Outpatient Management of Severe COPD

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A 67-year-old man presents with a history of dyspnea, which has progressed for the past several years. He began smoking cigarettes at 15 years of age and continues to smoke one pack per day. Worsening breathlessness forced him to retire as a laborer, and he has sought emergency care for what he calls bronchitis twice in the past year. His physical examination is notable for diminished breath sounds on auscultation, with a prolonged expiratory phase. Spirometry reveals severe airflow obstruction (ratio of forced expiratory volume in 1 second [FEV₁] to forced vital capacity [FVC], 0.43; FEV₁, 34% of the predicted value). How should this case be managed?

The Clinical Problem

The sentinel clinical feature of severe chronic obstructive pulmonary disease (COPD) is dyspnea on exertion. Its onset is usually insidious, and it may progress to severe disability over a period of years or decades. Other common symptoms include cough, sputum production, wheezing, and chest congestion. The principal pathological features of COPD are shown in Figure 1. Patients with severe COPD often have exacerbations that result in medical visits and hospitalizations. Chronic hypoxemia and hypercapnia may cause pulmonary hypertension and cor pulmonale. Patients with severe COPD are also at increased risk for other systemic diseases, including cardiovascular disease, osteoporosis, lung cancer, and depression.¹

COPD represents a growing global public health problem. In one population-based study conducted at multiple international sites, approximately 10% of participants 40 years of age or older were found to have airflow obstruction of at least moderate severity according to spirometric criteria.² Between 1970 and 2002, age-standardized rates of death from COPD increased by 103% in the United States, making it the fourth leading cause of death.³ Women accounted for most of this increase, and the rate of death from COPD among women now exceeds the rate among men.⁴ As COPD worsens, there is a precipitous increase in health care costs, much of which is attributable to hospital care for exacerbations.⁵

Strategies and Evidence

History and Physical Examination

Although COPD is more common with increasing age, it should be considered in all adults who report chronic respiratory symptoms, particularly dyspnea that limits ordinary activities. Cigarette smoking is by far the most important known cause of COPD, but clinically significant disease develops in only a small proportion of smokers. Other environmental risk factors, such as exposure to various industrial dusts and fumes, have also been identified.⁶,⁷ Physical examination may reveal a
barrel-shaped chest, inspiratory retraction of the lower ribs (Hoover’s sign), a prolonged expiratory phase, and use of the accessory muscles of respiration, but these findings are sometimes absent even in cases of severe disease.

SPIROMETRY AND OTHER TESTING
A medical history and physical examination may suggest COPD, but they are not reliable predictors of airflow obstruction; the diagnosis must be confirmed with the use of spirometry. Frequent-
ly, however, spirometry is not performed, and failure to obtain spirometric confirmation leads to misdiagnosis in many cases. Airflow obstruction as measured by spirometry is defined as a ratio of the postbronchodilator FEV₁ to FVC of less than 0.70. When airflow obstruction is present, its severity is classified according to the FEV₁ as a percentage of the predicted normal value (Table 1). Spirometry is essential in determining whether the probable cause of respiratory symptoms is COPD, but clinical criteria, such as the intensity of breathlessness in relation to specific tasks and the frequency of exacerbations, should also be used when evaluating the overall severity of disease.

Testing the reversibility of airflow obstruction with an inhaled bronchodilator may be of value at the initial evaluation because a very strong response might identify previously unsuspected asthma. An early age at the onset of symptoms, atopy, the absence of a history of smoking, episodic symptoms, and nighttime awakening are more suggestive of asthma than of COPD.

Labeling patients with COPD as “responders” or “nonresponders” according to arbitrary reversibility criteria is of little practical value because the improvement in lung function with bronchodilators, whether immediate or eventual, is small relative to measurement error. Consequently, spirometry is a poor guide for determining whether therapy should be continued or modified in an individual patient. Once a diagnosis of COPD has been established, there is usually little reason to repeat spirometry at subsequent visits, although serial spirometric measurement at yearly intervals (or longer) may provide some prognostic information. On occasion, it may be helpful in distinguishing pulmonary from nonpulmonary causes of worsening dyspnea.

A chest radiograph should be obtained to rule out other pulmonary diseases. Chest imaging with computed tomography is unnecessary unless another diagnosis is suspected or surgical therapy for COPD is being considered. Oximetry should be performed annually, particularly in patients with severe or very severe disease, since patients with chronic hypoxemia benefit from long-term oxygen therapy. Testing for genetically determined deficiencies of alpha₁-antitrypsin may be considered, particularly if COPD develops at a relatively young age or if there is a strong family history. This information may be useful for counseling purposes. Alpha₁-antitrypsin replacement therapy is available, though of uncertain benefit.

SMOKING CESSATION
In the Lung Health Study, a randomized trial of smoking cessation in patients with mild-to-moderate COPD, cessation of smoking slowed the decline in lung function and, at long-term follow-up, reduced the rate of death from any cause. Although similar studies involving patients with severe COPD have not been conducted, it is reasonable to assume that some health benefits accrue from smoking cessation at all stages of the disease. Information about smoking-cessation interventions targeted to patients with COPD is limited, so combinations of counseling and pharmacotherapy that are effective in the general population should also be used with these patients.

BRONCHODILATORS
Many patients with severe COPD obtain symptomatic relief from the use of inhaled bronchodilators. Short-acting β₂-adrenergic agonists (e.g., albuterol) and ipratropium bromide, a short-acting anticholinergic agent, are used singly and in combination. Long-acting bronchodilators are now commonly used, but a short-acting bronchodilator should be provided for rescue therapy (Table 2). Many patients prefer albuterol to ipratropium bromide because it is faster acting.

The inhaled long-acting β₂-agonists salmeterol and formoterol provide sustained bronchodilation for at least 12 hours, and the inhaled long-acting anticholinergic agent tiotropium for

### Table 1. Stage and Severity of COPD According to Postbronchodilator Spirometry

<table>
<thead>
<tr>
<th>Stage and Severity of COPD</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Stage 1 — mild</td>
<td>FEV₁/FVC &lt;0.70, FEV₁ ≥80% of predicted value</td>
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<tr>
<td>Stage 2 — moderate</td>
<td>FEV₁/FVC &lt;0.70, FEV₁ 50 to 79% of predicted value</td>
</tr>
<tr>
<td>Stage 3 — severe</td>
<td>FEV₁/FVC &lt;0.70, FEV₁ 30 to 49% of predicted value</td>
</tr>
<tr>
<td>Stage 4 — very severe</td>
<td>FEV₁/FVC &lt;0.70, FEV₁ &lt;30% of predicted value or FEV₁ &lt;50% of predicted value plus chronic respiratory failure</td>
</tr>
</tbody>
</table>

Adapted from the Global Initiative for Chronic Obstructive Lung Disease. COPD denotes chronic obstructive pulmonary disease, FEV₁ forced expiratory volume in 1 second, and FVC forced vital capacity.
Randomized trials have generally involved symptomatic patients with exacerbation-prone conditions who have FEV₁ values that are less than 60% of the predicted value. When used as monotherapy, both classes of long-acting bronchodilators confer similar benefits. They improve respiratory health status (according to patient scores on the St. George’s Respiratory Questionnaire) as compared with placebo, but mean improvement falls short of the 4-point change considered clinically meaningful for that instrument.

### Table 2. Medications Commonly Used in Outpatient Treatment of COPD.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mode of Delivery, Dose, and Frequency</th>
<th>Adverse Effects</th>
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<tbody>
<tr>
<td><strong>Short-acting bronchodilators</strong></td>
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<tr>
<td>β₂-Adrenergic agonist: albuterol</td>
<td>Inhaler: 90 µg per inhalation; 1 to 2 inhalations every 4 to 6 hr, as needed Nebulizer: 2.5 mg every 4 to 6 hr, as needed</td>
<td>Palpitations, tachycardia, tremor, hypersensitivity reaction</td>
</tr>
<tr>
<td>Anticholinergic agent: ipratropium</td>
<td>Inhaler: 17 µg per inhalation; 2 inhalations 4 times daily, up to 12 inhalations per day Nebulizer: 0.5 mg every 6 to 8 hr</td>
<td>Dry mouth, cough, blurred vision, hypersensitivity reaction</td>
</tr>
<tr>
<td>Combination short-acting bronchodilator: albuterol–ipratropium</td>
<td>Inhaler: 90 µg of albuterol and 18 µg of ipratropium per inhalation; 2 inhalations 4 times daily, up to 12 inhalations per day Nebulizer: 2.5 mg of albuterol and 0.5 mg of ipratropium per dose; 4 times daily, up to 2 additional doses per day</td>
<td>Palpitations, tachycardia, tremor, dry mouth, cough, blurred vision, hypersensitivity reaction</td>
</tr>
<tr>
<td><strong>Long-acting bronchodilators</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β₂-Adrenergic agonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Inhaler: 50 µg per inhalation; 1 inhalation twice daily</td>
<td>Dizziness, headache, tremor, throat irritation, hypersensitivity reaction</td>
</tr>
<tr>
<td>Formoterol</td>
<td>Inhaler: 12 µg per inhalation; 1 inhalation twice daily Nebulizer: 20 µg twice daily</td>
<td></td>
</tr>
<tr>
<td>Arformoterol</td>
<td>Nebulizer: 15 µg twice daily</td>
<td></td>
</tr>
<tr>
<td>Anticholinergic agent: tiotropium</td>
<td>Inhaler: 18 µg per inhalation; 1 inhalation each morning</td>
<td>Dry mouth, urinary retention, symptoms of narrow-angle glaucoma, hypersensitivity reaction</td>
</tr>
<tr>
<td><strong>Inhaled corticosteroids</strong></td>
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<tr>
<td>Fluticasone (dry powder)</td>
<td>Inhaler: 250 µg per inhalation; 1 to 2 inhalations twice daily</td>
<td>Sore throat, dysphonia, headache, nasopharyngitis, thrush, hypersensitivity reactions, possible pneumonia</td>
</tr>
<tr>
<td>Fluticasone (aerosol)</td>
<td>Inhaler: 220 µg; 1 to 2 inhalations twice daily</td>
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<tr>
<td>Budesonide</td>
<td>Inhaler: 160 µg; 2 inhalations twice daily</td>
<td></td>
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<tr>
<td>Beclomethasone</td>
<td>Inhaler: 80 µg; 2 inhalations twice daily</td>
<td></td>
</tr>
<tr>
<td>Mometasone</td>
<td>Inhaler: 220 µg; 1 to 2 inhalations twice daily</td>
<td></td>
</tr>
<tr>
<td>Combination β₂-adrenergic agonist bronchodilator–inhaled corticosteroid</td>
<td></td>
<td>Sore throat, dysphonia, headache, nasopharyngitis, thrush, hypersensitivity reaction, possible pneumonia, dizziness, tremor, throat irritation</td>
</tr>
<tr>
<td>Fluticasone–salmeterol (dry powder)†</td>
<td>Inhaler: 250 µg fluticasone, 50 µg salmeterol per inhalation; 1 inhalation twice daily</td>
<td>Nausea and vomiting, seizures, tremor, insomnia, multifocal atrial tachyarrhythmia, hypersensitivity reaction</td>
</tr>
<tr>
<td>Budesonide–formoterol†</td>
<td>Inhaler: 160 µg budesonide, 4.5 µg formoterol; 2 inhalations twice daily</td>
<td></td>
</tr>
<tr>
<td>Methylxanthine: theophylline (24-hr sustained-release formulation)</td>
<td>Pill: 200 to 800 mg per day, with low starting dose increased to obtain serum concentration of 8 to 12 µg/ml; once daily</td>
<td></td>
</tr>
</tbody>
</table>

* This is not a complete list of medications used for chronic obstructive pulmonary disease (COPD).
† This is the only formulation of this specific combination of drugs approved by the Food and Drug Administration for treatment of COPD.
‡ The dose of budesonide in the metering chamber is 180 µg, but the dose delivered to the patient is 160 µg.

At least 24 hours. Randomized trials have generally involved symptomatic patients with exacerbation-prone conditions who have FEV₁ values that are less than 60% of the predicted value. When used as monotherapy, both classes of long-acting bronchodilators confer similar benefits. They improve respiratory health status (according to patient scores on the St. George’s Respiratory Questionnaire) as compared with placebo, but mean improvement falls short of the 4-point change considered clinically meaningful for that instrument. Both classes of drugs also reduce the risk of exacerbation by 15 to 20% (relative risk reduc-
tion), and this may be their most important clinical benefit.\textsuperscript{14,21,22} Given that the average patient with severe COPD has about one exacerbation per year that requires medical attention, five to seven patients must be treated for 1 year to prevent a single event. Both classes of drugs have been shown to reduce hospitalizations, although the reductions have not been consistent.\textsuperscript{21,22}

Adverse events associated with long-acting bronchodilators are generally minor (Table 2). Although concerns have been raised about the cardiovascular safety of both classes of long-acting bronchodilators,\textsuperscript{23,24} no serious safety problems were identified in two large trials, one comparing salmeterol with placebo in 3045 patients followed for 3 years,\textsuperscript{21} and another comparing tiotropium with placebo in 5993 patients followed for 4 years.\textsuperscript{22}

Theophylline is infrequently used in current practice but may be considered in patients whose COPD is difficult to control. The target plasma level should be no higher than 12 μg per milliliter; higher levels are poorly tolerated in older patients.

**inhaled corticosteroids**

Inhaled corticosteroids are also widely prescribed for COPD. Similar to long-acting bronchodilators, inhaled corticosteroids reduce the frequency of exacerbations by 15 to 20% and also improve respiratory health status, but only modestly.\textsuperscript{14,21,22} The combination of an inhaled corticosteroid with a long-acting β2-agonist reduces exacerbations by about an additional 10% as compared with either therapy used alone.\textsuperscript{21}

Dysphonia and upper-airway thrush are the most common adverse events associated with inhaled corticosteroids. They have also been linked to an increased risk of pneumonia in patients with COPD, amounting to about 3 excess cases per 100 patient-years of exposure.\textsuperscript{25} However, the significance of this observation is uncertain, since chest radiographs were not required for the diagnosis of pneumonia, and inhaled corticosteroid use was not associated with increased mortality.

**oxygen**

Two randomized trials evaluated the use of oxygen therapy in patients with severe COPD and persistent hypoxemia.\textsuperscript{26,27} One was a 5-year study that compared the effects of oxygen use for 15 hours per day with no oxygen use. The other was a 3-year study of oxygen use for 18 hours per day as compared with 12 hours per day. Oxygen therapy proved beneficial: there was an absolute reduction in the rate of death from any cause of about 20 percentage points in both trials.

Arterial oxygen levels should be assessed when the patient is clinically stable, at rest, and breathing ambient air. If the partial pressure of arterial oxygen is at or below 55 mm Hg, or if the arterial oxygen saturation is at or below 88%, home use of oxygen should be prescribed for at least 18 hours daily, including sleep time, with flow rates that maintain the oxygen saturation above 90%. In randomized trials, home use of oxygen conferred no apparent survival advantage among patients with milder resting daytime hypoxemia (partial pressure of arterial oxygen, 56 to 65 mm Hg) or isolated nocturnal hypoxemia.\textsuperscript{28,29}

Clinicians frequently prescribe ambulatory oxygen therapy for patients who have normal oxygen levels at rest but who have transient desaturation during exercise. Some patients report that ambulatory oxygen therapy helps relieve exercise-related breathlessness. Whether this perceived benefit is due to oxygen supplementation or to a placebo effect remains unclear. Short-term, placebo-controlled trials have shown that oxygen therapy improves exercise endurance in a laboratory setting; however, efforts to show that ambulatory oxygen use improves respiratory quality of life or relieves symptoms during activities of daily living have been mostly unsuccessful.\textsuperscript{30,31}

**management of exacerbations**

Severe exacerbations of COPD have an adverse effect on health status and may cause permanent loss of lung function.\textsuperscript{32,33} Most exacerbations are thought to result from infection, but sputum smears and cultures offer little help in guiding therapy.

As compared with placebo, antibiotics decrease the relative risk of treatment failure (defined as no resolution or clinical deterioration) by approximately 50% when used for COPD exacerbations.\textsuperscript{34} Subgroup analysis suggests that antibiotics are most effective when cough and sputum purulence are present. Most trials suggesting the efficacy of antibiotics have compared the use of older antibiotics, such as amoxicillin,
trimethoprim–sulfamethoxazole, and the tetracyclines, with placebo. It is uncertain whether newer classes of antibiotics, such as macrolides and fluoroquinolones, are more effective. Initial outpatient treatment with antibiotics should be based on considerations of cost, safety, and local patterns of antibiotic resistance among the bacterial species commonly isolated from sputum during exacerbations, particularly *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. In randomized trials, the use of systemic corticosteroids as compared with placebo reduced the relative risk of treatment failure (as defined by intensification of therapy, rehospitalization, or a return to the emergency department) by about 30% in patients with COPD exacerbations who were hospitalized or seen in an emergency department. Severely symptomatic patients seen in an outpatient setting are also likely to benefit from systemic corticosteroids, although data from trials of outpatient corticosteroid therapy for severe symptoms are lacking. In most instances, 40 mg of prednisone taken once daily for 10 to 14 days should suffice. Courses of treatment that are extended for more than 14 days confer no added benefit and increase the risk of adverse events.

If an exacerbation is associated with increased breathlessness, patients should be encouraged to increase their use of short-acting bronchodilators. Anticholinergic and β₂-agonist bronchodilators appear to be equally effective, with little additive benefit from combined use.

### Pulmonary Rehabilitation

As airflow obstruction progresses, patients with COPD typically become increasingly sedentary, which leads to muscular and cardiovascular deconditioning. Increasing physical disability contributes to social isolation and depression, which are highly prevalent among patients with severe COPD. The primary goal of pulmonary rehabilitation is to reverse muscular and cardiovascular dysfunction through an individually designed program. Most programs are multidisciplinary; in addition to exercise, they include education, behavior modification, and interventions to improve social and psychological functioning. A typical program consists of supervised sessions, each lasting 3 to 4 hours, provided 3 times weekly for 6 to 12 weeks. Major contraindications to the use of such programs are inability to walk, unstable cardiovascular disease, and cognitive impairment. Randomized, controlled trials of pulmonary rehabilitation consist mostly of small, single-center studies, generally involving patients with severe disease according to spirometric criteria (FEV₁:FVC <0.70; FEV₁ 30 to 49% of predicted value). A systematic review concluded that pulmonary rehabilitation significantly improved both functional exercise capacity (assessed by measuring the distance walked in 6 minutes) and respi-

<table>
<thead>
<tr>
<th>Category</th>
<th>Inactivated Influenza Vaccine</th>
<th>Polysaccharide Pneumococcal Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target group</td>
<td>All patients with COPD, except those who are hypersensitive to any component of vaccine, particularly eggs</td>
<td>All patients with COPD, except those who are hypersensitive to any component of vaccine</td>
</tr>
<tr>
<td>Frequency</td>
<td>Annually, preferably before influenza season or at any time throughout season</td>
<td>For patients &lt;65 yr of age, once or twice in lifetime; for patients ≥65 yr of age, one-time revaccination if vaccinated ≥5 yr earlier and &lt;65 yr of age at time of primary vaccination</td>
</tr>
<tr>
<td>Evidence of efficacy in COPD</td>
<td>Data from a meta-analysis of a limited number of trials indicate substantial reduction in influenza-related respiratory illnesses; large cohort study showed significant association between vaccination and reductions in hospitalizations for pneumonia and influenza and in risk of death during influenza season in persons with chronic lung disease</td>
<td>Data from a meta-analysis of a limited number of trials showed no benefit in reducing COPD exacerbations; one large cohort study showed significant association between vaccination and reductions in hospitalizations for pneumonia and in risk of death in persons with chronic lung disease, but another study did not</td>
</tr>
</tbody>
</table>

* Adapted from the Advisory Committee on Immunization Practices: Recommended Adult Immunization Schedule, 2009.
ratory quality of life (evaluated on the basis of responses to the Chronic Respiratory Questionnaire). In the absence of a supervised continuation program, the improvement achieved during the active phase of rehabilitation erodes substantially over the following year.

**SURGICAL OPTIONS**

An option for selected patients with COPD is lung-volume reduction, which involves the resection of severely emphysematous tissue from both upper lobes, allowing the remaining lung tissue to expand and function more normally. In a randomized trial involving patients with severe COPD, this surgery was not associated with an overall reduction in mortality, as compared with the use of optimal medical therapy, although the surgery did result in improved lung function, exercise capacity, and respiratory quality of life. Mortality was reduced in the subgroup of patients who had predominant upper-lobe emphysema along with low exercise capacity at baseline; however, it should be noted that exercise capacity was not among the prespecified prognostic variables to be assessed.

Lung transplantation offers the only opportunity for severely disabled patients with COPD to resume normal daily activities, but the median survival rate after lung transplantation (about 5 years) remains far below that associated with the transplantation of other solid organs. It is not known whether the procedure reduces mortality, as compared with optimal medical therapy.
Table 4. Recommendations for Management of COPD.*

<table>
<thead>
<tr>
<th>Category</th>
<th>GOLD†</th>
<th>American Thoracic Society–European Respiratory Society‡</th>
<th>American College of Physicians§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications for spirometry</td>
<td>Presence of chronic respiratory symptoms; in the absence of symptoms, history of exposure to risk factors (e.g., cigarette smoking or occupational exposure)</td>
<td>Presence of chronic respiratory symptoms; in the absence of symptoms, history of exposure to risk factors (e.g., cigarette smoking or occupational exposure)</td>
<td>Presence of chronic respiratory symptoms, particularly dyspnea</td>
</tr>
<tr>
<td>Indications for treatment</td>
<td>FEV₁:FVC &lt;0.70, with any symptoms</td>
<td>FEV₁:FVC &lt;0.70, with any symptoms</td>
<td>Chronic respiratory symptoms and FEV₁ &lt;60% of predicted value</td>
</tr>
<tr>
<td>Medications recommended</td>
<td>Short-acting bronchodilator for GOLD stages 1 to 4; add LABA, LAAC, or both for GOLD stages 2 to 4; add inhaled corticosteroid for GOLD stages 3 to 4, if patient is prone to exacerbations¶</td>
<td>Short-acting bronchodilator for intermittent symptoms; add LABA or LAAC for persistent symptoms; if LABA or LAAC alone shows limited benefit, combine LABA or LAAC with inhaled corticosteroid</td>
<td>Monotherapy with LABA, LAAC, or inhaled corticosteroid for all symptomatic patients with FEV₁ &lt;60% of predicted value; consider combined therapy for the same patients; use of short-acting bronchodilators not addressed</td>
</tr>
<tr>
<td>Candidates for pulmonary rehabilitation</td>
<td>Patients with GOLD stages 2 to 4¶</td>
<td>All patients with dyspnea and exercise limitation in addition to COPD</td>
<td>Symptomatic patients with FEV₁ &lt;50% of predicted value</td>
</tr>
<tr>
<td>Indications for long-term oxygen therapy</td>
<td>Chronic hypoxemia with PaO₂ ≤55 mm Hg or SaO₂ ≤88% or chronic hypoxemia with PaO₂ of 55 to 60 mm Hg in presence of right-sided heart failure or polycythemia</td>
<td>Chronic hypoxemia with PaO₂ ≤55 mm Hg</td>
<td>Chronic hypoxemia with PaO₂ ≤55 mm Hg</td>
</tr>
</tbody>
</table>

* FEV₁ denotes forced expiratory volume in 1 second, FVC forced vital capacity, GOLD the Global Initiative for Chronic Obstructive Lung Disease, LAAC long-acting anticholinergic, LABA long-acting β₂-adrenergic agonist, PaO₂ partial pressure of oxygen in arterial blood, and SaO₂ arterial oxygen saturation.
† Data are from the Global Initiative for Chronic Obstructive Lung Disease.⁹
‡ Data are from Celli and MacNee.¹⁵
§ Data are from Qaseem et al.¹⁴
¶ GOLD identifies four stages of COPD, with 1 indicating mild COPD and 4 indicating very severe COPD.
Since he has severe, exacerbation-prone COPD, it would be reasonable to combine drugs from two of these three classes. A short-acting bronchodilator should be provided for rescue use. Even if symptoms do not abate, he should be urged to continue taking the medications, because they reduce the risk of a severe exacerbation. Like all patients, he should receive instruction in inhaler technique. (A video demonstrating inhaler technique is available at NEJM.org in an article by Hendeles et al.)

If the patient’s arterial oxygen saturation is 88% or lower at rest in a stable clinical state, long-term oxygen therapy should be prescribed and used for at least 18 hours each day. In the absence of a contraindication, he should receive influenza vaccination each autumn, as well as pneumococcal vaccination (with revaccination as needed). Pulmonary rehabilitation should be considered if it is accessible to the patient and if he has no medical contraindications.

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Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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