

New Perspectives in COPD Management

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CONTINUING MEDICAL EDUCATION

LEARNING OBJECTIVES

- Collaborate with patients to inform treatment decision-making that addresses their symptoms, goals, and concerns
- Individualize guideline-recommended therapy to reduce chronic obstructive pulmonary disease (COPD) exacerbations, improve lung function, manage daily symptoms such as breathlessness, and help achieve the patient's goals
- Select an inhaler and an optimal dose of medication to best meet a patient's needs and capabilities

KEY TAKEAWAYS

- The goal of treatment is to achieve and maintain stable disease by reducing both symptoms and the future risk of exacerbations.
- Holistic management consists of addressing 5 issues: 1) risk factors; 2) individualizing treatment; 3) comorbidities; 4) preventive therapy; and 5) self-management education to address patient's goals and preferences.
- Patients with COPD most likely to experience benefit with an inhaled corticosteroid (ICS) include those with ≥ 2 exacerbations and/or 1 hospitalization in the previous year.
- There is a continuous relationship between blood eosinophils and ICS benefit with those with blood eosinophil count < 100 cells/mL likely to achieve little or no benefit with ICS therapy.
- Single inhaler dual or triple therapy offers several advantages compared with separate inhaler dual or triple therapy, including improved symptom control, reduced rate and time to first moderate/severe exacerbation, and, for some patients, lower co-payments.

TARGET AUDIENCE

Family physicians and clinicians who wish to gain increased knowledge and greater competency regarding primary care management of COPD.

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BURDEN OF DISEASE

Chronic obstructive pulmonary disease (COPD) is well established as causing extensive morbidity and mortality among the 6.6% of adults with diagnosed COPD in the United

States.¹ The U.S. Burden of Disease Collaborators determined that COPD was responsible for 1.2 million years lived with disability, the eleventh leading cause, in 2016.² Morbidity from COPD may be affected by coexisting diseases, eg, car-

diovascular disease, musculoskeletal impairment, diabetes mellitus, gastroesophageal disease, osteoporosis, lung cancer, anxiety, and depression.³

Also in 2016, COPD was responsible for 2.3 million years of life lost, the third leading cause, or 501 years of life lost per 100,000 people.² In 2014, the death rate due to COPD in the United States was 39.1 deaths per 100,000 people and was higher in males than females (44.3 vs 35.6 deaths per 100,000 people, respectively).⁴ One-quarter of adults with COPD have never smoked.⁵ Geographic and sociodemographic patterns of COPD prevalence are similar among current smokers, former smokers, and adults who have never smoked.⁵

Exacerbations caused by COPD are associated with numerous negative outcomes, eg, accelerated decline in lung function, poor functional status and quality of life, and increased healthcare resource utilization. Severe exacerbations, ie, those requiring hospital admission, are associated with poor prognosis.⁶

CHANGING THE TREATMENT PARADIGM

For more than 20 years, the treatment of COPD has consisted of managing symptoms and preventing exacerbations.^{3,7} However, 20 years ago, controlling daily symptoms was especially challenging because of the limited effectiveness of available medications in treating symptoms and the underlying inflammation. Moreover, the duration of action of most medications was short, which required dosing multiple times daily. Consequently, much of the treatment focus was on reducing the severity of exacerbations once they occurred.

Fortunately, medications have become available that are more effective and have a longer duration of action. This has enabled the effective reduction of daily symptoms to be a realistic goal. This is fortuitous since compelling evidence has emerged as to the negative consequences of exacerbations, including increased risk for future exacerbations and death, as well as progressive decline in lung function.⁸⁻¹⁰

This changing paradigm has been embraced in the past few years by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). As identified by GOLD, the broad goal of treatment is to achieve and maintain stable disease. Although GOLD 2020 does not explicitly define stable disease, the objective is to reduce both symptoms and the future risk of exacerbations.³ This treat-to-target approach is increasingly employed in the treatment of individuals with other chronic diseases, eg, diabetes mellitus, inflammatory bowel disease, and rheumatoid arthritis. The treat-to-target approach involves employing treatment to first achieve the treatment target and then modifying treatment as needed to maintain the treatment target. In the case of COPD, the treatment target is stable disease. Therefore, when disease

control begins to deteriorate and symptoms increase but an acute exacerbation has not yet occurred, the patient should be empowered to intensify treatment. Action plans have been customarily aimed at treating an acute exacerbation; however, it is important for patients to know steps to intensify treatment at the onset of deteriorating symptoms, as is done for migraine headaches. A key item for inclusion in the written action plan is a reminder for the patient to contact their primary care clinician (PCC) at the time treatment is intensified, even if symptom stability is regained.

Effective self-management requires that the patient has the knowledge, motivation, and means to implement the treatment plan.¹¹ Effective communication and shared decision-making that engages the patient are key steps complemented with ongoing education and coaching by the multidisciplinary care team described below.¹² Shared decision-making should be utilized at each patient visit, with a key objective to solicit and address patient barriers, goals, and concerns. The treatment plan, as well as the written action plan, should be revised as needed.

HOLISTIC MANAGEMENT

Holistic management that places the patient at the center of care is a key to achieving and maintaining stable disease.¹¹ Five basic components of holistic management in individuals with COPD are 1) eliminate/minimize risk factors, 2) initiate individualized nonpharmacologic and pharmacologic therapy early in the disease course and intensify as needed using a treat-to-target approach, 3) identify and treat comorbidities, 4) provide preventive therapy, and 5) provide self-management education.³ Smoking cessation is of paramount importance, with support and treatment provided for the rest of the patient's life. The importance of a healthy diet should not be overlooked since a diet rich in antioxidants may have beneficial effects on lung function.¹³ Treatment cost and affordability are also important considerations and should be discussed with the patient.

Clinicians should consider and screen for comorbidities such as diabetes, cardiovascular disease, and depression. If found, clinicians should provide treatment with evidence-based therapies. Generally, the treatment of comorbidities does not alter COPD treatment, and the presence of COPD will not alter basic treatment of comorbid conditions. Treatment of individuals with COPD, such as with pulmonary rehabilitation, may have a beneficial impact on comorbidities, such as depression, anxiety, sleep disturbance, and fatigue.¹⁴⁻¹⁶ The overall treatment plan should be simplified as much as possible, including minimizing the number of medications and using combination medications, including inhalers. Assistance for smoking cessation is a key component of preventive therapy. In addition to practicing healthy

FIGURE 1. **ABCD assessment tool for selection of initial pharmacologic treatment**³

≥2 Moderate exacerbations or ≥1 leading to hospitalization	Group C LAMA	Group D LAMA or LAMA + LABA ^a or ICS + LABA ^b
0 or 1 Moderate exacerbations (not leading to hospital admission)	Group A Bronchodilator	Group B Long-acting bronchodilator (LAMA or LABA)
	mMRC 0-1; CAT <10	mMRC ≥2; CAT ≥10

CAT, COPD Assessment Test; mMRC, Modified British Medical Research Council Questionnaire.

^aConsider if highly symptomatic (eg, CAT >20).

^bConsider if eosinophil count ≥300 cells/microliter.

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lifestyle recommendations, individuals should be screened for lung cancer and should receive recommended vaccinations including pneumococcal, influenza, tetanus, diphtheria, pertussis (Tdap), shingles, and COVID-19.

Holistic management generally involves care provided by a multidisciplinary care team, with the PCC playing a key role in collaborating with the pulmonologist, chronic care managers, mental health clinician, respiratory therapist, physical therapist, and others. Collaboration among the multidisciplinary care team is especially important during any hospitalizations to ensure that transitions in care take place smoothly. Finally, although COPD is a progressive disease, a key role of the PCC is to nurture hope through close collaboration with the patient and provide assurances that treatment will be individualized to achieve treatment goals.

PHARMACOLOGIC TREATMENT

Initial

Initial pharmacologic treatment selection recommended by GOLD is guided by the revised ABCD assessment tool (FIGURE 1).³ This tool utilizes clinical parameters, ie, symptoms and history of exacerbations, but not airflow limitation as identified by spirometry. This separation acknowledges the limitations of lung function assessment in predicting symptom burden and risk of exacerbation and, therefore, pharmacologic treatment decisions, while remaining a key factor in diagnosis and prognosis assessments.

Bronchodilator therapy using a β_2 -agonist or antimuscarinic or a combination of these medications is the cornerstone of pharmacologic treatment for individuals with COPD as it increases the forced expiratory volume in 1 second (FEV₁) and/or improves other spirometric variables. Although bronchodilator therapy has not been shown to impact lung function decline,^{17,18} it has numerous other benefits, eg, reducing symptoms, improving health status,

and reducing exacerbation rates.¹⁹⁻²² Long-acting antimuscarinic (LAMA) therapy has a greater effect on reducing exacerbation rates than long-acting β_2 -agonist (LABA) therapy.^{23,24} Compared with monotherapy, combination LAMA/LABA therapy provides for greater improvement in lung function and patient-reported outcomes such as quality of life.²⁵⁻²⁸

Anti-inflammatory therapy using an inhaled corticosteroid (ICS) as monotherapy is not indicated in COPD management as it has not been shown to modify the long-term decline in FEV₁ or reduce mortality, symptom burden, or dynamic hyperinflation, the latter of which often leads to dyspnea.²⁹ Consequently, ICS therapy in combination with ≥1 long-acting bronchodilator(s) is recommended for patients with severe disease, eg, GOLD ABCD group D.³ Specifically, an ICS is recommended for patients with severe disease and an elevated blood eosinophil count. The eosinophil count helps predict the magnitude of the effect of ICS (in combination with bronchodilator therapy) in preventing future exacerbations.³⁰⁻³⁵ Patients with a blood eosinophil count >300 cells/ μ L are most likely to achieve treatment benefit with ICS therapy,³ although there is a continuous relationship between blood eosinophils and ICS benefit, and those with a blood eosinophil count >100 cells/ μ L are likely to achieve benefit with ICS therapy.³ Since the primary role is exacerbation prevention, patients most likely to benefit from ICS-containing therapy are those with high exacerbation risk, ie, ≥2 exacerbations and/or 1 hospitalization in the previous year.^{31,33,36} Thus, treatment decisions about ICS therapy should be based on the clinical assessment of exacerbation risk and should consider blood eosinophil count.³

TREATMENT DECISIONS ABOUT ICS THERAPY SHOULD BE BASED ON THE CLINICAL ASSESSMENT OF EXACERBATION RISK AND SHOULD CONSIDER BLOOD EOSINOPHIL COUNT.

TABLE 1. Checklist for the COPD follow-up office visit

- Repeat the CAT
 - Have patient complete in waiting room or examination room^a
 - Compare to previous CAT score to assess progressive symptoms like dyspnea
- Ask about:
 - Respiratory problems or events since last visit, particularly if they required an urgent care/emergency department visit
 - Changes in comorbidities
 - Changes in activity level (be specific)
 - Difficulties with prescription refills
 - Difficulties following the treatment plan
 - Satisfaction with treatment
- Check inhaler technique by observation
 - Can be done by trained staff
- Review medications patient is taking to be sure they are the ones prescribed
 - Requires patient to bring in actual medications instead of a list; telehealth may provide good opportunity for patient or family to bring medication to video device
 - Note brand and inhaler type may have been changed due to insurance
- Review patient's goals and action plan^a

CAT, COPD Assessment Test.

^aCan be facilitated by using the COPD Foundation application available at <https://bit.ly/2RwrX79>

Follow-up

Assessing the patient's response to treatment is essential at every visit (TABLE 1). Two validated tools that can be used are the Modified British Medical Research Council Dyspnea Scale (mMRC)³⁷ and the COPD Assessment Test (CAT).³⁸ However, the mMRC is of limited use since it measures only breathlessness and changes from 1 level to the next may not be very sensitive to changes in symptom burden or lung function decline. In contrast, the CAT is a broad measure of symptoms and is more inclusive of overall health status. While neither tool categorizes patients by symptom severity for the purpose of modifying treatment, using the CAT at every visit allows the clinician to assess health changes over time.

Patient assessment should also investigate any other changes in health or difficulties with treatment adherence the individual might be experiencing. As always, clear communication using shared decision-making can help quickly identify factors that might contribute to a change in disease stability. If the individual is experiencing difficulties or has concerns, it is important that solutions be found in collaboration with the patient and complemented by education and support so that the patient is willing and able to successfully implement the revised treatment plan. This is also the opportune time to reinforce nonpharmacologic treatment and inhaler technique.

FIGURE 2 outlines the recommended pathway for intensifying maintenance treatment in an individual who is experiencing

disease instability.³ The pathway does not include consideration of GOLD ABCD group identified at treatment initiation or disease duration.³ Treatment is modified based on whether dyspnea or exacerbations are the predominant treatable trait. The CAT is useful to identify trends and changes in symptom control. For individuals with dyspnea as the predominant trait who are treated with long-acting bronchodilator monotherapy, ie, LAMA or LABA, the addition of a second long-acting bronchodilator is appropriate. Alternatively, switching the inhaler device or molecules can be considered.

For an individual with exacerbations as the predominant trait, either dual or triple combination therapy is needed, with the choice based on current treatment as well as blood eosinophil count.³ For example, the addition of an ICS is recommended for a patient with blood eosinophil level >100 cells/ μ L who experiences an exacerbation despite good adherence to combination LABA/LAMA therapy.

Orally inhaled medications

To optimize inhalation therapy, inhaler selection must be individualized (TABLE 2).³⁹ Ease of use and convenience are factors patients consider important in the selection of an inhaler device. Therefore, selection must take into account patient capabilities and preferences, including experience with inhalers.^{40,41} Patient physical and cognitive limitations are important to consider as well. Device choice may also be

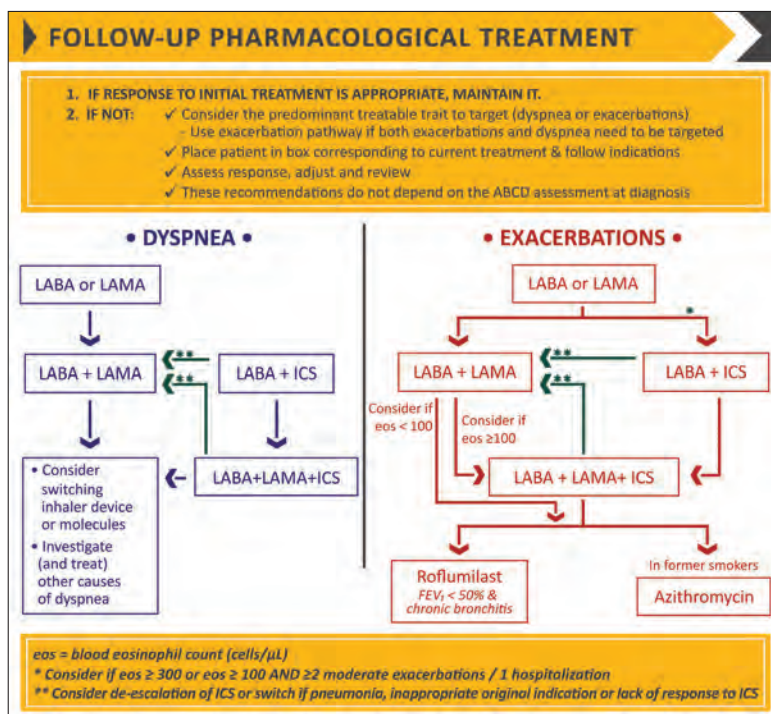
dictated by insurance coverage and co-payments, which are often very important to the patient.

In addition to demonstrating and verifying correct inhaler technique by watching the patient use the inhaler initially, inhaler technique should be reviewed and observed at each visit since a decline in correct inhaler technique is common within weeks to months of initial instruction.^{40,42-44}

For patients who require treatment with ≥ 2 inhaled medications, a single inhaler containing 2 or 3 medications, ie, single inhaler dual or triple therapy, should be used whenever possible. This not only reduces the amount of time required for medication administration, but it also simplifies the overall treatment plan. If individual inhalers must be used, the same inhaler device, eg, metered dose inhaler, dry powder inhaler, soft mist inhaler, should be used when possible to avoid patient confusion and errors in inhaler use.⁴⁵

Single inhaler triple therapy has been shown to provide significant improvement in symptom control and severity of exacerbations vs separate triple inhaler therapy.⁴⁶ Similarly, single inhaler triple

FIGURE 2. Follow-up pharmacologic treatment³



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TABLE 2. Advantages and disadvantages of inhaler devices³⁹

	Advantages	Disadvantages
Pressurized metered-dose inhaler (pMDI)	<ul style="list-style-type: none"> • High reproducibility between doses⁴⁸ • Independent of inspiratory flow rate⁴⁹ • Option for spacer add-on to optimize delivery⁴⁸ 	<ul style="list-style-type: none"> • Requires coordination of actuation and inhalation⁴⁸ • Many patients cannot use it correctly⁵⁰ • High oropharyngeal deposition⁵⁰
pMDI + spacer	<ul style="list-style-type: none"> • Compared with pMDI <ul style="list-style-type: none"> ◦ Easier to coordinate⁵⁰ ◦ Less oropharyngeal deposition⁵⁰ ◦ Higher lung deposition 	<ul style="list-style-type: none"> • Subject to static charge⁵⁰ • Compared with pMDI <ul style="list-style-type: none"> ◦ More expensive ◦ Less portable⁵⁰ ◦ Requires additional cleaning
Dry power inhaler (DPI)	<ul style="list-style-type: none"> • Does not contain propellant⁵⁰ • No coordination needed⁵⁰ • Quicker time to achieve mastery in technique⁵¹ 	<ul style="list-style-type: none"> • Requires minimum inspiratory flow⁵⁰ • Many patients cannot use it correctly⁵⁰ • Most types are moisture sensitive⁵⁰
Soft mist inhaler (SMI)	<ul style="list-style-type: none"> • Multidose device⁵⁰ • High lung deposition⁵⁰ • Does not contain propellant⁵⁰ 	<ul style="list-style-type: none"> • May require assembly • Requires some coordination of actuation and inhalation⁵² • Relatively expensive
Nebulizer	<ul style="list-style-type: none"> • May be used at any age⁵⁰ • No specific inhalation technique required⁵⁰ • May dispense drugs not available with pMDIs and DPIs⁵⁰ 	<ul style="list-style-type: none"> • Treatment times can be long⁵⁰ • Performance varies among nebulizers⁵⁰ • Risk of bacterial contamination⁵⁰ • Often requires separate administration for each medication used

therapy has been shown to provide significant improvement in rate of moderate/severe exacerbations and time to first moderate/severe exacerbation over 52 weeks vs single inhaler dual therapy.⁴⁷

The COPD Foundation provides video-based education related to the use of a wide variety of inhalers (<https://www.copdfoundation.org/Learn-More/Educational-Materials-Resources/Educational-Video-Series.aspx>). Additional resources include:

- American Thoracic Society/Mayo Clinic: <https://www.thoracic.org/professionals/clinical-resources/video-lecture-series/obstructive-lung-disease/asthma/inhaler-device-selection-and-technique.php>
- Asthma and Allergy Network: <https://allergyasthmanetwork.org/what-is-asthma/how-is-asthma-treated/>
- Centers for Disease Control and Prevention: https://www.cdc.gov/asthma/inhaler_video/default.htm ●

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