MedStar Health

Diagnosis and Management of COPD
Clinical Practice Guideline

"These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient's primary care provider-in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication but should be used with the clear understanding that continued research may result in new knowledge and recommendations."

More than 15 million Americans have been diagnosed with COPD. This likely grossly underestimates the true burden of COPD, with many people underdiagnosed. While death rates have been improving, COPD still accounts for more than 150,000 deaths each year.[1]

The MedStar Health Ambulatory Best Practices Committee endorses and accepts the recommendations for care in Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 Report and the accompanying 2023 GOLD Pocket Guide.[2] A complete copy of the documents can be accessed at no charge for personal use at: https://goldcopd.org/2023-gold-report-2/. Readers are encouraged to obtain copies of the entire document from the GOLD website. The included tables are from the 2023 GOLD document. The reader is referred to the complete document for expanded information and the references behind the key points. All images are copyrighted and used here with the permission of GOLD.

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Of note, in this era of the continuing COVID-19 pandemic, the CDC recognizes chronic lung disease, including COPD, as a risk factor for severe disease and the most recent GOLD Guideline includes a new chapter devoted to COVID-19 and COPD. Information is evolving rapidly in this area and the reader is encouraged to seek the most up-to-date information from a variety of other sources to supplement this guideline.

Initial Approval Date and Reviews:	Most Recent Revision and Approval Date: 2/2024	Next Scheduled Review Date:
Effective 2/2012, 2/2014, 2/2016, 2/2018, 2/2020, 2/2022, 2/2024	©Copyright MedStar Health, 2014	2/2026

DEFINITION AND OVERVIEW

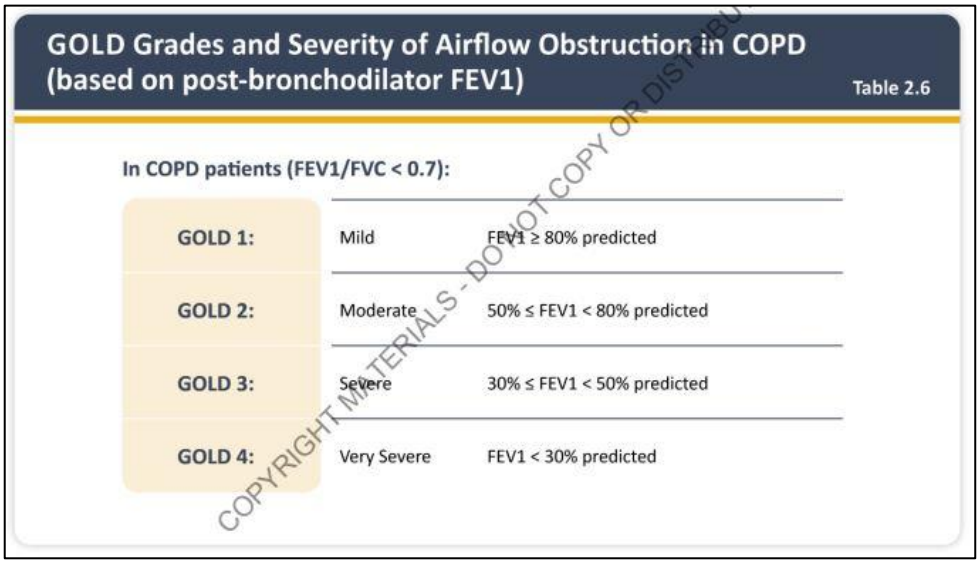
- **Definition**: Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms due to airway and/or alveoli abnormalities that cause persistent and often progressive airflow obstruction.
- **Causes and Risk Factors**
    - COPD results from interactions between a person's genetic risks and their environmental exposures.
    - The most common environmental exposures include tobacco smoking, poor indoor air quality (home use of biomass fuel and coal, occupational exposures), and outdoor air pollution.
- **Diagnostic criteria**
    - The presence of non-fully reversible airflow limitation (FEV1/FVC < 0.7 post-bronchodilation) measured by spirometry confirms COPD in the right clinical context.
    - Some people will have respiratory symptoms and/or structural lung lesions (bullae, blebs) and/or physiologic abnormalities (low-normal FEV1, hyperinflation, etc.) without the airflow obstruction in the previous bullet point. This is called "pre-COPD" and people with this are at risk of developing airflow obstruction over time.
- **Clinical presentation**
    - The most common respiratory symptoms include dyspnea, cough, activity limitation, and sputum production. People may experience acute exacerbations of these symptoms that require intervention.
    - People with COPD often have comorbid disease that can mimic or trigger acute exacerbations.

DIAGNOSIS AND INITIAL ASSESSMENT

- **Diagnosis**
    - COPD should be considered in any patient with the following key indicators.
        - Dyspnea that is progressive, worse with exercise, and persistent
        - Chronic cough, may be intermittent, may be productive or unproductive.
        - Recurrent wheezing
        - Recurrent lower respiratory tract infections
        - Risk factors – tobacco smoke, occupational exposures, indoor smoke, host factors such as genetics, low birthweight, etc.)

- Forced spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation.

- **Assessment**
  - The goals of COPD assessment are to determine the level of airflow limitation, 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.
  - Consider the use of lung volume measurement, diffusion capacity, exercise testing, and/or lung imaging if symptoms persist after initial treatment for COPD.
  - Concomitant chronic diseases 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 as they can influence mortality and hospitalizations independently.
  - Differential Diagnosis
    - A major differential diagnosis is asthma. Sometimes a clear distinction from COPD is not possible, in which case management is like that of asthma.
    - Other conditions to consider include congestive heart failure, bronchiectasis, tuberculosis, obliterative bronchiolitis, and diffuse pan bronchiolitis.



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

- The GOLD Grades in table 2.6 (prior page) provide a classification scheme for airflow limitation severity.
- Severity of symptoms can be assessed using the modified MRC (mMRC) dyspnea scale. However, because patients may experience symptoms beyond dyspnea, a comprehensive assessment of symptoms using a tool such as the COPD Assessment Test CAT is preferred.

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.

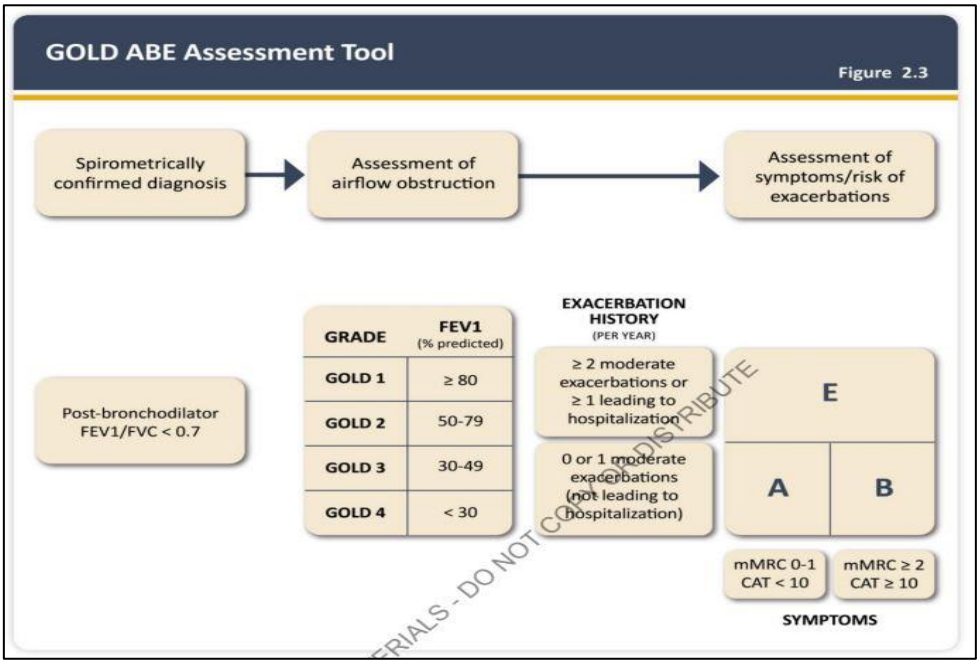
CAT™ Assessment Figure 2.2

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:** ☐

- ABCD assessment tool has been updated to better recognize the clinical relevance of exacerbations, independent of patient-reported symptoms. Groups A and B are unchanged, but groups C and D are merged in a single group termed "E."



PREVENTION AND MAINTENANCE THERAPY

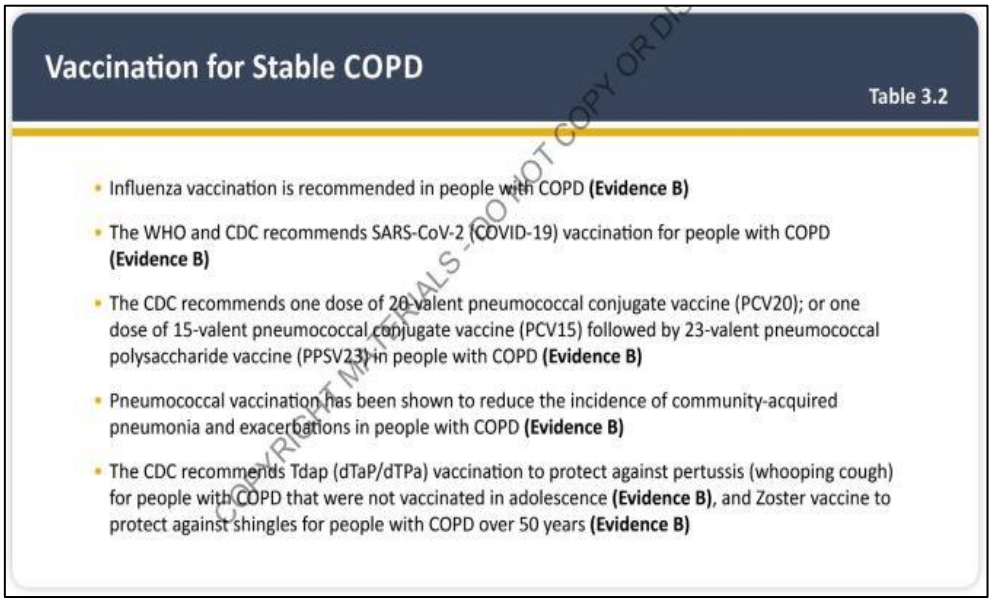
- **Tobacco Use**
  - Smoking cessation is key in management of COPD. Nicotine replacement therapy, pharmacologic products (bupropion, nortriptyline), and counseling are mainstays of treatment.
  - There is currently no evidence to support effectiveness or safety of e-cigarettes as a smoking cessation aid.
- **Medications**
  - Pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance. Data suggests that pharmacologic therapy may slow lung function decline and reduce mortality.

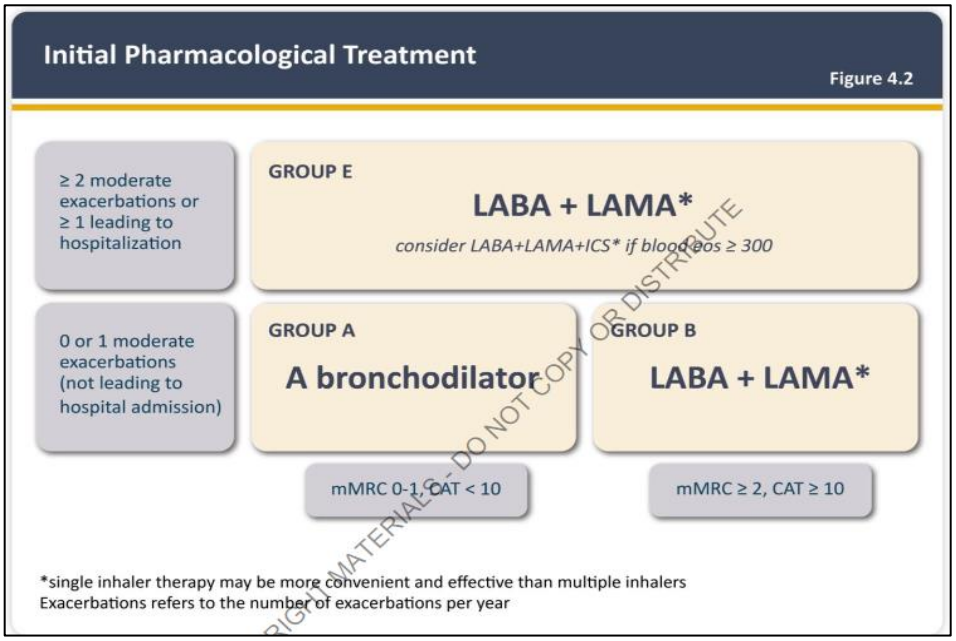
  - Each pharmacologic treatment regimen should be individualized and guided by the severity of symptoms, risk of exacerbations, side-effects, co-morbidities, drug availability and cost, and the patient's response, preference, and ability to use various drug delivery devices.
  - Inhaler technique needs to be assessed regularly.
- **Vaccinations**
  - People with COPD should receive COVID-19, influenza, pneumococcal, TDaP, and zoster vaccinations in accordance with recommended vaccine schedules (see Table 3.2 on next page for more information regarding updated recommendations for pneumococcal vaccines).
  - Be aware of new and developing recommendations regarding RSV vaccines – currently vaccination may be offered to people aged 60 and older using shared clinical decision-making.[3]
- **Oxygen**
  - In patients with severe resting chronic hypoxemia, 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.
- Pulmonary rehabilitation improves exercise capacity, symptoms, and quality of life across all grades of COPD severity.
- 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.

- **Initial Treatment** (See next page for diagram):
  - **Group A**
    - Start with a bronchodilator.
    - Long-acting bronchodilator is preferred, unless breathlessness is very rare.
  - **Group B**
    - Start with LABA+LAMA combination when possible.
    - Pulmonary rehabilitation
  - **Group E**
    - Start with LABA+LAMA combination, and add ICS if eosinophils are over 300 cells/uL, or there is a concomitant diagnosis of asthma.
    - Pulmonary rehabilitation

  - **All groups**
    - Provide a rescue short-acting bronchodilator for immediate symptom relief.
    - Recommend regular exercise.
    - Recommend updating vaccinations: flu, pneumococcal, pertussis, COVID-19, and shingles.

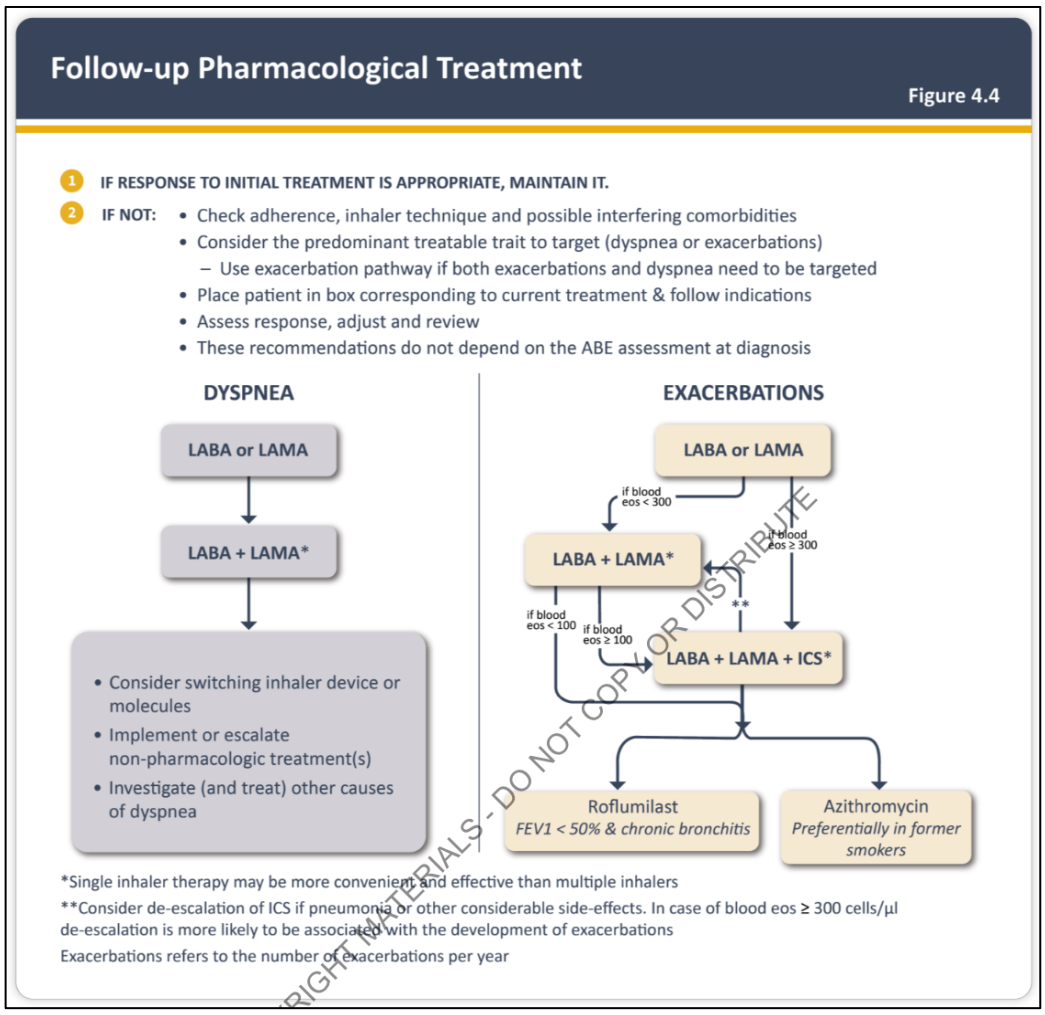




- **Key points for the use of bronchodilators**
  - LABAs and LAMAs are preferred over short acting agents except for patients with only occasional dyspnea (**Evidence A**), and for immediate relief of symptoms in patients already on long-acting bronchodilators.
  - Combined LAMA+LABA is preferred over the use of individual agents.
  - Inhaled bronchodilators are preferred over oral bronchodilators (**Evidence A**).
  - Theophylline is not recommended unless other long-term treatment bronchodilators are unavailable or unaffordable (**Evidence B**).
- **Key points for the use of anti-inflammatory agents**
  - Long term monotherapy with ICS is not recommended (**Evidence A**)
  - If there is an indication for ICS, the combination LABA+LAMA+ICS is preferred over LABA+ICS. This can be given as single or multiple inhaler therapy.
  - If patients with COPD have features of asthma, treatment should always contain an ICS.
  - If there is severe to very severe airflow limitation, chronic bronchitis, or exacerbations, the addition of a PDE4 inhibitor can be considered **(Evidence B**)
  - In former smokers with recurrent exacerbations despite appropriate therapy, can consider macrolides (azithromycin) (**Evidence B**)

- Statin therapy and/or beta blockers are not recommended for prevention of exacerbations (**Evidence A**).

- **Maintenance and Follow-up Treatment**



- **Key points for the use of other pharmacologic treatments**
  - 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 pulmonary hypertension secondary to COPD (**Evidence B**)

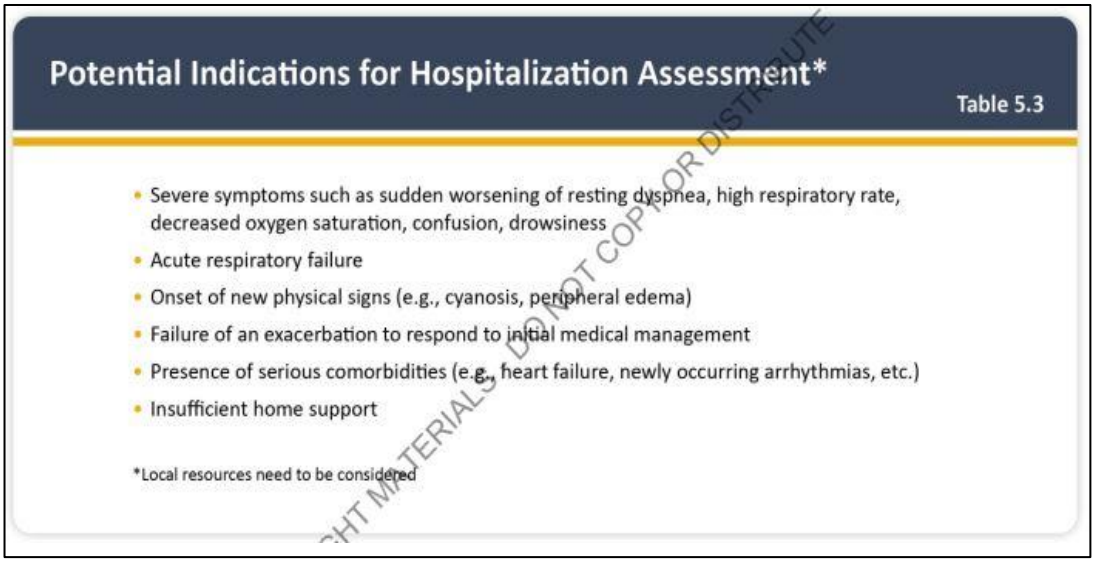
  - Low dose long acting oral and parenteral opioids may be considered for treating dyspnea in COPD patients with severe disease (**Evidence B**).
- **Non-pharmacologic management of COPD**
  - Smoking cessation
  - Recommend a combination of aerobic exercise (sustained effort or interval training) with strength training, as this has better outcomes than either method alone.
  - If in groups B or E, recommend formal rehabilitation program.
  - Nutritional support to prevent or treat COPD-associated malnutrition and weight loss.
  - Long term oxygen therapy if PaO2 is at or below 55 mmHg (SaO2 at or below 88%) with or without hypercapnia, or if PaO2 is between 55 mmHg and 60 mmHg (SaO2 of 88%) and there is evidence of pulmonary hypertension, congestive cardiac failure, or polycythemia.
  - Ventilatory support can be used in stable, very severe COPD – non-invasive devices can be used in the home setting.
  - Interventional bronchoscopy and surgery: lung volume reduction, surgical bullectomy, lung transplantation.

- **When to Refer to Pulmonology**
  - Uncontrolled symptoms despite inhaler therapy
  - Poor response to inhaler therapy
  - Frequent changes in medications
  - Advanced disease
  - Questionable diagnosis

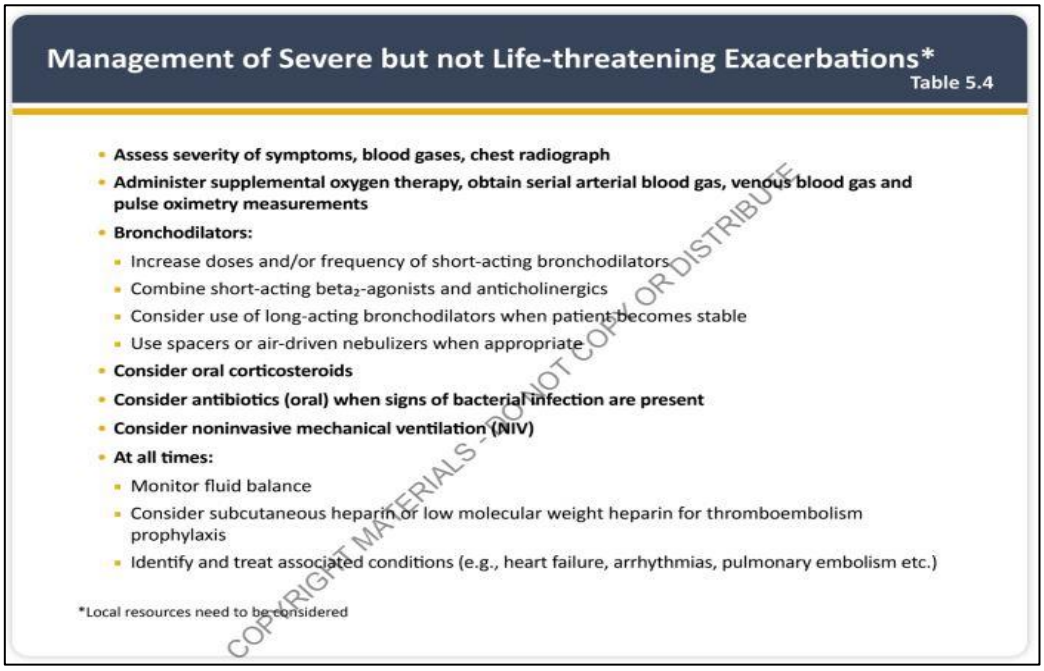
MANAGEMENT OF EXACERBATIONS

- An exacerbation of COPD is defined as an acute worsening of respiratory symptoms that results in additional therapy.
- As the symptoms are not specific to COPD, relevant differential diagnoses should be considered.
- Exacerbations of COPD can be precipitated by several factors. The most common causes are respiratory tract infections.
- The goal for treatment of COPD exacerbations is to minimize the negative impact of the current exacerbation and to prevent subsequent events.

- **Medications**
    - Short-acting inhaled beta2-agonists with or without short-acting anticholinergics are recommended as the initial bronchodilators to treat an acute exacerbation (**Evidence C**).
    - Maintenance therapy with long-acting bronchodilators should be initiated as soon as possible before hospital discharge.
    - Systemic corticosteroids can improve lung function (FEV1), oxygenation and shorten recovery time and hospitalization duration. Duration of therapy should not be more than 5-7 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 be 5-7 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**).
- Following an exacerbation, appropriate measures for exacerbation prevention should be initiated.



- **Recommended classification system for severity of COPD exacerbation:**
    - **No respiratory failure**: Respiratory rate: ≤ 24 breaths per minute; heart rate < 95 beats per minute, no use of accessory respiratory muscles; no changes in mental status; hypoxemia improved with supplemental oxygen given via Venturi mask 24-35% inspired oxygen (FiO2); no increase in PaCO2.
    - **Acute respiratory failure– non-life threatening**: Respiratory rate: > 24 breaths per minute; using accessory respiratory muscles; no change in mental status; hypoxemia improved with supplemental oxygen via Venturi mask > 35% FiO2; hypercarbia i.e., PaCO2 increased compared with baseline or elevated 50-60 mmHg.
    - **Acute respiratory failure – life threatening**: Respiratory rate: > 24 breaths per minute; using accessory respiratory muscles; acute changes in mental status; hypoxemia not improved with supplemental oxygen via Venturi mask or requiring FiO2 > 40%; hypercarbia i.e., PaCO2 increased compared with baseline or elevated > 60 mmHg or the presence of acidosis (pH ≤ 7.25).
- **Indications for Noninvasive Mechanical Ventilation**
    - Respiratory acidosis, severe dyspnea with signs of fatigue (accessory muscles, paradoxical abdominal motion, intercostal retractions
    - Persistent hypoxemia despite supplemental oxygen
- **Indications for Invasive Ventilation**
    - Unable to tolerate noninvasive ventilation.
    - Status post respiratory or cardiac arrest.
    - Persistent hypoxemia despite supplemental oxygen.
    - 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 arrythmias



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

COPD AND CO-MORBIDITIES

- COPD often exists with co-morbid diseases that may have a significant impact on disease course.
- In general, the presence of co-morbidities should not alter COPD treatment and co-morbidities should be treated per usual standards regardless of the presence of COPD.
- Lung cancer is frequently seen in patients with COPD and is a main cause of death.
  - Annual low-dose CT (LDCT) is recommended for lung cancer screening in patients with COPD due to smoking according to recommendations for the general population (ages 50-80, have a 20 pack-year history, currently smoke, or quit within the past 15 years, and will likely tolerate lung surgery and/or treatment of a lung tumor).[4.]
  - Annual LDCT is not recommended for lung cancer screening in patients with COPD not due to smoking due to insufficient data to establish benefit over harm.
- Cardiovascular diseases are common and important co-morbidities in COPD.
  - Heart failure prevalence in COPD ranges from 20-70% and may mimic COPD.
  - Ischemic heart disease: Increased incidence of cardiovascular events during and for at least 90 days after COPD exacerbation.

    - Arrythmias: Atrial fibrillation is very common and should not alter COPD treatment with long-acting beta-2 agonist therapy.
- Osteoporosis, depression/anxiety, and cognitive impairment are frequent, important co-morbidities 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.
- *See the full GOLD document for further recommendations.*

COVID-19 AND COPD

- Patients with COPD presenting with new or worsening respiratory symptoms, fever, and/or any other symptoms that could be COVID-19 related, even if these are mild, should be tested for possible infection with SARS-CoV-2.
- Patients should keep taking their oral and inhaled respiratory medication for COPD as directed.
- During periods of high prevalence of COVID-19 in the community, limit spirometry for patients requiring urgent or essential tests for the diagnosis of COPD, or to assess preoperative lung function.
- Patients should be encouraged to use reputable resources for medical information regarding COVID-19 and its management.

APPENDIX: MEDICATIONS FOR COPD[5]

a. Only long-acting inhalers specifically approved for COPD are included.
b. May differ from product labeling.
c. Wholesale cost for 30-day supply of highest strength of generic if available unless otherwise specified. For short-acting agents, cost is for 200 inhalations.

Inhalers for COPD			
Medication(a)	**Dosing Frequency(b)**	**Cost(c)**	**Adverse Reactions of Note**
Short-acting Bronchodilators			
Beta-2 agonists			
Albuterol (Salbutamol) (ProAir HFA, ProAir Digihaler, ProAir RespiClick, Proventil HFA, Ventolin HFA)	2 inhalations every 4-6 hours as needed	$91	Tachycardia, excitement/nervousness, tremors, paradoxical bronchospasm
Levalbuterol (Xopenex HFA)	2 inhalations every 4-6 hours as needed	$74	Headache, rhinitis
Anticholinergic			
Ipratropium (Atrovent HFA)	2 inhalations every 6 hours	Atrovent HFA $550	Bronchitis
Combination Beta-2 agonist/Anticholinergic			
Albuterol/ipratropium (Combivent Respimat)	1 inhalation four times daily; May take up to 2 additional inhalations daily as needed	Combivent Respimat $570	
Long-Acting Beta-2 agonists (LABAs)			
Olodaterol (Striverdi Respimat)	2 inhalations once daily	Striverdi Respimat $303	Nasopharyngitis
Salmeterol (Serevent Diskus)	1 inhalation twice daily	Serevent Diskus $508	Headache
Long-Acting Antimuscarinic agents (LAMAs)			
Aclidinium (Tudorza Pressair)	1 inhalation twice daily	Tudorza Pressair $374	
Tiotropium (Spiriva HandiHaler, Spiriva Respimat)	HandiHaler: 1 capsule inhaled once daily; each capsule should be inhaled twice. Respimat: 2 inhalations once daily	Spiriva HandiHaler $614 Respimat $614	Xerostomia, pharyngitis, upper respiratory tract infections
Umeclidinium	1 inhalation once daily	$386	

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(Incruse Ellipta)			
Combination LABA/LAMA			
Olodaterol/Tiotropium (Stiolto Respimat)	2 inhalations once daily	Stiolto Respimat $90	Nasopharyngitis
Vilanterol/Umeclidinium (Anoro Ellipta)	1 inhalation once daily	Anoro Ellipta $285	
Formoterol/Aclidinium (Duaklir Pressair)	1 inhalation twice daily	Duaklir Pressair $748	
Formoterol/Glycopyrrolate (Bevespi Aerosphere)	2 inhalations twice daily	Bevespi Aerosphere $503	
Combination LABA/Corticosteroid			
Formoterol/Budesonide (Breyna, Symbicort)	2 inhalations twice daily, except 1 inhalation twice daily with 400 mcg/12 mcg dosage	$403	Headache, nasopharyngitis, upper respiratory tract infections
Salmeterol/Fluticasone propionate (Advair Diskus, Advair HFA, AirDuo Digihaler, AirDuo RespiClick, Wixela Inhub)	1 inhalation twice daily	$163	Headache, upper respiratory tract infections
Vilanterol/Fluticasone furoate (Breo Ellipta)	1 inhalation once daily	$437	
Combination LABA/Corticosteroid/Anticholinergic			
Fluticasone/Umeclidium/ Vilanterol (Trelegy Ellipta)	1 inhalation once daily	$357	Nasopharyngitis, pharyngitis
Budesonide/Glycopyrrolate/ Formoterol (Breztri Aerosphere)	2 inhalations twice daily	$414	
Other Agents			
Methylxanthines			
Theophylline	Variable depending on formulation. Toxicity is dose related; drug levels should be monitored	$362 (generic twice daily product)	Tachycardia, headache, tremor, nausea
Systemic Corticosteroids			
Prednisone	Once daily by mouth (Usually, 40 mg once daily for 5 days)	$0.50 per day – therapy duration varies)	Increased appetite, fluid retention, electrolyte changes, weight gain, hypertension

Methylprednisolone	60-125 mg 1-4 times daily IV followed by oral therapy (prednisone preferred for oral route)	$4 -$8 per day – therapy duration varies	Hypertension, fluid retention, electrolyte changes
Phosphodiesterase-4 Inhibitor			
Roflumilast (Daliresp)	250 mcg once daily by mouth for 4 weeks followed by 500mcg once daily	$517	Weight loss, diarrhea

Patient Education:

https://www.cdc.gov/copd/infographics/copd-awareness.html

https://www.cdc.gov/copd/basics-about.html

https://www.uptodate.com/contents/chronic-obstructive-pulmonary-disease-copd-the-basics?search=COPD&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

https://www.uptodate.com/contents/medicines-for-chronic-obstructive-pulmonary-disease-copd-the-basics?search=COPD&topicRef=4649&source=see_link

Patient education videos (in English and in Spanish) on proper use of metered dose inhalers with and without spacers can be found at: https://www.cdc.gov/asthma/inhaler_video/default.htm

References:

1) https://www.cdc.gov/copd/data.html
2) Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Lung Disease 2023 Report. Global Initiative for Chronic Obstructive Lung Disease. Available from: http://www.goldcopd.org/.
3) Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices – United States, 2023. MMWR Morb Mortal Wkly Rep 2023; 72:793-801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4

4) Screening for Lung Cancer – US Preventive Services Task Force Recommendation Statement. JAMA. 2021; 325:962-970.

5) Drug Information Articles on https://www.uptodate.com/contents/table-of-contents/drug-information/general-drug-information (accessed January 8, 2024).