Optimizing COPD Outcomes in Primary Care

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Learning Objectives

▪ Recognize the symptoms and risk factors for COPD, as well as the importance of early recognition and routine spirometry in at-risk patients

▪ Explain the impact of disease severity and patient symptoms, needs, and preferences in providing individualized treatment with goals of slowing the decline of lung function, providing symptomatic relief, and managing disease-related exacerbations

▪ Review the safety and efficacy of new and emerging therapeutic options for patients with COPD

▪ Apply comprehensive knowledge to appropriately educate and counsel patients with COPD
Chronic Obstructive Pulmonary Disease (COPD)

- Characterized by
  - Chronic airflow limitation
  - Increased inflammatory response of the airways
  - Due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases

COPD Symptoms

- Most common respiratory symptoms include:
  - Dyspnea
  - Cough and/or sputum production
  - Wheezing
  - Chest tightness
  - Chest congestion
  - Patients tend to underreport these symptoms


COPD Mortality

- FOURTH leading cause of death in the U.S.
  - Worse in rural areas
  - Women
  - American Indian populations
  - More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally
    - 120,000 deaths annually in U.S.
  - Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population

COPD Risk Factors

- Cigarette smoke
- Occupational dust and chemicals
- Environmental tobacco smoke (ETS)
- Indoor and outdoor air pollution

Genes | Infections | Socio-economic status

Aging Populations

COPD Economic Burden

- Direct costs of COPD are $32 billion
- Indirect costs $20.4 billion
- COPD exacerbations account for the greatest proportion of the total COPD burden
- Co-morbidities amplify health care costs and resource utilization

Early Diagnosis of COPD and Assessment Tools

Global Strategy for Diagnosis, Management and Prevention of COPD 2018

https://goldcopd.org

Diagnosis and Initial Assessment

Key Points

▪ Consider COPD in any patient with:
  ▪ Dyspnea
  ▪ Chronic cough or sputum production
  ▪ And/or a history of exposure to risk factors

▪ Spirometry is required to make the diagnosis

▪ Goals of COPD assessment to guide therapy are to determine the:
  ▪ Level of airflow limitation
  ▪ Impact of disease on the patient’s health status
  ▪ And risk of future events (such as exacerbations, hospital admissions, or death)


Diagnosis of COPD

SYMPTOMS
shortness of breath
chronic cough
sputum

EXPOSURE TO RISK FACTORS
tobacco
occupation
indoor/outdoor pollution

SPIROMETRY:
Required to establish diagnosis

### Assessment of Airflow Limitation: Spirometry

- Perform spirometry after administration of an adequate dose of a short-acting inhaled bronchodilator to minimize variability
- A post-bronchodilator \( \text{FEV}_1 / \text{FVC} < 0.70 \) confirms the presence of airflow limitation
- Compare values to age-related normal values when possible to avoid overdiagnosis of COPD in the elderly


### A Quick Note: Asthma-COPD Overlap Syndrome

- A subset of patients will have asthma-COPD overlap syndrome (ACOS)
- Has features of both asthma and COPD
- Represents persistent airflow limitation in patients >40 YO with either a history of asthma or large bronchodilator reversibility
- Affects about a quarter of patients with COPD and almost a third of patients who previously had asthma
- Patients with ACOS have
  - significantly worse respiratory symptoms
  - poorer quality of life
  - increased risk of exacerbations and hospital admissions
- Using treatments developed for asthma or COPD that target eosinophilic, neutrophilic, or paucigranulocytic airway inflammation may help

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### Spirometry Testing

- **CPT codes**
  - 94010: $32.84 (FEV1/FVC)
  - 94060: $56.65 (spirometry before and after bronchodilator)
  - 94375: $36.81 (flow loop)
  - 94620: $64.59 (pulmonary stress test)

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### CAPTURE Questionnaire

**COPD Assessment in Primary Care To Identify Undiagnosed Respiratory Disease and Exacerbation risk.**

<table>
<thead>
<tr>
<th>Please answer each question</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Have you ever lived or worked in a place with dirty or polluted air, smoke, second-hand smoke, or dust?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>2. Does your breathing change with seasons, weather, or air quality?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>3. Does your breathing make it difficult to do things such as carry heavy loads, shovel dirt or snow, jog, play tennis, or swim?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>4. Compared to others your age, do you tire easily?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>5. In the past 12 months, how many times did you miss work, school, or other activities due to a cold, bronchitis, or pneumonia?</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

Martinez FJ, et al. *Am J Respir Crit Care Med.* 2017;195(6);
Assessment of COPD
Refined ABCD Assessment Tool

When assessing risk always choose the HIGHEST risk according to GOLD grade or exacerbation history.
Assessment of COPD
Global Strategy for Diagnosis, Management and Prevention of COPD

- Assess symptoms with either:
  - COPD Assessment Test (CAT)
    - An 8-item health status impairment in COPD (http://catestonline.org)
  - mMRC Breathlessness Scale
    (Breathlessness Measurement using the Modified British Medical Research Council) (https://www.medcalc.com)

COPD Assessment Test (CAT)

Reproduced from: COPD Assessment Test Healthcare Professional User Guide
Classification of Severity of Airflow Limitation in COPD*

In patients with FEV₁/FVC < 0.70

*Based on Post-Bronchodilator FEV₁

Case Study: David

Spirometry Test Results*

- FEV₁
  - Pre-bronchodilator: 2.22 L (69%)  
  - Postbronchodilator: 243 L (76%)  
- FVC
  - Pre: 4.22 L (107%)  
  - Post: 4.45 L (113%)  
- FEV₁/FVC
  - Pre: 53%  
  - Post: 55%  
- CAT test: 12

*Based on Post-Bronchodilator FEV₁

GOLD 1  
Mild predicted  
FEV₁ > 80%

GOLD 2  
Moderate predicted  
50% < FEV₁ < 80%

GOLD 3  
Severe 50% predicted  
30% < FEV₁ < 50%

GOLD 4  
Very Severe predicted  
FEV₁ < 30% predicted

Change 9%

Change 5%
Assessment of COPD
Refined ABCD Assessment Tool

When assessing risk always choose the HIGHEST risk according to GOLD grade or exacerbation history.
Individualizing Treatment in COPD

OVERALL KEY POINTS (1 of 3):

- **Smoking cessation is key.** Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates
- The effectiveness and safety of **e-cigarettes as a smoking cessation aid is uncertain** at present
- **Pharmacologic therapy can reduce COPD symptoms**, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance
- **Each pharmacologic treatment regimen should be individualized** and guided by the severity of symptoms, risk of exacerbations, side-effects, comorbidities, drug availability and cost, and the patient’s response, preference and ability to use various drug delivery devices
- **Inhaler technique needs to be assessed regularly**
Evidence Supporting Prevention & Maintenance Therapy

OVERALL KEY POINTS (2 of 3):

▪ **Influenza vaccination** decreases the incidence of lower respiratory tract infections

▪ **Pneumococcal vaccination** decreases lower respiratory tract infections

▪ **Pulmonary rehabilitation** improves symptoms, quality of life, and physical and emotional participation in everyday activities

▪ **Long-term oxygen therapy** improves survival in patients with severe resting chronic hypoxemia

▪ In patients with stable COPD and resting or exercise-induced moderate desaturation, long-term oxygen treatment should not be prescribed routinely. However, individual patient factors must be considered when evaluating the patient’s need for supplemental oxygen

Evidence Supporting Prevention & Maintenance Therapy

OVERALL KEY POINTS (3 of 3):

▪ In patients with severe chronic hypercapnia and a history of hospitalization for acute respiratory failure, **long-term non-invasive ventilation may decrease mortality** and prevent re-hospitalization

▪ In select patients with advanced emphysema refractory to optimized medical care, **surgical or bronchoscopic interventional treatments may be beneficial**

▪ **Palliative approaches** are effective in controlling symptoms in advanced COPD
Optimizing COPD Outcomes in Primary Care

### Manage Stable COPD: Non-pharmacologic

Global Strategy for Diagnosis, Management and Prevention of COPD

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Essential</th>
<th>Recommended</th>
<th>Depending on local guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Smoking cessation (can include pharmacologic treatment)</td>
<td>Physical activity</td>
<td>Flu vaccination</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pneumococcal vaccination</td>
</tr>
<tr>
<td>B, C, D</td>
<td>Smoking cessation (can include pharmacologic treatment)</td>
<td>Physical activity</td>
<td>Flu vaccination</td>
</tr>
<tr>
<td></td>
<td>Pulmonary rehabilitation</td>
<td></td>
<td>Pneumococcal vaccination</td>
</tr>
</tbody>
</table>

### Therapeutic Options: COPD Medications

Global Strategy for Diagnosis, Management and Prevention of COPD

<table>
<thead>
<tr>
<th>Beta₂-agonists</th>
<th>Methylxanthines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting beta₂-agonists</td>
<td>Inhaled corticosteroids</td>
</tr>
<tr>
<td>Long-acting beta₂-agonists</td>
<td></td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Combination long-acting beta₂-agonists + corticosteroids in one inhaler</td>
</tr>
<tr>
<td>Short-acting anticholinergics</td>
<td>Systemic corticosteroids</td>
</tr>
<tr>
<td>Long-acting anticholinergics</td>
<td></td>
</tr>
<tr>
<td>Combination short-acting beta₂-agonists + anticholinergic in one inhaler</td>
<td>Phosphodiesterase-4 inhibitors</td>
</tr>
</tbody>
</table>
Pharmacologic Treatment Algorithms
Global Strategy for Diagnosis, Management and Prevention of COPD

Comparative Attributes of Inhalers Used for COPD: DPI's

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
<th>Clinical Pearls</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
</table>
| Advair Diskus | Fluticasone/Salmeterol | • Profiled with dose counter  
• Twice daily dosing  
• One strength 250/50 | ✗ No breath and actuation coordination needed | ✗ Need to be able to inhale deep with good force  
✗ Preparation steps could be challenging for patients with arthritis, low dexterity or poor grip strength |
| Spiriva Handihaler | Tiotropium Bromide      | • Need to insert capsule before each use  
• Once daily dosing | | |
| ProAir Respiclek | Albuterol              | | | |
| Arcapta Neohaler | Indacaterol            | • Need to insert capsule before each use.  
• Once daily dosing | | |
| Tudorza Pressair | Aclidinium Bromide       | Twice daily dosing | | |
### Comparative Attributes of Inhalers Used for COPD: DPI’s (cont’d)

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
<th>Clinical Pearls</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incruse Ellipta</td>
<td>Umecilidium</td>
<td>Once daily dosing</td>
<td>![Checkmark] Preloaded inhalers with dose counter</td>
<td>![Cross] Hard to read information on the inhaler</td>
</tr>
<tr>
<td>Breo Ellipta</td>
<td>Fluticasone furoate and Vilanterol</td>
<td>Once daily dosing</td>
<td>![Checkmark] Single step for preparation making it easier for patients with poor grip strength or dexterity.</td>
<td></td>
</tr>
<tr>
<td>Anoro Ellipta</td>
<td>Umecilidium and Vilanterol</td>
<td>Once daily dosing</td>
<td>![Checkmark] Has a unique ventilation system at the mouth piece which allows for a steadier inhalation</td>
<td>![Checkmark] Easy to read dose counter</td>
</tr>
</tbody>
</table>

### Comparative Attributes of Inhalers Used for COPD: Soft Mist

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
<th>Clinical Pearls</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spiriva Respimat (2.5)</td>
<td>Tiotropium Bromide</td>
<td>One daily dosing</td>
<td>![Checkmark] Slow moving mist, can breathe slower and more normal</td>
<td>![Cross] Hard to turn canister</td>
</tr>
<tr>
<td>Striverdi Respimat</td>
<td>Olodaterol</td>
<td>Two inhalations once daily</td>
<td>![Checkmark] Better efficacy for drug administration</td>
<td>![Cross] Difficult to read dose counter</td>
</tr>
<tr>
<td>Stiolto Respimat</td>
<td>Tiotropium Bromide and Olodaterol</td>
<td>Two inhalations once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combivent Respimat</td>
<td>Ipratropium bromide and Albuterol Sulfate</td>
<td>Only product for COPD exacerbation that uses Respimat technology</td>
<td>![Checkmark] One inhalation 4 times daily</td>
<td></td>
</tr>
</tbody>
</table>

Bronchodilators

- Mainstay of pharmacological treatment
  - Short (albuterol) and long acting (formoterol, salmeterol, aformoterol)
  - Improve emptying of lungs, exercise tolerance and reduce hyperinflation


Anticholinergics

- Ipratropium bromide (Atrovent HFA)
  - 2 inhalations 4x per day
  - Contraindication: peanut allergy
- Tiotropium bromide (Spiriva)
  - 1 inhalation once daily
  - Indicated to reduce exacerbations
- Ipratropium bromide/albuterol (Combivent)
  - 2 puffs 4x per day

### Aclidinium Bromide Inhalation Powder

- **Brand name:** Tudorza pressair  
  - Anticholinergic  
  - Long-acting antimuscarinic agent; inhibits M3 receptor at smooth muscle leading to bronchodilation  
- **Indications:**  
  - Long-term maintenance treatment of bronchospasm associated with COPD  
- **Studies:**  
  - 3 pivotal trials  
  - 3 and 6 month clinical trials  
- **One inhalation (400 mcg) BID**


### Fluticasone Furoate and Vilanterol

- **Brand name:** Breo Ellipta  
- **Class:**  
  - Inhaled corticosteroid (ICS)  
  - Long-acting beta-2 agonist (LABA)  
- **Indications:**  
  - Once daily options for the maintenance of COPD and to reduce exacerbations  
  - Now indicated for ASTHMA; age 12 and up  
- **Efficacy:**  
  - Statistical improvement in FEV$_1$  
  - Reduction in exacerbations

Fluticasone Furoate and Vilanterol

- One inhalation (100 mcg/25 mcg) once daily
- Contraindications:
  - Milk proteins
- Drug-drug interactions:
  - Strong CY3A4 inhibitors (ketoconazole)
    - Increased systemic corticosteroid and CV effects
  - MAOI’s, TCA’s (increased vilanterol)
  - BB’s (bronchospasm)
  - Diuretics (hypokalemia)


Umeclidinium/Vilanterol

- Brand name: Anoro Ellipta
- Class: LAMA/LABA
  - First in this combination class
  - Two bronchodilators
- Indications:
  - Adults with COPD
- Dosage:
  - One inhalation (62.5 mcg/25 mcg) once daily
- Precautions:
  - Paradoxical bronchospasm
  - Cardiovascular disease
  - Uncontrolled hypertension
  - Narrow angle glaucoma
- Efficacy trials:
  - Statistical improvement in FEV₁
  - No indication to reduce exacerbations at present

### Long-Acting $\beta_2$-Adrenergic Agonist

- **Olodaterol** (Striverdi Respimat)
  - Indication: COPD
  - NOT indicated for asthma
  - Dosage: two inhalations once daily
  - Competing with: vilanterol, formoterol, salmeterol


### LABA/LAMA

- **Tiotropium bromide & olodaterol** (Stiolto Respimat)
  - Indication: Once daily for COPD
  - Combination: LAMA and LABA
  - 2 puffs once daily
  - Not indicated for asthma or for acute exacerbations

Emerging Treatments

- Potential therapeutic targets including COPD-related proinflammatory mediators and signaling pathways
- Some investigational compounds target
  - mucus hypersecretion
  - pulmonary hypertension
  - glucocorticoid sensitivity
- Large retrospective cohort study of COPD patients with diabetes found that the peroxisome proliferator-activated receptor γ (PPARγ) agonists rosiglitazone and pioglitazone with reduced COPD exacerbation rates
- Remember Asthma-COPD Overlap Syndrome: Subgroup identification may become more important


Long-term Oxygen Therapy

- Goal: Ensure adequate oxygen delivery to the vital organs by increasing the baseline PaO₂ at rest to
  \[ \text{PaO}_2 \geq 60 \text{ mm Hg at sea level and/ or producing a SaO}_2 \geq 90\% \]
- Indications to initiate long-term (> 15 hours/day) oxygen therapy:
  - PaO₂ < 55 mm Hg or SaO₂ < 88% with or without hypercapnia
  - PaO₂ 55-59 mm Hg or SaO₂ = 89% in the presence
    - cor pulmonale
    - right heart failure
    - polycythemia (hct> 56%)

Pulmonary Rehabilitation

- Exercise training
- Nutrition counseling
- Education
- Conducted over 6 weeks
- Improves exercise performance and reduces dyspnea (no improvement on FEV₁)


Surgery

- Bullectomy
- Lung Volume Reduction Surgery
- Lung Transplant Surgery

Exacerbations
Global Strategy for Diagnosis, Management and Prevention of COPD

An exacerbation of COPD is:

“An acute event characterized by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.”

- Classified as:
  - **Mild** (treated with short acting bronchodilators only, SABDs)
  - **Moderate** (treated with SABDs plus antibiotics and/or oral corticosteroids) or
  - **Severe** (patient requires hospitalization or visits the emergency room)
    Severe exacerbations may also be associated with acute respiratory failure


Exacerbations
Global Strategy for Diagnosis, Management and Prevention of COPD

- Most common causes
  - Viral upper respiratory tract infections
  - Infection of the tracheobronchial tree

Diagnosis relies exclusively on the patient’s clinical presentation (complaint of acute change of symptoms beyond normal day-to-day variation)

- Treatment goals:
  - Minimize the impact of the current exacerbation
  - Prevent the development of subsequent exacerbations

Management of Exacerbations
Global Strategy for Diagnosis, Management and Prevention of COPD

- **Oxygen** Titrate to improve the patient’s hypoxemia with a target saturation of 88-92%
- **Bronchodilators** Short-acting inhaled beta₂-agonists with or without short-acting anticholinergics are usually preferred
- **Systemic corticosteroids and antibiotics can**
  - Shorten recovery time
  - Improve lung function (FEV₁) and arterial hypoxemia (PaO₂)
  - Reduce the risk of early relapse, treatment failure, and length of hospital stay
  - A dose of 30-40 mg prednisolone per day for 5-7 days is recommended; antibiotics for no more than 5-7 days


Management of Exacerbations: Antibiotics
Global Strategy for Diagnosis, Management and Prevention of COPD

- Antibiotics should be given to patients with three cardinal symptoms:
  1. Increased dyspnea
  2. Increased sputum volume and
  3. Increased sputum purulence
- Who require mechanical ventilation

Management of Exacerbations: Antimicrobials
Global Strategy for Diagnosis, Management and Prevention of COPD

Prescribe antimicrobials to

- Patients with 3 cardinal symptoms:
  1. Increased dyspnea
  2. Increased sputum volume and
  3. Increased sputum purulence
- Individuals with 2 cardinal symptoms of COPD if one of the symptoms is increased purulence of sputum
- Individuals requiring hospitalization


Management of Exacerbations: Ventilation
Global Strategy for Diagnosis, Management and Prevention of COPD

- Non-invasive mechanical ventilation should be used first in COPD patients with acute respiratory failure who have no absolute contraindication
  - Improves gas exchange
  - Reduces work of breathing and the need for intubation
  - Decreases hospitalization duration
  - Improves survival
- Following an exacerbation, appropriate measures for exacerbation prevention should be initiated (see GOLD 2018 Chapter 3 and Chapter 4)
### Antimicrobial Therapy

**Mild to Moderate Exacerbations**

Antimicrobial therapy may not be indicated. If prescribed, consider spectrum of antimicrobial activity and side effects.

If prescribed, use one of the following:
1. Amoxicillin 875 mg BID x 5 – 7 days
2. TMP-SMX DS BID x 5 – 7 days
3. Doxycycline 100 mg BID x 5 - 7 days
4. Cephalosporin (cefdinir, cefpodoxime, cefuroxime)

**More Moderate - Severe Exacerbations**

Severe: hospital admission

Use one of the following:
1. Amoxicillin-clavulanate 875 mg BID x 5 – 7 days
2. Cephalosporin: 2nd – 3rd generation
3. Azithromycin or clarithromycin
4. Respiratory fluoroquinolone (moxifloxacin or levofloxacin)

### Manage Exacerbations: Indications for Hospital Admission

- Marked increase in symptom intensity
- Severe underlying COPD
- Onset of new physical signs
- Failure of an exacerbation to respond to initial medical management
- Presence of serious comorbidities
- Frequent exacerbations
- Older age
- Insufficient home support
Importance of Patient Education and Counseling in COPD Management

Unmet Patient Needs

Understanding of disease  Symptoms
Physical limitations  Emotional distress
Social isolation  Concerns about the future
Patient Education

- Comorbidities are common
  - Assess and educate
  - Watch for anxiety, depression, and isolation
- Proper inhaler technique
  - Evaluate with EVERY office visit
- Consider switching treatment modalities
  - Inhalers vs. nebulizers

Patient Lifestyle Modifications

- Smoking cessation
  - Couple with disease education
  - Individualize approach
    - Motivations
    - Treatment options
- Vaping
  - Is it better than smoking?
- Pulmonary Rehab
  - Improves lung function
  - May decrease $O_2$ necessity
Concerns About the Future

- People who have COPD understandably worry about their future, suffering, loss of independence, missing family milestones, and death
- Patients find comfort in and appreciate many different things, including good doctors, belief in God, medical advancements, having made plans for death, and family
- Many patients actively look for ways to improve their situations
  - Help patients connect to resources including psychological counseling
- Take a 360°, multidisciplinary approach to COPD, and ensure that patients have community linkages and receive constant, repetitive reinforcement of important messages

Summary

- COPD is a major cause of mortality and morbidity around the world
- Exacerbations and comorbidities contribute to the overall severity in individual patients. COPD is highly symptomatic disease
- Patients are plagued with progressive fatigue, dyspnea, depression, anxiety, insomnia that eventually require symptom-based palliative treatments
- Inhalers have been widely used in COPD for more than 60 years. They remain the cornerstone of treatment
- COPD patients reap considerable benefit from pulmonary rehabilitation (which is the most effective therapeutic strategy) to improve shortness of breath, health status and exercise tolerance
- Clinicians must educate and re-educate patients about their COPD and its management at every opportunity