

COPD and Gold Guideline update

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Objectives

1. **Identify** patients with COPD and **stratify** your approach according to disease severity
2. Utilize **pharmacotherapy** and pulmonary **rehabilitation** proportional to severity according to 2023 GOLD guidelines to maximize function
3. Identify when and how to have **advanced illness conversations** in patients with advanced COPD

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



Global Initiative for Chronic Obstructive Lung Disease (GOLD). <https://goldcopd.org/2023-gold-report-2/> (2023)

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COPD Definition

*A **Heterogeneous** lung condition characterized by **sputum** production and/or exacerbations) due to abnormalities of the **airways** (bronchitis, bronchiolitis) and/or **alveoli** (emphysema) that cause **persistent**, often progressive, **airflow obstruction***

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Causes and Risk Factors

- **Gene(G)-environment(E) interactions** occurring over the lifetime(T) of the individual that can damage the lungs and/or alter their normal development/aging processes.
- Environmental exposures leading to COPD are **tobacco smoking** and the inhalation of **toxic particles and gases** from household and outdoor air pollution and other environmental sources
- Host factors (including **abnormal lung development** and accelerated lung aging) can also contribute
- **α -1 antitrypsin deficiency** is caused by mutations in the SERPINA1 gene
- Other genetic variants have also been associated with reduced lung function and risk of COPD, but more rare

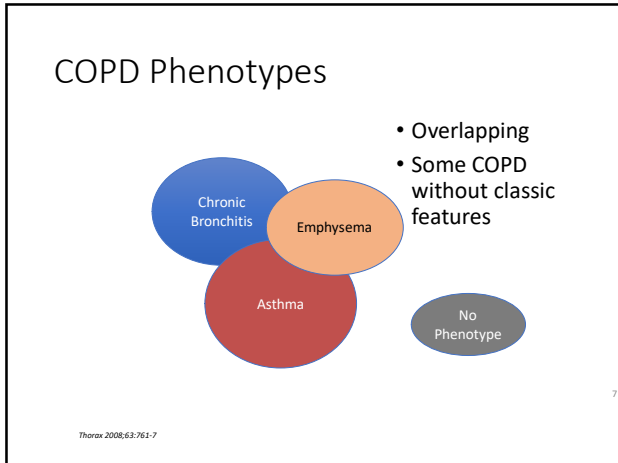
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Epidemiology of COPD

- Third leading cause of death in the US¹
- 15.2% of adults have a diagnosis of COPD in the US²
- \$49 billion dollars annually in the US³
- Worldwide, an estimated 74 million deaths are caused by COPD⁴
- More than ¾ of global cases are in LMIC (low to middle income countries)

¹ CDC 2016, ²Adeloye et al 2015, ³Ford et al, 2015, ⁴WHO Fact sheet 2016

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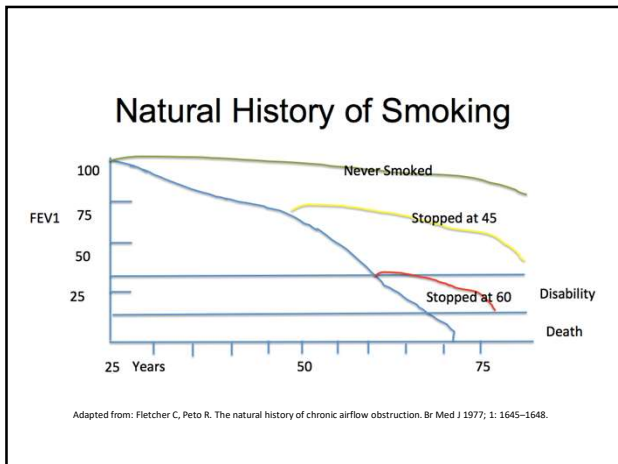
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But some surprises about Tobacco

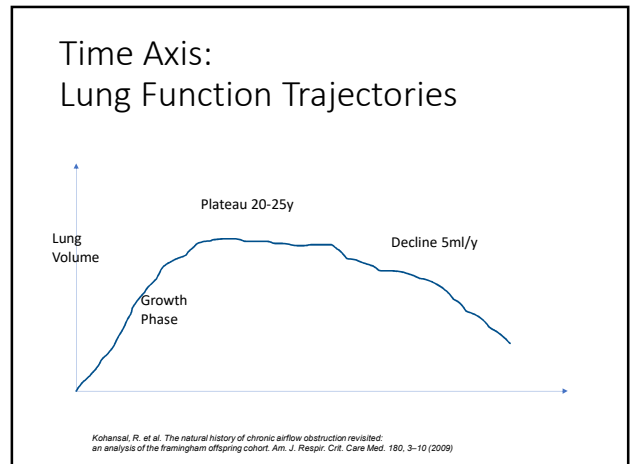
- Only 50% of smokers develop COPD
- Only 20% of 20 pack years develop COPD
- 20% of patients with COPD have never smoked

Wheaton, A. G. et al. Chronic obstructive pulmonary disease and smoking status—United States, 2017. MMWR Morb. Mortal. Wkly. Rep. 68, 533–538 (2019)

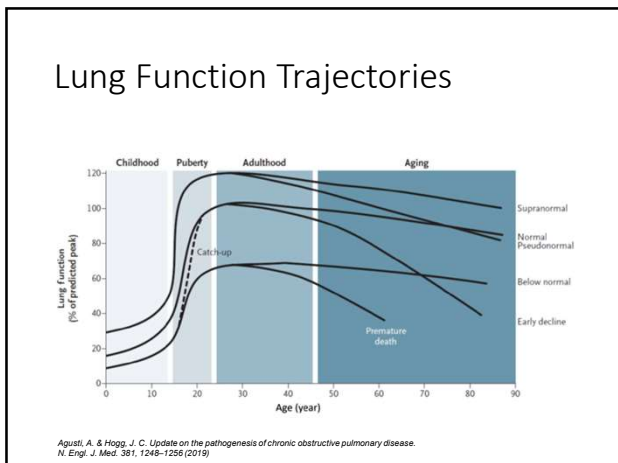
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COPD Etiotypes: Different Natural History

- Non smoking related COPD may have slower lung function decline
- GOLD is assessing variable recommendations depending on etiology
- Male and Female equal rates of COPD
- Female patients with greater risk of obstruction for same exposure

Amaral, A. F. S., Strachan, D. P., Burney, P. G. J. & Jarvis, D. L. Female smokers are at greater risk of airflow obstruction than male smokers. UK Biobank. Am. J. Respir. Crit. Care Med. 195, 1226–1238 (2017).
Sondyaji, R. & Chalmers, J. D. Just breathe: a review of sex and gender in chronic lung disease. Eur. Respir. Rev. 31, 210111 (2022)

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Diagnosis: Office Spirometry

FEV₁ Thresholds: Airflow Obstruction

- Grade 1: Mild FEV₁ > 80%
 - Grade 2: Moderate 50% < FEV₁ < 80%
 - Grade 3: Severe 30% < FEV₁ < 50%
 - Grade 4: Very Severe FEV₁ < 30%
- Compared with predicted values in patients with post-bronchodilator FEV₁/FVC < 70

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Severity of COPD

Obstruction = FEV₁/FVC < 70

Gold Class	Severity	FEV ₁
GOLD 1:	Mild	> 80% pred
GOLD 2:	Moderate	50%-80%
GOLD 3:	Severe	30%-50%
GOLD 4:	Very Severe	<30%

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Diagnostic Criteria FEV₁/FVC

- FEV₁/FVC < 0.7 (post-bronchodilation) measured by spirometry confirms the diagnosis of COPD
- Respiratory symptoms and/or structural lung lesions, low-normal FEV₁, gas trapping, hyperinflation, reduced lung diffusing capacity and/or rapid FEV₁ decline) without a reduced FEV₁/FVC = PRISM
- 'Pre-COPD': The term 'PRISM' (Preserved Ratio Impaired Spirometry) has been proposed to identify those with normal ratio but abnormal spirometry.
- Subjects with Pre-COPD or PRISM are at risk of developing airflow obstruction over time, but not all of them do

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Preserved Ratio Impaired Spirometry (PRISM)

- "Pre-COPD": normal spirometry but radiologic evidence of COPD
- PRISM (Preserved Ratio with Impaired Spirometry):
 - FEV₁/FVC not below 0.7 (therefore no obstruction) but reduced FEV₁



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No Asymptomatic Screening Spirometry

- For **asymptomatic** individuals without any significant exposure to tobacco or other risk factors, **screening spirometry is not indicated**
- In those with symptoms and/or risk factors (e.g., >20 pack-years of smoking, recurrent chest infections, prematurity or other significant early life events), spirometry should be considered as a valid method for **case finding**

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COPD with Comorbid Conditions

- Obesity effecting lung mechanics
- Secondary Pulmonary Hypertension
- Atrial Fibrillation
- Heart Failure with Preserved Lung Function (HFpEF)
- Coronary Artery Disease
- Heart Failure with Reduced Lung Function (HFrEF)

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Opportunities

- COPD is a common, **preventable, and treatable** disease, but extensive under-diagnosis and
- **Misdiagnosis** leads to patients receiving no treatment or incorrect treatment.
- **Earlier diagnosis** of COPD can have a very significant public-health impact.
- **Environmental** factors other than tobacco smoking can contribute to COPD,
- Can start **early in life** and affect young individuals, and that there are precursor conditions
- (Pre-COPD, **PRISM**), opens new windows of opportunity for its prevention, early diagnosis, and
- Prompt and appropriate therapeutic intervention.

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Chronic Cough

Intrathoracic

- Asthma
- Lung Cancer
- TB
- Bronchiectasis
- Left HF
- Interstitial Lung Disease
- Cystic Fibrosis
- Idiopathic Cough

Extrathoracic

- Chronic Allergic Rhinitis
- Post Nasal Drip Syndrome (PNDS)
- Upper Airway Cough Syndrome (UACS)
- GERD
- Medication (ACE)

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Auscultation/ Inhalation

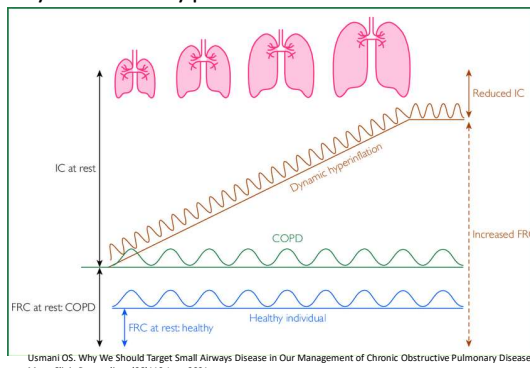
- Inspiratory and / or expiratory may vary
- Absence of Wheeze does not exclude COPD
- Often distant breath sounds limit auscultation due to hyperinflation



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Dynamic Hyperinflation



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OTHER TESTING	Asthma	COPD
Lung Function Test DLCO	N or slight high	Often reduced
LFT: ABG	Normal between exac.	May be chronically abn
LFT: (AHR) Airway Hyperresponsiveness	Not useful on its own But.... Favors Asthma	no
Imaging: HRCT	Normal though air trapping and bronchial thickening may be seen	Air trapping or Bullae. Bronchial Thickening & Pulm HTN
Atopy: IgE or skin test	Not essential but may be suggestive	Conforms to background prevalence (does not r/o COPD)
FENO	>50 ppb in non smoker supports Asthma dx	Usually normal, low in current smokers
Blood Eosinophils	Supports Asthma	May be present during exacerbation
Sputum analysis for inflammatory cells	Not well established	Not well established

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History

- Patient's exposure to risk factors
 - Smoking and environmental exposures (household/outdoor)
- Past medical history, including early life events (prematurity, low birthweight, maternal smoking during pregnancy, passive smoking exposure during infancy), asthma, allergy, sinusitis, or nasal polyps; respiratory infections in childhood; HIV; tuberculosis
- Family history of COPD or other chronic respiratory disease
- Pattern of symptom development:
 - COPD typically develops in adult life and most patients are conscious of increased breathlessness, more frequent or prolonged "winter colds,"
 - Often restriction exercise for a number of years before seeking medical help

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History 2

- Exacerbations or previous hospitalizations for respiratory disorder
- Presence of comorbidities, such as heart disease, osteoporosis, musculoskeletal disorders, anxiety and depression, and malignancies that may also contribute to restriction of activity.
- Impact of disease on patient's life, including limitation of activity, missed work and economic impact, effect on family routines, feelings of depression or anxiety, wellbeing, and sexual activity
- Social and family support available to the patient
- Possibilities for reducing risk factors, especially smoking cessation
- Weight loss, sarcopenia

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mMRC Dyspnea Scale

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

American Thoracic Society 1982 Am Rev Respir Dis. Nov;126(5): 952-6.

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COPD Assessment Test "CAT"

Symptom	Score 1 to 5	
Cough	0 no cough	5 "I cough all the time"
Phlegm	0 No Phlegm	5 "I'm completely full of Phlegm"
Chest Tightness	0 not tight	5 very tight
Breathlessness	0 "When I walk up a hill or a flight of stairs I'm not breathless"	5 very breathless
Activities	0 not limited	5 very limited
Confidence	0 confident leaving home	5 not confident to leave home
Sleep	0 Sleep soundly	5 Difficult Sleeping
Energy	0 Lots of energy	5 No Energy
	< 10	Low
	10 - 20	Medium
	21 - 30	High
	> 30	Very high

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Stratify Patients into 3 Groups



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TREATMENT PLANS

- Smoking Cessation
- Inhaler Choice and Technique
- Inhaled Medication Options
- Financial Implications

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Smoking cessation is key!

- Nicotine replacement and pharmacotherapy reliably increase long-term smoking abstinence rates
- Varenicline is the most effective agent with or without nicotine replacement, Bupropion is an alternative
- 40% of COPD patients still smoke
- Legislative smoking bans have been effective
- **Counseling**, delivered by healthcare professionals, **improve quit rates**
- Supplement with "quit lines" ie SAMHSA 800-662-4357
- There is **No** evidence for e-cigarettes as a smoking cessation aid at present
- Inhaler technique needs to be assessed regularly

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Pulmonary Rehabilitation

- Pulmonary rehabilitation:
 - Exercise training
 - Disease-specific education
- Improves exercise capacity, symptoms, and quality of life across all grades of COPD severity.
- Especially after hospital discharge for COPD exacerbation

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Oxygen & Surgery

- Severe resting chronic hypoxemia (PaO₂ ≤ 55 mmHg or < 60 mmHg if there is **cor pulmonale** or **secondary polycythemia**), long-term oxygen therapy improves survival.
- **Oxygen should not be routinely prescribed** for resting or exertional hypoxia
- Chronic **hypercapnia** and a history of hospitalization for acute respiratory failure, long-term **non-invasive ventilation** may decrease mortality and prevent re-hospitalization.
- **LVRS** (Lung Volume Reduction Surgery) for eligible patients with refractory symptoms and Emphysema

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BEST PRACTICES IN PULMONARY MEDICINE

Recommendations From Choosing Wisely

Recommendation	Sponsoring organization
For patients recently discharged from the hospital receiving supplemental home oxygen for an acute illness, do not renew the prescription without assessing the patient for ongoing hypoxemia.	American College of Chest Physicians/ American Thoracic Society

Source: For more information on Choosing Wisely, see <https://www.choosingwisely.org>. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see <https://www.aafp.org/pubs/afp/collections/choosing-wisely.html>.

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Vaccinations

- Influenza (B)
- Covid: SARS-CoV-2 (B)
- Pneumonia: PCV20 (or PCV15 followed by PPSV23) (B) Reduces exacerbations and CAP
- Pertussis Tdap if not vaccinated in adolescence (B)
- Zoster if >50 (B)
- RSV: In May 2023, the Food and Drug Administration (FDA) approved the first vaccines for prevention of RSV-associated LRTD in adults aged ≥60 years, especially those with chronic diseases

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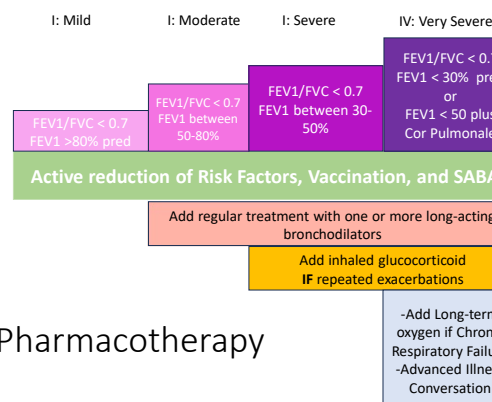
Exacerbation

Prednisone BLAST 40mg x 5d

- 40 mg prednisone-equivalent per day for 5 days is recommended¹
- Longer courses increase risk of pneumonia and mortality²
- Therapy with oral prednisolone is equally effective as intravenous administration³
- +/- Antibiotic

¹Leuppi, J. D., Schuetz, P., & Bingisser, R. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the reduce randomized clinical trial. *JAMA* 309, 2223-2231 (2013)
²Sivalalan, P. et al. COPD exacerbations: the impact of long versus short courses of oral corticosteroids on mortality and pneumonia: nationwide data on 67 000 patients with COPD followed for 12 months. *BMJ Open Respir. Res.* 6, e000407 (2019)
³de Jong, Y. P. et al. Oral or IV prednisolone in the treatment of COPD exacerbations: a randomized, controlled, double-blind study. *Chest* 122, 1741-1747 (2007)

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Inhaler Choice

- Availability (Cost)
- Part D or B ?
- Patient beliefs, satisfaction and preferences
- Shared decision making
- # of different devices
- Limit switching devices
- Cognition, dexterity and strength
- Inspiratory effort strong enough for DPI
- Slow Mist inhalers (SMI)
- Coordinate actuation with inhalation or use spacer (perhaps with mask)
- Size Portability

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Picture of Spacer and Mask



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Beta Agonists: SABA, LABA

- SABA (Short Acting Beta Agonists)
 - Fenoterol, Levalbuterol, Salbutamol/Albuterol
 - Terbutaline ?
 - Primatine? (Epinephrine)
 - FDA-approved asthma inhaler available over-the-counter
- LABA
 - Arformoterol, Formoterol, Indacaterol, Olodaterol, Salmeterol

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Muscarinic Antagonist and Beta Agonists and combinations

- SAMA
 - Ipratropium bromide
 - Oxitropium bromide
- LAMA
 - Acclidinium bromide
 - Glycopyrronium bromide
 - Tiotropium
 - Umeclidinium
 - Glycopyrrolate
 - Refenacin
- Combination SABA
 - Fenoterol/ipratropium
 - Salbutamol/ipratropium
- Combination LABA/LAMA
 - Formoterol/acclidinium
 - Formoterol/glycopyrronium
 - Indacaterol/glycopyrronium
 - Vilanterol/umeclidinium
 - Olodaterol/tiotropium

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Evidence of Benefit

- Bronchodilators are central to symptom management (A)
- SABA/SAMA improves symptoms and FEV1 (A)
- SABA/SAMA superior to either alone (A)
- LABA/LAMA improve lung function, dyspnea, health-status and exacerbation rates (A)
- LAMAs have greater impact on exacerbation and hospitalization rate (B)

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Evidence of Benefit

- LABA/LAMA increases FEV1 and reduces symptoms compared to monotherapy (A)
- LABA/LAMA reduces exacerbations compared to monotherapy (B)
- Tiotropium improves pulmonary rehabilitation exercise performance (B)
- Theophylline has small bronchodilator effect (A) and modest symptom improvement (B)

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Triple Drug Inhalers

- **Trelegy Ellipta:**
Fluticasone/umeclidinium/vilanterol
- **Trimbow:**
 - Beclometasone/formoterol/glycopyrronium
- **Breztri Aerosphere:**
 - Budesonide/formoterol/glycopyrrolate

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Inhaled and Oral Steroids (Inhaled Corticosteroids, ICS)

- ICS/LABA better than either in **reducing exacerbations** in moderate to severe COPD (A)
- Regular ICS **increases pneumonia** risk (A)
- Lower blood eosinophils associated with greater proteobacteria (Hemophilus), increased bacterial infection and pneumonia (B)
- Independent of ICS, eosinophil count <2% increased pneumonia risk (C)
- **Triple therapy** (LABA/LAMA/ICS) **improves lung function**, symptoms, health status and reduces exacerbations compared to monotherapy (A)
- Triple therapy versus LABA/LAMA **reduces mortality** in patients with frequent/ severe exacerbations (B)
- Long-term use of oral glucocorticoids has **numerous side effects** (A) and no benefit (C)

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Inhaled Steroid

STRONGLY FAVORS USE	History of hospitalization(s) for exacerbations of COPD
	>=2 moderate exacerbations of COPD per year
	Blood eosinophils >=300 cells/uL
FAVORS USE	1 moderate exacerbation of COPD per year
	Blood eosinophils 100-300 cells / uL
AGAINST USE	Repeated pneumonia events
	Blood eosinophils <100 cells/uL
	History of mycobacterial infection

Adapted from ERS 2019; European Respiratory Journal 52(6) 1801219; 13 Dec 2018

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Other Medications

- PDE4: Roflumilast improves lung function and reduces exacerbations in those already on LABA ICS (A)
- Antibiotics: Long term Azithromycin reduces exacerbations (A)
- Mucoregulators and Antioxidants: erdoisteine, carbocysteine and NAC reduce risk of exacerbations in **select population** (B)
- Other Antiinflammatories. Leukotriene modifiers (LTRA) have not been tested adequately in COPD
- Statins may help (C) ?

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Formulary Financial Impact Example

Cigna Houston			Humana Houston		
ASTHMA/COPD AGENTS			ASTHMA/COPD AGENTS		
Class	Drug	Tier	Class	Drug	Tier
LAMA	Incruse Ellipta	3	LAMA	Incruse Ellipta	NF
LABA/LAMA	Anoro Ellipta	3	LABA/LAMA	Anoro Ellipta	NF
SABA	Albuterol HFA	3	SABA	Albuterol HFA	3
	Ventolin HFA	3		Ventolin HFA	3
ICS-containing	Arnuly Ellipta, Flovent (Diskus & HFA), Breo Ellipta, Trelegy Ellipta	3	ICS-containing	Arnuly Ellipta, Flovent (Diskus & HFA), Breo Ellipta, Trelegy Ellipta	3
	Advair Diskus, Advair HFA	NF, 3		Advair Diskus, Advair HFA	3
	Wixela Inhub, Fluticasone/Salmeterol Diskus	2		Wixela Inhub, Fluticasone/Salmeterol Diskus	3
	Budesonide Nebs	3		Budesonide Nebs	4
LTRA	Montelukast tab/chew	1, 2	LTRA	Montelukast tab/chew	1, 1
	Montelukast pack	3		Montelukast pack	4

NF - Non-Formulary

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Formulary Variation

Aetna Houston			Blue Cross Houston		
ASTHMA/COPD AGENTS			ASTHMA/COPD AGENTS		
Class	Drug	Tier	Class	Drug	Tier
LAMA	Incruse Ellipta	3	LAMA	Incruse Ellipta	3
LABA/LAMA	Anoro Ellipta	3	LABA/LAMA	Anoro Ellipta	3
SABA	Albuterol HFA	2	SABA	Albuterol HFA	3
	Ventolin HFA	2		Ventolin HFA	3
ICS-containing	Arnuly Ellipta, Flovent (Diskus & HFA), Breo Ellipta, Trelegy Ellipta	3	ICS-containing	Arnuly Ellipta, Flovent (Diskus & HFA), Breo Ellipta, Trelegy Ellipta	3
	Advair Diskus, Advair HFA	3		Advair Diskus, Advair HFA	3
	Wixela Inhub, Fluticasone/Salmeterol Diskus	NF		Wixela Inhub, Fluticasone/Salmeterol Diskus	NF
	Budesonide Nebs	4		Budesonide Nebs	3
LTRA	Montelukast tab/chew	1, 1	LTRA	Montelukast tab/chew	1, 2
	Montelukast pack	2		Montelukast pack	2

NF - Non-Formulary

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COPAY \$47 per month

ASTHMA/COPD AGENTS		
Class	Drug	Tier
LAMA	Incruse Ellipta	NF
LABA/LAMA	Anoro Ellipta	NF
SABA	Albuterol HFA	3
	Ventolin HFA	3
ICS-containing	Arnuly Ellipta, Flovent (Diskus & HFA), Breo Ellipta, Trelegy Ellipta	3
	Advair Diskus, Advair HFA	3
	Wixela Inhub, Fluticasone/Salmeterol Diskus	3
	Budesonide Nebs	4
LTRA	Montelukast tab/chew	1,1
	Montelukast pack	4

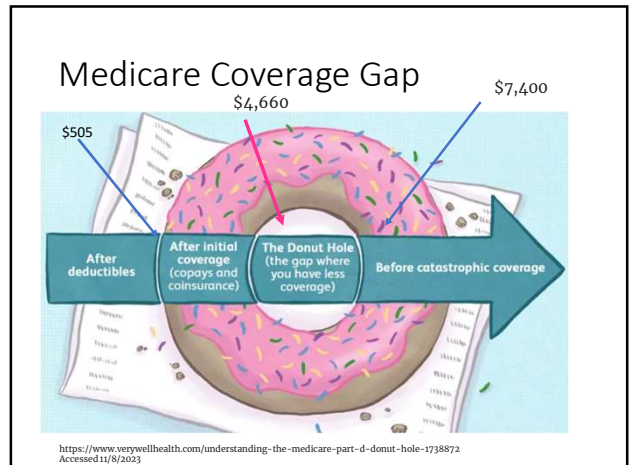
HUMANA MAPD 5-TIER FORMULARY COPAYS*			
Tier	Description	Preferred Retail (30- /90-D5)	Preferred Mail Order (90-D5)
1	Preferred Generic	\$0 / \$9	\$0
2	Generic	\$0-5 / \$30	\$0
3	Preferred Brand	\$47 / \$48	\$13
4	Non-Preferred	\$99-\$300 / \$291-\$500	\$287-\$290
5	Specialty	For 30-D5: Percent co-insurance varies by regional plan; Long-term supply is not available for drugs in Tier 5	Long-term supply is not available for drugs in Tier 5

For low-income subsidy (LIS) copays, [CLICK HERE](#)

* Copays listed are applicable to H-plans with the majority of P/A membership and only during the Initial Coverage Phase
D5 - Day Supply

\$100 copay for tier 4

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Trelegy Good RX Price ~\$700.00 per month

	HEB Grocery	\$677 retail Save 6%	\$635.63
	Randall's	\$793 retail Save 10%	\$640.25
	CVS Pharmacy	\$750 retail Save 12%	\$662.37
	Target (CVS)	\$750 retail Save 12%	\$662.37
	Kroger Pharmacy	\$766 retail Save 10%	\$664.95
	Walgreens	\$658 retail Save 22%	\$666.70

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Prescription Assistance

Trelegy Ellipta

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- ### Number Needed to Treat: NNT
- **Triple:** NNT 16 to reduce one exacerbation in 12 months
 - **Triple:** NNH 64 to cause one episode of Pneumonia compared to LAMA/LABA combination
 - **PDE4:** NNT 17 to prevent one exacerbation over 39 weeks
 - **Macrolide:** NNT 4 to prevent one exacerbation in 50 weeks (antibiotic resistance and QTc prolongation)

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Roger 65 COPD "D"

- Multiple inhalers, oxygen and a few hospitalizations for exacerbations
- Has begun to lose weight and has severe exercise restriction in spite of maximal treatment
- How would you bring up the topic?

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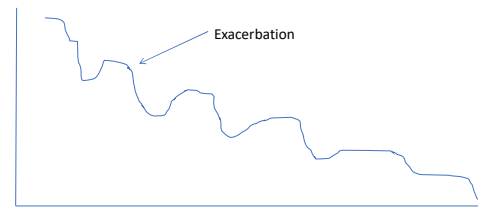
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How would you bring up the topic?

- A. Tell him, there is nothing more medicine can do
- B. Discuss how if he is intubated he will never come off the ventilator
- C. Say, "I'm worried about you because I see signs that your disease is getting much worse"

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Illness Trajectory: Chronic Illness Organ Failure COPD or CHF



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Introducing The Topic

- "After looking at what has been going on in the past year, I think we should talk about where this appears to be going"
- "How do you feel about continuing to go to the hospital?"
- "When this happens again do you want to go on a breathing machine?"
- "Since we know that COPD will likely take your life, have you thought what it will be like to die?"

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Key Points / Summary

- COPD?..... Chronic cough or sputum production, recurrent lower respiratory tract infections and/or risk factors
- Post Bronchodilator FEV1/FVC < 0.7 is mandatory to establish the diagnosis of COPD.
- Priorities:
 - Determine the severity of airflow obstruction
 - Impact of disease on the patient's health status
 - Risk of future events, exacerbation, hospitalization, death

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Key Points: Summary 2

- More testing if persistent symptoms after initial treatment
 - Full PFT, including lung volumes
- Concomitant chronic diseases (multimorbidity)
 - Cardiovascular disease
 - Skeletal muscle dysfunction
 - Metabolic syndrome
 - Depression, anxiety
 - Lung cancer

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Evidence Base Summary

Clinical recommendations	Evidence rating	Comments
Diagnosis confirmed by Spirometry	C	Consensus guidelines
Avoid Screening Spirometry	C	USPSTF D rating
LAMAs should be initial RX for mild symptoms and few exacerbations (LABA as alternative)	B	RCT LABA/LAMA combo even better
Long Term Oxygen if COPD with resting hypoxemia	B	Meta analysis of 5 studies
Avoid Oxygen if only moderate resting, nocturnal or exertional hypoxemia	B	Consensus guidelines and an RCT
Influenza and Pneumonia Vaccine	A	Cochrane Review

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