HIV-Related Lung Disease

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Pulmonary and Sleep Medicine
Learning Objectives
Upon completion of this presentation, learners should be better able to:

• Identify common Pulmonary complications associated with HIV
• Refer patients for appropriate diagnostic testing for COPD
• Manage stable outpatient COPD
• Recognize unique risks to inhaled corticosteroids in HIV-positive COPD patients

Faculty and Planning Committee Disclosures
Please consult your program book or the Conference App.

• GlaxoSmithKline (consulting in 2018)
• NIH grants for the study of lung disease in HIV

Off-Label Disclosure
The following off-label/investigational uses will be discussed in this presentation:

• Most inhaled corticosteroids are not labeled for use in chronic obstructive pulmonary disease (COPD)
cART Era HIV-Lung Diseases

- Bacterial pneumonia still problematic
cART Era HIV-Lung Diseases

- Bacterial pneumonia still problematic

- NCDs of the Lung
  - COPD
  - Lung Cancer
  - Pulmonary HTN
Lung cancer in HIV

Pulmonary Arterial HTN (PAH) in HIV

- Incidence 0.5% (1 in 200 patients)
  - Little change from pre-cART to modern cART era

- Mechanisms of how HIV leads to PAH unclear

- HIV is still part of a typical pulmonary HTN evaluation
cART Era HIV-Lung Diseases

- Bacterial pneumonia still problematic

- NCDs of the Lung
  - COPD
  - Lung Cancer
  - Pulmonary HTN

What is COPD?

- Collapsible
- Inflamed
- Fibrosed
Question:
Why does COPD cause shortness of breath with exertion?

Answer:
1) Hypoxia
2) Hypercarbia
3) Hyperinflation

Audience Response Question

Question:
Why does COPD cause shortness of breath with exertion?

Answer:
1) Hypoxia
2) Hypercarbia
3) Hyperinflation

ACTHIV
THE AMERICAN CONFERENCE FOR THE TREATMENT OF HIV

- Dyspnea with exertion
- Chronic cough/sputum
- Recurrent ‘bronchitis’ (exacerbations)

**Table 1** Annual median costs for COPD treatment based on disease severity

<table>
<thead>
<tr>
<th>Cost categories</th>
<th>Severity of COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stage I*</td>
</tr>
<tr>
<td>Total medication cost (%)</td>
<td>$512 (31)</td>
</tr>
<tr>
<td>Total non-medication costs (%)</td>
<td>$489 (29)</td>
</tr>
<tr>
<td>Hospitalization cost (%)</td>
<td>$680 (40)</td>
</tr>
<tr>
<td>Total cost</td>
<td>$1681</td>
</tr>
</tbody>
</table>

**Notes:** *P < 0.01 for each cost variable and total cost across the three severities of COPD. All figures are in US$ per patient.

Guarascio A. ClicioEcon Outcomes Res 2013:5:236-245
### COPD Co-Morbidities

- CVD
- Lung cancer
- Pulmonary HTN
- Osteoporosis
- Sarcopenia
- Cognitive dysfunction
- Depression / Anxiety

### COPD Diagnosis = SPIROMETRY

**Low FEV₁/FVC ratio**
# Prevalence of chronic obstructive pulmonary disease in the global population with HIV: a systematic review and meta-analysis

*Jean Joel Bigno, Angeladine Malaha Kenne, Serro Lem Asangbeh, Aurelie T Sibetchou*

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## LLN

<table>
<thead>
<tr>
<th>Study</th>
<th>LLN</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akahbi (2015)</td>
<td>43</td>
<td>356</td>
</tr>
<tr>
<td>George (2009)</td>
<td>20</td>
<td>234</td>
</tr>
<tr>
<td>Kuniaki (2016)</td>
<td>67</td>
<td>989</td>
</tr>
<tr>
<td>Makinson (2015)</td>
<td>75</td>
<td>338</td>
</tr>
<tr>
<td>Perhve-Yone (2015)</td>
<td>24</td>
<td>461</td>
</tr>
<tr>
<td>Vos (2017)</td>
<td>10</td>
<td>84</td>
</tr>
</tbody>
</table>

**Random-effects meta-analysis**

Heterogeneity: $I^2 = 92.7\%$ (95% CI 86–7–95.9), $t^2=0.0085$, $p=0.0001$

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<tr>
<th>Study</th>
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<tbody>
<tr>
<td>Akahbi (2015)</td>
<td>12.08</td>
<td>(8.88–15.32)</td>
</tr>
<tr>
<td>George (2009)</td>
<td>8.55</td>
<td>(5.39–12.80)</td>
</tr>
<tr>
<td>Kuniaki (2016)</td>
<td>6.77</td>
<td>(5.29–8.32)</td>
</tr>
<tr>
<td>Makinson (2015)</td>
<td>22.19</td>
<td>(17.87–27.00)</td>
</tr>
<tr>
<td>Perhve-Yone (2015)</td>
<td>3.21</td>
<td>(3.6–7.65)</td>
</tr>
<tr>
<td>Vos (2017)</td>
<td>1.90</td>
<td>(0.86–20.81)</td>
</tr>
</tbody>
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**Fixed-ratio**

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<tr>
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<tbody>
<tr>
<td>Akahbi (2015)</td>
<td>15.45</td>
<td>(11.86–19.63)</td>
</tr>
<tr>
<td>George (2009)</td>
<td>18.00</td>
<td>(13.82–22.82)</td>
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<tr>
<td>Kuniaki (2016)</td>
<td>10.46</td>
<td>(12.54–25.01)</td>
</tr>
<tr>
<td>Makinson (2015)</td>
<td>6.84</td>
<td>(3.66–10.87)</td>
</tr>
<tr>
<td>Vos (2017)</td>
<td>17.70</td>
<td>(11.16–26.00)</td>
</tr>
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**Random-effects meta-analysis**

Heterogeneity: $I^2 = 92.7\%$ (95% CI 86–7–95.9), $t^2=0.0085$, $p=0.0001$

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<tr>
<td>Akahbi (2015)</td>
<td>5.46</td>
<td>(4.13–7.06)</td>
</tr>
<tr>
<td>George (2009)</td>
<td>23.42</td>
<td>(15.94–32.41)</td>
</tr>
<tr>
<td>Makinson (2015)</td>
<td>2.13</td>
<td>(1.04–3.99)</td>
</tr>
<tr>
<td>Perhve-Yone (2015)</td>
<td>8.95</td>
<td>(6.76–11.57)</td>
</tr>
<tr>
<td>Vos (2017)</td>
<td>17.99</td>
<td>(12.84–22.07)</td>
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</tbody>
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**Random-effects meta-analysis**

Heterogeneity: $I^2 = 92.7\%$ (95% CI 86–7–95.9), $t^2=0.0085$, $p=0.0001$
Why is COPD Prevalence High in HIV?

Management of HIV-COPD

- Goals of COPD treatment
  - Prevent death
  - Reduce risk of exacerbations
  - Improve dyspnea / quality of life
Management of HIV-COPD

• Generally similar to non-HIV
  – Most effective intervention:
  – Oxygen for those with resting SpO2 ≤88%
  – Vaccinations
  – Pulmonary Rehabilitation
  – Inhalers
    • Short-acting bronchodilators
    • Long-acting bronchodilators
      – Long-acting beta agonists (LABA)
      – Long-acting muscarinic antagonists (LAMA)
    • Inhaled corticosteroids

Audience Response Question

Scenario: 60 y/o, cis-M, HIV+ for 15 years, on TDF/FTC/EVG/c, HIV-RNA <50 copies/mL, CD4+ 590 cells/mm³. Here for post-hospital discharge follow-up.

Medical History:
COPD, FEV₁ 1.98L [53% of predicted normal]
• Chronic sputum production; recurrent bronchitis—2 courses of antibiotics this winter. Recent 3-day hospitalization for COPD exacerbation.
• Former smoker (40 pack-years; quit 10 years ago).
Impaired Fasting Glucose
Osteopenia
Meds: Albuterol MDI prn; Guaifenesin QID; Stribild QDay; Tylenol prn.
PE: Normal vitals, SpO2 90% on room air
  Moderate expiratory wheezes.
The next most appropriate medication to add is:

a) Tiotropium (Long-acting muscarinic antagonist [LAMA])
b) Olodaterol (Long-acting beta agonist [LABA])
c) Fluticasone (Inhaled Corticosteroid [ICS])
d) Tiotropium + Olodaterol + Fluticasone (LABA + LAMA + ICS)

Inhaled Corticosteroids (ICS) in COPD

• ICS reduce risk of COPD exacerbations

• But ICS increase risk of bacterial pneumonia (Drummond B. JAMA 2008; Suissa S. Thorax 2013)

• And ICS interact with boosters (ritonavir and cobicistat)
  – Particularly strong interactions with fluticasone
  – Potentially less with beclomethasone (Boyd S. JAIDS 2013)
A Word About Inhalers in COPD

Prepare for first use

1. Remove clear base
   - Keep the cap closed.
   - Press the safety catch while firmly pulling off the clear base with your other hand.

2. Insert cartridge
   - Insert the narrow end of the cartridge into the inhaler.
   - Place the inhaler on a firm surface and push down firmly until it snaps into place.

3. Replace clear base
   - Put the clear base back into place until it clicks.
   - If the clear base doesn’t click, push down firmly against a firm surface (see step 2).

4. Turn
   - Keep the cap closed.
   - Turn the clear base in the direction of the arrows on the label until it clicks (half a turn).

5. Open
   - Open the cap until it snaps fully open.

6. Press
   - Press the dose-release button.
   - Close the cap.
   - Repeat steps 4-6 until a cloud is visible.
   - After a cloud is visible, repeat steps 4-6 three more times.

Daily use (TOP)

1. TURN
   - Keep the cap closed.
   - TURN the clear base in the direction of the arrows on the label until it clicks (half a turn).

2. OPEN
   - OPEN the cap until it snaps fully open.

3. PRESS
   - Breathe out slowly and fully.
   - Close your lips around the mouthpiece without covering the air vents.
   - While holding a slow, deep breath through your mouth, PRESS the dose-release button and continue to breathe in.
   - Hold your breath for 10 seconds or for as long as comfortable.
   - Repeat: TURN, OPEN, PRESS (TOP) for a total of 2 puffs.
Management of HIV-COPD

• Generally same as non-HIV
  – Most effective intervention:
  – Oxygen for those with resting SpO2 ≤88%
  – Vaccinations
  – Pulmonary Rehabilitation
  – Inhalers
    • Short-acting bronchodilators
    • Long-acting bronchodilators
      – Long-acting beta agonists (LABA)
      – Long-acting muscarinic antagonists (LAMA)
    • Inhaled corticosteroids
  – Multidisciplinary COPD Case Management?

COPD Management Guidelines

• Global Initiative for Chronic Obstructive Lung Disease (GOLD)
  – www.goldcopd.org

• American Thoracic Society (ATS)
  – www.thoracic.org/statements/copd
cART Era HIV-Lung Diseases

- Bacterial **pneumonia** still problematic

- NCDs of the Lung
  - **COPD**
  - **Lung Cancer**
  - Pulmonary HTN

These are my personal views, and not those of the US Government, Department of Veterans Affairs, or affiliated funders/institutions.
Supplemental Slides

Lung Cancer Screening in HIV

**USPSTF:**
- Age 55 – 80 years
- ≥30 pack-years of smoking
- Currently smoking or quit within past 15 years

- HIV+ = Diagnosed earlier, fewer pack-years, worse prognosis
Lung Cancer Screening in HIV

**Optimal screening criteria**

<table>
<thead>
<tr>
<th>Performance characteristics of variable screening thresholds for WIHS</th>
<th>Age</th>
<th>Pack-years</th>
<th>Quit time</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>USPSTF</td>
<td>55</td>
<td>30</td>
<td>15</td>
<td>16%</td>
<td>93%</td>
</tr>
<tr>
<td>Optimal</td>
<td>49</td>
<td>16</td>
<td>15</td>
<td>52%</td>
<td>75%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Performance characteristics of variable screening thresholds for MACS</th>
<th>Age</th>
<th>Pack-years</th>
<th>Quit time</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>USPSTF</td>
<td>55</td>
<td>30</td>
<td>15</td>
<td>24%</td>
<td>94%</td>
</tr>
<tr>
<td>Optimal</td>
<td>43</td>
<td>19</td>
<td>15</td>
<td>82%</td>
<td>76%</td>
</tr>
</tbody>
</table>

- Replacing age criteria with HIV markers did not improve test characteristics beyond already optimized criteria


Right now = USPSTF
Future = Tailored to HIV?