COPD Treatment
From the Office to the Hospital

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Disclosures

• Speakers’ Bureau for Astrazeneca Pharmaceuticals
Objectives

- Definition of COPD
- COPD Diagnosis
- Treatment of Stable COPD
- Treatment of COPD Exacerbations
Definition of COPD

A common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients.
COPD & Smoking Cessation

FEV₁ (% of value at age 25)

Smoked regularly and susceptible to its effects

Never smoked or not susceptible to smoke

Stopped smoking at 45

Stopped smoking at 65

Symptoms

Disability

Death

Age (years)

Fletcher C and Peto R. BMJ. 1977;1:1645-1648
Patient Case

• 67 y/o former smoker seen by his internist for increasing DOE and cough with mild sputum production. He c/o some mild wheezing. He estimates he can walk ~ 1 mile, but when he encounters hills or stairs, his dyspnea is worse. He is winded after one flight of stairs.

• Vitals: T 37.1° C, BP145/89, RR 14/min, HR 89, regular, O2 sat 92% on room air

• Exam reveals comfortable-appearing moderately overweight man. His thoracic excursion is slightly limited, mostly due to his body habitus. Lung auscultation reveals mildly reduced breath sounds without audible wheezes.
Diagnosis

- Symptoms and signs help you suspect COPD

- Diagnosis is made by spirometry with history
FEV1/FVC Ratio

- Hallmark of obstruction is decreased FEV1/FVC ratio
- Fixed FEV1/FVC ratio may lead to over-diagnosis in older patients and under-diagnosis in younger patients
- Reference equations should be used
## Spirometry

<table>
<thead>
<tr>
<th>Test</th>
<th>Reference</th>
<th>Confidence Interval</th>
<th>Pre-Meas</th>
<th>Pre-%Ref</th>
<th>Post-Meas</th>
<th>Post-%Ref</th>
<th>Post-%Chg</th>
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<tbody>
<tr>
<td>FVC</td>
<td>3.91</td>
<td>0.93</td>
<td>(2.58)</td>
<td>(66)</td>
<td></td>
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<tr>
<td>FEV1</td>
<td>2.75</td>
<td>0.79</td>
<td>(1.42)</td>
<td>(52)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC%</td>
<td>71</td>
<td>10</td>
<td>(55)</td>
<td></td>
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<td>PEF</td>
<td>6.86</td>
<td>2.32</td>
<td>5.66</td>
<td>82</td>
<td></td>
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<tr>
<td>FET100%</td>
<td></td>
<td></td>
<td>12.59</td>
<td></td>
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<td>FIVC</td>
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<td></td>
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<td>FVL ECode</td>
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<td></td>
<td>000000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Flow vs. Volume Graph:

- **PRE**: 
- **POST**: 

The University of Mississippi Medical Center

Education • Research • Healthcare
What is His COPD Severity?

1. Mild
2. Moderate
3. Severe
4. Very severe
COPD Classification of Severity

GOLD 1: Mild, FEV1 \(\geq 80\%\)

GOLD 2: Moderate, FEV1 50-80%,

GOLD 3: Severe, FEV1 30-50%,

GOLD 4: Very Severe, FEV1 <30%

FEV1/FVC < 70% in all above patients
Management of Stable COPD

- Drug Treatment
- Non-pharmacological treatments
Goals of Treatment

• Reduce Symptoms
  – Relieve symptoms
  – Improve exercise tolerance
  – Improve health status

• Reduce Risk
  – Prevent disease progression
  – Prevent and treat exacerbations
  – Reduce mortality
COPD Treatment Approach

- The overall approach to managing stable COPD characterized by a stepwise increase in the treatment, depending on the severity of the disease.

- None of the existing medications for COPD has been conclusively shown to modify the long-term decline in lung function that is the hallmark of this disease.

- Therefore, medications for COPD used to decrease symptoms and/or complications.
Patient Education

- Smoking cessation – reduce risk factors
- General outlook on life
- Proper use of inhalers
- Inhalers or nebulizer
- Dyspnea -- how to regard it and how to control it
- Exercise and pulmonary rehabilitation
- Home oxygen
- Health education can play a role in improving skills, ability to cope with illness, and health status
Bronchodilators

Bronchodilator medications central to symptom management in COPD

Choice between Beta\textsubscript{2}-agonist, anticholinergic, theophylline or combination therapy depends on availability and individual response in terms of symptoms relief and side effects

Bronchodilators (II)

- Bronchodilators prevent or reduce symptoms

- Long-acting inhaled bronchodilators more convenient

- Combining bronchodilators may improve efficacy and decrease the risk of side effects compared to increasing the dose of a single bronchodilator

Long-Acting Beta Agonists (LABA)

- 12-24 hours in duration of action allowing once twice daily dosing
  - Salmeterol, formoterol, indacaterol, olodaterol, vilanterol, arfomoterol

- Nebulized LABA
  - Arformoterol and formoterol
Anticholinergics

✧ Short acting (ipratropium) – Every 6-8 hours

✧ Long acting anticholinergics (LAMA) – Every 12 – 24 hours
  ✧ Aclidinium, glycopyrrolate, tiotripium, umeclidinium,
Theophylline

- Nonselective PDE inhibitor
- Modest bronchodilator effect compared to placebo
- Low dose reduces exacerbations
- Not recommended routinely unless other long acting bronchodilators are unavailable or unaffordable
Combination Bronchodilators

- SABA plus SAMA greater improvement in FEV₁ and symptoms than either drug alone
- LABA plus LAMA show significant increase in FEV1
  - More time to patient review outcomes

Inhaled Corticosteroids (ICS)

- Improve symptoms, lung function, and QOL and reduces frequency of exacerbations in those with FEV1 < 60% predicted
- Increased risk of pneumonia
- Long term monotherapy not recommended – less effective than combined LABA + ICS

LABA + ICS

- Improves lung function and health status and reduces exacerbations in moderate and severe COPD
- No difference in efficacy of once daily vs twice daily
- More triple therapy studies needed (LAMA, LABA, ICS)

PDE-4 Inhibitors

- Roflumilast (Daliresp®)
- Inhibits breakdown of intracellular cAMP
- Decreases neutrophil and eosinophils in sputum
- Not useful in acute exacerbations
- Don’t use in moderate to severe hepatic disease or in combination with theophylline
- Common side effects
  - Diarrhea, weight loss, nausea
- Decreases moderate to severe exacerbations by 15-18% in chronic bronchitis patients with severe COPD and at risk of exacerbations
<table>
<thead>
<tr>
<th>Statement</th>
<th>Score Options</th>
<th>Additional Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>I never cough</td>
<td>0 1 2 3 4 5</td>
<td>I cough all the time</td>
</tr>
<tr>
<td>I have no phlegm (mucus) in my chest at all</td>
<td>0 1 2 3 4 5</td>
<td>My chest is completely full of phlegm (mucus)</td>
</tr>
<tr>
<td>My chest does not feel tight at all</td>
<td>0 1 2 3 4 5</td>
<td>My chest feels very tight</td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am not breathless</td>
<td>0 1 2 3 4 5</td>
<td>When I walk up a hill or one flight of stairs I am very breathless</td>
</tr>
<tr>
<td>I am not limited doing any activities at home</td>
<td>0 1 2 3 4 5</td>
<td>I am very limited doing activities at home</td>
</tr>
<tr>
<td>I am confident leaving my home despite my lung condition</td>
<td>0 1 2 3 4 5</td>
<td>I am not at all confident leaving my home because of my lung condition</td>
</tr>
<tr>
<td>I sleep soundly</td>
<td>0 1 2 3 4 5</td>
<td>I don’t sleep soundly because of my lung condition</td>
</tr>
<tr>
<td>I have lots of energy</td>
<td>0 1 2 3 4 5</td>
<td>I have no energy at all</td>
</tr>
</tbody>
</table>

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## The MRC Breathlessness Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Degree of breathlessness related to activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not troubled by breathlessness except on strenuous exercise</td>
</tr>
<tr>
<td>2</td>
<td>Short of breath when hurrying on the level or walking up a slight hill</td>
</tr>
<tr>
<td>3</td>
<td>Walks slower than most people on the level, stops after a mile or so, or stops after 15 minutes walking at own pace</td>
</tr>
<tr>
<td>4</td>
<td>Stops for breath after walking about 100 yds or after a few minutes on level ground</td>
</tr>
<tr>
<td>5</td>
<td>Too breathless to leave the house, or breathless when undressing</td>
</tr>
<tr>
<td>Patient Category</td>
<td>Characteristics</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>A</td>
<td>Low risk, less symptoms</td>
</tr>
<tr>
<td>B</td>
<td>Low risk, more symptoms</td>
</tr>
<tr>
<td>C</td>
<td>High risk, less symptoms</td>
</tr>
<tr>
<td>D</td>
<td>High risk, more symptoms</td>
</tr>
</tbody>
</table>
Patient Case

71 y/o COPD patient who quit smoking 2 years ago comes in complaining of worsening dyspnea on exertion. Further discussion reveals that when he takes his inhaler every 6 hours prn, he does well for a few hours, but then it seems to wear off. He coughs when he gets a cold and has been treated for bronchitis twice in the past year. Physical exam and CXR are unremarkable. His FEV1 is 48% predicted and his FEV1/FVC ratio is 55%.

What changes in his medications do you make?

a) Order a home nebulizer
b) Add Advair®, Symbicort®, Breo®, Spiriva®, Tudorza®, Anoro®, or Stioloto®
c) Give him a tapering dose of oral prednisone
d) Order home oxygen PRN dyspnea
Group A Patients

- Few symptoms and low risk of exacerbations
- Gold Class 1 & 2
- First choice
  - Short-acting bronchodilator prn
- 2\textsuperscript{nd} choice
  - LABA, LAMA, or SABA+SAMA

Group B Patients

- More symptoms but low risk of exacerbations
- Gold Class 1 & 2
- First choice
  - LABA or LAMA
- 2nd choice (severe breathlessness)
  - LABA+LAMA
- Alternative choice
  - Short-acting bronchodilators, Theophylline

Group C Patients

- Few symptoms but high risk of exacerbations
- Gold Class 3 & 4
- First choice
  - ICS + LABA or LAMA
- 2nd choice
  - LABA+LAMA
- Alternative choice
  - PDE-4 inhibitor, Short-acting bronchodilators, Theophylline

Group D Patients

• More symptoms and high risk of exacerbations
• Gold Class 3 & 4
• First choice
  – ICS + LABA or LAMA
  – PDE-4 with bronchodilator (chronic bronchitis)
• 2nd choice
  – LABA+ICS+LAMA
  – PDE-4 with bronchodilator (chronic bronchitis)
• Alternative choice
  – Short-acting bronchodilators, Theophylline

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>First Choice</th>
<th>Second Choice</th>
<th>Alternative Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SABA prn or SAMA prn</td>
<td>LABA or LAMA or SABA + SAMA</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>LABA or LAMA</td>
<td>LAMA + LABA</td>
<td>SABA and/or SAMA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Theophylline</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA + LABA</td>
<td>PDE-4 inhibitor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SABA and/or SAMA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Theophylline</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA or LAMA</td>
<td>ICS + LAMA or ICS + LABA + LAMA or ICS + LABA + PDE-4 inhibitor or LAMA + LABA or LAMA + PDE-4 inhibitor</td>
<td>Carbocysteine</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>SABA and/or SAMA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Theophylline</td>
</tr>
</tbody>
</table>

ICS, inhaled corticosteroid; LABA, long-acting β₂-adrenergic agonist; LAMA, long-acting muscarinic antagonist (anticholinergic); PDE-4, phosphodiesterase-4; SABA, short-acting β₂-adrenergic agonist; SAMA, short-acting muscarinic antagonist.
Patient Case

70 y/o with severe COPD comes in complaining of progressive dyspnea. He was hospitalized and treated two weeks ago because of a COPD exacerbation. Since discharge he notices he can’t walk 50 yards to the mailbox because of dyspnea. He wants oxygen for home use. He smokes one pack of cigarettes daily.

What do you do next?
1. Prescribe oxygen at 2 liters continuously
2. Obtain RA O2 sat and prescribe oxygen only if sat or 88% or less
3. Tell him that starting pulmonary rehabilitation within 6 weeks of an exacerbation is too dangerous to do at this time.
4. Tell him yearly flu vaccines won’t decrease exacerbation risk
Home Oxygen

- Long-term oxygen (> 15 hours per day) to patients with chronic respiratory failure has been shown to increase survival.

- Indications for Home O2
  - PaO2 of 55 or less or SaO2 of 88% or less
  - PaO2 of 56-59 or SaO2 of 89% AND:
    - Cor pulmonale
    - Erythrocytosis (Hct > 55%)
Other Indication for Home Oxygen

• During Exertion
  – Reduction in PaO2 to 55 mmHg or less
  – Reduction in SaO2 to 88 percent or less

• Can be obtained during 6 minute walk test

• Document room air O2 sat, O2 sat during exertion, and O2 sat on oxygen at what flow
Pulmonary Rehabilitation

• Improves exercise capacity

• Reduces perceived intensity of breathlessness and anxiety and depression associated with COPD

• Improves health-related quality of life

• Reduces number of hospitalizations and days in hospital

• Early outpatient pulmonary rehab after hospitalization for an exacerbation safe and results in significant improvements in exercise capacity and health status at 3 months
Home Nebulizers

• Who needs a nebulizer
  – Patients with coordination problems
    ▪ Very old
    ▪ Very young
  – Hand problems/arthritis
  – Bronchospasm with MDI use
  – Very severe COPD (FEV1 < 30%)
COPD Exacerbation

• 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 warrants a change in regular medication in a patient with underlying COPD.
Exacerbations Drive Disease Progression

Patients with frequent exacerbations

- Lower quality of life
- Increased inflammation
- Faster disease progression
- Increased risk of recurrent exacerbations
- Increased likelihood of hospitalization
- Increased mortality rate

Patient Question
Which of the following statements is correct concerning COPD exacerbations?

1. No change in mortality after ED visits for COPD exacerbation

2. Mortality increases in COPD patients after admission for COPD exacerbation with hypercapnia.

3. No change in mortality with increased frequency of COPD exacerbations

4. No change in mortality with increased severity of COPD exacerbations.
AECOPD and Increased Mortality

Prospective cohort of 1016 adult patients with exacerbation of COPD and hypercapnia

<table>
<thead>
<tr>
<th>Hospital Stay</th>
<th>60 days</th>
<th>180 days</th>
<th>1 year</th>
<th>2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>11%</td>
<td>20%</td>
<td>33%</td>
<td>43%</td>
<td>49%</td>
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</tbody>
</table>

Who Is at Risk for Exacerbation?

- Increased age
- Severity of airway obstruction (FEV$_1$ impairment)
- Chronic bronchial mucous hypersecretion
- Longer duration of COPD
- Productive cough and wheeze
- Elevated cough and sputum
- Antibiotic or systemic corticosteroid use in the past year
- Prior use of medications for COPD
- Bacterial colonization
- Comorbid conditions (eg, cardiovascular disease)
- Poor health-related quality of life


Exacerbation Frequency Increases With Disease Severity

Results based on a cross-sectional observational study of ambulatory COPD patients in Spain. General practitioners (N=201) between October 1994 and May 1995 completed a questionnaire on COPD characteristics of 1001 patients.

Mortality Following ED Visit for COPD Exacerbation

- 5% at 30 Days
- 9% at 60 Days
- 11% at 90 Days
- 16% at 180 Days
- 23% at 1 Year
- 32% at 2 Years
- 39% at 3 Years

Antibiotics in Exacerbations

Antibiotics should be given to patients who:

- Have 3 cardinal symptoms:
  - Increased dyspnea
  - Increased sputum volume
  - Increased sputum purulence
- Require mechanical ventilation (invasive or non-invasive)
- 2 of 3 if one is sputum purulence
Systemic Steroids

- Chronic treatment with systemic corticosteroids should be avoided because of an unfavorable benefit-to-risk ratio.

- A 2-week tapering of oral steroids is as effective as a 6 week taper with less side effects.

- 5 days may be enough.
68 y/o patient with very severe COPD with FEV1 of 30% predicted c/o increased purulent sputum, increased dyspnea, and increased sputum volume. He has received steroids and antibiotics 3 times this year for COPD exacerbations.

- Which antibiotic should you prescribe for his COPD exacerbation?
  A. Macrolide
  B. Doxycycline
  C. Quinolone with anti-pseudomonal activity
  D. 2nd or 3rd generation cephalosporin
Management of AECOPD: Bacteria

I. Uncomplicated AECOPD
- Age < 65 years
- FEV\textsubscript{1} > 50% predicted
- < 4 AECOPDs/yr
- No comorbidity

II. Complicated AECOPD
- Age > 65 years
- FEV\textsubscript{1} < 50% predicted
- > 4 AECOPDs/year
- Comorbidity
- Abx use in past 3 months

Complicated AECOPD at Risk for Pseudomonas
- FEV\textsubscript{1} < 35% predicted
- Recurrent antibiotics
- Recurrent steroid courses
- Bronchiectasis

Group I plus
Other Gram negative enteric bacilli
Increased beta-lactam resistance

Group II plus
\textit{P. aeruginosa}

\textit{H. influenzae}
\textit{S. pneumoniae}
\textit{M. catarrhalis}
\textit{H. parainfluenzae}
Viral pathogens
\textit{M. pneumoniae}
\textit{C. pneumoniae}

Management of AECOPD: Antibiotics

I. Uncomplicated AECOPD
- Age < 65 years
- FEV$_1$ > 50% predicted
- < 4 AECOPDs/year
- No comorbidity

II. Complicated AECOPD
- Age > 65 years
- FEV$_1$ < 50% predicted
- > 4 AECOPDs/year
- Comorbidity
- Abx use in past 3 months

III. Complicated AECOPD at Risk for Pseudomonas
- FEV$_1$ < 35% predicted
- Recurrent antibiotics
- Recurrent steroid courses
- Bronchiectasis

Macrolide
- Doxycycline
- 2nd or 3rd generation
- Cephalosporin
- Respiratory quinolone

Respiratory quinolone
- Amoxicillin/clavulanate

Quinolone with anti-pseudomonal activity

Patient Case

- 65 y/o woman admitted to the ICU with COPD exacerbation. ABG 7.15/78/68 on 50% FiO2. Bipap 10/4 cm H20 with FiO2 50% is initiated. An hour later, her blood pressure drops from 140/85 to 110/60 mmHg. She is more lethargic on exam with O2 sat of 89%. She has T-wave inversions in anterior leads on EKG. Which of the following is the next step in her management?

1. Recheck an ABG
2. Increase O2 to maintain saturation of 92% or higher
3. Increase the expiratory setting by 5 cm H20
4. Intubate and provide mechanical support
5. Increase the inspiratory pressure setting by 3 cm H20.
NonInvasive Ventilation (NIV)

• Improves respiratory acidosis, reduces respiratory rate, severity of dyspnea, complications, ventilator associated pneumonia, and length of hospital stay

• Decreases mortality and need for intubation
Contraindications to NIV

- Respiratory Arrest
- Severe acid-base abnormalities
- Hemodynamic instability
- GI bleeding
- Acute myocardial ischemia or uncontrolled arrhythmias
- Inability to protect airway
- Excessive secretions
- Recent upper airway or GI surgery
- Uncooperative or agitated patient
Invasive Mechanical Ventilation

- Unable to tolerate NIV or NIV failure
- Severe dyspnea with use of accessory muscles and paradoxical abdominal motion
- Life-threatening hypoxemia
- Severe acidosis or hypercapnia
- Respiratory arrest
- Somnolence, impaired mental status
- Cardiovascular complications (hypotension, shock)
- Other complications (metabolic abnormalities, sepsis, pneumonia, pulmonary embolism, barotrauma, massive pleural effusion)

Influenza Vaccination

• Inactivated influenza vaccine reduces exacerbations in COPD patients

• The magnitude of this benefit due to reduction in exacerbations occurring ≥ 3 weeks after vaccination and due to influenza

• There is a mild increase in transient local adverse effects with vaccination, but no evidence exists of an increase in early exacerbations
Treating and preventing exacerbations are key goals in COPD disease management.

The goal of treatment is to minimize the impact of the current exacerbation and to prevent the development of subsequent exacerbations.

Infections are the predominant cause of exacerbations. Risk stratification is an appropriate approach to antibiotic choice in AECOPD.

Corticosteroids and NIV are useful in AECOPD.

Exacerbations can be prevented, multiple non-pharmacologic and pharmacologic interventions should be implemented especially in high-risk individuals.
Summary

- COPD characterized by airflow limitation
- Life prolonging measures
  - Stop smoking and oxygen for appropriate patients
- Pharmacotherapy
- Non-pharmacologic therapy
  - Pulmonary rehabilitation
- Yearly Influenza vaccine can decrease serious illness and death by about 50% in COPD patients
- Pneumococcal vaccine