Providers’ Best Practices Update: Asthma and COPD

Indian Health Service Conference
Sacramento, CA
May 4th, 2015

Nicholas Kenyon, MD
Professor and Chief
Division of Pulmonary, Critical Care, Sleep Medicine
Co-Director, UC Davis Asthma Network
University of California, Davis
Summary: Management of COPD & Asthma

- Epidemiology Trends for Asthma and COPD
- Definitions and Diagnostic Concerns
- Updates with the Management Guidelines
  - Similarities and Differences
- Treating Exacerbations of Asthma and COPD
- Novel Therapies for Asthma
- UC Davis Asthma and COPD Management Programs
Asthma in the Developed World, 1990-2008

Anandan et al. Allergy 2010
Global and regional trends in COPD mortality, 1990–2010
Burney et al. ERJ 2015
The Soaring Cost of a Simple Breath, NY Times
October 12th, 2013

40 million asthmatics in US; Asthma Costs are $56 billion/yr
The New Face of COPD

30 million COPD patients in US; COPD costs are $49 billion/yr

“In 14 years of modeling, this is my favorite shot of myself.”

Christy Turlington considers quitting smoking her biggest success. One of her biggest regrets is that she ever started.
COPD is much larger burden in hospital

- 1.5 million Emergency Department (ED) visits for severe COPD exacerbations in United States
  - 726,000 hospitalizations annually (48%)
  - 270,000 require mechanical ventilation
  - 120,000 deaths annually  
  
- 2 million Emergency Department (ED) visits attributed to acute asthma exacerbations annually in United States
  - 500,000 hospitalizations annually (25% of visits)
  - 25,000 intubations annually (5% of hospitalizations)
  - 5,000 deaths annually, majority occur outside hospital
### Summary of Asthma Measures by Race/Ethnicity

<table>
<thead>
<tr>
<th>Measures (All Ages Unless Otherwise Specified)</th>
<th>Black</th>
<th>AI/AN</th>
<th>White</th>
<th>Hispanic</th>
<th>A/PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime Asthma Prevalence (p. 31)</td>
<td>20.8%</td>
<td>21.2%</td>
<td>14.9%</td>
<td>10.0%</td>
<td>12.1%*</td>
</tr>
<tr>
<td>Current Asthma Prevalence (p. 31)</td>
<td>13.0%</td>
<td>15.6%</td>
<td>9.0%</td>
<td>5.9%</td>
<td>6.5%*</td>
</tr>
<tr>
<td>Percent with Well-Controlled Asthma (adults with current asthma, p. 52)</td>
<td>45.8%</td>
<td>52.0%†</td>
<td>54.7%</td>
<td>48.5%</td>
<td>58.1%*†</td>
</tr>
<tr>
<td>Asthma ED Visit Rate (per 10,000, p. 114)</td>
<td>157.5</td>
<td>26.9</td>
<td>38.6</td>
<td>43.2</td>
<td>17.9</td>
</tr>
<tr>
<td>Medi-Cal Asthma ED Visit Rate (per 10,000, p. 147)</td>
<td>317.0</td>
<td>227.7</td>
<td>164.9</td>
<td>115.1</td>
<td>60.8</td>
</tr>
<tr>
<td>Asthma Hospitalization Rate (per 10,000, p. 128)</td>
<td>29.0</td>
<td>4.7</td>
<td>7.6</td>
<td>8.7</td>
<td>6.1</td>
</tr>
<tr>
<td>Percent with Repeat Asthma Hospitalizations (p. 140)</td>
<td>18.8%</td>
<td>4.3%</td>
<td>11.3%</td>
<td>8.9%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Medi-Cal Asthma Hospitalization Rate (per 10,000, p. 151)</td>
<td>63.0</td>
<td>31.1</td>
<td>25.3</td>
<td>19.5</td>
<td>17.4</td>
</tr>
<tr>
<td>Asthma Death Rate (per million, p. 161)</td>
<td>32.7</td>
<td>6.8</td>
<td>11.5</td>
<td>9.0</td>
<td>15.2*</td>
</tr>
</tbody>
</table>

* Asian only (does not include Pacific Islanders)
† Unstable estimate – please note the wide confidence interval (see Technical Notes for details).
Age-Adjusted Asthma ED Visits per 10,000 California Residents by Race/Ethnicity and Age, 2010

Racial disparities persist across all ages, with Blacks having asthma ED visit rates that are 3–5 times higher than Whites. In the 65+ age group, the A/PI rate is slightly higher than among Whites, whereas their rate is much lower than Whites in all of the younger age groups.
California Department of Public Health, 2010

Medi-Cal Asthma Hospitalizations per 10,000 Continuously Enrolled Beneficiaries by Age and Race/Ethnicity, 2010
ACOS: Asthma COPD Overlap Syndrome
Zeki et al. J Asthma 2011; Louie et al. 2013
**Definition of Asthma**

A chronic inflammatory disorder of the airways in which many cells and elements play a role.

Chronic inflammation leads to an increase in airway hyper-responsiveness with recurrent episodes of wheezing, coughing, and shortness of breath.

Widespread, variable, and often reversible airflow limitation.

**Symptoms**
- cough
- sputum
- dyspnea

**Exposure to Risk Factors**
- tobacco
- occupation
- indoor/outdoor pollution

**Spirometry**
COPD : ATS/ERS Definition

• “COPD is a *preventable and treatable* disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal *inflammatory response* of the lungs to noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces *systemic consequences*.”

• Progressive disorder even when contributing factors are eliminated and aggressive therapy is instituted

American Thoracic Society 2004
www.thoracic.org/sections/copd/resources/copddoc.pdf
Asthma, or COPD or ACOS

59-year-old man
- FEV₁ 69% predicted
- Current smoker
- Productive cough in the morning
- No longer can walk up stairs
- ? Osteoporosis, coronary artery disease

42-year-old woman
- FEV₁ 66% predicted
- 10 pack-year history of smoking
- Increased shortness of breath when gardening
- ? Osteoporosis, coronary artery disease
ACOS: Asthma COPD Overlap Syndrome
Zeki et al. J Asthma 2011; Louie et al 2013

Louie et al.

Major criteria:
1. Physician diagnosis of asthma and COPD in the same patient
2. History or evidence of atopy—such as hay fever and elevated total IgE
3. >40 years old
4. Smoking >10 pack years
5. Post-Bronchodilator FEV1 < 80 % predicted and COPD per GOLD definition.

Minor criteria:
1. ≥15 % increase in post-bronchodilator FEV1 or
2. ≥12 % and ≥200 ml in post-bronchodilator FEV1
Percent of Adults Ever Diagnosed with COPD, by Asthma Status and Age, California 2009

Adults with current asthma are almost 8-10 more likely to have COPD than adults who have never had asthma.*

*Chi-square p<0.01 for all age groups
Atopic March—Allergic airway inflammation may begin in the skin and intestine.

Spergel  Ann Asthma All Immunol 2010
The Hygiene Hypothesis

Busse et al. NEJM 2000
Neither asthma nor chronic bronchitis is a single disease. It is a spectrum of airway disorders with common features.
What happens to the airway over a lifetime?
Asthma versus COPD: Pathobiology

**Asthma**
- Allergens
- Epithelial Cells
- CD4+ Cell (Th2)
- Mast Cell
- Eosinophils
- Small airway inflammation and smooth muscle hyperplasia with airway hyperresponsiveness
- Eotaxin, IL-4, IL-5, IL-13

**COPD**
- Cigarette Smoke
- Alveolar macrophage
- NF-kB
- Neutrophilis
- CD8+ Cell (Tc1)
- CD4+ Cell (Th1)
- Small airway inflammation with peribronchiolar fibrosis and centriacinar emphysema
- TNF-α, IL-8, IL-1β, IL-6

**Airflow Limitation**
- NOT FULLY REVERSIBLE

IL = interleukin; TNF = tumor necrosis factor.
COPD: Yes, there is bronchodilator reversibility.

**Short- and long-acting bronchodilators**
- May improve airflow obstruction and lung volumes
- Play a central role in the treatment of COPD

![Graph showing degree of responsiveness](image)

≥15% increase in FEV$_1$ was seen in 65.6% of patients

n=5,756

~54% of patients met ATS responsiveness criteria (≥12% + ≥200 mL)

COPD: Early Diagnosis Difficult

Significant Drops (50%) in Lung Function Are Often Required for Patients to Become Severely Symptomatic

- Dyspnea, Cough, Smoking history ≥10 pack-years
- Exercise Intolerance
- Exacerbations
- Hospitalizations
- Systemic Effects
- Respiratory Failure
- Pulmonary Hypertension
- Disability

*FEV1 % predicted

COPD: What do patients die from?

Death rate per 1,000 person-years

- Normal
- Restricted *
- GOLD 0
- GOLD 1
- GOLD 2
- GOLD 3/4

COPD
Heart Disease
Lung Cancer
Other

n = 15,759 adults age 43 to 66 years at baseline followed for up to 11 years

* Restricted category defined by FEV1/FVC > 0.70 and FVC < 80% predicted

Global Initiative for Chronic Obstructive Lung Disease (GOLD) Executive Summary. Updated 2009.
COPD: Spirometry = Severity

Post-bronchodilator FEV$_1$/FVC < 0.70 supports a COPD diagnosis
Post-bronchodilator FEV$_1$ % predicted determines severity:

<table>
<thead>
<tr>
<th>GOLD 1: Mild</th>
<th>FEV$_1$ &gt; 80% predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 2: Moderate</td>
<td>50% ≤ FEV$_1$ &lt; 80% predicted</td>
</tr>
<tr>
<td>GOLD 3: Severe</td>
<td>30% ≤ FEV$_1$ &lt; 50% predicted</td>
</tr>
<tr>
<td>GOLD 4: Very Severe</td>
<td>FEV$_1$ &lt; 30% predicted</td>
</tr>
</tbody>
</table>

Table adapted from the Global Strategy for Diagnosis, Management and Prevention of COPD 2013, © Global Initiative for Chronic Obstructive Lung Disease (GOLD), all rights reserved. Available from http://www.goldcopd.org.
### COPD: WHO/NIH GOLD Guidelines

**Figure 5-3-8. Therapy at Each Stage of COPD**

<table>
<thead>
<tr>
<th>Old</th>
<th>0: At Risk</th>
<th>I: Mild</th>
<th>II: Moderate</th>
<th>III: Severe</th>
<th>IV: Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>New</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Characteristics</td>
<td>Chronic symptoms</td>
<td>FEV_1/FVC &lt; 70%</td>
<td>FEV_1/FVC &lt; 70%</td>
<td>FEV_1/FVC &lt; 70%</td>
<td>FEV_1/FVC &lt; 70%</td>
</tr>
<tr>
<td></td>
<td>Exposure to risk factors</td>
<td>FEV_1 ≥ 80%</td>
<td>50% ≤ FEV_1 &lt; 80%</td>
<td>30% ≤ FEV_1 &lt; 50%</td>
<td>FEV_1 &lt; 30% or FEV_1 &lt; 50% predicted plus chronic respiratory failure</td>
</tr>
<tr>
<td></td>
<td>Normal spirometry</td>
<td>With or without symptoms</td>
<td>With or without symptoms</td>
<td>With or without symptoms</td>
<td></td>
</tr>
</tbody>
</table>

**Avoidance of risk factor(s); influenza vaccination**

*Add short-acting bronchodilator when needed*

*Add regular treatment with one or more long-acting bronchodilators*

*Add rehabilitation*

*Add inhaled glucocorticosteroids if repeated exacerbations*

*Add long-term oxygen if chronic respiratory failure*

*Consider surgical treatments*
COPD Assessment Scores

mMRC Dyspnea Score

• Grade 0: SOB w/ strenuous exercise

• Grade 1: SOB w/ hurrying on level ground or slight hill

• Grade 2: SOB w/ normal walking >100 meters; slower than others my age

• Grade 3: SOB after 100 meters

• Grade 4: SOB w/ ADLs or leaving the house

How is your COPD? Take the COPD Assessment Test (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

If you wish to complete the questionnaire by hand on paper, please click here and then print the questionnaire.

If you complete the questionnaire online, for each question below, click your mouse to place a mark (X) in the box that best describes you currently.

Example: I am very happy: 0 1 2 3 4 5 I am sad

<table>
<thead>
<tr>
<th>Question</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>I never cough</td>
<td>4</td>
</tr>
<tr>
<td>I cough all the time</td>
<td></td>
</tr>
<tr>
<td>I have no phlegm (mucus) in my chest at all</td>
<td>4</td>
</tr>
<tr>
<td>My chest is full of phlegm (mucus)</td>
<td></td>
</tr>
<tr>
<td>My chest does not feel tight at all</td>
<td>4</td>
</tr>
<tr>
<td>My chest feels very tight</td>
<td></td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am not breathless</td>
<td>5</td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am very breathless</td>
<td></td>
</tr>
<tr>
<td>I am not limited doing any activities at home</td>
<td>5</td>
</tr>
<tr>
<td>I am very limited doing activities at home</td>
<td></td>
</tr>
<tr>
<td>I am confident leaving my home despite my lung condition</td>
<td>5</td>
</tr>
<tr>
<td>I am not at all confident leaving my home because of my lung condition</td>
<td></td>
</tr>
<tr>
<td>I sleep soundly</td>
<td>5</td>
</tr>
<tr>
<td>I don’t sleep soundly because of my lung condition</td>
<td></td>
</tr>
<tr>
<td>I have lots of energy</td>
<td>5</td>
</tr>
<tr>
<td>I have no energy at all</td>
<td></td>
</tr>
</tbody>
</table>

Click to get your total score! 37
Management of COPD: WHO/NIH GOLD Guidelines

**Symptoms:** Based on mMRC or CAT scores

**Risk:** Based on GOLD grades and/or exacerbation history

**Spirometric Classification**
- Low risk: GOLD grades 1 and 2
- High risk: GOLD grades 3 and 4

**Exacerbation history (previous 12 months)**
- Low risk: 0 or 1
- High risk: >2 (or any hospitalization due to 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.)

Figure adapted from the Global Strategy for Diagnosis, Management and Prevention of COPD 2013, © Global Initiative for Chronic Obstructive Lung Disease (GOLD), all rights reserved. Available from http://www.goldcopd.org.
Management of COPD: WHO/NIH GOLD Guidelines

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.) Medications listed within each of the quadrants above are not necessarily in order of preference.

CAT=COPD assessment test; ICS=inhaled corticosteroid; LABA=long-acting beta agonist; LAMA=long-acting muscarinic antagonist; mMRC=modified British medical research council; SABA=short-acting beta agonist; SAMA=short-acting muscarinic antagonist

Figure adapted from the Global Strategy for Diagnosis, Management and Prevention of COPD 2013, © Global Initiative for Chronic Obstructive Lung Disease (GOLD), all rights reserved. Available from http://www.goldcopd.org.
COPD: The Goals of Care

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

Reduce Risk
- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

COPD management includes both pharmacologic and non-pharmacologic measures

Figure adapted from the Global Strategy for Diagnosis, Management and Prevention of COPD 2013, © Global Initiative for Chronic Obstructive Lung Disease (GOLD), all rights reserved. Available from http://www.goldcopd.org.
COPD: Key Activities

Early and correct diagnosis, i.e. FEV1 % < 70%
Staging disease severity, e.g. FEV1 % predicted
Phenotyping disease heterogeneity
Tobacco smoking cessation
Regular exercise and individualized pharmacotherapy
Palliative care with COPD action plan
Influenza vaccinations annually
Preventing acute COPD exacerbations
Consultation with pulmonologist in difficult cases
Providing education on patient self-management

Adapted after Center for Disease Control & Prevention
*MMWR* 2003; 52 (No. RR-6):1-8
Asthma: The Goals of Care

Reduce Symptoms

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

Reduce Risk

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

Asthma management includes both pharmacologic and non-pharmacologic measures

Figure adapted from NHLBI. National Asthma Education and Prevention Program. Full report of the Expert Panel: guidelines for the diagnosis and management of asthma (EPR-3), http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm
## Approach to Asthma: Classifying Control in Patients ≥12 Years

### Classification of Asthma Control

(Youths ≥12 years of age and adults)

<table>
<thead>
<tr>
<th>Components of Control</th>
<th>Well-Controlled</th>
<th>Not Well-Controlled</th>
<th>Very Poorly Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Impairment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2x/month</td>
<td>1-3x/month</td>
<td>≥4x/week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Some limitation</td>
<td>Extremely limited</td>
</tr>
<tr>
<td>Short-acting beta₂-agonist use for symptom control</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week</td>
<td>Several times per day</td>
</tr>
<tr>
<td>FEV₁ or peak flow</td>
<td>&gt;80% predicted/personal best</td>
<td>60-80% predicted/personal best</td>
<td>&lt;60% predicted/personal best</td>
</tr>
<tr>
<td>Validated questionnaires</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATAQ</td>
<td>0</td>
<td>1-2</td>
<td>3-4</td>
</tr>
<tr>
<td>ACQ</td>
<td>≤0.75</td>
<td>≥1.5</td>
<td>N/A</td>
</tr>
<tr>
<td>ACT</td>
<td>≥20</td>
<td>16-19</td>
<td>≤15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk</th>
<th>0-1 per year</th>
<th>2-3 per year</th>
<th>&gt;3 per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in lung growth</td>
<td>Evaluation requires long-term follow-up care.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-related adverse effects</td>
<td>Medication side effects vary in intensity. Level of intensity does not correlate to specific levels of control but should be considered in overall assessment of risk.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NHLBI. National Asthma Education and Prevention Program. Full report of the Expert Panel: guidelines for the diagnosis and management of asthma (EPR-3) Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm.**
Approach for Managing Asthmatics ≥ 12 Years of Age

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

STEP 1
PREFERRED
SABA PRN

STEP 2
PREFERRED
Medium-dose ICS
OR
Low-dose ICS + LABA

ALTERNATIVE
Cromolyn, Nedocromil, LTRA, or Theophylline

STEP 3
PREFERRED
Medium-dose ICS + LABA

OR
Medium dose ICS + either LTRA, Theophyllin or Zileuton

STEP 4
PREFERRED
High-dose ICS + LABA
AND
Consider Omalizumab for patients who have allergies

STEP 5
PREFERRED
High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies

STEP 6
PREFERRED
High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies

Step up if needed
(first, check adherence, environmental control, and comorbid conditions)

Step down if possible
(and asthma is well-controlled at least 3 months)

Intermittent Asthma

Patient Education and Environmental Control at Each Step

NHLBI. National Asthma Education and Prevention Program. Full report of the Expert Panel: guidelines for the diagnosis and management of asthma (EPR-3) DRAFT,
How might you differentiate Asthma from COPD?

- Childhood history of asthma
- Family history of asthma
- Atopy: RAST panel and total serum IgE
- Pulmonary Function Test: DLCO
- 6 min walk test: Oxygen saturation
- Methacholine challenge testing
- CXR/ Chest CT scan
- Exhaled Nitric Oxide FeNO
Exhaled breath nitric oxide predicts response to steroids in elderly patients with fixed airflow obstruction

46 patients, >50 yrs of age referred with fixed airflow obstruction. Subjects had bronchoscopic biopsy and HRCT + PFTs.

ATS recommends using FeNO in:

- diagnosing of eosinophilic airway inflammation
- determining likelihood of steroid responsiveness
- supporting the diagnosis of asthma
- monitoring airway inflammation

AJRCCM Sept 2011
Common Initial Management

- **Anti-Inflammatory drugs**
  - ED: IV corticosteroids within 1 hour  
    - 120 – 500 mg/d methylprednisolone
  - Inhaled corticosteroids
  - Oral prednisone for exacerbation

- **Bronchodilator drugs**
  - Short-acting $\beta_2$ agonists + ipratropium  
  - Long acting $\beta_2$ agonists + tiotropium
Not all asthmatics respond the same to steroids. Th2 High vs. Low Phenotype

Woodruff et al. AJRCCM 2009
More ‘targeted’ treatments: Asthma vs. COPD

- Leukotriene antagonists
  - Lipoxygenase inhibitor
  - LT receptor antagonist
- Magnesium
- Omalizumab (anti-IgE)
- Bronchial Thermoplasty
- Roflumilast
- Azithromycin

- Anti-IL5
  - Mepolizumab
- Anti-IL13
  - Lebrikizumab
- Anti-IL4/Anti-IL13
  - Dupilumab
Effectiveness of magnesium sulfate as initial treatment of acute severe asthma in children: a randomized, controlled trial
Torres et al Arch Pediatr 2012

SBT salbutamol
MPD methylprednisolone
CRIA respiratory failure

<table>
<thead>
<tr>
<th>Table 2a. Treatment group</th>
<th>Table 2b. Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBT 0.15 mg/kg x 3</td>
<td>SBT 0.15 mg/kg x 3</td>
</tr>
<tr>
<td>MPD 2 mg/kg IV</td>
<td>MPD 2 mg/kg IV</td>
</tr>
<tr>
<td>O₂</td>
<td>O₂</td>
</tr>
<tr>
<td>SO₄Mg 25 mg/kg</td>
<td>SBT 0.2 mg/kg x 3</td>
</tr>
<tr>
<td>SBT 0.2 mg/kg x 3</td>
<td></td>
</tr>
</tbody>
</table>

CRIA
Inadequate response:
SBT 0.15-0.4 mg/kg/h
Mechanical ventilation
Inadequate response

<table>
<thead>
<tr>
<th></th>
<th>Treatment group n= 76</th>
<th>Control group n= 67</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need of MV</td>
<td>5% (n= 4)</td>
<td>33% (n= 22)</td>
<td>0.001</td>
</tr>
<tr>
<td>Length-of-stay in MV (days) α</td>
<td>3 (1-6)</td>
<td>5 (2-12)</td>
<td>0.087</td>
</tr>
<tr>
<td>Total hospital length-of-stay α</td>
<td>7 (3-12)</td>
<td>19 (14-29)</td>
<td>0.046</td>
</tr>
<tr>
<td>Length-of-stay in PICU (days) α</td>
<td>2 (1-4)</td>
<td>10 (6-18)</td>
<td>0.0376</td>
</tr>
</tbody>
</table>
Effect of oral magnesium supplementation on measures of airway resistance and subjective assessment of asthma control and quality of life in men and women with mild to moderate asthma: a randomized placebo controlled trial.

Kazaks et al. J Asthma 2010

- **OBJECTIVE:** To determine if long term (6.5 month) treatment with oral Mg would improve asthma control and increase serum measures of Mg status in men and women with mild-to-moderate asthma.

- **SUBJECTS:** 55 males and females aged 21 to 55 years with mild to moderate asthma according to the 2002 National Heart, Lung, and Blood Institute (NHLBI) who used only beta-agonists or inhaled corticosteroids (ICS) as asthma medications were enrolled.

- **DESIGN:** Subjects were randomly assigned to consume 340 mg (170 mg twice a day) of Mg or a placebo for 6.5 months.

- **CONCLUSION:** Adults who received oral Mg supplements showed improvement in objective measures of bronchial reactivity to methacholine and PEFR and in subjective measures of asthma control and quality of life.
Anti-IgE (Omalizumab)


**TABLE II. Summary of timing of Xolair (omalizumab) adverse reactions**

<table>
<thead>
<tr>
<th>Timing of the reaction</th>
<th>First-third Xolair (omalizumab) dose (no. of events)</th>
<th>Fourth or later Xolair (omalizumab) dose (no. of events)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 min</td>
<td>11</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>30-60 min</td>
<td>6</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>1-2 h</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>2-12 h</td>
<td>4</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>&gt;12 h</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>9</td>
<td>41</td>
</tr>
</tbody>
</table>
Bronchial Thermoplasty #2:
Left: LLL Untreated, Right: RLL Treated
Effect of roflumilast on exacerbations in patients with severe chronic obstructive pulmonary disease uncontrolled by combination therapy (REACT): a randomised controlled trial.
Martinez et al Lancet 2015

2708 patients recruited

763 withdrew during screening or did not meet entry criteria

1945 patients randomly assigned

972 assigned to placebo

6 not given placebo

4 not given roflumilast

969 given roflumilast

269 discontinued roflumilast

82 adverse events

117 withdrew consent

11 chronic obstructive pulmonary disease exacerbation

5 predefined discontinuation criterion met

8 lost to follow-up

46 other reason

966 given placebo

192 discontinued placebo

29 adverse events

87 withdrew consent

18 chronic obstructive pulmonary disease exacerbation

1 predefined discontinuation criterion met

5 lost to follow-up

52 other reason

700 completed study

969 included in the intention-to-treat analysis

774 completed study

966 included in the intention-to-treat analysis

Mean rate of chronic obstructive pulmonary disease exacerbations per patient per year

- Intention to treat
- Per protocol

Number at risk
Patients with at least one exacerbation (n)

Severe exacerbations

Exacerbations leading to hospital admission

Placebo group vs Roflumilast group

Rate ratio (95% CI)

Two-sided p value

0.757 (0.601-0.952) 0.0175

0.668 (0.518-0.861) 0.0018

0.761 (0.604-0.960) 0.0209

FEV₁ (L)

Time (weeks)

Number at risk*
Prophylactic use of macrolide antibiotics for the prevention of chronic obstructive pulmonary disease exacerbation: a meta-analysis.
Ni et al. PLOS One 2015

Forest plot of risk ratios for exacerbations per patient per year treated with macrolides compared with the control.

<table>
<thead>
<tr>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Rate ratio and 95% CI</th>
<th>Relative weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suzuki (2001)</td>
<td>0.21 0.07 0.64 0.01</td>
<td></td>
<td>5.47</td>
</tr>
<tr>
<td>Banerjee (2005)</td>
<td>3.27 0.53 20.18 0.20</td>
<td></td>
<td>2.37</td>
</tr>
<tr>
<td>Seemungal (2008)</td>
<td>0.65 0.49 0.86 0.00</td>
<td></td>
<td>20.91</td>
</tr>
<tr>
<td>Blasi (2010)</td>
<td>0.24 0.10 0.59 0.00</td>
<td></td>
<td>7.49</td>
</tr>
<tr>
<td>He (2010)</td>
<td>0.55 0.31 0.98 0.04</td>
<td></td>
<td>12.98</td>
</tr>
<tr>
<td>Albert (2011)</td>
<td>0.83 0.72 0.95 0.01</td>
<td></td>
<td>24.47</td>
</tr>
<tr>
<td>Simpson (2014)</td>
<td>0.38 0.14 1.04 0.06</td>
<td></td>
<td>6.39</td>
</tr>
<tr>
<td>Uzun (2014)</td>
<td>0.58 0.42 0.80 0.00</td>
<td></td>
<td>19.91</td>
</tr>
<tr>
<td>Overall</td>
<td>0.58 0.43 0.78 0.00</td>
<td></td>
<td>100.00</td>
</tr>
</tbody>
</table>
Cytokines and Effector Cells of Interest in Asthma

**Key Cells**
- Eosinophil
- Mast cell
- Th2 lymphocyte
- Dendritic cell

**Key Cytokines**
- IL-4
- IL-5
- IL-13
- IL-17

Holgate et al. 2008
**Asthma:** Genotyping studies have led to new research avenues, but little change in therapeutics, in asthma.

- >100 genes associated with either asthma or atopy
- Most genes are related to either Th2 lymphocyte mediated inflammation or smooth muscle reactivity

Ober et al., Genes and Immunity 2007
The Black Box Warning on β-agonists

“We’ve got case reports of people dying, clutching their Serevent inhaler. But Serevent is still on the market.”

Dr. David Graham, October 2004
Salmeterol Multi-center Asthma Research Trial (SMART)

Hypothesis: Long-acting β-agonists would decrease near-fatal and fatal respiratory-related events

Goal: Enroll 60,000 patients

Design: RCT, 28 wk intervention of placebo vs. salmeterol

Interim analysis (25,858 patients)

- Non-significant increase in severe respiratory related events (<1% of subjects) in salmeterol group
- African Americans (17% of those enrolled) there was a significant increase in events (19 vs. 4; RR=4.6)
- 62% of African Americans were not on inhaled steroids

Nelson et al., Chest 2006
Polymorphisms of the β₂-adrenergic receptor

Population Genotype
Prevalence

16% Arg/Arg
37% Arg/Gly
47% Gly/Gly

McGraw et al., JCI 1998
Prospective trial of scheduled albuterol use by genotype (BARGE)

331 asthmatics
mild asthma
18-55 yrs age

55 Arg/Arg
37 randomized
17 albuterol
16 completed
20 placebo
17 completed

125 Gly/Gly
41 randomized
20 albuterol
17 completed
21 placebo
17 completed

Response to bronchodilators by genotype

Response to anti-cholinergic
UCAN Asthma Team (1998-2015)

- UCAN Clinic
  - Two pulmonary asthma specialists
  - Two full time respiratory therapists
  - “UCAN Quit” smoking cessation clinic,
  - Omalizumab clinic
  - Videolaryngoscopy clinic
  - Bronchial thermoplasty program
- Three additional bronchoscopists integrated into the UCAN team specifically to perform BT
- Authorization coordinator
- Bronchoscopy suite: Interventional pulmonary laboratory nurses and respiratory therapists specifically trained in BT
UC Davis Asthma Network (UCAN) clinics (1999-2008)

850 patients--74% Female, mean age 46.3±15.3
58.6% Severe persistent, 33.9% Moderate persistent

ER visits and admissions in the year before and after clinic enrollment

COPD hospitalizations increased from 459 in 2009 to 587 in 2011

Average cost per case increased nearly 2-fold from $14,259 to $26,355

Average LOS increased from 6.27 to 7.57 days in FY 2011

Total direct cost in FY 2011 for inpatient COPD care was 587 patients = $15,470,385
COPD Case Management Program

- Registered Respiratory Therapist COPD Case Manager Program at UCDMC (916)762-COPD from 7am-7pm
  - 130 Patients Hospitalized for AECOPD seen by CMs
  - Mean Age: **69 years** (range 46-88)
  - Men: **47%**
  - Women: **53%**
  - Patients with Prior COPD Education: **5%**
- Referral Source
  - Referred by MD: **21%**
  - Referred by RT: **15%**
  - Referred by EMR Screening Tool: **12%**
    - Use of this tool after development began 6/30/2012
  - Identified by Case Managers by Dx Code in EMR: **52%**
COPD is Treatable

- Diagnose
- Reduce Risk
- Reduce Symptoms
- Reduce Complications

- Spirometry
- Smoking Cessation
- Immunizations
- Reduce Other Exposures
- Bronchodilators
- Consider Inhaled Steroids
- Pulmonary Rehabilitation
- Treat Exacerbations (Flare Ups)
- Oxygen Use

We know there is no cure for COPD as of yet, but COPD is treatable. By taking your medications as prescribed to help slow the progression of this disease, you can reduce complications, such as an exacerbation. Slowing the progression of COPD can be done by:

Quitting smoking - You can add years on to your life and breathe better during those years if you quit smoking. Continuing to smoke reduces your lung function and can cause bad breathing days or flair ups.

Immunizations - Getting your flu shot and pneumonia vaccine when they are due can prevent respiratory illnesses that can lead to a COPD exacerbation.

Washing your hands - This is another way to help avoid infection. Approximately 60% of COPD exacerbations are caused by some sort of infection. We can reduce our risk by washing our hands as well as not touching our hands to our face. Waterless soap, wet wipes, and hand sanitizer can be kept handy.

Avoiding others who are sick - Staying away from friends and family who have a “cold” will prevent you from possibly contracting whatever bug they may have. When you have COPD, your “cold” can turn into an exacerbation. One week away from family and friends may save you a hospital visit.

Traveling with Oxygen

It is ok to travel with oxygen. It just requires some planning. It’s a good idea to call your healthcare provider before making travel arrangements and obtaining a copy of your oxygen prescription and any other paperwork you may need. Allow for plenty of time to have oxygen delivered, depending on where you are going, and how you plan to travel. Your healthcare provider or medical equipment company will help you with this. Before booking your trip, call the carrier or travel agent to find out the requirements for traveling with oxygen.

By Car

When traveling by car you will want to keep windows cracked for good air circulation. If you are using liquid oxygen, be sure to store the unit upright and secure it with a seatbelt if possible. DO NOT STORE OXYGEN IN THE TRUNK. It is too hot! DO NOT SMOKE or let anyone else smoke in the car.

By Bus or Train

You will likely be able to take your own oxygen delivery system on board, but you will need to call in advance to tell them you are traveling with oxygen. They may need to see a copy of your prescription prior to travel.

By Plane

Oxygen tanks are not allowed on airplanes. Many airlines supply oxygen for a fee. Call the airline well in advance to make arrangements. Keep in mind that airlines may supply oxygen on the plane, but not in the airport. You will need to arrange to have oxygen delivered to your destination, or on hand during a layover. If you are using oxygen at rest, you will need it on your flight. Discuss these travel plans with your doctor and discuss your oxygen use. Different airlines have different requirements, so check with your airline in advance to facilitate your travel.

By Ship

You can likely bring your own oxygen on board the cruise ship, but they may need a letter from your doctor along with a brief medical history and copy of your oxygen prescription. You must arrange for oxygen to be delivered to the cruise ship.
COPD Case Management Program

- COPD Care Coordination and Self Management proves to reduce Healthcare Resource Utilizations and Improve Patient Outcomes
  - Average LOS: 5.4 days
  - Decreased from 7.57 days for FY 2011
  - Projected cost savings of ~ $7,555 per admission
  - Average Hospitalizations in Past Year: 2.13
  - Bounce Back Rate to Date(<30 days after D/C): 6%
    - Decreased from 16% for FY 2011
    - Projected cost savings of ~ $1,300,000
  - Readmission Rate (>30 days after D/C): 23% (14 pts total)
  - Deaths After Enrolled In Program: 5
  - Patients Followed by PCP: 85%
  - UC Davis Patients: 60%
  - Patients with Follow Up Visit to PCP after D/C: 77%

Ann Intern Med 2011; 155: 179-191
Who should we refer?

- COPD GOLD Stages II through IV
- Difficult-to-control after rehabilitation
- Oxygen requirement
- ≥ 2 hospitalization for COPD per yr
- BMI < 21 kg/m²
- ICU admission for COPD
- Concomitant CHF
- Presence of anxiety or depression
- Patients unable to meet their ADLs
Clinical Pearls

1. There will be fewer asthmatics and more COPD patients requiring hospitalization in the future.

2. ACOS will continue to be a diagnostic conundrum.

3. Therapeutic considerations:
   • Consider magnesium
   • Roflumilast or azithromycin for COPD patients with frequent exacerbations
   • New small molecule therapies being developed for severe asthma

4. We must develop hospital programs to better manage the discharged COPD and COPD patient.

5. Fight the indifference of managing COPD.