

## CLINICAL PRACTICE GUIDELINE REVIEW WORKSHEET

Procedure: **Chronic Obstructive Pulmonary Disease**

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### MEMBERS PRESENT:

Credentialing/Peer Review Committee (see minutes)

### PURPOSE:

To guide the LHA network physicians in the diagnosis and treatment of Chronic Obstructive Pulmonary Disease (COPD). To prevent hospitalization and re-admission and to achieve best practice in managing COPD patients. This CPG is not intended to replace a physician's clinical medical judgment that should be based on current medical knowledge and practices.

### FINDINGS:

Chronic Obstructive Pulmonary Disease (COPD) is manifested by chronic cough, sputum production, wheezing and, in later stages, dyspnea, poor exercise tolerance, and signs/symptoms of right-sided heart failure. Symptomatic COPD affects more than 5 percent of the adult population, is the fourth leading cause of death, and the twelfth leading cause of morbidity in the United States. Affecting 16 million people, it accounts for 13,760,000 office visits and 297,000 hospitalizations annually (at a cost of \$18 billion). In more than 80 percent of cases, cigarette smoking is causally linked to the development of COPD. Smoking status should be assessed in all adults, and smokers should be advised to abstain from tobacco.

### RECOMMENDATIONS:

Liberty Health Advantage recommends the adoption of the Agency for Healthcare Research and Quality (AHRQ) Evidence Based Practice (EBP) program on *Management of Acute Exacerbations of Chronic Obstructive Pulmonary Disease and Use of Spirometry for Case Finding, Diagnosis, and Management of Chronic Obstructive Pulmonary Disease Summary, Evidence Report/Technology Assessment: Number 121*

### ATTACHMENTS:

No attachments

### Diagnosis:

COPD is diagnosed in symptomatic individuals through spirometric testing that demonstrates irreversible airflow obstruction.<sup>3</sup> Spirometry for case-finding diagnosis and management of all adults with persistent respiratory symptoms or having a history of exposure to pulmonary risk factors has been recommended in primary care settings for all current and former smokers as well as never smokers who have persistent respiratory symptoms or have history of exposure to other COPD risk factors. More than one-third of the adult U.S. population reported respiratory symptoms compatible with symptomatic COPD. Compared to clinical examination, spirometry plus clinical examination improves diagnostic accuracy of clinically significant disease in adults who report respiratory symptoms (especially dyspnea). Spirometry in addition to clinical examination improves COPD diagnostic accuracy compared to clinical examination alone and it is a useful diagnostic tool in individuals with symptoms suggestive of possible COPD. The primary benefit of spirometry is to identify individuals who might benefit from pharmacologic treatment in order to improve exacerbations. These include adults with symptomatic, severe to very severe airflow obstruction. In individuals where a diagnosis of asthma is suspected bronchodilator responsiveness, testing may be indicated.

The evidence **does not support** widespread use of spirometry in primary care settings for all adults with persistent respiratory symptoms or having a history of exposure to pulmonary risk factors for case-finding, improving smoking cessation rates, monitoring the clinical course of COPD, or adjusting COPD interventions. Routine spirometric testing in primary care settings is likely to result in considerable testing and treatment costs, resource utilization, and health care personnel time. It might reduce the number of individuals being labeled as having COPD or receiving disease-specific treatment in the absence of severe to very-severe airflow obstruction. However, it is likely to label a large number of individuals (many not reporting bothersome respiratory symptoms or having nondisabling symptoms) as diseased who would not benefit from testing or treatment.

Treatment effectiveness (beyond short acting medications used for "acute rescue therapy") is largely limited to reducing exacerbations among subjects who have bothersome dyspnea, frequent exacerbations, and severe to very-severe airflow obstruction. Nearly all the benefit from treatment could be obtained by reserving spirometry for those having activity limiting respiratory symptoms and targeting therapy to those who have reached a spirometric threshold of airflow obstruction of approximately a FEV1 less than 50 percent predicted.

The natural history of moderate to severe COPD is punctuated by acute exacerbations in which worsening symptoms of dyspnea and an increase in the amount or purulence of sputum may be accompanied by chest discomfort, fever, and other constitutional symptoms. The frequency of exacerbations varies widely from patient to patient, but is generally related to the severity and duration of the underlying COPD. Patients with a history of frequent exacerbations tend to continue to have a high frequency of exacerbations.

Acute exacerbations of COPD are associated with increased short-term mortality compared with stable COPD. Comorbid conditions, particularly heart diseases, are common among patients with COPD and contribute substantially to the mortality associated with acute exacerbations. Patients who survive exacerbations of COPD often experience important decrements in functional status and quality of life.

#### **Clinical Assessment:**

The diagnosis of acute exacerbation of COPD is generally made on clinical grounds; laboratory data such as ABGs and leukocyte counts are of little value. The principal findings concerning the clinical assessment of patients with acute exacerbation of COPD are as follows:

- Patients presenting with acute exacerbation of COPD have a relatively high rate of abnormalities (such as infiltrates or pulmonary edema) on chest roentgenography (CXR),

particularly when compared to previous series of patients with asthma, where relatively low rates of abnormalities have been found.

- Historical data and clinical signs and symptoms associated with two common comorbid conditions that often complicate the assessment of acute exacerbation of COPD—CHF and pneumonia—are significant but inexact predictors of two specific abnormalities on CXR, namely pulmonary edema and infiltrate, respectively.
- The prevalence of clinically unsuspected deep venous thrombosis (DVT) among patients hospitalized for acute exacerbation of COPD is high in some studies; however, few data are available to help quantify the risk for pulmonary embolus among patients with acute exacerbation of COPD with or without known DVT.
- Among patients presenting with acute exacerbation of COPD, forced expiratory volume in 1 second (FEV<sub>1</sub>) during exacerbation is not well correlated with PaO<sub>2</sub> (partial pressure of oxygen) without supplemental oxygen, but is correlated with PaCO<sub>2</sub> (partial pressure of carbon dioxide) and pH.
- Physician estimates of FEV<sub>1</sub> during acute exacerbation of COPD are generally inaccurate. Peak expiratory flow rate (PEFR) is not sufficiently well correlated with FEV<sub>1</sub> to substitute for it.
- Among patients on theophylline, neither clinical data on theophylline use (history of dosage, timing of last dose, past drug levels) nor other data (history of cigarette use, body weight) are accurate predictors of drug level during acute exacerbation of COPD.

### **Prognosis:**

Major findings related to prognosis are:

- While several factors are associated with worsening clinical condition in patients with acute exacerbation of COPD, no predictive model accurately predicts clinical outcomes, so ongoing clinical monitoring is needed for many patients.
- Among patients presenting with acute exacerbation of COPD and selected for outpatient treatment, cumulative relapse rates were between 11 percent and 17 percent at 48 hours and between 23 percent and 32 percent at 2 weeks. Hospitalization at index visit ranged from 24.2 percent to 71 percent among patients presenting to the emergency department (ED).
- Data from the previous history of individual patients—e.g., previous visit within 7 days, number of exacerbations in the past year, and relapsing on previous visits—were consistently identified as predictive of relapse. Also found to be predictive in several studies was baseline pulmonary function, as measured by FEV<sub>1</sub> or FVC (forced vital capacity). Data describing acute respiratory physiology, such as FEV<sub>1</sub> during exacerbation or arterial blood gases, predicted hospitalization or relapse. Data describing treatments used in the ED and clinical response were generally also predictive of hospitalization or later relapse.
- Among patients hospitalized for acute exacerbation of COPD and cared for in either ward beds or intensive care units, short-term or hospital mortality ranged from 4 percent to 26 percent. Study populations were not described well enough to explain these differences in overall mortality rates.
- The following are all associated with mortality due to acute exacerbation of COPD:

1. Acute physiology (as measured by arterial blood gases, FEV<sub>1</sub> during exacerbation, and scores from the Acute Physiology and Chronic Health Evaluation).
  2. Comorbid illness and other baseline, pre-exacerbation health status measures (such as body mass index and functional status).
  3. Cumulative or longitudinal data on the clinical course (e.g., baseline spirometry, number and frequency of previous acute exacerbations, and previous response to treatment of acute exacerbation of COPD).
- Acute respiratory physiology, as measured by blood gases, was predictive of the need for mechanical ventilation, as were baseline measures such as nutritional status.

## **Treatment**

### **Antibiotics**

The antibiotic drugs studied are tetracycline, doxycycline, chloramphenicol, penicillin plus streptomycin, ampicillin, amoxicillin, and cotrimoxazole. The major findings related to these drugs were:

- Placebo-controlled randomized trials of antibiotic treatment of acute exacerbations of COPD show overall evidence of improvement in pulmonary function.
- The included trials suggest that patients with more evidence of bacterial infection (sputum purulence) and more severe illness (worse PEFr) benefit more from antibiotics; however, this has not been conclusively demonstrated.

### **Bronchodilators**

The bronchodilators studied are:

- The anticholinergics ipratropium bromide and glycopyrrolate.
- The beta2-agonists albuterol (salbutamol).
- Fenoterol.
- Metaproterenol.
- Salmeterol.
- Terbutaline.
- The methylxanthines aminophylline and doxofylline.

The major findings related to this class of drugs are:

- Inhaled ipratropium and beta2-agonists are shown in comparative trials to have similar effects. However, neither class has demonstrated conclusive evidence of benefit in placebo or other no-treatment control trials. Most trials were too small to demonstrate a minimally clinically important benefit.
- Ipratropium is generally associated with fewer adverse effects than are the beta2-agonists, but it needs to be used cautiously in patients with pre-existing urinary retention problems. Beta2-agonists can cause cardiac arrhythmias in those predisposed to the condition. The arrhythmias are usually not life threatening.

- Bronchodilator therapy delivered by nebulizers and metered-dose inhalers (MDIs) show equivalent bronchodilation among patients with stable COPD. However, among patients with acute exacerbation of COPD, who may be unable to hold their breath, nebulizers may be necessary.
- Glycopyrrolate may have a synergistic effect in bronchodilation when given with a beta2-agonist.
- Parenteral aminophylline did not improve FEV<sub>1</sub>, hospitalization rates, or relapse in three placebo-controlled trials. Parenteral doxofylline did show a significant improvement in FEV<sub>1</sub> in a placebo-controlled trial. Moreover, methylxanthines have numerous, sometimes life-threatening, adverse effects and drug interactions.

### **Corticosteroids**

Principal findings related to corticosteroid treatment were the following:

- Several randomized controlled trials provided strong evidence that a course of systemic corticosteroids provides benefit in patients hospitalized with acute exacerbation of COPD. The risk of treatment failure was reduced by approximately 10 percent, and FEV<sub>1</sub> showed an improvement averaging about 0.1 liters in the first hours to days of treatment.
- Doses as low as prednisone 30 mg daily and duration as short as 3 days have been shown to be effective in single trials; however, the optimal dose and duration is not clear from available trials. A single well-designed trial found that there were no significant differences in clinical outcomes between a 2-week course of systemic corticosteroids and an 8-week course.
- Inhaled corticosteroids have not been tested adequately in patients with acute exacerbation of COPD.
- Adverse effects were common in patients treated for acute exacerbation of COPD with systemic corticosteroids. The most frequently observed adverse effect was hyperglycemia.

### **Mucous-Clearing Treatments**

Considered under this heading were mucolytic drugs and physical therapy interventions. The principal findings were:

- Available studies show no benefit from any of the mucolytic drugs studied (ambroxol, bromhexine, domiodol, potassium iodide, and S-carboxymethyl cysteine) in improving ventilatory function in acute exacerbation of COPD. Some studies reported subjective improvement in symptoms associated with decreasing sputum viscosity.
- Studies of chest percussion also failed to show any benefit in improving short-term ventilatory function in patients with acute exacerbation of COPD.

### **Noninvasive positive pressure ventilation (NPPV)**

Individual factors have been shown to be associated with the need for MV resulting from ARF in acute exacerbation. Acute respiratory physiology, as measure by blood gases, was associated with MV. Major findings related to NPPV are the following:

- NPPV is an effective alternative to mechanical ventilation by endotracheal intubation for some patients with acute respiratory failure secondary to acute exacerbation of COPD.

The selection of mask interface and/or ventilator mode can be important to patient cooperation and tolerance, and thus to the efficacy of the intervention. Each type of mask and

ventilation mode comes with its own set of morbidities. The pressure-support ventilation (PSV) and continuous or bi-level positive airway pressure modes of ventilation appear to be best tolerated and most effective for correcting hypercarbia. Assist control ventilation (ACV) mode with NPPV is generally poorly tolerated unless volume and rate are adjusted to the individual patient.

**Table 1**  
**Clinical staging of COPD - ATS 1995 guidelines<sup>1</sup>**

Stage	FEV <sub>1</sub>
I	≥ 50%
II	35–49%
III	< 35%

<sup>1</sup>Source: [American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1995;152\(5 Pt 2\):S77–121.](#) ATS = American Thoracic Society; COPD = chronic obstructive pulmonary disease; FEV<sub>1</sub> = forced expiratory volume in 1 second.

**Table 2**  
**Summary of effectiveness of treatments**

Treatment	Number of Studies	Highest Level of Evidence <sup>1</sup>	Summary Findings
Antibiotics	11	2b	Slight improvement in PEFr compared with control (NS) (patients with lower baseline function and more purulent sputum had the most benefit) Decreased symptom duration compared with control No significant difference in hospital length of stay
Bronchodilators Anticholinergics	8	1b	Improves FEV <sub>1</sub> , PaO <sub>2</sub> compared with

			control
			Not demonstrated superior to beta-agonists
			No difference in hospital admissions vs. control
Beta <sub>2</sub> -agonists	9	1b	Improves FEV <sub>1</sub> compared with control No change in PaO <sub>2</sub>
Methylxanthines	4	2b	Not demonstrated superior to ipratropium No effect on FEV <sub>1</sub> Significant adverse events associated with use
Combinations (ipratropium, albuterol, and aminophylline)	1	3b	No better FEV <sub>1</sub> , PaO <sub>2</sub> for combination compared with individual agents
Corticosteroids	6	1b	Improved FEV <sub>1</sub> compared with control Shorter hospital length of stay vs. placebo
Mucolytics	6	2b	No effect on FEV <sub>1</sub> No change in severity or duration of symptoms
Physical therapy	3	2b	No effect on FEV <sub>1</sub> No difference in hospital or ED length of stay
Noninvasive positive pressure ventilation	9	1b	Improves survival and decreases mortality associated with exacerbation Fewer complications than mechanical ventilation

<sup>1</sup>Levels of evidence are from [Ball, Sackett, Phillips, et al. \(1998\)](#). For studies regarding therapy/prevention or etiology/harm: 1b = individual RCT (with narrow confidence interval); 2b = individual cohort study (including low-quality RCT; e.g., < 80% followup); 3b = individual case-control study.

ED = emergency department; FEV<sub>1</sub> = forced expiratory flow in 1 second; NS = not significant; PaO<sub>2</sub> = partial pressure of oxygen, arterial; PEFr = peak expiratory flow rate

### Internet Citations:

Wilt TJ, Niewoehner D, Kim C, et al. *Use of Spirometry for Case Finding, Diagnosis, and Management of Chronic Obstructive Pulmonary Disease (COPD)*. Summary, Evidence Report/Technology Assessment: Number 121. AHRQ Publication Number 05-E017-1, August 2005. Agency for Healthcare Research and Quality, Rockville, MD.

<http://www.ahrq.gov/clinic/epcsums/spirosum.htm>

*Management of Acute Exacerbations of Chronic Obstructive Pulmonary Disease*. Summary, Evidence Report/Technology Assessment: Number 19. AHRQ Publication No. 00-E020, September 2000. Agency for Healthcare Research and Quality, Rockville, MD.

<http://www.ahrq.gov/clinic/epcsums/copdsum.htm>