Impact of COPD in Older Adults

In the United States and around the world, chronic obstructive pulmonary disease (COPD) is an often overlooked or misdiagnosed yet major cause of declining pulmonary function. COPD is a common cause of death, trailing cancer and heart disease and about the same as accidents worldwide and in the United States. COPD is more common in older adults, a time of life when several common conditions—particularly cardiovascular disease, depression, and anxiety—can contribute to symptoms similar to those of COPD. In such complicated clinical scenarios, people may attribute symptoms to aging, physical inactivity, or needing to lose weight. This creates challenges for patients, caregivers, and health professionals to recognize COPD and ensure the needed care that is imperative in optimizing health status, managing symptoms, and maintaining quality of life.

What can a knowledgeable team of health professionals do to recognize and support older adults with COPD? A lot, it turns out, when they understand the challenges faced by patients with this condition. The person with COPD has clear medical needs, but equally important are behavioral challenges such as smoking cessation and exercise. An important additional goal of care for patients later in their disease course is helping them overcome the stigma associated with smoking-related conditions and requiring oxygen therapy in public spaces so they can maintain their usual activities. Everyone caring for people with COPD must be strong advocates for adult immunizations; simply making the recommendation increases immunization rates and prevents morbidity and mortality. Research needs abound in preclinical, clinical, translational, and social realms. Patients and caregivers require education and support for COPD care, including regular and proper use of inhalers and nebulizers. Pulmonary rehabilitation is one of the most effective treatments for COPD symptoms, activity enhancement, and even prevention of hospitalizations; however, low reimbursement rates for pulmonary rehabilitation have resulted in inadequate numbers of programs, failure to refer appropriate individuals, and lack of access for most people with COPD.

This issue of What’s Hot focuses on the latest ideas about COPD and the best ways to approach care of patients living with this disease. Supported by a strong, interprofessional team, patients with COPD who are committed to overcoming its symptoms—and stigma—may be able to enjoy life on their own terms.
COPD is defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) as “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 and influenced by host factors, including abnormal lung development.” While most people with COPD have exposure to smoking, about 25% of affected Americans are individuals who have never smoked but have been exposed to other irritants, including pollution, occupational irritants, and smoke from other people’s tobacco use.

The airflow limitation in patients with COPD is not fully reversible, meaning that bronchodilators will not restore normal lung function. This is one of the ways that COPD is distinguished from asthma; for most individuals with asthma, bronchodilators can greatly improve lung function, with spirometry results often returning to normal.

Similar to other chronic conditions such as diabetes, COPD is underdiagnosed in the United States and worldwide.

COPD has been viewed as having two main phenotypes: chronic bronchitis (mucus secretion into the bronchial tree, defined clinically as cough present on most days for at least 3 consecutive months for 2 years or more) and emphysema (destruction of the gas-exchanging alveolar sacs of the lungs, resulting in trapping of air in the bronchioles, defined pathologically or by confirmatory evidence on chest computed tomography scan). Initial treatment for both of these phenotypes is similar (medications and nonpharmacologic interventions such as immunizations and smoking cessation); newer therapies are specific for people with chronic bronchitis, and endobronchial valves and lung volume reduction surgery are used in those with advanced emphysema.

Similar to other chronic conditions such as diabetes, COPD is underdiagnosed in the United States and worldwide. In a study of 44 sites in 27 countries, investigators identified people with chronic airflow limitation using pulmonary function tests (PFTs) and asked whether they had been diagnosed with COPD. Of those whose PFTs indicated COPD, 81.4% were not diagnosed; the highest percentage of individuals who were diagnosed with COPD was only 50% at one site in the United States (Lexington, KY).

Smoking is the most common cause of COPD in the United States, where an estimated...
30 million people have diagnosed or undiagnosed COPD. Greater numbers of men have smoked in the past, and deaths among men still exceed those among women. However, COPD death rates are falling among men while remaining the same among women (Figure 1). Since 2000, the number of American women dying of COPD has exceeded the number of men, and more women than men are currently living with COPD. About one-fourth of patients with COPD have never smoked; occupational and environmental exposures also contribute to disease, including exposure to smoke and irritants from use of biomass fuel for cooking or heating, as do early-life respiratory infections, asthma, and other factors.

COPD prevalence varies across the United States; it is particularly common in the “tobacco belt,” where crops are grown and usage is higher, and among lower socioeconomic groups. As shown in Figure 2, COPD is more common in certain areas where 3 to 4 times more patients have the disease than in other areas. COPD tends to be more prevalent in Appalachia, parts of the southeastern and southcentral United States, and states with high percentages of older residents, such as Florida and Arizona. Other demographic and socioeconomic factors that predict elevated risk of COPD include being aged 65 years or older; living in rural areas; people who are American Indians/Alaska natives or multiracial non-Hispanic; people who are unemployed, retired, or unable to work; people with less than a high school education; people who are divorced, widowed, or separated; people who are currently or have previously smoked; and people with a history of asthma.

**Figure 1. Age-Standardized Death Rates for COPD—United States, 1999–2014**

COPD = chronic obstructive pulmonary disease; ICD-10 = International Statistical Classification of Diseases-10th Revision.

Source: Reference 3.

**Figure 2. Distribution of the States Based on Age-Adjusted Percentage of Adults With COPD—United States, 2014–2015**

<table>
<thead>
<tr>
<th>1 Range: 3.7–4.6 (11 states)</th>
<th>2 Range: 4.8–5.4 (11 states)</th>
<th>3 Range: 5.5–5.9 (8 states)</th>
<th>4 Range: 6.1–7.1 (12 states)</th>
<th>5 Range: 7.2–12.0 (10 states)</th>
</tr>
</thead>
</table>

*Data derived from Centers for Disease Control and Prevention/Behavioral Risk Factor Surveillance System based on 2014–2015 data. In the box below the map, state scores are grouped in ranges of the percentage of adults with COPD.

COPD = chronic obstructive pulmonary disease.

Source: Figure 2 in Reference 5. Reprinted with permission from Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation.
COPD is a complex, multifactorial condition that results from the interplay of environmental, behavioral, and genetic factors (Table 1). Researchers are actively working to determine how these factors interact to produce the clinical presentation characteristic of patients with COPD: chronic respiratory symptoms, abnormalities in lung structures, and reductions in lung function.1,6

Cigarette smoking is the most common COPD risk factor. People who smoke are at greater risk of developing COPD and those who continue to smoke have symptoms that are generally worse, with greater declines in lung function and more exacerbations of greater severity. Yet fewer than half of heavy smokers develop COPD, and about one-quarter of patients with COPD in the United States are nonsmokers thus requiring the search for other risk factors such as occupational exposures that are often overlooked. In some countries, pollution from use of coal and other biomass energy sources used in cooking and heating are associated with higher rates of COPD among women. Women who smoke develop COPD at younger ages and with lower levels of smoking than men.1,4,6

Age-related mortality is greater in patients with COPD than in matched controls without COPD. Those with muco-obstructive forms of COPD can experience a rise in mucus concentrations, leading to mucus plaque and plug formation and blockage of small airways. Destruction of alveoli in patients with emphysema compromises gas exchange and can lead to respiratory failure. Cardiovascular disease and lung cancer are common concomitant conditions.7

Inflammation is a normal response to exposure to particulate matter and other chronic irritants associated with COPD. With chronic exposure and in those who are more susceptible to lung disease, this inflammation goes beyond the normal response. Through mechanisms such as oxidative stress, protease-antiprotease imbalance, and increased numbers of inflammatory cells and mediators, COPD develops and associated symptoms ensue.

Table 1. Factors Contributing to Development of COPD

<table>
<thead>
<tr>
<th>Categories of Factors</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetics</td>
<td>Hereditary deficiency of alpha-1 antitrypsin; increased risk of COPD in people with mutations in genes encoding matrix metalloproteinase 12 and glutathione S-transferase. Genome-wide studies have identified markers near several genetic loci associated with COPD, including those encoding the alpha-nicotinic acetylcholine receptor and hedgehog interacting protein.</td>
</tr>
<tr>
<td>Age and gender</td>
<td>Some age-related changes in the airways and lung parenchyma are similar to those of COPD. Increased disease severity in women may be the result of later diagnosis, but women could be more susceptible to the effects of tobacco and other factors contributing to COPD.</td>
</tr>
<tr>
<td>Lung growth and development</td>
<td>Conditions or diseases during gestation, birth, childhood, and adolescence can reduce maximal lung function and predispose individuals to development of COPD. Low birth weight and severe lung infections during early childhood affect lung function in adulthood, as can home overcrowding.</td>
</tr>
<tr>
<td>Exposure to particles</td>
<td>Cigarette smoking or secondhand exposure to tobacco smoke is the most common and consistent contributor to development of COPD. Smoking during pregnancy can affect lung growth and development in offspring. Occupational exposure to dusts, chemicals, and fumes are an underrecognized source of exposure. Urban air pollution exposes large numbers of people to detrimental particles. In developing countries, biomass [e.g., wood, coal, animal dung] fires used for heating and cooking in the home predispose people to develop COPD, especially women.</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td>People in poverty have greater risks of developing COPD, and lower socioeconomic status is associated with airflow obstruction, perhaps because of other factors that contribute to increased risk of lung problems.</td>
</tr>
<tr>
<td>Asthma and airway hyperreactivity</td>
<td>Patients with asthma and airway hyperreactivity have greater risks of developing COPD. Current evidence shows that COPD in people who smoke but do not have asthma has a very different pathology than when it occurs in nonsmokers with asthma, although it is unclear if the disease in these people with asthma is the same as COPD in people who have smoked.</td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>Chronic bronchitis has been associated with mucus hypersecretion, more rapid declines in lung function, and increased risk of exacerbations in some studies.</td>
</tr>
<tr>
<td>Infections</td>
<td>Severe childhood infection and prior tuberculosis are associated with decreases in lung function. Susceptibility to infections can increase risk of COPD exacerbations, but the exact nature of the relationship is unclear.</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease.

Source: Reference 1.

The Gerontological Society of America
Challenges in Diagnosis

Despite the serious morbidity associated with COPD and its link to increased mortality, diagnosis of the disease is challenging. The first hurdle in diagnosis begins with patients’ awareness of the disease and its risk factors and connecting those factors to symptoms they are experiencing. In one study, about 70% of American adults with spirometry-defined obstruction had not been diagnosed as having COPD, yet their all-cause mortality rates were significantly elevated [HR, 1.23; 95% CI, 1.08–1.40] compared with people with normal spirometry findings. Those with COPD diagnoses were also at increased risk of all-cause mortality [HR, 1.74; 95% CI, 1.45–2.09].

The COPD Foundation urges people to use its brief self-screening questionnaire to determine whether they might be at risk for COPD [see sidebar].

The diagnosis of COPD is limited by the continuing perception that it is a disease of older white men and by the narrow public awareness of the availability of treatment to improve symptoms. However, lung function peaks in early adulthood and then begins declining; the relevant metric is how quickly a person’s lung function declines. Because a number of interventions can optimize lung function, improve symptoms, increase health-related quality of life, and avoid complications and exacerbations, early diagnosis is critical for patients with COPD. Longitudinal studies show that about half of patients with COPD have accelerated declines in lung function; the other half started out with abnormal lung growth and development earlier in life, achieved lower peak lung function in early adulthood, and had normal rates of decline that compromised their lung function at earlier ages.

Establishing a Diagnosis of COPD

Pulmonary function testing, or spirometry before and after bronchodilator administration, is used to assess for COPD in at-risk patients and for those with suggestive symptoms. At-risk patients are those whose smoking history, occupational or environmental exposures, respiratory symptoms, and/or family history increase their risks of COPD. Patients with recurrent respiratory infections are also at increased risk for COPD. Suggestive symptoms are dyspnea, chronic cough, or sputum production; those with fatigue, weight loss, and anorexia—which can be presenting symptoms in those with severe or very severe COPD—should also be evaluated. Periodic monitoring of spirometry should be considered in patients with persistent symptoms and risk factors for COPD because disease may develop and progress over time.

All health facilities that care for patients with COPD should have access to properly maintained spirometers and staff trained in optimal technique and quality performance. During the test, patients take the deepest breath possible and then blow all of the air out of their lungs into the spirometer—continuing to exhale hard and fast for at least 6 seconds. The device calculates many values, but the two most important are the total amount of air exhaled, or forced vital capacity (FVC), and the amount exhaled during the first second, or forced expiratory volume in 1 second (FEV1).

A ratio of FEV1 to FVC of less than 0.7 post-bronchodilator in a patient with appropriate symptoms and exposure is consistent with COPD. A GOLD severity of grade 1 to 4 can then be assigned based on the FEV1 percentage predicted calculated in comparison with the predicted value based on the patient’s age, height, gender, and race, as shown in Figure 3. If a patient presents with an FEV1 value of 80% or more than predicted and an FEV1/FVC less than 0.7, the patient has COPD with a GOLD spirometry grade of 1 and can be managed with risk counseling and repeated spirometry monitoring.

Self-Screening Questionnaire for Identifying COPD Risk

The COPD Foundation suggests use of these “DRIVE4COPD” screener questions to aid patients in self-identifying as being at risk for COPD:

- During the past 4 weeks, how much of the time did you feel short of breath?
  - Responses: None, a little, some, most, or all of the time
- Do you ever cough up any “stuff,” such as mucus or phlegm?
  - Responses: No, never; only with occasional colds or chest infections; yes, a few days a month; yes, most days a week; yes, every day
- Please select the answer that best describes you in the past 12 months: I do less than I used to because of my breathing problems.
  - Responses: Strongly disagree; disagree; unsure; agree; strongly agree
- Have you smoked at least 100 cigarettes in your ENTIRE LIFE?
  - Responses: No; yes; don’t know
- How old are you?
  - Responses: 35–49; 50–59; 60–69; 70+

Responses are scored on a 0, 1, or 2 scale, as shown on the COPD Foundation website. Those with scores of 5 or greater should share the results with their health professional. People with lower scores who are experiencing breathing problems should also share the screening results with a health professional. Results are only for screening purposes; the diagnostic accuracy of screening questions is generally only fair and not sufficient to replace spirometry evaluation, the gold standard to confirm a diagnosis of COPD.
6MWD = 6-minute walk distance; BODE = body mass index, degree of airflow obstruction, severity of dyspnea, and exercise capacity (6-minute walking distance [6MWD]). CAT denotes COPD Assessment Test, DLco = diffusing capacity of the lung for carbon dioxide, FEV₁ = forced expiratory volume in 1 second, FVC = forced vital capacity, IC = inspiratory capacity, LVR = lung-volume reduction, mMRC = modified Medical Research Council dyspnea scale, RV = residual volume, and TLC = total lung capacity.

Those with FEV₁ values of 50% to 79% of predicted have GOLD grade 2 and may require further tests as outlined below. Patients with lower scores have GOLD grades 3 or 4; they should generally be referred to specialists or health professionals with experience in COPD management.¹

Further staging of COPD is used to refine therapy as the condition progresses. Two instruments have been recommended by the GOLD guidelines to standardize assessment of symptoms: the Modified Medical Research Council (mMRC) questionnaire and the COPD Assessment Test (CAT). In the mMRC questionnaire, participants rate their dyspnea symptoms by choosing one of the following statements¹:

- I only get breathless with strenuous exercise—(grade 0).
- I get short of breath when hurrying on the level or walking up a slight hill—(grade 1).
- 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—(grade 2).
- I stop for breath after walking about 100 meters or after a few minutes on the level—(grade 3).
- I am too breathless to leave the house or I am breathless when dressing or undressing—(grade 4).

The CAT has 8 questions, each rated from 0 to 5, that ask patients about their symptoms and daily activities (i.e., cough, mucus in the chest, chest tightness, breathlessness on exertion, activities limited by condition, confidence to leave the house, ability to sleep soundly, and energy level). The ratings are summed, giving a score of 0 to 40. Scores of 10 or greater are considered to represent a high COPD symptom burden.¹

As shown near the bottom of Figure 3, the mMRC or CAT score, along with 12-month history of exacerbations, can be used to guide therapy (see Treatment of COPD section).

There are no specific blood tests for diagnosis of COPD. However, all patients with COPD should have serum alpha-1 antitrypsin measured once. Alpha-1 antitrypsin deficiency requires additional evaluation for other manifestations of the genetic condition and can be treated with replacement therapy. While lower lobe predominant emphysema, early age of onset, phenotype, or family history are more suggestive of alpha-1 antitrypsin deficiency, diagnosis at a later age can be associated with more diffuse emphysema including the upper lobes. Measurement of blood eosinophil counts, as discussed further in the Pharmacologic Treatment section, can be helpful to identify patients who may be more responsive to inhaled corticosteroids.¹²
Treatment of COPD

A complex, progressive disease, COPD requires interventions from several types of health professionals with important roles to play and routine follow-up to monitor a patient’s health. The primary care clinician usually serves as the core of this interprofessional team, managing the patient’s overall therapy and referring complicated cases to pulmonologists and other specialists. All health professionals need to be aware of the underdiagnosis of COPD and watch for alarming signs and symptoms. The best intervention a health professional can make is to help people stop smoking before COPD develops; smoking cessation after COPD develops is likewise critically important and can slow progression of COPD. When possible, both children and adults should avoid indoor or outdoor pollutants, dusts, chemicals, and fumes to help prevent future COPD and reduce adverse effects in those with COPD.

People without a medical home or without a known diagnosis of COPD may first present at an emergency department. Emergency medicine health professionals should consider COPD in patients presenting with respiratory exacerbations; follow-up testing to determine a definitive diagnosis should be pursued in these patients. Other frontline health professionals, especially pharmacists, may notice or hear about fatigue and shortness of breath in patients seeking over-the-counter products or presenting prescriptions; pharmacists also provide education about smoking cessation, medication regimens, use and care of inhalers and nebulizers, and the need for vaccinations.

The COPD care team may include respiratory therapists, home care nurses, behavioral health professionals, palliative care staff, and others to help patients who have more severe COPD and comorbidities with care, including pulmonary rehabilitation, oxygen therapy, and other important nonpharmacologic interventions.1 The CAT is an important and valuable tool to monitor COPD symptoms and burden. It can be completed by patients while in the waiting room or at home using online tools and mobile apps developed by the COPD Foundation.9,13-15

Nonpharmacologic care is essential for all people with all types and levels of COPD; these therapies may include appropriate immunizations, support for daily activity, smoking cessation assistance, and for symptomatic COPD, pulmonary rehabilitation.

Nonpharmacologic care is essential for all people with all types and levels of COPD; these therapies may include appropriate immunizations, support for daily activity, smoking cessation assistance, and for symptomatic COPD, pulmonary rehabilitation. Pulmonary rehabilitation is a key but underused intervention for patients with COPD that can improve symptoms, restore quality of life, and improve physical and emotional participation in daily activities and prevent hospitalizations. Oxygen therapy may be required as symptoms progress and if hypoxemia is present. Prescribing the correct levels and devices for oxygen therapy is often improved with inclusion of specialists and respiratory therapists. Review of symptoms and exacerbation history is indicated for patients who have demonstrated desaturation at rest (≤88% or partial pressure of arterial oxygen [Pao2] ≤55 mm Hg at sea level).

Pharmacotherapy is central to the care of patients with GOLD grades 2 to 4. Review of symptoms should guide the addition of new drugs, and deprescribing is important to avoid unnecessary use of multiple agents, as discussed below.1

Exacerbations

The clinical course of COPD is often marked by exacerbations, which are flare-ups or episodes in which breathing worsens, usually in response to an irritant such as a viral upper respiratory infection, cigarette smoke, or pollution. Patients whose COPD is well controlled may go for long periods of time with no increase in symptoms, or they may have stable symptoms such as the same level of breathlessness, cough, and sputum production on most days. When an exacerbation occurs, the clinical picture changes. Signs and symptoms of an exacerbation may include persistent low-grade fever or an increased need for rescue medications to manage symptoms such as more breathlessness, increased coughing, more mucus or a change in color or thickness of the mucus, fatigue that lasts more than 1 day, and/or more wheezing than usual.

Exacerbations are common in patients with COPD, but every change in symptoms is not necessarily an exacerbation.1 When a patient has a change in symptoms, the first step is to confirm the exacerbation by ruling out conditions in the differential diagnosis: pneumonia, pleural effusion, pulmonary embolism, heart
Schedule a follow-up visit or telephone call, preferably within the first week after the quit date.

Assess the willingness to change and rationale of patient’s desire to quit (within the next 30 days).

At every visit, ask all patients whether they smoke. Add this to “vital signs” collected during patient intake.

Help the patient design a quit plan; provide pharmacologic supports and counseling; assist the patient in finding social support during and after the quit attempt; provide supplementary materials.

Schedule a follow-up visit or telephone call, preferably within the first week after the quit date.

---

Table 2. The 5 A’s for Smoking Cessation

<table>
<thead>
<tr>
<th>Ask</th>
<th>At every visit, ask all patients whether they smoke. Add this to “vital signs” collected during patient intake.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advise</td>
<td>In a clear, strong, and personalized manner, strongly urge all smokers to quit.</td>
</tr>
<tr>
<td>Assess</td>
<td>Assess the willingness to change and rationale of patient’s desire to quit (within the next 30 days).</td>
</tr>
<tr>
<td>Assist</td>
<td>Help the patient design a quit plan; provide pharmacologic supports and counseling; assist the patient in finding social support during and after the quit attempt; provide supplementary materials.</td>
</tr>
<tr>
<td>Arrange</td>
<td>Schedule a follow-up visit or telephone call, preferably within the first week after the quit date.</td>
</tr>
</tbody>
</table>

Source: References 1, 20, and 21.

Exacerbations of COPD can be managed with use of medications and interventions as presented later in the Pharmacologic Treatment section. Short-acting bronchodilators (SABDs) alone are useful when symptoms are mild; when symptoms are moderate, SABDs and systemic corticosteroids may be used with or without antibiotics. In a severe exacerbation, symptoms require inpatient or emergency department care for possible acute respiratory failure. Supplemental oxygen therapy, titrated to avoid hyperoxia, and noninvasive or invasive mechanical ventilation may be needed depending on the degree of ventilatory failure. The patient’s clinical condition must be managed aggressively and appropriate to the severity of symptoms and the goals of care.1,16

Smoking Cessation

Getting people to stop using the highly addictive substance nicotine is very difficult. Success rates for many programs are in the single digits, and it is not uncommon for people to require six to seven attempts before being successful. With proper behavioral and pharmacologic support and by treating smoking as a chronic disease, as many as 25% of smokers can achieve long-term abstinence.1 In discussing the importance of smoking cessation in patients at risk for or with COPD, listing the other health consequences of smoking can provide motivation: increased risk of numerous types of cancers, greater risk of premature death from cardiovascular disease, adverse pregnancy outcomes, and adverse effects on fertility in both men and women. Patients can also be asked what they would be able to do with greater mobility and more years of life, such as run around the yard with grandchildren or be able to care for their pets.

Nicotine-replacement therapy is the cornerstone of cessation efforts. Nicotine gums, inhalers, nasal sprays, transdermal patches, sublingual tablets, and lozenges have been shown to be effective for increasing abstinence rates in placebo-controlled clinical trials, particularly when dual therapies are used concomitantly. If the patient’s age and comorbidities allow, other pharmacologic agents can be used as replacements for nicotine replacement, including varenicline, bupropion, and nortriptyline; however, all three of these agents can produce adverse central nervous system effects in older adults, and nortriptyline is a Beers list medication because of its anticholinergic effects.1,17

E-cigarettes, first marketed in the United States in 2007, have been promoted for nicotine replacement in smoking cessation efforts. While e-cigarettes are potentially less harmful for nicotine delivery than combustible tobacco products, studies to date have not shown that these devices are effective for achieving long-term nicotine abstinence. In addition, the 2019 outbreak of lung injuries associated with e-cigarettes reminds health professionals how much is unknown. For patients with COPD, clinicians should advise strongly against use of e-cigarettes.1,18,19

Pharmacologic interventions should be paired with behavioral support programs to achieve maximal cessation rates. Motivational interviewing techniques can identify patients who are ready to quit, and programs such as the 5-step intervention are useful (Table 2). Physicians and other health professionals should counsel patients as they approach their quit dates; even a brief intervention improves smoking cessation rates.1,20

Immunizations

The influenza and pneumococcal vaccines are very important in patients with lung diseases, including COPD. These patients have increased risk of infections, and infections—including influenza—can increase risk for acute myocardial infarction and other serious cardiovascular events, reduce activities of daily living, and increase frailty and loss of independence.22

In strongly advocating for annual influenza vaccination, important points relevant to patients with COPD include the following1:

- Influenza vaccination reduces lower respiratory tract infections
Pneumococcal vaccine should also be given to patients with COPD, although recommendations for when to give the polysaccharide and conjugate vaccine differ by age. Advocacy for the two available adult pneumococcal vaccines has been complicated by recent changes in recommendations of the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention. From the standpoint of the older patient with COPD, the advantages of receiving both vaccines are clear.

All patients with COPD should receive the 23-valent pneumococcal polysaccharide vaccine (PPSV23) to help protect against pneumonia, regardless of age, according to the ACIP recommendations. Revaccination should occur after age 65 years or after 5 to 10 years have passed from the previous PPSV23 vaccination, depending on whether another immunocompromising condition is present.21

Whether or not older adults with COPD should receive the 13-valent pneumococcal conjugate vaccine (PCV13) is more controversial. In 2014, ACIP added a recommendation for this vaccine to adults aged 65 years or older [regardless of whether they have COPD]. In these patients—many of whom have never received a pneumococcal vaccine—the PCV13 is given first and the PPSV23 is given second because this sequence increases the response to the antigens.

ACIP reviewed this change in 2019 and found that herd immunity induced by vaccination of pediatric patients had muted the impact of the additional dose in older adults. The ACIP members responded by changing the PCV13 recommendation from a universal recommendation to one based on shared clinical decision-making by the patient and the health professional.

Nonetheless, the GOLD guidelines recommend vaccination with PCV13 for patients with COPD who are aged 65 years or older. Having both vaccines produces modest declines in target diseases in older adults, and in the 75-years- and older population, all-cause hospitalizations were unchanged by pediatric vaccinations, emphasizing the need for added protection in this older age group.24,25

In strongly advocating for pneumococcal vaccination, important points relevant to patients with COPD include the following1:

- PPSV23 is recommended for all adult patients with COPD, regardless of age, with consideration of revaccination at age 65 years and after 5 to 10 years have passed from initial vaccination.
- For older adults, PCV13 will increase immunity against vaccine-type pneumococcal strains and provide further protection against pneumonia and invasive pneumococcal disease.
- If a person 65 years or older has never received either vaccine and now wants to receive both, PCV13 should be given first and PPSV23 given 12 months later.

While outside the scope of the GOLD guidelines, shingles vaccine is important in maintaining health among older adults, and protection against pertussis is needed given recent outbreaks of this pathogen.

**Pharmacologic Treatment**

Drug therapy for stable COPD is guided by the intensity of patients’ symptoms (mMRC and CAT scores) and their risk for future exacerbations [based on 12-month exacerbation history]. Initial pharmacotherapy recommendations are summarized in Figure 4, which illustrates the ABCD system recommended in GOLD 2020, and maintenance regimens are detailed in Figure 5. SABDs can be used on an as-needed basis in patients categorized as Group A. Inhaled long-acting maintenance medications are the cornerstone of pharmacotherapy for patients in Groups B through D, with short-acting agents used for rescue therapy and other agents added as symptoms warrant.1

Maintenance bronchodilators fall into three categories:

- Long-acting muscarinic antagonists [LAMAs].
- Long-acting beta-adrenergic agonists [LABAs].
- Inhaled corticosteroids [ICS].

Because of the number of inhaled agents needed by most patients with COPD, combination products with two or three drugs are commonly used with a goal of increasing convenience, adherence, and in some cases effectiveness. Inhaled agents are recommended over orally administered bronchodilators; other than the controversial methylxanthines [e.g., theophylline], no oral bronchodilators are approved.
in the United States for COPD management. ICSs should not be used as monotherapy in patients with COPD because of an increased risk of death with inhaled fluticasone alone, compared with that agent plus salmeterol. While clinicians must balance benefits against potential risks, ICSs can increase patients’ risk of pneumonia and therefore are used more sparingly in those with COPD; this is the rationale for primarily using these agents in patients with asthmatic features or patients who have exacerbations despite LABA or LAMA therapy. In addition, ICS therapy can be withdrawn in patients with COPD who have not had any exacerbations within the past year.1,26

During maintenance therapy with long-acting agents, SABDs can be used as rescue therapy for short-term relief of occasional symptoms or increases in symptoms. Two types of SABDs are available; a short-acting beta-2 agonist can be combined with a short-acting muscarinic antagonist (SAMA) if neither alone relieves occasional symptoms. If symptoms are persistent, step-up therapy to long-acting bronchodilator monotherapy is usually preferred over combination SABD+SAMA treatment.27 Other modifications to pharmacotherapy are made as the disease progresses and patients demonstrate increased baseline respiratory symptoms and/or have exacerbations. Triple therapy with inhaled LAMA+LABA+ICS is indicated for step-up therapy following two or more exacerbations or one hospitalization for COPD. As shown in Figure 5, continued symptoms or exacerbations can be addressed with the addition of azithromycin, particularly in former smokers, or roflumilast in patients with symptoms of chronic bronchitis.1 The GOLD guidelines make these additional points about anti-inflammatory agents1:

- Long-term monotherapy with ICS is not recommended.
- ICS+LAMA+LABA improves spirometry and health status and decreases exacerbations compared with ICS+LABA and LAMA+LABA comparators in patients with COPD.
- Phosphodiesterase-4 inhibitors can be added to LABAs+LAMAs with or without ICS in patients with severe to very severe airflow limitation, chronic bronchitis, and exacerbations.
- Statin therapy is not recommended for prevention of COPD exacerbations.
- Antioxidant mucolytics are recommended only in selected patients.

Patients with hereditary deficiencies of alpha-1 antitrypsin may be candidates for alpha-1 antitrypsin augmentation therapy. Use of antilutivives is not recommended in patients with COPD, and drugs for primary pulmonary hypertension are not recommended when pulmonary hypertension is secondary to COPD. Patients with severe COPD symptoms may require low-dose, long-acting oral and parenteral opioids for palliative treatment of dyspnea. Use of benzodiazepines for palliative therapy has not been beneficial in clinical trials.1 Biologic agents under study for COPD include canakinumab [an interleukin (IL)-1beta antagonist], MEDI8986 (IL-1R1 antagonist), mepolizumab (IL-5 antagonist), benralizumab (IL-5R antagonist), ABX-IL8 (IL-8 antagonist), and infliximab [tumor necrosis factor–alpha antagonist]. Based on available results, patients with the eosinophilic endotype could be good candidates for therapy with some of these monoclonal antibodies because they target the cytokine/chemokine systems that produce inflammation in patients with COPD. In one analysis, mepolizumab reduced the risk of exacerbations, and benralizumab improved both FEV1 and health-related quality of life. None of these agents has received U.S. Food and Drug Administration approval for treatment of patients with COPD.28

Figure 4. Initial Pharmacologic Treatment of Patients With COPD

INHALATION DELIVERY DEVICES

Several devices are used to deliver inhaled medications: metered-dose...
Algorithm for Pharmacotherapy in Patients with a Confirmed Diagnosis of COPD.

Integration of the lung-function compromise, severity of symptoms, and risk of exacerbations helps determine disease severity. Milder disease may benefit from a single inhaled, long-acting bronchodilator, preferably a long-acting muscarinic antagonist (LAMA). In patients with more compromised lung function and infrequent exacerbations of moderate intensity, a LAMA combined with a long-acting beta-2 agonist (LABA) in a single inhaler or dual inhalers may be used. A history of asthma, allergies, or rhinitis or an elevated blood eosinophil count (>300 per cubic millimeter) favors the initial use of an inhaled glucocorticoid (IGC) combined with a LABA. If the symptoms and exacerbations persist (more than two exacerbations per year or one hospitalization for COPD), triple therapy consisting of a LAMA, a LABA, and an IGC is useful. An array of systemic therapies (azithromycin, roflumilast, xanthines, and antioxidants) may be considered as third-line agents. The use of biologic agents requires further studies to validate their efficacy. PDE4i denotes phosphodiesterase-4 inhibitor, and SABD short-acting bronchodilator.

COPD = chronic obstructive pulmonary disease; FEV1 = forced expiratory volume in 1 second; IGC = inhaled glucocorticoid (referred to in other figures and the text as inhaled corticosteroid, ICS); LABA = long-acting beta-2 agonist; LAMA = long-acting muscarinic antagonist; PDE4i = phosphodiesterase-4 inhibitor; SABD = short-acting bronchodilator.

inhalers (with or without spacers or breath actuation), dry powder inhalers (single dose or multidose), soft mist inhalers, nebulizers, and ancillary devices such as holding chambers. The classes of medications and specific agents differ in their types of delivery devices. The choice of delivery device must be individualized based on the patient’s medication needs, lung function, ability to use the device, and preferences; additional relevant factors include device availability, access, cost, and prescriber. Cost is a particularly important factor that should be discussed with patients because adherence is adversely affected when products are not covered by health insurance and/or have high copayment amounts.1

Patients should be educated on proper use of their devices using the “teach-back” method, and adherence to medications and proper use of devices should be checked at each clinic or refill visit. The teach-back method consists of showing the patient how to use the device and then asking the patient to demonstrate the method back to the educator. During this process, patient deficiencies in dexterity or cognition should be identified and addressed. For instance, holding chambers can be used to make administration easier in a patient with osteoarthritis of the hand who has poor “hand-lung coordination.” A caregiver may need to be involved with drug administration in patients with cognitive deficiencies that cannot be resolved or if patients are unable to administer the medication on their own. Education on care and cleaning of the specific device should be provided to the patient and/or caregiver. Proper use of inhalers should be validated each time the patient has an interaction with a member of the COPD health care team.27

Widely available videos can reinforce education on proper inhaler use after patients leave the health care setting. The COPD Foundation is a particularly good source of such videos and other information for patients living with COPD, including its COPD Pocket Consultant Guide mobile app (see Resources).15

Pulmonary Rehabilitation

As a disease that can impair pulmonary gas exchange, even mild cases of COPD can lead patients to avoid any exercise or physical exertion that causes dyspnea or fatigue. As a result, patients worry about the discomfort associated with dyspnea, further reinforcing the avoidance of exertion. COPD also affects the large muscles of the legs, where deconditioning and other factors lead the tissues to have decreased aerobic enzyme activity, a low fraction of aerobic fibers, fewer capillaries, inflammatory cells, and increased apoptosis. Consequently, muscle fatigue occurs at earlier points during exercise than in people without COPD. Cachexia—involuntary weight loss and depletion of lean muscle mass—can result, leading to a very poor prognosis.29

Pulmonary rehabilitation is an effective intervention to improve many of these effects, improve functional status and symptoms, avoid the decline into cachexia, and according to a recent study of Medicare beneficiaries, lower mortality risk 1 year later if provided within 3 months of hospitalization for COPD. This comprehensive intervention includes exercise training, education, and self-management techniques designed to change long-term behaviors. Most patients who are physically able to participate in pulmonary rehabilitation and are willing to commit to these changes with support will enjoy increased exercise tolerance, reduced dyspnea, and better quality of life.1,29,30

Patients who have unstable cardiac disease should be excluded from pulmonary rehabilitation programs; program adjustments can often be made for those with mobility issues other than COPD. Other relative contraindications include cognitive or psychiatric conditions that would limit patients’ ability to understand or cooperate with the treatment plan and its long-term behavioral changes. Before enrollment, health professionals in the primary care practice or in the rehabilitation program should assess patients with regard to their goals, specific health care needs, smoking status (some but not all programs exclude people who are continuing to smoke), nutritional health, self-management capacity, health literacy, psychological health, social circumstances, and comorbid conditions.1,29

Programs typically consist of two to three supervised and personalized sessions per week for 3 to 4 hours per session. Programs of 6 to 8 weeks in length have been shown to achieve optimal benefits; some programs last for up to 12 weeks, but no additional benefits of the added time have been demonstrated. Programs can be offered in hospital, ambulatory, and home settings, which may be particularly beneficial for patients who have transportation challenges or live far from the medical center.1,29 The benefits of pulmonary rehabilitation require that the patient continues with daily activity and other new techniques learned during the program. Some programs provide a maintenance program to help sustain changes. Telehealth or home-based pulmonary rehabilitation programs continue to be evaluated and have been helpful in some regions and situations, including ways of providing care during the coronavirus pandemic.31,32

Endurance exercise is the core of pulmonary rehabilitation, with particular attention given to the leg muscles through aerobic exercises such as walking, stationary cycling, and treadmill walking. Upper body strength is also addressed to help with standing and other activities. Resistance exercise is
used to increase both upper and lower limb strength. Flexibility, inspiratory muscle training, and neuromuscular electrical stimulation are sometimes added to the exercise component of the intervention. Other interventions include use of optimal bronchodilators and supplemental oxygen to maximize exercise endurance as well as education on the importance of smoking cessation, incorporation of exercise in the home setting, medication adherence, proper inhaler and nebulizer technique, and identification of anxiety and depression with referral for management.\textsuperscript{1,29}

Major challenges with pulmonary rehabilitation are insufficient availability of reimbursement for these services and perhaps because of that lack, a shortage of enough programs offering the intervention. Only about 3% of patients with COPD receive pulmonary rehabilitation, and the Medicare reimbursement for these programs is inadequate to cover the costs of the staff, medical director, site and equipment, and other expenses. These programs are similar in many respects to those providing cardiac rehabilitation, but that intervention is reimbursed at a much higher rate.\textsuperscript{33}

**Oxygen Therapy**

Oxygen therapy is an important option for patients with COPD; it is useful during exacerbations of COPD and allows patients to exercise, go on outings, and take airplane flights. However, the intervention is not useful in all situations, and like pulmonary rehabilitation, low levels of reimbursement are limiting its use. Oxygen is often part of the therapy for patients admitted to the emergency department or hospital for an exacerbation.\textsuperscript{34}

In patients with stable COPD with resting moderate hypoxemia or brief periods of moderate desaturation during exercise, long-term, 24-hour supplemental oxygen produced no significant changes in time to death or first hospitalization or other outcomes in the Long-Term Oxygen Treatment Trial (LOTT). In the LOTT study, moderate hypoxemia at rest was defined as oxyhemoglobin saturation by pulse oximetry of 89% to 93%, and moderate exercise-induced desaturation was defined as oxyhemoglobin saturation by pulse oximetry of 80% or greater for at least 5 minutes and less than 90% for 10 seconds or more during a 6-minute walk test. These data support the findings of earlier trials.\textsuperscript{35}

Guided by experienced practitioners, long-term oxygen—administration for more than 15 hours per day—increases survival in patients with COPD who frequently have low arterial oxygen saturation (Sao\textsubscript{2} <88%) or partial pressure of arterial oxygen (Pao\textsubscript{2} <55 mm Hg) at rest while breathing ambient air. Supplemental oxygen can be prescribed with a goal of keeping the Sao\textsubscript{2} at or above 90%. Effects of oxygen therapy should be reassessed at 60 to 90 days by checking the Sao\textsubscript{2} and Pao\textsubscript{2} while breathing ambient air to determine whether it remains useful and continues to be needed.\textsuperscript{1}

**Transitions of Care and Medication Reconciliation**

Transitions of care require careful attention as patients with COPD move from long-term care facilities or homes into the inpatient environment, skilled nursing facilities, and back. Because of formularies and preferred drug lists, patients may receive different agents within a medication class while hospitalized. If these agents are continued at discharge, patients and caregivers must be instructed on which of their home medications to discontinue. Medication reconciliation and education is needed when discharge medications are in different devices than those used previously and when dosing patterns are different. This medication review with deprescribing of duplicative agents is very important to avoid adverse effects and polypharmacy.

Clinicians should also ask about devices or medications patients may have obtained through family members or friends; nebulizers and SABDs in particular are commonly swapped among those with COPD.

Management of COPD often includes attention to associated conditions. Anxiety and depression are common in people living with COPD, as dyspnea and other symptoms keep patients on edge and the progressive nature of the diseases weighs on the psyche.\textsuperscript{1}

**End-of-Life Care**

As symptoms worsen and exacerbations become more common toward the end of life, palliative care can be very helpful for management of breathlessness, nutritional support, and fatigue as well as panic, anxiety, and depression. Patients and families should provide advance directives to guide care during this time. Discussions with patients and families should include resuscitation and place-of-death preferences. Hospice services are important end-of-life options for patients with very advanced or terminal illness.\textsuperscript{1}

**Conclusion**

For the millions of people with COPD—diagnosed or not—every day, every minute, every step can be affected by this chronic and progressive condition. Preventive measures are effective for helping people avoid COPD. Early diagnosis and optimal management through pulmonary rehabilitation, immunizations, smoking cessation support, behavioral changes, oxygen therapy when needed, management of associated comorbidities, and pharmacotherapy will enable people with COPD to improve symptoms, increase functional capacity, and live life to its fullest.
Resources

- **American Lung Association—Better Breathers Club** ([www.lung.org/support-and-community/better-breathers-club](http://www.lung.org/support-and-community/better-breathers-club)): A service that connects people living with lung disease to others in their community who want to become “better breathers.”

- **American Thoracic Society** ([www.thoracic.org/patients](http://www.thoracic.org/patients)): Resources for patients, families, and health professionals on lung disease and lung health.

- **COPD Foundation** ([www.copdfoundation.org](http://www.copdfoundation.org)): Online information about and support for COPD; COPD360social networking tool; COPD Pocket Consultant Guide mobile app (patient and provider view; available in mobile device app stores); DRIVE4COPD campaign.

- **National Heart, Lung, and Blood Institute—Learn More Breathe Better** ([www.nhlbi.nih.gov/BreatheBetter](http://www.nhlbi.nih.gov/BreatheBetter)): A national health program that provides resources and materials for patients with or at risk for lung diseases, health professionals, and organizations.

References


