COPD: What’s New with Diagnosis and Treatment?

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Following medical school, she completed her residency at the University of Missouri Kansas City Family Medicine Residency where she served as Chief Resident and earned a Master’s in Business Administration from Rockhurst University. She then completed fellowships in Operative Obstetrics and Faculty Development. Prior to her appointment as program director, Dr. Irwin served as the Family Medicine Clerkship Director for the University of Kansas School of Medicine-Wichita.

Dr. Irwin currently serves as the president elect of the Association of Family Medicine Residency Directors and on the board of trustees of the American Academy of Family Physicians Foundation. She also maintains a full spectrum clinical practice at the University of Kansas School of Medicine-Wichita Family Medicine Residency program at Wesley Medical Center.
Learning Objectives

- Describe best practices for the diagnosis of COPD
- Compare various treatment options to determine the best choice for an individual patient
- Appraise the latest evidence for diagnosis and management of COPD to determine if a practice change is warranted.
Epidemiology

- COPD projected to be the third leading cause of death worldwide by 2020\(^1\)
  - Cause of death of 3 million people 2012
    - 6% of all death globally
- Fifth leading cause of disability
- Chronic obstructive pulmonary disease accounts for 3.2% of all physician office visits annually\(^22\)
Quality of life

- Cross-sectional, prospective, observational study of 100 patients in Poland
- Quality of life higher in
  - Younger patients
  - Patients with higher levels of education
- No impact of gender, smoking, weight
COPD and Suicide

- COPD patients are 1.9 times more likely to commit suicide than people without COPD\(^{29}\)
The GOLD Method for Diagnosis

- Consensus opinion based upon literature
- Utilizes both spirometry and symptom assessment
GOLD Guidelines

- Global Initiative for Chronic Obstructive Lung Disease
- Initiated in 1998 by National Heart, Lung and Blood Institute
- Focus attention on the management and prevention of COPD
GOLD Guidelines

- Expert consensus document
- Diverse areas of interest- socioeconomics to education
- PubMed search of relevant literature for each update
- Most current recommendations published Nov 2018
  - Literature current through July 2018
Diagnosis

- History and physical exam findings should prompt consideration of spirometry
- Spirometry required for diagnosis
  - FEV₁/ FVC ratio of <0.70 with appropriate clinical context
Diagnosis

- **Dyspnea**
  - Progressive over time
  - Typically worse with exercise
  - Persistent

- **Chronic cough**
  - Productive of sputum not required for diagnosis, though sputum production in any pattern suggestive

- **Recurrent respiratory infections**

- **Exposure to risk factors**

- **Family history of COPD**
Risk Factors for COPD in US

- Tobacco smoke
  - Greater mortality than non-smokers$^2$
- Pipe, Cigar and Marijuana smoke$^3$
- Environmental smoke exposure$^4$
- Occupational exposures$^5$
- Genetic factors
- Asthma
- History of severe infections
- Poor lung development esp. associated with low birth weight
Marijuana and COPD$^{39}$

- Increases risk of COPD
- Few long term studies exist
- Occurs by increasing forced vital capacity
  - Rather than decrease in FEV₁
  - Likely due to acute bronchodilator effects
- Increased risk of bullae formation and barotrauma
Low birth weight and COPD\textsuperscript{40}

- Review of 16 studies of 69,365 individuals
- Increased risk of COPD with
  - Tobacco exposure in utero and early life
  - Low birth weight
  - Asthma as child
Socioeconomic Risk Factors

- **Indoor air pollution**
  - Women particularly who are exposed to wood burning in poorly vented dwellings\(^5\)

- **Poverty\(^6,7\)**
  - Higher risk of developing
    - Unclear if pollutant exposure, poor nutrition or increased infection risk is the cause
Should we screen patients with risk factor?

- Probably not
  - History and physical examination findings should prompt spirometry
  - Tobacco use, alone, for instance shouldn’t prompt screening

- Most groups do not recommend
  - ACP, GOLD, USPSTF
Diagnosis of COPD

- Assess with spirometry (FEV₁/FVC<0.7)
- Determine grade with GOLD 1-4 Classification
- Determine ABCD score
Spirometry Review

- Forced vital capacity (FVC)
  - Total volume of air exhaled during a maximal forced expiration effort

- Forced expiratory volume in 1 second (FEV1)
  - Volume of air exhaled in the first second after a maximal inhalation

- FEV1/ FVC ratio
  - Percentage of FVC expired in one second
Spirometry Review

<table>
<thead>
<tr>
<th></th>
<th>Predicted</th>
<th>Best</th>
<th>% of Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>3.66</td>
<td>3.14</td>
<td>86%</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>2.96</td>
<td>2.12</td>
<td>72%</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>81%</td>
<td>68%</td>
<td></td>
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</tbody>
</table>
Spirometry

- Useful, but not sufficient alone
- Useful for characterizing airflow limitation
- Does not correlate with impairment \(^9,10\)
- Perform to categorize patient COPD severity from an airflow perspective
## Spirometry

<table>
<thead>
<tr>
<th>Category</th>
<th>FEV₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>FEV₁ ≥ 80% Predicted</td>
</tr>
<tr>
<td>GOLD 2</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>50% ≤ FEV₁ ≤ 80% Predicted</td>
</tr>
<tr>
<td>GOLD 3</td>
<td>Severe</td>
</tr>
<tr>
<td></td>
<td>30% ≤ FEV₁ ≤ 50% Predicted</td>
</tr>
<tr>
<td>GOLD 4</td>
<td>Very Severe</td>
</tr>
<tr>
<td></td>
<td>FEV₁ ≤ 30% Predicted</td>
</tr>
</tbody>
</table>

Post Bronchodialator Measurements in Patients with FEV₁/FVC <0.70
Diagnosis of COPD

- Assess with spirometry (FEV₁/FVC<0.7)
- Determine grade with GOLD 1-4 Classification
- Determine ABCD score
Symptom Severity Assessment

- COPD Assessment Test (CAT) Recommended
  - Includes dyspnea symptoms and others
  - Likert style (0-5) questions addressing
    - Cough
    - Mucus production
    - Chest tightness
    - Breathlessness with exercise
    - Activity limitation
    - Confidence in leaving home
    - Sleep
    - Energy
  - Total Score 0-40
## ABCD Assessment Tool

<table>
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<tr>
<th></th>
<th>CAT&lt; 10</th>
<th>CAT&gt;10</th>
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<tr>
<td>0-1 exacerbations, 0 hospital admissions</td>
<td>A</td>
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</tr>
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<td>More than 2 exacerbations or more than 1 hospital admission</td>
<td>C</td>
<td>D</td>
</tr>
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</table>
GOLD 1-4 and ABCD

- Why does this matter?
  - Guides therapy
  - Provides a way to monitor disease progression
  - May help studies clarify treatment effectiveness
After the diagnosis

- Screen patients once for alpha-1 antitrypsin deficiency\(^8\)
  - Less than 20% normal is suggestive of deficiency
Treatment - Goals

- Reduce hospitalizations
- reduce exacerbations
- decrease dyspnea
- improve quality of life
- slow disease progression
- reduce mortality
Treatment Strategy

- Reduce Risk
  - Tobacco cessation counseling
- Implement initial treatment
- Assess symptoms and exacerbations
- Review inhaler technique
- Escalate or de-escalate as needed
- Consider pulmonary rehabilitation, nutrition, psychosocial support
  - Improves symptoms, but underutilized\textsuperscript{22}
Smoking Cessation

- Important first line treatment recommendation
- Remember to use pharmacotherapy as well as structured support
- Spirometry with lung age may help encourage cessation\textsuperscript{41}
Smoking Demographics

- Data from the 2011 U.S. National Health and Wellness Survey (n = 50,000).
- In 2011, 18% of US adults were current smokers
  - 27% of current smokers were attempting to quit
- Current smokers more likely to:
  - Be poor
  - Be non-Hispanic white
  - Have less education
  - Be uninsured
  - Demonstrate fewer health conscious behaviors like regular exercise, vaccination
Rural Tobacco Use in Adolescents

- National Youth Tobacco Survey data from 2011-2014
- Adults and adolescents in rural areas more likely to be tobacco users
  - E-cigarette use increasing everywhere (0.82% of youth age 11-17 in 2011, 8.62% in 2014)
  - Cigarette taxes, advertisement exposure and location predict adolescent smoking
- May see less urban-rural disparity with e-cigarette use
Tobacco cessation and Social Determinants

- Homeless smokers in Boston April 2014-July 2014 (N=306)
- Subsistence difficulties defines as difficulty finding shelter, food, clothing, wash space, bathroom facility
- Increased subsistence difficulty associated with more perceived barriers to quitting smoking
  - No association with cessation readiness or confidence
  - Less likely to remain abstinent once quit (OR=0.33)
Smoking cessation prescriptions\textsuperscript{32}

- National Ambulatory Medical Care Survey data from 2007 to 2012
- Average prescription rate of smoking cessation medication (varenicline, bupropion or NRT) over 5 years = 3.64%
- Hispanic race and depression = higher prescription rates
  - Driven by high rate of bupropion prescription
Treatment Strategy

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Bronchodilators

- Beta 2 Agonists and Anti-muscarinics
- Improve quality of life
- Decrease annual rate of FEV1 decline
- Decrease number of exacerbations
Beta 2 Agonists

- Short acting last 4-6 hours, long acting 12 hours
- Adverse effects: Tachycardia, Hypokalemia
- No association between beta2-agonist use and increased mortality with COPD\textsuperscript{12-14}
### Common Medications

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levalbuterol</td>
<td>Xopenex</td>
<td>Short acting beta agonist</td>
</tr>
<tr>
<td>Albuterol</td>
<td></td>
<td>Short acting beta agonist</td>
</tr>
<tr>
<td>Terbutaline</td>
<td>Brethine</td>
<td>Short acting beta agonist</td>
</tr>
<tr>
<td>Arformoterol</td>
<td>Brovana</td>
<td>Long acting beta agonist</td>
</tr>
<tr>
<td>Formoterol</td>
<td>Foradil</td>
<td>Long acting beta agonist</td>
</tr>
<tr>
<td>Indacaterol</td>
<td>Arcapta</td>
<td>Long acting beta agonist</td>
</tr>
<tr>
<td>Olodaterol</td>
<td>Striverdi</td>
<td>Long acting beta agonist</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Serevent</td>
<td>Long acting beta agonist</td>
</tr>
</tbody>
</table>
Antimuscarinics

- Block bronchoconstriction effects on smooth muscles
- Adverse effects: Dry mouth, urinary symptoms?
- Tiotropium improves health status, symptoms, effectiveness of pulmonary rehabilitation and reduce exacerbations and hospitalizations\textsuperscript{16-18}
## Common Medications

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<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipratropium bromide</td>
<td>Atrovent</td>
<td>Short acting antimuscarinic</td>
</tr>
<tr>
<td>Aclidinium bromide</td>
<td>Tudorza</td>
<td>Long acting antimuscarinic</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>Seebri</td>
<td>Long acting antimuscarinic</td>
</tr>
<tr>
<td>Tiotropium</td>
<td>Spiriva</td>
<td>Long acting antimuscarinic</td>
</tr>
<tr>
<td>Umeclidinium</td>
<td>Incruse Ellipta</td>
<td>Long acting antimuscarinic</td>
</tr>
</tbody>
</table>
Methylxanthines

- Narrow therapeutic window
- Adverse effects common
- Monitoring needed
- If trying, should discontinue if no improvement in several weeks of therapy
Phosphodiesterase 4 inhibitor

- Patients with severe or refractory symptoms
- Decreases exacerbations
- No improvement in quality of life or overall symptoms
# Common Medications

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminophylline</td>
<td></td>
<td>Methylxanthine</td>
</tr>
<tr>
<td>Theophylline</td>
<td></td>
<td>Methylxanthine</td>
</tr>
<tr>
<td>Roflumilast</td>
<td>Daliresp</td>
<td>Phosphodiesterase 4 inhibitor</td>
</tr>
</tbody>
</table>
# Combination Medications

<table>
<thead>
<tr>
<th>Medication #1</th>
<th>Medication #2</th>
<th>Medication #3</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salbutamol</td>
<td>Ipratropium bromide</td>
<td></td>
<td>Combivent, DuoNeb</td>
</tr>
<tr>
<td>Formoterol</td>
<td>Glycopyrrolate</td>
<td></td>
<td>Brevespi Aerosphere</td>
</tr>
<tr>
<td>Indacaterol</td>
<td>Glycopyrrolate</td>
<td></td>
<td>Utibron</td>
</tr>
<tr>
<td>Vilanterol</td>
<td>Umeclidinium</td>
<td></td>
<td>Anoro Ellipta</td>
</tr>
<tr>
<td>Olodaterol</td>
<td>Tiotropium</td>
<td></td>
<td>Stiolo Respimat</td>
</tr>
<tr>
<td>Formoterol</td>
<td>Budesonide</td>
<td></td>
<td>Symbicort</td>
</tr>
<tr>
<td>Formoterol</td>
<td>Mometasone</td>
<td></td>
<td>Dulera</td>
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<tr>
<td>Salmeterol</td>
<td>Fluticasone</td>
<td></td>
<td>Advair</td>
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<tr>
<td>Vilanterol</td>
<td>Fluticasone furoate</td>
<td></td>
<td>Breo Ellipta</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>Umeclidinium</td>
<td>Vilanterol</td>
<td>Trelegy</td>
</tr>
</tbody>
</table>
Inhaled Steroids and Pneumonia\textsuperscript{23}

- Review of 43 studies
- Typical patient was male, mean age of 63 with 40 pack year smoking history and FEV\textsubscript{1} less than 50% predicted
- Increase noted in non fatal pneumonia events with use of fluticasone or budesonide alone or in combination with a long acting beta agonist
  - OR = 1.78, 95% CI 1.50-2.12
- Increase in pneumonia, though no change in mortality as a result
# Initial Treatment Recommendations

<table>
<thead>
<tr>
<th></th>
<th>CAT&lt; 10</th>
<th>CAT≥10</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 exacerbations, 0 hospital admissions</td>
<td>A: Bronchodilator (short or long acting)</td>
<td>B: Long acting bronchodilator (antimuscarinic or beta 2 agonist)</td>
</tr>
<tr>
<td>More than 2 exacerbations or more than 1 hospital admission</td>
<td>C: Long acting anti-muscarinic</td>
<td>D: 1) Long acting antimuscarinic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2) If highly symptomatic- Long acting antimuscarinic and long acting beta agonist</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3) If high eosinophils, inhaled corticosteroid and long acting beta agonist</td>
</tr>
</tbody>
</table>
# Initial Treatment Recommendations - Example

<table>
<thead>
<tr>
<th></th>
<th>CAT&lt; 10</th>
<th>CAT&gt;10</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>0-1 exacerbations, 0 hospital admissions</strong></td>
<td>A: Albuterol</td>
<td>B: Salmeterol (Serevent) or Tiotropium (Spiriva)</td>
</tr>
<tr>
<td><strong>More than 2 exacerbations or more than 1 hospital admission</strong></td>
<td>C: Tiotropium (Spiriva)</td>
<td>D:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1) Tiotropium (Spiriva)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2) Vilanterol/Umeclidinum (Anoro Ellipta)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3) Formoterol/budesonide (Symbicort)</td>
</tr>
</tbody>
</table>
Treatment Strategy

- Reduce Risk
  - Tobacco cessation counseling
- Implement initial treatment
- Assess symptoms and exacerbations
- Review inhaler technique
- Escalate or de-escalate as needed
- Consider pulmonary rehabilitation, nutrition, psychosocial support
  - Improves symptoms, but underutilized\textsuperscript{22}
Inhaler Technique Matters

- Incorrect technique may be more than 53%\(^\text{42}\).
- Incorrect technique associated with higher symptoms score, increased cough, worse FEV\(_1\)\(^\text{42}\).
- Patients may make errors up to 20% of the time with inhaler\(^\text{43}\).
  - Of 60 expected doses, patient actually received 34 correctly on average in one study\(^\text{43}\).
Treatment Follow Up

- If initial treatment is working, continue it
- If treatment is not working, clarify
  - Dyspnea increased?
  - Increased exacerbations?
  - Both?
- Remember to vaccinate
Dyspnea- Escalating Treatment

- LAMA or LABA
  - Add the other agent

- LAMA and LABA
  - Switch inhaler device, molecule or treat other causes of dyspnea

- LABA and ICS
  - Add LAMA

- LAMA, LABA and ICS
  - Switch inhaler device, molecule or treat other causes of dyspnea
Dyspnea- De-escalating Treatment

- LABA and ICS
  - LABA and LAMA
- LAMA, LABA and ICS
  - LABA and LAMA
Exacerbations- Escalating Treatment

- **LAMA or LABA**
  - LABA and LAMA
  - LABA and ICS
- **LAMA and LABA**
  - Add ICS
  - Consider roflumilast if FEV$_1$<50% and chronic bronchitis
  - Consider azithromycin for 1 year in daily smokers
- **LABA and ICS**
  - Add LAMA
- **LAMA, LABA and ICS**
  - Consider roflumilast if FEV$_1$<50% and chronic bronchitis
  - Consider azithromycin for 1 year in daily smokers
Exacerbations- De-escalating Treatment

- LABA and ICS
  - Add LAMA and remove ICS
- LAMA, LABA and ICS
  - Remove ICS
Medication side effects

- COPD medications may increase risk of diabetes
- Analysis of 15,287 patients with COPD free of diabetes at baseline
  - 6.3% of population diagnosed with new onset diabetes during study
- Increased risk if individual using inhaled corticosteroids alone or in combination with statins or statins and antidepressants
COPD and Lung Cancer

- Meta-analysis of COPD associated with 5 year overall survival of lung cancer
  - Articles published before September 30, 2017
  - 29 studies, 70,111 patients
- Presence of COPD indicates poor survival for patients with lung cancer
Oxygen Therapy

- Oxygen does improve dyspnea and fatigue for those with moderate hypoxia.
- Does ambulatory oxygen help patients who otherwise don’t meet criteria for long term oxygen therapy?
  - Four studies of 331 participants.
  - No clear evidence to suggest that mortality or exercise capacity improve.
Treatment Strategy

- Reduce Risk
  - Tobacco cessation counseling
- Implement initial treatment
- Assess symptoms and exacerbations
- Review inhaler technique
- Escalate or de-escalate as needed
- Consider pulmonary rehabilitation, nutrition, psychosocial support
  - Improves symptoms, but underutilized\(^{22}\)
Pulmonary rehabilitation

- Strength and endurance training
- Educational, nutritional and psychosocial support
- Improves symptoms
- Improves exercise tolerance
- Very underutilized even in areas where readily available
Pulmonary Rehabilitation and Social Determinants

- Pulmonary rehabilitation adherence is generally low
- Study of adherence rates by social determinants found that
  - Low adherence increased with limited functional capacity and current smoking
    - Less than 35% of sessions attended
  - Moderate adherence increased with socioeconomic disadvantage
    - 35-85% of sessions attended
  - High adherence in groups with higher socioeconomic standing, non-smokers and higher functional capacity
Potential Biomarker

- 17 patients enrolled in study to isolate circulating pulmonary cells in peripheral blood
  - 6/17 had cells whereas no healthy volunteers had cells
  - Increased circulating pulmonary cells suggested increased severity of COPD

- Potential biomarker for severity?
Managing Exacerbations

- Acute worsening of respiratory symptoms requiring additional therapy
  - Mild: Treated with short acting bronchodilators only
  - Moderate: Add antibiotics and/or oral corticosteroids
  - Severe: Add hospitalization or visit to ER

- Most (80%) can be managed on outpatient basis
Interventions that Reduce Exacerbation Frequency

- Long acting beta 2 agonists
- Long acting antimuscarinics
- Long acting beta 2 agonists combined with inhaled corticosteroids
- Triple therapy (LABA, LAMA and ICS)
- Roflumilast
- Vaccines
- Long term macrolide therapy
- Smoking cessation
- Lung rehabilitation
Does Heliox help exacerbations?\textsuperscript{24}

- Heliox has low density which may decrease work of breathing
- Four studies reviewed (1997-2000)
  - Data obtained for 69 patients
  - Not significant change noted in FEV\textsubscript{1} or FVC when heliox used
- Insufficient evidence to justify use of Heliox. May benefit from additional studies in avoidance of mechanical ventilation
Prolonged antibiotics for COPD

- RCT of hospitalized patients with COPD
  - Inclusion criteria
    - Greater than 10 pack year history, more than 1 exacerbation in the prior year
  - Control group (n=154)
    - Acute treatment of steroids and antibiotics
  - Study group (n=147)
    - 500mg/day for 3 days of azithromycin plus 250mg BID for 3 months
  - Azithromycin group
    - Longer time to first re-hospitalization

Azithromycin as a prolonged course may reduce re-hospitalization
Length of Stay and Readmission$^{35}$

- Observational study of 33,558 veterans admitted to 130 VA hospitals 2008-2011
- Increased length of stay in hospital increases patient risk for readmission, not association at hospital level
Do residents make a difference?  

- Orlando community teaching hospital patients  
  January 2011-2014  
- 1419 patients, 306 on teaching service, 1113 on non-teaching service  
- Teaching service  
  - Lower cost per patient  
  - Shorter length of stay  
  - Less consultant use  
  - No change in mortality or readmission
Medicaid Expansion Impact

- Does having access to care through Medicaid increase diagnosis rates?
- 2011-2015 Behavioral Risk Factor Surveillance System data
- 521,622 respondents
  - Diagnosis of COPD did not change with expansion
    - Lack of health insurance decreased from 32% to 21%, diagnosis of COPD was unchanged
  - Diagnosis of COPD = 7% in Medicaid expansion states, 8% in non-expansion states
Do we follow GOLD?\(^{19}\)

- Retrospective chart review from 2 community clinics (n=101 patients)
  - No use of validated measures of dyspnea such as CAT
  - Only 21% had formal spirometry done
    - Of those with spirometry 31.5% were incorrectly diagnosed with COPD
  - Varied therapies not following GOLD guidelines
    - 42% of patients who qualified on long acting muscarinic inhalers
Questions?
References


References


References


