4 "Practice Changers" in Pulmonary Medicine for 2016

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Faculty Disclosures

• **Grant Support:**
  - Roche
  - Actelion
  - Ikaria
  - United Therapeutics
  - Gilead
  - Bayer
  - GeNO
  - Novartis
  - Chesi

• **Consulting and/or Speaker’s Bureau:**
  - Actelion
  - United Therapeutics
  - Gilead
  - Bayer
  - GeNO
  - Novartis

• **DSMB:**
  - Gilead
The 4 “Practice Changers”

• Suggest a novel treatment for patients with sleep apnea intolerant to PAP therapy
• Order lung cancer screening CT for appropriate patients
• Re-evaluate COPD documentation and treatment
• Consider PCV13 immunization for pneumococcal disease
Suggest a novel treatment for patients with sleep apnea intolerant to PAP therapy.
Obstructive Sleep Apnea Hypopnea Syndrome Pathophysiology

- Repetitive airway obstruction or collapse occurring during SLEEP
- To break an apnea the brain briefly “wakes up” causing sleep fragmentation
- During the apnea there is hypoxia, hypercapnia, and a rise in blood pressure:
  - Severity of derangement depends on length of apnea and oxygen stores in lung at onset of apnea
- By convention defined by apnea hypopnea index (AHI) $\geq 5$ with symptoms

Source: Atlanta Institute for ENT
Classification of Obstructive Sleep Apnea Based on Severity of Apnea-Hypopnea Index

• Apnea-Hypopnea Index (AHI) events/hour
  – Mild 5-15 events per hour
  – Moderate 15-30 events per hour
  – Severe > 30 events per hour

American Academy of Sleep Medicine, Sleep 22:667, 1999
Epidemiology

- Prevalence estimates from studies of mainly white men and women with BMI=25-28 demonstrate:
  - 1 in 5 adults has at least mild sleep apnea
  - 1 in 15 has at least moderate sleep apnea
  - 18 million people in US
- AHI>5 and daytime hypersomnolence in 2% women and 4% men (Young et al. NEJM, 1993)
- Prevalence of non-sleepy patients with OSA likely higher
Sleep Apnea Risk Factors at Presentation

Non-Modifiable

- Age
- Sex
- Race/Ethnicity
- Genetics
- Marfan’s, Down’s and Pierre Robin syndromes

Modifiable

- Obesity (BMI ≥ 30 kg/m²)
- Neuromuscular Disorders
- Craniofacial Abnormalities
- Endocrine Disorders
- Hormonal
# Epworth Sleepiness Scale

<table>
<thead>
<tr>
<th>Situation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and Reading</td>
<td></td>
</tr>
<tr>
<td>Watching TV</td>
<td></td>
</tr>
<tr>
<td>Sitting inactive in a public place</td>
<td></td>
</tr>
<tr>
<td>Passenger in a car</td>
<td></td>
</tr>
<tr>
<td>Lying down to rest in afternoon</td>
<td></td>
</tr>
<tr>
<td>Sitting, talking to someone</td>
<td></td>
</tr>
<tr>
<td>Sitting after lunch without alcohol</td>
<td></td>
</tr>
<tr>
<td>In a car, topped for minutes in traffic</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Likeliness of Dozing:</strong></td>
<td></td>
</tr>
<tr>
<td>0 – Never</td>
<td></td>
</tr>
<tr>
<td>1 – Slight Chance</td>
<td></td>
</tr>
<tr>
<td>2- Moderate Chance</td>
<td></td>
</tr>
<tr>
<td>3 – High Chance</td>
<td></td>
</tr>
</tbody>
</table>

Consequences of Untreated Sleep Apnea

- Hypersomnolence
  - Decreased job performance
  - Inattentiveness and Accidents
- Memory Problems
- Personality Changes
- Systemic Manifestations
  - Metabolic
    - Weight Gain
    - Insulin Resistance
  - Cardiovascular
  - Increased Inflammation
Typically 20% of patients will be unable to tolerate PAP therapy.
INSPIRE System for Hypoglossal Muscle Stimulation in OSA

**Implanted Components**

- **Stimulation Lead**
- **Implanted Pulse Generator (IPG)**
- **Sense Lead**

**Patient Programmer**
- Therapy ON/OFF
- Adjust amplitude
Patient Activates Therapy before Sleep

Patient Turns Therapy On

Patient can pause therapy during sleep

Therapy Active

Therapy Active

Therapy Duration

Start Delay
Effect of Stimulation

Therapy ON

Therapy OFF

30 seconds

EEG

EMG

Nasal Pressure

Thermo

Chest

Abdomen

SpO2
Important Selection Criteria

• Inability to use CPAP as therapy for >4 hours a night for >70% of nights
• AHI 20-65
• BMI <32, warning to BMI up to 35
• Age not specified but generally need to be in good health
• No lumps in nose or throat
• On Drug Induced Sedated Endoscopy (DISE): no concentric (camera shutter-like) closure of the back of the nose
STAR Efficacy Outcomes: Phase III Pivotal FDA Trial

- **Apnea Hypopnea Index Endpoint**
  - **Endpoint**: at least 50% responder rate (≥ 50% AHI reduction and AHI < 20 at 12 months – Sher criteria\(^1\))
  - **Outcome**: 66% responder rate at 12 months

![Graph showing median AHI reduction](image)

- **Baseline AHI**: 29.3
- **Month-12 AHI**: 9.0
- **68% reduction**

\(^1\) Sher et al, Sleep 1996

**N = 126**

**Strollo et al NEJM 2014**
Randomized Controlled Therapy Withdrawal Study

![Bar chart showing data comparison between baseline, month 12, and RCT for Maintenance and Withdrawal C groups.]

Strollo et al. *Otolaryngology -- Head and Neck Surgery* November 2014 151: 880-887
Order lung cancer screening CT for appropriate patients
Current Recommendations for Lung Cancer Screening*

• WHO?
  – Current or former smokers ages 55-74 in good health
  – > 30 pack-year history
  – Quit less than 15 years

• WHAT?
  – Low dose helical CT (LDCT)
  – Organized screening program that has experience in LDCT

• Screening should not be viewed as an alternative to smoking cessation

*(American College of Chest Physicians, American Society of Clinical Oncology, the American Thoracic Society, the National Comprehensive Cancer Network (NCCN) and the American Lung Association)
Utility of low dose CT screening for detection of lung cancer

High risk patients for lung cancer
- Current or previous smoker
- >30 pack/year history

Results
- 354 vs 442 deaths from lung cancer
- 20% reduction in lung cancer deaths in CT

Caveats
- Cost
- False (+) consequences
- Radiation effects

Cumulative Numbers of Lung Cancers and of Deaths from Lung Cancer in the National Lung Screening Trial

Additional Findings in National Lung Screening Trial

**Additional Findings**
- 39.1% of the LDCT group had at least 1 positive finding
- 24% of surgical procedures yielded a benign result
- 367/1060 cancers in the LDCT group were diagnosed either after the screening period or in patients missing screening.
- Number needed to screen to prevent 1 death was 320

**Potential Implications**
- Huge burden of workup and liability
- Non-trivial “unnecessary” procedures
- Do additional years of screening need to be done?
- Are we detecting non-lethal cancers?
- Can this change/cost

APPROVAL OF PAYMENT FOR LOW DOSE CT SCANNING FOR LUNG CANCER SCREENING IN HIGH RISK PATIENTS (2.5.2015)
Re-evaluate COPD documentation and treatment
Recently Approved COPD Treatments

• Oldaterol
  – Olodaterol (Striverdi Respimat)
  – Olodaterol and Tiotropium bromide (Stiloto™ Respimat®)

• Vilanterol + Fluticasone furoate + (Breo Ellipta)

• Umeclidinium
  – Umeclidinium (Incruse Ellipta)
  – Umeclidinium and Vilanterol inhalation powder (Anoro Ellipta)

• Aclidinium (Tudorza Pressair)

• Roflumilast (Daliresp®)
Recently Approved COPD Treatments

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• Roflumilast (Daliresp® )
Roflumilast (Daliresp)

- Phosphodiesterase E4 inhibitor
- Approval: 2011
- Indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.
- Dose 500 ug once daily
Recommendations for Use of Roflumilast in Primary Care

• Clear identification of patients eligible for roflumilast

• Phenotyping of patients in primary care
  – lung function measurement (FEV1<50%)
  – accurate health status classification
    • At least 1 exacerbation last year
    • Smoking > 20 pk/years
  – recording of chronic cough and regular sputum production

Additional Concerns with Roflumilast

- Roflumilast and suicidal thoughts or depression
- 20% of patients in trial had 5-10% weight loss
- GI Side effects
Q: Does the recent proliferation of new therapeutic agents for really change our treatment of COPD?  
A: Quite Possibly

Q: Should I think about COPD Patients Differently?  
A: Almost Certainly
2011+ Paradigm Shift in Global Recommendations for COPD Management

FEV1 Based Management Strategy with Some Escalation Based on Symptom Control

1) Reduce Symptoms
   - Relieve symptoms
   - Improve exercise tolerance
   - Improve health status

2) Reduce Risk
   - Prevent disease progression
   - Prevent and treat exacerbations
   - Reduce mortality
Therapy at Each Stage of COPD*

I: Mild

- FEV₁/FVC < 70%
- FEV₁ ≥ 80%
predicted

II: Moderate

- FEV₁/FVC < 70%
- 50% ≤ FEV₁ < 80%
predicted

III: Severe

- FEV₁/FVC < 70%
- 30% ≤ FEV₁ < 50%
predicted

IV: Very Severe

- FEV₁/FVC < 70%
- FEV₁ < 30%
predicted
or FEV₁ < 50%
predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination

*Add* short-acting bronchodilator (when needed)

*Add* regular treatment with one or more long-acting bronchodilators (when needed); *Add* rehabilitation

*Add* inhaled glucocorticosteroids if repeated exacerbations

*Add* long term oxygen if chronic respiratory failure.

*Consider* surgical treatments

*Postbronchodilator FEV₁ is recommended for the diagnosis and assessment of severity of COPD*
Exacerbation Frequency and Severity Both Increase Mortality Risk

Group A: patients with no acute exacerbations
Group B: patients with 1–2 acute exacerbations requiring hospital management
Group C: patients with ≥3 acute exacerbations

Group (1): no acute exacerbations
Group (2): acute exacerbations requiring emergency service visits without admission
Group (3): patients with acute exacerbations requiring one hospital admission
Group (4): patients with acute exacerbations requiring readmissions

### Combined Assessment of COPD

When assessing risk, choose the **highest risk** according to GOLD grade or exacerbation history. One or more hospitalizations for COPD exacerbations should be considered high risk.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Characteristic</th>
<th>Spirometric Classification</th>
<th>Exacerbations per year</th>
<th>CAT</th>
<th>mMRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low Risk Less Symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>&lt; 10</td>
<td>0-1</td>
</tr>
<tr>
<td>B</td>
<td>Low Risk More Symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>≥ 10</td>
<td>≥ 2</td>
</tr>
<tr>
<td>C</td>
<td>High Risk Less Symptoms</td>
<td>GOLD 3-4</td>
<td>≥ 2</td>
<td>&lt; 10</td>
<td>0-1</td>
</tr>
<tr>
<td>D</td>
<td>High Risk More Symptoms</td>
<td>GOLD 3-4</td>
<td>≥ 2</td>
<td>≥ 10</td>
<td>≥ 2</td>
</tr>
</tbody>
</table>
Tools Involved in Risk Assessment in Current GOLD Treatment Paradigm

• Simple spirometry
• COPD Assessment Test (CAT)
• Modified Medical Research Council Dyspnea Scale (mMRC)
Global Strategy for Diagnosis, Management and Prevention of COPD

Classification of Severity of Airflow Limitation in COPD*

<table>
<thead>
<tr>
<th>GOLD 1</th>
<th>Mild</th>
<th>( \text{FEV}_1 \geq 80% \text{ predicted} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 2</td>
<td>Moderate</td>
<td>( 50% \leq \text{FEV}_1 &lt; 80% \text{ predicted} )</td>
</tr>
<tr>
<td>GOLD 3</td>
<td>Severe</td>
<td>( 30% \leq \text{FEV}_1 &lt; 50% \text{ predicted} )</td>
</tr>
<tr>
<td>GOLD 4</td>
<td>Very Severe</td>
<td>( \text{FEV}_1 &lt; 30% \text{ predicted} )</td>
</tr>
</tbody>
</table>

*Based on Post-Bronchodilator \( \text{FEV}_1 \)

© 2015 Global Initiative for Chronic Obstructive Lung Disease
COPD Assessment Test (CAT)

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

SCORE
The COPD assessment test (CAT) assists prediction of COPD exacerbations in high-risk patients.

Figure 1. Adjusted time to first exacerbation by categorised baseline COPD assessment test (CAT) score.
Modified Medical Research Council Dyspnea Scale (mMRC)

- Grade 0: breathless with strenuous exercise
- Grade I: short of breath when hurrying on the level or walking up a slight hill
- Grade II: walking slower than people of the same age on the level because of breathlessness or having to stop for breath when walking at own pace on the level
- Grade III: stopping for breath after walking about 100 yards or after a few minutes on the level
- Grade IV: too breathless to leave the house or breathless when dressing or undressing
Figure 2. Survival shown as Kaplan-Meier curves according to the GOLD 2007 classification (left) and GOLD 2011 classification (right).

Lange et al.; Am J Respir Crit Care Med 2012, 186, 975-981.
Distribution and Prognostic Validity of the New Global Initiative for Chronic Obstructive Lung Disease Grading Classification New GOLD COPD Grading

Cox model adjusted by cohort

HR (95% CI)

COPD old GOLD II 1.78 (1.29-2.46)
COPD old GOLD III 2.84 (2.06-3.92)
COPD old GOLD IV 4.05 (2.57-6.72)

Cox model adjusted by cohort (differences between stages B and C disappears).

HR (95% CI)

COPD new GOLD B 1.70 (1.38-2.10)
COPD new GOLD C 1.69 (1.39-2.08)
COPD new GOLD D 2.79 (2.35-3.32)

**BODE Index for COPD Survival**

Use this calculator to calculate prognosis in COPD (Chronic Obstructive Pulmonary Disease) using the BODE Index.

<table>
<thead>
<tr>
<th><strong>FEV₁ (% predicted)</strong></th>
<th>≥65</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6-minute walk distance (m)</strong></td>
<td>≥350</td>
</tr>
<tr>
<td><strong>Modified MRC Dyspnea Scale</strong></td>
<td>0-1</td>
</tr>
</tbody>
</table>

0: Dyspneic on strenuous exercise
1: Dyspneic on walking a slight hill
2: Dyspneic on walking level ground; must stop occasionally due to breathlessness
3: Must stop for breathlessness after walking 100 yards or after a few minutes
4: Cannot leave house; breathless on dressing/undressing

<table>
<thead>
<tr>
<th><strong>Body Mass Index (kg/m²)</strong></th>
<th>&gt;21</th>
</tr>
</thead>
</table>

Submit

http://www.qxmd.com
Variables and Point Values Used for the Computation of the Body-Mass Index, Degree of Airflow Obstruction and Dyspnea, and Exercise Capacity (BODE) Index

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points on BODE Index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>FEV₁ (% of predicted)†</td>
<td>≥65</td>
</tr>
<tr>
<td>Distance walked in 6 min (m)</td>
<td>≥350</td>
</tr>
<tr>
<td>MMRC dyspnea scale‡</td>
<td>0–1</td>
</tr>
<tr>
<td>Body-mass index§</td>
<td>&gt;21</td>
</tr>
</tbody>
</table>

* The cutoff values for the assignment of points are shown for each variable. The total possible values range from 0 to 10. FEV₁ denotes forced expiratory volume in one second.

† The FEV₁ categories are based on stages identified by the American Thoracic Society.

‡ Scores on the modified Medical Research Council (MMRC) dyspnea scale can range from 0 to 4, with a score of 4 indicating that the patient is too breathless to leave the house or becomes breathless when dressing or undressing.

§ The values for body-mass index were 0 or 1 because of the inflection point in the inverse relation between survival and body-mass index at a value of 21.

Kaplan-Meier Survival Curves for the Four Quartiles of the Body-Mass Index, Degree of Airflow Obstruction and Dyspnea, and Exercise Capacity Index (Panel A) and the Three Stages of Severity of Chronic Obstructive Pulmonary Disease as Defined by the American Thoracic Society (Panel B)

Practical Office Implementation

1) COPD – FEV1 = 40% predicted, GOLD Class 3, CAT Score = 8, Type C, BODE 5 (0+2+2+1). Currently on LABA and LAMA. Completed pulmonary rehab, not LVRS candidate. Currently with adequate oxygenation.
Consider Vaccination with Pneumococcal Polysaccharide Conjugated Vaccine (PCV 13)
What is the difference between PCV13 and PPSV23 pneumococcal vaccines?

• PCV13 is a conjugated vaccine

• Difference in covered serotypes
  – Serotypes covered by PPSV23
    • 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F
  – Serotypes covered by PCV13
    • 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F
New Recommendations ACIP PCV13
Age > 65*

*To be re-evaluated in 2018
Original Article

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults

Marc J.M. Bonten, M.D., Ph.D., Susanne M. Huijts, M.D., Marieke Bolkenbaas, M.D., Chris Webber, M.D., Scott Patterson, Ph.D., Samantha Gault, M.B.A., Cornelis H. van Werkhoven, M.D., Anna M.M. van Deursen, M.D., Elisabeth A.M. Sanders, M.D., Ph.D., Theo J.M. Verheij, M.D., Ph.D., Michael Patton, B.Sc., Anne McDonough, M.P.H., Anita Moradoghli-Haftvani, B.Sc., Helen Smith, B.Sc., Tracey Mellelieu, B.Sc., Michael W. Pride, Ph.D., Graham Crowther, Ph.D., Beate Schmoele-Thoma, M.D., Daniel A. Scott, M.D., Kathrin U. Jansen, Ph.D., Rita Lobatto, M.D., Bas Oosterman, Ph.D., Nils Visser, M.Sc., Esther Caspers, M.Sc., Andre Smorenburg, M.Sc., Emilio A. Emini, Ph.D., William C. Gruber, M.D., and Diederick E. Grobbee, M.D., Ph.D.

N Engl J Med
Volume 372(12):1114-1125
March 19, 2015
Post Hoc Analysis of the Cumulative Episodes of the Primary and Secondary Efficacy End Points in the Per-Protocol Population.

Table 1. Baseline Characteristics of the Participants. *

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PCV13 Group (N=42,237)†</th>
<th>Placebo Group (N=42,255)†</th>
<th>All Participants (N=84,492)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>23,447 (55.5)</td>
<td>23,801 (56.3)</td>
<td>47,248 (55.9)</td>
</tr>
<tr>
<td>Female</td>
<td>18,790 (44.5)</td>
<td>18,454 (43.7)</td>
<td>37,244 (44.1)</td>
</tr>
<tr>
<td>Race — no. (%)‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>41,600 (98.5)</td>
<td>41,614 (98.5)</td>
<td>83,214 (98.5)</td>
</tr>
<tr>
<td>Black</td>
<td>146 (0.3)</td>
<td>140 (0.3)</td>
<td>286 (0.3)</td>
</tr>
<tr>
<td>Asian</td>
<td>277 (0.7)</td>
<td>292 (0.7)</td>
<td>569 (0.7)</td>
</tr>
<tr>
<td>Other</td>
<td>205 (0.5)</td>
<td>199 (0.5)</td>
<td>404 (0.5)</td>
</tr>
<tr>
<td>Unknown</td>
<td>9 (&lt;0.1)</td>
<td>10 (&lt;0.1)</td>
<td>19 (&lt;0.1)</td>
</tr>
<tr>
<td>Age at vaccination — yr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>72.8±5.7</td>
<td>72.8±5.6</td>
<td>72.8±5.7</td>
</tr>
<tr>
<td>Median (range)§</td>
<td>71.6 (61.9–101.1)</td>
<td>71.5 (63.3–99.5)</td>
<td>71.6 (61.9–101.1)</td>
</tr>
<tr>
<td>Age group — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;75 yr</td>
<td>29,006 (68.7)</td>
<td>29,064 (68.8)</td>
<td>58,070 (68.7)</td>
</tr>
<tr>
<td>≥75 and &lt;85 yr</td>
<td>11,727 (27.8)</td>
<td>11,753 (27.8)</td>
<td>23,480 (27.8)</td>
</tr>
<tr>
<td>≥85 yr</td>
<td>1504 (3.6)</td>
<td>1438 (3.4)</td>
<td>2942 (3.5)</td>
</tr>
</tbody>
</table>

* Plus–minus values are means ±SD. Additional characteristics are listed in Table S2 in the Supplementary Appendix.
PCV13 denotes 13-valent pneumococcal conjugate vaccine.
† The numbers of participants who received the study vaccine and for whom any safety data were available are shown. Four participants (three in the PCV13 group and one in the placebo group) were excluded because no safety data were available.
‡ Race was self-reported.
§ A total of 18 participants who were enrolled in the PCV13 group and 16 who were enrolled in the placebo group were younger than 65 years of age.
Table 3. Safety Outcomes.*

<table>
<thead>
<tr>
<th>Event</th>
<th>Safety Subgroup</th>
<th>P Value†</th>
<th>All Participants</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCV13 (N=1006)</td>
<td>Placebo (N=1005)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>no. (%)</td>
<td>no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse event within 1 mo after vaccination</td>
<td>188 (18.7)</td>
<td>144 (14.3)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Chronic medical condition diagnosed 1–6 mo after vaccination‡</td>
<td>17 (1.7)</td>
<td>12 (1.2)</td>
<td>0.46</td>
<td></td>
</tr>
<tr>
<td>Serious adverse event</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within 6 mo after vaccination</td>
<td>70 (7.0)</td>
<td>60 (6.0)</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Within 1 mo after vaccination</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>3006 (7.1)</td>
<td>3005 (7.1)</td>
<td>0.61</td>
<td>0.98</td>
</tr>
</tbody>
</table>

* The numbers of participants who received study vaccine and for whom any safety data were available are shown. Four participants (three in the PCV13 group and one in the placebo group) were excluded because they had no safety data. Listed are events that occurred at least once in any participant.
† A two-sided Fisher’s exact test was used to calculate the P value for the difference between percentages of participants who reported an event in each of the study groups.
‡ Newly diagnosed chronic medical conditions (including autoimmune or neuroinflammatory disease) were identified in subgroup participants by site staff members who conducted home visits; chronic medical conditions included conditions such as asthma, emphysema, hypertension, and cardiac failure.
• Among older adults, PCV13 was effective in preventing vaccine-type pneumococcal, bacteremic, and nonbacteremic community-acquired pneumonia and vaccine-type invasive pneumococcal disease but not in preventing community-acquired pneumonia from any cause.
Indications for PPSV23 Pneumococcal Vaccination in Patients 19-64 years old

- Cigarette smoking
- Chronic heart disease, including congestive heart failure and cardiomyopathy, but excluding hypertension
- Chronic lung disease, including asthma and chronic obstructive pulmonary disease
- Diabetes mellitus
- Alcoholism
- Chronic liver disease
Indication for PPSV23 +PCV13 age

• CSF Leak
• Cochlear Implant
• Asplenia
• Immunocompromised Patients
  – Immunodeficiency
  – HIV
  – ESRD
  – Leukemia, Lymphoma, Hodgkins Disease, Myeloma
  – Generalized Mailignancy
  – Solid Organ Transplant

MMWR 2014, 63:822
The 4 “Practice Changers”

• Suggest a novel treatment for patients with sleep apnea intolerant to PAP therapy
• Order lung cancer screening CT for appropriate patients
• Re-evaluate COPD documentation and treatment
• Consider PCV13 immunization for pneumococcal disease
QUESTIONS?
Global Strategy for Diagnosis, Management and Prevention of COPD
Manage Stable COPD: Pharmacologic Therapy

*(Medications in each box are mentioned in alphabetical order, and therefore not necessarily in order of preference.)*

<table>
<thead>
<tr>
<th>Patient</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>LAMA 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 PDE4-inh. or LABA and PDE4-inh.</td>
<td>SABA and/or SAMA Theophylline</td>
</tr>
<tr>
<td>D</td>
<td>ICS + LABA and/or LAMA</td>
<td>ICS + LABA and LAMA or ICS+LABA and PDE4-inh. or LAMA and LABA or LAMA and PDE4-inh.</td>
<td>Carbocysteine N-acetylcysteine SABA and/or SAMA Theophylline</td>
</tr>
</tbody>
</table>
Group A COPD Patients

- Patients have few symptoms and low risk of exacerbations
- A short-acting bronchodilator is recommended as first choice
  - Based on effect on lung function and breathlessness
- Combination of short-acting bronchodilators or introduction of a long-acting bronchodilator is recommended as second choice

<table>
<thead>
<tr>
<th>A</th>
<th>Short-acting anticholinergic prn or Short-acting beta₂-agonist prn</th>
<th>Long-acting anticholinergic or Long-acting beta₂-agonist or Short-acting beta₂-agonist and Short-acting anticholinergic</th>
<th>Theophylline</th>
</tr>
</thead>
</table>

# Short Acting Bronchodilators

<table>
<thead>
<tr>
<th>DRUG</th>
<th>TRADE NAME</th>
<th>Mechanism of Action</th>
<th>DOSING INTERVAL</th>
<th>MISC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol</td>
<td>Proventil®</td>
<td>Short Acting Beta 2 Agonist (SABA)</td>
<td>Q 4-6 hours</td>
<td>Also available as nebulized agent</td>
</tr>
<tr>
<td></td>
<td>Proair®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maxair®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipratropium Bromide</td>
<td>Atrovent®</td>
<td>Short Acting Antimuscarinic (SAMA)</td>
<td>Q 4-6 hours</td>
<td>Also available as nebulized agent</td>
</tr>
<tr>
<td>Albuterol + Ipratropium Bromide</td>
<td>Combivent®</td>
<td>SABA + SAMA</td>
<td>Q 6 hours</td>
<td>Also available as nebulized agent</td>
</tr>
</tbody>
</table>
Ipratropium Bromide and Albuterol (Combivent®)

- Inhaled short acting anti-cholinergic/short acting beta adrenergic combination

- FDA Approved: October 1996, May 27, 1999

- Indicated for use in patients with chronic obstructive pulmonary disease (COPD) on a regular aerosol bronchodilator who continue to have evidence of bronchospasm and who require a second bronchodilator

- 2 inhalations four times daily (18ug/103 ug per inhalation)
Short-acting Bronchodilators: Onset and Duration of Action

N=534
P<0.001 for the combination versus each agent alone

- Ipratropium + Albuterol (n=173)
- Ipratropium (n=176)
- Albuterol (n=165)

Group B COPD Patients

- Patients have more significant symptoms but still a low risk of exacerbations
- Long-acting bronchodilators are recommended as first choice
  - Choice is dependent on individual patient’s perception of symptom relief
- In patients with severe breathlessness, a combination of long-acting bronchodilators is recommended as second choice
- Alternative choices include short-acting bronchodilators and theophylline

| B | Long-acting anticholinergic or Long-acting beta$_2$-agonist | Long-acting anticholinergic and long-acting beta$_2$-agonist | Short-acting beta$_2$-agonist and/or Short-acting anticholinergic Theophylline |
Long Acting Antimuscarinics (LAMA)
Aclidinium (Tudorza Pressair)

• Inhaled long acting M3 blocker

• FDA Approval Date: July 23, 2012.

• Indicated for long-term maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

• Twice daily inhalation (400 ug)
Umeclidinium (Incruse Ellipta)

- Inhaled long acting M3 blocker
- FDA Approval Date: April 30, 2014.
- Indicated for long-term maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.
- Once daily inhalation (62.5 ug)
Tiotropium Bromide (Spiriva)

- Inhaled long acting M3 blocker
- FDA Approval Date: Jan 30, 2004 for COPD, Dec 18, 2009.
- Indicated for the long-term, once-daily, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), and for reducing COPD exacerbations.
- Handihaler: Once daily inhalation (18 ug)
- Respimat: Once daily inhalation of 2 puffs (2x 2.5 ug)
Efficacy and safety of umeclidinium plus vilanterol versus tiotropium, vilanterol, or umeclidinium monotherapies over 24 weeks in patients with chronic obstructive pulmonary disease: results from two multicenter, blinded, randomised controlled trials –Frequency of Exacerbation

## Long Acting Antimuscarinics (LAMA)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>TRADE NAME</th>
<th>INDICATION</th>
<th>DOSING INTERVAL</th>
<th>MISC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tiotropium Bromide</td>
<td>Spiriva®</td>
<td>Bronchodilation</td>
<td>qd</td>
<td>Decreased exacerbations</td>
</tr>
<tr>
<td>Umeclidinium</td>
<td>Incruse® Ellipta®</td>
<td>Bronchodilation</td>
<td>qd</td>
<td>Decreased exacerbations</td>
</tr>
<tr>
<td>Aclidinium</td>
<td>Tudorza® Pressair®</td>
<td>Bronchodilation</td>
<td>BID</td>
<td>Decreased exacerbations</td>
</tr>
</tbody>
</table>
Long Acting Beta- Agonist (LABA)
Olodaterol (Striverdi Respimat)

- Inhaled long acting β2-agonist
- Jul 31, 2014
- Indicated to control symptoms in adults with chronic obstructive pulmonary disease (COPD)
- Once daily inhalation (5 ug)
Clinical Data for Olodaterol

- Typically enrolled patients with moderate to severe COPD
- > 40 years old
- > 10 pack year smoking history

GSK Package Insert
Formoterol Fumarate (Foradil Aerolizer or Performist)

- Inhaled long acting anti-cholinergic/LABA combination


- Indicated for the long-term, twice daily (morning and evening) administration in the maintenance treatment of bronchoconstriction in patients with Chronic Obstructive Pulmonary Disease including chronic bronchitis and emphysema.

- 1 inhalation twice daily (12 ug per inhalation)
- 1 vial 20ug/2ml nebulized twice daily
Aformoterol (Brovana®)

- Inhaled long acting beta-agonist (LABA)

- Approved: Oct 6, 2006

- Indicated as a long-term, twice-daily (morning and evening), maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

- 15 ug nebulized twice daily
Bronchodilation of Brovana®
Indacaterol (Arcapta®)

- Inhaled long acting β2-agonist
- FDA Approval Date: Jul 1, 2011
- Indicated to control symptoms in adults with chronic obstructive pulmonary disease (COPD)
- Once daily inhalation (75 ug)
Salmeterol Xinafoate (Serevent®)

- Inhaled long acting β2-agonist
- FDA Approval Date: Sep 10, 2001
- Indicated for maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD)
- Twice daily inhalation (50 ug)
## Long Acting Beta-Agonist (LABA)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>TRADE NAME</th>
<th>INDICATION</th>
<th>DOSING INTERVAL</th>
<th>MISC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formoterol</td>
<td>Foradil®</td>
<td>Bronchodilation</td>
<td>BID</td>
<td>Decreased exacerbations, nebulized</td>
</tr>
<tr>
<td></td>
<td>Performist®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olodaterol</td>
<td>Incruse®</td>
<td>Bronchodilation</td>
<td>qD</td>
<td>Decreased exacerbations</td>
</tr>
<tr>
<td></td>
<td>Ellipta®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indacaterol</td>
<td>Arcapta®</td>
<td>Bronchodilation</td>
<td>qD</td>
<td></td>
</tr>
<tr>
<td>Salmeterol</td>
<td>Serevent®</td>
<td>Bronchodilation</td>
<td>BID</td>
<td></td>
</tr>
<tr>
<td>Aformoterol</td>
<td>Brovana®</td>
<td>Bronchodilation</td>
<td>BID</td>
<td>Neubulized only</td>
</tr>
<tr>
<td>Villaterol</td>
<td></td>
<td></td>
<td>qD</td>
<td>Only in combination</td>
</tr>
</tbody>
</table>
Combination Agents

• Inhaled LAMA/LABA
  – Tiotropium Bromide and Olodaterol (Stiloto™ Respimat®)
  – Umeclidinium and Vilanterol inhalation powder (Anoro Ellipta)
  – Aclidinium bromide/Formoterol fumarate*
  – Glycopyrronium bromide and Indacaterol maleate****

* Approved for use in EU
** Submitted for FDA approval by Novartis Early 2015
Umeclidiniumium and vilanterol inhalation powder (Anoro Ellipta)

- Inhaled long acting anti-cholinergic/LABA combination
- FDA Approval Date: December 18, 2013
- Indicated for maintenance of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema to improve patient symptoms.
- 1 inhalation daily (62.5ug/25 ug)
Clinical Studies

Tiotropium Bromide and Olodaterol (Stiloto™ Respimat®)

- Inhaled long acting anti-cholinergic/LABA combination

- Approved May 15, 2015

- Indicated for the long-term, once-daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema

- 2 inhalations once daily (2.5ug/2.5 ug per inhalation)
### Group C COPD Patients

| C | Long-acting anticholinergic and long-acting beta₂-agonist  
|   |   or  
|   | Long-acting anticholinergic and phosphodiesterase 4 inhibitor  
|   |   or  
|   | Long-acting beta₂-agonist and phosphodiesterase inhibitor  
|   | Short-acting beta₂-agonist and/or Short-acting anticholinergic  
|   | Theophylline |

Inhaled corticosteroid + long-acting beta₂-agonist  
or  
Long-acting anticholinergic

Combination Agents

• Inhaled LAMA/LABA
  – Tiotropium Bromide and Olodaterol (Stiloto™ Respimat®)
  – Umeclidinium and Vilanterol inhalation powder (Anoro Ellipta)
  – Glycopyrronium bromide and Indacaterol maleate****

• Inhaled Steroid/LABA
  – Fluticasone Propionate + Salmeterol (Advair® 250ug/50ug)
  – Budesonide + Formoterol (Symbicort ® 160ug/4.5ug)
  – Fluticasone furoate + Vilanterol (Breo™ Ellipta™)

• Inhaled SABA/SAMA
  – Ipratropium Bromide + Albuterol
    • Combivent ®
    • Duoneb ®

***** Submitted for FDA approval by Novartis Early 2015
Fluticasone+Salmeterol (Advair Discus)

- Advair Discus 250ug/50ug is indicated for the twice-daily maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. ADVAIR DISKUS 250/50 is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations.

- FDA Approval Date: Feb 27, 2009
- 1 puff inhaled twice daily
- 250 ug/50 ug per puff
Improvement in FEV1 by Fluticasone Propionate/Salmeterol vs Salmeterol

Change in FEV1 from Baseline (mL)

-120 -100 -80 -60 -40 -20 0 20 40

Weeks

Fluticasone propionate/salmeterol 250/50
Salmeterol

Screening
Randomization

4 week run-in period on FSC 250/50

Respiratory Medicine 2008 102, 1099-1108DOI: (10.1016/j.rmed.2008.04.019)
Reduction of Moderate to Severe COPD Exacerbations by Fluticasone Propionate/Salmeterol vs Salmeterol

Fluticasone propionate/salmeterol 250/50

Salmeterol

p=0.003 vs. Salmeterol

Number at Risk

Time to Event (Weeks)

Probability of No Mod/Sev Exacerbation (%)
Budesonide+Formoterol (Symbicort)

- SYMBICORT 160/4.5 is indicated for the maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.
- FDA Approval Date: Feb 27, 2009
- 2 puffs inhaled twice daily
- 160 ug/4.5 ug per puff
Fluticasone furoate + vilanterol (Breo™ Ellipta™)

- Inhaled long acting corticosteroid/LABA combination
- FDA Approval date: May 10, 2013
- Indicated for maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.
- BREO™ ELLIPTA™ is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations
- 1 inhalation daily (100 ug/25 ug)
Decrease in Clinical Exacerbations with Fluticasone furoate + vilanterol

- N= 1633 patients
- Moderate to Severe COPD
- Moderate Exacerbations = steroid and/or antibiotic
- Severe = hospitalization

Package Insert
Long Acting Combination LABA + Inhaled Corticosteroids (ICS)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>TRADE NAME</th>
<th>INDICATION</th>
<th>DOSING INTERVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluticasone Propionate + Salmeterol</td>
<td>Advair®</td>
<td>Maintenance + Decrease Exacerbations</td>
<td>1 puff BID</td>
</tr>
<tr>
<td>Budesonide + Formoterol</td>
<td>Symbicort®</td>
<td>Maintenance</td>
<td>2 puffs BID</td>
</tr>
<tr>
<td>Fluticasone furoate + vilanterol</td>
<td>Breo™ Ellipta™</td>
<td>Maintenance</td>
<td>1 puff qD</td>
</tr>
</tbody>
</table>
Increased risk of pneumonia with ICS use in patients with COPD: meta-analysis

- Significantly increased risk of serious pneumonia for
  - ICS vs placebo: risk ratio 1.51 (95%CI 1.08–2.10)
    285 events/3,881 patients vs 180 events/3,633 patients
  - ICS + LABA vs LABA: risk ratio 1.72 (95%CI 1.28–2.30)
    356 events/4,754 patients vs 217 events/4,728 patients
  - Total: ICS vs no ICS: risk ratio 1.60 (95%CI 1.33–1.92)
    641 events/8,635 patients vs 397 events/8,361 patients


CI, confidence interval; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; LABA, long-acting β₂-agonist.
Inhaled corticosteroids do not improve symptoms of breathlessness

Mean breathlessness symptom score after 52 weeks

Fluticasone propionate

Placebo

p=ns

ns = not significant

Roflumilast (Daliresp)

- Phosphodiesterase E4 inhibitor
- Approval: 2011
- Indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.
- Dose 500 ug once daily
Recommendations for Use of Roflumilast in Primary Care

• Clear identification of patients eligible for roflumilast

• Phenotyping of patients in primary care
  – lung function measurement (FEV1<50%)
  – accurate health status classification
    • At least 1 exacerbation last year
    • Smoking > 20 pk/years
  – recording of chronic cough and regular sputum production

Additional Concerns with Roflumilast

- Roflumilast and suicidal thoughts or depression
- 20% of patients in trial had 5-10% weight loss
- GI Side effects
<table>
<thead>
<tr>
<th>Group D COPD Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>D</strong></td>
</tr>
<tr>
<td>Inhaled corticosteroid + long-acting beta&lt;sub&gt;2&lt;/sub&gt;-agonist and/or Long-acting anticholinergic</td>
</tr>
</tbody>
</table>
| Inhaled corticosteroid plus long-acting anticholinergic and long-acting beta<sub>2</sub>-agonist  
  *or*  
  Inhaled corticosteroid plus long-acting beta<sub>2</sub>-agonist and phosphodiesterase 4 inhibitor  
  *or*  
  Long-acting beta<sub>2</sub>-agonist and long-acting anticholinergic  
  *or*  
  Long-acting anticholinergic and phosphodiesterase 4 inhibitor |
| Carbocysteine  
  Short-acting beta<sub>2</sub>-agonist  
  *and/or*  
  Short-acting anticholinergic  
  Theophylline |
Non-Pharmacologic Treatments for COPD

• Smoking Cessation
• Pulmonary Rehabilitation
• Oxygen Therapy
• Ventilatory Support
• Lung Volume Reduction Surgery
• Lung Transplantation
• Vaccination

From: Global Strategy for Diagnosis, Management and Prevention of COPD. GOLD Slideset 2015
## Manage Stable COPD: Non-pharmacologic

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Essential</th>
<th>Recommended</th>
<th>Depending on local guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Smoking cessation (can include pharmacologic treatment)</td>
<td>Physical activity</td>
<td>Flu vaccination Pneumococcal vaccination</td>
</tr>
<tr>
<td>B, C, D</td>
<td>Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation</td>
<td>Physical activity</td>
<td>Flu vaccination Pneumococcal vaccination</td>
</tr>
</tbody>
</table>

© 2014 Global Initiative for Chronic Obstructive Lung Disease
Decision tree for prevention of AECOPD according to three key clinical questions using the PICO format: nonpharmacologic therapies, inhaled therapies, and oral therapies. Note that the wording used is “recommended or not recommended” when the evidence was strong (level 1) or “suggested or not suggested” when the evidence was weak (level 2). AECOPD = acute exacerbation of COPD; ER = emergency room; ICS = inhaled corticosteroid; LABA = long-acting β₂-agonist; LAMA = long-acting muscarinic antagonist; PDE4 = phosphodiesterase 4; PICO = population, intervention, comparator, outcome; SABA = short-acting β₂-agonist; SAMA = short-acting muscarinic antagonist.
Selected Topics
Benefits of Pulmonary Rehab In Patients with COPD

• Improve exercise capacity
• Enhance quality of life (QOL)
• Decrease exacerbations within 30 days of discharge
• Impact on Hospitalization and Mortality*

*Inconsistently shown
## Mortality Benefits of Pulmonary Rehabilitation (N=246)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>(-) Rehab</th>
<th>(+) Rehab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital LOS for Respiratory Related Illness</td>
<td>↑25%</td>
<td>↓20%</td>
</tr>
<tr>
<td>Mortality for Respiratory Related Illness</td>
<td>39%</td>
<td>7%</td>
</tr>
<tr>
<td>BODE Score</td>
<td>↑4% (worsened)</td>
<td>↓19% (improved)</td>
</tr>
</tbody>
</table>

Cote CG, Celli BR Pulmonary rehabilitation and the BODE index in COPD. Eur Respir J. 2005;26(4):630
Surgical Options for Advanced COPD

- Lung Volume Reduction Surgery
- Lung Transplantation
Lung Volume Reduction Surgery

• Only for Select Emphysema Patients

• Selection Criteria
  – 45% < FEV1 < 25%
  – TLC >100%
  – RV > 150%

  – Post Rehab Exercise Capacity
    • 6MW > 140m
    • CPET with < 40 watts(men), <25 watts(women)
LVRS Results

FEV₁ = 1.60 L (37%)  
FEV₁ = 2.23 L (52%)
## LVRS Results

<table>
<thead>
<tr>
<th>Pulmonary Testing</th>
<th>Pre-LVRS</th>
<th>Post-LVRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV$_1$(L/min)</td>
<td>1.60 (37%)</td>
<td>2.23 (52%)</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>4.29 (76%)</td>
<td>4.70 (84%)</td>
</tr>
<tr>
<td>TLC (L)</td>
<td>9.21 (113%)</td>
<td>7.73 (94%)</td>
</tr>
<tr>
<td>RV(L)</td>
<td>4.77 (186%)</td>
<td>2.97 (116%)</td>
</tr>
</tbody>
</table>
Lung Volume Reduction Surgery

• Exclusions
  – BMI, > 31.1 kg/m$^2$ (men) or > 32.3 kg/m$^2$ (women)
  – PCO$_2$, > 60 mm Hg
  – PO$_2$, < 45 mm Hg on room air
  – Active Smoking or quit < 4 months
  – Alpha 1 Antitrypsin Disease
  – Non-Apical Distribution of Emphysema
Adult Lung Transplants
Major Indications by Year (Number)
Summary
Global Strategy for Diagnosis, Management and Prevention of COPD

Combined Assessment of COPD

*When assessing risk, choose the **highest** risk according to GOLD grade or exacerbation history. One or more hospitalizations for COPD exacerbations should be considered high risk.*

<table>
<thead>
<tr>
<th>Patient</th>
<th>Characteristic</th>
<th>Spirometric Classification</th>
<th>Exacerbations per year</th>
<th>CAT</th>
<th>mMRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low Risk Less Symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>&lt; 10</td>
<td>0-1</td>
</tr>
<tr>
<td>B</td>
<td>Low Risk More Symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>≥ 10</td>
<td>≥ 2</td>
</tr>
<tr>
<td>C</td>
<td>High Risk Less Symptoms</td>
<td>GOLD 3-4</td>
<td>≥ 2</td>
<td>&lt; 10</td>
<td>0-1</td>
</tr>
<tr>
<td>D</td>
<td>High Risk More Symptoms</td>
<td>GOLD 3-4</td>
<td>≥ 2</td>
<td>≥ 10</td>
<td>≥ 2</td>
</tr>
</tbody>
</table>
Manage Stable COPD: Goals of Therapy

- Relieve symptoms
- Improve exercise tolerance
- Improve health status
- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

© 2015 Global Initiative for Chronic Obstructive Lung Disease
• Avoidance of risk factors
  • smoking cessation
  • reduction of indoor pollution
  • reduction of occupational exposure

• Influenza vaccination
Manage Stable COPD: Key Points

• Identification and reduction of exposure to risk factors are important steps in prevention and treatment.

• Individualized assessment of symptoms, airflow limitation, and future risk of exacerbations should be incorporated into the management strategy.

• All COPD patients benefit from rehabilitation and maintenance of physical activity.

• Pharmacologic therapy is used to reduce symptoms, reduce frequency and severity of exacerbations, and improve health status and exercise tolerance.
Manage Stable COPD: Key Points

- Long-acting formulations of beta$_2$-agonists and anticholinergics are preferred over short-acting formulations. Based on efficacy and side effects, inhaled bronchodilators are preferred over oral bronchodilators.

- Long-term treatment with inhaled corticosteroids added to long-acting bronchodilators is recommended for patients with high risk of exacerbations.
• Long-term monotherapy with oral or inhaled corticosteroids is not recommended in COPD.

• The phosphodiesterase-4 inhibitor roflumilast may be useful to reduce exacerbations for patients with FEV$_1$ < 50% of predicted, chronic bronchitis, and frequent exacerbations.
Q: Does the recent proliferation of new therapeutic agents for really change our treatment of COPD?
A: Quite Possibly

Q: Should I think about COPD Patients Differently?
A: Almost Certainly
Appendix and Supplementary Slides
Carbocysteine
(R)-2-Amino-3-(carboxymethylsulfanyl)propanoic acid

• Not available in the United States
• Multiple Actions
  – muco-active drug
  – free radical scavenging
  – anti-inflammatory properties
ACIP Guidelines for Pneumococcal Vaccination

- **Pneumococcal vaccine-naïve persons aged ≥65 years**
  - PCV13 at age ≥65 years → PPSV23
  - ≥1 year

- **Persons who previously received PPSV23 at age ≥65 years**
  - PPSV23 already received at age ≥65 years → PCV13
  - ≥1 year

- **Persons who previously received PPSV23 before age 65 years who are now aged ≥65 years**
  - PPSV23 already received at age <65 years → PCV13 at age ≥65 years → PPSV23
  - ≥1 year
  - ≥1 year
  - ≥5 years
Multifactorial Approach to the COPD Patient

ALL PATIENTS
- Smoking cessation advice
- Patient education / self management
- Assess co-morbidity
- BMI: Dietary advice if >25, specialist dietary referral if <20
- Exercise promotion
- Pneumococcal vaccination
- Annual influenza vaccination

SYMPTOMS?
- Breathlessness
  - Short-acting bronchodilators (β-agonist/anticholinergic) for relief of symptoms
- Persistent symptoms
  - See pharmacotherapy algorithm (page 13)
- Productive cough
  - Consider mucolytics

FUNCTIONAL LIMITATION?
- MRC score ≥3
  - Optimise pharmacotherapy
  - See pharmacotherapy algorithm (page 13)
  - Offer pulmonary rehabilitation
  - Screen for anxiety/depression

EXACERBATIONS
- (Oral steroids/ antibiotics/ hospital admissions)
  - Discuss action plans including use of standby oral steroids and antibiotics

HYPOXIA?
- Oxygen saturation ≤92% at rest in air
  - FEV₁ <30% predicted
  - Refer for oxygen assessment

HYPOXIA?
- Oxygen saturation ≤92% at rest in air
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HOLISTIC CARE
- Check social support (e.g. carers and benefits)
- Treat co-morbidities
- Consider palliative therapy or secondary care referral for resistant symptoms
- Refer to specialist palliative care teams for end-of-life care

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Kevin Gruffydd-Jones Primary Care Respiratory Journal (2012) 21, 437–441
Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy

OTHER POSSIBLE TREATMENTS

- **GOLD 1**
  - CAT < 10 mMRC 0-1
  - Theophylline

- **GOLD 2**
  - CAT ≥ 10 mMRC ≥ 2
  - SABA and/or SAMA
  - Theophylline

- **GOLD 3**
  - 1 (not leading to hospital admission)
  - SABA and/or SAMA
  - Theophylline
  - N-acetylcysteine

- **GOLD 4**
  - 2 or more or ≥ 1 leading to hospital admission
  - Carbocysteine
  - SABA and/or SAMA
  - Theophylline

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# Therapeutic Options: COPD Medications

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Options</th>
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<tbody>
<tr>
<td>Beta$_2$-agonists</td>
<td>Short-acting beta$_2$-agonists</td>
</tr>
<tr>
<td></td>
<td>Long-acting beta$_2$-agonists</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Short-acting anticholinergics</td>
</tr>
<tr>
<td></td>
<td>Long-acting anticholinergics</td>
</tr>
<tr>
<td>Combination short-acting beta$_2$-agonists + anticholinergic</td>
<td>in one inhaler</td>
</tr>
<tr>
<td>Combination long-acting beta$_2$-agonist + anticholinergic</td>
<td>in one inhaler</td>
</tr>
<tr>
<td>Methylxanthines</td>
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<tr>
<td>Inhaled corticosteroids</td>
<td></td>
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<tr>
<td>Combination long-acting beta$_2$-agonists + corticosteroids</td>
<td>in one inhaler</td>
</tr>
<tr>
<td>Systemic corticosteroids</td>
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<tr>
<td>Phosphodiesterase-4 inhibitors</td>
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