

# COPD: Updating Our Diagnosis and Management

**Kaleb Veit, DO**

Assistant Professor

Department of Internal Medicine

Division of Pulmonary, Critical Care, and Sleep Medicine

University of Nebraska Medical Center



**University of Nebraska  
Medical Center**<sup>SM</sup>

**Global Initiative for  
Chronic Obstructive  
Lung Disease**

**2024**

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

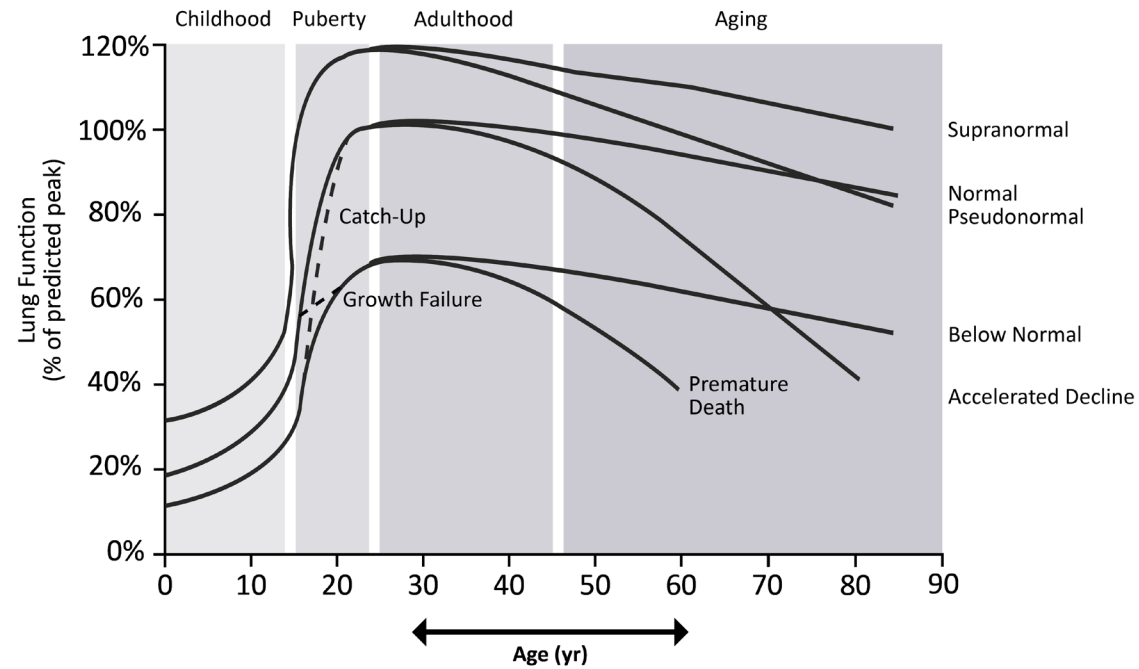
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# FEV1 Trajectories (TR) Over the Life Course

Figure 1.1

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



## Clinical Indicators for Considering a Diagnosis of COPD

Figure 2.1

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

### Dyspnea that is

Progressive over time

Worse with exercise

Persistent

### Recurrent wheeze

### Chronic cough

May be intermittent and may be non-productive

### Recurrent lower respiratory tract infections

### History of risk factors

Tobacco smoke (including popular local preparations)

Smoke from home cooking and heating fuels

Occupational dusts, vapors, fumes, gases and other chemicals

Host factors (e.g., genetic factors, developmental abnormalities, low birthweight, prematurity, childhood respiratory infections etc.)



## Other Causes of Chronic Cough

Figure 2.2

### INTRATHORACIC

- Asthma
- Lung Cancer
- Tuberculosis
- Bronchiectasis
- Left Heart Failure
- Interstitial Lung Disease
- Cystic Fibrosis
- Idiopathic Cough

### EXTRATHORACIC

- Chronic Allergic Rhinitis
- Post Nasal Drip Syndrome (PNDS)
- Upper Airway Cough Syndrome (UACS)
- Gastroesophageal Reflux
- Medication (e.g., ACE Inhibitors)



## Role of Spirometry in COPD

Figure 2.6

- **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



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

Figure 2.7

In COPD patients (FEV1/FVC < 0.7):

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



## Modified MRC Dyspnea Scale

Figure 2.8

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
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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





# CAT™ Assessment

Figure 2.9

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 <input checked="" type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I am very sad	Score
I never cough	0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 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 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 <input type="checkbox"/> 5	I have no energy at all	

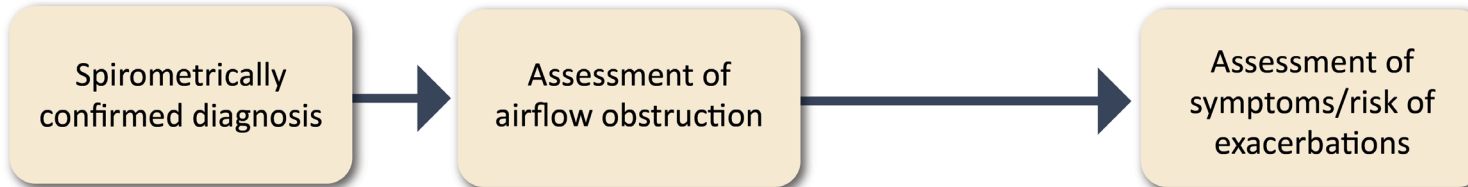
Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

**TOTAL SCORE:**



# GOLD ABE Assessment Tool

Figure 2.10



Post-bronchodilator FEV1/FVC < 0.7

GRADE	FEV1 (% predicted)	EXACERBATION HISTORY (PER YEAR)	SYMPTOMS	
<b>GOLD 1</b>	≥ 80	≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	<b>E</b>	
<b>GOLD 2</b>	50-79	0 or 1 moderate exacerbations (not leading to hospitalization)	<b>A</b>	<b>B</b>
<b>GOLD 3</b>	30-49			
<b>GOLD 4</b>	< 30		mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10



## Goals for Treatment of Stable COPD

Figure 3.1

- Relieve Symptoms
- Improve Exercise Tolerance
- Improve Health Status



**REDUCE SYMPTOMS**

**AND**

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



**REDUCE RISK**



## Identify & Reduce Risk Factor Exposure

Figure 3.3

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



## Brief Strategies to Help the Patient Willing to Quit

Figure 3.4

<b>ASK</b>	<p>Systematically identify all tobacco users at every visit</p> <p><i>Implement an office-wide system that ensures that, for EVERY patient at EVERY clinic visit, tobacco-use status is queried and documented</i></p>
<b>ADVISE</b>	<p>Strongly urge all tobacco users to quit</p> <p><i>In a clear, strong, and personalized manner, urge every tobacco user to quit</i></p>
<b>ASSESS</b>	<p>Determine willingness and rationale of patient's desire to make a quit attempt.</p> <p><i>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)</i></p>
<b>ASSIST</b>	<p>Aid the patient in quitting</p> <p><i>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</i></p>
<b>ARRANGE</b>	<p>Schedule follow-up contact</p> <p><i>Schedule follow-up contact, either in person or via telephone</i></p>



## Treating Tobacco Use and Dependence

Figure 3.5

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

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



## Vaccination for Stable COPD

Figure 3.6

- Influenza vaccination is recommended for 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) for people with COPD (**Evidence B**)
- Pneumococcal vaccination has been shown to reduce the incidence of community-acquired pneumonia and exacerbations for people with COPD (**Evidence B**)
- The CDC recommends the new respiratory syncytial virus (RSV) vaccine for individuals over 60 years and/or with chronic heart or lung disease (**Evidence A**)
- 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**)



# Initial Pharmacological Treatment

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

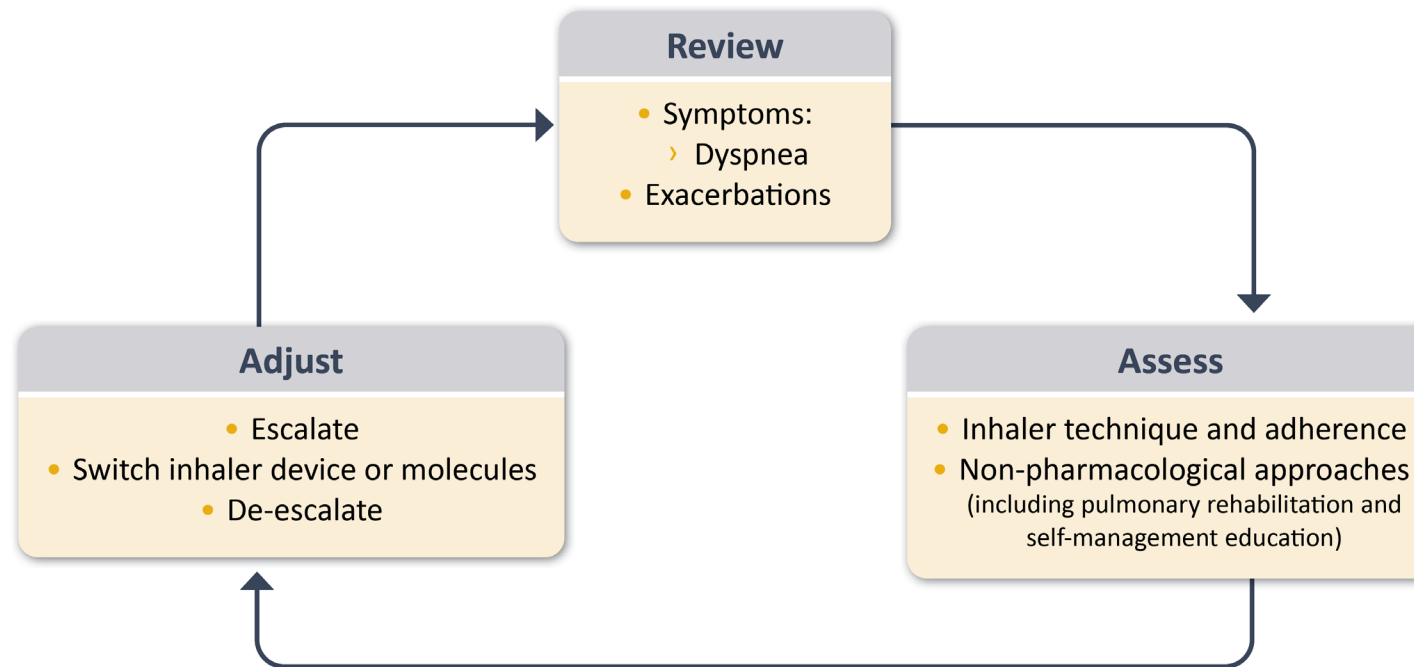
Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.





## Management Cycle

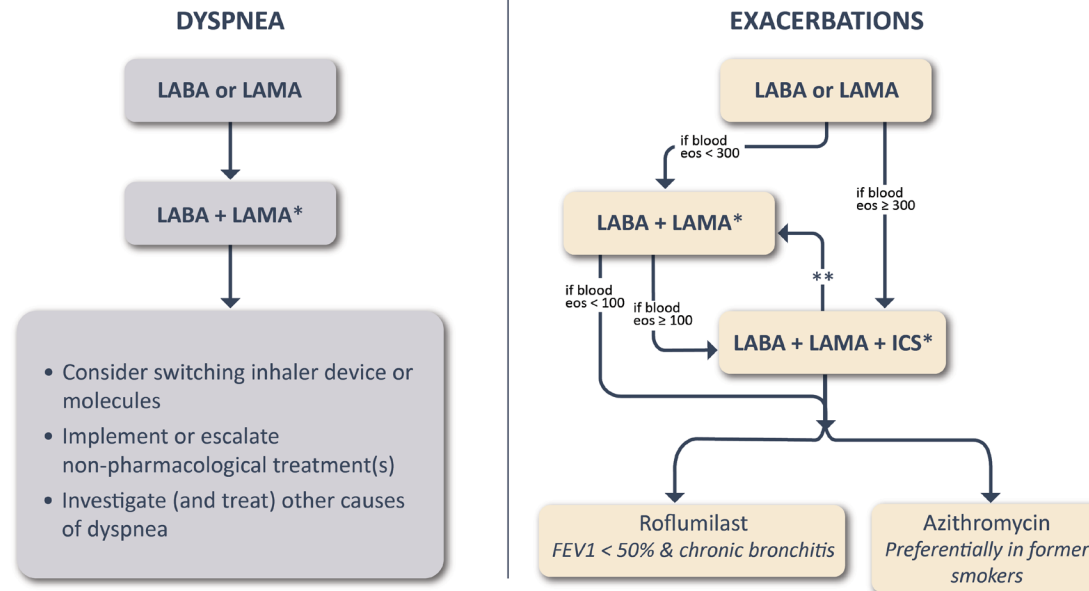
Figure 3.8



# Follow-up Pharmacological Treatment

Figure 3.9

- 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; single inhalers improve adherence to treatment

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

Exacerbations refers to the number of exacerbations per year



## Key Points for Inhalation of Drugs

Figure 3.10

- When a treatment is given by the inhaled route, the importance of education and training in inhaler device technique cannot be over-emphasized
- The choice of inhaler device has to be individually tailored and will depend on access, cost, prescriber, and most importantly, patient's ability and preference
- It is essential to provide instructions and to demonstrate the proper inhalation technique when prescribing a device, to ensure that inhaler technique is adequate and to re-check at each visit that patients continue to use their inhaler correctly
- Inhaler technique (and adherence to therapy) should be assessed before concluding that the current therapy is insufficient



## Basic Principles for Appropriate Inhalation Device Choice

Figure 3.11

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- 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 maneuver for the device must be assessed:
  - Dry powder inhalers are appropriate only if the patient can make a forceful and deep inhalation. Check visually that the patient can inhale forcefully through the device - if there is doubt assess objectively or choose alternative device
  - Metered-dose inhalers and, to a lesser extent, soft mist inhalers require coordination between device triggering and inhalation and patients need to be able to perform a slow and deep inhalation. Check visually that the patient can inhale slowly and deeply from the device - if there is doubt consider adding a spacer/VHC or choose an alternative device
  - For patients unable to use an MDI (with or without spacer/VHC), SMI or DPI a nebulizer should be considered
- Other factors to consider include size, portability, cost
- Smart inhalers may be useful if there are issues with adherence/persistence or inhalation technique (for devices that can check it)
- Physicians should prescribe only devices they (and the other members of the caring team) know how to use



# Non-Pharmacological Management of COPD\*

Figure 3.12

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

\*Can include pharmacological treatment



## Oxygen Therapy and Ventilatory Support in Stable COPD

Figure 3.14

### 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**)

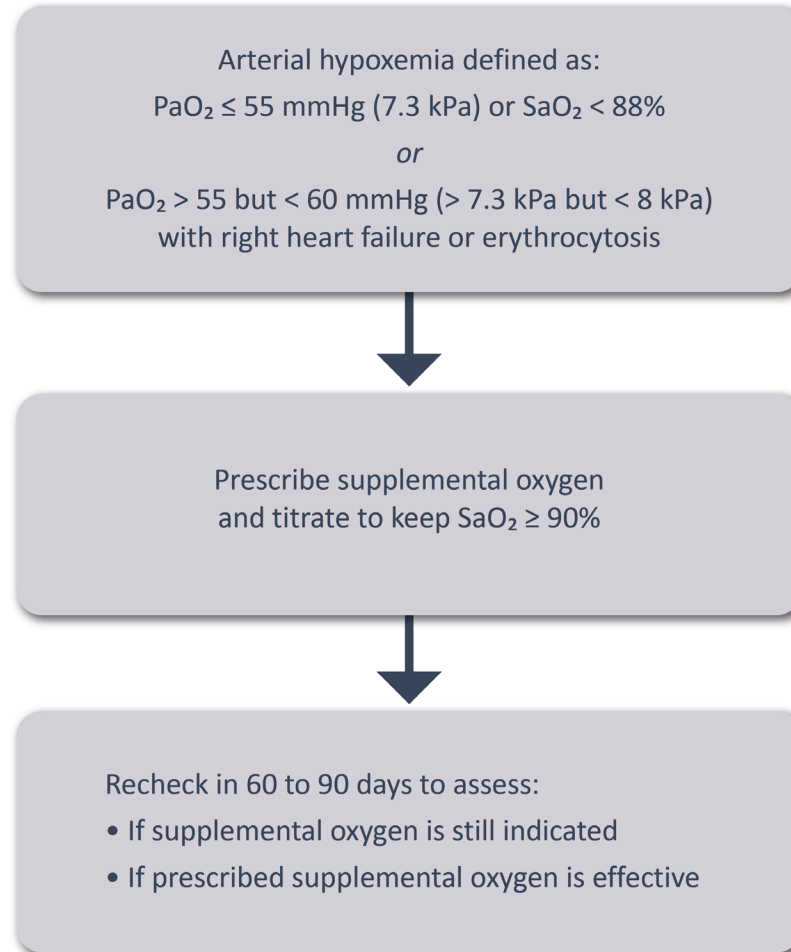
### Ventilatory Support

- NPPV may improve hospitalization-free survival in selected patients after recent hospitalization, particularly in those with pronounced daytime persistent hypercapnia ( $\text{PaCO}_2 > 53$  mmHg) (**Evidence B**)
- In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, long-term noninvasive ventilation may be considered (**Evidence B**)



## Prescription of Supplemental Oxygen to COPD Patients

Figure 3.15



## Palliative Care, End of Life and Hospice Care in COPD

Figure 3.16

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





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

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



# Commonly Used Maintenance Medications in COPD\*

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Generic Drug Name	Inhaler Type	DELIVERY OPTIONS			Duration of Action
		Nebulizer	Oral	Injection	
<b>BETA<sub>2</sub>-Agonists</b>					
<b>Short-acting (SABA)</b>					
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
<b>Long-acting (LABA)</b>					
Arformoterol		✓			12 hours
Formoterol	DPI	✓			12 hours
Indacaterol	DPI				24 hours
Olodaterol	SMI				24 hours
Salmeterol	MDI & DPI				12 hours
<b>Anticholinergics</b>					
<b>Short-acting (SAMA)</b>					
Ipratropium bromide	MDI	✓			6-8 hours
Oxipropium bromide	MDI				7-9 hours
<b>Long-acting (LAMA)</b>					
Acclidinium bromide	DPI				MDI 12 hours
Glycopyrronium bromide	DPI		solution	✓	12-24 hours
Tiotropium	DPI, SMI, MDI				24 hours
Umeclidinium	DPI				24 hours
Glycopyrronium		✓			12 hours
Revefenacin		✓			24 hours
<b>Combination Short-Acting Beta<sub>2</sub>-Agonist Plus Anticholinergic in One Device (SABA+SAMA)</b>					
Fenoterol/ipratropium	SMI	✓			6-8 hours
Salbutamol/ipratropium	SMI, MDI	✓			6-8 hours
<b>Combination Long-Acting Beta<sub>2</sub>-Agonist Plus Anticholinergic in One Device (LABA+LAMA)</b>					
Formoterol/acclidinium	DPI				12 hours
Formoterol/glycopyrronium	MDI				12 hours
Indacaterol/glycopyrronium	DPI				12-24 hours
Vilanterol/umeclidinium	DPI				24 hours
Olodaterol/tiotropium	SMI				24 hours
<b>Methylxanthines</b>					
Aminophylline			solution	✓	Variable, up to 24 hours
Theophylline (SR)			pill	✓	Variable, up to 24 hours
<b>Combination of Long-Acting Beta<sub>2</sub>-Agonist Plus Corticosteroid in One Device (LABA+ICS)</b>					
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
<b>Triple Combination in One Device (LABA+LAMA+ICS)</b>					
Fluticasone/umeclidinium/vilanterol	DPI				24 hours
Beclometasone/formoterol/glycopyrronium	MDI, DPI				12 hours
Budesonide/formoterol/glycopyrrolate	MDI				12 hours
<b>Phosphodiesterase-4 Inhibitors</b>					
Roflumilast			pill		24 hours
<b>Mucolytic Agents</b>					
Erdosteine			pill		12 hours
Carbocysteine <sup>†</sup>			pill		
N-acetylcysteine <sup>†</sup>			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.



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



## Anti-Inflammatory Therapy in Stable COPD

Figure 3.20

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<p><b>Inhaled Corticosteroids</b></p>	<ul style="list-style-type: none"> <li>Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease (<b>Evidence A</b>)</li> <li>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 (<b>Evidence A</b>)</li> <li>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</li> <li>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 (<b>Evidence A</b>). 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</li> <li>If patients with COPD have features of asthma, treatment should always contain an ICS</li> <li>Independent of ICS use, there is evidence that a blood eosinophil count &lt; 2% increases the risk of pneumonia (<b>Evidence C</b>)</li> <li>Combinations can be given as single or multiple inhaler therapy. Single inhaler therapy may be more convenient and effective than multiple inhalers</li> </ul>
<p><b>Oral Glucocorticoids</b></p>	<ul style="list-style-type: none"> <li>Long-term use of oral glucocorticoids has numerous side effects (<b>Evidence A</b>) with no evidence of benefits (<b>Evidence C</b>)</li> </ul>
<p><b>PDE4 Inhibitors</b></p>	<ul style="list-style-type: none"> <li>In patients with chronic bronchitis, severe to very severe COPD and a history of exacerbations:                             <ul style="list-style-type: none"> <li>Roflumilast improves lung function and reduces moderate and severe exacerbations (<b>Evidence A</b>)</li> </ul> </li> </ul>
<p><b>Antibiotics</b></p>	<ul style="list-style-type: none"> <li>Long-term azithromycin and erythromycin therapy reduces exacerbations over one year (<b>Evidence A</b>)</li> <li>Preferentially, but not only in former smokers with exacerbations despite appropriate therapy, azithromycin can be considered (<b>Evidence B</b>)</li> <li>Treatment with azithromycin is associated with an increased incidence of bacterial resistance (<b>Evidence A</b>) and hearing test impairments (<b>Evidence B</b>)</li> </ul>
<p><b>Mucoregulators and Antioxidant Agents</b></p>	<ul style="list-style-type: none"> <li>Regular treatment with mucolytics such as erdosteine, carbocysteine and NAC reduces the risk of exacerbations in select populations (<b>Evidence B</b>)</li> <li>Antioxidant mucolytics are recommended only in selected patients (<b>Evidence A</b>)</li> </ul>
<p><b>Other Anti-Inflammatory Agents</b></p>	<ul style="list-style-type: none"> <li>Statin therapy is not recommended for prevention of exacerbations (<b>Evidence A</b>)</li> <li>Simvastatin does not prevent exacerbations in COPD patients at increased risk of exacerbations and without indications for statin therapy (<b>Evidence A</b>). 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 (<b>Evidence C</b>)</li> <li>Leukotriene modifiers have not been tested adequately in COPD patients</li> </ul>



## Factors to Consider when Initiating ICS Treatment

Figure 3.21

### 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<sup>#</sup>  
 $\geq 2$  moderate exacerbations of COPD per year<sup>#</sup>  
 Blood eosinophils  $\geq 300$  cells/ $\mu$ L  
 History of, or concomitant asthma

#### FAVORS USE

1 moderate exacerbation of COPD per year<sup>#</sup>  
 Blood eosinophils 100 to  $< 300$  cells/ $\mu$ L

#### AGAINST USE

Repeated pneumonia events  
 Blood eosinophils  $< 100$  cells/ $\mu$ L  
 History of mycobacterial infection

<sup>#</sup>despite appropriate long-acting bronchodilator maintenance therapy (see Figures 3.7 & 3.18 for recommendations); \*note that blood eosinophils should be seen as a continuum; quoted values represent approximate cut-points; eosinophil counts are likely to fluctuate.

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## Other Pharmacological Treatments

Figure 3.22

### Alpha-1 Antitrypsin Augmentation Therapy

- Intravenous augmentation therapy may slow down the progression of emphysema (**Evidence B**)

### Antitussives

- There is no conclusive evidence of a beneficial role of antitussives in people with COPD (**Evidence C**)

### Vasodilators

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

### Opioids

- Low-dose long acting oral and parenteral opioids may be considered for treating dyspnea in COPD patients with severe disease (**Evidence B**)

### Pulmonary Hypertension Therapy

- Drugs approved for primary pulmonary hypertension are not recommended for patients with a pulmonary hypertension secondary to COPD (**Evidence B**)



## Pulmonary Rehabilitation, Self-Management and Integrative Care in COPD

Figure 3.23

<b>Pulmonary Rehabilitation</b>	<ul style="list-style-type: none"><li>• Rehabilitation is indicated in all patients with relevant symptoms and/or a high risk for exacerbation (<b>Evidence A</b>)</li><li>• Pulmonary rehabilitation improves dyspnea, health status and exercise tolerance in stable patients (<b>Evidence A</b>)</li><li>• Pulmonary rehabilitation reduces hospitalization among patients who have had a recent exacerbation (<math>\leq 4</math> weeks from prior hospitalization) (<b>Evidence B</b>)</li><li>• Pulmonary rehabilitation leads to a reduction in symptoms of anxiety and depression (<b>Evidence A</b>)</li></ul>
<b>Education and Self-Management</b>	<ul style="list-style-type: none"><li>• Education is needed to change patient's knowledge but there is no evidence that used alone it will change patient behavior (<b>Evidence C</b>)</li><li>• Self-management intervention with communication with a health care professional improves health status and decreases hospitalizations and emergency department visits (<b>Evidence B</b>)</li></ul>
<b>Integrated Care Programs</b>	<ul style="list-style-type: none"><li>• Integrative care and telehealth have no demonstrated benefit at this time (<b>Evidence B</b>)</li></ul>
<b>Physical Activity</b>	<ul style="list-style-type: none"><li>• Physical activity is a strong predictor of mortality (<b>Evidence A</b>). People with COPD should be encouraged to increase their level of physical activity although we still do not know how to best ensure the likelihood of success</li></ul>



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

Figure 3.24

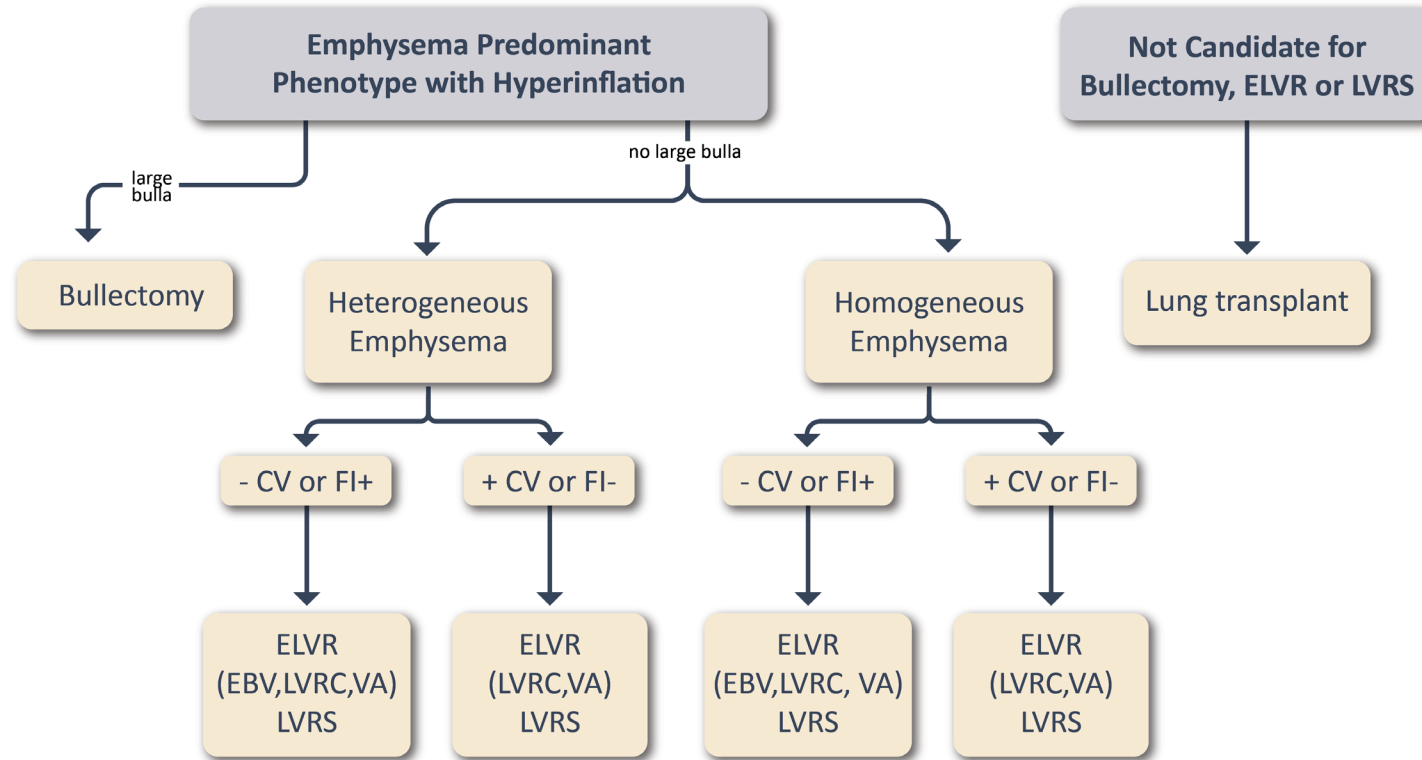
Symptoms	Chronic Mucus Production	Exacerbations	Dyspnea
Disorders	<ul style="list-style-type: none"> <li>Chronic bronchitis</li> </ul>	<ul style="list-style-type: none"> <li>Acute and chronic bronchitis</li> <li>Bulla</li> <li>Emphysema</li> <li>Tracheobronchomalcia</li> </ul>	<ul style="list-style-type: none"> <li>Bulla</li> <li>Emphysema</li> <li>Tracheobronchomalcia</li> </ul>
Surgical and Bronchoscopic Interventions	<ul style="list-style-type: none"> <li>Nitrogen cryospray</li> <li>Rheoplasty</li> </ul>	<ul style="list-style-type: none"> <li>Targeted lung denervation</li> </ul>	<ul style="list-style-type: none"> <li>Giant bullectomy</li> <li>Large airway stenting</li> <li>EBV</li> <li>Coil</li> <li>Thermal vapor ablation</li> <li>Lung sealants</li> <li>LVRS</li> <li>Lung transplantation</li> </ul>





# Surgical and Interventional Therapies in Advanced Emphysema

Figure 3.25



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.



# Interventional Therapy in Stable COPD

Table 3.26

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<b>Lung Volume Reduction Surgery</b>	<ul style="list-style-type: none"><li>• Lung volume reduction surgery improves survival in severe emphysema patients with an upper-lobe emphysema and low post-rehabilitation exercise capacity (<b>Evidence A</b>)</li></ul>
<b>Bullectomy</b>	<ul style="list-style-type: none"><li>• In selected patients, bullectomy is associated with decreased dyspnea, improved lung function and exercise tolerance (<b>Evidence C</b>)</li></ul>
<b>Transplantation</b>	<ul style="list-style-type: none"><li>• In appropriately selected patients with very severe COPD, lung transplantation has been shown to improve quality of life and functional capacity (<b>Evidence C</b>)</li><li>• In patients with very severe COPD (progressive disease, BODE score of 7 to 10, and not candidates for lung volume reduction) lung transplantation may be considered for referral with at least one of the following: (1) history of hospitalization for exacerbation associated with acute hypercapnia (<math>P_{CO_2} &gt; 50</math> mmHg); (2) pulmonary hypertension and/or cor pulmonale, despite oxygen therapy; or (3) <math>FEV_1 &lt; 20\%</math> and either <math>DL_{CO} &lt; 20\%</math> or homogenous distribution of emphysema (<b>Evidence C</b>)</li></ul>
<b>Bronchoscopic Interventions</b>	<ul style="list-style-type: none"><li>• 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 (<b>Evidence A</b>); Lung coils (<b>Evidence B</b>); Vapor ablation (<b>Evidence B</b>)</li></ul>
<b>Bronchoscopic Interventions Under Study</b>	<ul style="list-style-type: none"><li>• 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</li></ul>



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

Figure 4.1

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<b>Most frequent</b>	<b>Pneumonia</b>
	<ul style="list-style-type: none"><li>• Chest radiograph</li></ul>
	<b>Pulmonary embolism</b>
<b>Less frequent</b>	<ul style="list-style-type: none"><li>• Clinical probability assessment (Hemoptysis, surgery, fracture, history of cancer, DVT)</li><li>• D-dimer</li><li>• CT angiography for pulmonary embolism</li></ul>
	<b>Heart failure</b>
	<ul style="list-style-type: none"><li>• Chest radiograph</li><li>• NT Pro-Brain Natriuretic Peptide (Pro-BNP) and BNP</li><li>• Echocardiography</li></ul>
	<b>Pneumothorax, pleural effusion</b>
	<ul style="list-style-type: none"><li>• Chest radiograph</li><li>• Thoracic ultrasound</li></ul>
	<b>Myocardial infarction and/or cardiac arrhythmias (atrial fibrillation/flutter)</b>
	<ul style="list-style-type: none"><li>• Electrocardiography</li><li>• Troponin</li></ul>



## Potential Indications for Hospitalization Assessment\*

Figure 4.4

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

\*Local resources need to be considered



## Management of Severe but not Life-threatening Exacerbations\*

Figure 4.5

**Assess severity of symptoms, blood gases, chest radiograph**

---

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

---

**Bronchodilators:**

- Increase doses and/or frequency of short-acting bronchodilators
  - Combine short-acting beta 2-agonists and anticholinergics
  - Consider use of long-acting bronchodilators when patient becomes stable
  - Use spacers or air-driven nebulizers when appropriate
- 

**Consider oral corticosteroids**

---

**Consider antibiotics (oral) when signs of bacterial infection are present**

---

**Consider noninvasive mechanical ventilation (NIV)**

---

**At all times:**

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

\*Local resources need to be considered



## Key Points for the Management of Exacerbations

Figure 4.6

- Short-acting inhaled beta<sub>2</sub>-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 (FEV<sub>1</sub>), 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 Noninvasive Mechanical Ventilation (NIV)

Figure 4.8

**At least one of the following:**

- Respiratory acidosis ( $\text{PaCO}_2 \geq 6.0$  kPa or 45 mmHg and arterial  $\text{pH} \leq 7.35$ )
- Severe dyspnea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as use of respiratory accessory muscles, paradoxical motion of the abdomen, or retraction of the intercostal spaces
- Persistent hypoxemia despite supplemental oxygen therapy



## Indications for Invasive Mechanical Ventilation

Figure 4.9

- Unable to tolerate NIV or NIV failure
- Status post-respiratory or cardiac arrest
- Diminished consciousness, psychomotor agitation inadequately controlled by sedation
- Massive aspiration or persistent vomiting
- Persistent inability to remove respiratory secretions
- Severe hemodynamic instability without response to fluids and vasoactive drugs
- Severe ventricular or supraventricular arrhythmias
- Life-threatening hypoxemia in patients unable to tolerate NIV





## Discharge Criteria and Recommendations for Follow-up

Figure 4.10

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

### 1 – 4 Weeks Follow-up

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

### 12 – 16 Weeks Follow-up

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



# Interventions that Reduce the Frequency of COPD Exacerbations

Figure 4.11

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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)



## Common Risk Factors for the Development of Lung Cancer

Figure 5.1

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



# Questions?

[kveit@unmc.edu](mailto:kveit@unmc.edu)



**University of Nebraska  
Medical Center<sup>SM</sup>**