COPD 2020 Update

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MUSC

Disclosures

Consultant: AstraZeneca, CSL Behring, GlaxoSmithKline, Grifols, Inc, Uptake Medical

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Advisory Board: Vertex

Reference
Learning Objectives

1. Understand that COPD is a disease of the aging lung
2. Understand the definition and treatment of a COPD exacerbation
3. Define therapies that change outcomes in COPD

Current Definition of COPD

Chronic Bronchitis $\rightarrow$ Emphysema

COPD

Airflow Obstruction

Asthma

COPD in 2020

- 15 million Americans diagnosed
- Estimates suggest 12 million more undiagnosed
- 70% of COPD sufferers are in workforce
- COPD is now 2\textsuperscript{nd} leading cause of disability in US
- COPD is now 4\textsuperscript{th} leading cause of death in US
- Cost of care now over 50 billion dollars a year

What Did the BRFSS Tell Us?

- Prevalence in 18 and up age group: 6.1%
- Prevalence in 45 and up age group 9.0%
- Women reported higher COPD rates: 6.5% vs 5.3%
- 24.9% of those with COPD never smoked
- 43.2% saw physician re COPD in last year
- 17.7% ER visit or hospitalization in last year
COPD is My Favorite Disease to Treat.

• True, the challenge of multiple co-morbidities and long term nature of disease care is the reason I became a healthcare practitioner

• False, this is a challenging disease with frequent crises, ungrateful patients, and smoking addiction.
Cigarette Smoking- A Leading Cause of Preventable Death

MMWR 2008;57(45):1226–1228.

Spirometry

Volume Liters

FEV1

Normal

Obstruction

Restriction

FVC

Seconds

0 1 2 3 4 5 6

0 1 2 3 4 5 6
Spirometry Interpretation

- **FEV1/FVC < 0.70**
  - Obstruction
  - FEV1
  - Very Severe <30%
  - Severe 30-50%
  - Moderate 50-80%
  - Mild >80%
  - GOLD Stage: IV III II I

- **FEV1/FVC ≥ 0.70**
  - FVC < 80% Predicted
  - Probable Restriction

Comparison Between HTN and COPD

- **Hypertension**
  - Surrogate Marker:
  - Blood Pressure 140/80

- **COPD**
  - Surrogate Marker
  - FEV1/FVC < 0.7

Outcomes

- Angina
- MI
- Stroke
- CHF
- Dyspnea
- Exacerbations
- Respiratory Failure
Underdiagnosis of COPD

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-44</td>
<td>5.2%</td>
</tr>
<tr>
<td>45-54</td>
<td>7.2%</td>
</tr>
<tr>
<td>55-64</td>
<td>14.0%</td>
</tr>
<tr>
<td>65-74</td>
<td>20.7%</td>
</tr>
<tr>
<td>≥75</td>
<td>22.9%</td>
</tr>
</tbody>
</table>

Diagnosed with COPD

GOLD stage II or higher

Mannino DM, MMWR 2002; 51:1-16

CAPTURE™

For each question, place an X in the box with the answer that is best for you. There are no right or wrong answers, only answers which are right for you.

<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>

*COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease & Exacerbation Risk*
A Smoking Patient with Wheezing on Examination will Accurately be Diagnosed with COPD Without Spirometry

1. True, there are few alternative diagnoses and the medications have few side effects
2. False, there are many alternative diagnoses and therapy is lifelong and expensive.

Emphysema

Normal bronchiole and alveoli

Emphysema
Centrilobular

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Airflow Limitations in COPD

Chronic Obstructive Pulmonary Disease

Mucus hypersecretion (luminal obstruction)
Disrupted alveolar attachments (emphysema)
Mucosal and peribronchial inflammation and fibrosis (obliterative bronchiolitis)


Chronic Bronchitis

The presence of a chronic productive cough in 3 months of 2 successive years in patients with other causes of chronic cough excluded.
Risk Factors for COPD

- Smoking
- Tobacco in any form
- Marijuana
- Passive smoking
- Ambient air pollution (e.g. uranium)
- Hyperresponsive airways
- Alpha-1 antitrypsin deficiency
- HIV
- Marfan Syndrome, Ehler’s Danlos
- Cutis laxa
- Hypocomplementemic urticarial vasculitis
- Crack cocaine, IV Ritalin

Alpha-1 Antitrypsin Deficiency

Mean Age at first symptoms: 35 years
Mean Age at diagnosis: 41 years

Health Care Professionals Required To Make a Diagnosis

Stoller, Clev Clinic J Med 1994; 61:461
Impact of Smoking on AATD

**PI ZZ Smokers versus Non-smokers**

![](image)


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**Blood Tests for COPD**

- Alpha-1 antitrypsin level
- CBC with differential (Eosinophil >2%)
- IgE
Step Care Model for COPD

(1) Smoking Cessation
(2) Bronchodilator Therapy
   Ipratropium and/or Beta2-Agonist
(3) Exacerbation Prevention
   Regular Inhaled LAMA/LABA/Corticosteroid
(4) Targeted Therapy of Exacerbations
   A. Infectious → Antibiotic for 7-10 days
   B. Excess mucus → Mucolytic/expectorant for 2-8 wks
   C. Neither → Corticosteroid boost for 3-14 days
(5) Expectant Therapy
   A. Pulmonary Rehabilitation Program
   B. Nutrition
   C. Influenza and Pneumococcal Vaccination
   D. Oxygen
(6) Treat Hyperinflation-Lung Transplant or Volume Reduction

American Lung Association Report Card for Smoking Cessation

South Carolina 2020

- Smokefree Air F
- Tobacco Prevention and Control Spending F
- Cigarette Taxes F
- Cessation Coverage B
- Tobacco 21 F
South Carolina Spending on Tobacco Control 2019

- State Funding for Tobacco Control Programs: $5,000,000
- Federal Funding for State Tobacco Control Programs: $1,461,223
- Total Funding for State Tobacco Control Programs: $6,461,223
- CDC Best Practices State Spending Recommendation: $51,000,000
- Percentage of CDC Recommended Level: 12.7%
- State Tobacco-Related Revenue: $238,200,000

http://www.lung.org/our-initiatives/tobacco/reports-resources

GOLD COPD

Figure 2.4. The refined ABCD assessment tool

Spirometrically confirmed diagnosis → Assessment of airflow limitation → Assessment of symptoms/risk of exacerbations

Post-bronchodilator FEV/FVC < 0.7

FEV$_1$ (% predicted)

- GOLD 1: $\geq$ 80
- GOLD 2: 50-79
- GOLD 3: 30-49
- GOLD 4: < 30

Exacerbation history

- $\geq$ 2
- $\geq$ 1 leading to hospital admission
- 0 or 1 (not leading to hospital admission)

Symptoms

- mMRC 0-1: CAT $\leq$ 10
- mMRC $\geq$ 2: CAT $\geq$ 10

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Inhalers

Currently Available Single Agent Bronchodilators

<table>
<thead>
<tr>
<th>Drug</th>
<th>MDI 2 Puffs</th>
<th>DPI / Mist</th>
<th>Nebulizer Dose</th>
<th>MDI to Equal Neb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SABA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol (Ventolin, Proventil, Proair)</td>
<td>0.18 mg</td>
<td></td>
<td>2.5 mg</td>
<td>28</td>
</tr>
<tr>
<td>Levalbuterol (Xopenex)</td>
<td>0.09 mg</td>
<td></td>
<td>0.63-1.25 mg</td>
<td>14-28</td>
</tr>
<tr>
<td>Ipratropium (Atrovent)</td>
<td>0.36 mg</td>
<td></td>
<td>0.5 mg</td>
<td>28</td>
</tr>
<tr>
<td><strong>SAMA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol (Serevent)</td>
<td>0.42 mg</td>
<td>0.50 mg BID</td>
<td>20 mcg BID</td>
<td></td>
</tr>
<tr>
<td>Olodaterol (Striverdi)</td>
<td></td>
<td>2.5 mcg QD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formoterol (Foradil, Perforomist)</td>
<td>12 mcg BID</td>
<td></td>
<td>20 mcg BID</td>
<td></td>
</tr>
<tr>
<td>Arformoterol (Brovana)</td>
<td></td>
<td></td>
<td>15 mcg BID</td>
<td></td>
</tr>
<tr>
<td><strong>LABA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tiotropium (Spiriva)</td>
<td>0.18 mg QD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aclidinium (Tudorza)</td>
<td>0.4 mg BID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Umeclidinium (Incrueze)</td>
<td>62.5 mcg QD</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dolovich M, Dhand R. Lancet. 2011;377:1032-1045
ICS/LABA

Fluticasone propionate/ Salmeterol | GlaxoSmithKline, Elpen | Advair Diskus®, Advair HFA®
Budesonide/Formoterol | AstraZeneca | Symbicort®
Mometasone/Formoterol | Merck | Dulera®
Fluticasone furoate/ Vilanterol | GlaxoSmithKline | Breo Ellipta®
Fluticasone propionate/ Salmeterol | Teva/Mylan | AirDuo® Respliclick, Wixela®

LAMA/LABA

Tiotropium/Olodaterol | Boehringer Ingelheim | Stiolto®
Vilanterol/Umeclidinium bromide | GlaxoSmithKline | Anoro Ellipta®
Formoterol fumarate/ Glycopyrrolate | AstraZeneca | Bevespi Aerosphere®

LABA/LAMA/ICS

IMPACT Study
10,355 Patients– 1st Exacerbation Rate

<table>
<thead>
<tr>
<th>LAMA/LABA</th>
<th>UMEC-VI</th>
<th>(Anoro)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICS/LABA</td>
<td>FF-VI</td>
<td>(Breo)</td>
</tr>
<tr>
<td>ICS/LAMA/LABA</td>
<td>FF-UMEC-VI</td>
<td>(Trelegy)</td>
</tr>
</tbody>
</table>

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**Triple Therapy FF-UMEC-VI improves All Cause Mortality over UMEC-VI**

- **28.6 Relative Reduction (P=0.043)**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Mortality %</th>
</tr>
</thead>
<tbody>
<tr>
<td>FF-UMEC-VI Trelegy</td>
<td>2.14%</td>
</tr>
<tr>
<td>FF-VI Breo</td>
<td>2.35%</td>
</tr>
<tr>
<td>UMEC-VI Anoro</td>
<td>2.9%</td>
</tr>
</tbody>
</table>


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**Initial Pharmacologic Treatment by ABCD Group**

- **Group C**: LAMA
- **Group A**: A bronchodilator
- **Group D**: LABA=long-acting beta₂ agonists  
  LAMA=long-acting antimuscarinic antagonists  
  ICS=inhaled corticosteroids
- **Group B**: A long-acting bronchodilator (LABA or LAMA)*

*For patients with severe breathlessness, initial Rx with two bronchodilators may be considered
†Consider if there are concerns regarding asthma overlap or if eosinophils ≥ 300 cells/µl
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2019 GOLD Guidelines

- Recommendations are based on symptoms and exacerbation risk at diagnosis
- Based on the ABCD assessment scheme

Management Cycle

- REVIEW
  - Symptoms (dyspnea)
  - Exacerbations

- ASSESS
  - Inhaler technique and adherence
  - Nonpharmacological approaches (including pulmonary rehabilitation and self-management education)

- ADJUST
  - Escalate
  - Switch inhaler device or molecules
  - De-escalate

Follow-Up

- Recommendations are based on continued dyspnea and exacerbation risk
- The predominant treatable trait is used to guide treatment choice
- ABCD assessment scheme is not used to guide follow-up treatment

Exacerbations of COPD are Important

- More frequent and severe as lung function decreases
- Most common reason for hospitalization in COPD
- Associated with decreased health-related quality of life
- Associated with increased risk of mortality
- Major contributor to economic burden

An acute worsening of respiratory symptoms that results in additional therapy is defined as a COPD exacerbation

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COPD Exacerbations Requiring Hospitalization Are Associated With Increased Mortality

11% of patients with COPD died within 90 days of hospitalized exacerbation in a retrospective study of COPD exacerbation admissions (N=16,016)

3.6 Years Median Survival after first hospitalized exacerbation in a cohort of patients identified using healthcare databases and followed until death or end of study (N=73,106)

Management of Exacerbations

<table>
<thead>
<tr>
<th>Objective</th>
<th>Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td></td>
</tr>
<tr>
<td>Relieve dyspnea</td>
<td>SABA +/- SAMA</td>
</tr>
<tr>
<td>Reduce airway inflammation</td>
<td>Systemic corticosteroids</td>
</tr>
<tr>
<td>Improve lung function</td>
<td>Systemic corticosteroids</td>
</tr>
<tr>
<td>Eradicate infections</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Maintenance</td>
<td></td>
</tr>
<tr>
<td>Reduce risk of new exacerbation</td>
<td>Smoking cessation</td>
</tr>
<tr>
<td>Pharmacotherapy •LAMA, LABA, LABA/ICS, LABA/LAMA, LABA/LAMA/ICS</td>
<td></td>
</tr>
<tr>
<td>Immunizations •Influenza •Pneumonia</td>
<td></td>
</tr>
<tr>
<td>Pulmonary rehab</td>
<td></td>
</tr>
<tr>
<td>Self-management support</td>
<td></td>
</tr>
</tbody>
</table>
LABA/LAMA/ICS Combinations are Appropriate Therapy for All GOLD D Patients

1. False, exacerbations often can be decreased by less intensive therapy
2. True, exacerbations are expensive and the triple combination decreases mortality

Non-Drug Treatment of COPD

- Oxygen
- Chronic Non-invasive Ventilation
- Pulmonary Rehabilitation
- Devices
- Coils
- Endobronchial Valves
- Vapor
- Airway Denervation
- Lung Transplantation
One-way valves prevent air from entering the blocked emphysematous segment, while allowing the venting of expired gas and bronchial secretions, leading to atelectasis of the isolated segments with subsequent reduction in lung volume.

Coils are delivered to the lung in a straight configuration through a bronchoscope. Once deployed, LVRC reduces the diseased lung volume by coiling up thereby compressing the diseased tissue and allowing expansion of the healthier areas.

BTVA uses heated water vapor to produce a thermal reaction leading to an initial localized inflammatory response followed by permanent fibrosis and atelectasis with subsequent reduction in lung volume.

**Pulmonx Zephyr® Valve**
Emphysema Targeting

Lobar Exclusion
Occlude all airways supplying lobe


Key Inclusion/Exclusion Criteria

**Inclusion criteria**
- Age ≥ 35 years
- Bilateral emphysema (CT)
- Post BD FEV₁ ≤ 45 % predicted
- TLC > 100 % predicted
- RV ≥ 175 % predicted
- Dyspnea ≥ 2 (mMRC)
- Stopped cigarette smoking
- Completed pulmonary rehab w/in 6 months and/or regularly performing maintenance

**Exclusion criteria**
- Post BD FEV₁ < 20%
- DLCO < 20% predicted
- 6MWT < 140 m
- Recurrent RTI
- PH > 50 mmHg systolic
- Bullae > 1/3 lung
- Prior LVR Surgery, Lung Transplant, Lobectomy, or other LVR devices in either lung
- > 20 mg prednisone daily
Treatment Overview of COPD

### Nonpharmacological Approaches
- Smoking cessation
- Pulmonary rehabilitation
- Exercise
- Diet

### Pharmacological Approaches
- Pharmacotherapy for smoking cessation
- Vaccinations (eg, influenza, pneumococcal)
- Inhaled and other treatments

### Assessments and Education
- Inhaler techniques
- Patient adherence to therapy
- Understanding of multiple medication regimens
- Early recognition of exacerbations and symptom changes
- Regular HCP contact

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**Treatable Traits**

<table>
<thead>
<tr>
<th>LUNGS</th>
<th>MUSCLES</th>
<th>VASCULAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilatory Limited</td>
<td>Muscle Limited</td>
<td>Vascular Limited</td>
</tr>
<tr>
<td>(Airway clearance)</td>
<td>(Pulm Rehabilitation)</td>
<td>(Assure no Pulmonary Emboli or CHF)</td>
</tr>
<tr>
<td>Bronchospastic (Treat like asthma)</td>
<td>BMI/ Fat Free Mass (Diet and Exercise)</td>
<td>SpO2/ Exercise (More O2)</td>
</tr>
<tr>
<td>Hyperinflation and Dynamic Hyperinflation (Consider BLVR)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Conclusions

- Hospitalizations for COPD are the most costly aspect of care accounting for 50% of expenditures
- Patient phenotypes can be stratified and care enhanced by using the right drugs for the right patients
- The non-pharmacologic therapies are just as important as the drugs to ensure good outcomes.