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Highlights of the 2019 Update to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report and Their Application in Practice

Key Points

- The Global Initiative for Chronic Obstructive Lung Disease (GOLD) program releases consensus reports to provide evidence-based recommendations about the management and prevention of chronic obstructive pulmonary disease (COPD); the most recent major update occurred in November 2018.
- The 2019 GOLD strategy for COPD assessment now separates lung function measures from respiratory symptom scores because lung function is only weakly correlated to symptoms and health status impairment.
- The updated strategy now provides recommendations for initiation and maintenance of pharmacologic therapy in patients based on exacerbation risk and symptom scores, with consideration of blood eosinophil counts.
- Management of exacerbations now includes the prevention of future exacerbations, which may require adding another medication to the patient's maintenance regimen.

Introduction

Primary care providers play an important role in the management of chronic obstructive pulmonary disease (COPD), including diagnosis, treatment, and routine monitoring. COPD is the third leading cause of death in the United States and a major cause of morbidity, including visits to a health care provider, emergency department, or urgent care, as well as hospitalizations.^{1,2} Many patients have comorbid conditions (eg, cardiovascular disease) that may interfere with COPD management and increase health care resource utilization. COPD most commonly results from significant exposure to noxious gases or particles that lead to persistent respiratory symptoms and airflow limitation.^{2,3} Structural changes, small-airway narrowing, and lung tissue destruction occur as a result of chronic inflammation and prevent the airways from remaining open during expiration.² COPD is a heterogeneous disease with varying risk factors that may impact airflow differently⁴; cigarette smoking is the most common cause, but air pollution can also contribute.² Furthermore, asthma progression can result in fixed airflow limitation, predisposing individuals to development of COPD; some individuals may therefore have features of both diseases.^{2,5}

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) program was established in 1998 to provide recommendations for COPD management using the best scientific information available.² The first report was issued in 2001,⁶ and major revisions were published in 2006,⁷ 2011,⁸ 2017,⁹ and 2018.¹⁰ The GOLD Science Committee reviews published research on COPD management and prevention, examining its effect on the recommendations; members of the Committee are recognized leaders in COPD research and clinical practice. The 2019 GOLD report incorporates new information from literature published from January 2017 to July 2018 for diagnosis, assessment, and treatment of COPD.²

The aims of this newsletter are (1) to review the 2019 updates to the GOLD report, focusing on assessment goals, pharmacology, and exacerbation management; and (2) to illustrate patient care decisions based on the GOLD strategy in a case study, with an emphasis on early intervention to avoid exacerbations and achieve maximal bronchodilation.

Case Study

Paul is a 68-year-old male who presents to the clinic due to intermittent chronic cough with mucoid sputum for the past year. Over the previous 3 months, he developed persistent breathlessness with exertion and decided to seek medical advice and treatment. Paul is a current smoker, one-half of a pack per day for the past 35 years.

Note: This is a hypothetical case description for teaching purposes.

Revised COPD Assessment Goals

Any patient who presents with dyspnea, chronic cough, or sputum production should be further evaluated for COPD. A patient's history of exposure to risk factors should also be considered.² There are 3 goals of COPD assessment: (1) define the level of airflow limitation, (2) evaluate the effect of COPD on a patient's health status, and (3) evaluate the risk of future events, including exacerbations, hospitalizations, or death.²

To confirm a COPD diagnosis, spirometry is required; persistent airflow limitation is defined as a postbronchodilator forced expiratory volume in 1 second (FEV₁) to forced vital capacity (FVC) ratio <0.70.² Spirometry should be repeated for patients with postbronchodilator FEV₁/FVC between 0.60 and 0.80 to confirm obstruction. The severity of airflow limitation is classified on a numerical scale from 1 to 4 based on postbronchodilator FEV₁ % predicted values, as shown in **Figure 1**. The correlation between FEV₁, symptoms and health status impairment is weak, highlighting the need for symptom assessment.¹¹ GOLD no longer recommends the degree of reversibility of airflow limitation as a tool for therapeutic decision making.²

Figure 1. Classification of airflow limitation severity in patients with COPD, based on postbronchodilator FEV₁²

Increasing spirometric grade (GOLD 1-4) corresponds to more severe airflow limitation, measured by reduced FEV₁.

In patients with FEV ₁ /FVC <0.70:		
GOLD 1:	Mild	FEV ₁ ≥80% predicted
GOLD 2:	Moderate	50% ≤FEV ₁ <80% predicted
GOLD 3:	Severe	30% ≤FEV ₁ <50% predicted
GOLD 4:	Very Severe	FEV ₁ <30% predicted

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

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One measure used to assess symptoms and health status is the modified British Medical Research Council (mMRC) Questionnaire, which uses a 0 to 4 grading scale to characterize baseline dyspnea/breathlessness. However, there are many other symptoms of COPD, and therefore a more comprehensive assessment is recommended.² Another measure is the COPD Assessment Test (CAT[™]), an 8-item measure of the impact of COPD on the patient's health status; scores range from 0 to 40 (higher scores indicate more severe impact). These scores are used as a cut-point for making therapy decisions when a patient is experiencing fewer (CAT[™] <10) or more (CAT[™] ≥10) symptoms (**Figure 2**).^{2,12} Patients who have symptoms that are not responding to recommended medications should be referred to a pulmonary specialist.¹³

Figure 2. COPD Assessment Test (CAT[™])²

In the CAT[™], patients rate 8 items by describing their symptoms on a scale of 0 to 5. Higher scores indicate more severe impact; a total score of 10 is used as a cut-point for therapy.

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 1 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	
TOTAL SCORE				

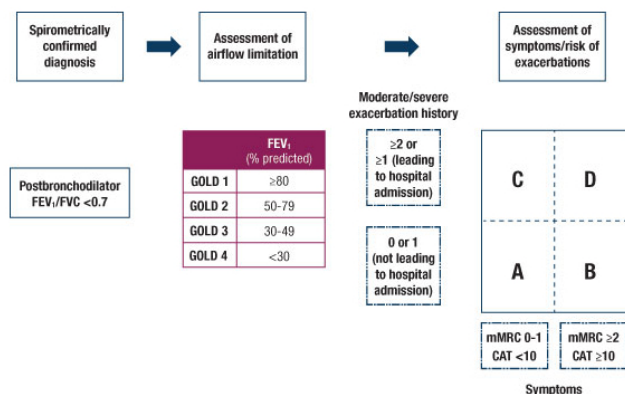
Abbreviation: COPD, chronic obstructive pulmonary disease.

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Exacerbation rates vary by patient. Patients with a history of exacerbations requiring hospitalization, oral corticosteroids (OCS), and/or antibiotics are most likely to have frequent exacerbations (≥2 per year) in the future.^{14,15} COPD is assessed by the spirometric grade (1-4; noted in **Figure 1**) and ABCD group, which also takes symptoms and exacerbation risk into account (**Figure 3**). If a patient has a marked difference between his or her spirometric grade (level of airflow limitation) and symptom assessment, further evaluation may be necessary, including specialist referral.²

Figure 3. The refined ABCD assessment tool²

Spirometric grading (GOLD 1-4) describes airflow limitation, whereas GOLD groups A-D describe symptoms/exacerbation risk. Combined assessment of these factors in COPD can guide therapy.



Abbreviations: CAT, COPD Assessment Test; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; mMRC, modified British Medical Research Council questionnaire (dyspnea).

From Global Initiative for Chronic Obstructive Lung Disease (GOLD), "Global strategy for the diagnosis,

Case Study (cont.)

A detailed medical history and physical assessment was conducted; Paul has a history of hypertension and obesity but no recurrent illnesses or hospitalizations. Spirometry provided an FEV₁/FVC ratio of 0.59 postadministration of a bronchodilator. FEV₁ was 68% predicted, which corresponds to spirometry grade GOLD 2 — moderate airflow limitation. Lung sounds were distant with prolonged expiration. Paul's CAT™ total score was 20. Based on his symptoms and exacerbation history, Paul's COPD assessment was Group B. He is started on a long-acting muscarinic antagonist (LAMA) with follow-up scheduled in 2 weeks. Instructions and demonstration of proper inhaler technique are provided, and a smoking cessation program is also reviewed.

Note: This is a hypothetical case description for teaching purposes.

Pharmacology of COPD Medications

Pharmacologic therapy can reduce symptoms, decrease risk of exacerbations, and improve exercise tolerance and health status.² Treatment should be individualized based on disease (symptom severity, exacerbation risk), drug (side effects of medication, availability/cost), and patient (comorbidities, preference and ability to use various devices) factors.²

Bronchodilators relax airway smooth muscle, improving expiratory flow and exercise performance by widening the airways; these medications are usually taken on a regular basis to relieve symptoms.² Beta₂-agonists stimulate beta₂-adrenergic receptors to cause relaxation of airway smooth muscle and are available in both short- (SABA) and long-acting (LABA) products.² LABA therapy has been shown to improve quality of life, reduce exacerbations, and improve lung function in patients with COPD.¹⁶ Muscarinic antagonists can open the airways by blocking the binding of acetylcholine to M3 muscarinic receptors in the airway smooth muscle and may also be either short- (SAMA) or long-acting (LAMA) products.² LAMAs have been associated with significant improvements in quality of life, as well as reductions in exacerbations and COPD-related hospitalizations.¹⁷ Methylxanthines are nonspecific phosphodiesterase inhibitors with a modest bronchodilator effect but are rarely used due to high toxicity.²

Anti-inflammatory agents primarily impact exacerbation risk. Inhaled corticosteroids (ICS) used in combination with LABA maintenance therapy improve lung function and health status and reduce exacerbations better than either agent alone.^{2,16,19} The likelihood of treatment benefit with ICS can be estimated using blood eosinophil count, with counts <100 cells/μL predicting little or no effect and counts >300 cells/μL suggesting greatest benefit with ICS.^{2,20} Triple therapy, which adds a LAMA to ICS/LABA therapy, can improve lung function and exacerbation risk.² Patients with higher exacerbation risk respond better to ICS-containing regimens, indicating that both blood eosinophil count and assessment of exacerbation risk should be considered to determine use of ICS.^{2,21,22} Oral corticosteroids are used in the acute management of COPD exacerbations but are not recommended for long-term daily treatment due to unfavorable long-term systemic effects.²

A phosphodiesterase-4 inhibitor can also reduce exacerbations and hospitalizations in combination with ICS/LABA therapy.² Antibiotics, particularly macrolide antibiotics, may be appropriate for patients who are former smokers and continue to have exacerbations despite triple therapy, but the risk of hearing loss and bacterial resistance with long-term antibiotic treatment should be considered.^{2,23,24}

Each of the therapies mentioned in this section is associated with potential adverse effects. When choosing a treatment for a specific patient, it is important to balance the benefits versus the risks. The revised GOLD 2019 report provides 2 models: (1) for the initiation of COPD treatments based on the ABCD assessment and (2) for maintenance treatment based on symptoms and exacerbations, including blood eosinophil count, that is not dependent on the ABCD assessment at diagnosis (Figure 4).²

Figure 4. Pharmacologic treatment algorithms by GOLD ABCD group²

A proposed model for treatment, including (A) initiation based on ABCD assessment and (B) maintenance treatment based on symptoms and exacerbations. Strategies for increasing or decreasing levels of intervention are based on available efficacy and safety data; response to treatment should always be reviewed because treatment escalation and de-escalation have not been well studied.

Figure 4A.

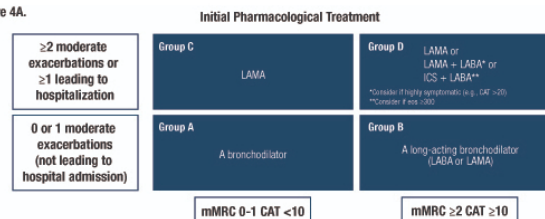
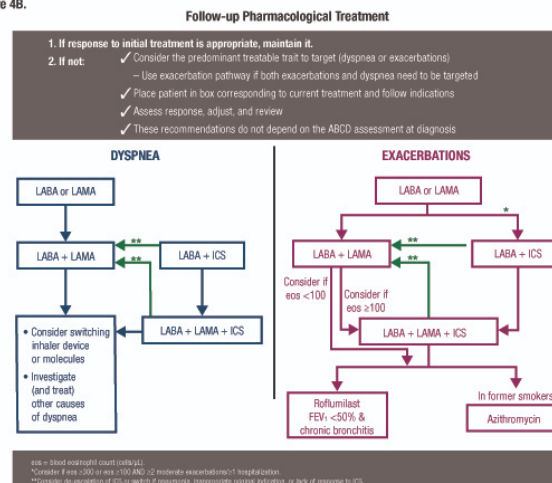


Figure 4B.



Abbreviations: CAT, COPD Assessment Test; eos, blood eosinophil count (cells/μL); FEV₁, forced expiratory volume in 1 second; GOLD, Global initiative for Chronic Obstructive Lung Disease; ICS, inhaled

corticosteroids; LABA, long-acting beta₂-agonist; LAMA, long-acting muscarinic antagonist; mMRC, modified British Medical Research Council questionnaire (dyspnea).

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Case Study (cont.)

Paul returns to the clinic with mild improvement in cough and breathlessness. FEV₁ is 75% predicted (GOLD 2), lung sounds remain unchanged, and CAT™ total score is 18. His blood eosinophil count is 80 cells/μL. Due to persistent symptoms, LAMA/LABA (long-acting beta₂-antagonist) is prescribed in place of LAMA, with follow-up in 2 weeks. Smoking cessation programs are reinforced, and the primary care provider ensures that Paul is up to date on his vaccines. Proper inhaler technique is reviewed.

Note: This is a hypothetical case description for teaching purposes.

All patients with COPD require routine follow-up that should include assessment of symptoms; monitoring of frequency, severity, and type of exacerbations; objective measurement of airflow limitation (FEV₁) using spirometry and functional capacity using a timed walking test; imaging if symptoms worsen; discussion of current therapeutic regimen, including dosage, adherence, and side effects; and review of inhaler technique.²⁵

Smoking Cessation

Smoking is the most common and avoidable risk factor for COPD.² For patients with COPD who smoke, cessation can significantly alter the progression of disease by slowing the progressive decline of lung function.²⁶ Furthermore, legislative smoking bans can lead to improved health outcomes, especially reducing exposure to secondhand smoke.²⁷ Pharmacologic therapies for smoking cessation include nicotine replacement (eg, patches), partial nicotine receptor agonists such as varenicline,²⁸ and certain antidepressants such as bupropion; the use of electronic cigarettes is controversial due to lack of supporting evidence.² Behavioral support, including counseling by health care providers, has also been shown to positively impact a patient's quitting success. A recent *Cochrane Database Review* of smoking cessation studies showed that, for patients with COPD who smoke, those who received a combination of high-intensity behavioral counseling and medication aimed at smoking cessation were more than twice as likely to quit as patients who received only behavioral support.²⁹ Health care providers can use the framework shown in **Figure 5** to guide smoking cessation discussions with their patients.²

Figure 5. A 5-step framework to help patients quit smoking²

Providers are encouraged to follow this "5-A" framework to identify patients who use tobacco and design a plan to help them quit.

- **ASK:** Systematically identify all tobacco users at every visit.
Implement an office-wide system that ensures that, for EVERY patient at EVERY clinic visit, tobacco-use status is queried and documented.
- **ADVISE:** Strongly urge all tobacco users to quit.
In a clear, strong, and personalized manner, urge every tobacco user to quit.
- **ASSESS:** Determine willingness and rationale of patient's desire to make a quit attempt.
Ask every tobacco user if he or she is willing to make a quit attempt at this time (eg, within the next 30 days).
- **ASSIST:** Aid the patient in quitting.
Help the patient with a quit plan; provide practical counseling; provide intra-treatment social support; help the patient obtain extra-treatment social support; recommend use of approved pharmacotherapy except in special circumstances; provide supplementary materials.
- **ARRANGE:** Schedule follow-up contact.
Schedule follow-up contact, either in person or via telephone.

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Vaccination

In a systematic review, polyvalent pneumococcal vaccinations were shown to reduce the likelihood of a COPD exacerbation and provide significant protection against community-acquired pneumonia.³⁰ These vaccinations are recommended for all patients aged 65 years and older.²

Management of Exacerbations

An acute worsening of respiratory symptoms that requires additional therapy defines an exacerbation of COPD.² Exacerbations may result in hospitalization and contribute negatively to patients' health status and disease progression.² Typically, exacerbations are triggered by viral respiratory infections, but they may also result from bacterial infections or environmental factors.³¹ The treatment required to manage an exacerbation defines its severity: mild exacerbations are treated with a SABA alone, whereas moderate exacerbations require a SABA plus antibiotic and/or a course of OCS. Severe exacerbations require hospitalization or emergency department visit(s) and may be associated with acute respiratory failure. **Figure 6** shows considerations for treatment of exacerbations.

Figure 6. Key considerations for management of exacerbations in patients with COPD²

The levels of evidence supporting the use of various agents in the management of exacerbations are summarized.

- Short-acting inhaled beta₂-agonists, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat an acute exacerbation (**Evidence C**).
- Systemic corticosteroids can improve lung function (FEV₁), oxygenation, and shorten recovery time and hospitalization duration. Duration of therapy should not 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**).

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second.

*Evidence A, sourced from randomized controlled trials with rich body of data; Evidence B, sourced from randomized controlled trials with limited body of data; Evidence C, sourced from nonrandomized trials and/or observational studies.

From Global Initiative for Chronic Obstructive Lung Disease (GOLD). "Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease," (2019). Reprinted with permission from GOLD.

Case Study (cont.)

Paul contacts the clinic to request a same-day sick appointment due to increasing shortness of breath, loose cough with mild clear sputum, increased nasal drainage, and fatigue over the past 3 days. His family members have been ill with upper respiratory infections. At the appointment, Paul's medical history is reviewed, and a physical assessment is completed. FEV₁ has decreased to 55% predicted from the previous visit, when FEV₁ was 72%. Oxygen saturation was 97% on room air, and CAT™ total score had increased to 26. Lung sounds remained clear and distant. A short-acting bronchodilator is added every 4 hours as needed and a 5-day oral prednisone burst of 40 mg/d is prescribed, with follow-up planned in 2 weeks.

Note: This is a hypothetical case description for teaching purposes.

Conclusions

Primary care providers play an important role in the assessment and management of COPD, including diagnosis, treatment, and routine monitoring. COPD assessment focuses on the patient's symptoms and risk of exacerbation; spirometry is used to confirm the diagnosis of COPD and objectively monitor patients over time. Various pharmacologic approaches are available for COPD treatment; recommendations for their use have been revised based on the ABCD groups and blood eosinophil count and include escalation/de-escalation strategies. Exacerbations suggest disease progression and require appropriate management. When a patient is not responding to treatment, a provider should refer the patient to a pulmonary specialist for further evaluation.

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