COPD: Updates in Diagnosis and Management

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Disclosures

Dr. Brown has no conflicts of interest

Dr. Montag Schafer has no conflicts of interest.

Unless otherwise specified, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report 2024 is the reference for the information presented.

Roadmap

- Review data on COPD in the United States
- Orient to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report
- Review major updates from 2023 and minor updates from 2024 for diagnosis and management of COPD
- Explore strategies for inhaler prescribing

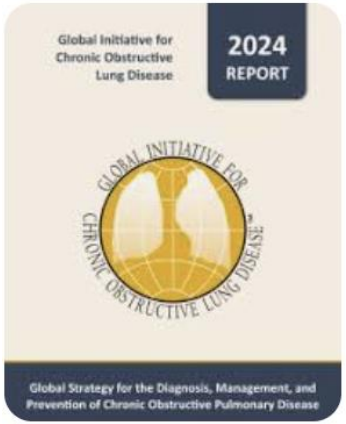
COPD in the United States

- Prevalence:
  - 6.5% of the United States adult population in 2021
  - 4.7% of Minnesota adult population
- Morbidity
  - 2nd leading cause of reduced DALY, 2nd to ischemic heart disease
- Mortality:
  - 6th leading cause of death in 2020
- Costs:
  - 49B healthcare costs 2020
  - 2.9B lost in 2010 due to employee absenteeism/missed work
- Care:
  - ~80% of patients diagnosed with COPD are managed by their primary care physician*

Centers for Disease Control and Prevention.
Ann Fam Med. 2022; 20(4): 319–327

Major Updates the 2023 GOLD Report

- New definitions for COPD and COPD exacerbations
- Expanded recognition of non-cigarette exposures as risk factors for COPD
- Simplified disease classification
- Updates in pharmacologic and non-pharmacologic management
- Specific treatment recommendations for COPD exacerbation
- Enhanced focus on reducing mortality in addition to morbidity

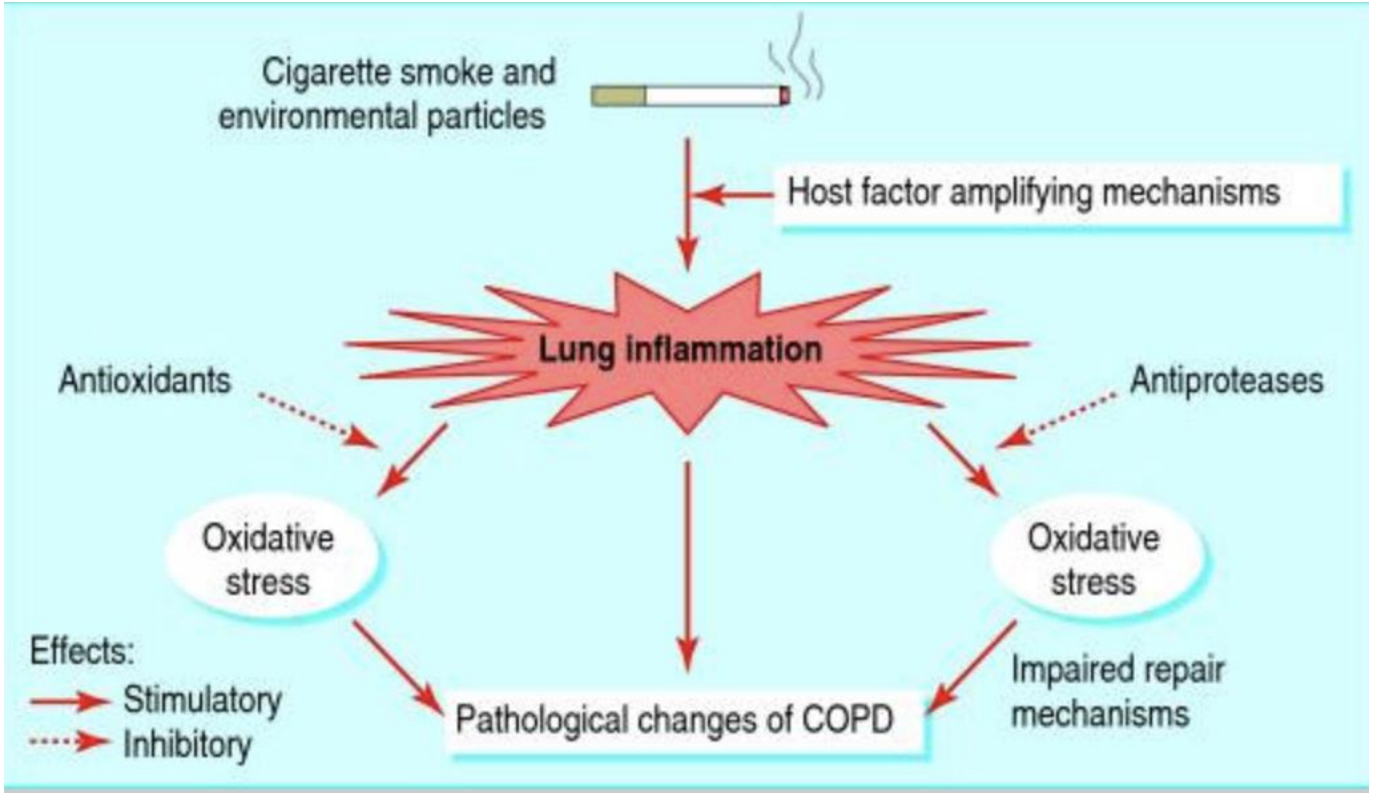


COPD Diagnosis

COPD Definition

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

Pathogenesis



BMJ. 2006 May 20; 332(7551): 1202–1204.

Proposed Taxonomy (Etiotypes) for COPD

Figure 1.2

Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	• Exposure to tobacco smoke, including *in utero* or via passive smoking • Vaping or e-cigarette use • Cannabis
Biomass and pollution exposure COPD (COPD-P)	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards
COPD due to infections (COPD-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD
COPD & asthma (COPD-A)	Particularly childhood asthma
COPD of unknown cause (COPD-U)	

*Adapted from Celli et al. (2022) and Stolz et al. (2022)

Clinical Indicators for Considering a Diagnosis of COPD

Consider the diagnosis of COPD, and perform spirometry, if any of these clinical indicators are present:

- Dyspnea that is progressive over time, worse with exercise or persistent
- Recurrent wheeze
- Chronic cough
- Recurrent lower respiratory tract infections
- History of risk factors

Role of Spirometry in COPD

- Diagnosis
- Assessment of severity of airflow obstruction
- Follow up assessment

Diagnosis

In the appropriate clinical context, the presence of non-fully reversible airflow limitation (i.e., FEV1/FVC < 0.7 **post-bronchodilation**) measured by spirometry confirms the diagnosis of COPD.

What if my patient doesn't met the spirometric criteria?

PreCOPD: individuals of any age who have respiratory symptoms and/or other detectable structural and/or functional abnormalities, in the absence of airflow obstruction or forced spirometry

PRISM: individuals with preserved ratio (FEV1/FVC$\geq$0.7 after bronchodilation) but impaired spirometry (FEV1<80% of reference, after bronchodilation)

Assigning GOLD Grade and Group

Initial Assessment

1. Severity of airflow limitation
2. Nature and magnitude of current symptoms
3. Previous history of moderate and severe exacerbations
4. Presence and type of other diseases (multimorbidity)

1. Airflow Limitation

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

Figure 2.7

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

2. Current Symptoms

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 ☐

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 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: ☐

3. History of Exacerbations

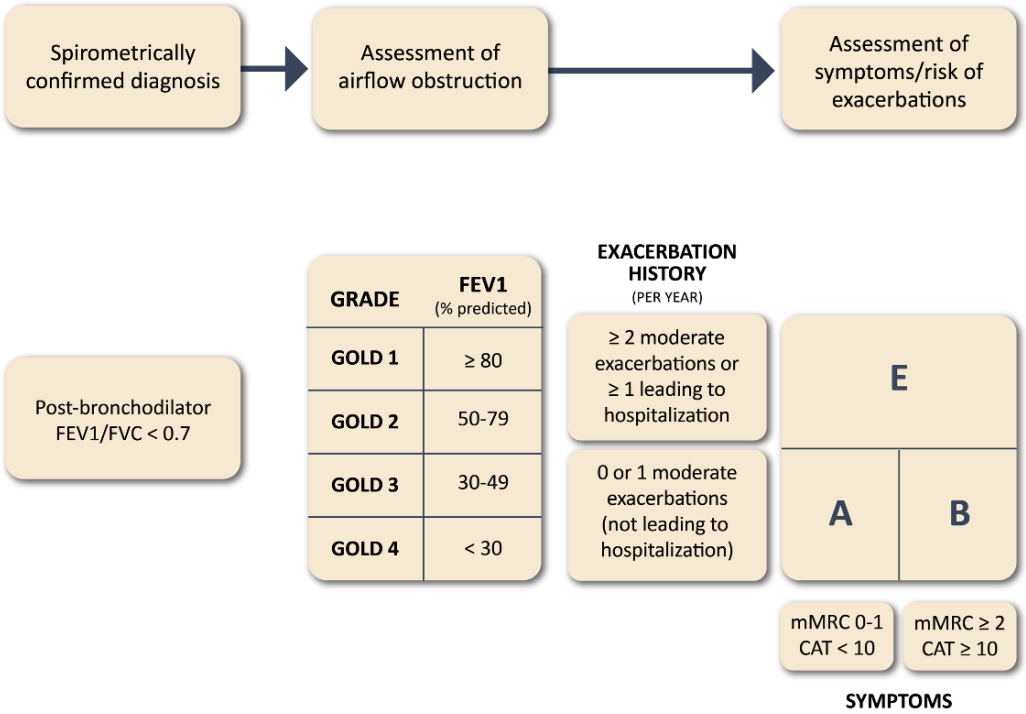
The best predictor of having frequent exacerbations (defined as two or more exacerbations per year) is the previous history of exacerbations.

4. Multimorbidity

- Comorbid conditions are common in patients with COPD
- Multimorbidity influences mortality and hospitalizations *independently* of the severity of airflow obstruction
- Comorbid conditions require the same treatment as those without COPD

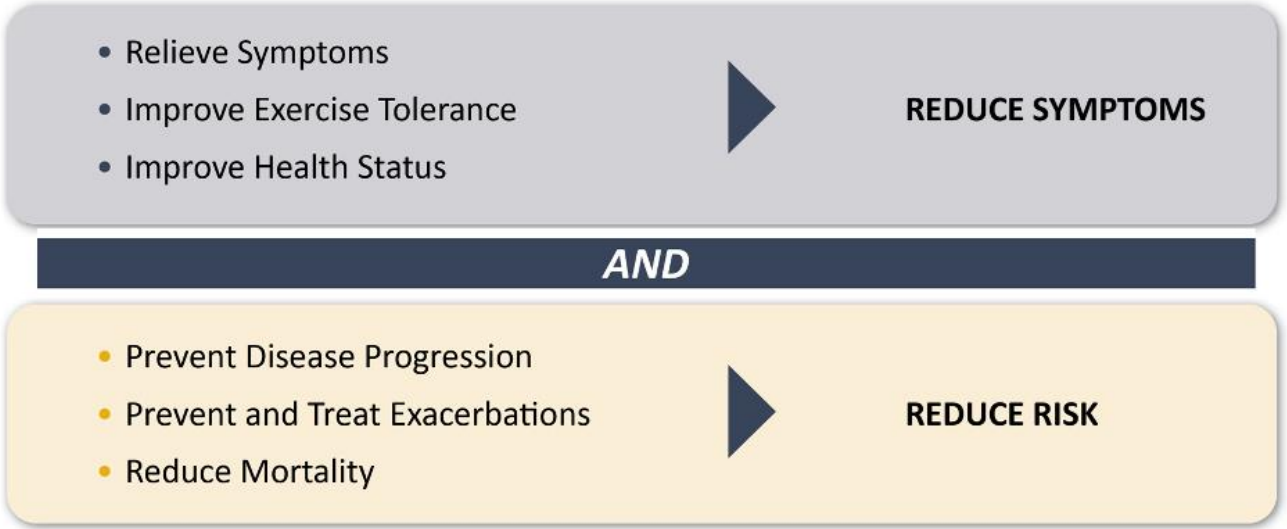
GOLD ABE Assessment Tool

Figure 2.10



Goals for Treatment of Stable COPD

Figure 3.1



Non-Pharmacologic Management of COPD

Non-Pharmacological Management of COPD*

Figure 3.12

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

*Can include pharmacological treatment

Non-Pharmacological Management of COPD*

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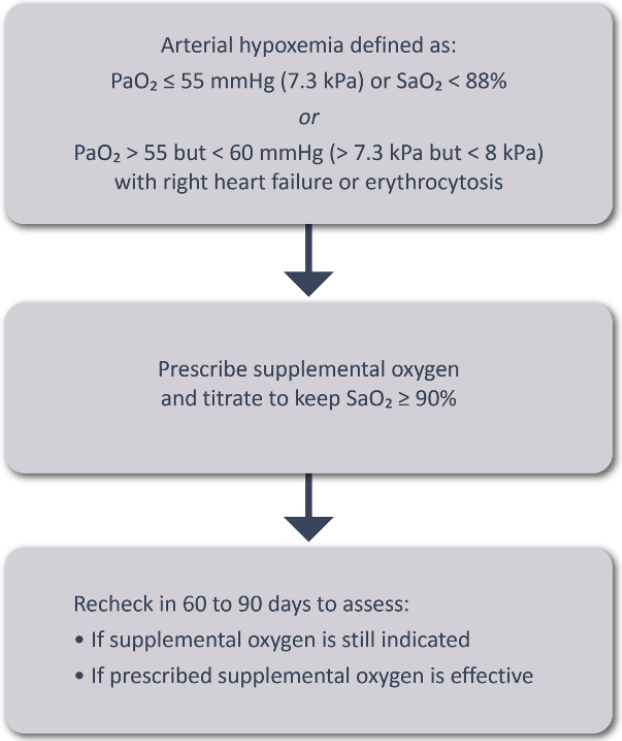
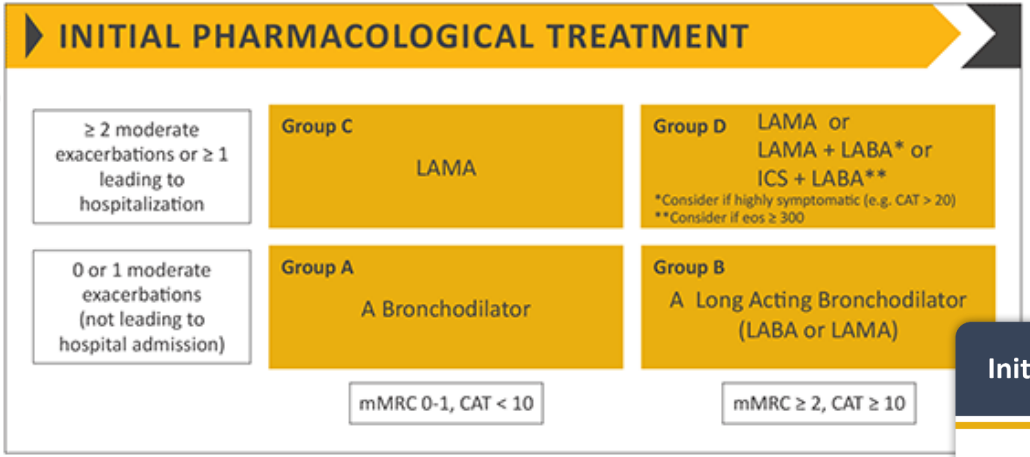
*Can include pharmacological treatment

Prescription of Supplemental Oxygen to COPD Patients

Figure 3.15

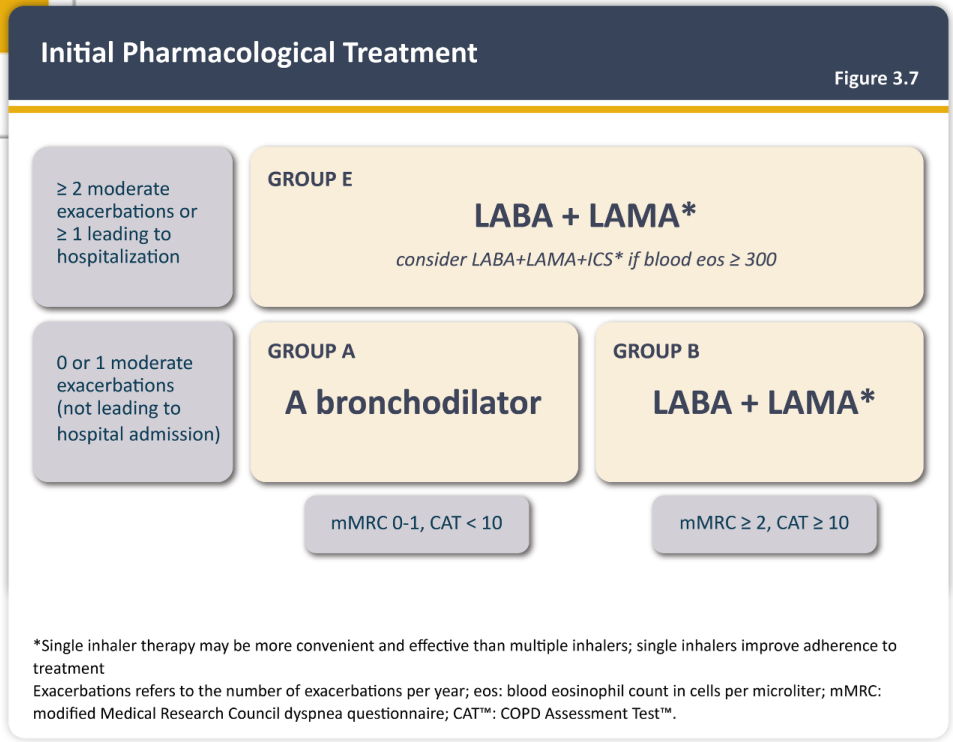


Choosing Pharmacotherapy


INITIAL PHARMACOLOGICAL TREATMENT
≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization
Group C
LAMA
Group D
LAMA or
LAMA + LABA* or
ICS + LABA**
*Consider if highly symptomatic (e.g. CAT > 20)
**Consider if eos ≥ 300
0 or 1 moderate exacerbations (not leading to hospital admission)
Group A
A Bronchodilator
Group B
A Long Acting Bronchodilator (LABA or LAMA)
mMRC 0-1, CAT < 10
mMRC ≥ 2, CAT ≥ 10

2022

2023


Initial Pharmacological Treatment
Figure 3.7
≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization
GROUP E
LABA + LAMA*
consider LABA+LAMA+ICS* if blood eos ≥ 300
0 or 1 moderate exacerbations (not leading to hospital admission)
GROUP A
A bronchodilator
GROUP B
LABA + LAMA*
mMRC 0-1, CAT < 10
mMRC ≥ 2, CAT ≥ 10
*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment
Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.

Group B: LABA + LAMA

- When initiating treatment with a long-acting bronchodilator the preferred choice is a combination of LABA and LAMA
- Combination therapy with LABA and LAMA increases FEV1 and reduces symptoms and exacerbations superior to monotherapy
- If a LABA+LAMA combination is not considered appropriate, there is no evidence to recommend one class of long-acting bronchodilators over another (LABA or LAMA) for initial relief of symptoms in this group of patients.

EMAX Trial

- Population
  - CAT ≥ 10
  - GOLD Grade 2 and 3
  - ≤1 moderate exacerbation and no severe exacerbations in the previous year
- Intervention/Comparison
  - LABA/LAMA vs. LAMA vs. LABA
- Outcome
  - Primary: FEV1; Secondary: Symptom assessment
- Results
  - Combination therapy significantly improved FEV1 and symptoms

Respir Res. 2019;20(1):238.

Group E: LABA + LAMA *Consider addition of ICS

- LABA-LAMA therapy considered the highest ranked treatment to reduce exacerbations when compared to single long-acting bronchodilator therapy
- Similar to group B, provided there are no issues regarding availability, cost and side-effects LABA+LAMA is the preferred choice.

Group E: LABA + LAMA *Consider addition of ICS

- Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease
- GOLD report recommends against the use of LABA-ICS combination. If there is an indication for an ICS the combination, LABA-LAMA-ICS has been shown to be superior
    - Triple therapy has been shown to be superior to LABA-ICS, LAMA-LABA and LAMA monotherapy in regards to improving lung function and symptoms and exacerbations
    - Recent data suggests a beneficial effect on mortality in symptomatic COPD treatments with a history of frequent or severe exacerbations with triple therapy compared to LABA-LAMA combination

IMPACT and ETHOS Trials

- Population
  - CAT score ≥10
  - GOLD Grade 2 with history of >2 moderate or >1 severe COPDe in last year
  - GOLD Grade >3 with history of >1 moderate or severe COPDe in the last year
    - Moderate COPDe - requiring antibiotics or systemic glucocorticoids
    - Severe COPDe - requiring hospitalization
- Intervention/Comparison
  - LABA-LAMA-ICS vs. LAMA-LABA vs. LABA-ICS
- Primary Outcome
  - Annual rate of moderate or severe COPDe - ITT
- Results
  - Lower rate of moderate and severe COPDe in triple therapy group

COPDe: COPD exacerbations

N Engl J Med. 2018;378(18):1671-1680.
N Engl J Med. 2020;383(1):35-48

IMPACT and ETHOS Trials - Secondary Analyses

- Missing data limited all-cause mortality assessment in original trials, leading to secondary analyses after additional data was collected
    - Found reduction in all-cause mortality in triple therapy groups

Am J Respir Crit Care Med. 2020;201(12):1508-1516
Am J Respir Crit Care Med. 2021;203(5):553-564.

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

Figure 3.17

Therapy	RCT*	Treatment effect on mortality	Patient characteristics
Pharmacotherapy			
LABA+LAMA+ICS[1]	Yes	Single inhaler triple therapy compared to dual LABD therapy relative risk reduction: IMPACT: HR 0.72 (95% CI: 0.53, 0.99)[1a] ETHOS: HR 0.51 (95% CI: 0.33, 0.80)[1b]	Symptomatic people with a history of frequent and/or severe exacerbations
Non-pharmacological Therapy			
Smoking cessation[2]	Yes	HR for usual care group compared to intervention group (smoking cessation) HR 1.18 (95% CI: 1.02, 1.37)[2]	Asymptomatic or mildly symptomatic
Pulmonary rehabilitation[3#]	Yes	Old trials: RR 0.28 (95% CI 0.10, 0.84)[3a] New trials: RR 0.68 (95% CI 0.28, 1.67)[3b]	Hospitalized for exacerbations of COPD (during or ≤ 4 weeks after discharge)
Long-term oxygen therapy[4]	Yes	NOTT: ≥ 19 hours of continuous oxygen vs ≤ 13 hours: 50% reduction[4a] MRC: ≥ 15 hours vs no oxygen: 50% reduction[4b]	PaO_2 ≤ 55 mmHg or < 60 mmHg with *cor pulmonale* or secondary polycythemia
Noninvasive positive pressure ventilation[5]	Yes	12% in NPPV (high IPAP level) and 33% in control HR 0.24 (95% CI 0.11, 0.49)[5]	Stable COPD with marked hypercapnia
Lung volume reduction surgery[6]	Yes	0.07 deaths/person-year (LVRS) vs 0.15 deaths/person-year (UC) RR for death 0.47 (p = 0.005)[6]	Upper lobe emphysema and low exercise capacity

*RCT with pre-specified analysis of the mortality outcome (primary or secondary outcome); #Inconclusive results likely due to differences in pulmonary rehabilitation across a wide range of participants and settings.

1. a) IMPACT trial (Lipson et al. 2020) and b) ETHOS trials (Martinez et al. 2021); 2.Lung Health Study (Anthonisen et al. 2005); 3. a) Puhan et al. (2011) and b) Puhan et al. 2016; 4. a) NOTT (NOTT, 1980) and b) MRC (MRC, 1981); 5. Kohlein trial (Kohlein et al. 2014); 6. NETT trial (Fishman et al. 2003)

ICS: inhaled corticosteroid; IPAP: inspiratory positive airway pressure; LABA: long-acting beta$_2$-agonist; LABD: long-acting bronchodilator; LAMA: long-acting anti-muscarinic; LTOT: long-term oxygen therapy; NPPV: noninvasive positive pressure ventilation; LVRS: lung volume reduction surgery; UC: usual treatment control group.

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#**
	≥ 2 moderate exacerbations of COPD per year#
	Blood eosinophils ≥ 300 cells/µL
	History of, or concomitant asthma
FAVORS USE	1 moderate exacerbation of COPD per year#
	Blood eosinophils 100 to < 300 cells/µL
AGAINST USE	**Repeated pneumonia events**
	Blood eosinophils < 100 cells/µL
	History of mycobacterial infection

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

Group E: LABA + LAMA *Consider addition of ICS

- If patients with COPD have a concurrent diagnosis of asthma, treatment should follow asthma treatment guidelines

Anti-Inflammatory Treatments - PDE4 Inhibitor

- In patients with severe to very severe airflow limitation (GOLD Groups 3-4, i.e. FEV1 < 50%), chronic bronchitis and a history of exacerbations the addition of a PDE4 inhibitor to a treatment with long-acting bronchodilators with or without an ICS can be considered
    - Chronic bronchitis defined as chronic cough, sputum production for at least 3 months for 2 years or more
- PDE4 improves lung function and reduces moderate and severe exacerbations
- PDE4 improves lung function and reduces exacerbations in patients on LABA-ICS combinations

PDE4 Inhibitor

- Roflumilast
  - 250 mcg once daily for 4 weeks, followed by 500 mcg once daily.
  - Note: An initial dose of 250 mcg once daily is recommended for the first 4 weeks of treatment in an attempt to improve tolerability. However, this is not considered a therapeutic dose and the effect of this approach on long-term tolerability is uncertain.
    - ADRs: Headache (4%), dizziness (2%), insomnia (2%), Weight loss (5% to 10% of body weight: 8% to 20%; >10% loss: 7%), Diarrhea (10%), nausea (5%), decreased appetite (2%), Influenza (3%), Back pain (3%)

Anti-Inflammatory Treatments - Antibiotics

- Long-term azithromycin and erythromycin reduces exacerbations over one year
    - There are **no data** showing the efficacy or safety of chronic azithromycin treatment to prevent exacerbations beyond one-year of treatment.
        - Azithromycin 250 mg/day or 500 mg TIW
        - Erythromycin 250 mg BID
- A post-hoc analysis suggests lesser benefit in active smokers
- Treatment with azithromycin is associated with an increased incidence of bacterial resistance and hearing test impairments

Overcoming Cost Concerns - Low Time Burden

- GoodRx.com or similar program

Overcoming Cost Concerns - High Time Burden

- Branded medications
  - Manufacturer Patient Assistance Programs
    - Requires annual renewal
    - Subject to income requirements
- Medicare
  - Part D: Apply for Extra Help Program, application available online
    - Subject to income requirements
  - Part B: Use of nebulized products
    - Drug classes available: LABA and LAMA
- Use of Canadian pharmacy
  - https://www.cipa.com/cipa-safe-pharmacies

Adjusting Therapy

Follow-up Management

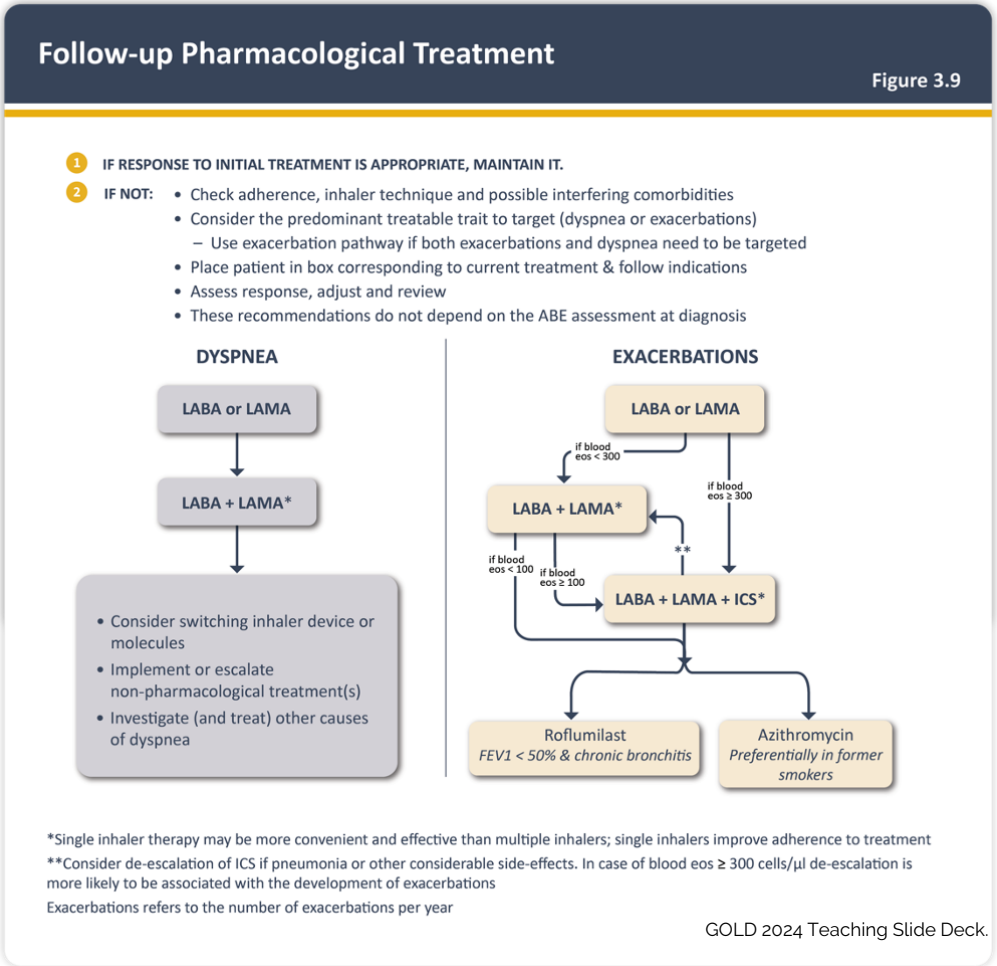
Key Points for Inhalation of Drugs

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

Follow-up Management

- Based on two key **treatable traits**
  - Persistence of dyspnea
  - Occurrence of exacerbations
  - If both, then go with exacerbation route
- Algorithm designed to facilitate management of patients taking maintenance regimens, at any point in time



GOLD 2024 Teaching Slide Deck.

Meaningful Change in CAT score

A difference or change of 2 or more units over 2 to 3 months in a patient suggests a clinically significant difference or change in health status.

A note on ICS-LABA

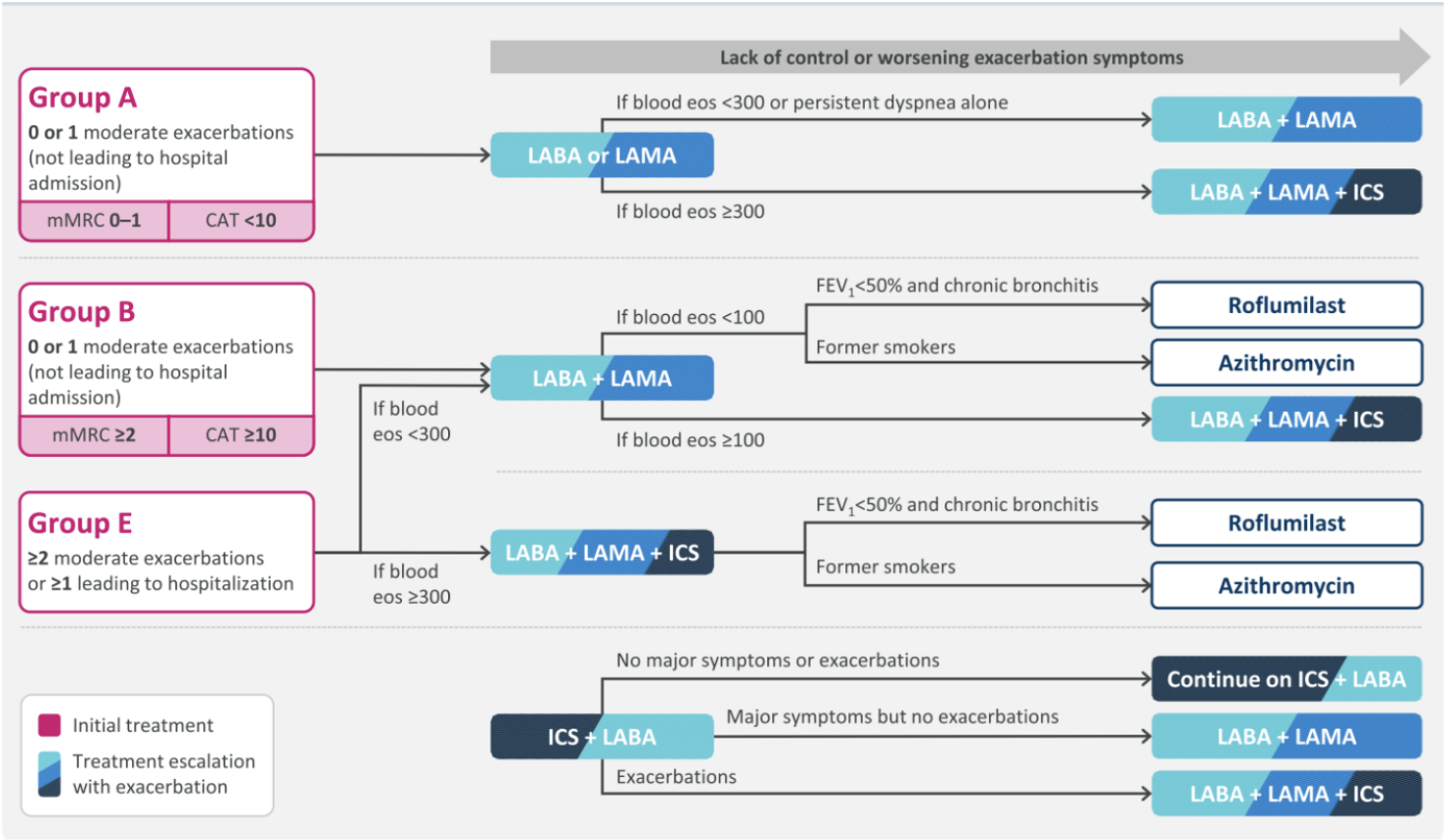
If a patient with COPD and no features of asthma has been **treated** with **LABA+ICS** and is **well controlled** in terms of symptoms and exacerbations, **continuation with LABA+ICS is an option**.

Yet, if the patient has:

a) further exacerbations = escalate to LABA+LAMA+ICS

b) major symptoms = switch to LABA+LAMA

Alternative Visualization of Pharmacologic Recommendations



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Select Tools

Inhaler Charts

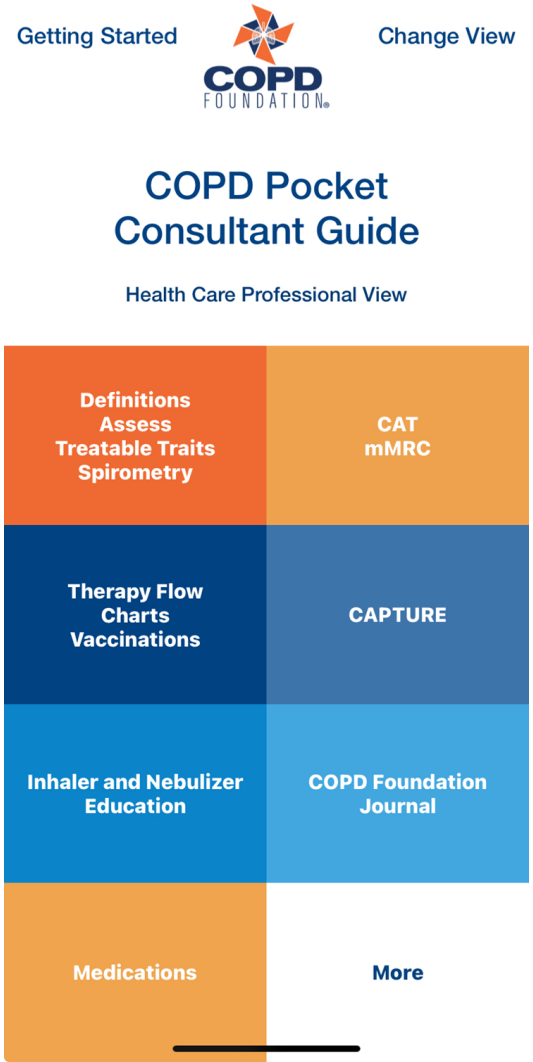
z.umn.edu/COPDInhalers

Minnesota Medicaid Formulary Review

z.umn.edu/medicaidformulary

Inhaler Education Instructional Videos

- The COPD Foundation
  - Website: COPD Inhaler Educational Video Series
  - Mobile app: COPD Pocket Consultant Guide
  - Written material available in a variety of languages



The COPD Foundation Website / Mobile App,

Thank You!

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