

# Prevention, Diagnosis & Treatment of COPD

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## Summary

COPD is a preventable and treatable disease that results in significant morbidity, mortality, and costs. Treatment uses a stepped care approach utilizing inhaled medications and nonpharmacologic therapy. Smoking cessation, both on an individual and societal basis, is the most important factor in fighting COPD.

## Key Points

- Smoking cessation can prevent development of COPD and progression once the disease has developed.
- Oxygen therapy, in appropriate patients, can reduce mortality.
- At this time, no medication has been shown to reduce COPD mortality.
- First line therapy is inhaled long acting beta agonists or tiotropium.
- The future should bring additional therapies, which hopefully will impact disease progression and mortality.

CHRONIC OBSTRUCTIVE PULMONARY disease (COPD) is defined by airflow limitation that is not fully reversible and is progressive. Although not previously understood, it is now known that there is a significant inflammatory component to the COPD disease process. These patients have an abnormal inflammatory response to particles or gases and significant inflammatory extra pulmonary effects of the disease. COPD is preventable and treatable. Twenty-four million people in the United States are estimated to have COPD, but only 12 million are diagnosed. Identifying these patients early for treatment to prevent progression is a challenge to primary care physicians.

The demographics of COPD, traditionally perceived as a disease of elderly men, are changing. Currently, 70 percent of patients are younger than 65, and 60 percent are women. Women appear more susceptible to the adverse effects of smoking.

COPD is the fourth-leading cause of death in the United States, and is predicted to be the third leading cause by 2020. Exhibit 1 compares the mortality rates from COPD in men and women from 1980 to 2000.<sup>1</sup> Currently, one person dies of COPD in the United States every four minutes. Since 2002, more women die annually from COPD than men. It also results in 1.5 million emergency room visits

and 726,000 hospital admissions annually. The total costs of the disease are estimated at \$34 billion per year.

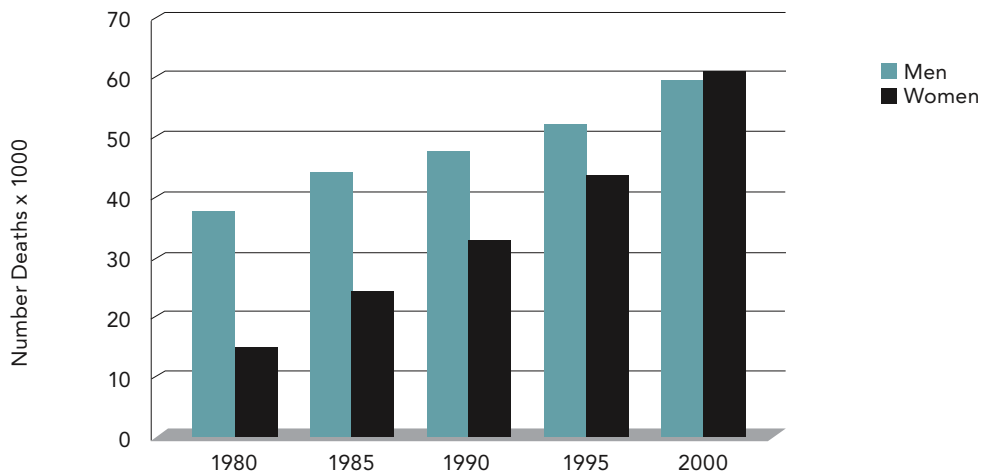
Ninety percent of COPD cases are smoking related, but only 25 percent of smokers develop COPD. It is not known what factors, other than gender, make some people more susceptible to the effects of smoking. Although lung function typically declines with aging, susceptible smokers have a much more rapid decline (Exhibit 2).<sup>2</sup> Other causes of COPD include work exposures, inherited alpha-1 antitrypsin deficiency, second-hand smoke, indoor and outdoor pollution, and childhood infections.

The most important way to prevent COPD is smoking cessation. As shown in Exhibit 2, smoking cessation is important because lung function deterioration will slow down significantly. Reduced occupational and pollution exposures, and alpha-1 antitrypsin replacement in appropriate patients are other prevention strategies.

There are two major guidelines for the identification and management of COPD.<sup>3,4</sup> The Global Obstructive Lung Disease (GOLD) guidelines are international guidelines for application around the world. The American Thoracic Society (ATS) guidelines, while good, are about 5 years out of date.

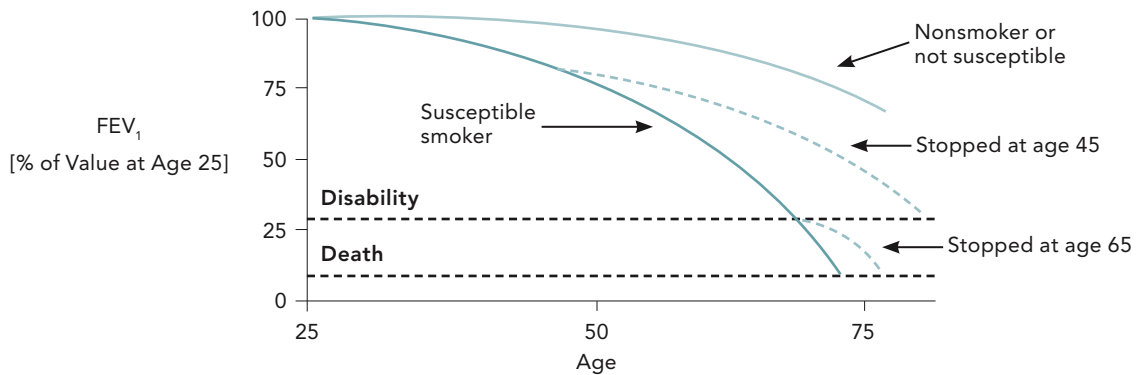
Screening for COPD is done with spirometry.

Exhibit 1: COPD Mortality by Gender, U.S., 1980-2000



Reference: 1

Exhibit 2: Natural History of COPD



Screening smokers with symptoms (such as cough, sputum production, shortness of breath) is cost effective. A smoker's cough is not a normal part of smoking; it usually indicates damage to the lungs. Patients with risk factors for COPD, other than smoking, also should be screened.

For a diagnosis of COPD, asthma, heart failure, pulmonary fibrosis, and pulmonary embolus have to be ruled out. About 10 to 15 percent of patients have symptoms suggestive of both asthma and COPD. The initial workup of a patient with COPD will include history, physical exam, spirometry, radiographic assessment, oxygenation assessment, nutritional/weight assessment, genetic assessment, and smoking assessment. A history of smoking (especially greater than 10 pack years), shortness of breath,

slowly progressive course, chronic cough (with or without sputum), and/or onset of symptoms in the 40s are suggestive of COPD. On spirometry, a forced vital capacity (FVC) of less than 70 percent is evidence of obstructive lung disease. The forced expiratory volume in 1 second (FEV-1) is used to determine the severity of the obstruction.

Nutritional assessment in patients with COPD is often overlooked. Underweight patients with COPD have higher mortality and hospitalization rates. Excessive weight also increases the risk of complications.

Genetic assessment is important to identify the one percent of the COPD population that has alpha-1 antitrypsin deficiency. The management guidelines recommend screening all COPD patients for

deficiency. Markers of alpha-1 antitrypsin deficiency are early onset emphysema (< 45 years of age), emphysema without other risk factors, lower lobe bullous disease, and a positive family history. There are probably genetic reasons why only 25 percent of smokers develop COPD but these have not been identified.

Prevention of COPD is very important. The best way to prevent the disease is smoking cessation. Smoking results in significant costs, morbidity, and mortality. Smoking kills more than 430,000 Americans each year and causes COPD, cancer, heart disease, stroke, and adverse pregnancy outcomes. Smoking causes \$50 billion in health costs and \$50 billion in lost productivity each year. Despite public knowledge of the dangers of smoking, 25 percent of adult Americans smoke and 3,000 adolescents become regular smokers every day.

All patients should be assessed at every visit for smoking with a smoking assessment as the fifth vital sign measured at each visit. Smokers should be advised to quit at each visit because it has been shown that the number one reason why smokers quit is because they've been advised to do so from a physician. The readiness to quit also should be assessed in all smokers. (Exhibit 3)

Success with smoking cessation requires a combination approach of behavioral counseling and pharmacotherapy.<sup>5</sup> Tobacco dependence is a chronic disease that is treated most effectively with multiple modalities. Smoking cessation with no assistance results in about a five percent success rate and therefore, is not effective in most patients. Pharmacotherapy is a key element of all treatment strategies. The only time pharmacotherapy is not recommended is when contraindications are present, the patient smokes less than 10 cigarettes per day, or the patient is pregnant, breastfeeding or an adolescent. With medication alone, there is about a 10 percent success rate. Counseling alone also has a 10 percent success rate. Intensive counseling combined with pharmacotherapy has a 30 percent success rate. Tobacco dependence treatment should be a covered service under managed care for all patients.

COPD does result in extrapulmonary effects. Bone density is significantly affected in patients with COPD for a variety of factors - inactivity, multiple courses of corticosteroids, and COPD itself. Fifty percent or more of COPD patients have osteoporosis. All patients with COPD should have a bone density screening. Depression, coronary heart disease, and lung cancer also are common comorbid conditions in patients with COPD.

The goals of COPD treatment are relief of symptoms, improved exercise tolerance, improved health

### Exhibit 3: The 5 As

- **ASK** about tobacco use
- **ADVISE** to quit
- **ASSESS** willingness to make a quit attempt
- **ASSIST** in quit attempt
- **ARRANGE** for follow-up

status, prevention and treatment of complications, prevention and treatment of exacerbations, prevention of disease progression, and reduced mortality. For most patients, current treatments can accomplish all of these goals except prevention of disease progression and reduction of mortality. Only smoking cessation can prevent disease progression. Oxygen therapy, in appropriate patients, can reduce mortality but, at this time, no medication has been shown to reduce COPD mortality.

The four components of therapy are 1) assessment and monitoring of disease, 2) risk factor reduction, 3) management of stable COPD, and 4) management of exacerbations. Assessment and monitoring is done with spirometry and symptoms. The strategies for risk factor reduction are smoking cessation and avoidance of occupational exposures. To prevent exacerbations, influenza and pneumonia vaccinations are recommended.

An important component of managing stable COPD is patient education. Patients should be educated on disease awareness, risk factor reduction, how and when to use medications, how to recognize early symptoms of an exacerbation, need for healthy lifestyle, nutrition, and exercise. Early recognition of an exacerbation can help keep the patient out of the hospital.

The GOLD guidelines outline a step care approach to pharmacotherapy (Exhibit 4).<sup>3</sup> Because no medication has been shown to slow disease progression or prolong life, pharmacotherapy selection should be symptom based and individualized for each patient. Additional medications are added as the patient has progression. Patients with mild disease may only need inhaled medications as needed. Moderate severity disease is where quality of life is being affected. At this level, patients will need routine therapy with a long acting beta agonist. At a severe level, the patient will be unable to walk any distance without symptoms. At a severe level or higher, inhaled corticosteroids are added if exacerbations are occurring.

To allow application in many different countries, the GOLD guidelines do not specify a bronchodilator of choice. Beta agonists, anticholinergics, and

#### Exhibit 4: GOLD Guidelines

##### Stage I: Mild Disease

- Avoid risk factors
- Short-acting bronchodilators PRN

##### Stage II: Moderate

- Avoid risk factors
- Short-acting bronchodilators PRN
- Regular therapy with one or more bronchodilators
- Pulmonary rehab

##### Stage III: Severe

- Avoid risk factors
- Short-acting bronchodilators PRN
- Regular therapy with one or more bronchodilators
- Pulmonary Rehab
- Consider inhaled steroids for repeated exacerbations

Reference: 6

##### Stage IV: Very Severe

- Avoid risk factors
- Short-acting bronchodilators PRN
- Regular therapy with one or more bronchodilators
- Consider inhaled steroids for repeated exacerbations
- Oxygen if indicated
- ?? surgery

Reference: 3

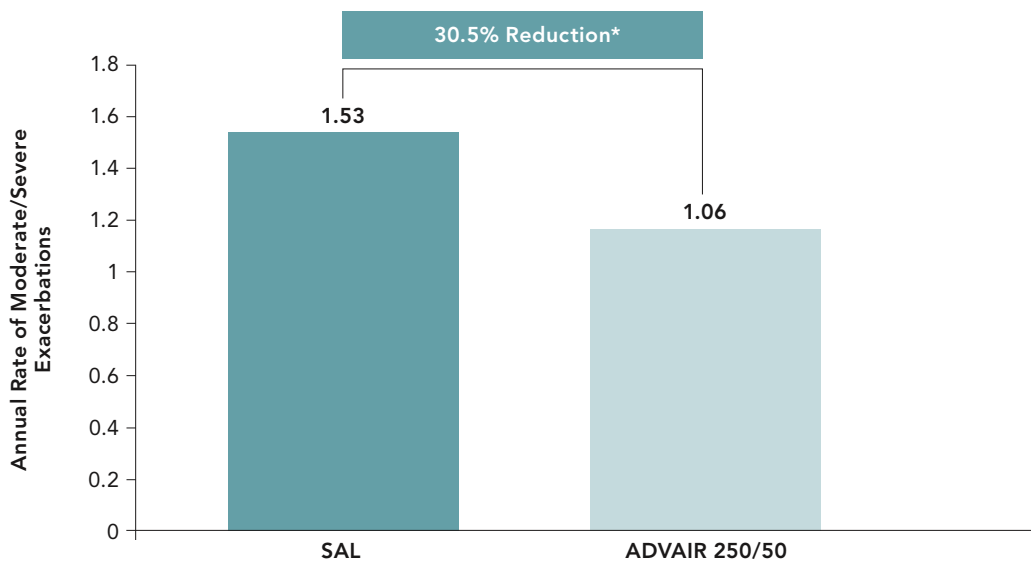
theophylline are all considered acceptable alternatives. Theophylline is used very little for COPD in the United States. The guidelines do say that inhaled is better than oral, long-acting is better than short, and if one bronchodilator is not effective, add a second. The choice of bronchodilator should be based

on efficacy, individual response, and side effects.

Standard practice in the United States is to use long acting beta agonists (LABA) or tiotropium, an inhaled anticholinergic, as first line therapy. The combination of these two is used in more severe and/or symptomatic disease. Inhaled corticosteroids have a definite role in patients with severe disease (FEV-1 less than 50 percent) with repeated exacerbations.

Nonpharmacologic therapy may include oxygen, pulmonary rehabilitation, lung volume reduction, and lung transplant. Oxygen, if necessary, should be used for at least 16 hours per day to have a significant impact on mortality. Pulmonary rehabilitation, although difficult to find, results in improvement in dyspnea, health-related quality of life, and walking distance. Although initial reports with lung reduction surgery looked promising, a nationwide trial did not show significant overall benefit. A small subset of patients with heterogeneous emphysema, upper lobe predominant disease, and poor exercise capacity did benefit but this is not a common surgical procedure. Lung transplantation has limited utility in COPD. Those patients who can be listed for a transplant have very severe disease and are relatively young (less than 70 at most centers). Transplants can improve quality of life but have not been shown to improve longevity; thus they are not widely utilized.

#### Exhibit 5: Combination Therapy Significantly Reduces Exacerbations



SAL- salmeterol ADVAIR 250/50- make salmeterol/fluticasone

\*Negative binomial model, P < 0.001

The final component of management is dealing with exacerbations. Exacerbation in COPD is defined as an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication. Exacerbations are common with 50 to 77 percent of patients having at least one exacerbation per year. Fifty to 75 percent of all COPD costs are for exacerbation treatment.

The most common causes of an exacerbation are infection and air pollution. The cause of one third of exacerbations cannot be identified. Inhaled beta agonists with or without anticholinergics and oral steroids are effective for treating exacerbations. Patients with clinical signs of airway infection (sputum purulence) may benefit from antibiotic treatment.

It is important to prevent exacerbations because frequent COPD exacerbations are associated with a higher rate of decline in lung function and lower quality of life. Influenza and pneumonia vaccination are important strategies to prevent infection related exacerbations. Inhaled corticosteroids, alone or in combination with long acting beta agonists, have been shown to reduce the frequency of exacerbations. One study found a 30.5 percent decrease with the combination of fluticasone and salmeterol (Exhibit 5).<sup>6</sup>

To improve compliance, once a day inhaled therapy with single and combination agents will be available in the near future. Other strategies in trials are combinations of long acting beta agonists and long acting muscarinic agents and triple therapy with beta agonists, inhaled corticosteroids, and muscarinic agents. Specific phosphodiesterase (PDE-4) inhibitors also are under study.

The far future will bring medication to slow progression and reverse damage. More effective smoking cessation treatments, better genetic testing for identification of additional enzyme deficiencies. Markers for COPD susceptibility, and medication responsiveness also are on the horizon. In the nonpharmacologic realm, additional ways of redirecting airflow away from diseased lung tissue such as endobronchial valves and fibrin glue also are under study.

## Conclusion

The treatment of COPD has progressed significantly during the past twenty years. Medications are available that, when used appropriately, can manage patient symptoms and reduce the rate of exacerbations. Pharmacotherapy for smoking cessation has improved quitting rates. New therapies that alter

the natural history of this disease will hopefully be available in the near future. **JMCM**

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