RATIONALE

Chronic Obstructive Pulmonary Disease (COPD) remains a major public health problem. It is a major cause of chronic morbidity and mortality and is the fourth leading cause of death in the United States. Further increases in prevalence and mortality are predicted in the coming decades. In the United States in 2007, the direct and indirect costs of COPD to society and the healthcare system exceeded $42 billion. While there is no current cure, there is strong evidence that early intervention and improved management can impact outcomes. The purpose of this practice guideline is to increase recognition and reduction of COPD risk factors and to support effective management of COPD once it is diagnosed.

These practice guidelines are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and patient in light of all of the circumstances presented by that patient.

DEFINITION

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an inflammatory response of the lung to noxious particles or gases. The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person. The impact of COPD on an individual patient depends on the severity of symptoms, systemic effects, and any comorbidities the patient may have – not just on the degree of airflow limitation. A careful differential diagnosis and comprehensive assessment of severity of comorbid conditions should be performed in every patient with chronic airflow limitation.

The most commonly encountered risk factor for COPD is cigarette smoking. Incorporation of smoking cessation programs is a key element of COPD prevention as well as an important intervention for patients who already have the disease. At every possible opportunity individuals who smoke should be encouraged to quit.

While disease prevention is the ultimate goal, once COPD has been diagnosed effective management includes four components:
(1) assess and monitor disease;
(2) reduce risk factors;
(3) manage stable COPD;
(4) manage exacerbations.
Management should be aimed at the following goals:

- Relieve symptoms
- Prevent disease progression
- Improve exercise tolerance
- Improve health status
- Prevent and treat complications
- Prevent and treat exacerbations
- Reduce mortality

[In this guideline, levels of evidence are assigned to management recommendations where appropriate. See Appendix A for a description of these levels.]

COMPONENT I: ASSESS AND MONITOR DISEASE

ASSESSMENT

The characteristic symptoms of COPD are chronic and progressive dyspnea, cough, and sputum production. Chronic cough and sputum production may precede the development of airflow limitation by many years. This pattern offers a unique opportunity to identify smokers and others at risk for COPD, and intervene when the disease is not yet a major health problem. Conversely, significant airflow limitation may develop without chronic cough and sputum production.

The diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease. Spirometry is required to confirm the diagnosis and determine the degree of airflow limitation.

Symptoms

<table>
<thead>
<tr>
<th>Key Indicators for Considering a Diagnosis of COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD. <strong>Spirometry is essential to establish a diagnosis of COPD</strong></td>
</tr>
</tbody>
</table>

**Dyspnea** that is:
- Progressive (worsens over time)
- Usually worse with exercise
- Persistent (present most days)
- Described by the patient as an "increased effort to breathe," "heaviness," "air hunger," or "gasping."

**Chronic Cough**
- May be intermittent and may be unproductive

**Chronic sputum production:**
- Any pattern of chronic sputum production may indicate COPD.

**History of exposure to risk factors, especially:**
- Tobacco smoke.
- Occupational dusts and chemicals
- Smoke from home cooking and heating fuels.

Dyspnea is the symptom that interferes most with a patient’s daily life and health status. When taking the medical history of the patient, it is therefore important to explore the impact of dyspnea and other symptoms on daily activities, work, and social activities (see Appendix B), and provide treatment accordingly.

**Spirometry**

The diagnosis should be confirmed by spirometry. Access to spirometry is key to the diagnosis of COPD (see Appendix D). Spirometry should measure

- the volume of air forcibly exhaled from the point of maximal inspiration (forced vital capacity, FVC) and
- the volume of air exhaled during the first second of this maneuver (forced expiratory volume in one second, FEV1).

The ratio of these two measurements (FEV1/FVC) should be calculated. Patients with COPD typically show a decrease in both FEV1 and FVC. The presence of a postbronchodilator FEV1/FVC < 0.70 and FEV1 < 80% predicted confirms the presence of airflow limitation that is not fully reversible.
Universally applicable reference values for FEV1 and FVC are not available. Where possible, values should be compared to age-related normal values to avoid over-diagnosis of COPD in the elderly and underdiagnosis in adults younger than 45 years, especially of mild disease. Using the fixed ratio (FEV1/FVC) is particularly problematic in milder patients who are elderly as the normal process of aging affects lung volumes.

**Normal Spirogram and Spirogram Typical of Patients with Mild to Moderate COPD***

*Postbronchodilator FEV1 is recommended for the diagnosis and Assessment of severity of COPD.*

**Assessment of COPD Severity**
Assessment is based on the patient’s level of symptoms, the severity of the spirometric abnormality, and the presence of complications such as respiratory failure, right heart failure, weight loss, and arterial hypoxemia.

| Classification of COPD Severity and Stages Based on Post-Bronchodilator FEV1 |
|-------------------------------|---------------------------------|--------------------------|
| Stage                      | Spirometric results | Symptoms                             |
| Stage I: Mild              | FEV1/FVC <0.70, FEV1 ≥80% predicted | Cough & sputum production may be present, but not always. Individual usually unaware that lung function is abnormal |
| Stage II: Moderate         | FEV1/FVC <0.70, 50% ≤FEV1 <80% predicted | Shortness of breath typically developing on exertion. Cough and sputum production sometimes also present. Patients |
### Classification of COPD Severity and Stages Based on Post-Bronchodilator FEV₁

<table>
<thead>
<tr>
<th>Stage</th>
<th>FEV₁/FVC</th>
<th>FEV₁</th>
<th>Staging Criteria</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage III: Severe</td>
<td>&lt;0.70 30% ≤FEV₁ &lt;50% predicted</td>
<td>Greater shortness of breath, reduced exercise capacity, fatigue, and repeated exacerbations that have an impact on patients’ quality of life.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IV: Very Severe</td>
<td>&lt;0.70 FEV₁ &lt;30% predicted or FEV₁ &lt;50% predicted plus chronic respiratory failure (PaO₂ &lt;60 mmHg +/- PaCO₂ &gt;50 mm Hg)</td>
<td>Quality of life is very appreciably impaired and exacerbations may be life-threatening</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Some patients may have cough or sputum production yet have no spirometric abnormality. Not all these individuals will go on to develop COPD, but the presence of these symptoms should help define a high-risk population that should be targeted for preventive intervention, especially smoking cessation support. **Even minor respiratory symptoms are not normal and may be markers of future ill health.**

### Medical History
- A detailed medical history should include:
- Exposure to risk factors (such as personal smoking, indoor and outdoor air pollution, occupational exposures), including intensity and duration.
- Past medical history, including asthma, allergy, sinusitis or nasal polyps, respiratory infections in childhood, and other respiratory diseases.
- Family history of COPD or other chronic respiratory disease.
- Pattern of symptom development.
- History of exacerbations or previous hospitalizations for respiratory disorder.
- Presence of comorbidities, such as heart disease, malignancies, osteoporosis, and musculoskeletal disorders, which may also contribute to restriction of activity.
- Appropriateness of current medical treatments.
- Impact of disease on patient’s life, including limitation of activity; missed work and economic impact; effect on family routines; and feelings of depression or anxiety.
- Social and family support available to the patient.
- Possibilities for reducing risk factors, especially smoking cessation.

### Physical Examination
Though an important part of patient care, a physical examination is rarely diagnostic in COPD. Physical signs of airflow limitation are usually not present until significant impairment of lung function has occurred and their detection has a relatively low sensitivity and specificity. Findings suggestive of COPD (especially more advanced disease) include:
- prolonged expiratory phase
- wheezing, rhonchi
- increased A-P chest diameter (barrel chest)
- clinical signs of right heart failure (ankle edema, increase in jugular venous pressure)

### Additional Investigations
(for patients with diagnosed COPD at Stage II or above)
• Bronchodilator reversibility testing: To rule out a diagnosis of asthma, particularly in patients with an atypical history (e.g., asthma in childhood and regular night waking with cough and wheeze).
• Chest X-ray: Seldom diagnostic in COPD but valuable to exclude alternative diagnoses such as pulmonary tuberculosis, and identify comorbidities such as cardiac failure.
• Arterial blood gas measurement: Perform in patients with FEV1 < 50% predicted or with clinical signs suggestive of respiratory failure or right heart failure. The major clinical sign of respiratory failure is cyanosis. Clinical signs of right heart failure include ankle edema and an increase in the jugular venous pressure. Respiratory failure is indicated by PaO2 < 8.0 kPa (60 mm Hg), with or without PaCO2 > 6.7 kPa (50 mm Hg) while breathing air at sea level.
• Alpha-1 antitrypsin deficiency screening: Perform when COPD develops in patients of Caucasian descent — under 45 years or — with a strong family history of COPD.

Differential Diagnosis of COPD
In some patients with chronic asthma, a clear distinction from COPD is not possible using current imaging and physiological testing techniques and it is assumed that asthma and COPD coexist in these patients. In these cases, current management is similar to that of asthma. Other potential diagnoses are usually easier to distinguish from COPD.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Suggestive features*</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>Onset in mid-life.</td>
</tr>
<tr>
<td></td>
<td>Symptoms slowly progressive.</td>
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<tr>
<td></td>
<td>Long history of tobacco smoking.</td>
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<tr>
<td></td>
<td>Dyspnea during exercise.</td>
</tr>
<tr>
<td></td>
<td>Largely irreversible airflow limitation.</td>
</tr>
<tr>
<td>Asthma</td>
<td>Onset early in life (often childhood).</td>
</tr>
<tr>
<td></td>
<td>Symptoms vary from day to day.</td>
</tr>
<tr>
<td></td>
<td>Symptoms at night/early morning.</td>
</tr>
<tr>
<td></td>
<td>Allergy, rhinitis, and/or eczema also present.</td>
</tr>
<tr>
<td></td>
<td>Family history of asthma.</td>
</tr>
<tr>
<td></td>
<td>Largely reversible airflow limitation.</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Fine basilar crackles on auscultation.</td>
</tr>
<tr>
<td></td>
<td>Chest X-ray shows dilated heart, pulmonary edema.</td>
</tr>
<tr>
<td></td>
<td>Pulmonary function tests indicate volume restriction, not airflow limitation</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>Large volumes of purulent sputum.</td>
</tr>
<tr>
<td></td>
<td>Commonly associated with bacterial infection.</td>
</tr>
<tr>
<td></td>
<td>Crackles on auscultation/clubbing of fingers.</td>
</tr>
<tr>
<td></td>
<td>Chest X-ray/CT shows bronchial dilation, bronchial wall thickening.</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Onset all ages.</td>
</tr>
<tr>
<td></td>
<td>Chest X-ray shows lung infiltrate or nodular lesions.</td>
</tr>
<tr>
<td></td>
<td>Microbiological confirmation.</td>
</tr>
<tr>
<td></td>
<td>High local prevalence of tuberculosis.</td>
</tr>
<tr>
<td>Obliterative bronchiolitis</td>
<td>Onset in younger age, nonsmokers.</td>
</tr>
<tr>
<td></td>
<td>May have history of rheumatoid arthritis or exposure to fumes.</td>
</tr>
<tr>
<td></td>
<td>CT on expiration shows hypodense areas.</td>
</tr>
<tr>
<td>Diffuse panbronchiolitis</td>
<td>Most patients are male and nonsmokers.</td>
</tr>
<tr>
<td></td>
<td>Almost all have chronic sinusitis.</td>
</tr>
<tr>
<td></td>
<td>Chest X-ray and HRCT show diffuse small centrilobular nodular opacities and hyperinflation.</td>
</tr>
</tbody>
</table>
*These features tend to be characteristic of the respective diseases, but do not occur in every case. For example, a person who has never smoked may develop COPD; asthma may develop in adult and even elderly patients.

**MONITORING**

- Ongoing monitoring and assessment in COPD ensures that the goals of treatment are being met and should include evaluation of:
  - Disease progression and development of complications
  - Exposure to risk factors, especially tobacco smoke
  - Pharmacotherapy and other medical treatment
  - Exacerbation history
  - Comorbidities

The best way to detect changes in symptoms and overall health status is to ask the patient the same questions at each visit. *(see Appendix B)*

**Monitor Disease Progression and Development of Complications**

COPD is usually a progressive disease. Lung function can be expected to worsen over time, even with the best available care. Symptoms and objective measures of airflow limitation should be monitored to determine when to modify therapy and to identify any complications that may develop.

Follow-up visits should include:

- a physical examination
- discussion of symptoms, particularly any new or worsening symptoms.
- Spirometry, if there is a substantial increase in symptoms or a complication or for yearly monitoring of disease progression. The development of respiratory failure is indicated by a PaO2 < 8.0 kPa (60 mm Hg) with or without PaCO2 > 6.7 kPa (50 mm Hg) in arterial blood gas measurements made while breathing air at sea level.

Measurement of pulmonary arterial pressure is not recommended in clinical practice as it does not add practical information beyond that obtained from knowledge of PaO2.

**Monitor Pharmacotherapy and Other Medical Treatment**

In order to adjust therapy appropriately as the disease progresses, each follow-up visit should include a discussion of the current therapeutic regimen to monitor:

- dosages of various medications,
- adherence to the regimen,
- inhaler technique,
- effectiveness of the current regime at controlling symptoms, and
- side effects of treatment.

**Monitor Exacerbation History:**

Evaluate:

- frequency and severity of exacerbations
- likely causes of exacerbations and
- psychological wellbeing.

Note:

- increased sputum volume,
- acutely worsening dyspnea,
- presence of purulent sputum
- hospitalizations, including the facility, duration of stay, and any use of critical care or intubation
Estimate severity by:
- increased need for bronchodilator medication or inhaled (or oral) glucocorticosteroids
- need for antibiotic treatment.

**Monitor Comorbidities:** Comorbidities are common in COPD and can be categorized into the following four groups:
- Common pathway diseases: other smoking-related diseases, e.g. ischemic heart disease, lung cancer
- Complicating conditions – arise as a complication of COPD, e.g. pulmonary hypertension, right heart failure
- Coincidental conditions - coexisting as a part of the aging process, e.g. arthritis, diabetes, bowel or prostate cancer, depression, Parkinson’s disease, dementia
- Inter-current illnesses – acute illnesses, like upper respiratory tract infections, that may have a more severe impact in patient with COPD.

These comorbidities may become harder to manage when COPD is present, either because COPD adds to the total level of disability or because COPD therapy adversely affects the comorbid disorder. The focus should be on identification and management of these individual problems in line with local treatment guidance.

**COMPONENT II: REDUCE RISK FACTORS**

**Smoking Cessation Intervention Process:** Smoking cessation is the single most effective—and cost effective—way to reduce exposure to COPD risk factors. All smokers—including those who may be at risk for COPD as well as those who already have the disease—should be offered the most intensive smoking cessation intervention feasible.
- Even a brief (3-minute) period of counseling to urge a smoker to quit results in smoking cessation rates of 5-10%. At the very least, this should be done for every smoker at every health care provider visit
- Pharmacotherapy (nicotine replacement, buproprion/nortryptiline, and/or varenicline) is recommended when counseling is not sufficient to help patients stop smoking. Special consideration should be given before using pharmacotherapy in people smoking fewer than 10 cigarettes per day, pregnant women, adolescents, and those with medical contraindications.
- Use “5A” strategy (Ask, Advise, Assess, Assist, Arrange) to help patients willing to quit. See NHPRI Guideline for Smoking Cessation in Primary Care and NHPRI Guideline for Smoking Cessation in Pregnancy.

**Occupational Exposures:** Emphasize primary prevention, which is best achieved by elimination or reduction of exposures to various substances in the workplace. Secondary prevention, achieved through surveillance and early detection, is also important.

**Indoor and Outdoor air pollution:** Advise patients to monitor public announcements of air quality and, depending on the severity of their disease, avoid vigorous exercise outdoors or stay indoors altogether during pollution episodes.

**COMPONENT III: MANAGE STABLE COPD**

The overall approach to managing stable COPD should be individualized to address symptoms and improve quality of life. The overall approach to managing stable COPD should be characterized by an increase in treatment, depending on the severity of the disease and the clinical status of the patient. Management of COPD is based on an individualized assessment of disease severity and response to various therapies.

**Education**
Education plays an important role in smoking cessation and can also play a role in improving skills, ability to cope with illness and health status. (A) The topics that seem most appropriate for an education program include:
- smoking cessation;
- basic information about COPD and pathophysiology of the disease;
• general approach to therapy and specific aspects of medical treatment;
• self-management skills;
• strategies to help minimize dyspnea;
• advice about when to seek help;
• self-management and decision-making during exacerbations; and
• advance directives and end-of-life issues.

Pharmacotherapy
Pharmacotherapy is used to
• prevent and control symptoms
• reduce frequency and severity of exacerbations
• improve health status,
• improve exercise tolerance.

None of the existing medications for COPD have been shown to modify the long-term decline in lung function that is the hallmark of this disease (A), although here is limited evidence that regular treatment with long-acting B2-agonists, inhaled glucocorticosteroids, and its combination can decrease the rate of decline of lung function. (B)

• Bronchodilator medications: central to the symptomatic management of COPD. (A) They are given on an as-needed basis for relief of persistent or worsening symptoms or on a regular basis to prevent or reduce symptoms.
  o Principal bronchodilator treatments: B2-agonists, anticholinergics, and methylxanthines used singly or in combination. (A)
  o Inhaled therapy is preferred; attention to effective drug delivery and training in inhaler technique (recheck at each visit) is essential
  o Regular treatment with long-acting bronchodilators is more effective and convenient than treatment with short-acting bronchodilators. (A)
  o Combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation for equivalent or lesser side effects.

• Glucocorticosteroids (A):
  o regular treatment with inhaled glucocorticosteroids reduces frequency of exacerbations for symptomatic COPD patients with FEV1 < 50% predicted and repeated exacerbations (e.g. 3 in three years).
  o Inhaled glucocorticosteroid combined with a long-acting B2-agonist is more effective than individual components in reducing exacerbations and improving lung function and health status. (A)
  o In patients with FEV1 < 60%, treatment with long-acting B2-agonist, inhaled glucocorticosteroid and its combination decreased the rate of decline of lung function.
  o Longterm treatment with oral glucocorticosteroids is not recommended. (A)

• Vaccines:
  o influenza vaccines can reduce serious illness. (A)
  o pneumococcal polysaccharide vaccine is recommended for all COPD patients 65 years and older and for those COPD patients younger than age 65 with an FEV1 < 40% predicted (B)

• Alpha-1 antitrypsin augmentation therapy: not recommended except sometimes for young patients with severe hereditary alpha-1 antitrypsin deficiency and established emphysema.

• Antibiotics: not recommended except for treating infectious exacerbations of COPD and other bacterial infections

• Mucolytic agents: widespread use not recommended (D)

• Antitussives: not recommended in stable COPD (D)

• Others:
  o Nedocromil and leukotriene modifiers not recommended
  o Endothelin-receptor antagonist antagonist bosentan should not be used with severe COPD.
Non-pharmacologic treatment

- **Pulmonary Rehabilitation**: goals are to reduce symptoms, improve quality of life, and increase participation in everyday activities. Includes:
  - **Exercise training**: all COPD patients benefit from exercise training programs, improving with respect to both exercise tolerance and symptoms of dyspnea and fatigue.
  - **Nutrition counseling**: both overweight and underweight can be a problem. A reduction in body mass index (BMI) is an independent risk factor for mortality in COPD patients. (A)
  - **Education** (see above)

- **Oxygen**: long-term administration of oxygen (> 15 hours per day) to patients with chronic respiratory failure has been shown to increase survival. (A) Initiate oxygen therapy for patients with Stage IV: Very Severe COPD if:
  - PaO2 is at or below 7.3 kPa (55 mm Hg) or SaO2 is at or below 88%, with or without hypercapnia;
  - PO2 is between 7.3 kPa (55 mm Hg) and 8.0 kPa (60 mm Hg) or SaO2 of 89%, if there is evidence of pulmonary hypertension, peripheral edema suggesting congestive heart failure, or polycythemia (hematocrit > 55%).

  The goal of long-term oxygen therapy is to increase the baseline PaO2 at rest to at least 8.0 kPa (60 mm Hg) at sea level, and/or produce SaO2 at least 90%, which will preserve vital organ function by ensuring an adequate delivery of oxygen. A decision about the use of long-term oxygen should be based on the waking PaO2 values.

- **Surgical Treatments**:
  - Bullectomy is effective in reducing dyspnea and improving lung function in carefully selected patients with Stage IV: Very Severe COPD. (C)
  - Lung volume reduction surgery (LVRS) can be considered in carefully-selected patients with upper-lobe emphysema and low exercise capacity; it has been shown to increase PaO2 and decrease use of supplemental oxygen during treadmill walking, and self-reported use of oxygen during rest, exertion, and sleep for up to 24 months post-procedure.
  - Lung transplantation: in carefully selected patients with very advanced COPD it has been shown to improve quality of life and functional capacity. (C) Criteria for referral include FEV1 <35% predicted, PaO2 <7.3-8.0 kPa (55-60 mm Hg), PaCO2 > 6.7 kPa (50 mm Hg) and secondary pulmonary hypertension.

- **Mechanical ventilation**: there is no convincing evidence that mechanical ventilator support has a role in the routine management of stable COPD. However, the combination of non-invasive intermittent positive pressure ventilation (NIPPV) with long-term oxygen therapy may be of some use in a selected subset of patients, particularly in those with pronounced daytime hypercapnia (PCO2>50 mm Hg).

<table>
<thead>
<tr>
<th>Therapy at Each Stage of COPD</th>
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<tbody>
<tr>
<td><strong>I: Mild</strong></td>
</tr>
<tr>
<td>- FEV1/FVC &lt; 0.70</td>
</tr>
<tr>
<td>- FEV1 ≥ 80%</td>
</tr>
<tr>
<td>- With or without symptoms</td>
</tr>
</tbody>
</table>

- Active reduction of risk factors (especially smoking cessation)
- Influenza vaccine
- Add short-acting bronchodilator (when needed)
- Add regular treatment with one or more long-acting bronchodilators (when needed)
- Add rehabilitation
- Add inhaled glucocorticosteroids if repeated exacerbations
COMPONENT IV: MANAGE EXACERBATIONS

An exacerbation of 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 in a patient with underlying COPD. The most common causes of an exacerbation are infection of the tracheobronchial tree and air pollution, but the cause of about one-third of severe exacerbations cannot be identified. (B)

Diagnosis and assessment of severity

- **Medical history:**
  - Symptoms: increased breathlessness, often accompanied by wheezing and chest tightness, increased cough and sputum, change of color and/or tenacity of sputum, fever
  - Duration of worsening and/or new symptoms
  - Severity of FEV1
  - Prior arterial blood gas measurements for comparison
  - Any change in mental status (especially for patients with Stage IV COPD)
  - Number of previous episodes (exacerbations/hospitalizations)
  - Comorbidities
  - Present treatment regimen

Physical signs of severity include:

- Use of accessory respiratory muscles
- Paradoxical chest wall movements
- Worsening or new onset of central cyanosis
- Hemodynamic instability
- Signs of right heart failure including peripheral edema
- Reduced alertness

- **Laboratory tests**
  - Pulse oximetry can be used to evaluate patient’s oxygen saturation and need for supplemental oxygen therapy.
  - Arterial blood gas measurement (in hospital, to assess severity of exacerbation):
    - PaO2 < 8.0 kPa (60 mm Hg) and/or SaO2 < 90% with or without PaCO2 > 6.7 kPa, (50 mmHg) when breathing room air indicates respiratory failure.
    - Moderate-to-severe acidosis (pH < 7.36) plus hypercapnia (PaCO2 > 6-8 kPa, 45-60 mm Hg) in a patient with respiratory failure is an indication for mechanical ventilation.
  - Chest X-ray: Chest radiographs (posterior/anterior plus lateral) identify alternative diagnoses that can mimic the symptoms of an exacerbation.
  - ECG: Aids in the diagnosis of right ventricular hypertrophy, arrhythmias, and ischemic episodes.
  - The presence of purulent sputum during an exacerbation of symptoms is sufficient indication for starting empirical antibiotic treatment.
  - Sputum culture and antibiogram to identify infection if there is no response to initial antibiotic treatment.
  - Biochemical tests to detect electrolyte disturbances, poor glucose control, and poor nutrition.
  - Whole blood count can identify polycythemia or bleeding.
  - Spirometry and PEF not recommended since measurements are not accurate during an acute exacerbation.
Differential Diagnosis
A diagnosis of pulmonary embolism should be considered in patients with exacerbation severe enough to warrant hospitalization, especially in those with intermediate-to-high pretest probability of pulmonary embolism.

Patients with apparent exacerbations of COPD that do not respond to treatment (10-30% of patients with apparent COPD exacerbations) should be re-evaluated for other medical conditions that can aggravate symptoms or mimic COPD exacerbations, which include:

- Pneumonia
- Congestive heart failure - elevated serum levels of brain-type natriuretic peptide, in conjunction with other clinical information, identifies patients with acute dyspnea secondary to congestive heart failure and enables them to be distinguished from patients with COPD exacerbations
- Pneumothorax
- Pleural effusion
- Pulmonary embolism
- Cardiac arrhythmia.

Non-compliance with the prescribed medication regimen can also cause increased symptoms that may be confused with a true exacerbation.

Management - Home Care or Hospital Care for End-Stage COPD Patients?
The risk of dying from an exacerbation of COPD is closely related to

- The development of respiratory acidosis,
- The presence of serious comorbidities, and
- The need for ventilatory support.

Patients lacking these features are not at high risk of dying, but those with severe underlying COPD often require hospitalization in any case. Attempts at managing such patients entirely in the community have met with limited success, but returning them to their homes with increased social support and a supervised medical care program after an initial emergency room assessment has been much more successful.

<table>
<thead>
<tr>
<th>Indications for Hospital Assessment or Admission for COPD Exacerbations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Marked increase in intensity of symptoms, such as sudden development of resting dyspnea</td>
</tr>
<tr>
<td>• Severe underlying COPD</td>
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<tr>
<td>• Onset of new physical signs (e.g., cyanosis, peripheral edema)</td>
</tr>
<tr>
<td>• Failure of exacerbation to respond to initial medical management</td>
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<tr>
<td>• Significant comorbidities</td>
</tr>
<tr>
<td>• Frequent exacerbations</td>
</tr>
<tr>
<td>• Newly occurring arrhythmias</td>
</tr>
<tr>
<td>• Diagnostic uncertainty</td>
</tr>
<tr>
<td>• Older age</td>
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<tr>
<td>• Insufficient home support</td>
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</table>

Home Management
There is increasing interest in home care for end-stage COPD patients, although there are so far no exact criteria for this approach as opposed to hospital treatment. Home management includes the following components:

- **Bronchodilators:** Increase dose and/or frequency of existing short-acting bronchodilator therapy, preferably with B2-agonists. If not already used, add anticholinergics until symptoms improve.
- **Glucocorticosteroids:** Systemic glucocorticosteroids are beneficial in management of COPD exacerbations to shorten recovery time and improve lung function (FEV1) and hypoxemia (PaO2). They may also reduce risk of early relapse and treatment failure.
- If baseline FEV1 < 50% predicted, add 30-40 mg oral prednisolone per day for 7-10 days to the bronchodilator regimen.

- Budesonide alone, or in combination with formoterol, may be an alternative to oral glucocorticosteroids in the treatment of exacerbations and is associated with significant reduction of complications.

- Antibiotics – see discussion in Hospital Management section.

### Hospital Management

The first actions when a patient reaches the emergency department are

- To provide supplemental O2 therapy
- To determine whether exacerbation is life threatening and thus requires ICU admission.

<table>
<thead>
<tr>
<th>Indications for ICU Admission of patients with COPD Exacerbations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Severe dyspnea that responds inadequately to initial emergency therapy</td>
</tr>
<tr>
<td>• Changes in mental status (confusion, lethargy, coma)</td>
</tr>
<tr>
<td>• Persistent or worsening hypoxemia (PaO2 &lt; 5.3 kPa, 40 mmHg) and/or severe/worsening hypercapnia (PaCO2 &gt; 8.0 kPa, 60 mmHg) and/or severe/worsening respiratory acidosis (pH &lt; 7.25) despite supplemental oxygen and noninvasive ventilation</td>
</tr>
<tr>
<td>• Need for invasive mechanical ventilation</td>
</tr>
<tr>
<td>• Hemodynamic instability – need for vasopressors</td>
</tr>
</tbody>
</table>

Management of severe but not life-threatening exacerbations of COPD can be in the Emergency Department or the hospital and includes the following measures:

- Assess severity of symptoms, blood gases, chest X-ray
- Administer controlled oxygen therapy and repeat arterial blood gas measurement after 30-60 minutes to ensure satisfactory oxygenation (PaO2 > 8.0 kPa, 60 mm Hg or SaO2 > 90%) without CO2 retention or acidosis.
  - **Bronchodilators**: short-acting inhaled B2-agonists are the preferred bronchodilators for treatment of COPD exacerbations. (A) Increase doses and/or frequency
  - Combine B2-agonists and anticholinergic if no prompt response to B2-agonists alone
  - Use spacers or air-driven nebulizers
  - Consider adding intravenous mehylxanthines, if needed (B)
- Add oral or intravenous glucocorticosteroids (A) - 30-40 mg oral prednisolone daily for 7-10 days.
- Consider antibiotics (oral or occasionally intravenous) when signs of bacterial infection. (B) Antibiotics should be given to:
  - Patients with exacerbations of COPD with the following three cardinal symptoms: increased dyspnea, increased sputum volume, and increased sputum purulence (B)
  - Patients with exacerbations of COPD with two of the cardinal symptoms, if increased purulence of sputum is one of the two symptoms (C)
  - Patients with a severe exacerbation of COPD that requires mechanical ventilation (invasive or noninvasive) (B)
- **Mechanical ventilatory support** - used to decrease mortality and morbidity and to relieve symptoms.
  - Noninvasive mechanical ventilation (NIV) using either negative or positive pressure devices: improves respiratory acidosis, decreases respiratory rate, severity of breathlessness, and length of hospital stay (A). Also reduces mortality and/or intubation rate. **Indications for NIV** include:
    - Moderate to severe dyspnea with use of accessory muscles and paradoxical abdominal motion
    - Moderate to severe acidosis (pH ≤ 7.35) and/or hypercapnia (PaCO2 > 6.0 kPa, 45 mm Hg)
    - Respiratory frequency > 25 breaths/minute
Relative contraindications for NIV include:
- Respiratory arrest
- Cardiovascular instability (hypotension, arrhythmias, myocardial infarction)
- Change in mental status; uncooperative patient
- High aspiration risk
- Viscous or copious secretions
- Recent facial or gastroesophageal surgery
- Craniofacial trauma
- Fixed nasopharyngeal abnormalities
- Burns
- Extreme obesity

Invasive mechanical ventilation: indications for initiating this therapy include:
- Unable to tolerate NIV (see contraindications above) or NIV failure
- Severe dyspnea with use of accessory muscles and paradoxical abdominal motion
- Respiratory frequency > 35 breaths/minute
- Life-threatening hypoxemia
- Severe acidosis (pH < 7.25) and/or hypercapnia (PaCO2 > 8.0 kPa, 60 mm Hg)
- Respiratory arrest
- Somnolence, impaired mental status
- Cardiovascular complications (hypotension, shock)
- Other complications (metabolic abnormalities, sepsis, pneumonia, pulmonary embolism, barotraumas, massive pleural effusion)

The use of invasive ventilation in end-stage COPD patients is influenced by the likely reversibility of the precipitating event, the patient’s wishes, and the availability of intensive care facilities.

- At all times:
  - Monitor fluid balance and nutrition
  - Consider deep venous thrombosis prophylaxis (mechanical devices, heparins) in immobilized, polycythemic, or dehydrated patients
  - Encourage sputum clearance (stimulate coughing and low-volume forced expirations; manual or mechanical chest percussion and postural drainage as indicated)
  - Identify and treat associated conditions (e.g., heart failure, arrhythmias)
  - Closely monitor condition of the patient

Hospital discharge and follow-up:
Discharge criteria for patients with COPD exacerbations include:
- Inhaled B2-agonist therapy is required no more frequently than every 4 hrs.
- Patient, if previously ambulatory, is able to walk across room
- Patient able to eat and sleep without frequent awakening by dyspnea
- Patient has been clinically stable for 12-24 hrs.
- Arterial blood gases have been stable for 12-24 hrs.
- Patient (or home caregiver) fully understands correct use of medications
- Follow-up and home care arrangements have been completed (e.g., visiting nurse, oxygen delivery, meal provisions)
- Patient, family, and physician are confident patient can manage successfully at home.

Follow-up assessment should be done 4-6 weeks after discharge from the hospital for exacerbations of COPD and should include assessment of:
- Ability to cope in usual environment
- Measurement of FEV1
- Reassessment of inhaler technique
- Understanding of recommended treatment regimen
Need for long-term oxygen therapy and/or home nebulizer (for patients with Stage IV COPD)

Use of a **written action plan** in COPD increases appropriate therapeutic interventions for COPD exacerbations but does not decrease health-care resource utilization. *(B)*

**SOURCE**

Neighborhood has adopted the COPD guidelines developed through the Global Initiative for the Diagnosis, Management and Prevention of Chronic Obstructive Lung Disease. The reference document for the current guideline is *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease*. Updated 2009 (www.goldcopd.com)

**REVIEW AND APPROVAL**

Neighborhood Health Plan of RI Clinical Affairs Committee, at least biannually or more often as needed.
**APPENDIX A**

**Description of Levels of Evidence**
Levels of evidence are assigned to management recommendations where appropriate, as described in the following table:

<table>
<thead>
<tr>
<th>Evidence Category</th>
<th>Sources of Evidence</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Randomized controlled trials (RCTs). Rich body of data.</td>
<td>Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.</td>
</tr>
<tr>
<td>B</td>
<td>Randomized controlled trials (RCTs). Limited body of data.</td>
<td>Evidence is from endpoints of intervention studies that include only a limited number of patients, posthoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.</td>
</tr>
<tr>
<td>C</td>
<td>Nonrandomized trials. Observational studies.</td>
<td>Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.</td>
</tr>
<tr>
<td>D</td>
<td>Panel Consensus Judgment.</td>
<td>This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was deemed insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria</td>
</tr>
</tbody>
</table>
### APPENDIX B

**Evaluation Tools**

#### Questionnaire for Assessing the Severity of Breathlessness

Please check the box that applies to you (one box only)

- [ ] I only get breathless with strenuous exercise
- [ ] I get short of breath when hurrying on the level or walking up a slight hill
- [ ] I walk slower than people of my same age on the level because of breathlessness, or I have to stop for breath when walking at my own pace on the level.
- [ ] I stop for breath after walking about 100 yards or after a few minutes on the level
- [ ] I am too breathless to leave the house or I am breathless when dressing or undressing

#### Suggested Questions for Follow-Up Visits

**Monitor exposure to risk factors:**
- Has your exposure to risk factors changed since your last visit?
- Since your last visit, have you quit smoking or are you still smoking?
- If you are still smoking, how many cigarettes/how much tobacco per day?
- Would you like to quit smoking?
- Has there been any change in your working environment?

**Monitor disease progression and development of complications:**
- How much can you do before you get short of breath? (see questionnaire above)
- Has your breathlessness worsened, improved, or stayed the same since your last visit?
- Have you had to reduce your activities because of your breathing or any other symptom?
- Have any of your symptoms worsened since your last visit?
- Have you experienced any new symptoms since your last visit?
- Has your sleep been disrupted by breathlessness or other chest symptoms?
- Since your last visit, have you missed any work and/or had to see a doctor because of your symptoms?

**Monitor pharmacotherapy and other medical treatment:**
- What medicines are you taking?
- How often do you take each medicine?
- How much do you take each time?
- Have you missed or stopped taking any regular doses of your medicine for any reason?
- Have you had trouble filling your prescriptions?
- Please show me how you use your inhaler.
- Have you tried any other medicines or remedies?
- Has your treatment been effective in controlling your symptoms?
- Has your treatment caused you any problems?

**Monitor exacerbation history:**
- Since your last visit, have you had any episodes or times when your symptoms were a lot worse than usual?
- If so, how long did the episode(s) last? What do you think caused the symptoms to get worse? What did you do to control the symptoms?

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1. Modified from a British Medical Research Council questionnaire
2. These questions are examples and do not represent a standardized assessment instrument. The validity and reliability of these questions have not been assessed.
### APPENDIX C

#### Commonly Used Formulations of Drugs used in COPD

<table>
<thead>
<tr>
<th>Medication</th>
<th>Inhaler (µg)</th>
<th>Solution for nebulizer (mg/ml)</th>
<th>Oral</th>
<th>Vials for Injection (mg)</th>
<th>Duration of Action (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B2-agonists- short-acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenoterol</td>
<td>100-200 (MDI)</td>
<td>1</td>
<td>0.5% (syrup)</td>
<td></td>
<td>4-6</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>0.21, 0.42</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salbutamol (albuterol)</td>
<td>100, 200 (MDI &amp; DPI)</td>
<td>5</td>
<td>5 mg (pill)</td>
<td>0.24% (syrup)</td>
<td>0.1, 0.5</td>
</tr>
<tr>
<td>Terbutaline</td>
<td>400, 500 (DPI)</td>
<td>-</td>
<td></td>
<td>0.2, 0.25</td>
<td>4-6</td>
</tr>
<tr>
<td><strong>B2-agonist - Long-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formoterol</td>
<td>4.5-12 (MDI&amp;DPI)</td>
<td>0.01*</td>
<td></td>
<td></td>
<td>12+</td>
</tr>
<tr>
<td>Arformoterol</td>
<td>0.0075</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol</td>
<td>25-50 (MDI &amp; DPI)</td>
<td></td>
<td></td>
<td></td>
<td>12+</td>
</tr>
<tr>
<td><strong>Anticholinergics- short-acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium bromide</td>
<td>20,40 (MDI)</td>
<td>0.25, 0.5</td>
<td></td>
<td></td>
<td>6-8</td>
</tr>
<tr>
<td>Oxitropium bromide</td>
<td>100 (MDI)</td>
<td>1.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anticholinergics - Long-acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tiotropium</td>
<td>18 (DPI), 5 (SMI)</td>
<td></td>
<td></td>
<td></td>
<td>24+</td>
</tr>
<tr>
<td><strong>Combination short-acting B2-agonists plus anticholinergic in one inhaler</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fenoterol/ Ipratropium</td>
<td>200/80 (MDI)</td>
<td>1.25/0.5</td>
<td></td>
<td></td>
<td>6-8</td>
</tr>
<tr>
<td>Salbutamol/ Ipratropium</td>
<td>75/15 (MDI)</td>
<td>0.75/4.5</td>
<td></td>
<td></td>
<td>6-8</td>
</tr>
<tr>
<td><strong>Methylxanthines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aminophylline</td>
<td></td>
<td>200-600 mg (pill)</td>
<td>240</td>
<td>Variable, up to 24</td>
<td></td>
</tr>
<tr>
<td>Theophylline (SR)</td>
<td></td>
<td>100-600 mg (pill)</td>
<td></td>
<td>Variable, up to 24</td>
<td></td>
</tr>
<tr>
<td><strong>Inhaled glucocorticosteroids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>50-400 (MDI &amp; DPI)</td>
<td>0.2-0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide</td>
<td>100, 200, 400 (DPI)</td>
<td>0.20, 0.25, 0.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone</td>
<td>50-500 (MDI&amp;DPI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>100 (MDI)</td>
<td>40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Combination long-acting B2-agonists plus glucocorticosteroids in one inhaler</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formoterol/Budesonide</td>
<td>4.5/160, 9/320 (DPI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol/Fluticasone</td>
<td>50/100, 250, 500 (DPI)</td>
<td>25/50, 125, 250 (MDI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Systemic glucocorticosteroids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td></td>
<td>5-60 mg (pill)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td></td>
<td>4, 8, 16 mg. (pill)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Formoterol nebulized solution is based on the unit dose vial containing 20 µgm in a volume of 2.0 ml
APPENDIX D

SPIROMETRY FOR DIAGNOSIS OF COPD

Spirometry is a simple test to measure the amount of air a person can breathe out, and the amount of time taken
to do so. Spirometry measurements used for diagnosis of COPD include:
- FVC (Forced Vital Capacity): maximum volume of air that can be exhaled during a forced maneuver
- FEV1 (Forced Expired Volume in one second): volume expired in the first second of maximal expiration after a maximal inspiration. This is a measure of how quickly the lungs can be emptied.
- FEV1/FVC: FEV1 expressed as a percentage of the FVC gives a clinically useful index of airflow limitation.
The ratio FEV1/FVC is between 70-80% in normal adults; a value less than 70% indicates airflow limitation
and the possibility of COPD.
FEV1 is influenced by the age, sex, height and ethnicity, and is best considered as a percentage of the predicted
normal value. Appropriate normal values for the local populations should be used.

Why do Spirometry for COPD?
- Spirometry is needed to make a firm diagnosis of COPD
- Together with the presence of symptoms, spirometry helps stage COPD severity and can be a guide to
  specific treatment steps.
- A normal value for spirometry effectively excludes the diagnosis of clinically relevant COPD
- The lower the percentage predicted FEV1, the worse the subsequent prognosis
- FEV1 declines over time and faster in COPD than in healthy subjects. Spirometry can be used to
  monitor disease progression, but to be reliable the intervals between measurements must be at least 12
  months.