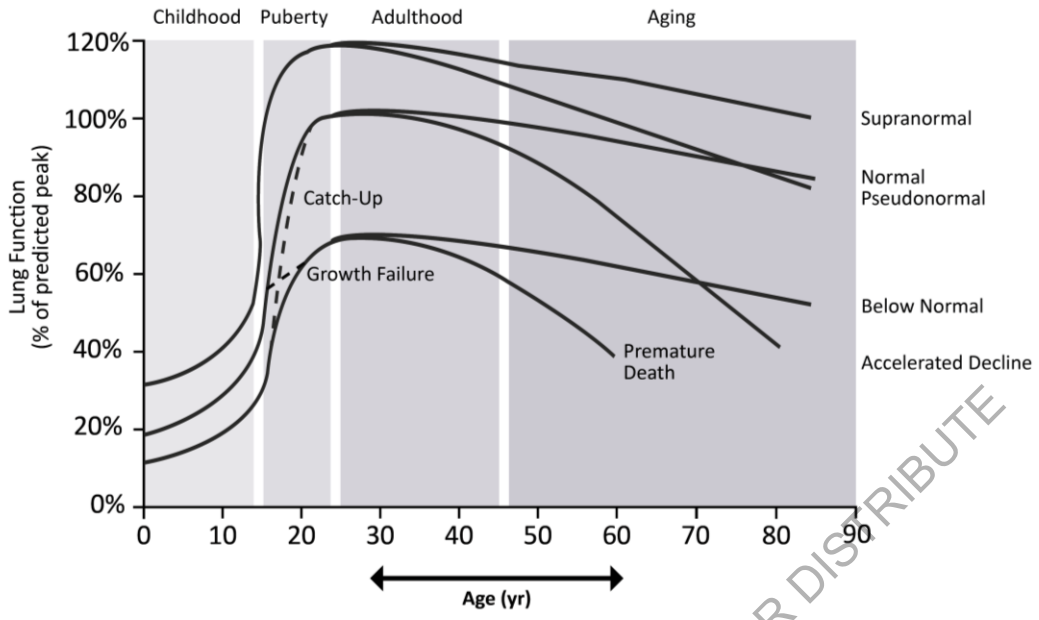
Clinical Presentation

- 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 as well. 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.

FEV1 Trajectories (TR) Over the Life Course



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

Proposed Taxonomy (Etiotypes) for COPD

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 AND ASSESSMENT

KEY POINTS:

- 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 for the disease, but **spirometry** showing the presence of a post-bronchodilator FEV1/FVC < 0.7 is **mandatory** to establish the diagnosis of COPD.
- The goals of the initial COPD assessment are to determine the severity of airflow obstruction, the impact of disease on the patient's health status, and the risk of future events (such as exacerbations, hospital admissions, or death), to guide therapy.
- Additional clinical assessment, including the measurement of lung volumes, diffusion capacity, exercise testing and/or lung imaging may be considered in COPD patients with persistent symptoms after initial treatment.
- Concomitant chronic diseases (multimorbidity) occur frequently in COPD patients, 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.

Clinical Indicators for Considering a Diagnosis of COPD

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.)

Other Causes of Chronic Cough

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

Differential Diagnosis of COPD

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

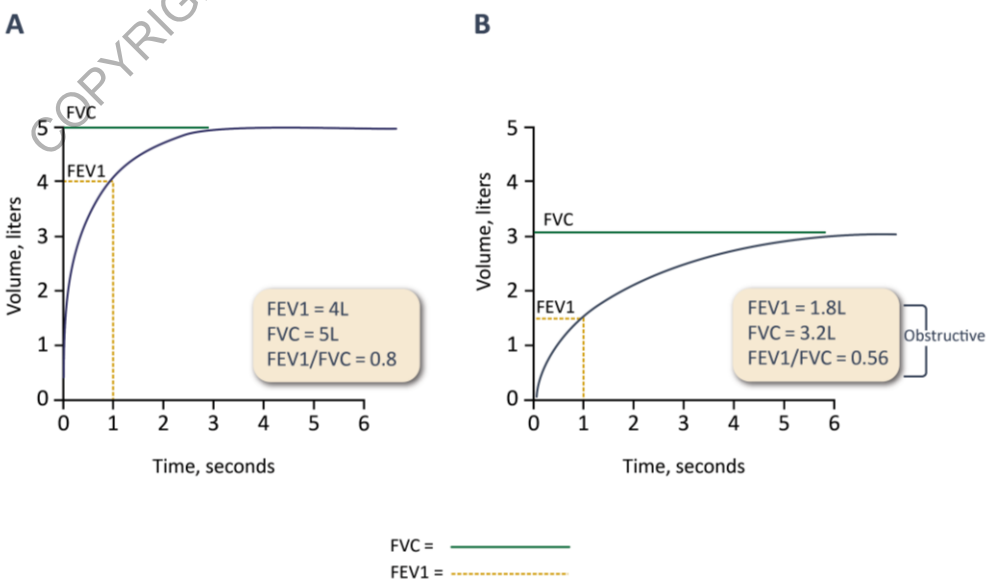
These features tend to be characteristic of the respective diseases, but are not mandatory. For example, a person who has never smoked may develop COPD (especially in LMICs where other risk factors may be more important than cigarette smoking).

Considerations in Performing Spirometry

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 taken from the technically acceptable curve with the largest sum of FVC and FEV1
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; [b]Pellegrino *et al.* Eur Respir J 2005; 26(5): 948.

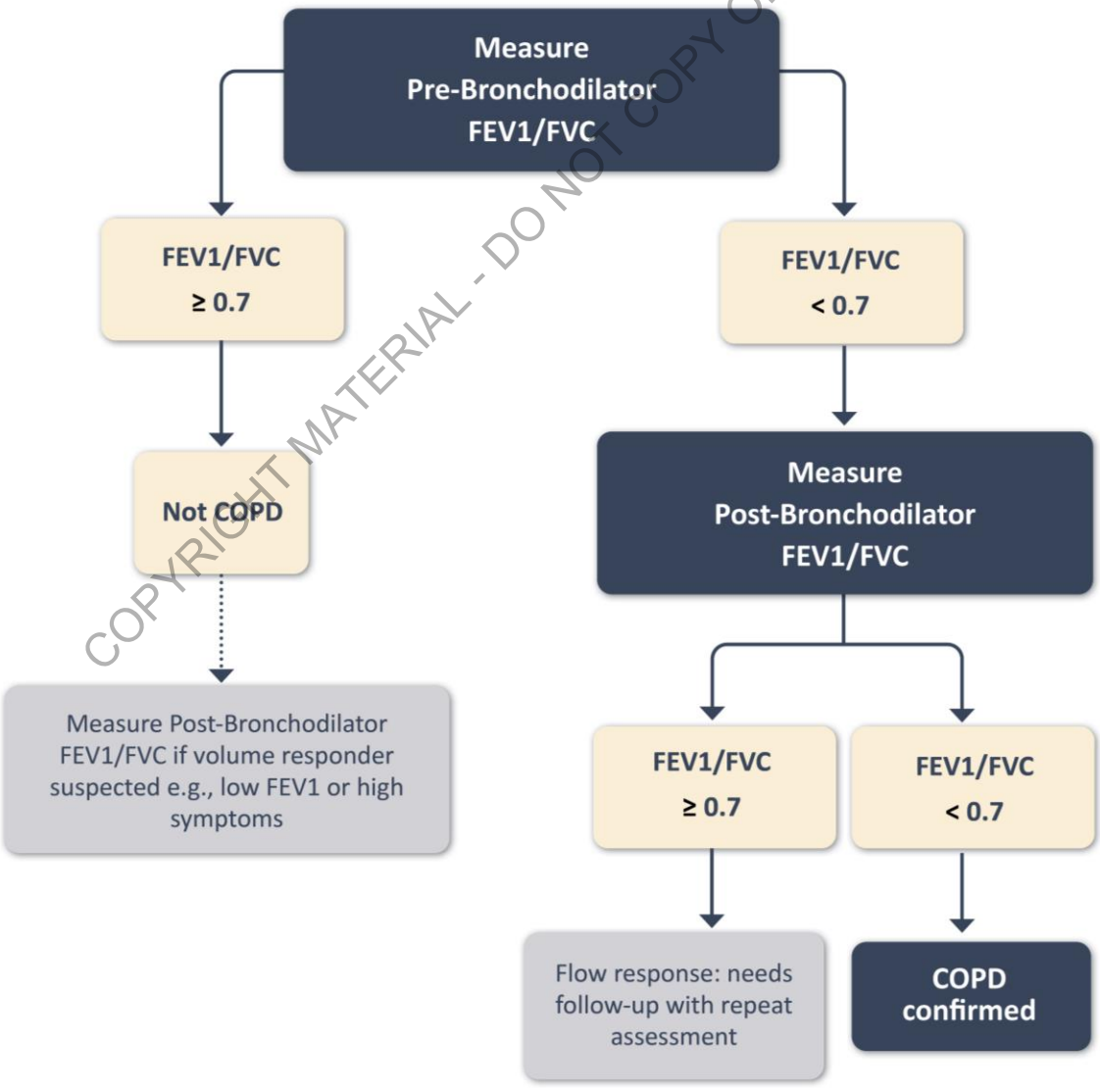
A. Spirometry - Normal Trace B. Spirometry - Airflow Obstruction



Role of Spirometry in COPD

- **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

Pre- and Post- Bronchodilator Spirometry



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

In COPD patients (FEV1/FVC < 0.7):

GOLD 1:	Mild	FEV1 ≥ 80% predicted
GOLD 2:	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3:	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4:	Very Severe	FEV1 < 30% predicted

Modified MRC Dyspnea Scale

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

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

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

CAT™ Assessment

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: ☐

GOLD ABE Assessment Tool

Spirometrically confirmed diagnosis → Assessment of airflow obstruction → Assessment of symptoms/risk of exacerbations

Post-bronchodilator FEV1/FVC < 0.7

GRADE	FEV1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

EXACERBATION HISTORY (PER YEAR)

	SYMPTOMS	
≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	E	
0 or 1 moderate exacerbations (not leading to hospitalization)	A	B
	mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10

Use of CT in Stable COPD

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

KEY POINTS:

- 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.

- The main treatment goals are to reduce symptoms and future risk of exacerbations. The management strategy of stable COPD should be predominantly based on the assessment of symptoms and the history of exacerbations.

- Pharmacotherapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance. Data suggest beneficial effects on rates of lung function decline and mortality.

- Each pharmacological treatment regimen should be individualized and guided by the severity of symptoms, risk of exacerbations, side-effects, comorbidities, drug availability and cost, and the patient's response, preference, and ability to use various drug delivery devices.

- Inhaler technique needs to be assessed regularly.

- COVID-19 vaccines are highly effective against SARS-CoV-2 infection and people with COPD should have the COVID-19 vaccination in line with national recommendations.

- Influenza vaccination and pneumococcal vaccination decrease the incidence of lower respiratory tract infections.

- The CDC recommends: the Tdap vaccination (dTaP/dTPa; pertussis, tetanus and diptheria) for COPD patients who were not vaccinated in adolescence; routine use of shingles vaccine in all COPD patients; the new respiratory syncytial virus (RSV) vaccine for individuals over 60 years and/or with chronic heart or lung disease.

- Pulmonary rehabilitation with its core components, including exercise training combined with disease-specific education, improves exercise capacity, symptoms, and quality of life across all grades of COPD severity.

- 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 oxygen therapy improves survival.

- In patients with stable COPD and resting or exercise-induced moderate desaturation, long-term oxygen treatment should not be prescribed routinely. However, individual patient factors must be considered when evaluating the patient's need for supplemental oxygen.

- In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, long-term non-invasive ventilation may decrease mortality and prevent re-hospitalization.

- 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.

Goals for Treatment of Stable COPD

- Relieve Symptoms
- Improve Exercise Tolerance
- Improve Health Status

▶ **REDUCE SYMPTOMS**

AND

- Prevent Disease Progression
- Prevent and Treat Exacerbations
- Reduce Mortality

▶ **REDUCE RISK**

Management of COPD

Diagnosis

- Symptoms
- Risk factors
- Spirometry (repeat if borderline)

Initial Assessment

- FEV1 – ***GOLD 1 - 4***
- Symptoms (CAT or mMRC) } **GOLD ABE**
- Exacerbation history
- Smoking status
- Blood eosinophil count
- α1- antitrypsin
- Comorbidities

Initial Management

- Smoking cessation
- Vaccination
- Active lifestyle and exercise
- Initial pharmacotherapy
- Self management education
  - risk factor management
  - inhaler technique
  - breathlessness
  - written action plan
- Manage comorbidities

Adjust

- Pharmacotherapy
- Non-pharmacological therapy

Review

- Symptoms (CAT or mMRC)
- Exacerbations
- Smoking status
- Exposure to other risk factors
- Inhaler technique & adherence
- Physical activity and exercise
- Need for pulmonary rehabilitation
- Self management skills
  - breathlessness
  - written action plan
- Need for oxygen, NIV, lung volume reduction, palliative approaches
- Vaccination
- Management of comorbidities
- Spirometry (at least annually)

Vaccination for Stable COPD

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)**
- Either one dose of 21-valent pneumococcal conjugate vaccine (PCV21) or one dose PCV20, as recommended by the CDC **(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 ≥ 60 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) for people with COPD that were not vaccinated in adolescence, as recommended by the CDC **(Evidence B)**
- Zoster vaccine to protect against shingles for people with COPD aged > 50 years, as recommended by the CDC **(Evidence B)**

Identify & Reduce Risk Factor Exposure

- 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, if possible **(Evidence D)**

Treating Tobacco Use and Dependence

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

Brief Strategies to Help the Patient Willing to Quit

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*

Initial Pharmacological Treatment

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization

GROUP E

LABA + LAMA*

consider LABA+LAMA+ICS if blood eos ≥ 300*

0 or 1 moderate exacerbations (not leading to hospital admission)

GROUP A

A bronchodilator

mMRC 0-1, CAT < 10

GROUP B

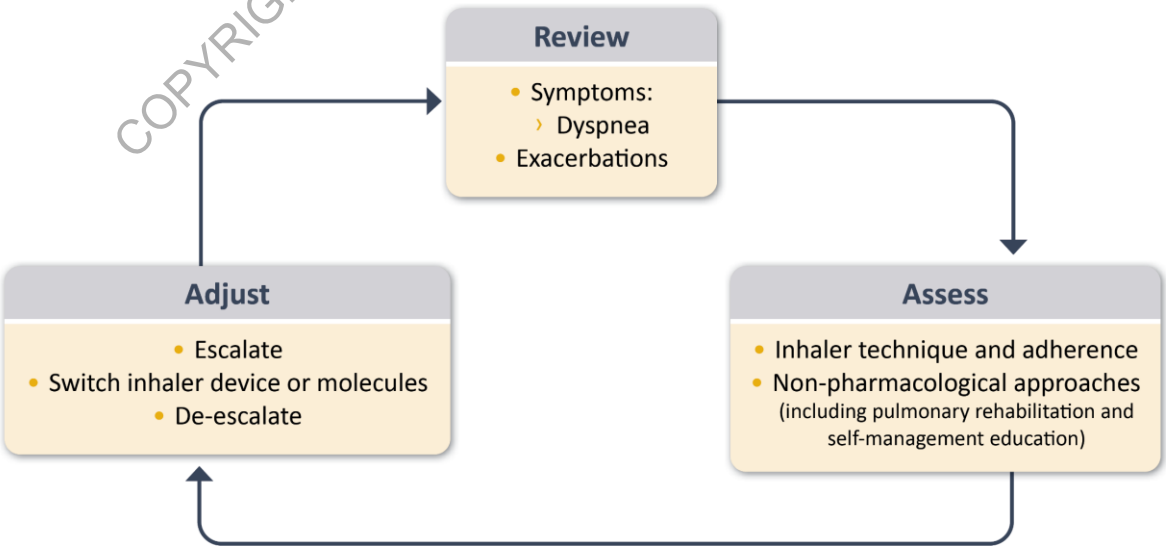
LABA + LAMA*

mMRC ≥ 2, CAT ≥ 10

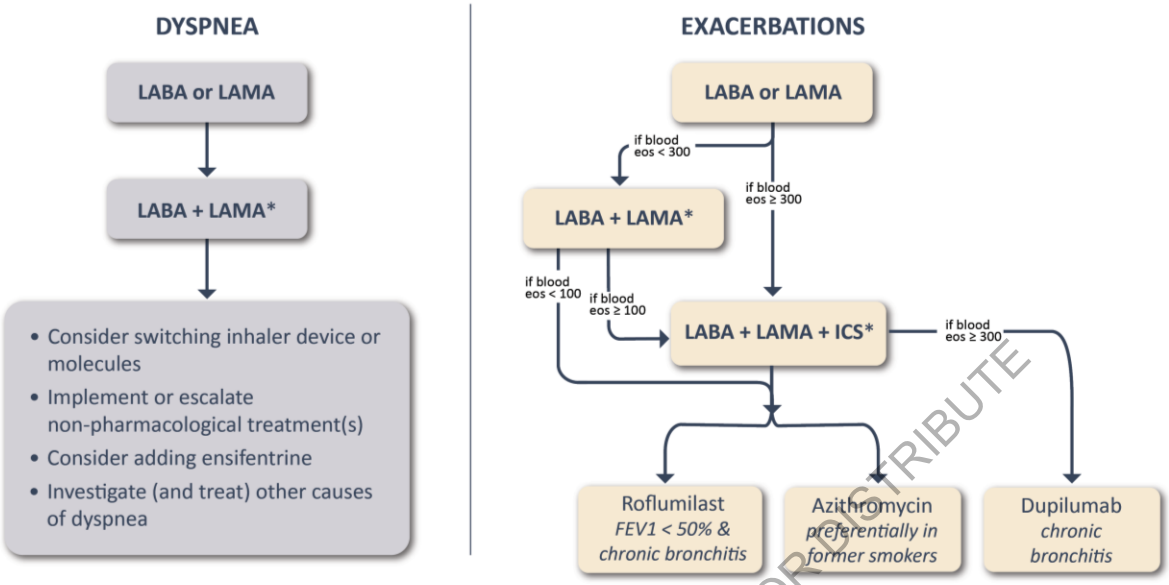
*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

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

Management Cycle



Follow-up Pharmacological Treatment



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

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

Exacerbations refers to the number of exacerbations per year.

Key Points for Inhalation of Drugs

- 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

- 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.

Non-Pharmacological Management of COPD*

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

*Can include pharmacological treatment

Follow-up of Non-Pharmacological Treatment

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

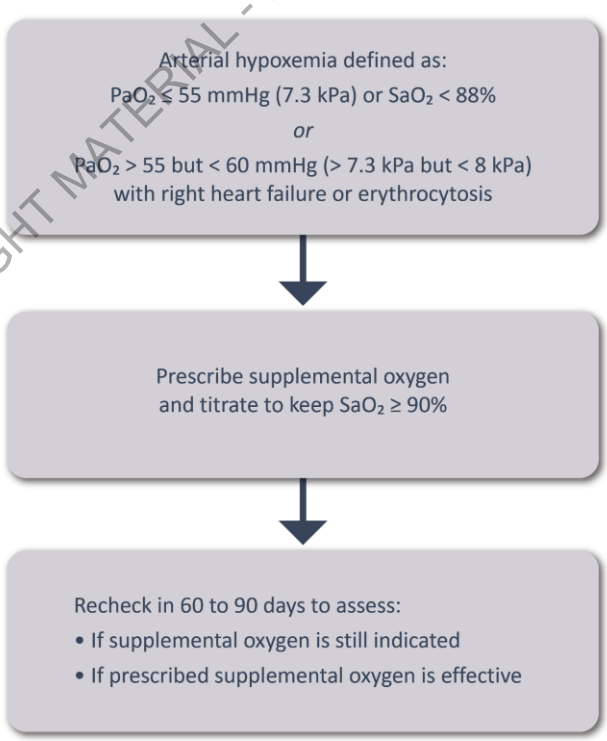
- Self-management education (written action plan) that is personalized with respect to:
  - Avoidance of aggravating factors
  - How to monitor/manage worsening of symptoms
  - Contact information in the event of an exacerbation
- Pulmonary rehabilitation (PR) program and/or maintenance exercise program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

Oxygen Therapy and Ventilatory Support in Stable COPD

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

Prescription of Supplemental Oxygen to COPD Patients



Palliative Care, End of Life and Hospice Care in COPD

- 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)**

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

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 anti-muscarinic; LTOT: long-term oxygen therapy; NPPV: noninvasive positive pressure ventilation; LVRS: lung volume reduction surgery; UC: usual treatment control group.

Maintenance Medications in COPD*

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
Glycopyrronium		✓		12 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

*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.

Bronchodilators in Stable COPD

- 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)**

Anti-Inflammatory Therapy in Stable COPD

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 NAC 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, chronic bronchitis and higher blood eosinophil counts (≥ 300 cells/µL): ▪ Dupilumab reduces exacerbations, improves lung function and quality of life **(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

Factors to Consider when Initiating ICS Treatment

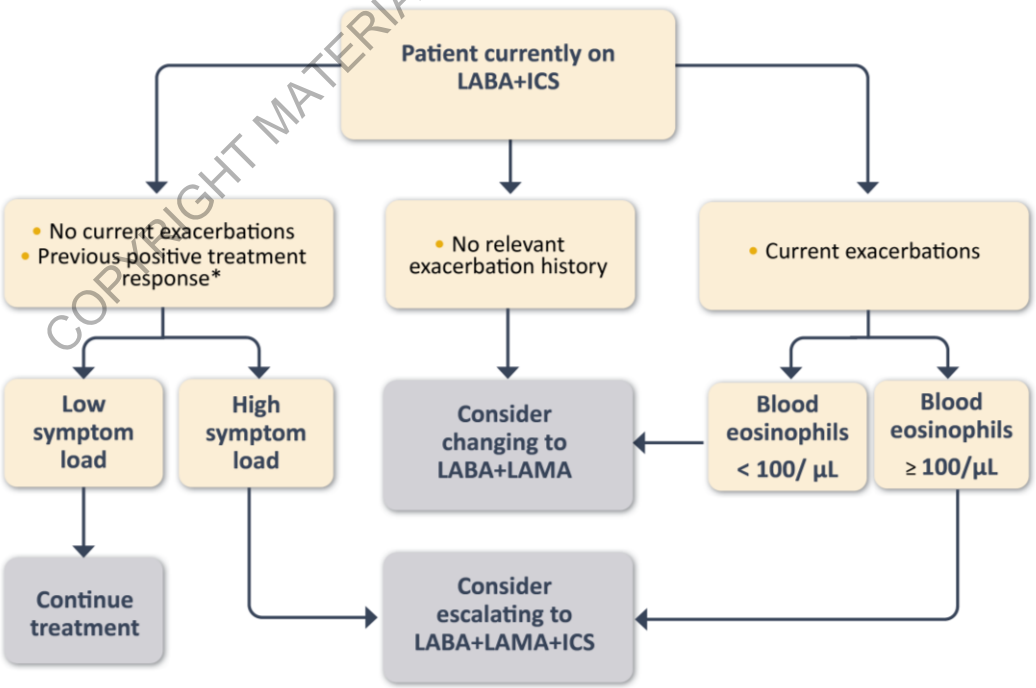
Factors to consider when adding ICS to long-acting bronchodilators:

(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 3.7 & 3.18 for recommendations); *note that blood eosinophils should be seen as a continuum; quoted values represent approximate cut-points; eosinophil counts are likely to fluctuate.

Management of Patients Currently on LABA+ICS



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

Other Pharmacological Treatments

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**)

Pulmonary Rehabilitation, Self-Management and Integrative Care in COPD

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)**
Education and 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)**
Integrated Care Programs	• Integrative care and telehealth have no demonstrated benefit at this time **(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 although we still do not know how to best ensure the likelihood of success

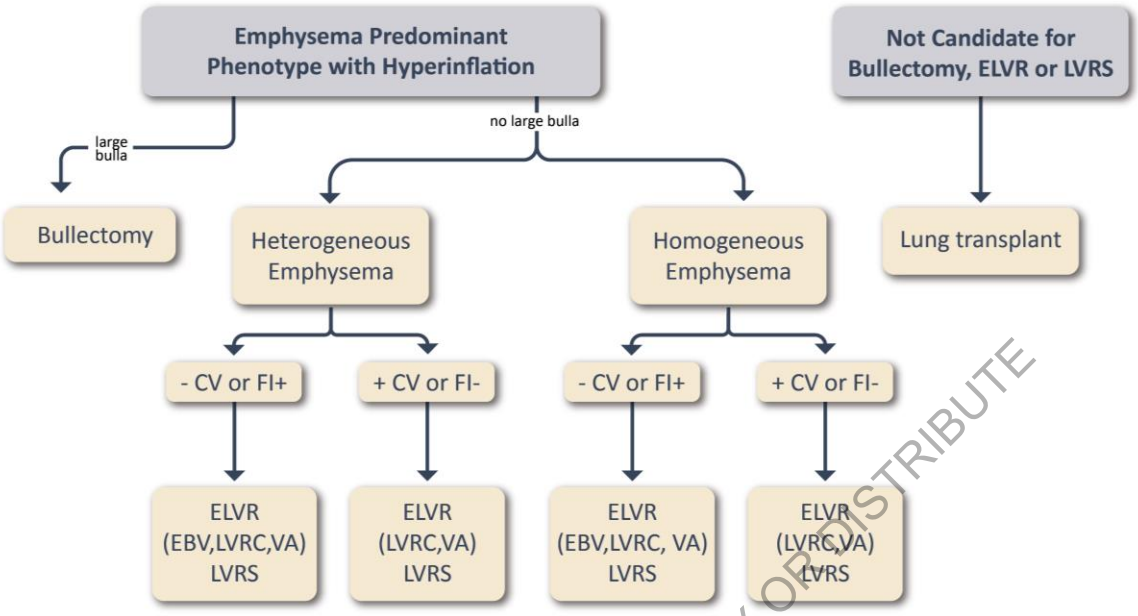
Overview of Current and Proposed Surgical and Bronchoscopic Interventions for People with COPD

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

Interventional Therapy in Stable COPD

Lung Volume Reduction Surgery	• Lung volume reduction surgery improves survival in severe emphysema patients with an upper-lobe emphysema 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 (Pco_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 III trials are currently being conducted to determine the efficacy of treatments for patients with refractory exacerbations and chronic bronchitis using cryospray, rheoplasty and targeted lung denervation technology

Surgical and Interventional Therapies in Advanced Emphysema



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.

MANAGEMENT OF EXACERBATIONS

KEY POINTS:

- An exacerbation of COPD is defined as an event characterized by dyspnea and/or cough and sputum that worsen over < 14 days. Exacerbations of COPD are often associated with increased local and systemic inflammation caused by airway infection, pollution, or other insults to the lungs.
- As the symptoms are not specific to COPD relevant differential diagnoses should be considered, particularly pneumonia, congestive heart failure and pulmonary embolism.
- The goals for treatment of COPD exacerbations are to minimize the negative impact of the current exacerbation and to prevent subsequent events.
- Short-acting inhaled beta$_2$-agonists, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat an exacerbation.
- Maintenance therapy with long-acting bronchodilators should be initiated as soon as possible. In patients with frequent exacerbations and elevated blood eosinophil levels addition of inhaled corticosteroids to the double bronchodilator regimen should be considered.
- In patients with severe exacerbations, systemic corticosteroids can improve lung function (FEV1), oxygenation and shorten recovery time including hospitalization duration. Duration of therapy should not normally be more than 5 days.
- Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should be 5 days.
- Methylxanthines are not recommended due to increased side effect profiles.
- Non-invasive mechanical ventilation should be the first mode of ventilation used in COPD patients with acute respiratory failure who have no absolute contraindication because it improves gas exchange, reduces work of breathing and the need for intubation, decreases hospitalization duration and improves survival.
- Exacerbation recovery time varies, taking up to 4-6 weeks to recover, with some patients failing to return to the pre-exacerbation functional state. Following an exacerbation, appropriate measures for exacerbation prevention should be initiated (see previous section).

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

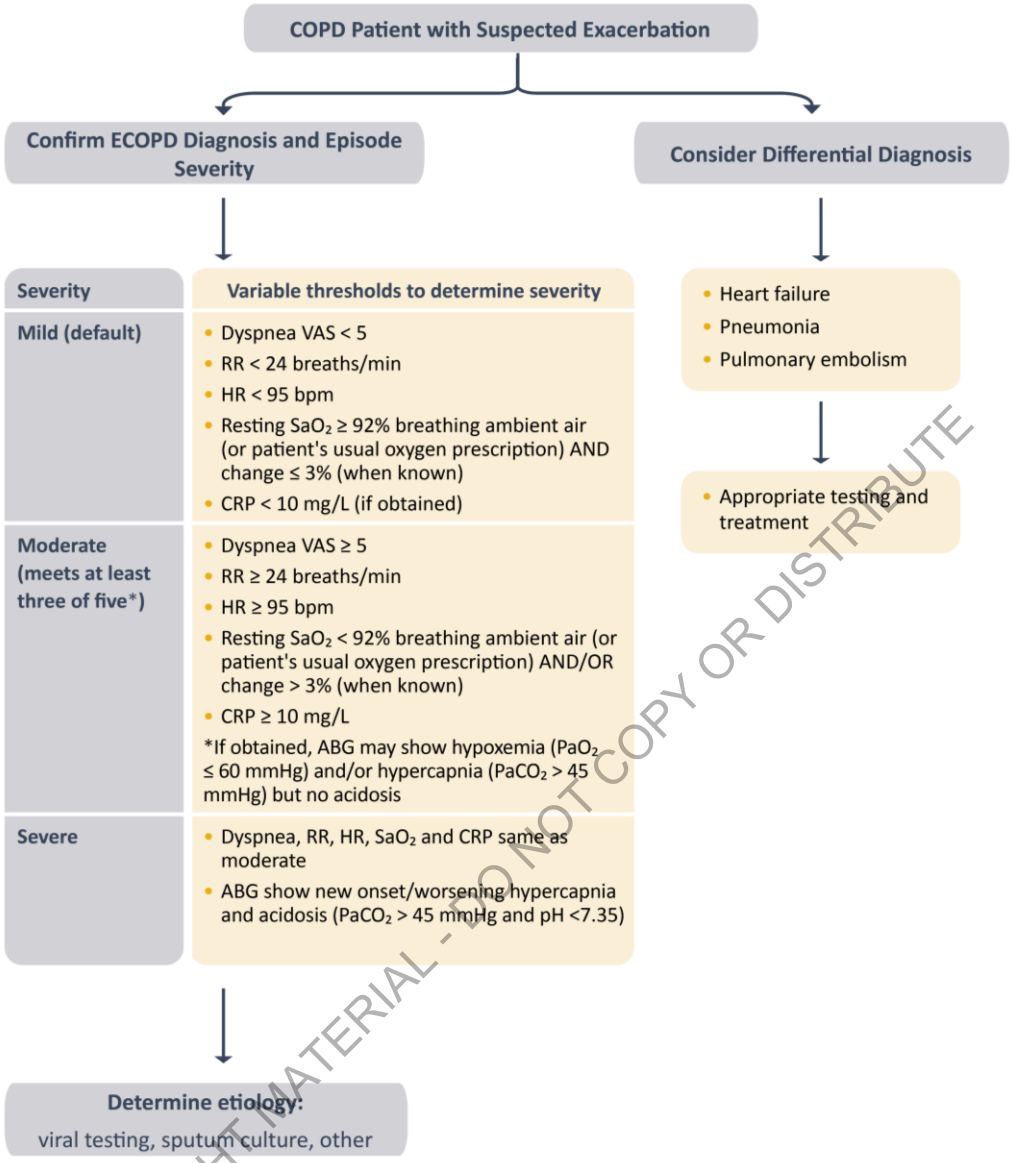
Most frequent	**Pneumonia**	• Chest radiograph
	Pulmonary embolism	• Clinical probability assessment (Hemoptysis, surgery, fracture, history of cancer, DVT) • D-dimer • CT angiography for pulmonary embolism
	Heart failure	• Chest radiograph • NT Pro-Brain Natriuretic Peptide (Pro-BNP) and BNP • Echocardiography
Less frequent	**Pneumothorax, pleural effusion**	• Chest radiograph • Thoracic ultrasound
	Myocardial infarction and/or cardic arrhythmias (atrial fibrillation/flutter)	• Electrocardiography • Troponin

Exacerbations: Diagnosis and Assessment

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

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

Classification of the Severity of COPD Exacerbations



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

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

Potential Indications for Hospitalization Assessment*

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

*Local resources need to be considered

Management of Severe but not Life-threatening Exacerbations*

Assess severity of symptoms, blood gases, chest radiograph

Administer supplemental oxygen therapy, obtain serial arterial blood gas, venous blood gas and pulse oximetry measurements

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) when signs of bacterial infection are present

Consider noninvasive mechanical ventilation (NIV)

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

Key Points for the Management of Exacerbations

- 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 should not normally be more than 5 days **(Evidence A)**
- Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should normally be 5 days **(Evidence B)**
- Methylxanthines are not recommended due to increased side effect profiles **(Evidence B)**
- Non-invasive mechanical ventilation should be the first mode of ventilation used in COPD patients with acute respiratory failure who have no absolute contraindication because it improves gas exchange, reduces work of breathing and the need for intubation, decreases hospitalization duration and improves survival **(Evidence A)**

Indications for Respiratory or Medical Intensive Care Unit Admission*

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

*Local resources need to be considered.

Indications for Noninvasive Mechanical Ventilation (NIV)

At least one of the following:

- Respiratory acidosis ($PaCO_2$ ≥ 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

Indications for Invasive Mechanical Ventilation

- Unable to tolerate NIV or NIV failure
- 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
- Life-threatening hypoxemia in patients unable to tolerate NIV

Discharge Criteria and Recommendations for Follow-up

1. Full review of all clinical and laboratory data
2. Check maintenance therapy and understanding
3. Reassess inhaler technique
4. Ensure understanding of withdrawal of acute medications (steroids and/or antibiotics)
5. Assess need for continuing any oxygen therapy
6. Provide management plan for comorbidities and follow-up
7. Ensure follow-up arrangements: early follow-up < 4 weeks, and late follow-up < 12 weeks as indicated
8. All clinical or investigational abnormalities have been identified

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: CAT 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: CAT or mMRC
- Determine status of comorbidities

Interventions that Reduce the Frequency of COPD Exacerbations

Intervention Class	Intervention
Bronchodilators	LABAs LAMAs LABA + LAMA
Corticosteroid-containing regimens	LABA + ICS LABA + LAMA + ICS
Anti-inflammatory (non-steroid)	Roflumilast Dupilumab
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)

COPD AND COMORBIDITIES

KEY POINTS:

- COPD often coexists with other diseases (comorbidities) that may have a significant impact on disease course.
- In general, the presence of comorbidities should not alter COPD treatment and comorbidities should be treated per usual standards regardless of the presence of COPD.
- Cardiovascular diseases are common and important comorbidities in COPD.
- Lung cancer is frequently seen in people with COPD and is a major cause of death.
    - Annual low-dose CT scan (LDCT) is recommended for lung cancer screening in people with COPD due to smoking according to recommendations for the general population
    - Annual LDCT is not recommended for lung cancer screening in people with COPD not due to smoking due to insufficient data to establish benefit over harm
- Osteoporosis and depression/anxiety are frequent, important comorbidities in COPD, are often under-diagnosed, and are associated with poor health status and prognosis.
- Gastroesophageal reflux (GERD) is associated with an increased risk of exacerbations and poorer health status.
- When COPD is part of a multimorbidity care plan, attention should be directed to ensure simplicity of treatment and to minimize polypharmacy.

Common Risk Factors for the Development of Lung Cancer

- 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

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

COPD and PAH (Group 1 PH)	• Treat as PAH with comorbidity according to 2022 ESC/ERS PH guidelines
COPD and CTEPH (Group 4 PH)	• Treat as CTEPH according to 2022 ESC/ERS PH guidelines
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

Description of Levels of Evidence

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.

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 **CAT:** /40	*Maintenance Medication and adherence:* ☐ SABA ☐ LABA/LAMA ☐ LABA ☐ LABA/ICS ☐ LAMA ☐ ICS/LABA/LAMA ☐Other: *Non pharmacological Rx:* O2: CPAP: BIPAP :

2. COVID-19 – If patient is feeling unwell, check other symptoms: ☐ Fever____ ☐ Sore throat ☐ Anosmia ☐ Others_____

Contact with someone COVID-19 positive? ☐ no ☐ yes Tested for COVID-19? ☐ 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/ER	Where	Date	Length	Reason (Dx)

Comments:

5. COPD Self-management (healthy behaviors) – Integrated (patient has used it in his 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 need:

6. MAIN ISSUES

1.	*2.*	*3.*

7. SUMMARY, INTERVENTIONS & PLAN

(healthcare professional name & signature)

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 – COVID-19**
    a. Assess whether the patient has any symptoms of COVID-19 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 COVID-19 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.[4] 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 ER visits**
    a. Write down recent admissions and ER 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 it will be in-person or remote).

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