Global Initiative for Chronic Obstructive Lung Disease

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Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease

Case #1

- 1. A 62-year-old man is evaluated for chronic cough productive of thin clear sputum and dyspnea on exertion that has worsened over the last 2 years. He has a 54-pack-year smoking history. Medical history is otherwise unremarkable, and he takes no medications.
- On physical examination, vital signs are normal. The patient coughs during the examination, and mild expiratory wheezing is heard over the posterior lung fields. Cardiac examination is normal.
- Chest radiograph shows hyperinflated lungs with a flattened diaphragm without infiltrates.
- Spirometry shows an FEV1/FVC ratio of 0.65 and an FEV1 of 52% of predicted without a significant bronchodilator response.
- Which of the following is the most likely diagnosis?
- A Asthma
- B Bronchiectasis
- C COPD
- D Desquamative interstitial pneumonia

Case #2

- A 62-year-old man is evaluated during a follow-up visit for COPD. He continues to smoke one pack daily and has a 40-pack-year history. He can walk rapidly on a level surface but has breathlessness walking up a slight hill. He has not been hospitalized or seen urgently for an exacerbation. Medications are salmeterol and tiotropium.
- On physical examination, vital signs are normal. Oxygen saturation is 92% with the patient breathing ambient air. Faint expiratory wheezing is present.
- Spirometry shows an FEV1/FVC ratio of 0.58, and FEV1 is 62% of predicted.
- Which of the following is the most appropriate additional therapy?
- A Chronic azithromycin therapy
- B Prednisone
- C Pulmonary rehabilitation
- D Smoking cessation

Case#3

- A 59-year-old man is seen in a follow-up visit for a 6-month history of progressively worsening chronic cough productive of small amounts of thin clear sputum and dyspnea on exertion. He has shortness of breath when he walks quickly and when he walks uphill. He has a 45-pack-year smoking history but quit 2 years ago. He has been using albuterol as needed since his diagnosis of COPD 3 months ago, but he remains symptomatic.
- On physical examination, oxygen saturation is 95% with the patient breathing ambient air. Scattered expiratory wheezing is heard. Cardiac examination is normal.
- Chest radiograph from 3 months ago shows flattened diaphragm but no infiltrate.
- Spirometry at the time of diagnosis showed reduced postbronchodilator FEV1/FVC ratio and FEV1 of 69% of predicted.
- Which of the following is the most appropriate pharmacologic treatment?
- A Inhaled fluticasone propionate–salmeterol
- B Inhaled tiotropium bromide
- C Prednisone
- D Roflumilast

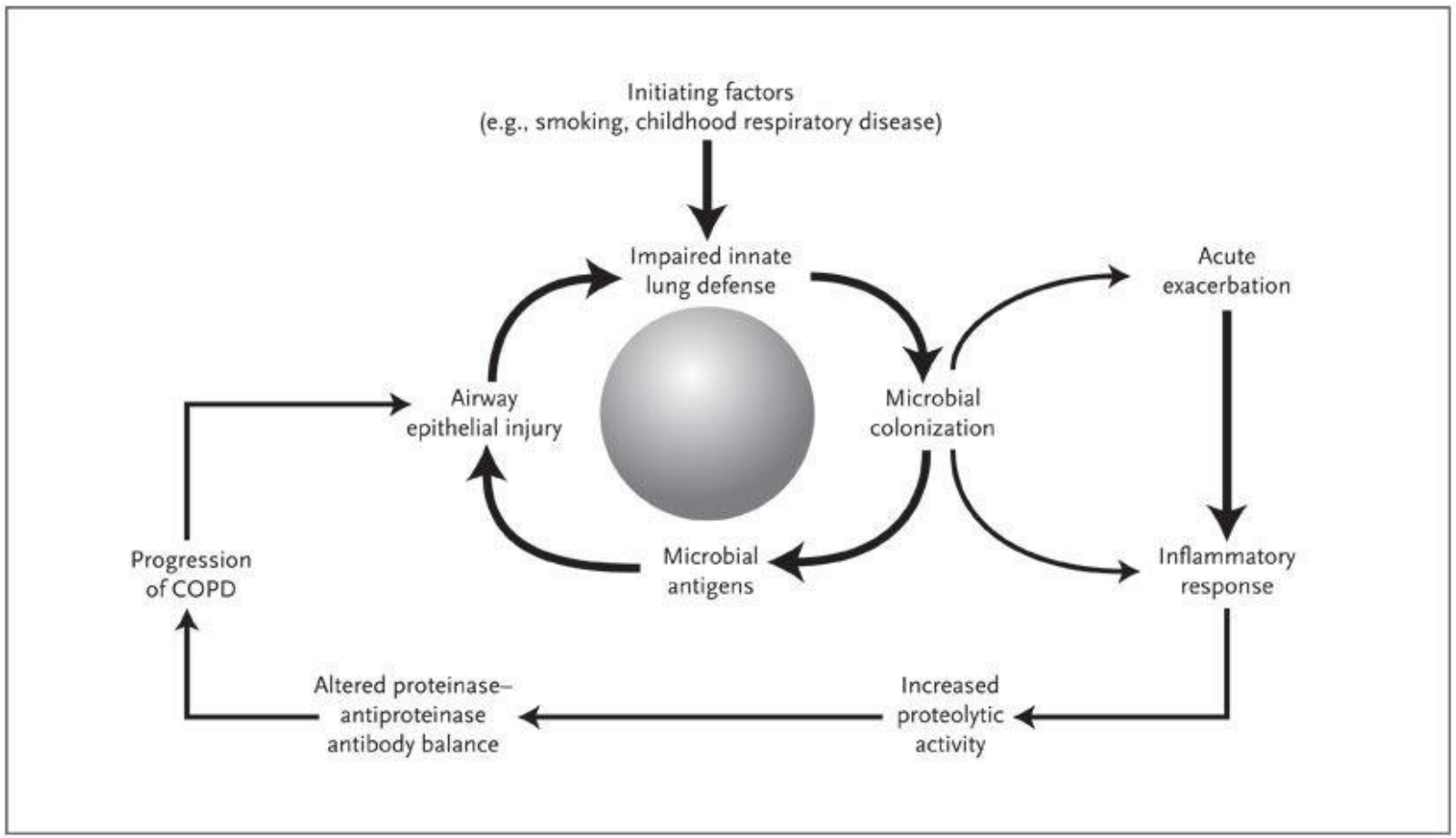
Objectives

- Define COPD based on pathophysiology and spirometry.
- Describe the different stages of COPD severity by Gold criteria, including mMRC and how COPD assessment test is utilized.
- Know the recommended treatment for each stage of COPD severity.
- Describe the diagnosis and management strategy of COPD exacerbation.

COPD

- Amongst the 10 leading causes of death in the United States
- Affects roughly 13 million Americans
- Annually ± 800,000 patients are hospitalized with COPD
- One in five patients are readmitted after discharge from index COPD admission.
- Readmissions after discharge from a COPD hospitalization cost ∼$13 billion and are associated with poor outcomes

Puebla Neira DA, Hsu ES, Kuo YF, Ottenbacher KJ, Sharma G. Readmissions Reduction Program: Mortality and Readmissions for Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2021 Feb 15;203(4):437-446. doi: 10.1164/rccm.202002-0310OC. PMID: 32871097; PMCID: PMC7885833.



Sethi S, Murphy TF. N Engl J Med 2008;359:2355-2365.

Description of Levels of Evidence

Table A

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 (methodologic 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.

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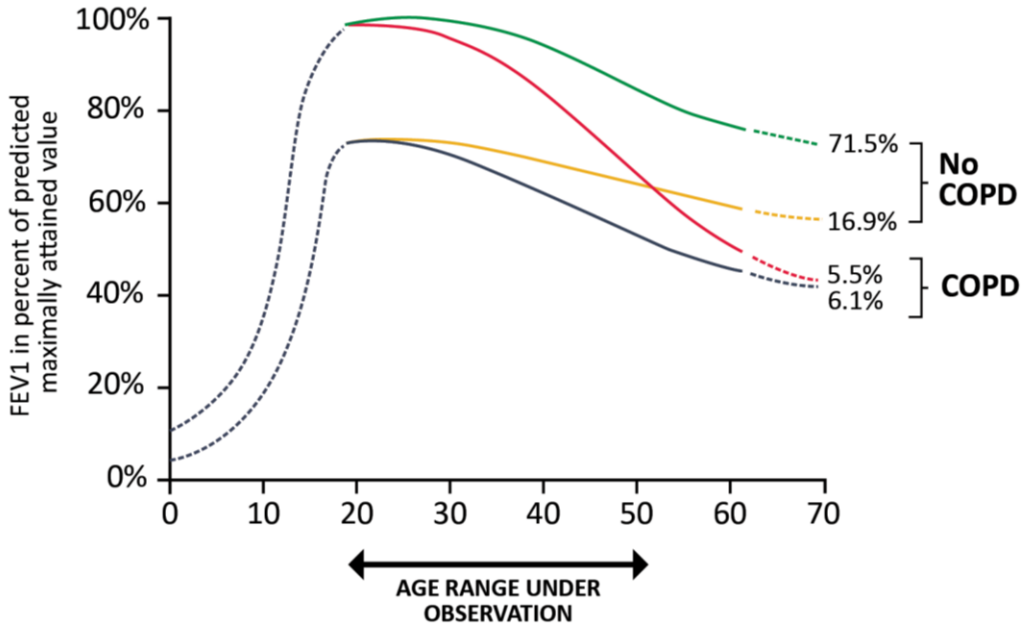
FEV1 Trajectories (TR) Over the Life Course

Figure 1.1



Note: This is a simplified diagram of FEV1 progression over time. In reality, there is heterogeneity in the rate of decline in FEV1 owing to the complex interactions of genes with environmental exposures and risk factors over an individual's lifetime [adapted from Lange et al. NEJM 2015;373:111-22].

Proposed Taxonomy (Etiotypes) for COPD

Table 1.1

Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	• 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)

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Clinical Indicators for Considering a Diagnosis of COPD

Table 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 unproductive
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

Table 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 (PNDS) • Upper Airway Cough Syndrome (UACS) • Gastroesophageal Reflux • Medication (e.g., ACE Inhibitors)

Differential Diagnosis of COPD

Table 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 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

Table 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 < 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, sex, and race • The presence of a postbronchodilator 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.

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

Figure 2.1

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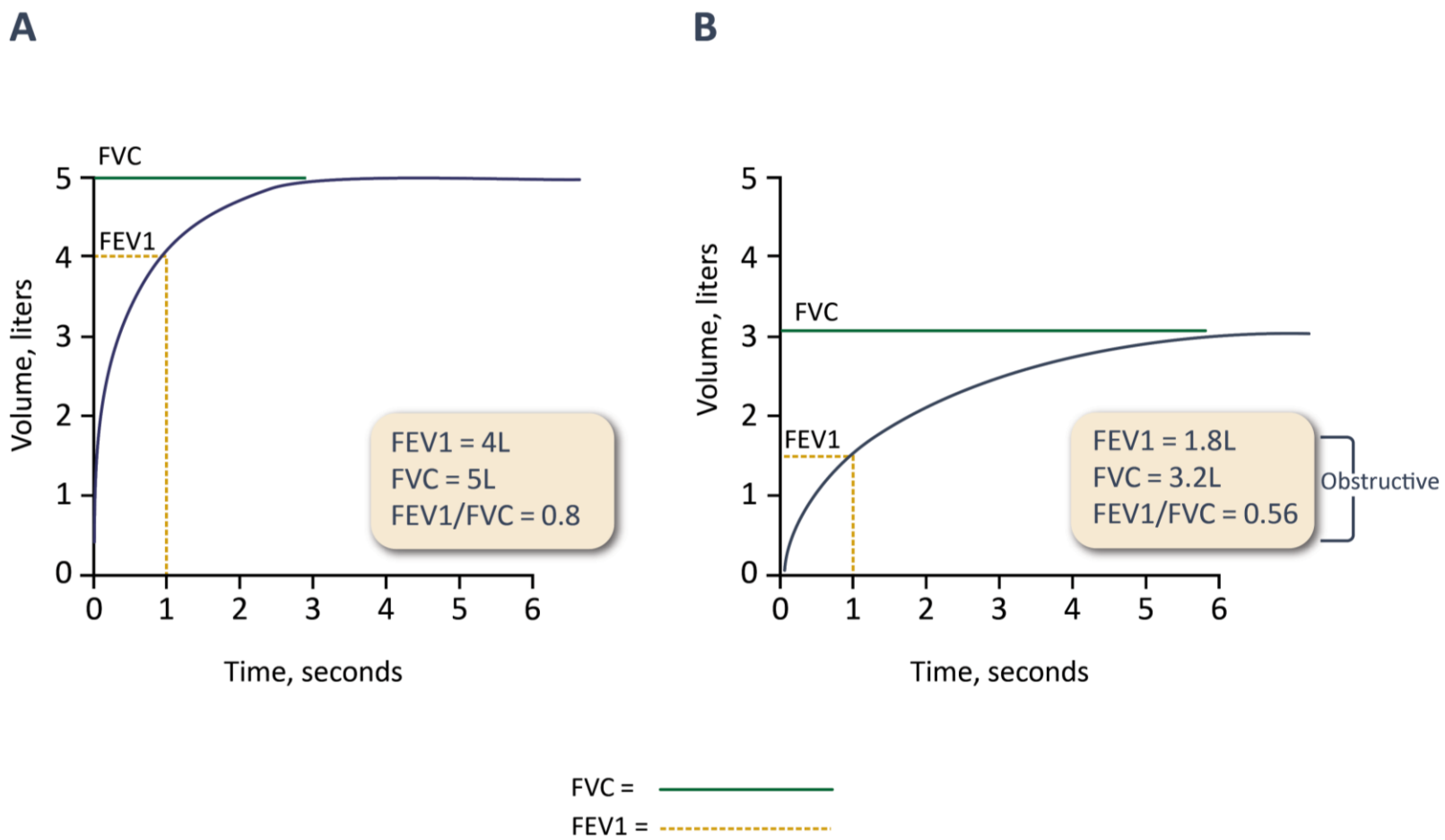
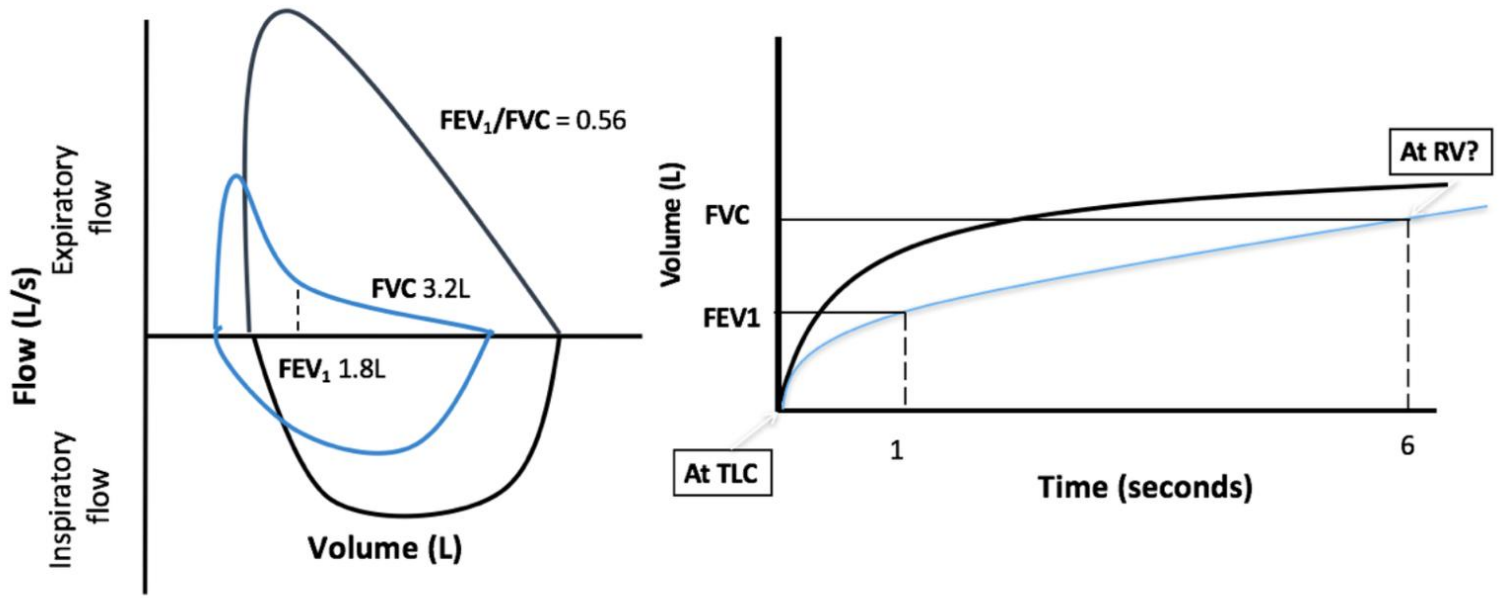


Obstructive Lung Disease



https://www.grepmed.com/images/1749/flowvolumeloops-obstructive-diagnosis-copd-pfts

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Role of Spirometry in COPD

Table 2.5

- **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

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

Table 2.6

In COPD patients (FEV1/FVC < 0.7):

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

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Modified MRC Dyspnea Scale

Table 2.7

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

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

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

CAT™ Assessment

Figure 2.2

For each item below, place a mark (x) in the box that best describes you currently.
Be sure to only select one response for each question.

EXAMPLE: I am very happy	0 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™ 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**
bronchitis: I never cough	0 1 2 3 4 5	I cough all the time	
bronchitis: I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
dyspnea: My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
dyspnea: 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	
dyspnea: I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
dyspnea: 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	
Comorbid conditions: I sleep soundly	0 1 2 3 4 5	I don‘t sleep soundly because of my lung condition	
Comorbid conditions: 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: ◯

THE REFINED ABCD ASSESSMENT TOOL

Spirometrically Confirmed Diagnosis

Post-bronchodilator $FEV_1/FVC < 0.7$

Assessment of airflow limitation

Grade	FEV_1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

Assessment of symptoms/risk of exacerbations

Moderate or Severe Exacerbation History

≥2 or ≥ 1 leading to hospital admission

0 or 1 (not leading to hospital admission)

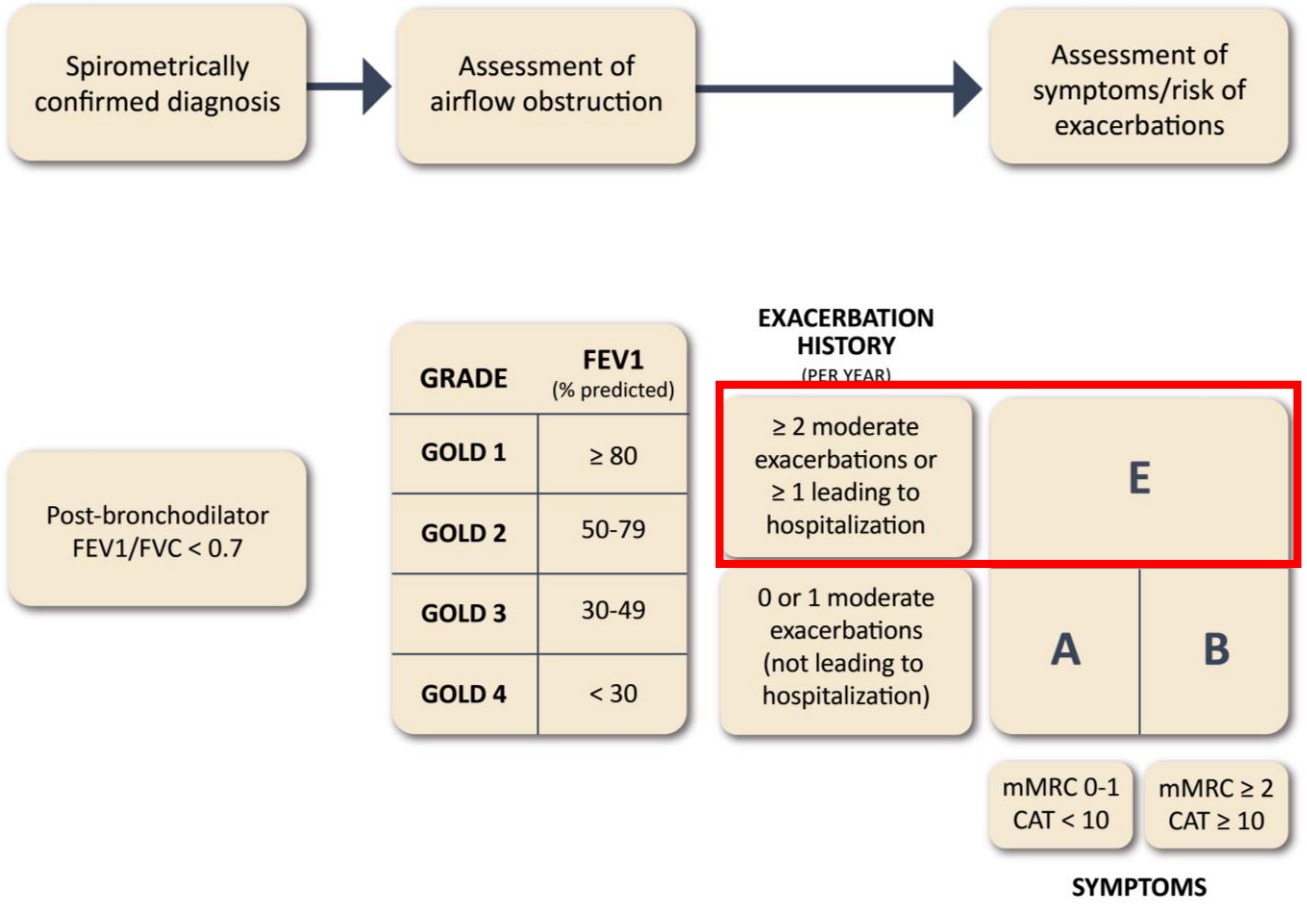
C	D
A	B

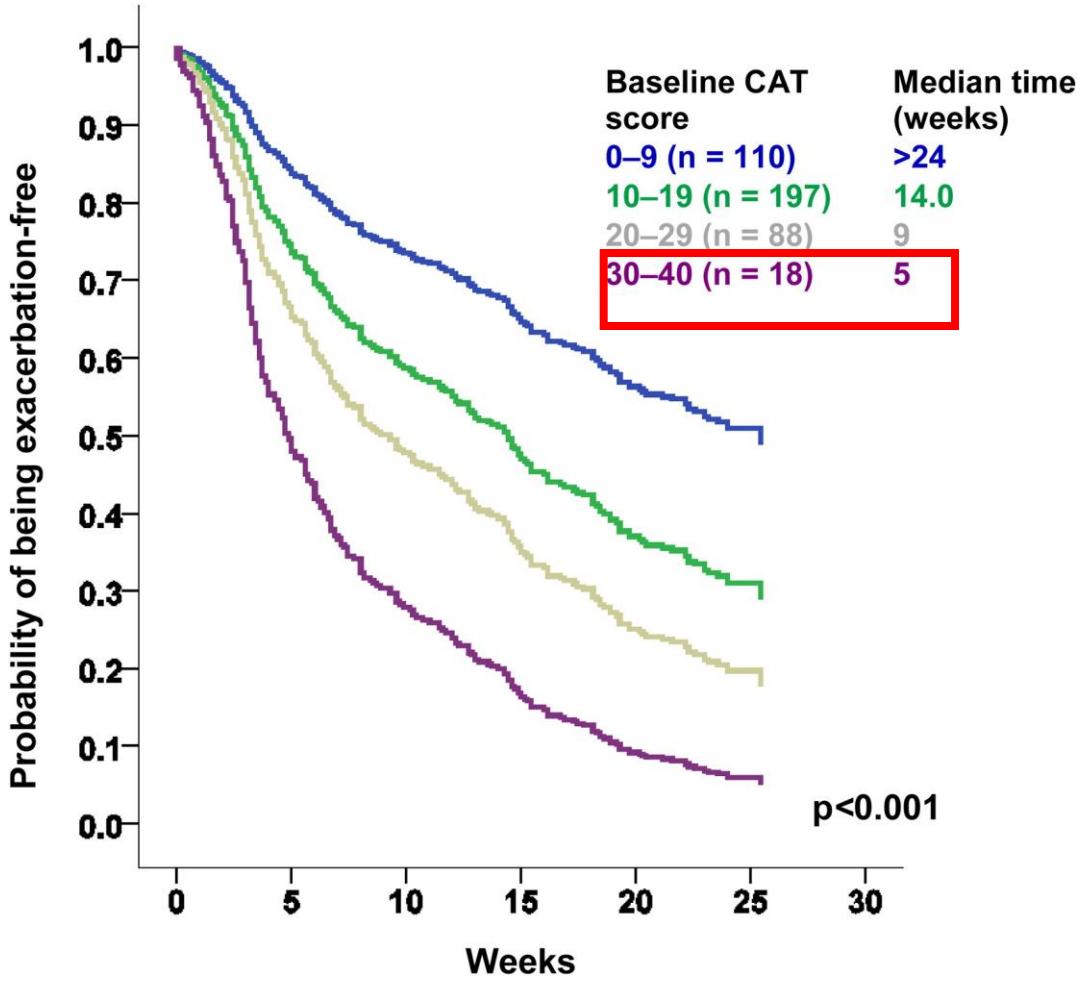
mMRC 0-1 CAT < 10 | mMRC ≥ 2 CAT ≥ 10

Symptoms

GOLD ABE Assessment Tool

Figure 2.3





Sang-Do Lee, et al. The COPD assessment test (CAT) assists prediction of COPD exacerbations in high-risk patients, Respiratory Medicine, Volume 108, Issue 4, 2014, Pages 600-608, ISSN 0954-6111, https://doi.org/10.1016/j.rmed.2013.12.014.

Commonly Used Maintenance Medications in COPD*

Table 3.3

Generic Drug Name	Inhaler Type	DELIVERY OPTIONS			Duration of Action
		Nebulizer	Oral	Injection	
BETA$_2$-Agonists					
Short-acting (SABA)					
Fenoterol	MDI	✓	pill, syrup		4-6 hours
Levalbuterol	MDI	✓			6-8 hours
Salbutamol (albuterol)	MDI & DPI	✓	pill, syrup, extended release tablet	✓	4-6 hours 12 hours (ext. release)
Terbutaline	DPI		pill	✓	4-6 hours
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,				MDI 12 hours
Glycopyrronium bromide	DPI		solution	✓	12-24 hours
Tiotropium	DPI, SMI, MDI				24 hours
Umeclidinium	DPI				24 hours
Glycopyrrolate		✓			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	✓			6-8 hours
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	✓	Variable, up to 24 hours
Theophylline (SR)			pill	✓	Variable, up to 24 hours
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-4 Inhibitors					
Roflumilast			pill		24 hours
Mucolytic Agents					
Erdosteine			pill		12 hours
Carbocysteine†			pill		
N-acetylcysteine†			pill		

*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

Table 3.4

- Inhaled bronchodilators in COPD are central to symptom management and commonly given on a regular basis to prevent or reduce symptoms **(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 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)**
- 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)**
- Tiotropium improves the effectiveness of pulmonary rehabilitation in increasing exercise performance **(Evidence B)**
- Theophylline exerts a small bronchodilator effect in stable COPD **(Evidence A)** and that is associated with modest symptomatic benefits **(Evidence B)**
- Single inhaler therapy may be more convenient and effective than multiple inhalers

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Anti-Inflammatory Therapy in Stable COPD

Table 3.5

Inhaled Corticosteroids	• 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)** • Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease **(Evidence A)** • Lower blood and sputum eosinophils are associated with greater presence of proteobacteria, notably *Haemophilus*, increased bacterial infections & pneumonia • Independent of ICS use, there is evidence that a blood eosinophil count < 2% increases the risk of pneumonia **(Evidence C)** • 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 suggest a 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 • 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)**

PDE4 Inhibitors	• In patients with chronic bronchitis, severe to very severe COPD and a history of exacerbations:
	  ▪ A PDE4 inhibitor improves lung function and reduces moderate and severe exacerbations **(Evidence A)**
	  ▪ A PDE4 inhibitor improves lung function and decreases exacerbations in patients who are on fixed-dose LABA+ICS combinations **(Evidence A)**

Antibiotics	• Long-term azithromycin and erythromycin therapy reduces exacerbations over one year **(Evidence A)** • Treatment with azithromycin is associated with an increased incidence of bacterial resistance **(Evidence A)** and hearing test impairments **(Evidence B)**
Mucoregulators and Antioxidant Agents	• Regular treatment with mucolytics such as erdosteine, carbocysteine and NAC reduces the risk of exacerbations in select populations **(Evidence B)**
Other Anti-Inflammatory Agents	• 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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Factors to Consider when Initiating ICS Treatment

Figure 3.1

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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 Table 3.4 and Figure 4.3 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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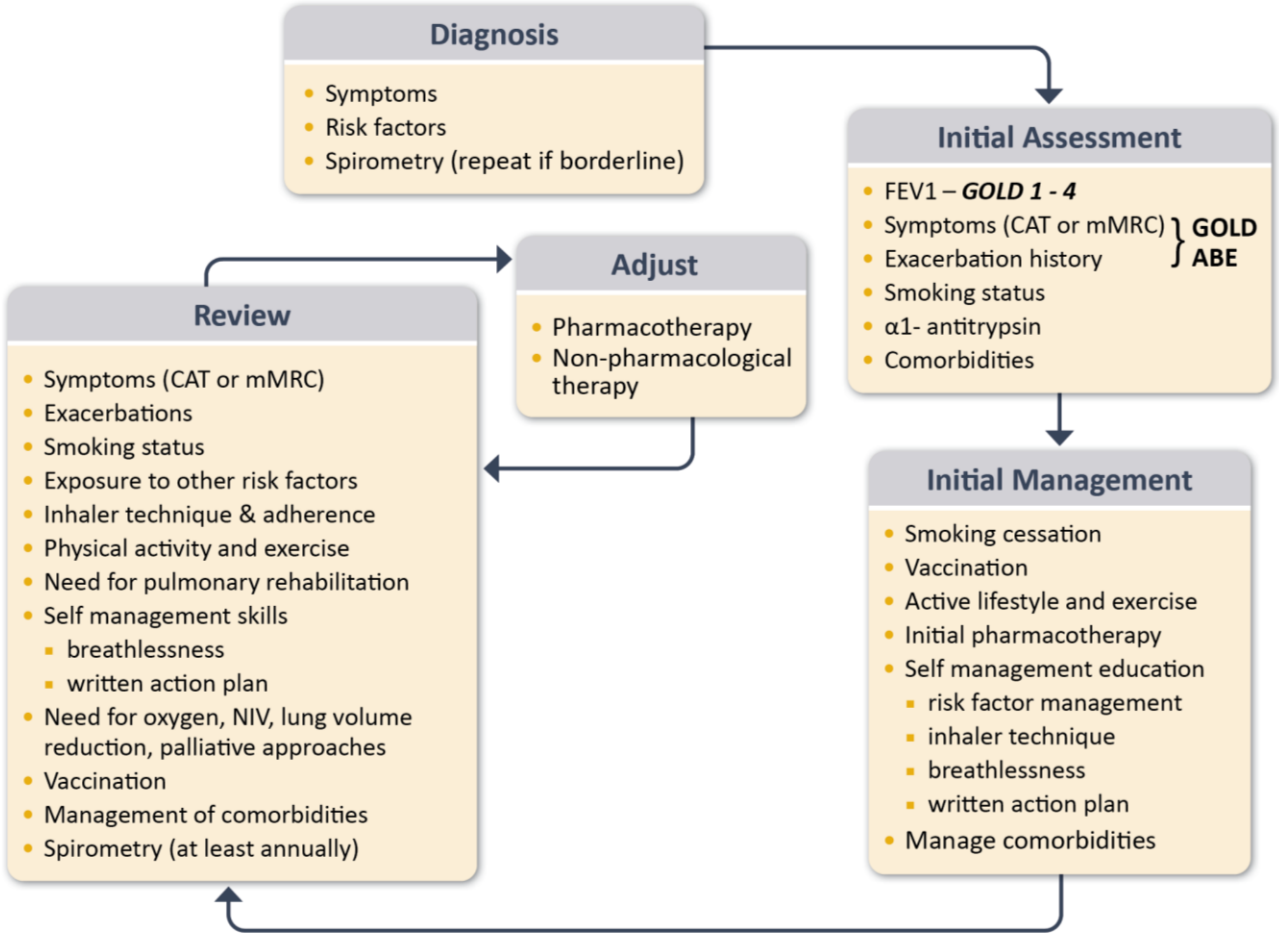
Management of COPD

Figure 4.1



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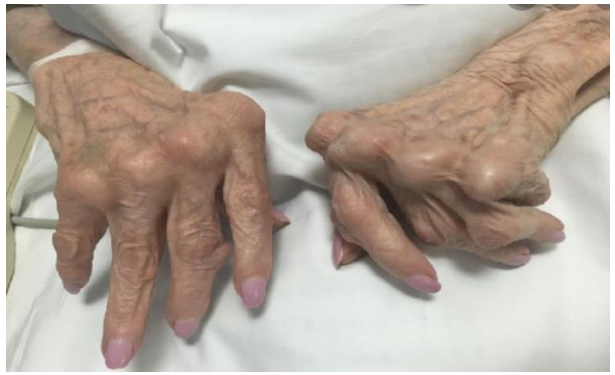
Goals for Treatment of Stable COPD

Table 4.1

Key Points for Inhalation of Drugs

Table 4.4

- 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 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



https://www.orthobullets.com/basic-science/9085/rheumatoid-arthritis

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https://www.gtsimulators.com/products/adult-tracheostomy-care-manikin-lf01168u

- https://www.youtube.com/watch?v=NWGvBMBXcRA
- https://www.youtube.com/watch?v=U1NV10RuV6Y
- https://www.youtube.com/watch?v=fHYTz-ZoRLw

Basic Principles for Appropriate Inhalation Device Choice

Table 4.5

- 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. Ideally, only one device type should be used
- 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 manoeuvre 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 chose 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 chose 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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Key Points for the Use of Bronchodilators

Table 4.6

- 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
- When initiating treatment with long acting bronchodilators the preferred choice is a combination of a long-acting muscarinic antagonist and a long acting ß2-agonist. In patients with persistent dyspnea on a single long acting bronchodilator treatment should be escalated to two **(Evidence A)**. The combination can be given as single inhaler or multiple inhaler treatment
- Inhaled bronchodilators are recommended over oral bronchodilators **(Evidence A)**
- Theophylline is not recommended unless other long-term treatment bronchodilators are unavailable or unaffordable **(Evidence B)**

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Key Points for the Use of Anti-Inflammatory Agents

Table 4.7

- Long-term monotherapy with ICS is not recommended **(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. This combination can be given as single or multiple inhaler therapy.
- If patients with COPD have features of asthma, treatment should always contain an ICS
- In patients with severe to very severe airflow limitation, chronic bronchitis and exacerbations the addition of a PDE4 inhibitor to a treatment with long acting bronchodilators with/without ICS can be considered **(Evidence B)**
- Preferentially, but not only in former smokers with exacerbations despite appropriate therapy, macrolides, in particular azithromycin, can be considered **(Evidence B)**
- Statin therapy and/or beta-blockers are not recommended for prevention of exacerbations **(Evidence A)**

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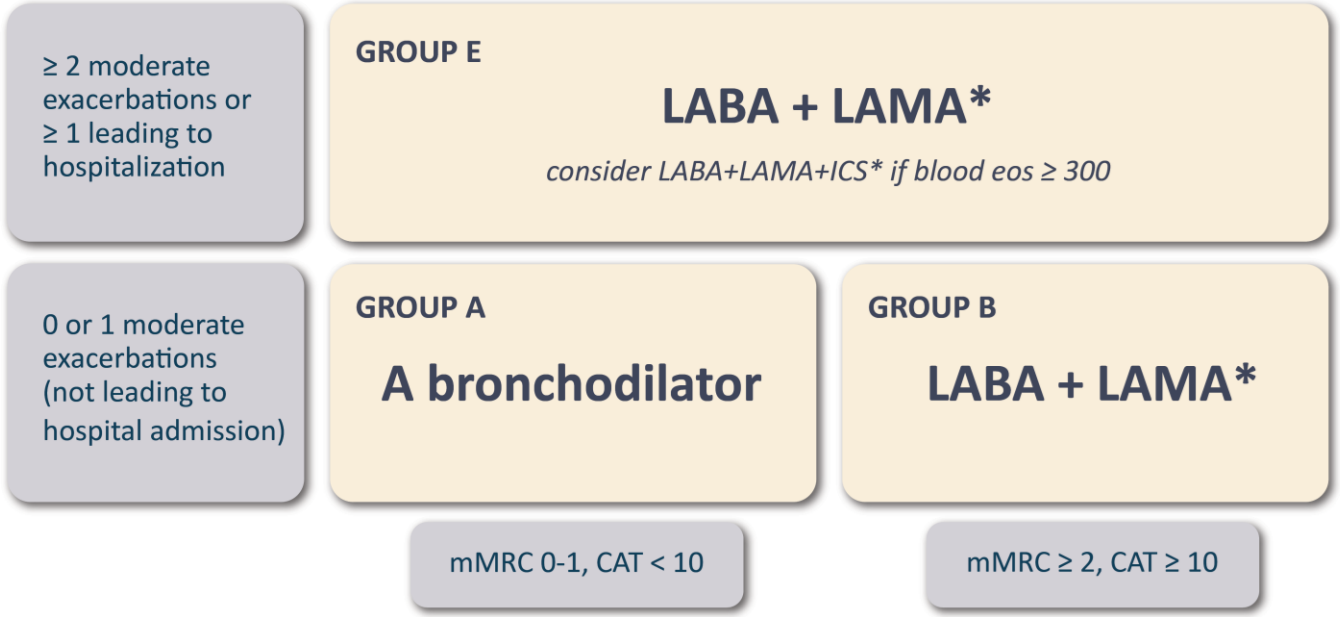
Key Points for the Use of Other Pharmacological Treatments

Table 4.8

- Patients with severe hereditary alpha-1 antitrypsin deficiency and established emphysema may be candidates for alpha-1 antitrypsin augmentation therapy **(Evidence B)**
- Antitussives cannot be recommended **(Evidence C)**
- Drugs approved for primary pulmonary hypertension are not recommended for patients with a pulmonary hypertension secondary to COPD **(Evidence B)**
- Low-dose long acting oral and parenteral opioids may be considered for treating dyspnea in COPD patients with severe disease **(Evidence B)**

Initial Pharmacological Treatment

Figure 4.2



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

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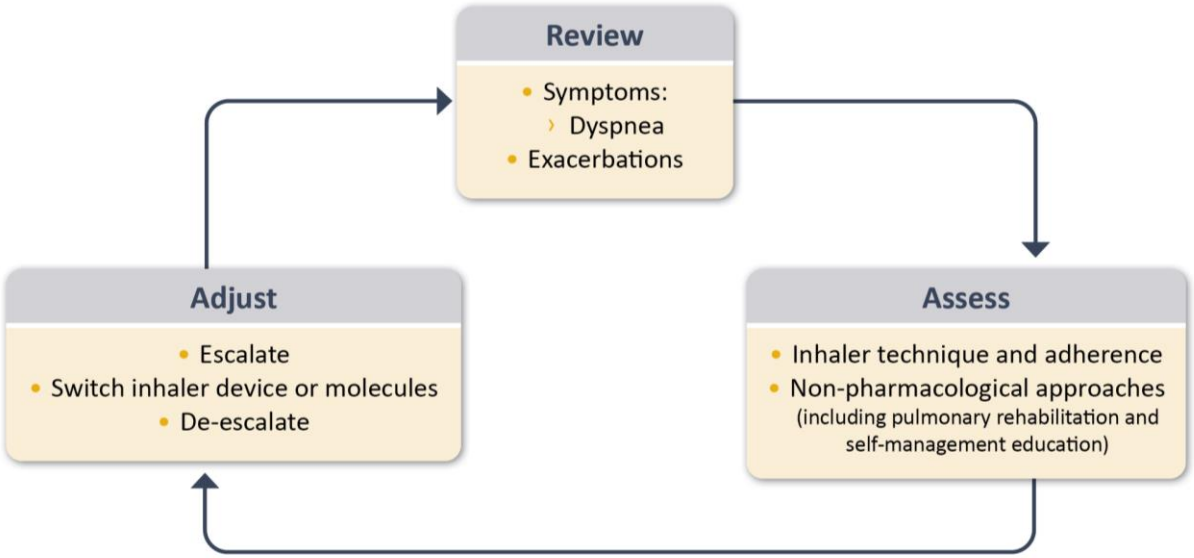
Management Cycle

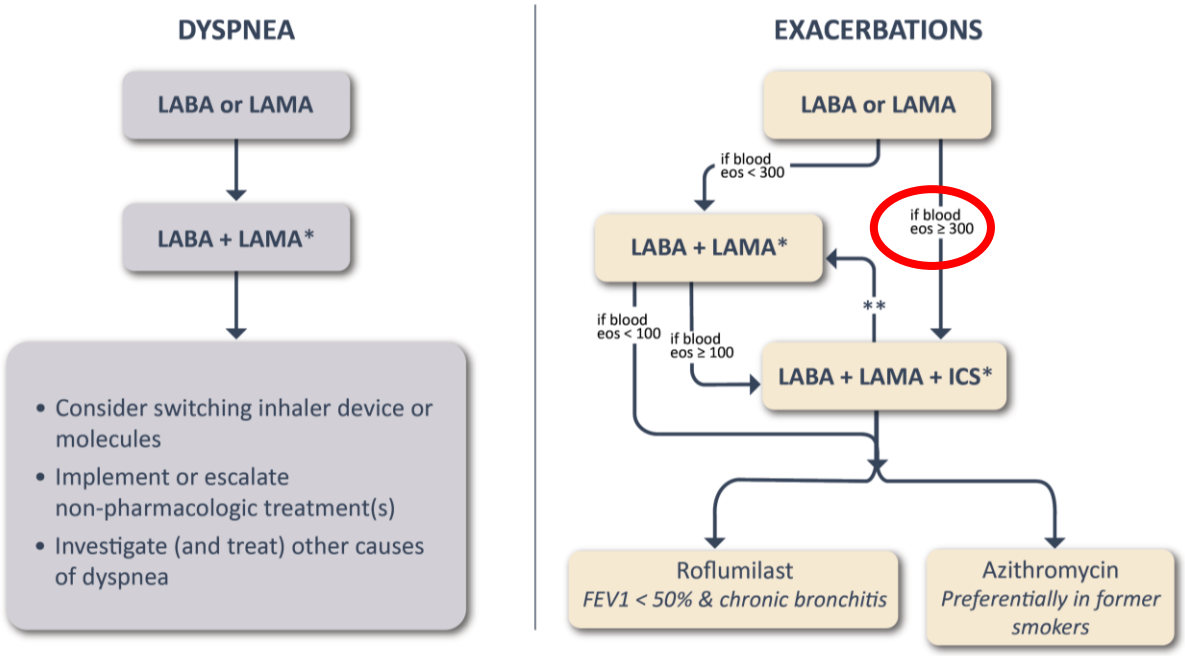
Figure 4.3



Follow-up Pharmacological Treatment

Figure 4.4

1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - Check adherence, inhaler technique and possible interfering comorbidities
   - Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - Place patient in box corresponding to current treatment & follow indications
   - Assess response, adjust and review
   - These recommendations do not depend on the ABE assessment at diagnosis



*Single inhaler therapy may be more convenient and effective than multiple inhalers

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

Exacerbations refers to the number of exacerbations per year

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Non-Pharmacologic Management of COPD*

Table 4.9

Patient Group	Essential	Recommended	Depending on Local Guidelines
A	Smoking Cessation (can include pharmacological treatment)	Physical Activity	Flu Vaccination Pneumococcal Vaccination Pertussis Vaccination COVID-19 Vaccinations Shingles Vaccination
B and E	Smoking Cessation (can include pharmacological treatment) Pulmonary Rehabilitation	Physical Activity	Flu Vaccination Pneumococcal Vaccination Pertussis Vaccination COVID-19 Vaccinations Shingles Vaccination

*Can include pharmacologic treatment

Follow-Up of Non-Pharmacological treatment

Table 4.10

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

- Flu 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

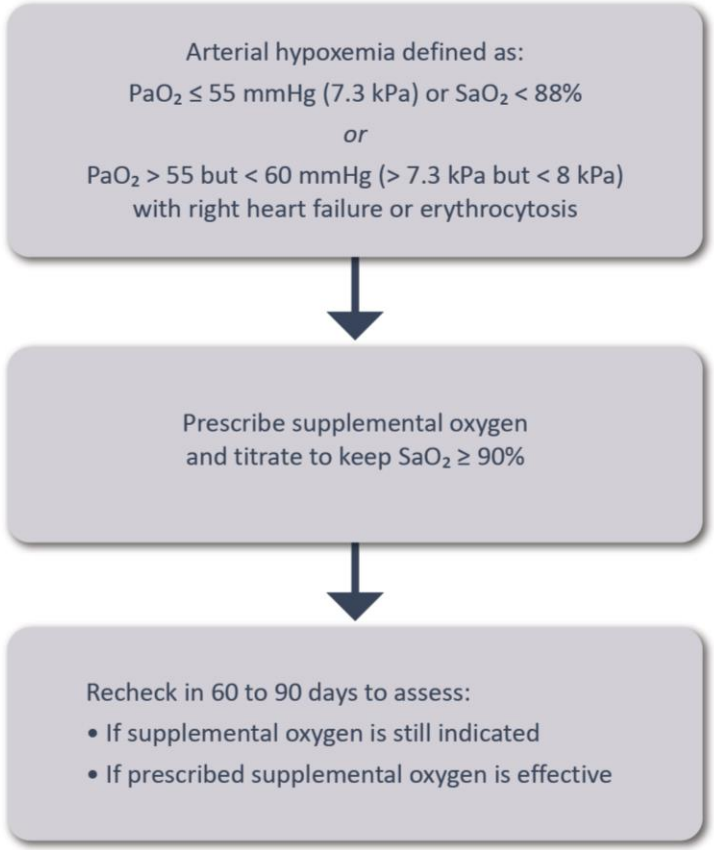
EXACERBATIONS

- 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

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.

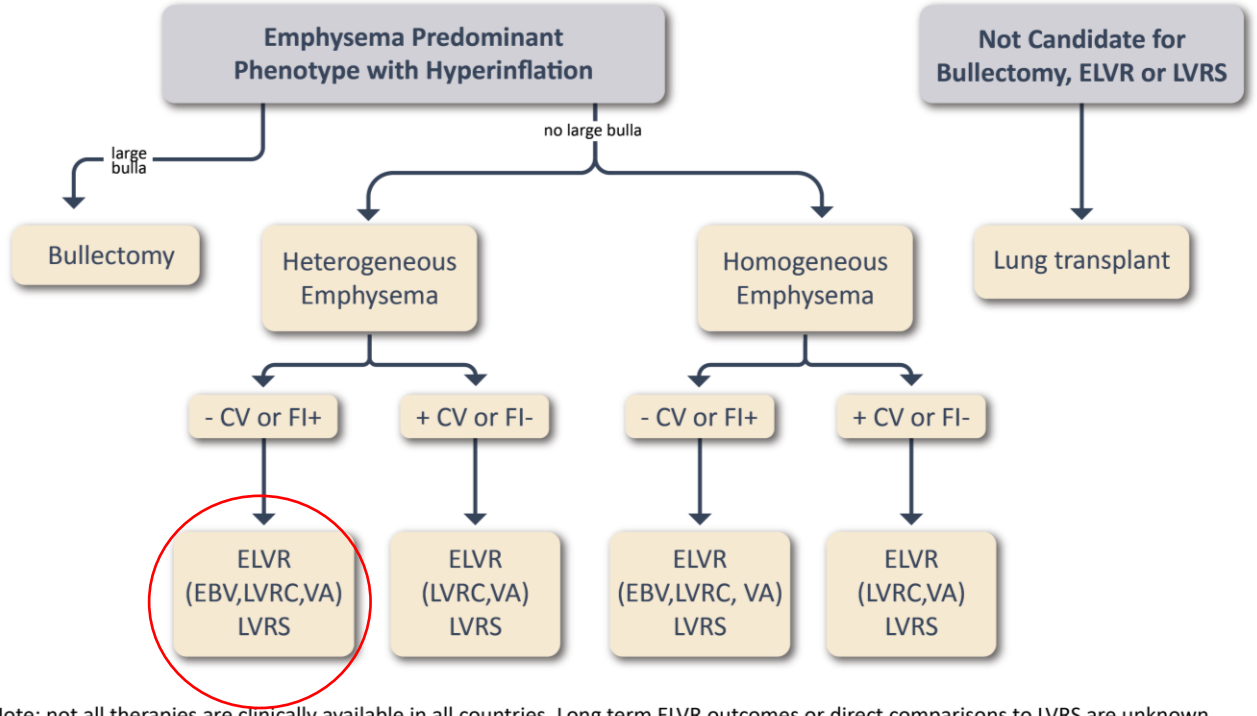
Prescription of Supplemental Oxygen to COPD Patients

Figure 4.5



Surgical and Interventional Therapies in Advanced Emphysema

Figure 4.6



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

Key Points for the Use of Non-Pharmacological Treatments

Table 4.11

Education, Self-Management and Pulmonary Rehabilitation	• Education is needed to change patient's knowledge but there is no evidence that used alone it will change patient behavior • Education self-management with the support of a case manager with or without the use of a written action plan is recommended for the prevention of exacerbation complications such as hospital admissions **(Evidence B)** • Rehabilitation is indicated in all patients with relevant symptoms and/or a high risk for exacerbation **(Evidence A)** • Physical activity is a strong predictor of mortality **(Evidence A)**. People with COPD should be encouraged to increase the level of physical activity although we still don't know how to best insure the likelihood of success
Vaccination	• Influenza vaccination is recommended in people with COPD **(Evidence B)** • The WHO and CDC recommends SARS-CoV-2 (COVID-19) vaccination for people with COPD **(Evidence B)** • The CDC recommends one dose of 20-valent pneumococcal conjugate vaccine (PCV20); or one dose of 15-valent pneumococcal conjugate vaccine (PCV15) followed by 23-valent pneumococcal polysaccharide vaccine (PPSV23) in people with COPD **(Evidence B)** • Pneumococcal vaccine has been shown to reduce the incidence of community-acquired pneumonia and exacerbations in people with COPD **(Evidence B)** • The CDC recommends Tdap (dTaP/dTPa) vaccination to protect against pertussis (whooping cough) for people with COPD that were not vaccinated in adolescence **(Evidence B)**, and Zoster vaccines to protect against shingles for people with COPD over 50 years **(Evidence B)**
Nutrition	• Nutritional supplementation should be considered in malnourished patients with COPD **(Evidence B)**
End of Life and Palliative Care	• 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)**
Treatment of Hypoxemia	• In patients with severe resting hypoxemia long-term oxygen therapy is indicated **(Evidence A)** • In patients with stable COPD and resting or exercise-induced moderate desaturation, long term oxygen treatment should not be routinely prescribed. However, individual patient factors may be considered when evaluating the patient's needs for supplemental oxygen **(Evidence A)** • Resting oxygenation at sea level does not exclude the development of severe hypoxemia when travelling by air **(Evidence C)**
Treatment of Hypercapnia	• In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, long term noninvasive ventilation may be considered **(Evidence B)**
Intervention Bronchoscopy and Surgery	• Lung volume reduction surgery should be considered in selected patients with upper-lobe emphysema **(Evidence A)** • In selected patients with a large bulla surgical bullectomy may be considered **(Evidence C)** • In select patients with advanced emphysema, bronchoscopic interventions reduce end-expiratory lung volume and improve exercise tolerance, quality of life and lung function at 6-12 months following treatment. Endobronchial valves **(Evidence A)**; Lung coils **(Evidence B)**; Vapor ablation **(Evidence B)** • In patients with very severe COPD (progressive disease, BODE score of 7 to 10, and not candidate 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)**

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

Table 5.1

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

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Diagnosis and Assessment

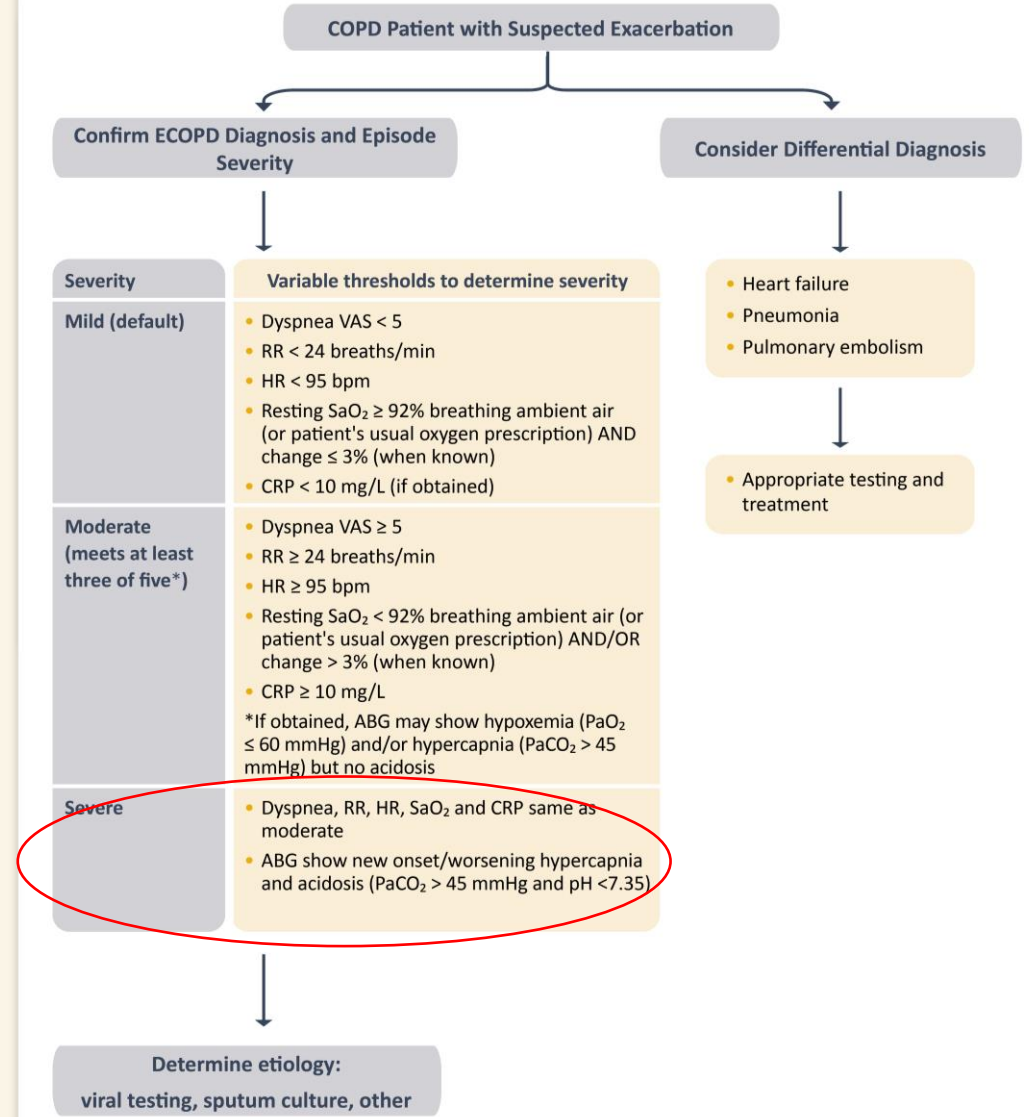
Table 5.2

1.	Complete a thorough clinical assessment for evidence of COPD and potential respiratory and nonrespiratory 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.	Establish the cause of the event (viral, bacterial, environmental, other).

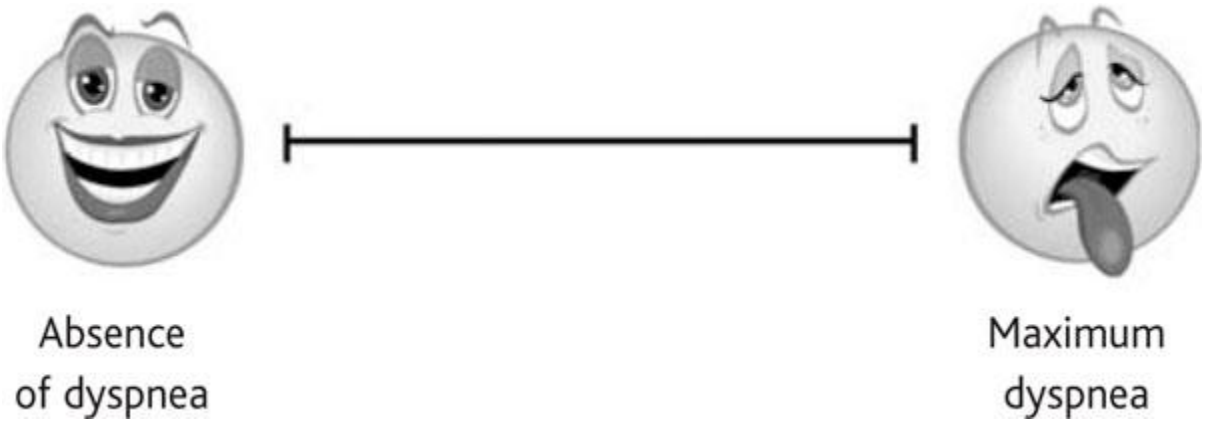
Definition of abbreviations: COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; VAS = visual analog scale.

Classification of the Severity of COPD Exacerbations

Figure 5.1



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.



Crisafulli, E., Clini, E.M. Measures of dyspnea in pulmonary rehabilitation. *Multidiscip Respir Med* **5**, 202 (2010).

Potential Indications for Hospitalization Assessment*

Table 5.3

- 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

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Management of Severe but not Life-threatening Exacerbations*

Table 5.4

- **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

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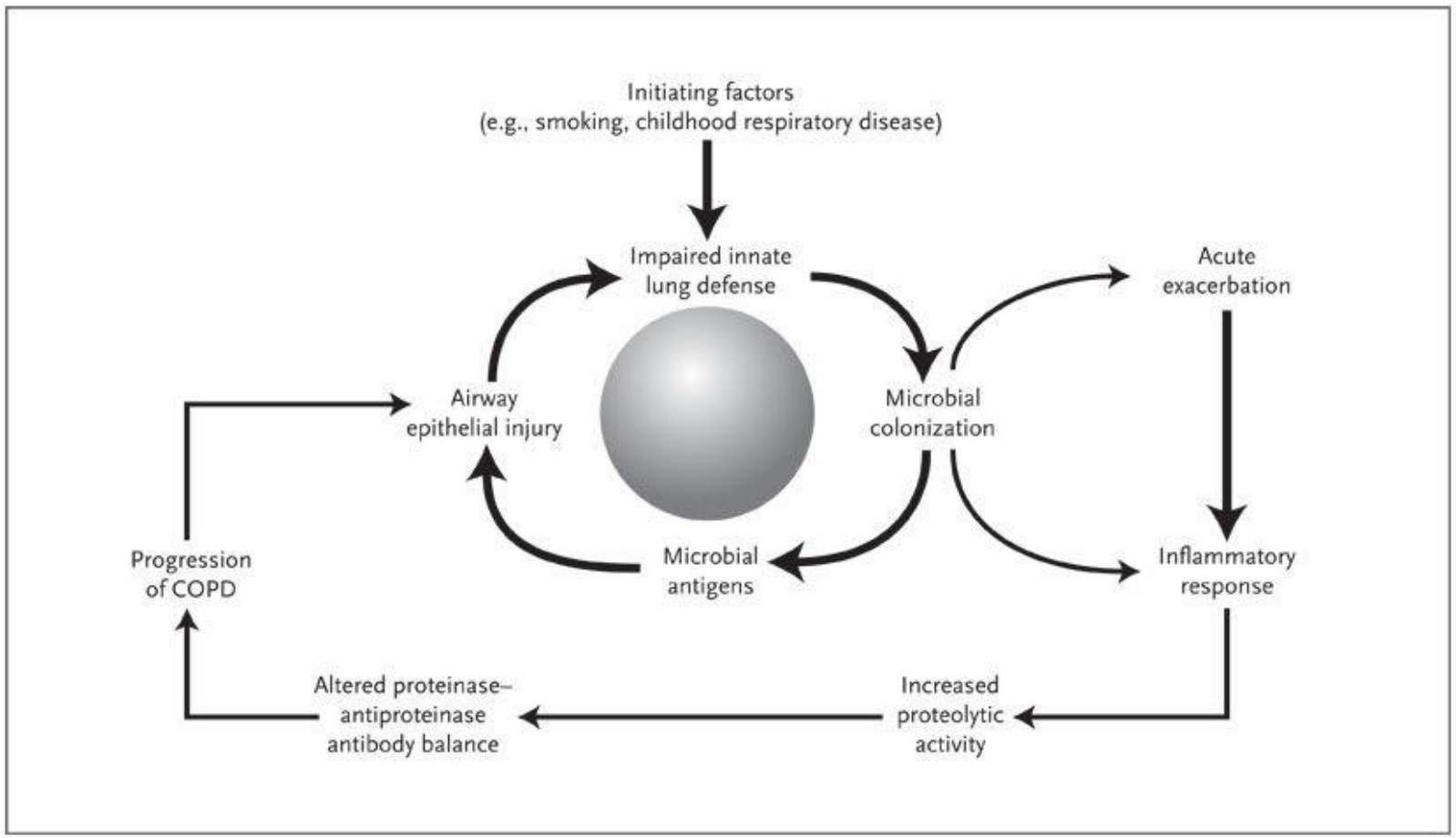
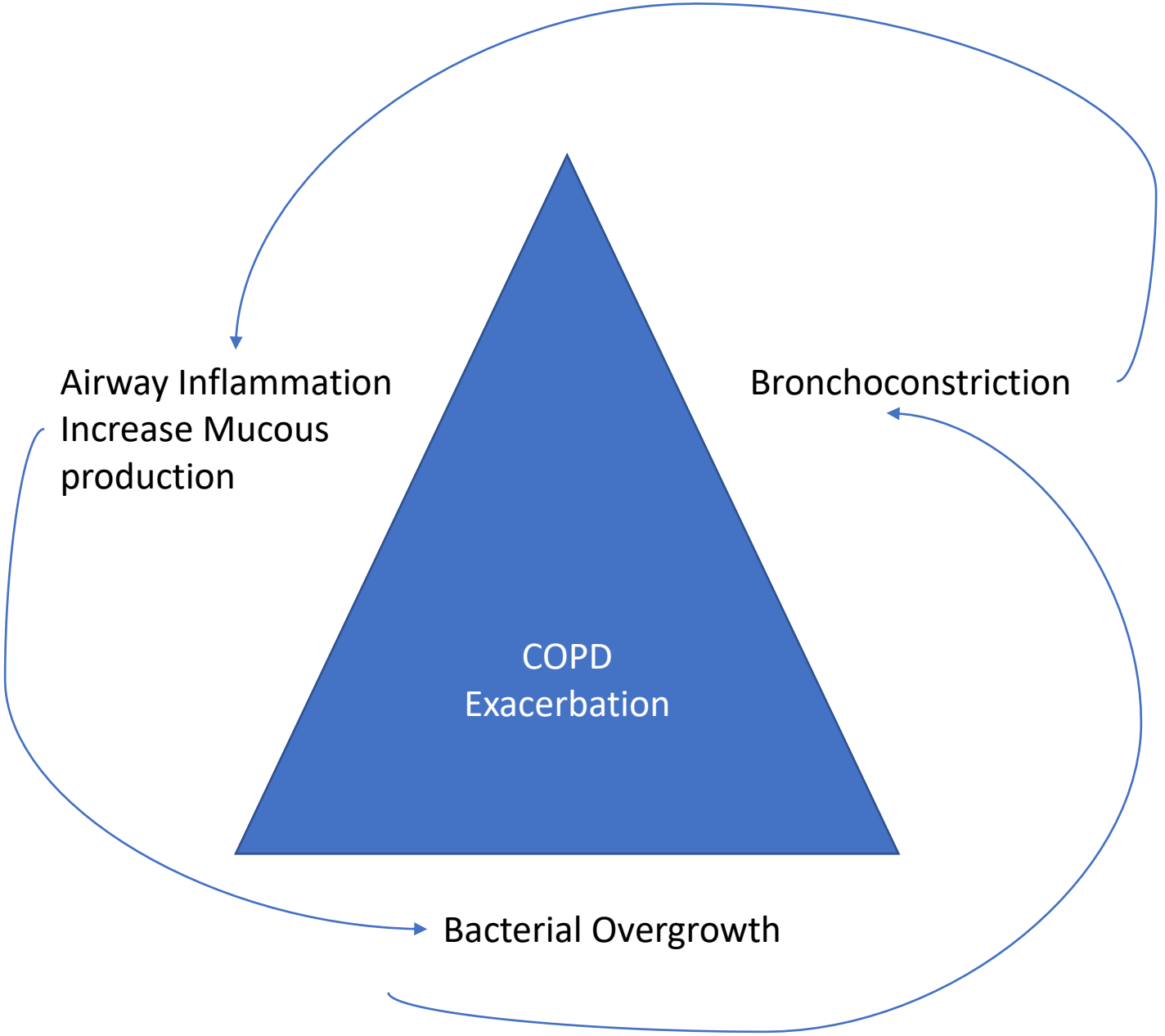


Sethi S, Murphy TF. N Engl J Med 2008;359:2355-2365.



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Key Points for the Management of Exacerbations

Table 5.5

- 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*

Table 5.6

- 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)

Table 5.7

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

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Indications for Invasive Mechanical Ventilation

Table 5.8

- 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

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Discharge Criteria and Recommendations for Follow-up

Table 5.9

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 and understanding 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 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

Table 5.10

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

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

Table 3.6

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.

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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 **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 *Comments:*

Hospital/ER	Where	Date	Length	Reason (Dx)

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)

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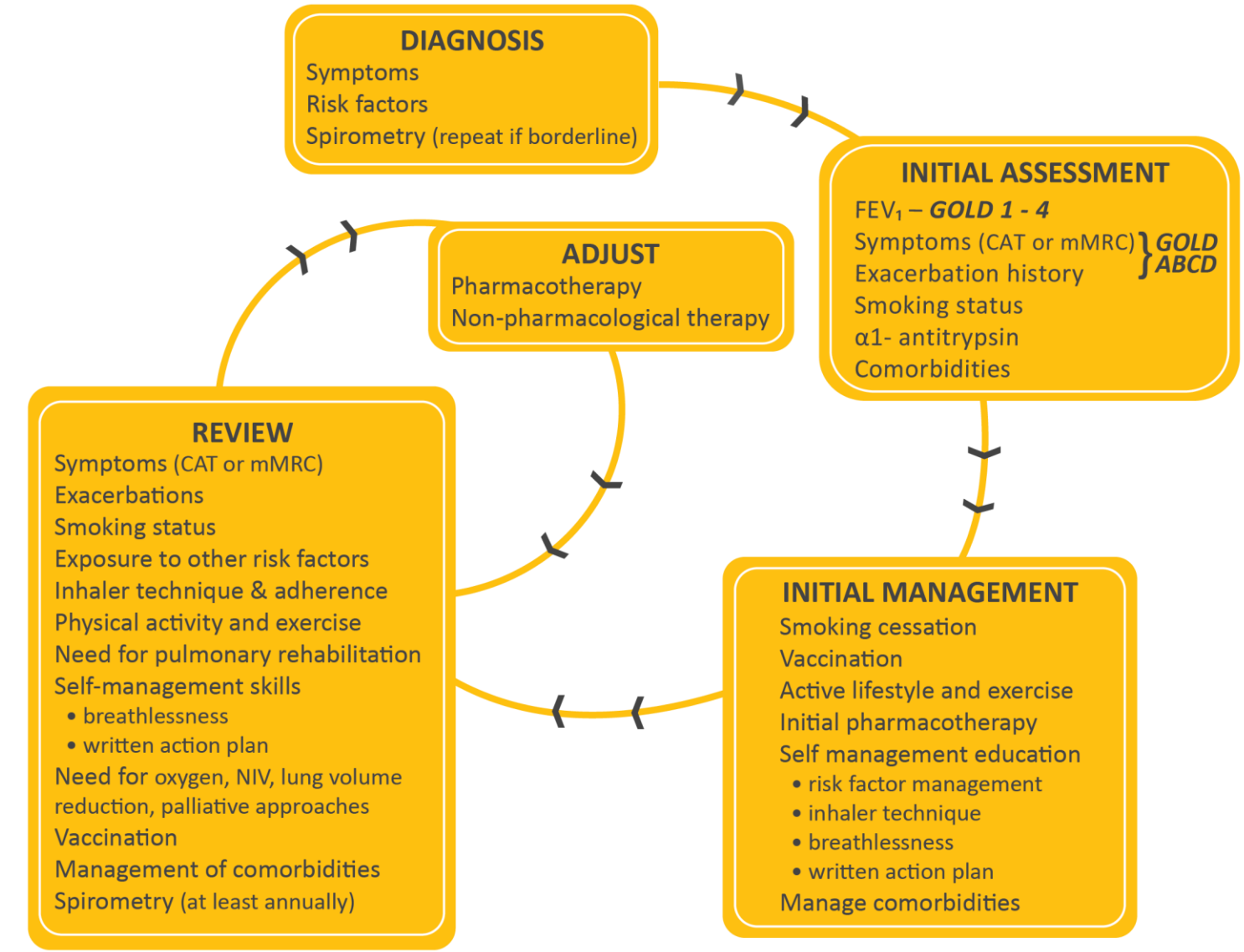
Case #1

- 1. A 62-year-old man is evaluated for chronic cough productive of thin clear sputum and dyspnea on exertion that has worsened over the last 2 years. He has a 54-pack-year smoking history. Medical history is otherwise unremarkable, and he takes no medications.
- On physical examination, vital signs are normal. The patient coughs during the examination, and mild expiratory wheezing is heard over the posterior lung fields. Cardiac examination is normal.
- Chest radiograph shows hyperinflated lungs with a flattened diaphragm without infiltrates.
- Spirometry shows an FEV1/FVC ratio of 0.65 and an FEV1 of 52% of predicted without a significant bronchodilator response.
- Which of the following is the most likely diagnosis?
- A Asthma
- B Bronchiectasis
- C COPD
- D Desquamative interstitial pneumonia

Case #2

- A 62-year-old man is evaluated during a follow-up visit for COPD. He continues to smoke one pack daily and has a 40-pack-year history. He can walk rapidly on a level surface but has breathlessness walking up a slight hill. He has not been hospitalized or seen urgently for an exacerbation. Medications are salmeterol and tiotropium.
- On physical examination, vital signs are normal. Oxygen saturation is 92% with the patient breathing ambient air. Faint expiratory wheezing is present.
- Spirometry shows an FEV1/FVC ratio of 0.58, and FEV1 is 62% of predicted.
- Which of the following is the most appropriate additional therapy?
- A Chronic azithromycin therapy
- B Prednisone
- C Pulmonary rehabilitation
- D Smoking cessation

MANAGEMENT OF COPD



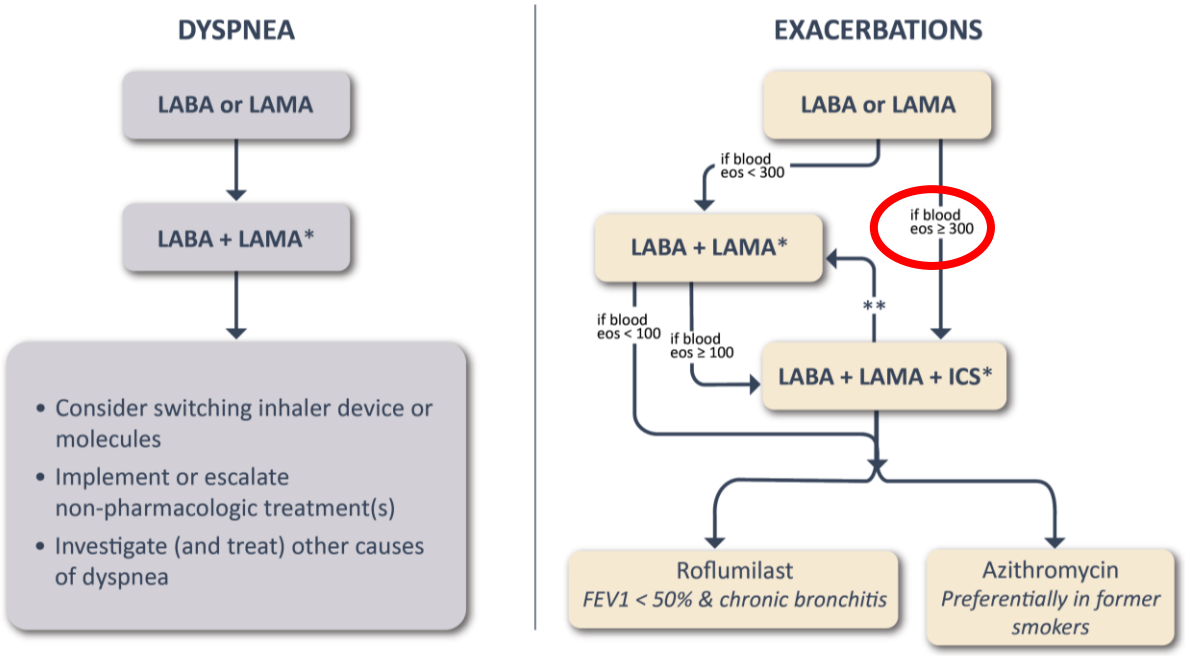
Case#3

- A 59-year-old man is seen in a follow-up visit for a 6-month history of progressively worsening chronic cough productive of small amounts of thin clear sputum and dyspnea on exertion. He has shortness of breath when he walks quickly and when he walks uphill. He has a 45-pack-year smoking history but quit 2 years ago. He has been using albuterol as needed since his diagnosis of COPD 3 months ago, but he remains symptomatic.
- On physical examination, oxygen saturation is 95% with the patient breathing ambient air. Scattered expiratory wheezing is heard. Cardiac examination is normal.
- Chest radiograph from 3 months ago shows flattened diaphragm but no infiltrate.
- Spirometry at the time of diagnosis showed reduced postbronchodilator FEV1/FVC ratio and FEV1 of 69% of predicted.
- Which of the following is the most appropriate pharmacologic treatment?
- A Inhaled fluticasone propionate–salmeterol
- B Inhaled tiotropium bromide
- C Prednisone
- D Roflumilast

Follow-up Pharmacological Treatment

Figure 4.4

1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - Check adherence, inhaler technique and possible interfering comorbidities
   - Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - Place patient in box corresponding to current treatment & follow indications
   - Assess response, adjust and review
   - These recommendations do not depend on the ABE assessment at diagnosis



*Single inhaler therapy may be more convenient and effective than multiple inhalers

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

Exacerbations refers to the number of exacerbations per year

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Thank you

Questions?

Common Risk Factors for Development of Lung Cancer

Table 6.1

- Age > 55
- Smoking history > 30 pack years
- Presence of emphysema by CT scan
- Presence of airflow limitation FEV1/FVC < 0.7
- BMI < 25 kg/m^2
- Family history of lung cancer

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Key Points for the Management of Stable COPD During COVID-19 Pandemic

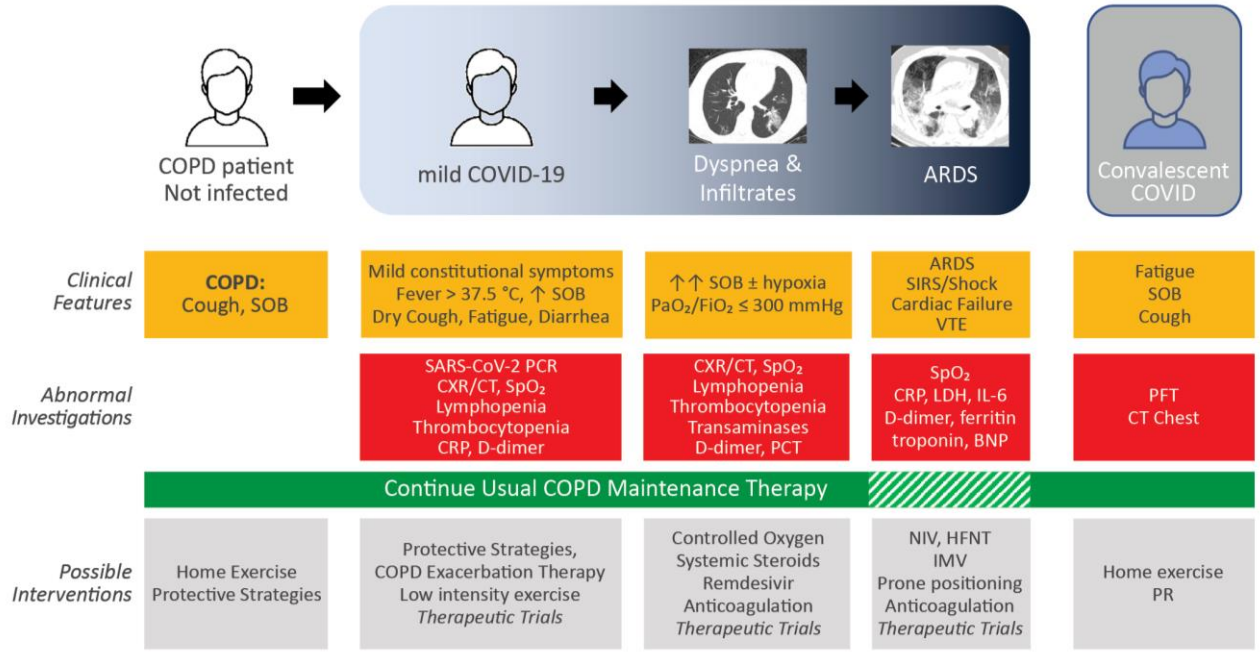
Table 7.1

Protective Strategies	• Follow basic infection control measures • Wear a face covering • Consider shielding/sheltering-in-place • Have the COVID-19 vaccinations in line with national recommendations
Investigations	• Only essential spirometry at times of high prevalence of COVID-19
Pharmacotherapy	• Ensure adequate supplies of medications • Continue unchanged including ICS
Non-pharmacological Therapy	• Ensure annual influenza vaccination • Maintain physical activity

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™

COVID-19 & COPD

Figure 7.1



(ARDS, Adult respiratory distress syndrome; BNP, brain natriuretic peptide; CRP, C reactive protein; CT, computed tomography; CXR, chest radiograph; HFNT, high flow nasal therapy; IL-6, interleukin 6; IMV, invasive mechanical ventilation; LDH, lactate dehydrogenase; NIV, non-invasive ventilation; PCT, procalcitonin; PFT, pulmonary function tests; PR, pulmonary rehabilitation; SOB, Shortness of breath; SpO_2 , peripheral oxygen saturation; VTE, venous thromboembolism)

Halpin et al. 2020. Global Initiative for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease: The 2020 GOLD Science Committee Report on COVID-19 & COPD. Published Ahead of Print: https://www.atsjournals.org/doi/abs/10.1164/rccm.202009-3533SO
The American Journal of Respiratory and Critical Care Medicine is an official journal of the American Thoracic Society

Key Points for the Management of Patients with COPD and Suspected or Proven COVID-19

Table 7.2

SARS-CoV-2 Testing	• Swab/saliva PCR if new or worsening respiratory symptoms, fever, and/or any other symptoms that could be COVID related
Other Investigations	• Avoid spirometry unless essential • Consider CT for COVID pneumonia and to exclude other diagnoses e.g. PE • Avoid bronchoscopy unless essential • Assess for co-infection
COPD Pharmacotherapy	• Ensure adequate supplies of medication • Continue maintenance therapy unchanged including ICS • Use antibiotics and oral steroids in line with recommendations for exacerbations • Avoid nebulization when possible
COPD Non-Pharmacological Therapy	• Maintain physical activity as able
Protective Strategies	• Have the COVID-19 vaccinations in line with national recommendations • Follow basic infection control measures • Maintain physical distancing • Wear a face covering
COVID-19 Therapy	• Use antivirals, corticosteroids, IL-6 receptor blockers and baricitinib as recommended for patients with COVID-19 • Use HFNT or NIV for respiratory failure if possible • Use invasive mechanical ventilation if HFNT or NIV fails • Post COVID-19 rehabilitation • Ensure appropriate post COVID-19 follow-up

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GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™

Use of CT in Stable COPD

Table 2.8

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 15-45% 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

Brief Strategies to Help the Patient Willing to Quit

Table 3.1

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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Vaccination for Stable COPD

Table 3.2

- Influenza vaccination is recommended in people with COPD **(Evidence B)**
- The WHO and CDC recommends SARS-CoV-2 (COVID-19) vaccination for people with COPD **(Evidence B)**
- The CDC recommends one dose of 20-valent pneumococcal conjugate vaccine (PCV20); or one dose of 15-valent pneumococcal conjugate vaccine (PCV15) followed by 23-valent pneumococcal polysaccharide vaccine (PPSV23) in people with COPD **(Evidence B)**
- Pneumococcal vaccination has been shown to reduce the incidence of community-acquired pneumonia and exacerbations in people with COPD **(Evidence B)**
- The CDC recommends Tdap (dTaP/dTPa) vaccination to protect against pertussis (whooping cough) for people with COPD that were not vaccinated in adolescence **(Evidence B)**, and Zoster vaccine to protect against shingles for people with COPD over 50 years **(Evidence B)**

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

Table 3.6

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.

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Other Pharmacological Treatments

Table 3.7

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)**

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Pulmonary Rehabilitation, Self-Management and Integrative Care in COPD

Table 3.8

Pulmonary Rehabilitation	• 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 alone has not been shown to be effective **(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)**

Palliative Care, End of Life and Hospice Care in COPD

Table 3.9

- Opiates, neuromuscular electrical stimulation (NMES), oxygen and fans blowing air on to the face can relieve breathlessness **(Evidence C)**
- In malnourished patients, nutritional supplementation 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)**

Oxygen Therapy and Ventilatory Support in Stable COPD

Table 3.10

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)**

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

Figure 3.2

	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

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Interventional Therapy in Stable COPD

Table 3.11

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)**
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

Treating Tobacco Use and Dependence: A Clinical Practice Guideline — Major Findings & Recommendations

Table 4.2

- 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, 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

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Identify & Reduce Risk Factor Exposure

Table 4.3

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