Relevance to Population: COPD affects 12 million people in the United States, making it the 4th leading cause of mortality and the 2nd leading cause of disability. It is predicted that these statistics will increase by 30% by 2020 due to the aging population and prevalence of tobacco use (Buist et al. 2005). In 2009, COPD was one of the top 10 diagnoses for inpatient admissions of UPMC Health Plan members. Although COPD cannot be cured, use of the following evidence-based guidelines for management of COPD can control symptoms, slow disease progression, and improve quality of life.

Definition: Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease with both pulmonary and extra-pulmonary effects. Its pulmonary component is characterized by chronic airflow limitation that is not fully reversible. It is usually progressive and associated with an inflammatory response of the lung to noxious particles or gases. The extra-pulmonary effects, which include weight loss, nutritional abnormalities, skeletal muscle dysfunction, and increased risk for cardiovascular disease, may contribute to the severity of COPD in individual patients.

Clinical Indicators Measured by UPMC Health Plan:
1. The percentage of members 40 years of age and older with a new diagnosis or newly active chronic obstructive pulmonary disease (COPD) who received appropriate spirometry testing to confirm the diagnosis. HEDIS®
2. The percentage of COPD exacerbations for members 40 years of age and older who had an acute inpatient discharge or ED encounter during the measurement year and who were dispensed appropriate medications
   - Dispensed a systemic corticosteroid within 14 days of the event
   - Dispensed a bronchodilator within 30 days of the event. HEDIS®

Population Covered by Guideline: All adult members with stable COPD and acute exacerbations of COPD.

Goals of Therapy—Management of COPD and Prevention of Disease Progression:
- Relieve symptoms
- Improve health status
- Reduce mortality
- Prevent disease progression
- Prevent and treat complications
- Improve exercise tolerance
- Prevent and treat exacerbation

Key Points: Spirometry is essential for confirming the diagnosis and classifying the severity of COPD.
- Spirometry is recommended in all smokers over the age of 40 to establish a diagnosis of COPD.
- Spirometry should be performed yearly in any patient with a diagnosis of COPD.
- Spirometry should be considered in asymptomatic patients ≥ 45 y/o who have ≥ 10 pack/year smoking history (patients often ignore or deny symptoms, and COPD is commonly under-diagnosed in its early stages when smoking cessation may be most beneficial).
- Spirometry can determine level of severity, but other factors, including symptoms, exacerbations, and comorbid conditions, must be accounted for in the determination of therapy for COPD.
- Spirometry should be performed when the patient is clinically stable and free from infection.
- Pre-dose and peak FEV₁ should be measured before and after administering a bronchodilator to determine the percentage of reversibility.
### Spirometric Classification of COPD Severity Based on Post-Bronchodilator FEV₁

Assign the patient to the highest severity level in which any feature occurs.

<table>
<thead>
<tr>
<th>COPD Severity Category</th>
<th>Degree of Airflow Limitation</th>
<th>FEV₁ (% predicted)</th>
<th>FEV₁/FVC Ratio (% predicted)</th>
<th>Typical Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I: Mild</td>
<td>Mild airflow limitation</td>
<td>FEV₁ ≥ 80%</td>
<td>FEV₁/FVC &lt; 70%</td>
<td>Chronic cough with or without sputum; Little or no dyspnea</td>
</tr>
<tr>
<td>II: Moderate</td>
<td>Worsening airflow limitation</td>
<td>50% ≤ FEV₁ &lt; 80%</td>
<td>FEV₁/FVC &lt; 70%</td>
<td>Dyspnea developing on exertion; Cough sputum production; General reduction in breath sounds; Presence of wheeze; Hypoxemia may be present</td>
</tr>
<tr>
<td>III: Severe</td>
<td>Further worsening of airflow</td>
<td>30% ≤ FEV₁ &lt; 50%</td>
<td>FEV₁/FVC &lt; 70%</td>
<td>Increased shortness of breath with any exertion or at rest; Reduced exercise capacity; Fatigue; Wheeze and cough prominent</td>
</tr>
<tr>
<td>IV: Very Severe</td>
<td>Severe airflow limitation</td>
<td>FEV₁ &lt; 30% OR FEV₁ &lt; 50% plus chronic respiratory failure</td>
<td>FEV₁/FVC &lt; 70%</td>
<td>Presence of chronic respiratory failure; Lung hyperinflation; Cyanosis; peripheral edema; Polycythemia; Hypoxemia and hypercapnea; Cor pulmonale (right heart failure)</td>
</tr>
</tbody>
</table>

### Key Messages:
- **Treating acute exacerbation (AE) episodes is not sufficient! Prevention and early treatment is critical!**
- **Spirometry** is essential for confirming the diagnosis of COPD (GOLD, 2007).
- **Smoking Cessation** is the single most effective intervention to reduce the risk of developing COPD and to slow its progression; however, other risk factors, such as occupational dusts and chemicals and indoor air pollution should also be taken into account (GOLD 2007).
- **Oxygen** administration long-term ≥ 15 hours/day has been shown to increase survival in patients with hypoxemia.
- **Pharmacotherapy** according to Stepwise Therapy can improve clinical outcomes.
- **Any patient with uncontrolled symptoms and or frequent exacerbations of COPD should be referred to pulmonary specialist.**
- **Pulmonary rehabilitation,** either through a home exercise program for mild disease or a hospital-based program for more advanced disease, is essential to decrease symptoms, exacerbations, and health care utilization.
- **Surgical options such as lung volume reduction surgery** can improve symptoms and prolong survival in appropriately selected patients.
- **Living Wills and Durable Powers of Attorney** are important to discuss with patients in the long-term management of COPD.

### Consequences of acute exacerbations:
- Negative impact on symptoms and quality of life (Seemungal 2000)
- Accelerated decline in FEV₁ (Donaldson et al. 2002)
- Increased mortality with exacerbations (Soler-Cataluna et al. 2005)
- Increased Health Resource Utilization and Direct Costs (Bourbeau et al. 2003)
Manage COPD with a **Stepwise approach** according to the severity classification. (GOLD, 2007)

Stepwise approach for managing COPD:

- Treatment for stable COPD should be reserved for patients who have respiratory symptoms and FEV$_1$ less than 60% predicted as documented by spirometry. (Qaseem et al. 2007).
- The Stepwise approach is meant to assist, not replace, the clinical decision making required to meet individual patient needs.
- COPD Severity Class is a guide for the treatment of COPD, but is not the absolute determinant; severity and persistence of symptoms, frequency of exacerbations and comorbid conditions must also be considered in the selection of optimal therapy.
- Provide patient education on self-management and controlling risk and environmental factors.
- Consultation with a pulmonary specialist may be indicated at any stage of the disease to:
  - Confirm the diagnosis
  - Facilitate tobacco cessation
  - Consideration of lung volume reduction or transplantation
  - Optimize treatment if disability progresses, symptoms are uncontrolled, or there are recurrent exacerbations.

### Therapy at Each Stage of COPD (GOLD 2007)

**Post Bronchodilator FEV$_1$ is recommended for the diagnosis and assessment of severity of COPD.**

<table>
<thead>
<tr>
<th>Stratification</th>
<th>I: Mild</th>
<th>II: Moderate</th>
<th>III: Severe</th>
<th>IV: Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV$_1$/FVC</td>
<td>FEV$_1$/FVC &lt; 70%</td>
<td>FEV$_1$/FVC &lt; 70%</td>
<td>FEV$_1$/FVC &lt; 70%</td>
<td>FEV$_1$/FVC &lt; 70%</td>
</tr>
<tr>
<td>FEV$_1$ ≥ 80% predicted</td>
<td>50% ≤ FEV$_1$ &lt; 80% predicted</td>
<td>30% ≤ FEV$_1$ &lt; 50% predicted</td>
<td>FEV$_1$ &lt; 30% OR FEV$_1$ &lt; 50% predicted</td>
<td>FEV$_1$ &lt; 30% OR FEV$_1$ &lt; 50% predicted</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Active reduction of risk factors; influenza vaccination</th>
<th>Add short-acting bronchodilator when needed</th>
<th>Pneumococcal vaccine for all COPD patients; ACIP recommends revaccination once ≥ 5 yrs after 1st dose</th>
<th>Add regular treatment with ≥ 1 long-acting bronchodilators (when needed). Add pulmonary rehabilitation.**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider adding</td>
<td>Add inhaled corticosteroids if repeated exacerbations</td>
<td></td>
<td></td>
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<tr>
<td>inhaled corticosteroid to long-acting bronchodilator(s) if:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Frequent exacerbations</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• Poor symptom control</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• Asthma overlap (Expert opinion – Dr. Frank Sciurba)</td>
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<tr>
<td>** Add long-term oxygen therapy for chronic respiratory failure**</td>
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<tr>
<td>** Consider surgical treatments (Lung-Volume Reduction Surgery [LVRS])***</td>
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</tr>
</tbody>
</table>
*Pulmonary Rehabilitation:
- Increase exercise capacity and conditioning.
- Improve quality of life,
- Reduce symptoms.
- Reduce exacerbations and hospitalizations.
- Presently there is still not sufficient evidence that it improves survival.
- Evidence-based clinical practice guidelines published in May 2007 issue of *Chest* recommending the following:
  ✓ Pulmonary rehabilitation should be implemented immediately following a hospital discharge.
  ✓ Long-term programs (12 weeks) that include a home maintenance program have more sustained benefits.
  ✓ Therapy should include a combination of aerobic and strength training to increase muscle strength and muscle mass.
  ✓ Inspiratory muscle training as part of a comprehensive pulmonary rehabilitation program may improve dyspnea, walking distance, and health-related quality of life scores, but multiple study limitations reduce the strength of this recommendation and do not clarify optimal selection of patients or regimens for IMT. (GOLD 2008) (Shoemaker et al.)
  ✓ Oxygen therapy should be used during all exercise for patients who have exercise-induced hypoxemia, but may also be used to increase the endurance of those who do not have exercise-induced hypoxemia during high-intensity workouts.
- Educational components on self-management and prevention/treatment of exacerbations should be included. (Barclay et al. 2007)

**Long-Term Oxygen Therapy:**
Use of long-term oxygen therapy (> 15 hours per day) should be based on waking PaO2 values.
- If PaO2 ≤ 55 mmHg or O2 sat < 88% on RA, with or without hypercapnia OR
- PaO2 between 55 mmHg and 60 mmHg or O2 sat of 88% if there is:
  ➢ Peripheral edema suggesting pulmonary hypertension;
  ➢ CHF;
  ➢ Polycythemia (Hct > 55%); or
  ➢ Other comorbidity such as mental status changes associated with hypoxemia.
- Resting hypoxemia should be treated with continuous, 24-hour therapy.

Lightweight portable devices are essential to optimize mobility.

***Lung Volume Reduction Surgery:** Appears to be beneficial when performed in carefully selected COPD patients and should be performed at CMS certified centers experienced in this procedure. Consider for patients with predominantly upper lobe emphysema and low lung function (FEV₁ less than 45% predicted and significant impairment in quality of life.) Patients should be referred to the LVRS coordinator (412 647-5266) for more detailed radiographic, cardiac, and exercise evaluation to determine candidacy. There is evidence of improved outcomes after LVRS, as follows:
- Increased PaO₂ and decreased use of supplemental oxygen with exercise, rest and sleep for up to 24 months post-procedure (GOLD 2009).
- Improved longevity, exercise tolerance and health related quality of life up to 4.3 years post procedure (Naunheim et al. 2006)
- Reduced frequency of COPD exacerbations and increased the time to first exacerbation. (GOLD 2008) (Washko et al.)

**Lung Transplantation:** Consider for COPD patients with very severe disease who meet criteria and have no contraindications to the surgery. Such patients should be referred to the UPMC Lung Transplant Center for evaluation.
Key Points about Pharmacotherapy Management of COPD:
- Inhaled therapy is preferable to systemic therapy. (GOLD 2007)
- Bronchodilator medications are central to the symptomatic management of COPD. They are given either on an as-needed basis for relief of persistent or worsening symptoms, or on a regular basis to prevent or reduce symptoms. (GOLD 2007)
- Principal bronchodilators include β2-agonists, anticholinergics, and methylxanthines used singly or in combination. (GOLD 2007)
- Albuterol is the preferred bronchodilator for acute symptoms because of its rapid onset of action.
- Long-acting inhaled bronchodilators (LABA), including nebulized formulations (GOLD 2009), are more effective and convenient than short-acting agents, (GOLD 2007) and they are associated with decreased frequency of exacerbations and increased quality of life.
- Tiotropium is more effective and convenient (once daily) and should replace the use of Ipratropium (four times daily) in moderate-severe stable COPD.
- Use of inhaled anticholinergic plus sympathomimetic bronchodilators can result in meaningful increases in lung function even in patients with moderate to severe COPD. (GOLD 2008)
- Most studies indicate that existing medications for COPD do not modify the long-term decline in lung function, but there is limited evidence that regular therapy with LABA, ICS, or both can reduce the decline in lung function (Celli et al. 2008).
- Treatment with long-acting anticholinergic drugs improve the effectiveness of pulmonary rehabilitation. (GOLD 2008)
- For Stage III: Severe COPD and Stage IV: Very Severe COPD and individuals with repeated exacerbations combination therapy may be synergistic:
  - Combining bronchodilators with different mechanisms and durations of action may improve efficacy and reduce the risk of side effects. (GOLD 2007)
  - For use in appropriately selected patients, inhaled corticosteroids combined with long-acting bronchodilators are more effective than either agent used alone; clinical trials have demonstrated this combination results in (Calverly et al. 2007):
    - Significant improvement in pre-dose bronchodilator and peak FEV1
    - Significant reduction in hospitalizations for COPD exacerbation
    - Significant improvement in quality of life scores
    - Trend toward, but not a significant reduction in, mortality from COPD
  - Adding Tiotropium to long-acting beta-agonists + inhaled corticosteroids may add further synergism from combined mechanisms of action (small airway bronchodilator + large airway bronchodilator + anti-inflammatory).
- Prescribe one of the following maintenance monotherapies for symptomatic patients with COPD and FEV1 less than 60% predicted: long-acting inhaled β-agonists, long-acting inhaled anticholinergics, or inhaled corticosteroids. (Qaseem et al. 2007)
- Consider combination inhaled therapies for symptomatic patients with COPD and FEV1 less than 60% predicted. (Qaseem et al. 2007)
- Inhaled corticosteroids alone or in combination products can increase the risk of pneumonia in COPD patients.
- Evidence for use of mucolytics in COPD is mixed and does not support routine use. Patients with very viscous sputum may receive limited benefit from mucolytics and there is circumstantial evidence they may reduce exacerbations in COPD patients who have not been treated with inhaled glucocorticosteroids. (GOLD 2008)
- Acute exacerbations of COPD should be treated early and aggressively with:
  - Oral antibiotics (IV if hospitalization requires)
  - Oral systemic steroids (IV if hospitalization required)
- Chronic treatment with systemic steroids should be avoided because of an unfavorable benefit to risk ratio.
### Pharmaceutical Interventions for Inhaled Agents and Dosing Information

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Drug Category</th>
<th>Dosing Information &amp; Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β₂ AGONIST</strong>&lt;br&gt;Short-acting</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Albuterol</td>
<td>Ventolin HFA®, Proventil HFA®, Proair HFA®</td>
<td>Short-acting β₂ agonist</td>
<td>2-4 puffs as needed every 4-6 hours</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>Xopenex HFA®</td>
<td>Short-acting β₂ agonist</td>
<td>2 puffs every 4-6 hours (theoretical benefits over Albuterol not demonstrated; 3rd line after Albuterol &amp; Ipratropium in COPD)</td>
</tr>
<tr>
<td>Albuterol + Ipratropium</td>
<td>Combivent®</td>
<td>Short-acting β₂ agonist + short-acting anticholinergic</td>
<td>2-4 puffs QID; greater bronchodilation effect than each alone, but similar effect probably achieved by doubling the dose of each drug</td>
</tr>
<tr>
<td><strong>β₂ AGONIST</strong>&lt;br&gt;Long-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Serevent Discus®</td>
<td>Long-acting β₂ agonist</td>
<td>1 puff BID; higher and longer bronchodilation effect than other β₂ agonists</td>
</tr>
<tr>
<td>Formoterol</td>
<td>Foradil®</td>
<td>Long-acting β₂ agonist</td>
<td>1 puff BID; similar to Salmeterol, but has quicker onset of action</td>
</tr>
<tr>
<td><strong>ANTICHOLINERGICS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium</td>
<td>Atrovent®</td>
<td>Short-acting anticholinergic</td>
<td>2-4 puffs QID; maintenance only, not PRN for acute symptoms</td>
</tr>
<tr>
<td>Tiotropium</td>
<td>Spiriva®</td>
<td>Long-acting anticholinergic</td>
<td>1 capsule inhaled daily; replaces Ipratropium</td>
</tr>
<tr>
<td><strong>INHALED CORTICOSTEROID</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>Qvar®</td>
<td>Inhaled Corticosteroid</td>
<td>1-8 puffs (40-320mcg) twice daily</td>
</tr>
<tr>
<td>Budenoside DPI</td>
<td>Pulmicort®</td>
<td>Inhaled Corticosteroid</td>
<td>1 – 8 puffs (180-1440 mcg) daily divided in 2 doses</td>
</tr>
<tr>
<td>Flunisolide</td>
<td>Aerobid®</td>
<td>Inhaled Corticosteroid</td>
<td>2 – 8 puffs (500 – 2000 mcg) daily divided in 2 doses</td>
</tr>
<tr>
<td>Fluticasone 44</td>
<td>Flovent 44®</td>
<td>Inhaled Corticosteroid</td>
<td>2 – 6 puffs (88 – 264 mcg) daily divided in 2 doses</td>
</tr>
<tr>
<td>Fluticasone 110</td>
<td>Flovent 110®</td>
<td>Inhaled Corticosteroid</td>
<td>2 – 16 puffs (220 – 1760 mcg) daily divided in 2 doses</td>
</tr>
<tr>
<td>Fluticasone 220</td>
<td>Flovent 220®</td>
<td>Inhaled Corticosteroid</td>
<td>2– 8 puffs (440– 1760 mcg) daily divided in 2 doses</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>Azmacort®</td>
<td>Inhaled Corticosteroid</td>
<td>8-16 puffs (600 – 1200 mcg) daily divided in 3 – 4 doses</td>
</tr>
<tr>
<td>Mometasone</td>
<td>Asmanex®</td>
<td>Inhaled Corticosteroid</td>
<td>1-2 puffs (220-440 mcg) once or twice daily</td>
</tr>
<tr>
<td>Generic Name</td>
<td>Brand Name</td>
<td>Drug Category</td>
<td>Dosing Information &amp; Comments</td>
</tr>
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<td>---------------------------------------------------------------------</td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>Alvesco®</td>
<td>Inhaled Corticosteroid</td>
<td>1-4 puffs (80mcg-320mcg) twice daily</td>
</tr>
<tr>
<td>Fluticasone 100 + Salmeterol 50</td>
<td>Advair 100/50®</td>
<td>Combination long-acting β₂ agonist + Inhaled Corticosteroid</td>
<td>1 puff (100 mcg Fluticasone + 50 mcg Salmeterol) every 12 hrs</td>
</tr>
<tr>
<td>Fluticasone 250 + Salmeterol 50</td>
<td>Advair 250/50®</td>
<td>Combination long-acting β₂ agonist + Inhaled Corticosteroid</td>
<td>1 puff (250 mcg Fluticasone + 50 mcg Salmeterol) every 12 hrs</td>
</tr>
<tr>
<td>Fluticasone 500 + Salmeterol 50</td>
<td>Advair 500/50®</td>
<td>Combination long-acting β₂ agonist + Inhaled Corticosteroid</td>
<td>1 puff (500 mcg Fluticasone + 50 mcg Salmeterol) every 12 hrs</td>
</tr>
<tr>
<td>Formoterol/ Budesonide</td>
<td>Symbicort®</td>
<td>Combination long-acting β₂ agonist + Inhaled Corticosteroid</td>
<td>2 puffs(80-160mg/4.5mg) twice daily</td>
</tr>
</tbody>
</table>

Oxygen Therapy:
- Long-term oxygen therapy (more than 15 hours per day) improves survival and quality of life in hypoxemic patients:
  - PaO₂ ≤ 55 mmHg/SaO₂ ≤ 88% on RA with or without hypercapnea **OR**
  - PaO₂ of 55-60 mmHg/SaO₂ of 88% with coexisting pulmonary hypertension, peripheral edema suggesting CHF, or polycythemia (Hct > 55%).
- Pulse oximetry is useful to monitor oxygen saturation and to adjust the oxygen flow setting.
- Titrate oxygen to a flow rate sufficient to maintain PaO₂ ≥ 60mmHg/SpO₂ ≥ 90% with exercise. (GOLD 2007)
- Consider overnight pulse oximetry and/or referral for sleep evaluation if nocturnal/sleep desaturation is suspected.
- ABG measurement should be considered to initiate oxygen therapy and/or to assess for hypercapnea in the following clinical circumstances:
  - Clinical suspicion of hypercapnea (asterixis, headache, hypersomnolence, altered mental status)
  - FEV₁ < 1.0
  - Morbid obesity
  - Excessive daytime somnolence
  - Right heart failure/cor pulmonale
  - Severe airflow obstruction

Brief Strategies to Help the Patient Willing to Quit Smoking:
- **ASK**: Systemically identify all tobacco users at every visit.
- **ADVISE**: Strongly urge all tobacco users to quit.
- **ASSESS**: Determine willingness to make a quit attempt.
- **ASSIST**: Aid the patient in quitting.
- **ARRANGE**: Schedule follow-up contact.

For additional information go to [www.upmchealthplan.com](http://www.upmchealthplan.com)

**Clinical practice guidelines** are designed to assist clinicians by providing a framework for the evaluation and treatment of patients.

**Additional Resources for UPMC Health Plan Members**
- **MyHealth Advice Line** is staffed by experienced Registered Nurses and is available 24/7 to provide telephone support to members. Call 1-866-918-1591. TTY/TDD users should call 1-866-918-1593.
Health Coach Programs provide intensive case management for members with specific chronic illnesses or conditions. The programs are built upon best practices and accepted clinical guidelines and include:

- Diabetes
- Asthma/COPD
- Cardiovascular
  - Heart failure
  - Coronary artery disease
  - Hypertension
  - Hyperlipidemia.
  - Behavioral Health

Members and providers can obtain additional information about the health coach programs by calling **1-866-778-6073**.

- Online interactive preventive health programs and resources are available in partnership with WebMD at [www.upmchealthplan.com](http://www.upmchealthplan.com).
  - MyHealth OnLine Tobacco Cessation Program
  - MyHealthOnLine Physical Activity Program
  - MyHealthOnLine Nutrition Program
  - MyHealthOnLine Weight Management Program
  - MyHealthOnLine Stress Management Program
  - MyHealthOnLine Emotional Health Program

Scientific Evidence Sources:


Bourbeau J. "Self-Management of Acute Exacerbations." Clinical Consensus on COPD, 2-3rd March 2007, Presentation. AE is to COPD what MI is to CAD! slide # 12.


Global Initiative for Chronic Obstructive Lung Disease; Institute for Clinical Systems Improvement Health Care Guidelines for Chronic Obstructive Pulmonary Disease (2007).

Global Initiative for Chronic Obstructive Lung Disease; Institute for Clinical Systems Improvement Health Care Guidelines for Chronic Obstructive Pulmonary Disease (2008).

Global Initiative for Chronic Obstructive Lung Disease; Institute for Clinical Systems Improvement Health Care Guidelines for Chronic Obstructive Pulmonary Disease (2009).


