Objectives

• Describe the impact of asthma and COPD in the U.S

• Outline the latest treatment guidelines for asthma and COPD

• Discuss currently available treatment options with emphasis on recently approved medications for asthma and COPD
# Key Differences in Clinical Presentation Between Asthma and COPD

<table>
<thead>
<tr>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Onset early in life (often childhood)</td>
<td>• Onset in midlife</td>
</tr>
<tr>
<td>• Symptoms vary from day to day</td>
<td>• Symptoms slowly progressive</td>
</tr>
<tr>
<td>• Symptoms at night/early morning (acid reflux)</td>
<td>• Long smoking history</td>
</tr>
<tr>
<td>• Allergic rhinitis and/or eczema also present</td>
<td>• Dyspnea during exercise</td>
</tr>
<tr>
<td>• Family history of asthma</td>
<td>• Partially reversible airflow limitation</td>
</tr>
<tr>
<td>• Largely reversible airflow limitation</td>
<td></td>
</tr>
</tbody>
</table>

Inflammation: Asthma vs. COPD

- Inflammation is an important component in the pathogenesis of asthma and COPD
- The inflammatory response in asthma and COPD is markedly different, although there is some overlap
- Predominant inflammatory cells in asthma:
  - Eosinophils, Mast cells, CD4+ T lymphocytes
- Predominant inflammatory cells in COPD:
  - Neutrophils, CD8+ T lymphocytes, Macrophages
Asthma Impact in the United States

- 25.7 million people affected
- Prevalence increased 75% from 1980 to 1994
  - 111 per 1000 people
- Per year
  - 10.4 million asthma-related outpatient visits
  - 1.8 million emergency room (ER) visits
  - 5000 deaths
  - >$9.4 billion in direct costs; $4.6 billion in indirect costs
- Impact on Children
  - 9 million children have been diagnosed with asthma
  - >4 million children had an asthma attack in the past year
  - Prevalence 122 per 1000 people ≤18 years of age
  - 14 million missed school days per year
  - 40% of children whose parents have asthma will develop asthma
Goal of Asthma Therapy: Achieve Control

**Reduce Impairment**

- Prevent chronic and troublesome symptoms
- Require infrequent use of inhaled SABA (≤2 days/week)
- Maintain (near) “normal” pulmonary function
- Maintain normal activity levels
- Meet patients’ expectations of, and satisfaction with, asthma care

**Reduce Risk**

- Prevent recurrent exacerbations
- Minimize need for emergency department visits or hospitalizations
- Prevent progressive loss of lung function
- Provide optimal pharmacotherapy, with minimal or no adverse effects

Available at: http://www.nhlbi.nih.gov/guidelines/asthma/epr3/resource.pdf
Main Components of Asthma Management

I. Initial Assessment and Continuous Monitoring

• Monitor symptoms, exacerbations, quality of life
• Periodic pulmonary function tests
# Classifying Severity in Patients ≥12 Years Not Currently Taking Long-Term Controllers

## Components of Severity

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Classification of Asthma Severity (Youths ≥12 of Age and adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>Intermittent</td>
</tr>
<tr>
<td>&lt;2 days/week</td>
<td>Mild</td>
</tr>
<tr>
<td>&gt;2 days/week but not daily</td>
<td>Severe</td>
</tr>
<tr>
<td><strong>Nighttime awakenings</strong></td>
<td>&lt;2x/month</td>
</tr>
<tr>
<td>&gt;1x/week but not nightly</td>
<td>Daily</td>
</tr>
<tr>
<td><strong>Short-acting β&lt;sub&gt;2&lt;/sub&gt;-agonist use for symptom control</strong></td>
<td>&lt;2 days/week</td>
</tr>
<tr>
<td>&gt;2 days/week but not daily</td>
<td>Daily</td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>None</td>
</tr>
<tr>
<td>Minor limitation</td>
<td>Some limitation</td>
</tr>
<tr>
<td>Extremely limited</td>
<td></td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td>&lt;2 days/week</td>
</tr>
<tr>
<td>&gt;2 days/week but not daily</td>
<td>Daily</td>
</tr>
<tr>
<td>Normal FEV&lt;sub&gt;1&lt;/sub&gt; between exacerbations</td>
<td>Mild</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; &gt;80% predicted</td>
<td>Severe</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC normal</td>
<td></td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; &lt;80% predicted</td>
<td></td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC reduced 5%</td>
<td></td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; &lt;60% predicted</td>
<td></td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC reduced &gt;5%</td>
<td></td>
</tr>
<tr>
<td>Risk</td>
<td>0-2/year</td>
</tr>
<tr>
<td>(consider frequency and severity)</td>
<td>Frequency and severity may fluctuate over time</td>
</tr>
<tr>
<td>Relative annual risk of exacerbations may be related to FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td></td>
</tr>
</tbody>
</table>

### Components of Severity

#### Impairment

<table>
<thead>
<tr>
<th>Component</th>
<th>Classification of Asthma Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Well-Controlled</strong></td>
<td><strong>Not Well-Controlled</strong></td>
</tr>
<tr>
<td>Symptoms</td>
<td>&lt;2 days/week</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>&lt;2/month</td>
</tr>
<tr>
<td>Short-acting $\beta_2$-agonist use for symptom control</td>
<td>&lt;2 days/week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
</tr>
<tr>
<td>FEV1 or peak flow</td>
<td>&gt;80% pred/personal best</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Validated questionnaires</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ATAQ</td>
<td>0</td>
<td>1-2</td>
</tr>
<tr>
<td>ACQ</td>
<td>&lt;0.75</td>
<td>&gt;1.5</td>
</tr>
<tr>
<td>ACT</td>
<td>&gt;20</td>
<td>16-19</td>
</tr>
</tbody>
</table>

#### Risk

<table>
<thead>
<tr>
<th>Exacerbations</th>
<th>0-1 per year</th>
<th>2-3 per year</th>
<th>&gt;3 per year</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Reduction in lung growth</th>
<th>Evaluation requires long-term follow-up care.</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Treatment-related adverse effects</th>
<th>Medication side effects vary in intensity from none to very troublesome. Level of intensity does not correlate to specific levels of control but should be considered in overall assessment of risk.</th>
</tr>
</thead>
</table>

Main Components of Asthma Management

I. Initial Assessment and Continuous Monitoring
   • Monitor symptoms, exacerbations, quality of life
   • Periodic pulmonary function tests

II. Control of Triggers
   • Cigarette smoke
   • Irritants (at work or at home)
   • Air Pollutants
   • Allergens
   • Rx of diseases exacerbating diseases: GERD, allergic rhinitis, sinusitis
I TOLD YOU CIGARS WERE BAD FOR YOU!
Main Components of Asthma Management

I. Initial Assessment and Continuous Monitoring
   • Monitor symptoms, exacerbations, quality of life
   • Periodic pulmonary function tests

II. Control of Triggers
   • Cigarette smoke
   • Irritants (at work or at home)
   • Air Pollutants
   • Allergens
   • Rx of diseases exacerbating diseases: GERD, allergic rhinitis, sinusitis

III. Pharmacotherapy
Medications for Asthma

Long-Term Control
- Corticosteroids
- Long-acting, inhaled beta$_2$ agonists (salmeterol and formoterol)
- Leukotriene Modifiers (montelukast and zafirlukast, zileuton)
- Theophylline
- Omalizumab

Quick Relief
- Short-acting, inhaled beta$_2$ agonists
- Systemic corticosteroids
- Inhaled anticholinergics (ipratropium)
New Drug Approval

• **Arnuity Ellipta** - A once daily fluticasone dry powder inhaler

• For maintenance treatment of asthma

• Approved in 100mcg and 200mcg dosing system
Taking Control in Asthma Management

Level of Control

- Well Controlled
  - Maintain and Find Lowest Controlling Step

- Not Well Controlled
  - Consider Stepping Up to Gain Control

- Very Poorly Controlled
  - Step Up Until Controlled

Treatment Action

Treatement Steps

- Step 1
- Step 2
- Step 3
- Step 4
- Step 5
- Step 6
STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS ≥ 12 YEARS AND ADULTS

Intermittent Asthma

Persistent Asthma: Daily Medication
Consult with asthma specialist if step 4 or higher care is required
Consider consultation at step 3

Quick-Relief Medication for All Patients
SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of systemic oral corticosteroids may be needed.
• Use of beta₂-agonist >2 days a week for symptom control (not prevention of EIB) indicates inadequate control and the need to step up treatment.

Step 1
Preferred:
SABA prn

Step 2
Preferred:
Low-dose ICS
Alternative:
LTRA
Cromolyn
Theophylline

Step 3
Preferred:
Medium-dose ICS+LABA

Alternative:
Low-dose ICS+either LABA, LTRA, Theophylline Or Zileutin

Step 4
Preferred:
High dose ICS + LABA

AND
Consider Olamizumab for patients with allergies

Step 5
Preferred:
High-dose ICS + LABA + oral Corticosteroid

AND
Consider Olamizumab for patients with allergies

Step 6
Preferred:
High-dose ICS + LABA + oral Corticosteroid

AND
Consider Olamizumab for patients with allergies

Step up if needed (check adherence, environmental control and comorbidities)

Step down if possible
(asthma well controlled for 3 months)

Assess Control

Patient Education and Environmental Control at Each Step
## STEP 1 - Intermittent

<table>
<thead>
<tr>
<th>Long-Term-Control</th>
<th>Quick-Relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>No daily medication needed</td>
<td>Short-acting bronchodilators: Inhaled beta$_2$-agonists as needed for symptoms</td>
</tr>
</tbody>
</table>
## STEP 2 - Mild Persistent

<table>
<thead>
<tr>
<th>Long-Term Control</th>
<th>Quick-Relief</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daily medications:</strong></td>
<td>Short-acting bronchodilators: inhaled beta(_2)-agonists as needed</td>
</tr>
<tr>
<td><strong>Anti-inflammatory:</strong></td>
<td></td>
</tr>
<tr>
<td>inhaled corticosteroids (low dose)</td>
<td></td>
</tr>
<tr>
<td><strong>Alternatives:</strong></td>
<td></td>
</tr>
<tr>
<td>Leukotriene Modifiers</td>
<td></td>
</tr>
<tr>
<td>(zafirlukast, montelukast or zileuton)</td>
<td></td>
</tr>
<tr>
<td>Sustained-release theophylline</td>
<td></td>
</tr>
</tbody>
</table>
Options for Monotherapy for Treatment of Mild Persistent Asthma

- Inhaled corticosteroids are the most potent and effective long term control therapy
- Some alternatives to inhaled corticosteroids are effective as single agents
- Choices include:
  - Theophylline
  - Leukotriene modifiers (montelukast, zafirlukast)
Inhaled Corticosteroids: First-line Therapy for Persistent Asthma

- Reduce asthma symptom severity
- Improve quality of life
- Improve pulmonary function
- Reduce rescue inhaler use
- Reduce exacerbations/hospitalizations/mortality
- Reduce bronchial hyperreactivity
- Slow deterioration of lung function
- May prevent airway remodeling
START* Trial: Time to First Severe Asthma Related Event in Mild Asthma

*START: Steroid Treatment as Regular Therapy in Early Asthma

**Number at risk**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Budesonide</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3568</td>
<td>3597</td>
</tr>
<tr>
<td>1</td>
<td>2865</td>
<td>2998</td>
</tr>
<tr>
<td>2</td>
<td>2600</td>
<td>2722</td>
</tr>
<tr>
<td>3</td>
<td>2438</td>
<td>2570</td>
</tr>
</tbody>
</table>

44% risk reduction with ICS

## Theophylline

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relaxes smooth airway</td>
<td>Serum concentration must be monitored</td>
</tr>
<tr>
<td>May have anti-inflammatory and immunomodulatory effects</td>
<td>High incidence of side effects</td>
</tr>
<tr>
<td>Affordable</td>
<td>Low efficacy</td>
</tr>
<tr>
<td></td>
<td>More data needed on low-dose theophylline as add-on therapy to ICS</td>
</tr>
<tr>
<td></td>
<td>Low adherence rates</td>
</tr>
</tbody>
</table>


# Leukotriene Receptor Antagonists

**Montelukast, Zafirlukast**

## Advantages
- Minimal adverse effects
- Improve pulmonary function
- Reduce EIB
- Prevent allergen-induced inflammation
- Improve QoL
- High compliance rates, convenient dosing
- Systemic delivery may target upper and smaller airways

## Disadvantages
- Less potent anti-inflammatory effect than ICS
- Less effect on airway responsiveness compared to ICS
- Poor predictors of response

*Zileuton is another medication approved for the treatment of asthma. It is an orally active inhibitor of 5-lipoxygenase that also inhibits leukotrienes. Please see zileuton prescribing information for a safety and efficacy profile of this medication.*


Step 3: Moderate-Persistent

Long-Term-Control

*Daily medications:*
- Low-medium dose ICS + inhaled LABA

*Alternatives:*
- Medium dose ICS
- Low-medium dose ICS + Leukotriene modifier or Sustained-release theophylline

Quick-Relief

*Short-acting bronchodilators:*
- Inhaled $\beta_2$-agonist, as needed

*Severe Persistent Asthma approach is similar with more intensive therapy*
# Long-acting $\beta_2$-agonists

**Salmeterol, Formoterol**

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce exacerbations</td>
<td>Potential for reduced effect with long-term treatment</td>
</tr>
<tr>
<td>Improve pulmonary function</td>
<td>Not recommended as monotherapy</td>
</tr>
<tr>
<td>Reduce airway responsiveness</td>
<td>Genetic differences put some patients at risk for worsening</td>
</tr>
<tr>
<td>Provide bronchodilation</td>
<td>asthma</td>
</tr>
<tr>
<td>Prevent nocturnal asthma</td>
<td></td>
</tr>
</tbody>
</table>

Concerns about LABAs

- Serevent Nationwide Surveillance Study (SNS; 1993)
  - Significantly more deaths in patients taking LABA vs. SABA
- Salmeterol Multicenter Asthma Research Trial (SMART; 2006)
  - Significantly more deaths in patients taking LABA vs. placebo

FDA LABA Safety Requirements
February 18, 2010

1. LABAs must be used in combination with an asthma controller medication
2. Only patients whose asthma cannot be adequately controlled with asthma controller medications should use LABAs long term
3. LABAs should be discontinued if possible once asthma controlled
4. Combination LABA/ICS products should be used for pediatric and adolescent patients
Xolair (Omalizumab) Anti-IgE

✓ Dosing based on IgE levels and weight
✓ Indicated for ages over 12 years old
✓ In conjunction with other meds
✓ Must have evidence of specific allergy sensitivity
✓ Used for those with poorly controlled asthma and non-compliant with standard recommended therapy
✓ Delivered by SQ injection Cost ~ $10,000/yr (range $7500-$40,000)
Effects of Omalizumab as Add-on to ICS/LABA

Main Components of Asthma Management

I. Initial Assessment and Continuous Monitoring
   • Monitor symptoms, exacerbations, quality of life
   • Periodic pulmonary function tests

II. Control of Triggers
   • Cigarette smoke
   • Irritants (at work or at home)
   • Air Pollutants
   • Allergens
   • Rx of diseases exacerbating diseases: GERD, allergic rhinitis, sinusitis

III. Pharmacotherapy

IV. Asthma Education
Component 4: Asthma Education

Key Educational Messages for Asthma

- Basic Facts About Asthma
  - Contrast normal and asthmatic airways

- Roles of Medications
  - Long-term-control and quick-relief medications

- Relevant Environmental Control Measures

- When and How To Take Rescue Actions
  (Action Plan)

- Skills
  - Inhalers, spacers, symptom and peak flow monitoring, early warning signs of attack
Asthma Action Plan

Every patient with persistent asthma should have a written home management plan.
Conclusion

- Inhaled corticosteroids are the most effective long term control therapy
- Combining ICS with long-acting beta agonists is the recommended strategy for moderate and severe disease
- Other agents are effective as monotherapy or in combination with ICS
- Patient education and periodic monitoring and assessment are important components to optimize outcomes
What Is COPD?

- COPD is a **preventable and treatable disease** state characterized by airflow limitation that is not fully reversible.

- The airflow limitation is usually **progressive** and is associated with an **abnormal inflammatory response** of the lungs to noxious particles or gases, primarily caused by cigarette smoking.

- Although COPD affects the lungs, it also produces significant **systemic consequences**.

The Impact of COPD in the United States

In 2010, COPD accounted for

- 10.3 million physician office visits/y
- 1.5 million ED visits
- 699,000 hospital discharges

• Costly

- Direct: ≈$27 billion/y
- Indirect: ≈$20 billion/y

• 3rd leading cause of death

• 4th leading cause of hospital readmissions

COPD in Younger Patients and Women Is on the Rise

Reality: COPD afflicts the working-age population.

Reality: COPD is also a disease of women.

1Mannino, et al. *MMWR.* 2002; 51(6 suppl):1-16. Netter illustrations used with permission from Icon Learning Systems, a division of MediMedia USA, Inc. All rights reserved.
Risk Factors for COPD

Key Risk Factors for COPD

Smoking
(~90% of cases)
- Current or former smoker

Genetic factors
- Alpha-1 antitrypsin deficiency
  (~1% of cases)
  - Can cause COPD even without smoking history/environmental exposure

Environmental exposure
(~10% of cases)
- Long-term exposure to chemicals, dust, or fumes in the workplace; second hand smoke
- Household exposures; (eg, biomass cooking)

Age
- >40 years of age

References:
Key Indicators for Considering a Diagnosis of COPD

- Consider a diagnosis of COPD, and perform spirometry, if any of these indicators* are present in an individual >40 years of age
  - Exertional dyspnea
  - Chronic cough
  - Chronic sputum production
  - History of exposure to risk factors (eg, tobacco smoke)

* These indicators are not diagnostic in themselves, but the presence of multiple key indicators increases the probability of a COPD diagnosis.

Smoking....Is it Really a Killer??

Who said cigarettes kill?

I'm 48 and still feeling good.
Improving Outcomes in COPD

• Early diagnosis and accurate assessment
  – Identifying patients at risk
  – Using appropriate diagnostic approaches, ruling out other mimickers
  – Early treatment

• Implementing optimal management
  – Reducing exposures to risk factors and triggers
  – Non-pharmacological approaches
  – Pharmacological treatments

• Incorporating self-management skills through education and collaboration with a health care team
  – Improve adherence

Goals of Management

Airflow Limitation
- Improve Lung Function
- Slow FEV1 Decline

Symptom Burden
- Improve Symptoms

Exacerbations
- Prevent and Manage Exacerbations

Functional Limitations
- Improve Health Status and Exercise Tolerance

Reduce Hospital Admissions and Mortality

Changes in GOLD Guidelines 2010 vs 2011

Patient assessment criteria*

* Assessment should also include an assessment of potential patient comorbidities

mMRC: Modified Medical Research Council Dyspnea Scale, CAT: COPD Assessment Test
## mMRC Dyspnea Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Degree of Breathlessness Related to Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not troubled by breathlessness except with strenuous exercise</td>
</tr>
<tr>
<td>2</td>
<td>Short of breath when hurrying on level ground or walking up a slight hill</td>
</tr>
<tr>
<td>3</td>
<td>Walks slower than most on level ground, or has to stop for breath when walking at own pace</td>
</tr>
<tr>
<td>4</td>
<td>Stops for breath after walking about 100 yards or after a few minutes on level ground</td>
</tr>
<tr>
<td>5</td>
<td>Too breathless to leave the house or breathless when dressing</td>
</tr>
</tbody>
</table>

mMRC, modified Medical Research Council
GOLD Spirometric Criteria for COPD Severity Based on Postbronchodilator $FEV_1$ Measurement

<table>
<thead>
<tr>
<th>GOLD stage</th>
<th>Spirometric Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I: Mild</td>
<td>$FEV_1/FVC &lt;0.70$</td>
</tr>
<tr>
<td></td>
<td>$FEV_1 \geq 80%$ predicted</td>
</tr>
<tr>
<td>Stage II: Moderate</td>
<td>$FEV_1/FVC &lt;0.70$</td>
</tr>
<tr>
<td></td>
<td>$50% \leq FEV_1 &lt; 80%$ predicted</td>
</tr>
<tr>
<td>Stage III: Severe</td>
<td>$FEV_1/FVC &lt;0.70$</td>
</tr>
<tr>
<td></td>
<td>$30% \leq FEV_1 &lt; 50%$ predicted</td>
</tr>
<tr>
<td>Stage IV: Very Severe</td>
<td>$FEV_1/FVC &lt;0.70$</td>
</tr>
<tr>
<td></td>
<td>$FEV_1 &lt; 30%$ predicted or $FEV_1 &lt; 50%$ predicted plus chronic respiratory failure</td>
</tr>
</tbody>
</table>

**COPD diagnosis: Postbronchodilator $FEV_1/FVC$ ratio <0.7**

$FEV_1$=forced expiratory volume in 1 second; FVC=forced vital capacity.

Factors Associated With Increased Risk for Exacerbations

- Increased age
- Severity of airway obstruction (FEV$_1$ impairment)
- Chronic bronchial mucus 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 (e.g., cardiovascular disease)
- Poor health-related quality of life


### Combined Assessment of COPD

Choose the **highest** risk according to GOLD grade or exacerbation history.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Characteristic</th>
<th>Spirometric Classification</th>
<th>Exacerbations per year</th>
<th>mMRC</th>
<th>CAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low Risk Less Symptoms</td>
<td>GOLD 1-2</td>
<td>≤1</td>
<td>0-1</td>
<td>&lt;10</td>
</tr>
<tr>
<td>B</td>
<td>Low Risk More Symptoms</td>
<td>GOLD 1-2</td>
<td>≤1</td>
<td>≥2</td>
<td>≥10</td>
</tr>
<tr>
<td>C</td>
<td>High Risk Less Symptoms</td>
<td>GOLD 3-4</td>
<td>≥2</td>
<td>0-1</td>
<td>&lt;10</td>
</tr>
<tr>
<td>D</td>
<td>High Risk More Symptoms</td>
<td>GOLD 3-4</td>
<td>≥2</td>
<td>≥2</td>
<td>≥10</td>
</tr>
</tbody>
</table>
COPD Pharmacological Agents Approved in the U.S.

**Bronchodilators**

**Short-acting**
- β-Agonists (SABA)
  - Albuterol
  - Pirbuterol
  - Levalbuterol
- Anticholinergic (SAMA)
  - Ipratropium

**Long-acting**
- β-Agonists (LABA)
  - Salmeterol
  - Formoterol
  - Arformoterol
  - Indacaterol
- Anticholinergic (LAMA)
  - Tiotropium
  - Aclidinium
  - Umeclidinium
- LABA + LAMA
  - Umeclidinium + Vilanterol
- Theophylline

**Anti-Inflammatory**

**ICS+LABA**
- Fluticasone + Salmeterol
- Budesonide + Formoterol
- Fluticasone Furoate + Vilanterol

**PDE-4 Inhibitors**
- Roflumilast

**Systemic Steroids**
- Prednisone
- Methylprednisolone
Pharmacological Management of COPD

• Guideline-recommended COPD treatment
  - Improves lung function
  - Minimizes symptoms
  - Improves QoL
  - Prevents exacerbations

• Wide variety of options including new agents
  - Appropriate treatment selection hinges on GOLD staging
  - Before stepping up/modifying treatment, re-evaluate
    Treatment goals
    Clinical phenotype
    Comorbidities
    Adherence
## Initial Pharmacologic Management of COPD

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Recommended First Choice*</th>
<th>Alternative Choice*</th>
<th>Other Possible Treatments*†</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>SAMA prn or SABA prn</td>
<td>LAMA or LABA or SABA and SAMA</td>
<td>Theophylline</td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>LAA and LABA</td>
<td>SABA and/or SAMA Theophylline</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA and LABA or LAMA and PDE-4 inhibitor or LABA and PDE-4 inhibitor</td>
<td>SABA and/or SAMA Theophylline</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA and/or LAMA</td>
<td>ICS + LABA and LAA or ICS + LABA and PDE-4 inhibitor or LAMA and LABA or LAMA and PDE-4 inhibitor</td>
<td>Carbocysteine SABA and/or SAMA Theophylline</td>
</tr>
</tbody>
</table>

*Medications in each box are in alphabetical order, not necessarily in order of preference.
†Medications in this column can be used alone or in combination with other options in the recommended first choice and alternative choice columns.

Rationale for Early Treatment in COPD

• The effect of treatment on lung function may be more marked in patients who are younger and in those with less severe disease\textsuperscript{1-4}

• Lung function deteriorates more rapidly during the less severe, early stages of COPD\textsuperscript{3}

• LABA and LAMA are recommended initial maintenance therapy for patients who are symptomatic but at low risk of exacerbations\textsuperscript{5}

• Lack of data in treatment-naïve patients with mild or moderate airflow limitation

COPD Comorbidities

- Skeletal muscle abnormalities
- Depression
- Hypertension
- Diabetes
- Coronary-artery disease
- Heart failure (>20%)
- Pulmonary infections
- Cancer
- Pulmonary vascular disease
- Osteoporosis (up to 70%)
- Metabolic syndrome (perhaps 50%)
Many Patients Remain Symptomatic on “Mono-Bronchodilator” Therapy

- A significant proportion of patients with COPD remain symptomatic when receiving a single bronchodilator\(^1,2\)

**Current guidelines recommend adding a second bronchodilator to treatment regimens in moderate COPD to optimize symptom benefit for patients\(^2\)**

- Combining bronchodilators of different pharmacologic classes may improve efficacy and decrease the risk of side effects compared to increasing the dose of a single bronchodilator\(^2\)

- As airflow obstruction becomes more severe, a LAMA plus a LABA combination has been advocated\(^3\)

THE PROBLEM WITH COMBINATION THERAPY?

TOO MANY INHALERS.

I CAN'T BREATHE!
Withdrawal of Inhaled Glucocorticoids and Exacerbations of COPD

Helgo Magnussen, M.D., Bernd Disse, M.D., Ph.D., Roberto Rodriguez-Roisin, M.D., Anne Kirsten, M.D., Henrik Watz, M.D., Kay Tetzlaff, M.D., Lesley Towse, B.Sc., Helen Finnigan, M.Sc., Ronald Dahl, M.D., Marc Decramer, M.D., Ph.D., Pascal Chanez, M.D., Ph.D., Emiel F.M. Wouters, M.D., Ph.D., and Peter M.A. Calverley, M.D., for the WISDOM Investigators*

CONCLUSIONS

In patients with severe COPD receiving tiotropium plus salmeterol, the risk of moderate or severe exacerbations was similar among those who discontinued inhaled glucocorticoids and those who continued glucocorticoid therapy. However, there was a greater decrease in lung function during the final step of glucocorticoid withdrawal. (Funded by Boehringer Ingelheim Pharma; WISDOM ClinicalTrials.gov number, NCT00975195.)
Novel Pharmacological Targets in COPD

• Novel formulations of existing medications
  – Ultra LABAs (indacaterol, oladaterol)
  – Ultra LAMAs (aclidinium, umeclidinium, glycopyrinium)
  – LABA/LAMA combinations (vilianterol/umeclidinium, indacaterol/glycopyrrolate, formoterol/glycopyrrolate)
  – LABA/ICS combinations (vilianterol/fluticasone)
  – Nebulized bronchodilators and combination therapies
Recently Approved Medications

Umeclidinium and Vilanterol
(Anoro Ellipta™)

Fluticasone furoate and Vilanterol
(Breo Ellipta™)
Breo Ellipta & Anoro Ellipta

**Breo Ellipta™**

- **Mechanism**
  - Long-acting inhaled corticosteroid and beta₂ agonist

- **Cost**: AWP = $123/mo

**Anoro Ellipta™**

- **Mechanism**
  - Long-acting anticholinergic and beta₂ agonist

- **Cost**: none available

Manufacturer: GlaxoSmithKline
Aclidinium (Tudorza Pressair™)

- FDA-approved for the long-term maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. (July 23, 2012)

- Manufacturer
  - Forest Pharmaceuticals, Inc.

- Mechanism of Action
  - Long-acting anti-muscarinic agent with similar affinity to the M1 to M5 subtypes of muscarinic receptors
  - In the airways, it exhibits pharmacological effects through inhibition of M1 receptor
Aclidinium (Tudorza Pressair™)

- Approved dosing
  - COPD:
    - 400mcg inhaled twice daily → No dosage adjustments
    - Inhalation powder: the multi-dose device is a dry powder inhaler metering 400 mcg of aclidinium bromide per actuation
Warnings and Precautions

- Contraindications: None
- Warnings and Precautions
  - Potential worsening of narrow angle glaucoma
  - Potential worsening of urinary retention
    - Absolute bioavailability of ~ 6% in healthy adults
    - Use as indicated by guidelines; educate patients and monitor, especially in BPH/LUTB
- Drug interactions
  - Limited potential for CYP450 Interactions → no studies
- Side effects:
- Cost: currently covered under Tricare
Where does Tudorza™ fit?

- Alternative to tiotropium
- Limited clinical evidence, no head-to-head clinical comparison to other long-acting bronchodilators
- At this point, Aclidinium (Tudorza™) would only be preferred if cost was substantially less
New Drug Approval

• Striverdi Respimat (olodaterol Respimat) received FDA approval for the treatment of COPD
  • Long-acting beta-adrenergic agonist (LABA)

FYI - Spiriva is due to lose patent protection soon ... a once-daily combination of olodaterol and tiotropium is being investigated

7/31/2014  FDA News and Events
The new Respimat inhaler delivers the drug in a mist form. The traditional inhaler, known as a HandiHaler, uses a dry powder form of the drug. Both have been shown to be equally safe and effective for COPD patients.
A large proportion (49-76%) of patients use their inhalers incorrectly. GOLD guidelines recommend rechecking inhaler technique at each patient visit.

## Misuse of Inhalers Is Common in COPD (≥3% of Patients)

<table>
<thead>
<tr>
<th>Metered Dose Inhalers</th>
<th>Percent of patients</th>
<th>Dry Powder Inhalers</th>
<th>Percent of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to coordinate MDI actuation with inhalation</td>
<td>27</td>
<td>Not holding device correctly</td>
<td>35</td>
</tr>
<tr>
<td>Too short a breath hold after inhalation</td>
<td>26</td>
<td>Exhaling through mouthpiece</td>
<td>19</td>
</tr>
<tr>
<td>Too rapid an inspiratory flow</td>
<td>19</td>
<td>Not exhaling to residual volume before inhaling</td>
<td>24</td>
</tr>
<tr>
<td>Inadequate shaking/mixing before use</td>
<td>13</td>
<td>Not inhaling forcefully</td>
<td>17</td>
</tr>
<tr>
<td>Abrupt discontinuation of inspiration as aerosol hits throat</td>
<td>6</td>
<td>Inadequate or no breath hold</td>
<td>23</td>
</tr>
<tr>
<td>Actuating MDI at total lung capacity</td>
<td>4</td>
<td>Exhaling into mouthpiece after inhaling</td>
<td>20</td>
</tr>
<tr>
<td>Firing MDI multiple times during a single inhalation</td>
<td>3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Rau JL. *Respir Care.* 2006;51:158-172.
Clinician’s Factors That Determine Selection of Delivery System

- Accurate and Consistent Drug Delivery
- Robust
  low intrinsic airflow resistance

Deliver wide range of therapies

Cost/Reimbursement/Insurance coverage

Patient’s disease severity

Liked by patients

Ease of Use

Type of prescribed Medication:
ICS vs. bronchodilators

Clinical Efficacy
Patent’s Factors That Determine Selection of Delivery Method

- Lifestyle/Preference
- Disease Severity
- Cost/Reimbursement
- Clinical Setting and Caregiver Capability/Preference
- Physical Ability/Dexterity
- Cognitive Ability
- History of Compliance
Strategies to Ensure Adherence

- Educate patients about COPD and treatments
- Support self-efficacy; encourage and praise successes
- Set treatment goals
- Ask about device preference
- Use “teach back” method
- Train patients on proper use of devices periodically
- Ask about side effects
- Urge patients to complete treatment course—even if they feel better
Summary

• COPD continues to be a major public health problem

• Early diagnosis and staging using spirometry are essential

• Smoking cessation prevents the rapid deterioration of lung function and improves survival

• Other non-pharmacologic approaches are available and need to be considered

• Currently available medications for COPD can reduce or abolish symptoms, increase exercise capacity, reduce the number and severity of exacerbations, and improve health status.

• Novel interventions are under development but are still experimental
Questions ???