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Individualized Care in COPD: Updated Guidelines from Revised GOLD 2017 Report

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Abstract

Chronic obstructive lung disease (COPD) is a major cause of morbidity and mortality around the world. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) program provides evidence based guidelines to optimize management of patients with COPD. The Global Strategy for Diagnosis, Management and Prevention of COPD 2017 report incorporates many changes based on updated research published through 2016. It includes new strategies to promote individualized care with the goal of improving patient-centered outcomes. The new definition, revised combined assessment tool and the new approaches to management of COPD are highlighted in our review.

Keywords: COPD assessment; Gold 2017 guidelines; Gold 2017 update; COPD treatment; COPD outpatient management; Global initiative for chronic obstructive lung disease; Chronic obstructive pulmonary disease

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Introduction

Chronic obstructive lung disease (COPD) is a major cause of chronic morbidity and is the fourth leading cause of mortality worldwide [1]. In the USA, it is the third leading cause of death as well as the second leading cause of reduced disability-adjusted life years (DALYs) [2,3]. The disease burden is projected to continue to rise worldwide because of ongoing exposure to COPD risk factors and aging of the population [4]. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) program was initiated in 1988 to optimize management of COPD and promote prevention worldwide. In 2001, it published its first report "Global Strategy for Diagnosis, Management and Prevention of COPD" to provide clinicians with evidence-based management guidelines. The GOLD Science Committee periodically revises the report based on new research findings. The 2017 report represents the fourth major revision based on publications through 2016 related to pathophysiology, diagnosis, assessment and approaches to management of COPD [5]. Our review highlights the GOLD updates on outpatient management of stable COPD. These updates are of relevance to primary care providers as well as pulmonary specialists.

Diagnosis of COPD

GOLD's definition of COPD was changed in its 2017 report to "A common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases" [5]. The prior definition referenced inflammation, comorbidities and exacerbations but this new simplified definition brings focus to the typical clinical picture at time of presentation. COPD should be considered in any individual who has dyspnea, chronic cough, chronic sputum production or recurrent lower respiratory tract infections and a history of exposure to risk factors. The updated list of risk factors in GOLD 2017 report adds genetic and individual factors (**Table 1**).

Since symptoms associated with COPD are nonspecific and overlap with cardiac, systemic and other pulmonary disorders, spirometry is required to confirm COPD. Spirometry reliably measures forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC). The ratio of these two measurements (FEV_1/FVC) is used to determine presence or absence of airflow limitation. Per GOLD guidelines, a post-bronchodilator FEV_1/FVC ratio of <0.70 identifies persistent airflow limitation. This differs from ATS guidelines that recommend using ratio less than lower limits of normal (FEV_1/FVC <LLN) to identify airflow limitation

Table 1 Risk factors for COPD.

Host factors
Genetic (family history, alpha-1 antitrypsin deficiency) Individual (low birth weight, childhood infections)
Tobacco smoke
Smoke from home cooking and heating fuels Industrial dust and chemical fumes
Adapted from "From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease [GOLD] 2017". Copyright 2017 by Global Initiative for Chronic Obstructive Lung Disease.

[6]. While more data are needed to determine ideal diagnostic spirometry criterion, GOLD favors use of fixed ratio for its simplicity and consistency. However, clinicians should be mindful that using FEV_1/FVC ratio <0.70 to define airflow limitation may result in over-diagnosis in the older individuals, and under-diagnosis in adults <45 years, especially in the presence of mild disease [7,8].

Initial COPD Assessment

The goals of initial COPD assessment are to determine the severity of airflow limitation, the impact of disease on the patient's health status, and the risk of future events (such as exacerbations, hospital admissions, or death). Comorbidities contribute significantly to morbidity and mortality associated with COPD. Thus, assessment of all these factors is required to provide individualized treatment for each patient.

Assessment of air flow limitation: Classification of severity of airflow limitation is based on post-bronchodilator FEV_1 (**Table 2**). The degree of reversibility on post-bronchodilator spirometry does not add to differential diagnosis or predict response to therapy [9].

Assessment of symptoms: Severity of airflow limitation has a weak correlation with symptoms and impairment of a patient's health-related quality of life. Several tools are available to specifically measure burden of disease. GOLD favors the use of the Modified British Medical Research Council (mMRC) dyspnea scale (**Table 3**) and COPD assessment test (CAT) (**Table 4**), primarily for their ease of use in clinical practice [10,11]. CAT is favored over mMRC dyspnea scale as it allows a more comprehensive assessment of symptoms beyond just breathlessness. mMRC grade 0-1 and CAT score <10 indicate a low-symptom profile.

Assessment of risk for exacerbations: An exacerbation of COPD is defined as "Acute worsening of respiratory symptoms that result in additional therapy". COPD exacerbations are associated with accelerated rate of decline in FEV_1, deterioration in health status and risk of death [12,13]. The most reliable way of assessing future risk of exacerbations is to look at treated exacerbations in the past. Increased risk of exacerbations is defined as 2 or more exacerbations per year or 1 exacerbation leading to hospital admission. In patients not on inhaled steroid treatment, GOLD 2017 updated guidelines incorporate increased blood eosinophil count as a predictor of exacerbations [14,15]. However, prospective clinical trials are needed to establish blood eosinophil cut-off values that can be used in clinical decisions. GOLD 2017 report recommends that most therapeutic decisions be based on ABCD assessment tool that grades severity of disease based on symptoms and risk for exacerbations. This tool is presented in **Figure 1**.

Assessment of comorbidities: Common comorbidities associated with COPD include cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression, anxiety and lung cancer [16-18]. Comorbidities can occur with any degree of airflow limitation. They diminish the quality of life, and increase hospitalization and mortality rates; 60% of patients with COPD die from other causes [19-21]. Therefore, clinicians should look for these conditions in all patients diagnosed with COPD, and treat them appropriately. Comprehensive COPD evaluation protocol includes diagnosis, assessment of severity of airflow limitation, assessment of severity of symptoms, assessment of risk of exacerbations and identification of comorbidities that add to disease burden for each individual patient (**Figure 2**).

Additional Testing

Imaging: Chest X-ray is used primarily to exclude alternative diagnoses. CT chest is not routinely recommended but is needed if considering invasive treatment for COPD.

Lung volumes and diffusion capacity: These tests may be considered to look for other conditions when the degree of air flow limitation does not explain dyspnea.

Oximetry and arterial blood gases (ABGs) measurement: Pulse oximetry should be performed for all stable patients with FEV_1 <35% predicted or with clinical signs of respiratory failure and/or right heart failure. ABGs measurement is indicated for all patients with baseline pulse oximetry saturation level <92%.

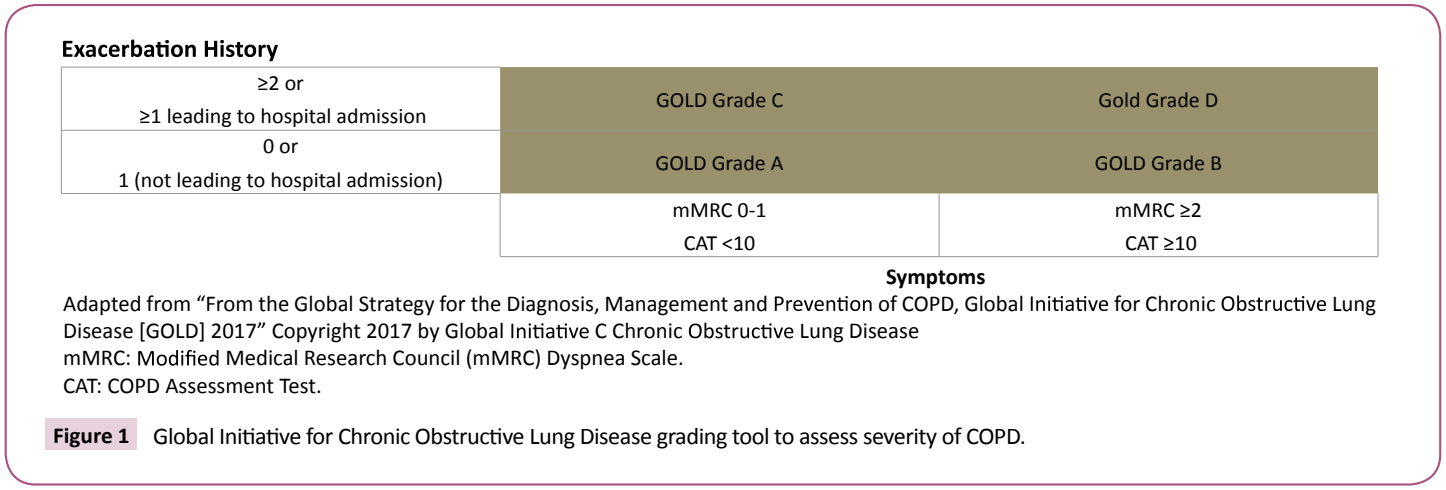
Screening for alpha-1 antitrypsin (AAT) deficiency: Patients from areas with high prevalence of alpha-1 antitrypsin deficiency and with earlier presentation [<45 years with pan lobular emphysema] should be screened for AAT deficiency.

Exercise testing: Walking distance measured by the six-minute walk test or the shuttle walk test is used to assess degree of disability and mortality risk, and to monitor response to pulmonary rehabilitation [22-24].

Composite scores: The BODE (Body mass index, Obstruction, Dyspnea, and Exercise) index are easy to calculate and is a better predictor of survival than any of its single components [25].

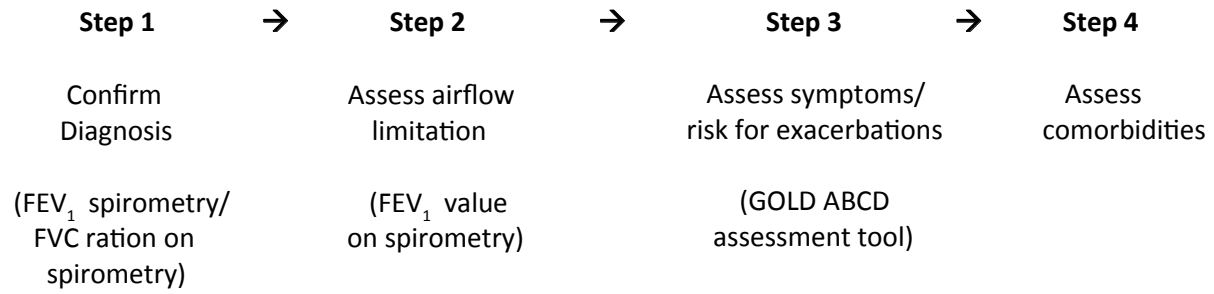
Outpatient Management of COPD

Treatment of COPD is targeted at reducing symptoms, exacerbations, hospitalizations and mortality as well as improving overall health status. To achieve these goals, a multipronged



Adapted from "From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease [GOLD] 2017" Copyright 2017 by Global Initiative C Chronic Obstructive Lung Disease
mMRC: Modified Medical Research Council (mMRC) Dyspnea Scale.
CAT: COPD Assessment Test.

Figure 1 Global Initiative for Chronic Obstructive Lung Disease grading tool to assess severity of COPD.



FEV_1: Forced Expiratory Volume in 1 second.
FVC: Forced Vital Capacity.

GOLD ABCD: Global Initiative for Chronic Obstructive Lung Disease tool to assess severity of COPD

Figure 2 Stepwise comprehensive COPD assessment (based on GOLD 2017 report).

Table 2 GOLD Classification of airflow limitation based on post-bronchodilator FEV_1.

GOLD 1	Mild	FEV_1 ≥ 80% predicted
GOLD 2	Moderate	FEV_1 50% to < 80% predicted
GOLD 3	Severe	FEV_1 30% to <50% predicted
GOLD 4	Very severe	FEV_1 <30% predicted

Adapted from "From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017". Copyright 2017 by Global Initiative for Chronic Obstructive Lung Disease.

FEV_1: Forced expiratory volume in 1 second.

Table 3 Modified Medical Research Council (mMRC) Dyspnea Scale.

mMRC grade 0	I only get breathless with strenuous exercise	☐
mMRC grade 1	I get short of breath when hurrying on the level or walking up a light hill	☐
mMRC grade 2	I walk slower than other 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	☐
mMRC grade 3	I stop for breath after walking about 100 meters or after a few minutes on the level	☐
mMRC grade 4	I am too breathless to leave the house or I am breathless when dressing or undressing	☐

Adapted from "Standardized questionnaire on respiratory symptoms: a statement prepared and approved by the MRC Committee on the Aetiology of Chronic Bronchitis (MRC breathlessness score). BMJ (1960) 2: 1662".

Table 4 COPD assessment test.

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 questions				Score
Example	I am very happy	⓪①②⊗④⑤	I am very sad	③
	I never cough	⓪①②③④⑤	I cough all the time	
	I have no phlegm (mucus) in my chest at all	⓪①②③④⑤	My chest is completely full of phlegm	
	My chest does not feel tight at all	⓪①②③④⑤	My chest feels very tight	
	When I walk up a hill or one flight of stairs I am not breathless	⓪①②③④⑤	When I walk up a hill or one flight of stairs I am very breathless	
	I am not limited doing any activities at home	⓪①②③④⑤	I am very limited doing activities at home	
	I am confident leaving my home despite my lung condition	⓪①②③④⑤	I am not at all confident leaving my home because of my lung condition	
	I sleep soundly	⓪①②③④⑤	I don't sleep soundly because of my lung condition	
	I have lots of energy	⓪①②③④⑤	I have no energy at all	
			Total Score	

Adapted from: "Development and first validation of the COPD Assessment Test. Eur Respir J (2009) 34: 648-654".

Table 5 Pharmacological treatment strategies by GOLD Grade.

GOLD Grade A	Single bronchodilator → alternative class of bronchodilator if needed → discontinue if appropriate
GOLD Grade B	LABA or LAMA → LABA/LAMA if symptoms persist
GOLD Grade C	LAMA → LABA/LAMA (preferred) or LABA/ICS if exacerbations
GOLD Grade D	LABA/LAMA → LABA/LAMA/ICS if symptoms/exacerbations (preferred)* or LABA/ICS → LABA/LAMA/ICS if symptoms/exacerbations or LAMA → LABA/LAMA→ LABA/LAMA/ICS if symptoms/exacerbations If further exacerbations, consider: Roflumilast (FEV_1<50%, chronic bronchitis) or Macrolide (former smoker) If stable on LABA/LAMA/ICS, consider de-escalation to LABA/LAMA

LABA: Long-Acting Beta-Agonists
LAMA: Long-Acting Muscarinic Antagonists
LABA/LAMA is more effective than LABA or LAMA or ICS/LABA for decreasing exacerbations
ICS: Inhaled Corticosteroid
FEV_1: Forced expiratory volume in 1 second.
Adapted from "From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017". Copyright 2017 by Global Initiative for Chronic Obstructive Lung Disease.

management strategy that includes pharmacological as well as non-pharmacological interventions is required. Interventions should be tailored to the individual patient's needs based on COPD assessment protocol outlined in **Figure 2**. Some key changes in management included in GOLD 2017 report are:

- The pharmacologic regimen is based primarily on GOLD ABCD grade of disease. The primary role for spirometry is confirmation of diagnosis, prognostication and follow-up assessment. Spirometry does have a more prominent role in therapeutic decisions if there is significant discrepancy between spirometry and symptoms or when invasive therapies for COPD are being considered.
- Treatment escalation and de-escalation strategies are outlined to accommodate shifts in degree of baseline symptoms and pattern of exacerbations.
- Invasive interventional therapy options are listed for selected patients with emphysema and hyperinflation.

Pharmacologic Therapy

Pharmacologic therapy is effective at reducing symptoms and exacerbations but has not been shown to modify the decline in lung function [12,26–29]. Many classes of medications are available to treat COPD as highlighted below. The mainstay of pharmacologic treatment in patients with COPD, however, continues to be inhaled bronchodilators (beta2-agonists and anti-muscarinic drugs) and inhaled corticosteroids **(Table 5).**

Beta2 agonists: Short acting beta2 agonists (SABA) as well as long acting beta2 agonists (LABA) have a defined role in management. Unlike asthma, there is no association between use of this class and increased mortality in COPD [30-37].

Antimuscarinic drugs: Short acting muscarinic antagonists (SAMAs) and long acting muscarinic antagonists (LAMAs) have an important role in management of COPD. LAMA (Tiotropium)

has been shown to have greater effect on reducing exacerbations compared to LABA treatment [38,39]. Because of concerns regarding adverse cardiovascular effects associated with this class, FDA conducted a review in 2009 and concluded that LAMA (Tiotropium) added to other standard therapies had no effect on cardiovascular risk [40].

Inhaled corticosteroids (ICS): In patients with moderate to very severe COPD and exacerbations, an ICS combined with a LABA is more effective than either component alone in improving lung function, health status and reducing exacerbations but it has no impact on survival [41-44]. Inhaled steroids may be more effective in reducing exacerbations in patients with eosinophilia [45,46].

Oral steroids: Oral glucocorticoids which play a significant role in the acute management of exacerbations have no role in the chronic daily treatment in COPD because of a lack of benefit and a high rate of systemic complications.

Phosphodiesterase-4 (PDE4) inhibitor: Roflumilast reduces moderate and severe exacerbations in patients with chronic bronchitis and severe COPD. However, it has more adverse effect than inhaled medications [47,48].

Antibiotics: Macrolides (azithromycin, erythromycin) prescribed for anti-inflammatory effects may reduce exacerbation rates but are associated with increased bacterial resistance and ototoxicity [49,50]. Impact to prevent COPD exacerbations beyond one year is unknown.

Mucolytics: In COPD patients not on inhaled corticosteroids, carbocysteine and/or N-acetylcysteine may reduce exacerbations and improve health status [51].

Methylxanthine: Theophylline has modest bronchodilator effect but toxicity limits its usage. Its side effect profile includes arrhythmias and convulsion which can prove to be fatal.

Alpha1 antitrypsin (AAT) augmentation: Never or ex-smokers with FEV_1 of 35-60% and AAT deficiency are considered most suitable for AAT augmentation therapy. Patients with FEV>=65% may also be considered if there is evidence of progressive lung disease despite other optimal therapy. In view of the cost of therapy and lack of evidence for much benefit, discussion with individual patient is recommended before initiation of therapy [52].

Non-pharmacologic Therapies

Smoking cessation: It is the only evidence-based intervention that slows the accelerated decline in lung function in people with COPD [53]. Interventions include counseling and pharmacological therapy. While a clear relation exists between the intensity of counseling and smoking cessation, as little as three minutes of counseling can lead to successful cessation [54,55]. The pharmacological therapy options include nicotine replacement (gum, inhaler, nasal spray, transdermal patch, sublingual tablet, or lozenge), and medication such as varenicline, bupropion or nortriptyline. Concomitant use of counseling and pharmacological therapy increases effectiveness of intervention [56]. Role of e-cigarettes as nicotine replacement therapy is unclear based on currently available data. In addition, avoidance of other risk factors such as occupational dusts, air pollutants, fumes and gases that contribute to airway disease should be emphasized.

Vaccination: All COPD patients should receive influenza vaccination. Influenza vaccination in patients with COPD reduces severe lower respiratory tract infections and mortality, and over time reduces risk of ischemic heart disease [57,58]. Pneumococcal vaccination is recommended per CDC guidelines. Specific effects of Pneumococcal vaccination on infections and mortality in patients with COPD is unclear [59,60].

Pulmonary rehabilitation: Pulmonary rehabilitation is defined as "A comprehensive intervention based on thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, self-management intervention aiming at behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors." [61] It is recommended for all patients that continue to be symptomatic after optimization of pharmacologic therapy. It can be conducted in inpatient or outpatient settings including the patient's home. It is one of the most cost effective strategies to improve shortness of breath, health status and exercise tolerance across all grades of COPD severity [62-64].

Self-management interventions: Self-management interventions include training in self-recognition of exacerbations, coping with breathlessness, increasing physical activity and improving nutrition in malnourished individuals. Self-management interventions that include action plans for worsening symptoms decrease respiratory-related as well as all cause hospitalizations [65].

Invasive therapy: Recommendations for invasive therapies are included for the first time in the GOLD 2017 report. Bullectomy, bronchoscopic lung volume reduction (BLVR) and lung volume reduction surgery (LVRS) improve health outcomes in carefully selected subset of patients [66-69]. Extent and pattern of emphysema on high-resolution computed tomography (HRCT), presence of inter-lobar collateral ventilation, patient and provider preferences and local expertise are important considerations when considering invasive treatment options for patients. For selected patients with very severe COPD, lung transplantation should be considered. Patients should be informed that it improves QOL but not survival [70,71].

Palliative care: The goal of palliative care is to prevent and relieve suffering, and to optimize quality of life [72]. Opiates, neuromuscular electrical stimulation (NMES), chest wall vibration (CWV), fans blowing air onto the face, oxygen, pulmonary rehabilitation, and non-invasive ventilation all reduce breathlessness [73-79]. Cognitive behavioral therapy and mind-body interventions [e.g., mindfulness-based therapy, yoga, and relaxation] can reduce anxiety and dyspnea and improve lung function, exercise capacity and fatigue [80]. Nutritional supplementation supports weight gain, respiratory muscle strength and overall health-related quality of life in malnourished patients. Fatigue may be reduced by self-management education, pulmonary rehabilitation, nutritional support and mind-body

interventions [81,82]. Prediction of 6-month survival in patients with end-stage COPD is unreliable and therefore early discussion of advance care planning is recommended [83]. Discussing issues surrounding death with compassion can reduce anxiety for patients and their families and avoid unnecessary, unwanted and costly invasive approaches [84]. For patients with terminal illness, hospice services may be beneficial.

Oxygen and non-invasive positive pressure ventilation: Oxygen administration (> 15 hours per day) improves survival in patients with severe resting hypoxemia [85]. In patients with overlap syndrome (both COPD and obstructive sleep apnea), continuous positive airway pressure (CPAP) improves survival and reduces hospitalizations [86]. There is conflicting data on the use of non-invasive positive pressure ventilation (NIPPV) on survival and re-hospitalization in chronic hypercapneic COPD. NIPPV should always be managed by providers familiar management of hypercapneic respiratory failure.

Monitoring and Follow-up

Follow-up visits should include symptom evaluation as well as discussion of treatment regimen. For patients on inhalers, inhaler technique should be checked during each visit. There is no evidence for superiority of any one type of hand held device over others. For patients that are able to use their prescribed devices properly, nebulized therapy offers no additional advantage [87-89]. Thus, it is important to assess patient's physical and medical conditions to determine the most suitable inhaler device for them. Spirometry is recommended at least once a year in all patients. If there is a clear worsening of symptoms, imaging may be indicated. Step up in therapy to prevent future exacerbations and step down in therapy in stable patients should be implemented as needed during the follow up visits **(Table 5).**

Conclusion

COPD is a major cause of morbidity and mortality in the USA and around the world. Based on review of literature published through 2016, the GOLD 2017 report includes major changes in guidelines for assessment as well as treatment. All providers that treat patients with COPD should be aware of these updated strategies that promote symptom control, improve quality of life and reduce COPD associated mortality.

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