Breathing New Air Into the Treatment of COPD & Asthma

Timothy J. Barreiro, DO, MPH, FCCP, FACP, FACOI
Section Chair, Pulmonary & Critical Care Medicine
Associate Professor of Internal Medicine
NIH Health Minority & Harvard Macy Scholar
Ohio University Heritage College of Osteopathic Medicine
Northeast Ohio Medical University
Director, St. Elizabeth Pulmonary Health & Research Center
Disclosures Information
2016 Annual Convention and Scientific Sessions

• I have no relevant or non relevant financial relationship with a commercial interest in this subject or other subject matter.

• I have no financial relationships to disclose.

• I will not discuss off label use or investigational use in my presentation.

• I will discuss the following off label use and/or investigational use in my presentation:
Lecture Objectives

• Introduce new and interesting issues related to the diagnosis, assessment and management of obstructive pulmonary disease (COPD), Asthma and Overlaps.

• Discuss how to individualize pharmacological therapy in airflow obstruction.

• Examine contemporary strategies to assess, manage, and reduce exacerbations (multisystems).
We Know Airflow Disease Is Important

Respiration: The essence of life

“The Lord formed a man from the dust and breathed into his nostrils the breath of life, and the man became a living being” (Genesis)

Absence of a breathing is tested with a CO2 challenge

Obstructive Pulmonary Diseases are not glamorous
The Diseases are NOT Sexy

I miss my lung, Bob.
Why It Matters
Major Health Problem

• 30% increase in deaths worldwide in the past 10 years.

• The 3\textsuperscript{rd} leading cause of death.

• Adults with COPD (compared to general population)
  • Unable to work (24% vs. 5%)
  • Activity limitations (50% vs. 17%)
  • Difficulty walking, climbing stairs (38% vs. 11%)
  • Require specialized equipment (22% vs. 7%)

The Longitudinal History

- Accidents: Decreased by 100% from 1970 to 2002.
- COPD: Increased by 100% from 1970 to 2002.
- Diabetes: Increased by 3% from 1970 to 2002.

JAMA 2008; 294: 1255-1259
What Went Wrong In Obstructive Pulmonary Disease
# Airflow Heterogeneity

<table>
<thead>
<tr>
<th>PT # 1</th>
<th>PT # 2</th>
<th>PT # 3</th>
<th>PT # 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>58 y</td>
<td>62 y</td>
<td>69 y</td>
<td>72 y</td>
</tr>
<tr>
<td>FEV1: 28%</td>
<td>FEV1: 33%</td>
<td>FEV1: 35%</td>
<td>FEV1: 34%</td>
</tr>
<tr>
<td>MRC: 2/4</td>
<td>MRC: 2/4</td>
<td>MRC: 3/4</td>
<td>MRC: 4/4</td>
</tr>
<tr>
<td>PaO2: 70 mmHg</td>
<td>PaO2: 57 mmHg</td>
<td>PaO2: 66 mmHg</td>
<td>PaO2: 60 mmHg</td>
</tr>
<tr>
<td>6MWD: 540 m</td>
<td>6MWD: 400 m</td>
<td>6MWD: 230 m</td>
<td>6MWD: 154 m</td>
</tr>
<tr>
<td>BMI: 30</td>
<td>BMI: 21</td>
<td>BMI: 34</td>
<td>BMI: 24</td>
</tr>
<tr>
<td>SCORE: 3</td>
<td>SCORE: 6</td>
<td>SCORE: 7</td>
<td>SCORE: 9</td>
</tr>
</tbody>
</table>
FEV₁ 88% predicted
FEV₁ % 72%
Interpretation: Normal

FEV₁ 102% predicted
FEV₁ % 73%
Interpretation: Normal

FEV₁ 81% Predicted
FEV₁ % 74%
Interpretation: Normal
The Proportional Venn Diagram of Obstructive Lung Disease*

Non-proportional Venn diagram of COPD showing subsets of patients with chronic bronchitis, emphysema, and asthma. The subsets comprising COPD are shaded.

http://dx.doi.org/10.1378/chest.124.2.474
The Proportional Venn Diagram of Obstructive Lung Disease*

Proportional Venn diagram of COPD showing subsets of patients with chronic bronchitis, emphysema, and asthma. The subsets comprising COPD are shaded.

Figure Legend:
Proportional Venn diagram of OLD and airflow obstruction in the United States (NHANES III surveys from 1988 to 1994) in participants aged ≥ 50 years. Open circles within each area represent the proportion of OLD patients with objective airflow obstruction according to spirometry measurements. Note that there are eight open circles, one for each of the seven mutually exclusive conditions plus one on the right that represents participants with airflow obstruction who did not receive an OLD diagnosis.
Asthma and Chronic Obstructive Pulmonary Disease Overlap Syndrome:

Copenhagen City Heart Study
N = 8,382
22 year follow up

Lange P. Lancet Resp Med 2016
Percentage of Patient with Overlap

http://dx.doi.org/10.1378/chest.124.2.474
Asthma and Chronic Obstructive Pulmonary Disease Overlap Syndrome

Mean Annual Health Care Cost ($ per patient

Asthma

ACOS

% Hospitalization

% ED Visit

p=0.0001

p=0.0001

p=0.0001

Gerhardsson de Verdier M Value Health 2015; 18: 759
Asthma and Chronic Obstructive Pulmonary Disease Overlap Syndrome

- Sleep Apnea
- Diabetes
- GERD
- Allergies
- Hypertension
- Dyslipidemia

Percent (%)

Frequency of exacerbations among patients with ACOS, COPD & Asthma

<table>
<thead>
<tr>
<th>Study</th>
<th>ACOS</th>
<th>COPD</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardin et al.</td>
<td>1.4</td>
<td>0.8</td>
<td>0.1</td>
</tr>
<tr>
<td>Miravitles et al.</td>
<td>1.6</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Menezes et al.</td>
<td>1.5</td>
<td>0.3</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Exacerbations rates per year

- Hardin et al.: p < 0.001
- Miravitles et al.: p < 0.001
- Menezes et al.: p < 0.002


Overlap Syndrome

• Why is the Overlap between Asthma and COPD important?

• Patients are rarely included in clinical trials.

• ~ 50% develop fixed airflow limitations over the course of their lifetime.
  • ? corticosteroid resistance.

• May not be related to smoking.

• Diagnostic & prognostic purposes are unclear at present time.
Obstructive Pulmonary Disease Risk & Smoking Cessation

Study of 749 men followed for 8 years. 1977

Course of Lung Function

Percent of predicted Forced Expiratory Volume $\times$ (of Value at Birth)

- Continuous Smokers
- Childhood Asthma
- Poverty
- Pollution
- Viral Inf. (adenovirus)
- Bronchopulmonary Dysplasia
- Prematurity (<37 wks)
- Low Birth Weight

Never smoked or not susceptible to smoke

Adapted from Martinez, F et al. NEJM. 2016; 375: 871 – 8.
Airway Function in early infancy & by age 22 years: a non-selective longitudinal cohort study

123 babies born Tucson Lung function at 2 m and 11, 16, & 22 Years

Figure: Predicted mean values for lung function in males at ages 11, 16, and 22 years by length-adjusted infant VmaxFRC

Predicted values were standardised to the mean height and weight for male participants at ages 11, 16, and 22 years. We included an interaction term between survey (age 11, 16, and 22) and quartiles of infant VmaxFRC in the random-effects models. P values were estimated at each survey from the models.

Adapted from Stern D et al. Lancet 2007; 370: 758–64
The Natural History Analysis of the Framingham Offspring Cohort

**Figure.** Mean FEV1 values (expressed as percent of its value at the age of 25) by age, for healthy never-smokers (NS), and continuous smokers (CS). (A) Data for males and (B) for females. The mean FEV1 decline value (and 95% confidence intervals) for males was 38.2 ml (33.9–42.6) and for females 23.9 ml (20.9–27.0), with a P value < 0.001. *P < 0.05 versus healthy never-smokers.

Adapted from Kohasnsal R, et al. Am J Respir Crit Care Med. 2009; 180: 3 – 10
Kalhan R et al. AJM 2010 123, 468. e1 – 468.e7
Birth - Course of Lung Function

Forced Expiratory Volume$_1$ (% of Value at Age 25)

Birth

25

50

75

Age (years)

Normal Group

COPD Group

Determinants of loss

Lower BMI
Pollution (Geography)
Poverty
Lower CC16 levels

Current Smoking
Female gender
Exacerbations (freq)
No Pharmacology Rx
Emphysema (+)
Lower BMI
Lower CC16 levels

Adapted from Lange P et al. NEJM. 2015; 372: 2
What Can Be Done?

Severity

Onset

Death

Time

Biochemical & Cellular events

Physiologic alterations

Clinical & Radiographic Signs

Pathologic evidence
Biomarkers in COPD Patients

Lung Health Study, n = 4,803
Follow up = 22 years
FEV1 = 76.2%
Age = 56 years old

p < 0.0001

Man et al. Thorax 2016; 61: 349
Biomarkers

CRP - Sensitive, but lacks Specificity

Relative Risk of Mortality for 1 SD increase in CRP

- Respiratory (non-malignant)
- Lung Cancer
- Cardiovascular Disease
- Breast Cancer
- GI (non-malignant)
- Violence/Suicide/Trauma

Management / Treatment Goals

• Improve dyspnea

• Improved functional capacity

• Improve quality of life

• Reduce mortality

• Reduce infections & exacerbations

• Improve FEV$_1$ (lung function)
The Gift That Keep Giving

Tobacco, a gift of the Americas to the Old World

Tobacco smoking was used in the Americas for thousands of years before the arrival of Europeans.

Rodrigo de Jerez returned with Cristobal Colon and was jailed by the inquisition for 7 years because “only a possessed person could blow smoke from the mouth”.

1492
and having lighted one part of it, by the other they suck, absorb, receive that smoke inside with the breath, by which they become benumbed and almost drunk, and so it is said they do not feel fatigue. These musket they call tobacos. I knew Spaniards who were accustomed to take it, and being reprimanded for it, by telling them it was a vice, they replied they were unable to cease using it. I do not know what relish or benefit they found in it.
LUNG HEALTH STUDY: Benefits of Smoking Cessation

Usual Care
n = 1964

Sustained quitters
Change status
Continuous smokers

Quitters
Intermittent
Smokers

Do win!

n= 5887

Usual Care
n = 1964

Continuous smokers

P =

Forced Expiratory Volume
1
(% of Value at Age 25)

85
80
70
60
50

11
0
2
5

Years

Combination Therapies

- Combination Therapies
  - LAMA / LABA combinations
    - Aclidinium/indacaterol [Bretaris Genuair]
    - Umeclidinium/vilanterol [Anoro Ellipta]
    - Tiotropium/olodaterol [Stiolto Respimat]
    - Glycopyrronium/indacaterol [Ultibro Breezhaler]

Improved FEV1
Improved QoL scores

Chest 2016; 149: 1181
Global Strategy for Diagnosis, Management and Prevention of COPD

Pharmacologic Therapy = First Choice

<table>
<thead>
<tr>
<th>Exacerbations per year</th>
<th>GOLD 4</th>
<th>GOLD 3</th>
<th>GOLD 2</th>
<th>GOLD 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 or more</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 1 leading to hospital admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (not leading to hospital admission)</td>
<td>B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **C**: CAT < 10 mMRC 0-1
  - ICS + LABA
  - or
  - LAMA

- **D**: CAT ≥ 10 mMRC ≥ 2
  - ICS + LABA
  - and/or
  - LAMA

- **A**: SAMA prn
  - or
  - SABA prn

- **B**: LABA
  - or
  - LAMA

Adapted from © 2015 Global Initiative for Chronic Obstructive Lung Disease
Clinical Stage | GOLD Stage | Inhaled therapy | Non-pharmacological therapy
---|---|---|---
At risk | 0 | SAMA, SABA, or SAMA + SABA | Smoking Cessation, Avoidance of exposure
Intermittent symptoms | 1 | LAMA+SABA | Vaccinations [Influenza, Pneumococcal; (23,13)], Shingles
Persistent symptoms | 2 | LABA+SAMA Except pure asthma | Pulmonary Rehabilitation, Exercise prescription
Maintenance therapy | | | |
Having exacerbations | 3 | LAMA + LABA w/(+ICS) | |
Uncontrolled disease | | | |
Respiratory failure | 4 | Clinical phenotyping (+) ICS to above / (Azithromycin, Daliresp) | Supplemental O2, LVRS, Lung transplantation
End-stage disease | | | |
Prevention of exacerbation is key treatment goal for patients with airflow obstruction.

COPD exacerbations

- Impaired quality of life
- Accelerated lung function decline
- Frequent hospitalizations
- Increased mortality
Exacerbations are Associated with a Decline in Health Status

Exacerbation Frequency

SGRQ (total score decline)

Increase rate FEV1, of decline

None
Infrequent
Frequent

SGRQ = St. George's Respiratory Questionnaire

Frequent exacerbation are associated with increased mortality

Soler-Cataluna et al. Thorax 2005; 60 : 925 - 931
In the POET Study, Treatment with tiotropium or salmeterol

Probability of a first exacerbation of chronic obstructive pulmonary disease (COPD) in the tiotropium and salmeterol groups

Hazard Ratio 0.83
p<0.001 log-rank test

Exacerbations delayed 42 days
17% reduction in risk

Hazard Ratio 0.72
p<0.001 log-rank test

Kaplan–Meier Curves for the Primary and Selected Secondary Outcomes.

Experience of frequent exacerbations despite treatment

In the POET Study, a proportion of patients still experience >2 exacerbations during the study period while receiving treatment with tiotropium or salmeterol.

Subgroup Analysis from POET-COPD Study

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Tiotropium</th>
<th>Salmeterol</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yr)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;55</td>
<td>237/655</td>
<td>258/665</td>
<td>0.88 (0.74–1.05)</td>
<td>0.76</td>
</tr>
<tr>
<td>≥55 to &lt;65</td>
<td>484/1462</td>
<td>522/1426</td>
<td>0.87 (0.77–0.98)</td>
<td></td>
</tr>
<tr>
<td>≥65</td>
<td>556/1590</td>
<td>634/1578</td>
<td>0.83 (0.74–0.93)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.83</td>
</tr>
<tr>
<td>Male</td>
<td>913/2759</td>
<td>1016/2747</td>
<td>0.86 (0.78–0.94)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>364/948</td>
<td>398/922</td>
<td>0.84 (0.73–0.97)</td>
<td></td>
</tr>
<tr>
<td><strong>COPD severity stage (GOLD)</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>Stage II</td>
<td>561/1781</td>
<td>635/1833</td>
<td>0.88 (0.79–0.99)</td>
<td></td>
</tr>
<tr>
<td>Stage III</td>
<td>589/1597</td>
<td>627/1545</td>
<td>0.86 (0.77–0.97)</td>
<td></td>
</tr>
<tr>
<td><strong>Smoking status</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.64</td>
</tr>
<tr>
<td>Noncurrent smoker</td>
<td>678/1929</td>
<td>746/1896</td>
<td>0.84 (0.75–0.93)</td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>599/1778</td>
<td>668/1773</td>
<td>0.87 (0.78–0.97)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>&lt;20</td>
<td>105/286</td>
<td>134/271</td>
<td>0.66 (0.51–0.85)</td>
<td></td>
</tr>
<tr>
<td>≥20 to &lt;25</td>
<td>455/1230</td>
<td>501/1254</td>
<td>0.89 (0.79–1.02)</td>
<td></td>
</tr>
<tr>
<td>≥25 to &lt;30</td>
<td>424/1276</td>
<td>468/1284</td>
<td>0.87 (0.76–0.99)</td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td>293/915</td>
<td>311/860</td>
<td>0.85 (0.72–1.00)</td>
<td></td>
</tr>
<tr>
<td><strong>Use of inhaled glucocorticoids at baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.41</td>
</tr>
<tr>
<td>Yes</td>
<td>785/1986</td>
<td>839/1955</td>
<td>0.87 (0.79–0.96)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>492/1721</td>
<td>575/1714</td>
<td>0.82 (0.73–0.92)</td>
<td></td>
</tr>
</tbody>
</table>
FLAME is the first study to demonstrate superiority of Ultibro® Breezhaler® in exacerbations

1680 pts

indacaterol–glycopyrronium group

indacaterol–salmeterol–fluticasone group

The indacaterol–glycopyrronium group had a delay to first and 11% lower exacerbation rate salmeterol–fluticasone group

(3.59 vs. 4.03; rate ratio, 0.89; 95% confidence interval [CI], 0.83 to 0.96; P=0.003)
Inhaled Corticosteroids

- Limited efficacy vs. Placebo in monotherapy
  - Inconsistent prevention of FEV$_1$ decline
  - Reduced exacerbations (decline 0.19 per patient per year)
  - Slowed rate of QoL decline
  - Large role with asthma overlap patients
  - Increase risk of dysphonia & oral candidiasis
  - Debatable increase risk of pneumonia
    - Recent date does not support his risk?
Inhaled Corticosteroids in DUAL Therapy

- **TORCH**: salmeterol + fluticasone vs. Individual components or placebo
  - Reduced exacerbation, improved health status and FEV$_1$
  - Almost reduced mortality (vs. placebo) $p=0.054$

- **INSPIRE**: Salmeterol + fluticasone vs Tiotropium (Spiriva)
  - No difference in exacerbation rate
  - Reduced overall mortality in combination (HR 0.48)
  - Improved health scores

Am J Respir Crit Care med 2008; 177: 19
Withdrawal of Inhaled Steroids and Exacerbations of COPD

N = 2488

Severe – Very Severe COPD
One exacerbation /12 m

Continued ICS  n = 1244
Discontinued ICS  n = 1244

Outcomes:
1st exacerbation
Lung functions
QoL

A  Moderate or Severe COPD Exacerbation
Hazard ratio, 1.06 (95% CI, 0.94–1.19)
P = 0.35 by Wald’s chi-square test

No. at Risk
IGC continuation 1243 1059 927 827 763 694 646 615 581 14
IGC withdrawal 1242 1090 965 825 740 688 646 607 570 19

Roflumilast (Daliresp)

- Reduced exacerbation by 13%
- Higher rate of adverse events & withdrawal
- Side effect may limit tolerability
  - Psychiatric symptoms
  - Weight loss
  - Diarrhea, nausea, headaches
  - Contraindicated in advanced liver disease

Azithromycin

- Macrolide antibiotic (1 year)

- Decreased frequency of exacerbations (HR 0.73)
  - Median time to first exacerbation was 266 days among patients receiving azithromycin compared with 174 days in the placebo group (P < 0.001).

- More patient with improved QoL
  - The frequency of exacerbations also was significantly decreased in the azithromycin group.

- Concerns
  - Cardiovascular disease debated (prolonged QT)
  - Hearing loss (25% vs. 20%)
  - Drug Resistance (did develop)

Am J Respir Crit Care med 2014; 189: 1173
Management of pulmonary disease beyond the lungs

- Osteoporosis
- Muscle Wasting
- Obesity / Underweight
- Depression / Anxiety
- Metabolism Disorders
- Cognitive dysfunction

Morbidity & Mortality
A Prospective Study of COPD & Risk for Cognitive Impairment

**Figure Legend:**

Adjusted Kaplan-Meier Plots of Chronic Obstructive Pulmonary Disease (COPD) and Risk for Mild Cognitive Impairment (MCI)

A, Relationship between COPD (present or absent) and the percentage of participants free of MCI. B, Relationship between COPD duration (>5 vs ≤5 years) or no COPD and the percentage of participants free of MCI, with age as the time scale.

Majority of morbidity & mortality in COPD is related to extrapulmonary manifestations.

SOB

skeletal muscle dysfunction

reduced exercise tolerance

muscle wasting

skeletal muscle weakness.

Normal = Dark Cell are Type II Fibers

COPD

Destruction of connective tissue, loss of type II fibers, disorganized tissue

Adapted from: Sin DD and Man SFP. Thorax 2006; 61: 1-3
Body Mass, Fat-Free Mass, and Prognosis in Patients with Chronic Obstructive Pulmonary Disease from a Random Population Sample: Finding from the Copenhagen City Heart Study

- 1898 pts with COPD
- Bioelectric impedance measurement
- 7 year follow-up
  - ♂ FFMI 16kg/m²
  - ♀ FFMI 18.7 kg/m²

Vestbo J et al. AJRCCM 2006;173:79-83
Ferreira IM et al. Cochrane Database Sys Rev 2012 12: CD000998
Body Mass, Fat-Free Mass, and Prognosis in Patients with Chronic Obstructive Pulmonary Disease from a Random Population Sample: Finding form the Copenhagen City Heart Study

<table>
<thead>
<tr>
<th></th>
<th>Low FFMI</th>
<th>Low BMI</th>
<th>Normal BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Mortality</td>
<td>1.5</td>
<td>1.8</td>
<td>1.3</td>
</tr>
<tr>
<td>COPD Mortality</td>
<td>2.4</td>
<td>3.2</td>
<td>2.0</td>
</tr>
</tbody>
</table>
**Nutritional Supplementation has uncertain effects on patient important outcomes**

**NUTRITIONAL SUPPLEMENTATION VS. PLACEBO OR USUAL DIET (CONTROL) IN STABLE COPD**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th># of trails (n)</th>
<th>At end of Intervention</th>
<th>Change from baseline to end of Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Supplement</td>
<td>Control</td>
</tr>
<tr>
<td>Mean weight, kg</td>
<td>14 (512)</td>
<td>57</td>
<td>56</td>
</tr>
<tr>
<td>Mean 6-min walk distance, m</td>
<td>5 (142)</td>
<td>411</td>
<td>397</td>
</tr>
<tr>
<td>Health Related QoL Score, total</td>
<td>4 (130)</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Management of pulmonary disease beyond the lungs

60-yr-old pts with echocardiographically confirmed CHF (n=5201)
60-yr-old pts with clinically & spirometry confirmed COPD (n=5218)
Management of pulmonary disease beyond the lungs

<table>
<thead>
<tr>
<th>Baseline Echocardiogram</th>
<th>CHF Group</th>
<th>COPD Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection Fraction %</td>
<td>32± 8</td>
<td>Pt &lt;40% = 30</td>
</tr>
<tr>
<td>LVEDP</td>
<td>59.7 ± 9</td>
<td>47.4 ± 5</td>
</tr>
<tr>
<td>PA Systolic Pressure (mmHg)</td>
<td>39.8</td>
<td>Pt = 7 (diastolic dysfunction)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Baseline Lung Function</th>
<th>CHF Group</th>
<th>COPD Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD I (FEV₁%&lt;70, FEV₁≥ 80%)</td>
<td>13 (6.5%)</td>
<td>55 (25.2%)</td>
</tr>
<tr>
<td>GOLD II (50% ≤ FEV₁ ≥ 80%)</td>
<td>36 (17.9%)</td>
<td>112 (51.4%)</td>
</tr>
<tr>
<td>GOLD III (30% ≤ FEV₁ ≤ 50%)</td>
<td>25 (12.9%)</td>
<td>35 (16%)</td>
</tr>
<tr>
<td>GOLD IV (FEV₁ ≤ 30% or ≤ 50% / RF)</td>
<td>1 (0.5%)</td>
<td>16 (7.3%)</td>
</tr>
</tbody>
</table>

Totals = 37.3% w/ COPD

Totals = 17% w/ HF
Kaplan–Meier estimates of survival of patients with chronic obstructive pulmonary disease with left ventricular dysfunction (-----) and without left ventricular dysfunction (-------). **Hazard ratio 2.34** (95% CI 0.99–5.54); \( p=0.053 \).

Kaplan–Meier estimates of survival of patients with chronic heart failure with airway obstruction (-----) and without airway obstruction (-------). **Hazard ratio 0.77** (95% CI 0.37–1.58); \( p=0.474 \).
Obstructive Pulmonary Disease Summary

• Remains a major cause of morbidity and mortality.

• There have been new insights into its pathophysiology & the role of inflammation.

• Management required a multisystem approach.

• We must look beyond the lungs to care for these patients.