Analysis of the Current Care Model of the COPD Patient: A Health Outcomes Assessment and Economic Evaluation

NEIL B. MINKOFF, MD

ABSTRACT

OBJECTIVE: Because chronic obstructive pulmonary disease (COPD) is a common but serious illness affecting millions worldwide, we present an overview of the disease and discuss its underdiagnosis and treatment options.

SUMMARY: COPD, a disease encompassing emphysema and chronic bronchitis, is associated with cigarette smoking, chronic exposure to environmental pollutants, and, occasionally, genetic conditions. The disease is severely underdiagnosed and underrecognized. The economic costs of COPD, which accounted for about 14 million office visits and 3.5 million hospital days in 1993, are estimated at more than \$7 billion, and another \$8 billion worth of productivity was lost to morbidity and mortality in the same year.¹ The death rate from COPD is rising, principally among women. Uniform diagnosis and treatment standards are now being realized. The American Thoracic Society and European Respiratory Society recommend treatment, based on worsening symptoms, with bronchodilators and, in more advanced cases, inhaled corticosteroids. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) treatment algorithm also uses a step-care approach. The GOLD guidelines recommend a management program that prevents disease progression, relieves symptoms, improves exercise tolerance and health status, and prevents and treats complications and exacerbations, thereby reducing mortality. The GOLD guidelines recommend avoiding risk factors, using short- or long-acting bronchodilators, and adding rehabilitation and inhaled glucocorticoids. In severe cases, the GOLD guidelines recommend long-term oxygen administration and even surgery. Decisions in managing COPD require a consideration of multiple outcomes measures. Although spirometry remains the foundation for diagnosis and demonstration of efficacy, the patients and their families may be more concerned with symptoms, quality of life, and prevention of exacerbations. In patients with COPD, bronchodilators such as tiotropium produce significant improvements in all of these outcomes measures.

CONCLUSIONS: COPD is a common disease that substantially affects patients, health care systems, and society. With increasing awareness of the disease, improved diagnostic guidelines, and newer cost-effective pharmacologic regimens, this chronic progressive disorder can be effectively recognized and treated, helping to improve patients' overall health and quality of life.

KEYWORDS: Chronic obstructive pulmonary disease (COPD); Treatment, lung diseases, obstructive; Emphysema; Chronic bronchitis

J Manag Care Pharm. 2005;11(6)(suppl S-a):S3-S7

Author

NEIL B. MINKOFF, MD, is medical director of pharmacy and associate medical director of network medical management, Harvard Pilgrim Health Care, Wellesley, Massachusetts, and an instructor of medicine, Harvard Medical School.

AUTHOR CORRESPONDENCE: Neil B. Minkoff, MD, Medical Director, Pharmacy, Harvard Pilgrim Health Care, 93 Worcester St., Wellesley, MA 02481.

Tel: (617) 509-0170; Fax: (617) 509-9141; E-mail: neil_minkoff@hphc.org

Copyright© 2005, Academy of Managed Care Pharmacy. All rights reserved.

Chronic Obstructive Pulmonary Disease (COPD)

Definition

COPD is a mixture of separate disease processes that are characterized by chronic inflammation throughout the airways, parenchyma, and pulmonary vasculature.² Most notably, the diseases that fall under the umbrella term of COPD are emphysema and chronic bronchitis. Specifically, emphysema is marked by alveolar wall destruction and irreversible enlargement of the air spaces distal to the terminal bronchioles; chronic bronchitis is defined as a productive cough present for 3 months in each of 2 consecutive years in the absence of other identifiable causes of excessive mucus production. Objectively, COPD is diagnosed through pulmonary function testing (spirometry). In the early stages of the disease, the forced expiratory volume (FEV₁), the amount of air that can be expelled from the lungs in 1 second, is <80% of that expected. In addition, a ratio of FEV₁ over forced vital capacity (FVC), or the volume of air forcibly exhaled after deep inspiration, is <70% of what is considered normal in a person at this stage. Over time, these percentages decrease as the disease progresses to more advanced stages.

Symptoms

The main symptoms of COPD are chronic cough, mucus production, and dyspnea. Even during the early stages of the disease, coughing is usually chronic and productive and tends to persist over several months and even years. Significant production of mucus (sputum) is often associated with the cough. Dyspnea, a hallmark symptom of COPD, is usually noticed first as shortness of breath on exertion. All of these symptoms are progressive.

The underlying causes of these symptoms are multifactorial. One main cause is emphysema: a progressive destruction of alveolar tissue and related vasculature, limiting the surface area for oxygen and carbon dioxide exchange, and the resulting hypoxemia produces pulmonary vasoconstriction. Fibrosis in bronchial walls and smooth muscle contraction around bronchial tubes results in airway narrowing and dyspnea. Bronchospasm, repeated smooth muscle contraction, causes the patient to cough and expel sputum. Progressive blockage of the airways by exudates and mucus also contributes to symptoms of coughing and dyspnea.

Risk Factors

The single most prevalent risk factor for COPD is cigarette smoking,³ to the extent where smoking cessation or even a decrease in smoking can substantially reduce the risk for the development and rate of progression of COPD.⁴ In addition, epidemiologic studies have implicated childhood respiratory infections as an independent

FIGURE 1 Proportion of 1965-1998 Rate Percentage Change in Age-Adjusted Deaths in the United States

Source: Global Initiative for Chronic Pulmonary Disease. GOLD Teaching Slide #10.²⁴
COPD=chronic obstructive pulmonary disease; CVD=cardiovascular disease.

risk factor for the subsequent development of persistent asthma and COPD.⁵ A relatively rare genetic condition, alpha₁ antitrypsin (AAT) deficiency, is also a potential risk for pulmonary disease such as emphysema and COPD.^{6,7} Another main risk factor for developing COPD is chronic exposure to fumes, chemical substances, and dust in the workplace—usually factories. For example, inhalation of grain dust, coal, other mineral dusts, isocyanates, heavy metal adhesives, and welding fumes have been linked to COPD in mining, quarrying, construction, textile, and wood industries.⁸

Impact of COPD

The prevalence of COPD may be much greater than published data indicate because the disease is usually not diagnosed until it is sufficiently advanced to give rise to obvious symptoms.⁹ Although it has been traditionally considered a disease of the elderly, COPD definitely afflicts the working-age population as well.¹⁰ According to the 1995 National Ambulatory Medical Care Survey, approximately 70% of COPD patients were under the age of 65 years, and they accounted for 67% of total COPD office visits and 43% of all hospitalizations.¹⁰ Another common misconception is that COPD is uncommon in the general population.¹¹ It is, in fact, a common chronic disease. In a survey of patients with chronic diseases, the prevalence of COPD was comparable with that of diabetes, asthma, and congestive heart failure in the 45- to 64-year-old age group and increased in prevalence in older patients.¹¹ The disease has been more prevalent in men than in women, but some recent studies suggest that this may be changing. One study showed that, in 2002, more than 33% of COPD patients were female, a figure that is likely to increase.¹² The women's death rate due to COPD is also rising. According to a 2002 mortality and morbidity report,¹³ during the period 1980-2000, the COPD death rate of women rose 2.8 times, from 20.1

to 56.7 per 100,000 women; this is compared with a more modest increase in the death rate for men, from 73.0 to 82.5 per 100,000 men. Meanwhile, in 2000, the number of women dying from COPD surpassed the number of men dying from the disease (59,936 women versus 59,118 men) for the first time.

Mortality, Morbidity, Economic and Human Burdens

COPD often escapes diagnosis and treatment, and primary care physicians and patients underrecognize the large impact of this disease.^{12,13} In 2000, an estimated 10 million U.S. adults reported physician-diagnosed COPD. COPD represents massive and growing economic and social burdens in terms of mortality and morbidity. In 2000, COPD was the second leading cause of disability after heart disease.¹⁴ In that same year, COPD was responsible for 8 million physician office and hospital outpatient visits, 1.5 million emergency department visits, 726,000 hospitalizations, and 119,000 deaths.¹³ In 1997 in the United States alone, obstructive lung disease (i.e., chronic bronchitis, emphysema, asthma) was the fourth most common cause of death, accounting for more than 109,000 deaths.¹³ By 2020, COPD is expected to rise from the fourth to the third leading cause of death. As shown in Figure 1, this is largely because of a continuing reduction in mortality from coronary heart disease and stroke.¹²

The economic burden of COPD is enormous. According to the National Heart, Lung, and Blood Institute, the direct total costs for COPD grew from \$18 billion to \$20.9 billion between 2002 and 2004,^{2,14} a rise attributed to increased hospitalizations. In 2002, COPD was responsible for 1,763 million bed days and 57.5 million lost work days, making it the sixth worst disease for lost work days in the United States.¹⁵ Exacerbations of respiratory symptoms are common and a primary contributor of morbidity, mortality, and costs of the illness.¹⁶ As the disease progresses and exacerbations increase, the patients' health-related quality of life dramatically deteriorates¹⁷ as they experience progressively worsening impairments in their ability to socialize, work, and even walk. Therefore, reducing exacerbations and improving life quality are two of the major outcome measures of treatment.

Treatment of COPD: Differing Approaches

Nonpharmacologic Treatments

There are several nonpharmacologic treatments for COPD, many of which are adjuncts to pharmacologic therapy. *Oxygen therapy*, or the long-term administration of pure oxygen (>15 hours daily) is usually introduced in severe (Stage IV) COPD.² *Ventilatory support* may be administered in severe and end-stage patients.² Several surgical options are also used in more advanced cases of COPD. *Bulectomy* in selected patients can be effective for reducing dyspnea and improving lung function; *lung-volume reduction surgery* is still an unproven palliative procedure; and *lung transplantation*, indicated only for very advanced, end-stage COPD, has been shown to improve quality of life and functional capacity.² *Pulmonary rehabilitation programs* (PRPs) are specifically

designed for patients with chronic lung disease.¹⁸ PRPs focus on improving the quality of life for patients by adhering to a variety of objectives, such as disease education, coping methods, physical exercise strategies, and the importance of self-esteem.¹⁸ While PRPs are recommended as an integral aspect of care for COPD,¹⁹ these programs alone may not improve pulmonary measures. A longitudinal study of one PRP on health outcomes of 36 patients with COPD ($FEV_1 < 60\%$ predicted)²⁰ showed improvement in exercise endurance, reduced dyspnea and hospitalization/length of stay, and improved quality of life. However, in this study, objective measures of lung function (FEV_1 , FVC) or oxygen saturation did not improve during the 12 months following completion of the PRP.

COPD Treatment Algorithms

American Thoracic Society (ATS) European Respiratory Society (ERS) Treatment Algorithm

There has been an increasing focus on treatment standards that incorporate pharmacologic agents with known efficacy. The ATS and ERS published a 2004 update to its treatment algorithm, which recommended step therapy on the basis of worsening symptoms (Figure 2).⁹ According to the ATS/ERS treatment guidelines, patients with intermittent COPD symptoms (coughing, wheezing, exertional dyspnea) should be treated with a short-acting bronchodilator or oral or inhaled anticholinergic agent. Patients with more persistent symptoms (dyspnea, night waking) are recommended for treatment with a long-acting bronchodilator² plus additional reliever medications. If there is only a limited benefit to this approach, alternative classes of drugs or combinations of long-acting bronchodilators and inhaled corticosteroids are recommended. Because of its anticholinergic effects, theophylline is recommended as a third-line agent but is not favored because of the need for drug-level monitoring and certain drug-drug interactions.

Global Initiative for Chronic Obstructive Lung Disease (GOLD) Treatment Algorithm

The other treatment algorithm comes from the GOLD guidelines.¹⁶ The goals outlined in the GOLD guidelines are to (1) prevent disease progression, (2) relieve symptoms, (3) improve exercise tolerance and health status, (4) prevent and treat complications and exacerbations, and (5) reduce mortality.

The GOLD criteria classify COPD into 5 stages:

1. *Stage 0* identifies those patients who are at risk for COPD, such as a patient who has chronic symptoms but normal spirometry measures and is exposed to risk factors, such as cigarette smoking.
2. *Stage I* is mild COPD with an $FEV_1/FVC < 70\%$ and $FEV_1 \geq 80\%$ predicted, with or without symptoms.
3. *Stage II* is moderate, characterized by worsening airflow limitation ($50\% \leq FEV_1 < 80\%$ predicted) and, usually, progression of symptoms, with shortness of breath developing on exertions. Patients often seek medical attention at this stage

FIGURE 2 Algorithm for Pharmacological Treatment of COPD

COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; LA-BD = long-acting bronchodilator; SA-BD = short-acting bronchodilator.

Assess effectiveness by treatment response criteria. If FEV_1 is $< 50\%$ predicted and exacerbations of COPD requiring a course of oral corticosteroid or antibiotic occurred at least once within the last year, consider adding regular ICS. If an ICS and a long-acting β -agonist are used, prescribe a combination inhaler. After Celli et al., Figure 1.⁹

because of dyspnea or exacerbation of their disease.

4. *Stage III* is severe COPD characterized by worsening airflow limitation ($30\% \leq FEV_1 < 50\%$ predicted) and repeated exacerbations.
5. By *Stage IV*, there is severe airflow restriction ($FEV_1 < 30\%$ predicted), or the presence of chronic respiratory failure.

As shown in Table 1, the GOLD treatment recommendation uses a step-therapy approach. At Stage 0, the patient should avoid risk factors and obtain an influenza vaccination. As the patient begins to develop mild COPD in Stage I, short-acting bronchodilators should be added. At Stage II (moderate) COPD, regular treatment with at least one long-acting bronchodilator and adjuvant pulmonary rehabilitation is recommended. At Stage III (severe), if the patient continues to have multiple exacerbations, an inhaled corticosteroid is added. By Stage IV (very severe), long-term oxygen therapy is required if there is chronic respiratory failure, and physicians should consider surgical therapy. By Stage IV, patients who need the surgery are often poorer surgical candidates because of significant heart strain and chronic anoxia.

Analysis of the Current Care Model of the COPD Patient: A Health Outcomes Assessment and Economic Evaluation

TABLE 1 Global Initiative for Chronic & Obstructive Lung Disease Schematic: Therapy at Each Stage of Chronic Obstructive Pulmonary Disease

Stage 0. At Risk	Stage I. Mild	Stage II. Moderate	Stage III. Severe	Stage IV. Very Severe
Avoidance of risk factor(s); influenza vaccination				
	Add short-acting bronchodilator when needed			
		Add regular treatment with one or more long-acting bronchodilators Add rehabilitation		
			Add inhaled glucocorticosteroids if repeated exacerbations	
				Add long-term oxygen if chronic respiratory failure Consider surgical treatments

Adapted from Pauwels et al., Table 8.¹⁶

Bronchodilators

Bronchodilators are a central medication class for managing COPD. A patient's symptom relief and adverse-event profile may help direct the type of bronchodilator therapy: anticholinergic, β -agonist, or theophylline. Bronchodilators are prescribed as needed or regularly to prevent or reduce symptoms. The long-acting bronchodilators are more effective and convenient, but acquisition cost is more expensive. Rather than increasing the dose of a specific bronchodilator, it has been theorized that combining short-acting bronchodilators may improve efficacy and decrease the risk of adverse reactions by reducing the dose of one or both agents.¹⁶

COPD is a long-term chronic condition that requires ongoing treatment. Reducing exacerbations can help to lower the costs of treatment. Two separate publications have demonstrated the cost-savings potential of bronchodilators in treating COPD. Friedman et al. evaluated 2 double-blind, randomized, prospective studies with a total of 1,067 patients with COPD that compared inhaled ipratropium/albuterol combination therapy with either drug alone for the treatment of COPD.²¹ Compared with albuterol alone, both the combination therapy and ipratropium alone decreased exacerbations by 33%, translating to a 24% lower cost in each group. The reduced costs resulted from reductions in add-on therapy and hospitalizations. As a result, the total cost of treatment over the duration of the study period was significantly less for ipratropium (\$156 per patient) and ipratropium plus albuterol (\$197 per patient) than for albuterol (\$269 per patient). Increased cost-effectiveness, defined as total estimated treatment cost per mean change in FEV₁, was observed in both treatment arms containing ipratropium. A second study assessed the economic impact of combined inhaled bronchodilator therapy in treating COPD.²² A total of 641 patients were treated with a combination of ipratropium and albuterol in one inhaler while 411 patients received both ipratropium bromide and albuterol in separate

inhalers. Although patients using the combination inhaler did not differ in treatment outcomes from patients in the comparator arms, they realized a significant cost savings due to a difference in medication costs.

Measuring Treatment Outcomes

COPD is a progressive disease with frequent exacerbations that deteriorate patients' ability to walk, participate in social activities, and work. Therefore, COPD management assessment must take into consideration improvements in exacerbations and hospitalization as well as other health-related measures such as quality of life and patients' self-assessments.

These measurements are important in assessing successful treatment outcomes and were demonstrated in 2 one-year, head-to-head studies in patients receiving tiotropium 18 μ g once daily (n = 356) or ipratropium 40 μ g 4 times daily (n = 179).²³ Overall, tiotropium led to significant improvements in all of the primary study outcome measures. FEV₁ at one year improved by 0.12 $\pm$ 0.01 L with tiotropium and declined by 0.03 $\pm$ 0.02 L with ipratropium ($P < 0.001$). Significant improvement in PEF, salbutamol use, Transition Dyspnea Index focal score, and the St. George's Respiratory Questionnaire total and impact scores were seen with tiotropium ($P < 0.01$). Also, tiotropium reduced the number of exacerbations by 24%, ($P < 0.01$) and increased time to first exacerbation ($P < 0.01$) and time to first hospitalization for a COPD exacerbation ($P < 0.05$) compared with ipratropium. The number of exacerbations per patient per year was reduced by 24%, and the number of exacerbation days was reduced by 39% for patients receiving tiotropium. The time to first exacerbation was significantly longer in patients receiving tiotropium. Finally, the proportion of patients hospitalized for a COPD exacerbation in the year-long study was significantly reduced in those receiving tiotropium.

While adjunctive therapies, such as pulmonary rehabilitation programs, can be helpful in controlling symptoms and improving quality of life, they do not improve lung function in patients with COPD.¹⁹ To evaluate effective therapy, one must also examine cost-effective therapy to make decisions based on patients' coverage and what would constitute appropriate therapy. Overall, decisions in managing COPD require a consideration of multiple outcome measures, including reductions in exacerbations and hospitalizations. Although spirometry remains the foundation for diagnosis and demonstration of drug efficacy, patients and their families may be more concerned with symptoms, quality of life, and prevention of exacerbations.

Conclusions

COPD is a common disease that substantially affects patients and health care systems and is associated with increasing economic and social burdens. COPD ranks as the fourth leading cause of death in the United States, surpassed only by heart disease, cancer, and cerebrovascular disease. The disease is associated with

Analysis of the Current Care Model of the COPD Patient: A Health Outcomes Assessment and Economic Evaluation

frequent and progressively worsening exacerbations, which are associated with high levels of morbidity and mortality. Despite the substantial burden of illness and the available treatment options, COPD continues to present challenges to patients and physicians. Physicians can help to increase awareness of the disease and increase their patients' understanding of treatment options and guidelines, particularly early in the course of this disease. Placebo-controlled trials and head-to-head comparison trials demonstrate the efficacy of tiotropium as a drug for the maintenance treatment of COPD.

DISCLOSURES

This article is based on the proceedings of an American College of Clinical Pharmacy symposium held on October 25, 2004, in Dallas, Texas, which was supported by an educational grant from Boehringer Ingelheim Pharmaceuticals, Inc. and Pfizer, Inc. The author received an honorarium from the Postgraduate Institute for Medicine for participation in the symposium upon which this article is based. He discloses no potential bias or conflict of interest relating to this article.

REFERENCES

1. Smith, M. Breathing lessons: the costs of COPD—Chronic obstructive pulmonary disease. Available at: http://www.findarticles.com/p/articles/mi_m0903/is_n10_v14/ai_18769614. Accessed June 16, 2005.
2. Global Initiative for Chronic Obstructive Lung Disease (GOLD), World Health Organization (WHO), National Heart, Lung, and Blood Institute (NHLBI). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease; 2004. Available at: <http://www.goldcopd.com>. Accessed May 19, 2005.
3. Man SFP, McAlister F, Anthonisen N, Sin D. Contemporary management of chronic obstructive pulmonary disease. *JAMA*. 2003;290:2313-16.
4. Doherty DE, Briggs DD, Jr. Chronic obstructive pulmonary disease: epidemiology, pathogenesis, disease course, and prognosis. *Clin Cornerstone*. 2004;(suppl 2):S5-S16.
5. Hogg JC. Childhood viral infection and the pathogenesis of asthma and chronic obstructive lung disease. *Am J Respir Crit Care Med*. 1999;160(5 pt 2):S26-S28.
6. Wadsworth ME, Vinall LE, Jones AL, et al. Alpha₁-antitrypsin as a risk for infant and adult respiratory outcomes in a national birth cohort. *Am J Respir Cell Mol Biol*. 2004;31:559-64.
7. Lieberman J, Winter B, Sastre A. Alpha₁-antitrypsin Pi-types in 965 COPD patients. *Chest*. 1986;89:370-73.
8. Rahman Q, Nettesheim P, Smith K, Seth P, Selkirk J. International conference on environmental and occupational lung diseases. *Environ Health Perspect*. 2001;109:425-31.
9. Celli BR, MacNee W. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*. 2004;23:932-46.
10. Sin DD, Stafinski T, Ng YC, Bell NR, Jacobs P. The impact of chronic obstructive pulmonary disease on work loss in the United States. *Am J Respir Crit Care Med*. 2002;165:704-07.
11. Lucas J, Schiller J, Benson V. Summary health statistics for U.S. adults: National Health Interview Survey, 2001. *Vital Health Stat*. 2004;10(218). Available at: http://www.cdc.gov/nchs/data/series/sr_10/sr10_218.pdf. Accessed May 16, 2005.
12. Mannino DM, Gagnon RC, Petty TL, Lydick E. Obstructive lung disease and low lung function in adults in the United States: data from the National Health and Nutrition Examination Survey, 1988-1994. *Arch Intern Med*. 2000;160:1683-89.
13. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance—United States, 1971-2000. *MMWR Surveill Summ*. 2002;51(6):1-16.
14. Clancy C. *Improving Health Care for Americans with Disabilities*. Bethesda, MD: Agency for Healthcare Research and Quality: U.S. Dept of Health and Human Services; 2002. AHRQ Publication no. 02-M016.
15. Druss B, Marcus S, Olsson M, Pincus H. The most expensive medical conditions in America. *Health Aff (Millwood)*. 2002;21:105-11.
16. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS, for the GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop Summary. *Am J Respir Crit Care Med*. 2001;163:1256-76.
17. Donohue JF, van Noord JA, Bateman ED, et al. A 6-month, placebo-controlled study comparing lung function and health status changes in COPD patients treated with tiotropium or salmeterol. *Chest*. 2002;122:47-55.
18. Mayo Clinic. Pulmonary Rehabilitation Program at Mayo Clinic in Rochester. Available at: <http://www.mayoclinic.org/pulmonary-rst/pulmrehabprgm.html>. Accessed May 17, 2005.
19. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 1995;152(5 pt 2):S77-S121.
20. Hui KP, Hewitt AB. A simple pulmonary rehabilitation program improves health outcomes and reduces hospital utilization in patients with COPD. *Chest*. 2003;124:94-97.
21. Friedman M, Serby CW, Menjoge SS, et al. Pharmacoeconomic evaluation of a combination of ipratropium plus albuterol compared with ipratropium alone and albuterol alone in COPD. *Chest*. 1999;115:635-61.
22. Benayoun S, Ernst P, Suissa S. The impact of combined inhaled bronchodilator therapy in the treatment of COPD. *Chest*. 2001;119:85-92.
23. Vincken W, van Noord JA, Greefhorst AP, et al. Improved health outcomes in patients with COPD during 1 yr's treatment with tiotropium. *Eur Respir J*. 2002;19:209-16.
24. Global Initiative for Chronic Obstructive Lung Disease. Additional GOLD resources. GOLD teaching slide set. Available at: <http://www.goldcopd.com>. Accessed May 19, 2005.