

# Evidence-Based Approach to Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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**C**hronic obstructive pulmonary disease (COPD) is a common chronic disease with high morbidity and mortality worldwide. A recent study conducted to determine the global burden of COPD using recent diagnostic criteria<sup>1</sup> estimated that the prevalence of moderate to severe COPD is 10.1%.<sup>2</sup> A large percentage of these individuals are asymptomatic and undiagnosed. According to the 2002 estimates of the World Health Organization, COPD is the fifth leading cause of death in high-income countries, the third leading cause in middle-income countries, and the ninth leading cause in low-income countries.<sup>3</sup> In the United States, an estimated 24 million adults have COPD (only 12 million are diagnosed),<sup>4</sup> and it is the fourth leading cause of death among adults.<sup>5</sup>

Acute exacerbations of COPD are common in patients with moderate to severe disease. These patients experience 2 exacerbations per year on average, with a median recovery time of 7 days.<sup>6</sup> Exacerbations of COPD lead to substantial economic losses in terms of medical costs, absenteeism, and loss of productivity at work,<sup>7</sup> and can have a negative impact on patients' daily life and health-related well-being.<sup>8</sup> Acute exacerbations are primarily responsible for the direct cost of COPD associated with emergency department visits and hospitalizations.<sup>4</sup> In 2000, COPD exacerbations accounted for approximately 1.5 million emergency department visits, 726,000 hospitalizations, and 119,000 deaths.<sup>5</sup> Exacerbations also lead to frequent physician office visits. The indirect costs of COPD include the activity and functional limitations of individuals diagnosed with this condition.

Given the substantial burden of COPD, appropriate management of acute COPD exacerbations is essential. This article presents an evidence-based approach to managing acute exacerbations of COPD based on current guidelines, with a focus on strategies that have been shown to improve patient outcomes.

## OVERVIEW OF COPD

The definition of COPD has changed significantly over

## TAKE HOME POINTS

- An exacerbation of chronic obstructive pulmonary disease (COPD) often presents as a sustained increase in symptoms of dyspnea, cough, and sputum production.
- Diagnosis of an exacerbation requires a careful history, physical examination, and diagnostic tests to exclude other pulmonary or cardiac diseases that present in a similar manner.
- Patients with an acute exacerbation of COPD are classified as having mild, moderate, or severe disease according to the severity of their symptoms and findings on physical examination and diagnostic tests.
- Moderate to severe COPD exacerbations require hospitalization.
- Inhaled bronchodilators, oral or intravenous steroids, and antibiotics have been shown to be effective in the treatment of an acute exacerbation.
- Noninvasive positive pressure ventilation has been shown to decrease intubation rates, length of hospital stay, and mortality in those who present with respiratory failure and acidosis.
- Smoking cessation counseling, self-management education, influenza vaccine, and pulmonary rehabilitation have all been shown to be effective in preventing further exacerbations.

the past decade as our understanding of the pathogenesis and management of the disease has improved. Current guidelines on COPD diagnosis and treatment from the American Thoracic Society (ATS) and European

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Respiratory Society (ERS) do not use the traditional terms *chronic bronchitis* and *emphysema* but rather define COPD as a progressive yet preventable and treatable disease with the characteristic feature of airflow obstruction that is not completely reversible.<sup>1</sup> The guidelines classify the severity of COPD on the basis of a postbronchodilator forced expiratory volume in 1 second/forced vital capacity ratio ( $FEV_1/FVC$ ) and the percentage of predicted  $FEV_1$ . There are 5 categories: at risk ( $FEV_1/FVC > 0.7$ ,  $FEV_1$  % predicted  $> 80$ ), mild ( $\leq 0.7$ ,  $> 80$ ), moderate ( $\leq 0.7$ ,  $\geq 50$ ), severe ( $\leq 0.7$ ,  $\geq 30$ ), and very severe ( $\leq 0.7$ ,  $< 30$ ).

The limitation of airflow in COPD is triggered by noxious stimuli that lead to chronic inflammation, edema, and secretions.<sup>9</sup> Inflammation promotes remodeling in the form of squamous metaplasia of the epithelium of small airways, hypertrophy of smooth muscles, and peribronchial fibrosis. A host of cytokines have been identified as critical players in inducing and maintaining this state of chronic inflammation. Some of these, such as C-reactive protein, tumor necrosis factor- $\alpha$ , interleukin (IL)-6, IL-8, and IL-10, are being investigated as biomarkers for predicting the intensity of inflammation.<sup>10</sup>

Cigarette smoking is the most common cause for the development of COPD worldwide. Other exogenous risk factors include passive smoking,<sup>11</sup> occupational exposure to noxious particles,<sup>12</sup> and air pollution.<sup>13</sup> Endogenous factors such as genetic factors<sup>14</sup> and airway hyperreactivity<sup>15</sup> also affect an individual's susceptibility to the disease.

#### **DEFINITION OF ACUTE COPD EXACERBATION**

Many different definitions for COPD exacerbation have been used in the medical literature. A common definition used in COPD studies over the past decade was formulated by Anthonisen and colleagues,<sup>16</sup> who defined an exacerbation based on 3 major clinical features: worsening of dyspnea, increase in sputum production, and increase in sputum purulence. According to this definition, the presence of all 3 features indicates a severe exacerbation, 2 features indicates a moderate exacerbation, and 1 major feature in conjunction with 1 minor feature (eg, increase in wheezing or coughing, fever, upper respiratory symptoms in the past 5 days, and increase in heart rate or respiratory rate by approximately 20%) indicates a mild exacerbation. A limitation of this definition is that it was designed for studies investigating the use of antibiotics in COPD and thus emphasizes features that are indicative of an underlying infectious cause of exacerbation. In addition, no prospective studies have validated the

association between these features and the severity of an exacerbation.

A consensus definition issued by a working group of US and European respiratory physicians in 2000<sup>17</sup> and amended in 2003<sup>18</sup> defines a COPD exacerbation as "a sustained worsening of the patient's condition from the stable state and beyond normal day-to-day variations that is acute in onset and may warrant additional treatment in a patient with underlying COPD." This definition has several strengths. It is independent of the etiology of the exacerbation, disease severity at baseline, and severity of the exacerbation itself. It also does not specify the presence or absence of any clinical symptoms, signs, or lung function parameters to define the exacerbation, which allows inclusion of even mild exacerbations for which the patient may not necessarily seek medical care. However, using this definition to detect an acute exacerbation would require patients to maintain a daily symptom diary. Also, although this consensus definition has a high sensitivity for detecting exacerbations, it lacks the specificity required by a clinician to make an accurate diagnosis and determine the etiology and severity of the exacerbation, especially in patients with daily symptoms, which often vary on a day-to-day basis.

#### **ETIOLOGY**

Respiratory infectious agents, particularly viruses and bacteria, have been implicated as a major risk factor for the development of a COPD exacerbation. Viral infections with or without superimposed bacterial infection account for approximately one third of infectious exacerbations.<sup>19</sup> The role of bacterial infection in COPD exacerbation is controversial because bacteria have been isolated in up to one third of patients with stable COPD.<sup>20</sup> A number of studies have shown that the concentration of bacterial pathogens significantly increases in the distal airways in up to 50% of patients during an acute exacerbation of COPD, implying an underlying infectious etiology.<sup>21,22</sup> *Haemophilus influenzae* and *Streptococcus pneumoniae* are the most commonly isolated pathogens, while atypical bacteria account for 5% to 10% of exacerbations.<sup>23</sup> Gram-negative enteric bacilli and *Pseudomonas aeruginosa* are associated with severe COPD at baseline, use of systemic steroids, and antibiotic use in the preceding 3 months.<sup>24</sup> In addition, there is a subgroup among patients with stable moderate to severe COPD who are more susceptible to frequent exacerbations, leading to extensive utilization of health resources, a rapid decline in lung function ( $FEV_1$ ), and a poor quality of life.<sup>25</sup> These patients are more likely to have bacterial colonization of their

**Table 1.** Common Symptoms of Chronic Obstructive Pulmonary Disease Exacerbation

Pulmonary	Extrapulmonary
Dyspnea	Fever
Cough	Symptoms of common cold
Increase in sputum production	Sore throat
Increase in sputum purulence	Malaise
Chest tightness	Fatigue
Chest congestion	
Wheezing	

airways.<sup>26</sup> It has been postulated that these colonizing bacteria may be the trigger for chronic and progressive inflammation of the airways.

Another factor linked to COPD exacerbations is air pollution. A number of studies have shown that an increase in the level of air pollutants is associated with hospital admissions related to COPD exacerbation.<sup>27,28</sup> Also, worsening of a serious underlying comorbid condition such as congestive heart failure or renal insufficiency can precipitate an exacerbation.

#### DIAGNOSTIC EVALUATION AND RISK STRATIFICATION

Patients with COPD can present with a wide range of nonspecific symptoms. **Table 1** provides a list of common symptoms experienced during an exacerbation. A prospective study that followed 101 patients with moderate to severe COPD for a period of 2.5 years showed that the onset of symptoms of exacerbation occurs up to 7 days prior to a significant decrease in lung function manifested as reduced FEV<sub>1</sub>, FVC, and peak expiratory flow rate (PEFR).<sup>6</sup> Another prospective cohort study of factors that lead to reporting of an acute exacerbation of COPD found that up to 60% of exacerbations are not reported.<sup>29</sup> The total number of symptoms experienced at onset and the need for rescue medications were strongly associated with increased reporting of events. The symptoms that triggered the most reporting were coughing and sputum production, and those that triggered the least reporting were symptoms of cold and wheezing.<sup>29</sup>

The work-up of an acute exacerbation of COPD includes a thorough patient history, physical examination, and diagnostic tests to exclude other or coexisting diseases and to determine the etiology and severity of the exacerbation. The common presenting symptoms of an exacerbation are not specific, and thus it is important to perform a comprehensive physical examination, especially of the pulmonary and cardiovascular system,

**Table 2.** Differential Diagnosis of Chronic Obstructive Pulmonary Disease Exacerbation

Cardiac	Pulmonary
Acute coronary syndrome	Pneumonia
Congestive heart failure	Pneumothorax
Arrhythmias	Pleural effusion
Thromboembolic	Bronchiolitis obliterans organizing pneumonia
Pulmonary embolism	

to narrow the differential diagnosis (**Table 2**). Diagnostic tests such as oxygen saturation, arterial blood gases, chest radiograph, electrocardiogram, blood cell counts, electrolytes, and gram stain and culture of the sputum are also used to exclude other important differentials, such as pneumonia, congestive heart disease, acute coronary syndrome, and pulmonary embolism. The choice of these tests depends on the clinical presentation of the patient, underlying patient risk factors, and physical examination findings. Measurement of oxygen saturation and arterial blood gases are used to assess the severity of an exacerbation and make appropriate clinical decisions regarding management.

The ATS/ERS task force classified the severity of COPD exacerbations into 3 levels (**Table 3**).<sup>1</sup> The first level represents a mild to moderate exacerbation in a hemodynamically stable patient with mild to moderate COPD at baseline. These patients are unlikely to have a history of frequent exacerbations or serious comorbid conditions. Patients assigned to the second level of severity are hemodynamically stable, have moderate to severe COPD at baseline, and are likely to have a history of frequent exacerbations and significant comorbidity. The presence of tachypnea, use of accessory muscles, and failure of rescue therapy are signs included in this level. Level 3 patients have severe COPD at baseline and are hemodynamically unstable with impending or actual respiratory failure and end-organ damage.

#### MANAGEMENT

Management of COPD exacerbations is based on the severity of the exacerbation, with more intensive and invasive measures required as the severity increases (**Figure**). Bronchodilators and corticosteroids are used to treat all patients with COPD exacerbation, and antibiotics are used to treat patients with symptoms suggestive of an infectious etiology and patients with moderate to severe exacerbations. Antibiotics also may be used in patients with mild exacerbations based on the premise that patients have a higher degree of

**Table 3.** Assessment of Severity of an Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Clinical History	Level 1	Level 2	Level 3
Comorbid conditions*	Unlikely	Likely	Very likely
Frequent exacerbations	Unlikely	Likely	Very likely
Baseline COPD severity	Mild-moderate	Moderate to severe	Severe
Physical findings			
Hemodynamic evaluation	Stable	Stable	Unstable
Tachypnea, use of accessory respiratory muscles	None	Present	Present
Persistent symptoms after initial therapy	None	Present	Present

Adapted with permission from Celli BR, Macnee W; ATS/ERS Task Force. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper [published erratum appears in Eur Respir J 2006;27:242]. Eur Respir J 2004;23:940.

COPD = chronic obstructive pulmonary disease.

\*The more common comorbid conditions associated with poor prognosis are coronary artery disease, congestive heart failure, diabetes mellitus, liver failure, and renal insufficiency.

bacterial colonization during an exacerbation than at baseline,<sup>21,22</sup> and these organisms may contribute to an inflammatory response. However, no clinical trials have demonstrated a beneficial effect of antibiotics in these patients, and the decision to initiate antibiotic therapy for treating mild exacerbations is based on clinical judgment. The dose, frequency, duration of treatment, and choice of antibiotics change with the severity of the disease.

Patients with a mild exacerbation receive level 1 interventions and can be treated on an outpatient basis if they do not have underlying comorbidities and frequent exacerbations. Patients with a moderate to severe exacerbation require all level 1 interventions and may require supplemental oxygen due to hypoxemia. These patients are treated in the hospital. Patients presenting with hemodynamic instability require level 1 interventions and oxygen and may need invasive or non-invasive ventilatory support. These patients are treated in special care units or intensive care units (ICUs).

### Inhaled Bronchodilators

Systematic reviews have clearly documented that inhaled bronchodilators play an important role in improving lung function in patients with COPD exacerbation.<sup>30</sup> Both short-acting  $\beta$ -agonist and anticholinergic inhaled bronchodilators are comparable in their ability to significantly improve FEV<sub>1</sub>, and there is an additive effect when both bronchodilators are used together.<sup>30</sup>

### Corticosteroids

Use of oral and intravenous steroids is a standard of care for COPD exacerbation. The largest study that documented the benefit of steroids in exacerbations was a double-blind randomized trial that included 271

patients admitted for acute exacerbation of COPD at 25 Veterans Affairs medical centers.<sup>31</sup> This study showed that administration of steroids was associated with improvement of lung function, shorter length of hospitalization, and decrease in treatment failure. It also showed that a 2-week course is as effective as an 8-week course.<sup>31</sup> The most common side effect associated with the use of steroids in COPD exacerbation was hyperglycemia. Oral and intravenous forms of steroids are equally effective.<sup>32</sup> In addition, use of inhaled steroids either alone or with long-acting  $\beta$ -agonists in the treatment of stable COPD results in decreased rates of exacerbation.<sup>33</sup> A meta-analysis of 47 primary studies indicated that inhaled steroids reduce the rate of exacerbations and the rate of deterioration in the quality of life in patients with COPD, although they do not affect lung function or mortality.<sup>34</sup>

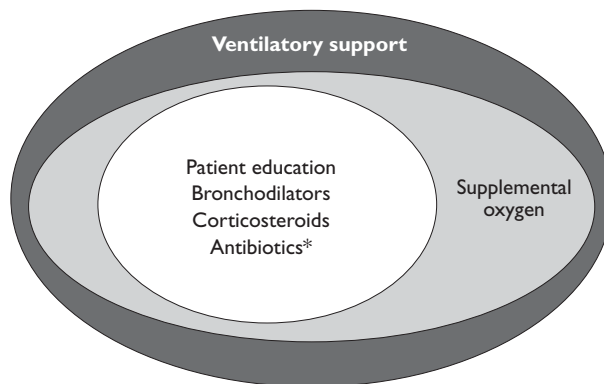
### Antibiotics

Randomized controlled trials of antibiotic therapy in COPD exacerbation and meta-analyses of these trials have demonstrated that antibiotics are beneficial in those presenting with symptoms that indicate an underlying infectious etiology and in patients with a moderate to severe exacerbation. Russo et al<sup>35</sup> reviewed 10 placebo-controlled trials to determine the role of antibiotics in patients with exacerbation and no evidence of pneumonia or underlying asthma. Six trials failed to indicate a clear advantage, but 4 trials showed earlier symptomatic recovery and earlier improvement in PEFr of patients treated with antibiotics. Patients with more cardinal symptoms of infection (dyspnea, increase in sputum volume, increase in sputum purulence) appeared to derive greater benefit from antibiotics.<sup>35</sup> In another study that compared 2 groups of patients who

presented to the emergency department due to exacerbation, patients treated with antibiotics had a lower rates of relapse, hospitalization, and intubation as compared with those not prescribed antibiotics. In this study, even patients with mild symptoms at presentation benefited from antibiotics. The 2 groups were similar in regard to severity of underlying COPD and severity of the acute exacerbation.<sup>36</sup> A systematic meta-analysis of 11 placebo-controlled studies performed in various settings (3 outpatient, 7 inpatient, 1 ICU) found that antibiotic use decreased treatment failure by 46% as compared with placebo, although there was substantial variation in the findings across the studies. Stratification by patient setting decreased this variability and showed that antibiotics reduced mortality and treatment failure in inpatients but not in outpatients.<sup>37</sup> Finally, a Cochrane database review of 11 randomized controlled trials also showed that antibiotics reduced treatment failure and short-term mortality rates among patients who had moderate or severe exacerbations with increased cough and sputum purulence.<sup>38</sup>

The choice of an antibiotic and duration of therapy depend on the severity of the exacerbation. In patients with an exacerbation of mild to moderate severity, an antibiotic course of 5 days or less has been shown to be equivalent to a 5-day or longer course.<sup>39</sup> When choosing an antibiotic, it is important to understand the pathogens involved at different levels of severity of COPD exacerbation. A more severe exacerbation requiring hospitalization indicates the possibility of an increasingly virulent and/or resistant organism requiring institution of broad spectrum antibiotics. A surveillance study carried out in 1999–2000 to evaluate the frequency and antimicrobial susceptibility of pathogens causing community-acquired pneumonia, COPD exacerbation, and sinusitis in 674 community-based practices across the United States showed that *S. pneumoniae*, nontypeable *H. influenzae*, and *Moraxella catarrhalis* account for most exacerbations.<sup>40</sup> A high level of resistance in *S. pneumoniae* to both penicillin and macrolides was noted in this study. *H. influenzae* was also found to have increased resistance to ampicillin. These patterns of resistance varied from region to region, and thus the antimicrobial susceptibility patterns of these organisms at institutional and regional levels should be taken into account prior to prescribing antibiotics for an exacerbation. Also, patients with severe COPD at baseline, elderly patients, and those receiving multiple antibiotics were more susceptible to resistant pathogens, such as gram-negative bacilli and *P. aeruginosa*.<sup>40</sup> These risk factors should be considered when prescribing antibiotics for acute exacerbations of COPD.

- Level 1: Mild to moderate COPD exacerbation
- Level 2: Moderate to severe COPD exacerbation
- Level 3: Severe COPD exacerbation



**Figure.** Stepwise approach to the management of acute exacerbation of chronic obstructive pulmonary disease (COPD). \*In mild exacerbations, antibiotics may be used when an infectious etiology is suspected.

A meta-analysis of 12 randomized controlled trials that compared first-line antibiotic agents (eg, amoxicillin, doxycycline, trimethoprim/sulfamethoxazole) with second-line agents (eg, second- and third-generation cephalosporins and quinolones) for COPD exacerbation concluded that second-line treatment resulted in fewer treatment failures.<sup>41</sup> The 2 groups were no different in terms of side-effect profiles. Another meta-analysis of 19 randomized controlled trials found that macrolides, quinolones, and amoxicillin/clavulanate are equally effective for treatment of COPD exacerbation.<sup>42</sup> Therefore, patients who have more severe symptoms of exacerbation, those who require hospitalization for an exacerbation, or those at risk for resistant pathogens would benefit from the use of second-line antibiotics.

### Oxygen

Patients presenting to the emergency department with COPD exacerbation may be hypoxic and acidotic, and use of oxygen therapy is an important intervention in those presenting with hypoxia to prevent acidosis. However, patients with COPD often have elevated CO<sub>2</sub> levels at baseline and are at risk for oxygen-induced hypercapnia. Mechanisms for oxygen-induced hypercapnia include suppression of hypoxic drive to ventilation and an increase in ventilation-perfusion mismatch and Bohr's dead space secondary to reduced hypoxic vasoconstriction.<sup>43</sup> It has been documented that high-concentration oxygen therapy leads to worsening acidosis and CO<sub>2</sub> retention.<sup>44</sup> On the other

hand, another study found no difference between patients admitted to the ICU for COPD exacerbation who were assigned to receive oxygen therapy titrated to a  $\text{PaO}_2$  exceeding 6.6 kPa (50 mm Hg;  $n = 17$ ) versus a  $\text{PaO}_2$  exceeding 9 kPa (70 mm Hg;  $n = 17$ ).<sup>45</sup> Specifically, the 2 groups were not statistically different in terms of percentage of patients requiring mechanical ventilation or death rate. The ATS/ERS guidelines recommend that the goal of inpatient oxygen therapy is to maintain an oxygen saturation of 90% or greater and a  $\text{PaO}_2$  above 60 mm Hg.<sup>1</sup> It also emphasizes that prevention of tissue hypoxia is a priority followed by prevention of  $\text{CO}_2$  retention.

### **Ventilatory Support**

Ventilatory support is vital in patients who present with hypoxic and/or hypercapnic respiratory failure. Both noninvasive and invasive forms of support have been successfully used in COPD exacerbation. A meta-analysis of 14 randomized controlled trials involving patients admitted to the hospital with acute respiratory failure secondary to exacerbation showed that use of noninvasive positive pressure ventilation (NPPV) leads to shorter hospital stay, decreased rate of intubation, and decreased mortality.<sup>46</sup> Six of these studies showed that improvement in acidosis, hypoxia, and hypercapnia was observed only 1 hour after institution of NPPV. Monitoring of hemodynamic stability and frequent measurement of blood gases to evaluate for hypoxia and hypercapnia are crucial for patients on NPPV. Invasive ventilation is required if respiratory function does not improve or worsens as indicated by worsening respiratory acidosis, hypoxia, or hypercapnia as well as development of altered mentation or hemodynamic instability.<sup>47</sup> NPPV has also been found to be useful in weaning patients intubated for COPD exacerbation, with studies showing that it reduces weaning time and shortens the duration of the ICU stay.<sup>48,49</sup>

NPPV is not appropriate in all situations. Contraindications include respiratory arrest, cardiovascular instability (eg, hypotension, arrhythmias, myocardial infarction), impaired mental function, copious secretions, recent facial and gastroesophageal surgery, craniofacial trauma, burns, and extreme obesity.<sup>1</sup> In addition, there is a lack of sufficient evidence for the role of NPPV in conditions such as pneumonia, sepsis, pulmonary embolism, and acute lung injury; in these situations, invasive ventilation is the preferred option.

### **MORTALITY AND PROGNOSIS**

Patients with an exacerbation who are admitted to the ICU have a poor prognosis. A retrospective cohort

study in 57 patients admitted to the ICU reported an inpatient mortality rate of 24%, and 90% of these patients were intubated for a mean intubation period of 2.3 days.<sup>50</sup> The 6-month, 1-year, 3-year, and 5-year mortality rates were 39%, 43%, 61%, and 76%, respectively. Factors associated with poor prognosis in the ICU setting in this study were increased age, previous history of mechanical ventilation, malnutrition, and higher disease severity on admission as measured by the Acute Physiology and Chronic Health Evaluation (APACHE II). A prospective multicenter cohort study followed 362 ICU admissions in 42 ICUs in 40 different US hospitals for severe COPD exacerbation. The mortality rate in this study was also 24%, but it increased significantly in elderly patients. The mortality rate was 30% at hospital discharge, 41% at 90 days, 47% at 180 days, and 59% at 1 year.<sup>51</sup>

Patients admitted to a nonintensive hospital setting with COPD exacerbation also have high mortality rates both during (6%–8%) and after hospitalization.<sup>52,53</sup> In a prospective cohort study, the 6-month, 1-year, and 5-year mortality rates of patients hospitalized with COPD exacerbation were 13%, 22%, and 36%, respectively.<sup>54</sup> The mortality rate for elderly patients at 6 months postdischarge was 20%, indicating that age is an important risk factor for mortality.<sup>55</sup> In addition to age, poor functional status and lower body mass index were independent risk factors in the elderly. Other predictors of mortality include use of oral steroids, severe chronic COPD, comorbidities (eg, underlying cardiac, liver, or renal dysfunction), symptoms of depression, and prior hospital admission.<sup>52,53,55</sup>

Predictors of frequent hospitalizations secondary to COPD exacerbation include severity of COPD, psychological stress, poor ambulatory status, hypercapnia at discharge, and hospitalization in the previous year.<sup>56–59</sup> The presence of systemic inflammatory markers such as fibrinogen has also been shown to independently increase the risk of exacerbations.<sup>60</sup>

### **PREVENTION**

Prevention is an important part of management of COPD exacerbations given the increased health care utilization, mortality, and morbidity associated with these episodes. Interventions that have been shown to be effective in preventing further exacerbations include patient education, influenza vaccine, long-term steroid therapy (discussed in Management section), and pulmonary rehabilitation. The key components of patient education are smoking cessation counseling and instruction on self-management of COPD. Smoking cessation is the only way to slow the progression of

COPD. The Lung Health Study proved that smoking cessation leads to a decreased rate of decline of FEV<sub>1</sub> in mild to moderate COPD irrespective of age, duration of smoking, and severity of lung disease.<sup>61</sup> Smoking cessation also significantly decreases chronic cough, sputum production, dyspnea, and wheezing in patients with mild to moderate disease.<sup>62</sup> In both studies, the effects of smoking cessation were noted in patients with less severe disease; hence it is crucial to intervene at an early stage.

Prospective randomized clinical trials in patients with moderate to severe COPD have shown that providing education on self-management of COPD leads to fewer emergency department and office visits and increases work productivity.<sup>63</sup> In 1 trial, self-management reduced hospital admissions by approximately 40%.<sup>64</sup> A Cochrane review of 14 controlled trials related to self-management education in COPD demonstrated a significant decrease in the likelihood of at least 1 hospital admission among patients receiving self-management education versus those receiving usual care.<sup>65</sup>

Unfortunately, there are no recommendations regarding the content or form of material for effectively educating patients on COPD self-management. To address this issue, Adams et al<sup>66</sup> conducted a quantitative meta-analysis of 32 studies (including 20 randomized controlled trials) that evaluated components of the chronic care model (CCM) as interventions for preventing exacerbations and reducing health care utilization in adults with COPD. The CCM model coordinates basic elements of the health care system (eg, self-management support, delivery system design, decision support) to enhance the quality of care of a chronic disease. These authors found that interventions with 2 or more CCM components resulted in lower rates of hospitalizations and emergency room visits; however, the interventions did not impact lung function or the functional status of the patients.<sup>66</sup> This study suggests that patients being treated for an acute COPD exacerbation should receive support regarding managing their disease at home in the form of education or information about the disease, including its treatment and prevention; access to a health care professional for follow-up; identification of possible barriers to care; and provider feedback.

Patients with COPD may benefit from influenza vaccination and pulmonary rehabilitation. Influenza vaccine has been shown to decrease the incidence of COPD exacerbation during the 3- to 4-week period following vaccination.<sup>67</sup> The pneumococcal vaccines are also recommended in elderly patients to decrease the risk of pneumococcal bacteremia.<sup>68</sup> However, no ran-

domized controlled trials supporting the effectiveness of vaccination in COPD patients have been conducted. A systematic review of randomized controlled trials showed that pulmonary rehabilitation after an acute COPD exacerbation reduces the risk of hospitalization and mortality.<sup>69</sup>

## CONCLUSION

An acute exacerbation can serve as a window of opportunity for improving management of COPD as it brings the patient in touch with health care services and professionals. The aim of hospitalization should be appropriate diagnosis and evidence-based management of the exacerbation using bronchodilators, antibiotics, and steroids, in addition to use of oxygen and ventilatory support in those with moderate to severe exacerbation. However, treatment should focus on not only symptom relief but should also include preventive aspects such as patient education regarding self-management and smoking cessation, follow-up, and vaccination.

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