

# Chronic Obstructive Pulmonary Disease: Epidemiology, Management, and Impact on North Carolina

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**Chronic obstructive pulmonary disease (COPD) affects millions of people worldwide, resulting in morbidity, mortality, and substantial utilization of health care resources. This review focuses on the epidemiology of COPD, management strategies, and the health and economic impact of this condition in North Carolina.**

**C**hronic obstructive pulmonary disease (COPD) is a common respiratory disorder characterized by non-reversible airflow obstruction. When a susceptible individual is exposed to a noxious substance, pathophysiologic changes take place in the small airways, lung parenchyma, and pulmonary vasculature that cause airflow limitation. These changes result in the clinical manifestations of COPD: dyspnea, cough, hypoxemia, and mucous production. Acute exacerbations and comorbidities add to the overall severity and complications of the disease.

COPD is a major cause of morbidity and mortality worldwide [1]. The disease also uses a large portion of health care resources and is a significant social and economic burden. The Global Initiative for Chronic Obstructive Lung Diseases (GOLD), a program shaped by committees made up of international experts, seeks to raise awareness of COPD among health care professionals in order to improve prevention and management. The initiative has established evidence-based guidelines that are considered to be the standard of care [1]; these guidelines focus on the diagnosis, management, and prevention of COPD. This article reviews the epidemiology and basic management of COPD according to the GOLD guidelines and describes the effects of the disease in North Carolina.

## Epidemiology

Recent data suggest that COPD is more prevalent among smokers (current and past), people over the age of 40 years, and men [1]. COPD is a major cause of chronic morbidity—including hospitalizations, dyspnea, and health care utilization—and in 2010 it was the third leading cause of death worldwide [2]. The social and economic ramifications of managing this disease are considerable and are increasing. In the United States, the direct and indirect costs of COPD are estimated to be \$29.5 billion and \$20.4 billion, respectively [1].

In North Carolina, COPD is common and has increased the utilization of health care resources. Analysis of data from the 2007 and 2009 Behavioral Risk Factor Surveillance System surveys showed that, in North Carolina, 5.7% of respondents (2,187 out of 26,227) reported having been diagnosed with COPD [3]. Although COPD is more common among men, COPD-related mortality among woman in North Carolina is increasing, with the death rate increasing from 12.9 to 59.1 per 100,000 population from 1980 through 2006. Mortality among men in North Carolina also increased during this period, but this increase was much smaller, from 72.9 to 83.7 per 100,000 population [4]. Additionally, from 2003 to 2007, there were 33,507 hospital discharges in North Carolina with a diagnosis of COPD, and the charges for these hospitalizations totaled \$421.6 million; these numbers are greater than those for 1995-1999, when there were 28,496 hospital discharges with a diagnosis of COPD, with charges totaling \$225.7 million [5].

## Risk Factors

COPD results from the interaction of genetic and environmental factors. This interaction is best demonstrated by hereditary deficiency of alpha-1 antitrypsin (AAT), which is a well-documented risk factor for COPD [1]. Patients with COPD who are younger than 45 years of age or who live in an area with a high prevalence of AAT deficiency should undergo testing for this deficiency [1].

The main risk factor for developing COPD is cigarette smoking. Data clearly show that smokers have more symptoms, a higher rate of decline in lung function, and a higher rate of mortality than do nonsmokers [6]. Passive exposure to secondhand tobacco smoke can lead to respiratory symptoms and COPD [7].

In North Carolina, approximately 21% of adults and 11% of youth aged 12-17 years are current smokers [8]. During the period 2000-2004, the average annual smoking-attributable mortality rate among North Carolinians aged

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35 years or older was 298.4 deaths per 100,000 population [8], which translates to about 12,000 deaths each year as a result of tobacco use. Most of these deaths are the result of COPD. In 2012, North Carolina Prevention Partners released a prevention report card [9] affirming that smoking is still the leading cause of preventable death in the state. According to the report, 60.5% of serious smokers in North Carolina are trying to quit, compared with 52% nationwide.

Although smoking is the most common risk factor for acquiring COPD, environmental or occupational exposure to organic or inorganic dust particles also places an individual at significant risk. Occupational exposures account for 10% to 20% of the symptoms and functional impairment associated with COPD [1]. The burning of substances such as wood, animal dung, or coal can lead to COPD. In particular, indoor pollution from biomass cooking in poorly ventilated areas is an important risk factor for the disease [10]. Exposure to outdoor pollutants appears to have some impact on the development of COPD, but the effect is small compared with that of cigarette smoking [1].

## Diagnosis and Staging

The diagnosis of COPD is based on 3 considerations: a history of symptoms consistent with the disease (dyspnea, cough, and sputum production), a history of exposure to 1 or more noxious substances known to be a risk factor for COPD, and measurement of airflow obstruction. Treatment is based on the severity of symptoms and the degree of airflow limitation.

The most accurate method of demonstrating airflow limitation is spirometry, which involves measuring 2 respiratory variables. Forced expiratory volume in 1 second ( $FEV_1$ ) is the amount of air that can be forcibly blown out during the first second of forced exhalation after complete inhalation. Forced vital capacity (FVC) is the total amount of air forcibly exhaled after a complete inhalation. The GOLD guidelines for diagnosis and management of COPD state that airflow obstruction is present when the  $FEV_1/FVC$  ratio is less than .70 when measured after administration of a short-acting inhaled bronchodilator [1]. However, using this fixed cutoff to define airflow limitation may result in overdiagnosis of COPD [1].

Depending on the degree of airflow obstruction, the severity of COPD is classified as stage 1, 2, 3, or 4. (Spirometric cutpoints are listed in Table 1.) Staging of COPD helps to determine therapy. Also, a higher GOLD stage (indicating worsening of airflow limitation) correlates with increased risk of exacerbations of COPD, a higher number of hospitalizations, and a higher 3-year mortality rate [1].

## Prevention and Management

Prevention of disease is the ultimate goal. Once COPD has been diagnosed, however, effective management should be aimed at reducing symptoms and reducing risk of exacerbations, disease progression, and death [1].

**Prevention.** COPD can be relatively easily prevented by not smoking cigarettes, avoiding secondhand smoke, and avoiding the inhalation of other noxious particles, such as chemical dust and fumes, both at home and in the workplace. The use of personal protective equipment and adherence to Occupational Safety and Health Administration standards as it pertains to workplace exposure are recommended and may help to decrease contact with noxious fumes and chemicals.

Public health policies and educational efforts are aiming to decrease North Carolinians' exposure to cigarette smoke and other noxious particles that are found indoors. North Carolina has taken measures to help control exposure to secondhand smoke among the general public. In 2009 the North Carolina General Assembly passed a law [11] banning smoking in almost all restaurants and bars.

It also may be appropriate to pursue legislation that minimizes occupational exposure to toxic particles by implementing engineering control and elimination of these particles—for example, by providing appropriate ventilation or finding substitutes for toxic substances. Such legislation could help to prevent work-related COPD.

**Nonpharmacologic management.** In patients for whom it is indicated, long-term oxygen therapy (more than 15 hours per day) has been shown to decrease mortality rates and hospitalization rates [12, 13]. To be an appropriate candidate for such therapy, the patient must have partial pressure of oxygen ( $Pao_2$ ) at or below 55 mm Hg or oxygen saturation ( $Sao_2$ ) at or below 88% on arterial blood gas analysis, when measured on room air. Either of these findings can occur with or without hypercapnia (increased carbon dioxide), and the measurement must be confirmed twice over a 3-week period. For patients who have pulmonary hypertension, peripheral edema, or polycythemia (hematocrit greater than 55%), long-term oxygen therapy is appropriate if  $Pao_2$  is between 55 mm Hg and 60 mm Hg or  $Sao_2$  is 88% [1].

Pulmonary rehabilitation has been shown to improve dyspnea, to enhance quality of life, to decrease hospitalizations, to decrease the number of days spent in the hospital, and to enhance exercise capacity; it may even improve survival [1]. Rehabilitation programs attempt to address the muscle wasting, deconditioning, depression, social isolation, and weight loss that often accompany COPD. Active smoking status is no longer an exclusion criterion, and pulmonary rehabilitation programs may include smoking cessation counseling.

**Pharmacologic management.** Smoking cessation remains the only intervention that can attenuate the age-related decline in  $FEV_1$  experienced by patients with COPD [14]. Brief physician counseling alone is associated with a 5% to 10% smoking cessation rate [1]. Nicotine replacement products, varenicline, and bupropion are additional first-line options.

Bronchodilators include beta-agonists and muscarinic antagonists, both of which are available in short-acting and

long-acting formulations. Despite the myriad of bronchodilators and inhaled corticosteroids available, none have been shown to modify the long-term decline in lung function that is associated with COPD, nor have any been shown to conclusively improve mortality. The role of these agents in COPD management is to decrease symptoms and exacerbations and to improve exercise tolerance and quality of life.

The GOLD 2013 guidelines recommend using bronchodilators and/or inhaled corticosteroids based on the patient's symptoms and his or her risk of exacerbations (Table 1). Symptoms are assessed using an instrument such as the Modified Medical Research Council Dyspnea Scale or the COPD Assessment Test; for example, if a patient walks slower than his or her peers because of dyspnea, that would be a symptom of COPD. A patient has a high risk of exacerbation if he or she has experienced 2 or more exacerbations in the past year or if his or her FEV<sub>1</sub> is less than 50% of the predicted value when measured with post-bronchodilator spirometry [1].

The recommended treatment for patients with less severe symptoms and a low risk of exacerbations is a short-acting muscarinic antagonist or a short-acting beta-agonist. In patients with moderate to severe disease, triple therapy with a long-acting beta-agonist, a long-acting muscarinic antagonist, and an inhaled corticosteroid improves lung function and may also improve quality of life and decrease exacerbations requiring hospitalization [15]. Long-term monotherapy with an inhaled corticosteroid is not recommended given the adverse effects of this drug, which include pneumonia, and the relatively decreased efficacy of such therapy. Likewise, the adverse effects of long-term oral corticosteroids—which include osteoporosis, cataracts, muscle wasting, and weight gain—make these agents unappealing. Strong evidence argues against their use as long-term monotherapy [1].

Roflumilast, the first phosphodiesterase-4 inhibitor to be approved for treatment of COPD, exerts an anti-inflammatory effect by inhibiting the breakdown of intracellular cyclic adenosine monophosphate. Multiple studies have

shown that use of this agent decreases moderate exacerbations requiring steroids and decreases severe exacerbations requiring hospitalization [16]. The rate of discontinuation is higher with roflumilast than placebo (14% versus 11%), usually due to headache, diarrhea, or weight loss [16]. Given the long half-life of roflumilast (17 hours) and the even longer half-life of the active metabolite roflumilast N-oxide (30 hours), every-other-day dosing may be considered for patients who are experiencing side effects, although the drug's efficacy may be attenuated on such a schedule. Current guidelines recommend that clinicians consider adding roflumilast to the treatment regimen if patients have a high risk of exacerbations (that is, if patients have an FEV<sub>1</sub> less than 50% of the predicted value or they have experienced 2 or more exacerbations in the past year) [1].

Finally, influenza vaccination in patients with COPD has been shown to decrease exacerbations of the disease, although it does not decrease hospitalizations or mortality [17]. The GOLD 2013 guidelines recommend yearly administration of either killed viruses or live-inactivated viruses [1].

**Surgical therapy.** Lung volume-reduction surgery (LVRS) is a surgical procedure that removes parts of the patient's lungs in order to decrease hyperinflation. LVRS has been shown to decrease the mortality rate in patients whose exercise capacity after rehabilitation is poor and who have severe emphysema that predominantly affects the upper lobes; however, LVRS is costly compared with medical therapy [1]. Lung transplantation is an option for patients with severe COPD and has been shown to improve quality of life and to decrease mortality [1].

## Conclusion

COPD is a debilitating disease that results in substantial morbidity and mortality as well as significant utilization of health care resources. The major risk factor for developing COPD is tobacco smoking. In North Carolina, much work remains to be done in terms of tobacco cessation, given the significant smoking rates among the state's adults and chil-

**TABLE 1.**  
Recommended Therapy for Each Stage of Chronic Obstructive Pulmonary Disease<sup>a</sup>

GOLD stage	Recommended therapy according to GOLD guidelines					
	Influenza vaccine	Short-acting bronchodilator	Long-acting bronchodilator (1 or more)	Pulmonary rehabilitation	Inhaled corticosteroid if repeated exacerbations	Long-term oxygen therapy; consider surgical procedures
1. Mild FEV <sub>1</sub> > 80%	Yes	Yes	No	No	No	No
2. Moderate FEV <sub>1</sub> 50%–80%	Yes	Yes	Yes	Yes	No	No
3. Severe FEV <sub>1</sub> 30%–50%	Yes	Yes	Yes	Yes	Yes	No
4. Very severe FEV <sub>1</sub> < 30%	Yes	Yes	Yes	Yes	Yes	Yes

Note. GOLD, Global Initiative for Chronic Obstructive Lung Diseases.

<sup>a</sup>GOLD stage is based on the severity of airflow limitation measured in terms of forced expiratory volume in 1 second (FEV<sub>1</sub>), as a percentage of the predicted value, after administration of a short-acting bronchodilator.

dren. Prevention is the key to success. This can be accomplished by aggressive education and through public health policy (eg, the banning of smoking in certain public areas). Emphasis needs to be placed not only on smoking cessation but also on the reduction of occupational exposure to noxious particles. Strategies to prevent work-related COPD include exposure controls such as elimination, engineering controls, diesel filters, administrative controls, and personal protective equipment.

For those who already have COPD, smoking cessation is essential and can reduce mortality. Long-term oxygen therapy also reduces mortality in patients for whom it is indicated. The goals of therapy are to reduce symptoms and to reduce the risk of disease progression, exacerbations, and death. Pharmacologic management of COPD should follow the GOLD guidelines, which recommend a stepwise addition of pharmacologic treatments based on the severity of the disease. **NCMJ**

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