Update in COPD

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Objectives

- **Burden of disease:**
  - Understand the need for early recognition, prevention, and treatment of COPD

- **COPD diagnosis:**
  - Importance of spirometry, symptom and exacerbation assessment

- **Treatment:**
  - Review current GOLD guidelines

- **Asthma / COPD Overlap**

- **The Future of COPD:**
  - Current Clinical Trials
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“COPD, a common **preventable and treatable** disease is characterized by persistent airflow limitation.”

“Airflow limitation is usually progressive and is **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 is a Major Public Health Problem

- 16.3 million office visits each year due to COPD\textsuperscript{1}
- 672,000 hospitalizations each year for COPD\textsuperscript{2}
  - 21\% mortality rate at one year after being hospitalized for a COPD exacerbation in a large VA cohort\textsuperscript{3}
- COPD is currently the 3rd-leading cause of death in the United States\textsuperscript{4}
- Total costs for COPD estimated at $49.9 billion in 2007

Percent Change in Age-Adjusted US Death Rates

Coronary Heart Disease: -59%
Stroke: -64%
Other CVD: -35%
COPD: +163%
All Other Causes: -7%

## COPD: Risk Factors

<table>
<thead>
<tr>
<th>Established</th>
<th>Probable</th>
<th>Possible</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cigarette smoking</strong></td>
<td><strong>Exposure to primary and secondary smoke</strong></td>
<td><strong>Low birth weight</strong></td>
</tr>
<tr>
<td>Occupational exposure</td>
<td><strong>Hyperactive airways</strong></td>
<td><strong>Childhood respiratory infections</strong></td>
</tr>
<tr>
<td>( \alpha_1 )-Antitrypsin deficiency (genetic abnormality)</td>
<td><strong>Alcohol</strong></td>
<td><strong>Family history</strong></td>
</tr>
<tr>
<td>Air pollution</td>
<td><strong>Poverty</strong></td>
<td><strong>Atopy</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>IgA deficiency</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Blood type A</strong></td>
</tr>
</tbody>
</table>

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Spirometry Steps For Suspected COPD

**STEP 1**

- OAD (COPD or Asthma)
  - FEV$_1$/FVC <70%
  - FEV$_1$/FVC >70%
  - Normal

**STEP 2**

- FVC
  - >80%
  - Obstructive disease only
  - <80%
  - Concomitant restrictive component

- WNL >80%
  - FVC

- <80%
  - Restrictive Airways Disease
Disease must be detectable in an early stage: Lung Function Over Time

Adapted from Fletcher et al. BMJ. 1977;1:1645-1648.
Underdiagnosis of COPD in the United States

Diagnosed with chronic bronchitis or emphysema
Airflow limitation (GOLD 1 or higher)

Rate per 1000 of Population

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Diagnosed with chronic bronchitis or emphysema</th>
<th>Airflow limitation (GOLD 1 or higher)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-44</td>
<td>22.9%</td>
<td>7.2%</td>
</tr>
<tr>
<td>45-54</td>
<td>14%</td>
<td>20.7%</td>
</tr>
<tr>
<td>55-64</td>
<td>14%</td>
<td>20.7%</td>
</tr>
<tr>
<td>65-74</td>
<td>22.9%</td>
<td>7.2%</td>
</tr>
<tr>
<td>/=75</td>
<td>22.9%</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

The Argument for Selective Screening

1. During the past 4 weeks, how much of the time did you feel short of breath?
   - None of the time
   - A little of the time
   - Some of the time
   - Most of the time
   - All of the time

2. Do you ever cough up any “stuff,” such as mucus or phlegm?
   - No, never
   - Only with occasional colds or chest infections
   - Yes, a few days a month
   - Yes, most days a week
   - Yes, every day

3. Please select the answer that best describes you in the past 12 months.
   I do less than I used to because of my breathing problems.
   - Strongly disagree
   - Disagree
   - Unsure
   - Agree
   - Strongly agree

4. Have you smoked at least 100 cigarettes in your ENTIRE LIFE?
   - No
   - Yes
   - Don’t know

5. How old are you?
   - Age 35 to 49
   - Age 50 to 59
   - Age 60 to 69
   - Age 70+

Martinez, et al., COPD, 2008;5:85. “COPD Screener”
Symptoms in COPD

- Expiratory Flow Limitation
  - Breathlessness
    - Deconditioning
    - Inactivity
  - Reduced exercise capacity
    - Poor Quality of Life
Exacerbation Frequency Increases With Disease Severity

![Bar chart showing exacerbation frequency per year for different ranges of % Predicted FEV1: >60% (1.6), 40%-59% (1.9), and <40% (2.3).]

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.

Exacerbation was defined as an increase in dyspnea, sputum volume, and/or sputum purulence.

Frequency of Exacerbations Is Associated With a Decline in Lung Function

Exacerbations Per Year

FEV$_1$, mL/year

-25.3*

-46.1

*P<0.001

Results based on a secondary analysis of 32 patients who recorded daily FEV$_1$. The median rate of exacerbations seen at clinic was 1.5 per patient per year.

Patients With Frequent Exacerbations Had Significantly Worse Quality of Life

Mean Difference: -15.1*
Mean Difference: -21.9*
Mean Difference: -12.2*
Mean Difference: -14.1*

P ≤ 0.002

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- **The Future of COPD:**
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Goal of the Combined COPD Assessment is to stratify subjects based on
- Risk for exacerbations, hospitalizations and death
- Symptoms

Metrics used to stratify
- FEV1% predicted
- Exacerbation history
- Symptoms using either the modified Medical Research Council (mMRC) dyspnea score or the COPD Assessment Test (CAT) score
### Classification of Airflow Limitation

<table>
<thead>
<tr>
<th>Classification</th>
<th>Severity</th>
<th>FEV1 Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD I</td>
<td>Mild</td>
<td>FEV1 $\geq$ 80% predicted</td>
</tr>
<tr>
<td>GOLD II</td>
<td>Moderate</td>
<td>50% $\leq$ FEV1 $&lt; 80$% predicted</td>
</tr>
<tr>
<td>GOLD III</td>
<td>Severe</td>
<td>30% $\leq$ FEV1 $&lt; 50$% predicted</td>
</tr>
<tr>
<td>GOLD IV</td>
<td>Very Severe</td>
<td>FEV1 $&lt; 30$% predicted</td>
</tr>
</tbody>
</table>

In patients with FEV1/FVC $< 0.70$
GOLD 2011 Consensus Statement

Symptoms
(mMRC or CAT score)

Risk
(GOLD Classification of Airflow Limitation)

(A) mMRC 0-1
CAT < 10

(B) mMRC > 2
CAT ≥ 10

(C) mMRC 0-1
CAT < 10

(D) mMRC > 2
CAT ≥ 10

Risk (Exacerbation history)

≥ 2

1

0
### Modified Medical Research Council Questionnaire for Assessing Breathlessness

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>I only get breathless with strenuous exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>I get short of breath when hurrying on the level or walking up a slight hill</td>
</tr>
<tr>
<td>Grade 2</td>
<td>I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level</td>
</tr>
<tr>
<td>Grade 3</td>
<td>I stop for breath after walking about 100 m or after a few minutes on the level</td>
</tr>
<tr>
<td>Grade 4</td>
<td>I am too breathless to leave the house or I am breathless when dressing or undressing</td>
</tr>
</tbody>
</table>
CAT: COPD Assessment Test

I never cough 0 1 2 3 4 5 I cough all the time

I have no phlegm (mucus) in my chest at all 0 1 2 3 4 5 My chest is completely full of phlegm (mucus)

My chest does not feel tight at all 0 1 2 3 4 5 My chest feels very tight

When I walk up a hill or one flight of stairs I am not breathless 0 1 2 3 4 5 When I walk up a hill or one flight of stairs I am very breathless

I am not limited doing any activities at home 0 1 2 3 4 5 I am very limited doing activities at home

I am confident leaving my home despite my lung condition 0 1 2 3 4 5 I am not at all confident leaving my home because of my lung condition

I sleep soundly 0 1 2 3 4 5 I don’t sleep soundly because of my lung condition

I have lots of energy 0 1 2 3 4 5 I have no energy at all

FEV₁ and Risk for Exacerbations, Hospitalization and Death

Combined placebo data from TORCH, Uplift and ECLIPSE

<table>
<thead>
<tr>
<th>GOLD spirometric level</th>
<th>Exacerbations / year</th>
<th>Hospitalizations / year</th>
<th>3-year mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD I</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>GOLD II</td>
<td>0.7 – 0.9</td>
<td>0.11 – 0.2</td>
<td>11%</td>
</tr>
<tr>
<td>GOLD III</td>
<td>1.1 – 1.3</td>
<td>0.25 – 0.3</td>
<td>15%</td>
</tr>
<tr>
<td>GOLD IV</td>
<td>1.2 – 2.0</td>
<td>0.4 – 0.54</td>
<td>24%</td>
</tr>
</tbody>
</table>

2011 GOLD Consensus Report [www.goldcopd.com](http://www.goldcopd.com)
Exacerbations become more frequent and more severe as severity of COPD increases

ECLIPSE study (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints)

- A large, observational cohort of 2138 patients followed for 3 years
  - age 40-75 years, ≥10 pack-year smoking history, postbronchodilator FEV$_1$ < 80% of predicted, FEV$_1$/FVC ratio < 0.7

- Exacerbations were defined as events that resulted in treatment with antibiotics and/or corticosteroids (moderate) or that led to hospitalization.

Results:

- Exacerbations were found to be more frequent and more severe as the patient's disease worsened.

- Single best predictor of exacerbations, across GOLD stages II through IV, was a history of exacerbations.

- Subjects with 2 or more exacerbations was the most stable “phenotype”

Relationship between FEV1 and Quality of Life
GOLD 2011 consensus statement

A

Short of breath walking on the level? NO

2 or more Exacerbations in Prior Year? NO AND

FEV1>50%

B

FEV1>50%

C

Short of breath walking on the level? NO

2 or more Exacerbations in Prior Year? YES

OR

FEV1<50%

D

FEV1<50%

Short of breath walking on the level? YES

2 or more Exacerbations in Prior Year? YES or

OR

FEV1<50%
Achievable Outcomes of Therapy in COPD

- Bronchodilators are effective in improving airflow and lung volume
- Symptomatic patients with appropriate treatment can expect
  - Relief of dyspnea
  - Improvement of exercise tolerance
  - Improvement of quality of life
  - Decrease in exacerbations

GOLD 2007 Treatment Overview

GOLD Stage

- **I Mild**
  - Active reduction of risk factors: influenza vaccine
  - Add short-acting bronchodilators when needed

- **II Moderate**
  - Add regular Rx with ≥1 long-acting bronchodilator when needed. Add rehabilitation

- **III Severe**
  - Add inhaled corticosteroids (ICS) if repeated exacerbations

- **IV Very Severe**
  - Add $O_2^*$
  - Consider surgery

* If chronic respiratory failure.

### GOLD 2011 Treatment Overview

<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>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>LAMA &amp; LABA</td>
<td>SABA and/or SAMA Theophylline</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA &amp; LABA</td>
<td>PDE4 inhibitor SABA and/or SAMA Theophylline</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA or LAMA</td>
<td>ICS &amp; LAMA or ICS &amp; LABA &amp; LAMA or ICS &amp; LABA &amp; PDE4 inhibitor or LAMA &amp; LABA or LAMA &amp; PDE4 inhibitor</td>
<td>Carbocysteine SABA and/or SAMA Theophylline</td>
</tr>
<tr>
<td>Patient Group</td>
<td>First Choice</td>
<td>Second Choice</td>
<td>For Whom is this Appropriate?</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------------------------------</td>
<td>---------------------------------------------</td>
<td>------------------------------------------------------------------</td>
</tr>
<tr>
<td>A</td>
<td>SAMA PRN or SABA PRN</td>
<td>LAMA or LABA or SABA and SAMA</td>
<td>Not short of breath on the level &lt; 2 exacerbations in prior year FEV1&gt;50%</td>
</tr>
<tr>
<td>B</td>
<td>LAMA or LABA</td>
<td>LAMA &amp; LABA</td>
<td>Short of breath on the level &lt; 2 exacerbations in prior year FEV1&gt;50%</td>
</tr>
<tr>
<td>C</td>
<td>ICS + LABA or LAMA</td>
<td>LAMA &amp; LABA</td>
<td>Not short of breath on the level ≥ 2 or more Exacerbations in FEV1&lt;50%</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA or LAMA</td>
<td>ICS &amp; LAMA or ICS &amp; LABA &amp; LAMA or ICS &amp; LABA &amp; PDE4 inhibitor or LAMA &amp; LABA or LAMA &amp; PDE4 inhibitor</td>
<td>Short of breath on the level ≥ 2 or more Exacerbations in FEV1&lt;50%</td>
</tr>
</tbody>
</table>
“New Kids on the Block”

- **Roflumilast** (Daliresp)
  - PDE4 inhibitor
  - Indicated for exacerbation reduction in patients with history of exacerbations AND chronic cough and sputum production
  - QD dosing

- **Aclidinium** (Tudorza)
  - Long-acting anticholinergic
  - BID dosing
  - Indicated for maintenance therapy in COPD

- **Indacaterol** (Arcapta)
  - Long-acting beta-agonist
  - QD dosing
  - Indicated for maintenance therapy in COPD
“New Kids on the Block”

- **Fluticasone/Vilanterol (Breo)**
  - ICS/LABA
  - Indicated for maintenance treatment of COPD
  - QD dosing

- **Vilanterol/Umeclidinium (Anoro)**
  - LABA/LAMA
  - Indicated for maintenance therapy in COPD
  - QD dosing

- **Umeclidinium (Incruse)**
  - Long-acting anticholinergic
  - QD dosing
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Asthma-COPD overlap syndrome (ACOS) is characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. ACOS is therefore identified by the features that it shares with both asthma and COPD.
Asthma / COPD Overlap

- **Step 1:** Does the patient have chronic airway disease?
- **Step 2:** The syndromic diagnosis of asthma, COPD and ACOS in an adult patient?
- **Step 3:** Spirometry
- **Step 4:** Commence initial therapy
Asthma / COPD Overlap

Step 1: Does the patient have chronic airway disease?
- Clinical history
  - Cough, sputum, dyspnea, wheeze
  - Tobacco history
- Physical Exam
  - Hyperinflation, wheezing
- Radiology
  - Hyperinflation, airway thickening, emphysema
Asthma / COPD Overlap

Step 2: The syndromic diagnosis of asthma, COPD and ACOS in an adult patient.

- Assemble the features that favor a diagnosis of asthma or COPD
- Compare the number of features in favor of a diagnosis of asthma vs COPD
- Having 3 or more features listed for either asthma or COPD in absence of those for alternative diagnosis provides strong likelihood of diagnosis.
- When a patient has a similar number of features of both asthma and COPD, diagnosis of ACOS should be considered.
### Table 2a. Usual features of asthma, COPD and ACOS

<table>
<thead>
<tr>
<th>Feature</th>
<th>Asthma</th>
<th>COPD</th>
<th>ACOS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of onset</strong></td>
<td>Usually childhood onset but can commence at any age.</td>
<td>Usually &gt; 40 years of age</td>
<td>Usually age ≥40 years, but may have had symptoms in childhood or early adulthood</td>
</tr>
<tr>
<td><strong>Pattern of respiratory symptoms</strong></td>
<td>Symptoms may vary over time (day to day, or over longer periods), often limiting activity. Often triggered by exercise, emotions including laughter, dust or exposure to allergens</td>
<td>Chronic usually continuous symptoms, particularly during exercise, with ‘better’ and ‘worse’ days</td>
<td>Respiratory symptoms including exertional dyspnea are persistent but variability may be prominent</td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td>Current and/or historical variable airflow limitation, e.g. BD reversibility, AHR</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;, may be improved by therapy, but post-BD FEV&lt;sub&gt;1&lt;/sub&gt;/FVC &lt; 0.7 persists</td>
<td>Airflow limitation not fully reversible, but often with current or historical variability</td>
</tr>
<tr>
<td><strong>Lung function between symptoms</strong></td>
<td>May be normal between symptoms</td>
<td>Persistent airflow limitation</td>
<td>Persistent airflow limitation</td>
</tr>
<tr>
<td><strong>Past history or family history</strong></td>
<td>Many patients have allergies and a personal history of asthma in childhood, and/or family history of asthma</td>
<td>History of exposure to noxious particles and gases (mainly tobacco smoking and biomass fuels)</td>
<td>Frequently a history of doctor-diagnosed asthma (current or previous), allergies and a family history of asthma, and/or a history of noxious exposures</td>
</tr>
<tr>
<td><strong>Time course</strong></td>
<td>Often improves spontaneously or with treatment, but may result in fixed airflow limitation</td>
<td>Generally, slowly progressive over years despite treatment</td>
<td>Symptoms are partly but significantly reduced by treatment. Progression is usual and treatment needs are high</td>
</tr>
<tr>
<td><strong>Chest X-ray</strong></td>
<td>Usually normal</td>
<td>Severe hyperinflation &amp; other changes of COPD</td>
<td>Similar to COPD</td>
</tr>
<tr>
<td><strong>Exacerbations</strong></td>
<td>Exacerbations occur, but the risk of exacerbations can be considerably reduced by treatment</td>
<td>Exacerbations can be reduced by treatment. If present, comorbidities contribute to impairment</td>
<td>Exacerbations may be more common than in COPD but are reduced by treatment. Comorbidities can contribute to impairment</td>
</tr>
<tr>
<td><strong>Typical airway inflammation</strong></td>
<td>Eosinophils and/or neutrophils</td>
<td>Neutrophils in sputum, lymphocytes in airways, may have systemic inflammation</td>
<td>Eosinophils and/or neutrophils in sputum.</td>
</tr>
</tbody>
</table>

### Table 2b. Features that favor asthma or COPD

<table>
<thead>
<tr>
<th>Favors Asthma</th>
<th>Favors COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset before age 20 years</td>
<td>Onset after age 40 years</td>
</tr>
<tr>
<td>Variation in symptoms over minutes, hours or days</td>
<td>Persistence of symptoms despite treatment</td>
</tr>
<tr>
<td>Symptoms worse during the night or early morning</td>
<td>Good and bad days but always daily symptoms and exertional dyspnea</td>
</tr>
<tr>
<td>Symptoms triggered by exercise, emotions including laughter, dust or exposure to allergens</td>
<td>Chronic cough and sputum preceded onset of dyspnea, unrelated to triggers</td>
</tr>
<tr>
<td>Record of variable airflow limitation (spirometry, peak flow)</td>
<td>Record of persistent airflow limitation (post-bronchodilator FEV&lt;sub&gt;1&lt;/sub&gt;/FVC &lt; 0.7)</td>
</tr>
<tr>
<td>Lung function normal between symptoms</td>
<td>Lung function abnormal between symptoms</td>
</tr>
<tr>
<td>Previous doctor diagnosis of asthma</td>
<td>Previous doctor diagnosis of COPD, chronic bronchitis or emphysema</td>
</tr>
<tr>
<td>Family history of asthma, and other allergic condi</td>
<td>Heavy exposure to a risk factor: tobacco smoke, biomass fuels</td>
</tr>
<tr>
<td>No worsening of symptoms over time. Symptoms vary either seasonally, or from year to year</td>
<td>Symptoms slowly worsening over time (progressive course over years)</td>
</tr>
<tr>
<td>May improve spontaneously or have an immediate response to BD or to ICS over weeks</td>
<td>Rapid-acting bronchodilator treatment provides only limited relief.</td>
</tr>
</tbody>
</table>

*Syndromic diagnosis of airways disease: how to use Table 2b*

Shaded columns list features that, when present, best distinguish between asthma and COPD. For a patient, count the number of check boxes in each column. If three or more boxes are checked for either asthma or COPD, that diagnosis is suggested. If there are similar numbers of checked boxes in each column, the diagnosis of ACOS should be considered. See Step 2 for more details.
Asthma / COPD Overlap

- Step 3: Spirometry – essential in all patient suspected of chronic airway disease

<table>
<thead>
<tr>
<th>Spirometric variable</th>
<th>Asthma</th>
<th>COPD</th>
<th>ACOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal FEV₁/FVC pre- or post BD</td>
<td>Compatible with diagnosis</td>
<td>Not compatible with diagnosis</td>
<td>Not compatible unless other evidence of chronic airflow limitation</td>
</tr>
<tr>
<td>Post-BD FEV₁/FVC &lt; 0.7</td>
<td>Indicates airflow limitation but may improve spontaneously or on treatment</td>
<td>Required for diagnosis (GOLD)</td>
<td>Usually present</td>
</tr>
<tr>
<td>FEV₁ ≥80% predicted</td>
<td>Compatible with diagnosis (good asthma control or interval between symptoms)</td>
<td>Compatible with GOLD classification of mild airflow limitation (categories A or B) if post-BD FEV₁/FVC &lt; 0.7</td>
<td>Compatible with diagnosis of mild ACOS</td>
</tr>
<tr>
<td>FEV₁ &lt;80% predicted</td>
<td>Compatible with diagnosis. Risk factor for asthma exacerbations</td>
<td>An indicator of severity of airflow limitation and risk of future events (e.g., mortality and COPD exacerbations)</td>
<td>An indicator of severity of airflow limitation and risk of future events (e.g., mortality and exacerbations)</td>
</tr>
<tr>
<td>Post-BD increase in FEV₁ &gt;12% and 200 ml from baseline (reversible airflow limitation)</td>
<td>Usual at some time in course of asthma, but may not be present when well-controlled or on controllers</td>
<td>Common and more likely when FEV₁ is low, but ACOS should also be considered</td>
<td>Common and more likely when FEV₁ is low, but ACOS should also be considered</td>
</tr>
<tr>
<td>Post-BD increase in FEV₁ &gt;12% and 400 ml from baseline (marked reversibility)</td>
<td>High probability of asthma</td>
<td>Unusual in COPD. Consider ACOS</td>
<td>Compatible with diagnosis of ACOS</td>
</tr>
</tbody>
</table>

ACOS: asthma-COPD overlap syndrome; BD: bronchodilator; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; GOLD: Global Initiative for Obstructive Lung Disease.
Step 4: Initiation of Treatment

- If asthma or ACOS is suspected or if there is uncertainty in diagnosis of COPD, treat as if asthma
  - Treatment should include an ICS
  - Long-acting beta2-agonist (LABA) should be continued or added
  - These patients should not be treated with LABA without ICS
- If assessment suggests COPD, treatment with bronchodilator should be commenced, but not ICS alone
- Smoking cessation, pulmonary rehabilitation, vaccinations appropriate for all
Asthma / COPD Overlap

- Step 5: referral for specialized investigations if necessary
  - Persistent symptoms despite treatment
  - Diagnostic uncertainty

<table>
<thead>
<tr>
<th>Lung function tests</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLCO</td>
<td>Normal (or slightly elevated).</td>
<td>Often reduced.</td>
</tr>
<tr>
<td>Arterial blood gases</td>
<td>Normal between exacerbations</td>
<td>May be chronically abnormal between exacerbations in more severe forms of COPD</td>
</tr>
<tr>
<td>Airway hyperresponsiveness (AHR)</td>
<td>Not useful on its own in distinguishing asthma from COPD, but high levels of AHR favor asthma</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Imaging</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>High resolution CT Scan</td>
<td>Usually normal but air trapping and increased bronchial wall thickness may be observed.</td>
<td>Low attenuation areas denoting either air trapping or emphysematous change can be quantitated; bronchial wall thickening and features of pulmonary hypertension may be seen.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inflammatory biomarkers</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test for atopy (specific IgE and/or skin prick tests)</td>
<td>Modestly increases probability of asthma; not essential for diagnosis</td>
<td>Conforms to background prevalence; does not rule out COPD</td>
</tr>
<tr>
<td>FENO</td>
<td>A high level (&gt;50 ppb) in non-smokers supports a diagnosis of eosinophilic airway inflammation</td>
<td>Usually normal. Low in current smokers.</td>
</tr>
<tr>
<td>Blood eosinophilia</td>
<td>Supports asthma diagnosis</td>
<td>May be present during exacerbations</td>
</tr>
<tr>
<td>Sputum inflammatory cell analysis</td>
<td>Role in differential diagnosis is not established in large populations</td>
<td></td>
</tr>
</tbody>
</table>
STEP 1  DIAGNOSE CHRONIC AIRWAYS DISEASE
Do symptoms suggest chronic airways disease?

Yes  No  Consider other diseases first

STEP 2  SYNDROMIC DIAGNOSIS IN ADULTS
(i) Assemble the features for asthma and for COPD that best describe the patient.
(ii) Compare number of features in favour of each diagnosis and select a diagnosis

<table>
<thead>
<tr>
<th>Feature: if present suggests</th>
<th>ASTHMA</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Before age 20 years</td>
<td>After age 40 years</td>
</tr>
<tr>
<td>Pattern of symptoms</td>
<td>Variation over minutes, hours or days</td>
<td>Persistent despite treatment</td>
</tr>
<tr>
<td></td>
<td>Worse during the night or early morning</td>
<td>Good and bad days but always daily symptoms and exertional dyspnoea</td>
</tr>
<tr>
<td></td>
<td>Triggered by exercise, emotions including laughter, dust or exposure to allergens</td>
<td>Chronic cough &amp; sputum preceding onset of dyspnea, unrelated to triggers</td>
</tr>
<tr>
<td>Lung function</td>
<td>Record of variable airflow limitation (spirometry or peak flow)</td>
<td>Record of persistent airflow limitation (FEV1/FVC &lt; 0.7 post-BD)</td>
</tr>
<tr>
<td>Lung function between symptoms</td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Past history or family history</td>
<td>Previous doctor diagnosis of asthma</td>
<td>Previous doctor diagnosis of COPD, chronic bronchitis or emphysema</td>
</tr>
<tr>
<td></td>
<td>Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)</td>
<td>History of respiratory symptoms or smoking</td>
</tr>
<tr>
<td>Time course</td>
<td>No worsening of symptoms over time</td>
<td>Symptoms slowly worsening over time (progressive course over years)</td>
</tr>
<tr>
<td></td>
<td>Variation in symptoms either seasonally, or from year to year</td>
<td>Rapid-acting bronchodilator treatment provides only limited relief</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Normal</td>
<td>Severe hyperinflation</td>
</tr>
</tbody>
</table>

NOTE: These features best distinguish between asthma and COPD. Several positive features (3 or more) for either asthma or COPD suggest that diagnosis. If there is a similar number for both asthma and COPD, consider diagnosis of ACOS.

DIAGNOSIS

<table>
<thead>
<tr>
<th>Asthma</th>
<th>Some features of asthma</th>
<th>Features of both</th>
<th>Some features of COPD</th>
<th>Possibly COPD</th>
<th>COPD</th>
</tr>
</thead>
</table>

CONFIDENCE IN DIAGNOSIS

<table>
<thead>
<tr>
<th>Asthma</th>
<th>Possible asthma</th>
<th>Could be ACOS</th>
<th>Possibly COPD</th>
<th>COPD</th>
</tr>
</thead>
</table>

STEP 3  PERFORM SPIROMETRY
Marked reversible airflow limitation (pre-post bronchodilator) or other proof of variable airflow limitation

FEV1/FVC < 0.7 post-BD

STEP 4  INITIAL TREATMENT*

*Consult GINA and GOLD documents for recommended treatments.

- **Asthma drugs**
  - No LABA monotherapy
  - Asthma drugs No LABA monotherapy
  - ICS and consider LABA or LAMA
- **COPD drugs**
  - COPD drugs

STEP 5  SPECIALISED INVESTIGATIONS or REFER IF:

- Persistent symptoms and/or exacerbations despite treatment.
- Diagnostic uncertainty (e.g. suspected pulmonary hypertension, cardiovascular diseases and other causes of respiratory symptoms).
- Suspected asthma or COPD with atypical or additional symptoms or signs (e.g. haemoptysis, weight loss, night sweats, fever, signs of bronchiectasis or other structural lung disease).
- Few features of either asthma or COPD.
- Comorbidities present.
- Reasons for referral for either diagnosis is outlined in the GINA and GOLD strategy reports.
ACOS Treatments on the Horizon?

- IL-5 inhibitors (mepolizumab, benralizumab) currently being studies in both asthma and COPD

A Phase 2a Study Of Benralizumab, An Anti-Interleukin-5 Receptor A Monoclonal Antibody, In Adults With Chronic Obstructive Pulmonary Disease And Sputum Eosinophilia

C. E. Brightling¹, R. Van Der Merwe²,³, D. She⁴, C. Birrell²,
¹University Of Leicester, Leicester, United Kingdom, ²MedImmune, Cambridge, United Kingdom, ³, ⁴MedImmune, Gaithersburg, MD

CONCLUSIONS: Benralizumab depleted both peripheral blood and sputum eosinophils in subjects with COPD and sputum eosinophilia. Although the primary endpoint was not met, benralizumab significantly improved FEV₁ over placebo. A positive correlation appeared to be present between increased baseline blood eosinophil count and efficacy parameters.
Objectives

▪ Burden of disease:
  ▪ Understand the need for early recognition, prevention, and treatment of COPD

▪ COPD diagnosis:
  ▪ Importance of spirometry, symptom and exacerbation assessment

▪ Treatment:
  ▪ Review current GOLD guidelines

▪ Asthma / COPD Overlap

▪ The Future of COPD:
  ▪ Current Clinical Trials
Future Directions: COPD Phenotypes

Clinical Commentary

Chronic Obstructive Pulmonary Disease Phenotypes
The Future of COPD

“A single or combination of disease attributes that describe differences between individuals with COPD as they relate to clinically meaningful outcomes (symptoms, exacerbations, response to therapy, rate of disease progression or death).”

Defined by symptoms, radiology, physiology, biologic markers

Ultimately have similar biologic or physiologic mechanisms

Han, et al. AJRCCM 2010;182:598.
Spiromics

Subpopulations and Intermediate Outcome Measures in COPD Study
Study Aims

Subgroup Finding

To identify homogeneous subgroups of COPD patients for targeted enrollment in future therapeutic clinical trials

Intermediate Outcomes

To identify and perform preliminary validation of intermediate biological or clinical outcomes for use as clinical trial endpoints
Summary

- GOLD Consensus Report aids with disease staging and treatment selection

- Symptoms, Exacerbation History and FEV1 should be assessed for all COPD patients

- Therapy for COPD can:
  - Improve symptoms
  - Improve lung function
  - Improve exercise tolerance
  - Decrease exacerbation frequency

- Asthma and COPD may be hard to distinguish
  - ICS/LABA appropriate initial therapy for ACOS