Session 1: Optimizing Treatment in Patients with Stable COPD

Learning Objectives

1. Perform spirometry in patients with symptoms suggestive of chronic obstructive pulmonary disease (COPD) to confirm diagnosis and determine disease severity.

2. Develop treatment plans for COPD patients that are based on their symptoms and FEV1 values.
Session 1

Optimizing Treatment in Patients with Stable COPD

Faculty

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Stephen Rennard, MD, is Larson Professor of Medicine in the pulmonary and critical care medicine section of the department of pathology and microbiology and the department of genetics, cell biology, and anatomy at the University of Nebraska Medical Center in Omaha. He received an AB with honors in folklore and mythology from Harvard University and an MD with honors from the Baylor College of Medicine in Houston, Texas. He completed internal medicine training at Barnes Hospital, Washington University, in St. Louis, Missouri, and trained in pulmonary diseases at the National Institutes of Health, where he remained for seven years, conducting research in the cell biology of lung disease.

Dr Rennard currently serves on the board of directors of the COPD Foundation and the Alpha-1 Foundation. He is a member of the National Heart Lung Education Program Executive Committee and is the chair of the steering committee for SPIROMICS. He is an external advisor to the Thomas Petty Aspen Lung Conference and the University of California, Davis Pulmonary Training Grant.

Dr Rennard maintains an active program of clinical investigation in COPD and smoking cessation and a program of basic research in the mechanisms of lung tissue repair and remodeling, including the role of stem cells in disease pathogenesis and repair.

Faculty Financial Disclosure Statement
The presenting faculty reports the following:
Dr Rennard receives consulting fees from ABIM, APT Pharma, Align2Action, and AstraZeneca.
Optimizing Treatment in Patients with COPD

Stephen Rennard, MD

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Learning Objectives

- Perform spirometry in patients with symptoms suggestive of chronic obstructive pulmonary disease (COPD) to confirm diagnosis and determine disease severity.
- Develop comprehensive treatment plans for COPD patients that are based on their symptoms and FEV1 values.

Pre-ARS 1

Which of the following regarding the National Lung Screening Trial (NLST) is TRUE?

1. There was 20% mortality reduction in lung cancer in the CT group compared to the X-ray group
2. The rate of false positives in both the CT and X-ray groups was acceptably low at about 30%
3. The findings of the study can be extrapolated to all persons with a least a 10-year smoking history
4. All of the above

Pre-ARS 2

Initiating COPD drug therapy with a long-acting bronchodilator is indicated in:

1. Asymptomatic patients with mild COPD
2. Symptomatic patients with mild COPD
3. All of the above
4. None of the above since an inhaled corticosteroid is recommended as initial COPD therapy

Pre-ARS 3

The goal of long-term oxygen therapy (LTOT) in COPD patients with severe resting hypoxemia is to maintain a PaO2 of:

1. > 90 mm Hg
2. > 80 mm Hg
3. > 70 mm Hg
4. > 60 mm Hg
**Case 1: Kevin**

- A 53-year-old male presents for evaluation, accompanied by his wife
- He has no specific complaints but just wants “a check up”
- PMH: significant only for mild HTN, well-controlled on diuretic
  - SH:
    - Employed as an executive
    - Smoked 1.5 packs of cigarettes per day for 30 years; has cut back ½ pack per day × 6 months
    - Minimal alcohol
    - Mostly sedentary other than walking the dog and an occasional golf game

**Kevin**

- He denies respiratory complaints
- His wife interjects by saying he sometimes has a morning cough
- She is concerned about his smoking and asks about breathing tests and a CT scan to check for lung cancer
- Physical examination, lungs: unremarkable

**Kevin**

Would you order spirometry for this patient?

1. Yes
2. No
3. Not sure

**Spirometry**

- Crucial diagnostic test for patients with respiratory symptoms
  - combination of chronic cough, sputum production, or exertional dyspnea and either smoking or other exposures associated with risk
- Not recommended for “screening” of asymptomatic smokers
- Providing smokers with spirometry results not shown to improve smoking cessation rates

**COPD in the United States**

- Underdiagnosed and misdiagnosed
- Affects 5% of the adult population
  - Nearly 10 million diagnosed in 2010
- 3rd leading cause of death
- 12th leading cause of morbidity

**Prevalence of COPD in the United States 2007-2009**

- More common in women across most age groups

### GOLD Classification of COPD

<table>
<thead>
<tr>
<th>COPD Staging*</th>
<th>FEV₁/FVC Ratio</th>
<th>FEV₁, % predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I Mild</td>
<td>&lt; 70%</td>
<td>≥ 80% predicted</td>
</tr>
<tr>
<td>Stage II Moderate</td>
<td>&lt; 70%</td>
<td>50% to &lt; 80% predicted</td>
</tr>
<tr>
<td>Stage III Severe</td>
<td>&lt; 70%</td>
<td>30% to &lt; 50% predicted</td>
</tr>
<tr>
<td>Stage IV Very Severe</td>
<td>&lt; 70%</td>
<td>&lt; 30% predicted or &lt; 50% predicted plus chronic respiratory failure</td>
</tr>
</tbody>
</table>

*Severity determined by post-bronchodilator values

FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity

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### GOLD Guidelines

**Assess and Monitor Disease**

The GOLD Standard

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### Spirometry: Normal

![Spirometry: Normal](image)

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### Spirometry: Obstruction

![Spirometry: Obstruction](image)

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### COPD Assessment: A New Model

![COPD Assessment: A New Model](image)
Kevin

At the insistence of his wife, you agree to order spirometry.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Observed</th>
<th>Predicted</th>
<th>% Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁</td>
<td>3.22l</td>
<td>3.88</td>
<td>83%</td>
</tr>
<tr>
<td>FVC</td>
<td>4.73l</td>
<td>4.88</td>
<td>97%</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>08%</td>
<td>79.5%</td>
<td>85%</td>
</tr>
</tbody>
</table>

Kevin

Would you prescribe drug therapy at this point?

1. Yes
2. No
3. Unsure

No Proven Benefit of Drug Therapy in Asymptomatic Patients with COPD

Mild to Moderate Airflow Obstruction
- (FEV₁/FVC < 0.70 and FEV₁ > 50% Predicted)

OR

No Airflow Obstruction
- (FEV₁/FVC Ratio > 0.70)

Neither long-acting bronchodilators nor inhaled corticosteroids have been shown to prevent development of symptoms.


Dynamic Lung Volume Regulation in COPD Compared to Normal

Effect of Tiotropium on Dynamic Hyperinflation

What did Subjects Die From?

- Normal Lungs
- Moderate COPD
- Severe COPD

Mannino et al, Thorax, 2003
Relationship of FEV1 to Cardiac Risk: *hospitalization or death*

Si et al. Chest 127; 1952, 2005

- NHANES follow up dataset
- Age 40-60
- 1861 subjects
- Assess cardiac events
- FEV1

Kevin

What additional tests would you order?

1. CXR
2. Chest CT
3. Chest MRI
4. None are indicated

National Lung Screening Trial (NLST)

- Evaluated the efficacy of low-dose CT for lung cancer screening
- 53,454 current and former smokers aged 55-74 years with a history of > 30 pack-years
- Patients randomized to low-dose CT vs chest radiography offered at baseline and at 2 annual follow-up visits (3 screenings total)

NLST Results

Trial terminated early at an interim analysis due to a significant difference between groups that met a pre-specified stopping rule

- 20.0% mortality reduction from lung CA in CT group (95% CI, 6.8 to 26.7; P = 0.004; 346 vs 425 deaths/26K)
- Cancers discovered after a positive low-dose CT screening test were more likely to be early stage than those discovered after chest radiography
- 320 = Number needed to screen with low-dose CT to prevent 1 death from lung cancer

Potential Harms of Lung Cancer Screening

- Total false-positive screening results (3 screenings*)
  - Low-dose CT 96.4%
  - Radiography 94.5%
- Exposure to low-dose CT radiation increases cancer risk
- For 25% of false-positive CT, subjects underwent additional procedures and were exposed to higher doses of radiation
- False sense of security to smokers with negative screening result

*Subjects diagnosed with lung CA after first screening were not offered additional screening

NLST Take-Away Messages

- Study findings can only be extrapolated to persons aged 55-74, with a minimum 30 pack-year history, who are still smoking or have quit within 15 years.
- Smoking avoidance must continue to be the goal to prevent lung cancer morbidity/deaths and other diseases.
- Guidelines from U.S. Preventative Services Task Force and Canadian Task Force for Preventive Health Care do not recommend lung cancer screening, even in persons who smoke.

But …
National Comprehensive Cancer Network (NCCN)

2012 Recommendations for Lung Cancer Screening
Baseline low-dose CT, then annual screening for 3 years until age 74*
• Persons aged 55-74 with at least 30 pack-year smoking history and cessation for < 5 years
• Persons aged ≥ 50 with at least 20 pack-year history and one additional risk factor:
  – history of other cancer, lung disease, family history, radon exposure, occupational exposure

*Uncertainty about appropriate duration of screening and age to stop screening


Case 2: Barbara

• A 57-year-old woman presents for a health maintenance visit.
• PMH is significant for hyperlipidemia
• She is a former smoker, 40 pack-years, who quit 6 years ago. She works in an office
• Upon questioning, she admits she’s “slowed down a little bit” in terms of her activities as she gets out of breath more easily than she used to. She denies any recent change in exercise tolerance, exertional chest pain, or acute respiratory symptoms
• Physical examination is unremarkable

Barbara

How would you classify the severity of her disease?
1. Mild
2. Moderate
3. Severe
4. Very severe

Barbara

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Observed</th>
<th>Predicted</th>
<th>% Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁</td>
<td>1.89l</td>
<td>1.53</td>
<td>58%</td>
</tr>
<tr>
<td>FVC</td>
<td>1.4</td>
<td>2.11</td>
<td>63%</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>33%</td>
<td>33%</td>
<td>96%</td>
</tr>
</tbody>
</table>

ACP Clinical Practice Guidelines 2011

Diagnosis and Management of Stable Chronic Obstructive Pulmonary Disease: A Clinical Practice Guideline Update

American College of Physicians
American College of Chest Physicians
American Thoracic Society
European Respiratory Society

Drug Therapy Recommendations for Symptomatic Patients with Stable COPD

<table>
<thead>
<tr>
<th>Spirometry Results</th>
<th>Treatment</th>
<th>Recommendation Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁: 60%-80% predicted</td>
<td>Inhaled bronchodilators (LAAC or LABA) may be used</td>
<td>Weak; low-quality evidence</td>
</tr>
<tr>
<td>FEV₁ &lt; 60% predicted</td>
<td>MONOTHERAPY WITH INHALED LAAC OR LABA RECOMMENDED</td>
<td>Strong; moderate-quality evidence</td>
</tr>
<tr>
<td>Combination therapy with inhaled LAAC, LABA, or ICS may be used</td>
<td>Weak; moderate-quality evidence</td>
<td></td>
</tr>
</tbody>
</table>

NOTE: Occasional use of short-acting inhaled bronchodilators for acute symptom relief is not addressed in recommendations

LAAC = long-acting anticholinergic
LABA = long-acting beta agonist
ICS = inhaled corticosteroid

Inhaled Monotherapy

• LAAC or LABA reduce exacerbations and improve health-related quality of life
• Benefit of reduced mortality, hospitalizations, dyspnea not established
• ICS not a preferred monotherapy because of side effects
• Pooled analyses of monotherapy trials show no outcome differences among specific agents; however, recent large trials have shown some benefit of one monotherapy over another
• Monotherapy selection should be based on patient preference, side effects, cost


Combination Therapy

• When to use combination therapy over monotherapy not clearly established
• Benefit of decreased exacerbations and mortality not consistently shown
• Modest increase in adverse events compared to monotherapy
• Most studied combination: LABA plus ICS


Barbara

With appropriate therapy, over time you would expect her lung function to:

1. Improve
2. Remain the same
3. Decline

The Natural History of COPD


Can Anything Slow COPD Progression?

➢ Use of inhaled therapies in asymptomatic COPD patients has no impact on the rate of long-term FEV₁ decline or on development of symptoms.

➢ Neither monotherapy nor combination therapy in symptomatic COPD patients impact rate of FEV₁ decline to a clinically meaningful degree.

➢ However, smoking cessation significantly slows rate of FEV₁ decline.


FEV₁ Decline: ECLIPSE

Mean decline in all subjects was 33±2 mL/year

Significant variation in decline (or increase) observed between subjects

ECLIPSE 3 year data

LUNG HEALTH STUDY: Benefits of smoking cessation


- N=5887 usual care
- N=1964 usual care
- N=1964 smoking intervention
- N=1962 placebo
- N=1961 ipratropium

• sustained quitters
• changes in status
• sustained smokers


Natural History of Chronic Obstructive Pulmonary Disease: benefits of smoking cessation


- Non-smokers
  - Yearly
  - 5 years
  - 11 years
  - FEV-1

- Healthy smokers
  - 19.6 ml/year
  - 32.5 ml/year
  - Quitters > 40
  - 28.9 ml/year

Case 3: Walter

- A 68-year-old man recently underwent coronary artery stenting 1 week ago after presenting with unstable angina
- He is a 40 pack-year smoker who quit during his recent hospitalization
- PMH: HTN and COPD diagnosed 10 years ago
- His last COPD exacerbation was 8 months ago. He has never been hospitalized for respiratory issues, although he has been treated for exacerbations “once or twice a year” for the past several years

Walter

- PE: Normal VS. Somewhat barrel chested. Chest is resonant to percussion. Breath sounds are decreased diffusely. No wheezing or rales present.
- Previous meds: States he uses his inhalers—LABA and ICS
- New meds: Antithrombotic therapy, beta-blocker, ARB, statin, anxiolytic

Measurement | Observed | Predicted | % Predicted
---|---|---|---
FEV<sub>1</sub> | 1.5l | 3.18 | 47%
FVC | 2.7l | 4.72 | 58%
FEV<sub>1</sub>/FVC | 55% | 57.4% | 82%

Walter

How would you classify the severity of his COPD?

1. Mild
2. Moderate
3. Severe
4. Very severe
**COPD Assessment: A New Model**

Increasing Risk

GOLD classification

<table>
<thead>
<tr>
<th>Increasing</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>mMRC &lt;2</td>
<td>mMRC &gt;2</td>
</tr>
<tr>
<td>CAT &lt;10</td>
<td>CAT &gt;10</td>
</tr>
</tbody>
</table>

Increasing Symptoms

**Walter**

What treatment regimen would you prescribe?

1. Add third inhaler
2. Add daily oral prednisone
3. Add prophylactic antibiotic
4. Add pulmonary rehabilitation

**Treatments to Prevent Exacerbations**

- Long-acting anti-muscarinic bronchodilators
- Long-acting β-agonist/inhaled glucocorticoid
- PDE4 inhibitors

*Antibiotics
  - *Azithromycin
  - *Moxifloxacin
- *N-acetyl cysteine
- *Theophylline

*not FDA approved for this indication

**Pulmonary Rehabilitation**

**American Thoracic Society/European Respiratory Society Statement on Pulmonary Rehabilitation**

- Evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities
- Proven benefits
  - reduces dyspnea
  - increases exercise performance
  - improves health-related quality of life
- Unproven long-term goals
  - hospital admission prevention
  - reduced length of hospital stay
  - improved self-management, less reliance on medical care

**Benefits of Combined Tiotropium and Pulmonary Rehabilitation**

- 91 COPD subjects
  - Tiotropium N=47
  - Placebo N=44
- Initiate therapy
- After 4 weeks, initiate rehabilitation
- Monitor
  - Exercise performance
  - Dyspnea
  - Health status (QoL)

**Pulmonary Rehabilitation**

**Exercise program**

- Minimum 20 sessions at least 3 times per week
- High-intensity exercise, when possible, provides greater physiologic benefit
- Interval training may provide higher exercise levels in more symptomatic patients
- Both upper and lower extremity training
- Combination endurance and strength training has multiple beneficial effects and is well tolerated
Pulmonary Rehabilitation

- Body composition interventions
  - Caloric supplementation for patients with BMI < 21, significant involuntary weight loss, or depletion in fat-free mass (FFM) or lean body mass
  - Anabolic steroids, testosterone, growth hormone, megesterol acetate have been investigated*
  - Obese patients: nutritional education, restricted calorie meal planning, psychological support
- Screen for anxiety and depression
- Self-management education

*Not FDA-approved for this indication


Long Term Oxygen Therapy (LTOT) in COPD

LTOT used ≥ 15 hours daily to maintain a PaO₂ > 60 mmHg for COPD patients who have severe resting hypoxemia decreases morbidity and mortality

Indications
- Arterial PO₂ (PaO₂) ≤ 55 mmHg or an arterial oxygen saturation (SaO₂) ≤ 88%
- PaO₂ ≤ 59 mmHg or an SaO₂ ≤ 89%, if there is evidence of cor pulmonale, right heart failure, or erythrocytosis
- Oxygen may be prescribed during sleep with documented nocturnal hypoxemia with signs or symptoms
- Oxygen may be prescribed during exercise if there is a reduction of PaO₂ to ≤ 55 mmHg or SaO₂ ≤ 88% during exercise


Prescribing Oxygen Therapy

- Setting flow rate: goal PaO₂ of 60-65 mmHg or an SaO₂ of 90%-92%
- The oxygen flow rate often needs to be increased during exertion.
- Portable or wearable oxygen systems can encourage or maintain an active lifestyle.
- Overnight oximetry and/or clinical evaluation for sleep-disordered breathing may be appropriate for selected patients.

COPD Severity and Survival: More Than Just PFTs

BODE Index is better predictor of survival than PFTs alone.
- Incorporates
  - FEV₁ predicted levels: ≥ 65 % to ≤ 35%
  - 6-minute walk test: > 350 m to ≤ 150 m
  - Dyspnea scale: 0 (with strenuous exercise) to 4 (eg, with dressing)
  - BMI: ≤ 21 or ≥ 21

Example:
BODE Index of 8 = 52-month mortality approximately 80%

http://www.qxmd.com/calculate-online/respirology/bode-index


Beta-Blockers in Patients with COPD

- Cardioselective beta-blockers are not associated with increased respiratory symptoms or inhaler use in patients with COPD.
- Patients with COPD and comorbid cardiac conditions should be treated with cardioselective beta-blockers as these agents are safe and associated with significant reductions in morbidity and mortality.
- Treatment with beta-blockers may reduce the risk of exacerbations and improve survival in patients with COPD, possibly as a result of dual cardiopulmonary protective properties.

Case 4: Carol

- A 56-year-old woman presents for evaluation of productive cough and exertional breathlessness, progressive over last several years.
- She reports at least one episode of “bad bronchitis” per year over last several years.
- PMH: She had an episode of severe pneumonia as a child, for which she was hospitalized, otherwise unremarkable
- She has a minimal smoking history of < 5 pack-years, and last smoked at age 25. Her husband is a former smoker. She has no history of occupational exposures or respiratory exposures via hobbies, and there are no pets in the home
- ROS: She has lost “a few pounds” because her appetite “just isn’t what is used to be.” Otherwise negative
- PE: Thin woman, normal VS; lungs are clear to percussion; coarse inspiratory rales are present at the bases and anteriorly on the right; no wheezing

Carol: Spirometry

- FEV₁ = 72% predicted
- FEV₁/FVC = 66%
- Residual volume/total lung capacity (RV/TLC) = 40 (elevated)
- DLCO (Diffusion capacity) = 64%

Carol: Chest X-ray

Carol

What diagnosis is most likely?

1. Bronchiectasis
2. COPD
3. Cystic fibrosis
4. Gastroesophageal reflux disease (GERD)

Bronchiectasis

- Respiratory disease characterized by the abnormal dilatation of airways
- Broad array of causes/associated diseases
  - Cystic fibrosis
  - Prior severe pneumonia
  - Immunoglobulin deficiency, ciliary dyskinesia, etc.
  - Collagen vascular/autoimmune diseases
  - Non-tuberculous mycobacterial infection
- Commonly associated with sputum production and obstruction on PFT, mimicking COPD
Carol
What would be your next step?
1. Order sputum for AFB
2. Order sweat chloride test
3. Place PPD
4. Pulmonary consultation
5. Order chest CT

Carol
• Culture
  – Pseudomonas aeruginosa
  – Nocardia
• Clinically is presumed to have Mycobacterium avium complex (MAC)

Case 5: Darryl
• A 44-year-old male complains of episodic non-productive cough and intermittently diminished exercise tolerance, worse certain times of year
• History of asthma as a child, but he “outgrew it” and hasn’t been on medications for years
• Lifetime non-smoker, though he was heavily exposed to second-hand smoke while growing up
• Works in sales. No occupational exposures. Has a dog, but no cats or birds
• Physical exam is unremarkable

Is this COPD?
• Most likely diagnosis is asthma
• COPD is an umbrella term used to describe chronic lung diseases that are characterized by progressive limitations of expiratory airflow
• More than 80% of patients with COPD have a history of smoking. Those who don’t usually have history of exposure to inhaled irritants
• A subset of patients with chronic longstanding asthma develop irreversible obstruction

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Observed</th>
<th>Predicted</th>
<th>% Predicted</th>
<th>Post-bronchodilator</th>
<th>% Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁</td>
<td>3.45l</td>
<td>4.21</td>
<td>82%</td>
<td>4.04</td>
<td>17%</td>
</tr>
<tr>
<td>FVC</td>
<td>4.86l</td>
<td>5.23</td>
<td>93%</td>
<td>5.34</td>
<td>10%</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>0.71</td>
<td>0.804</td>
<td>98%</td>
<td>0.76</td>
<td>96%</td>
</tr>
</tbody>
</table>
### COPD and Asthma

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>COPD</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker or ex-smoker</td>
<td>Nearly all</td>
<td>Possibly</td>
</tr>
<tr>
<td>Symptoms when aged younger than 35 years</td>
<td>Rare</td>
<td>Often</td>
</tr>
<tr>
<td>Chronic productive cough</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>Persistent</td>
<td>Variable</td>
</tr>
<tr>
<td>Variables with SOB and/or wheezing</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Atopic symptoms and seasonal allergies</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Significant diurnal variability</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Favorable response to ICS</td>
<td>Inconsistent</td>
<td>Consistent</td>
</tr>
</tbody>
</table>


### Summary

- COPD is lung disease characterized by progressive, irreversible airflow obstruction
- Symptoms include breathlessness and chronic productive cough
- Most COPD is related to cigarette smoking
- Other forms of obstructive lung disease include:
  - Bronchiectasis
  - Asthma

### Post-ARS 1

Which of the following regarding the NLST is TRUE?

1. There was 20% mortality reduction in lung cancer in the CT group compared to the X-ray group
2. The rate of false positives in both the CT and X-ray groups was acceptably low at about 30%
3. The findings of the study can be extrapolated to all persons with at least a 10-year smoking history.
4. All of the above

### Post-ARS 2

Initiating COPD drug therapy with a long-acting bronchodilator is indicated in:

1. Asymptomatic patients with mild COPD
2. Symptomatic patients with mild COPD
3. All of the above
4. None of the above since an inhaled corticosteroid is recommended as initial COPD therapy

### Post-ARS 3

The goal of LTOT in COPD patients with severe resting hypoxemia is to maintain a PaO2 of:

1. > 90 mmHg
2. > 80 mmHg
3. > 70 mmHg
4. > 60 mmHg
Questions
?