

## COPD: A Renewed Focus

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## Disclosures

- No Business Interests
- No Consulting
- No Speakers Bureau
- No Off Label Use to Discuss



## Objectives

- Master the definition of COPD
- List factors that impact economics and QoL associated with acute exacerbations
- List medications classes used for treatment
- Review new GOLD risk stratification
- List risk factors for acute exacerbations
- List risk factors for re-admission post exacerbation
- List strategies to reduce re-admission



## COPD Definition

- A Chronic Preventable and Treatable Disease
- Persistent Airflow Limitation
- Progressive
- Chronic Inflammatory Response



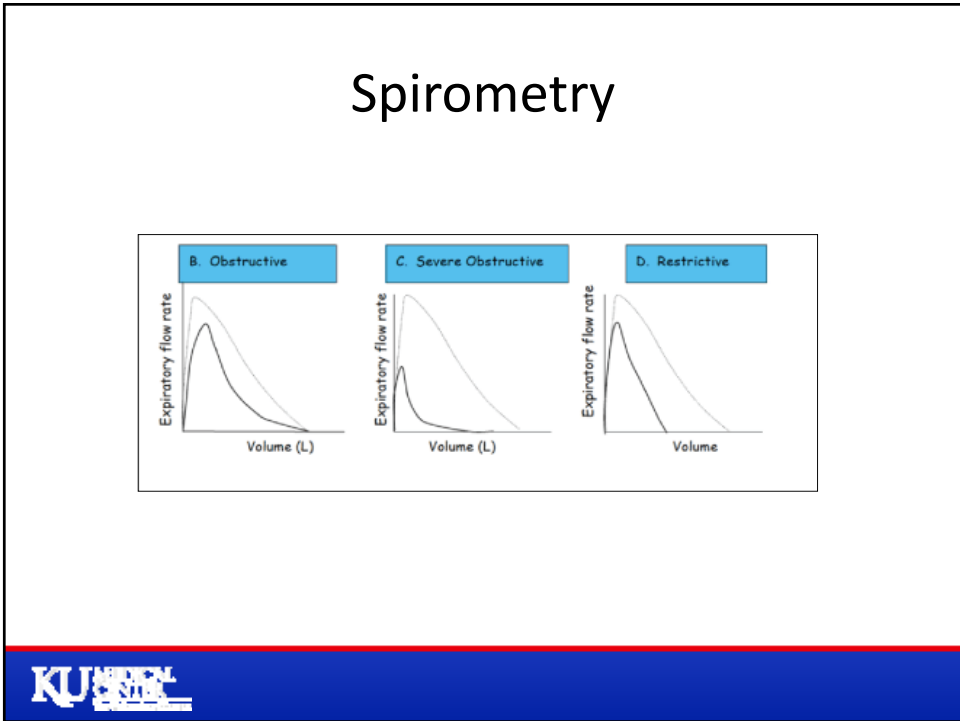
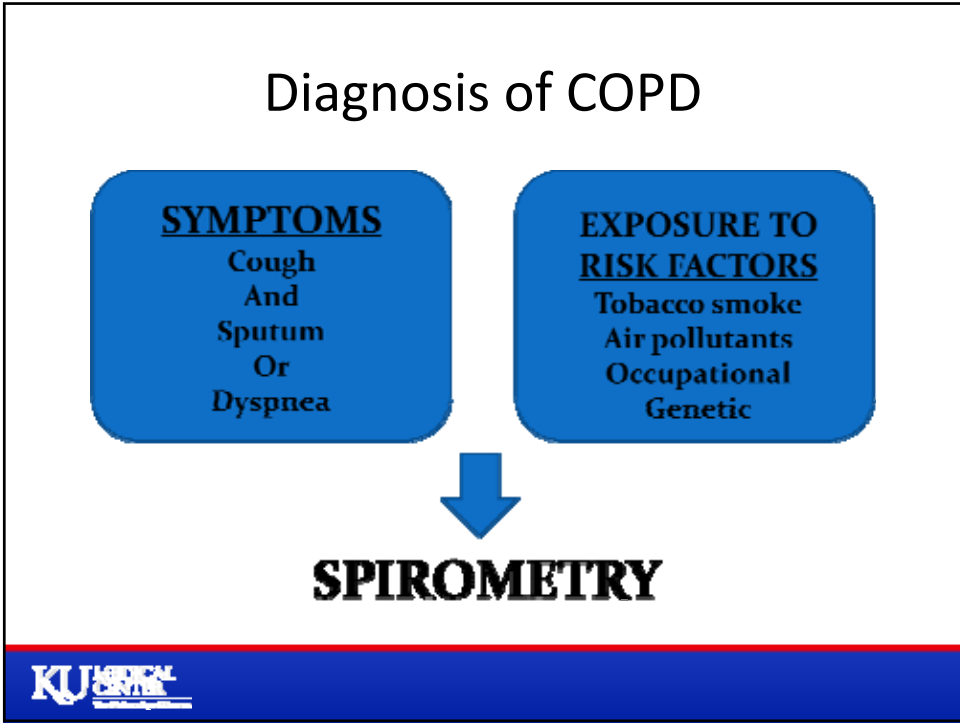
- Which of the following patients should undergo spirometry?
  - A. 35 year old smoker with symptoms
  - B. 45 year old smoker without symptoms
  - C. 55 year old previous smoker without symptoms
  - D. 55 year old smoker without symptoms and a family history of emphysema



## Diagnosis of COPD

- Spirometry
  - Any smoker with symptoms
  - Any risk factor with symptoms
- Screening Not Beneficial





# Diagnosis of COPD

## ATS Guidelines

- FEV<sub>1</sub>/FVC Ratio (FEV<sub>1</sub>%)
  - Less than LLN
- Rate Severity
  - FEV<sub>1</sub> Percent Predicted
- Underestimates OLD
  - Elderly

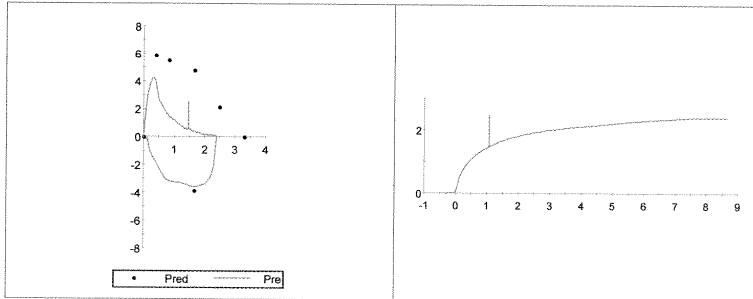
## GOLD Guidelines

- FEV<sub>1</sub>/FVC Ratio (FEV<sub>1</sub>%)
  - Less than 70%
- Rate Severity
  - FEV<sub>1</sub> Percent Predicted
- Underestimates OLD
  - Young
- Overestimates OLD
  - Elderly



ID: 1330363      BMI 19.3      Date: 07/12/2013  
 Height: 60.00      Age: 19      Room: IP-1514  
 Weight: 99.00      Sex: Female      Race: Caucasian

--- SPIROMETRY ---	Pre-Bronch				Post-Bronch		
	Actual	Pred	LLN	%Pred	Actual	%Pred	%Chng
FVC (L)	2.40	3.31	2.70	72			
FEV1 (L)	1.48	2.96	2.45	50			
FEV1/FVC (%)	62	87	77	71			
FEV1/SVC (%)		89					
FEF 25-75% (L/sec)	0.67	3.53	2.44	19			
FEF Max (L/sec)	4.19	5.90	4.04	71			



# Inflammation of COPD

## COPD

- Inflammatory Cells
  - Neutrophils
  - Cytotoxic T Cells
- Inflammatory Mediators
  - TNF- $\alpha$
  - IL-8
  - ROS
- Effects
  - Peripheral airways
  - Parenchyma

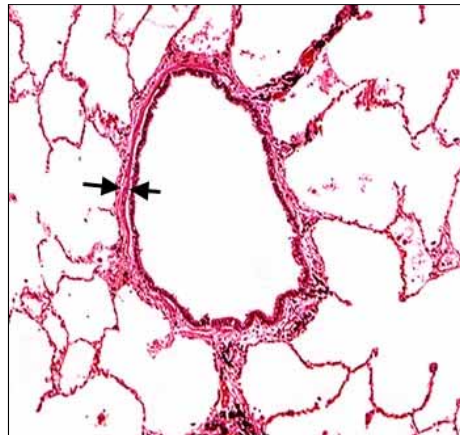
## Asthma

- Inflammatory Cells
  - Mast Cells
  - Eosinophils
- Inflammatory Mediators
  - Leukotriene
  - IL-4
  - IL-5
- Effects
  - All airways
  - Parenchyma sparing

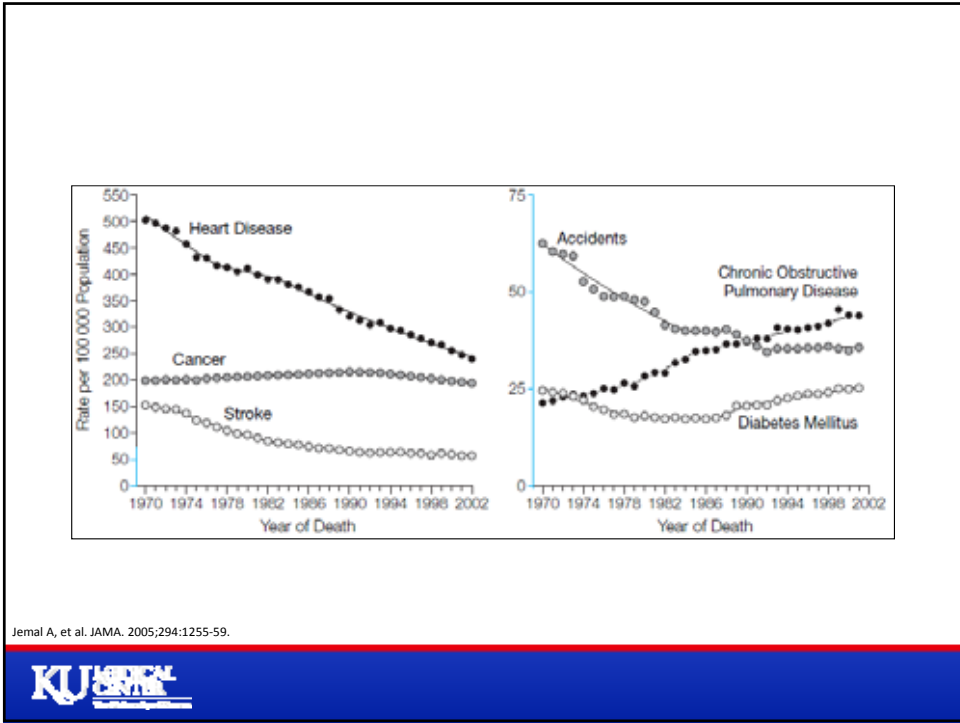


# Inflammation of COPD

Normal Airway







## Epidemiology of COPD

- Affects 12 million Americans
- 3<sup>rd</sup> Leading Cause of Death in the US
  - 800,000 Hospitalizations
  - 143,000 Deaths
- Second Leading Cause of Disability
- Cost
  - \$50 billion spent annually in the US
  - Acute exacerbations leading contributor

CDC. 2012, vol 61, no 6. [http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61\\_06.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_06.pdf).  
 Am J Respir Crit Care Med. 2013;187(4):347-365





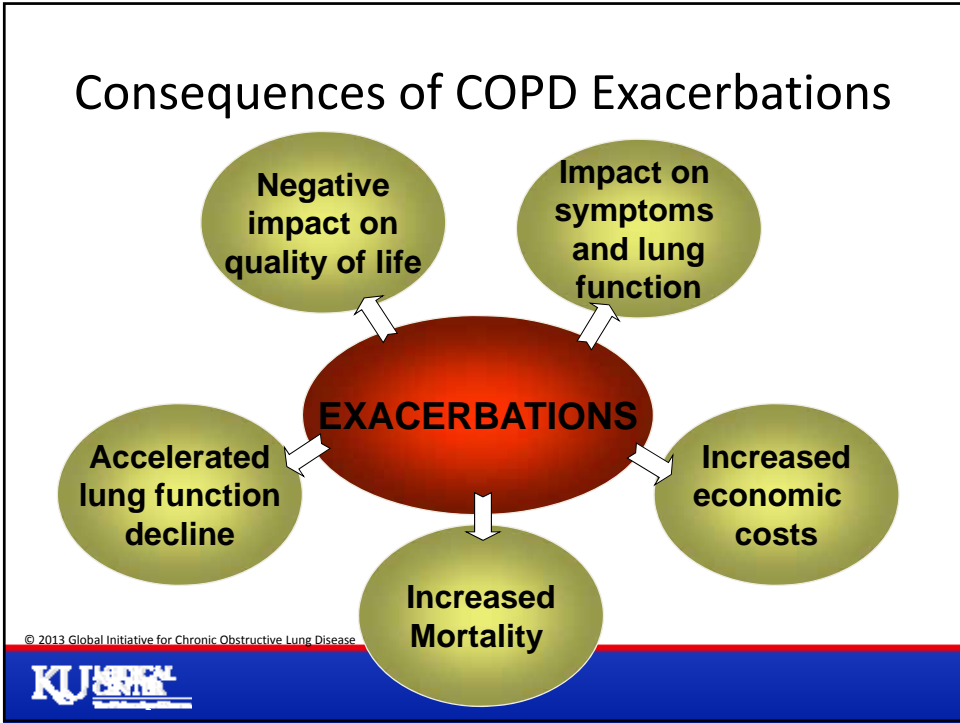
- Which of the following interventions has clearly been shown to reduce mortality associated with COPD?
  - A. Smoking cessation
  - B. Use of a combination LABA/ICS
  - C. Use of long acting muscarinic antagonists
  - D. Use of short acting bronchodilators
  - E. Use of systemic corticosteroids



## Treatment of COPD

- Goals
  - Improve Quality of Life
  - Symptom Control
  - Reduce Exacerbations





- ### COPD Exacerbation
- Risk Factors for Re-Admission
    - Prolonged Hospital Stay
    - Number of Exacerbations
    - Age
    - Co-morbidities
- Jencks SF, et al. NEJM. 2009;360:1418-28.  
Hurst JR, et al. AJRCCM. 2009;179:369-74.
-

## COPD Exacerbations

- Interventions to Reduce Re-admissions
  - Discharge Planning
  - Close Follow-up
  - Patient Education

Boland M, et al. BMC Pulm Med. 2013;13:40.



## Treatment of COPD

- Patient Education
  - Disease Course
  - Risk Factors
  - Smoking Cessation
  - Inhaler Utilization
    - Spacers
  - Immunization

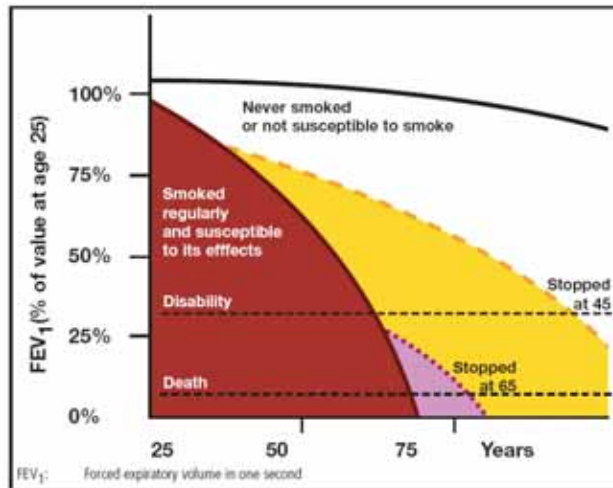


## Treatment of COPD

- Smoking Cessation
  - Nicotine Replacement
  - Behavioral Modification Meds
  - Counselling and Support
    - KanQuit.org

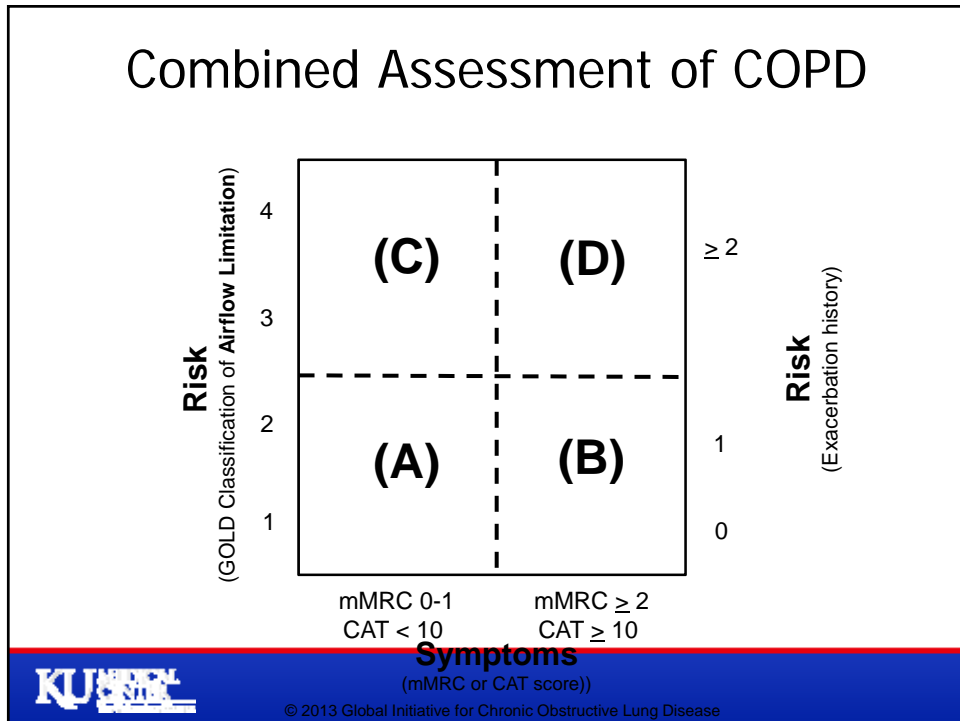
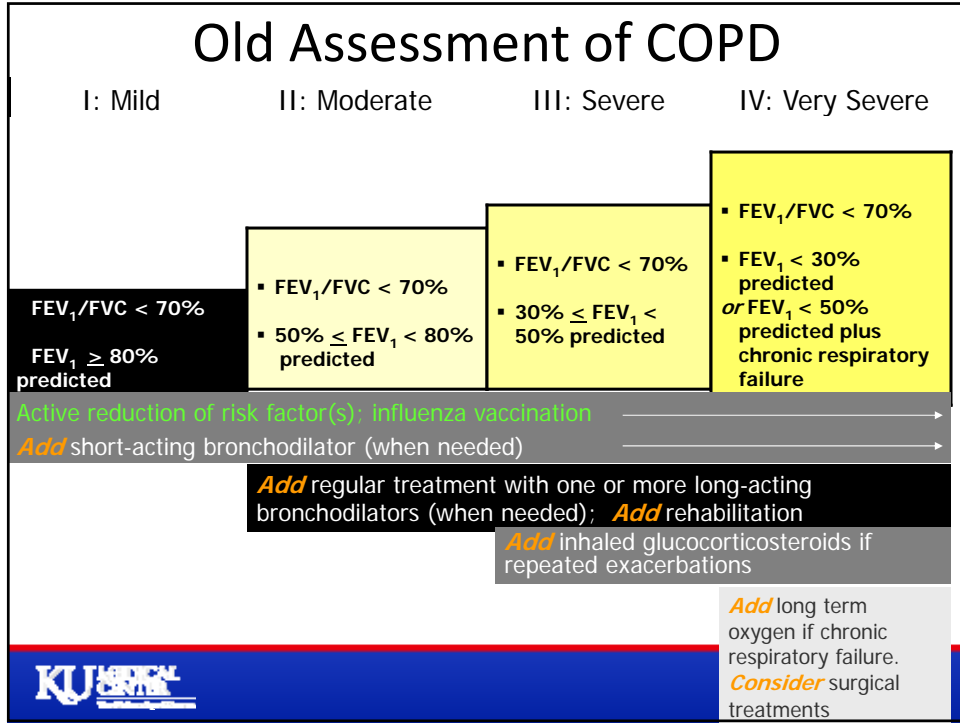


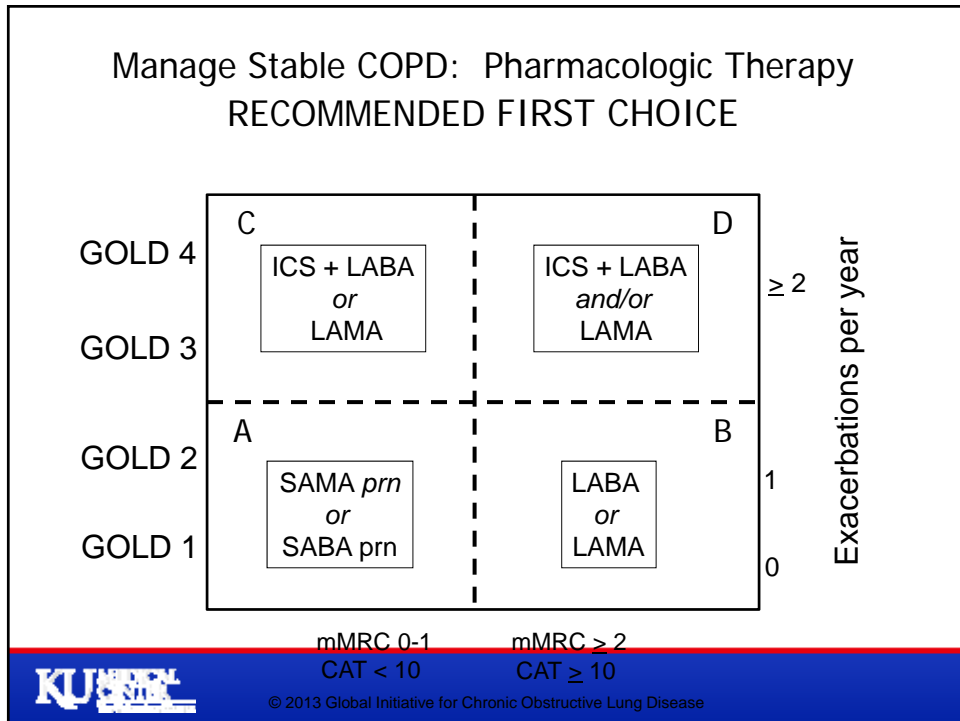
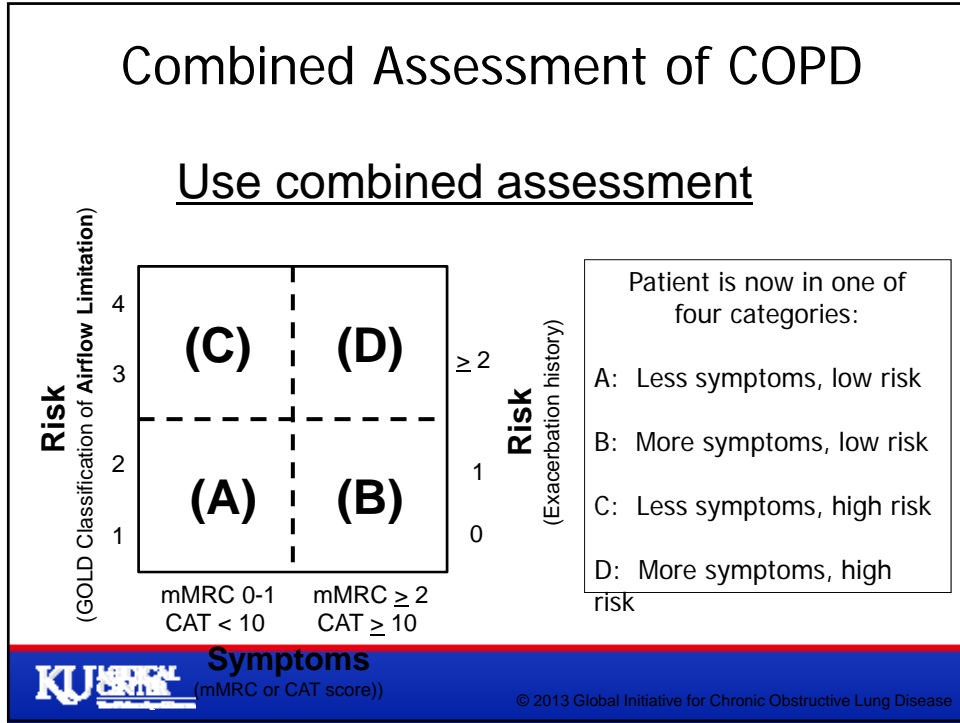
## Smoking Cessation



Fletcher c, Peto R. Brit Med J. 1977;1:1645.







## Treatment of COPD

- Pharmacotherapy in COPD
  - Not shown to alter progressive decline of FEV1
  - Does not improve mortality\*

\*Am J Respir Crit Care Med Vol 180. pp 948-955, 2009



## Treatment of COPD

- |  |  |
|--|--|
| <ul style="list-style-type: none"> <li>▪ Bronchodilators           <ul style="list-style-type: none"> <li>▪ Cornerstone of COPD Treatment</li> <li>▪ Anticholinergics               <ul style="list-style-type: none"> <li>▪ Ipratropium</li> <li>▪ Tiotropium</li> <li>▪ Aclidinium</li> </ul> </li> <li>▪ Beta2-agonist               <ul style="list-style-type: none"> <li>▪ Albuterol</li> <li>▪ Salmeterol</li> <li>▪ Formoterol</li> <li>▪ Arformoterol</li> </ul> </li> <li>▪ Methylxanthines               <ul style="list-style-type: none"> <li>▪ Theophylline</li> </ul> </li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>▪ Anti-inflammatory           <ul style="list-style-type: none"> <li>▪ ICS</li> <li>▪ Phosphodiesterase-4 inhibitor               <ul style="list-style-type: none"> <li>▪ Raflumilast</li> </ul> </li> <li>▪ Macrolides               <ul style="list-style-type: none"> <li>▪ Azithromycin</li> </ul> </li> </ul> </li> </ul> |
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## Bronchodilators

- Physiologic Effects
  - Smooth Muscle Relaxation
  - Improve FEV1
  - Decrease Air-Trapping
    - Dynamic hyperinflation
- Non-Bronchodilator Effects of Beta-Agonists
  - Improve ciliary-beat
  - Improve mucocilliary clearance
  - Decrease vascular permeability
  - Inhibit neutrophil adhesion
  - Increase neutrophil apoptosis



## Treatment of COPD

- Clinical Effects of Bronchodilators
  - Decreased Dyspnea
  - Increased Exercise Tolerance
  - Increased Sleep Quality
  - Increased Quality of Life
  - Decreased Exacerbations

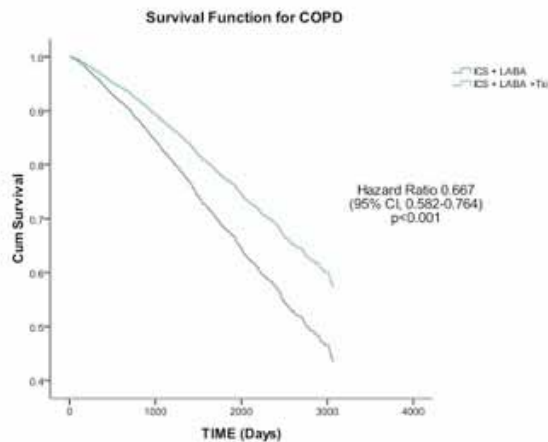
Tashkin, DP, et al. Chest 2004;125:249.





## Long-Acting Bronchodilators

- None Improve Mortality
- No Difference in Exacerbation Reduction
  - When LABA used w/ ICS
- All Improve QOL
  - Salmeterol/Fluticasone>Tiotropium
- Unclear of Impact of ICS causing Pneumonia
  - Didn't affect Mortality
- Combination of All Three Classes Likely Beneficial



Am J Respir Crit Care Med 183:2011:A1611



## Treatment of COPD

- Roflumilast
  - Phosphodiesterase-4 inhibitor
  - Reduce inflammation via inhibition of
    - Chemotaxis, leukocyte activation, and cytokine production
  - Improves FEV1
  - Reduces exacerbations in patients with severe disease and having exacerbations.
  - Side Effects:
    - Nausea, diarrhea, weight loss, and headache

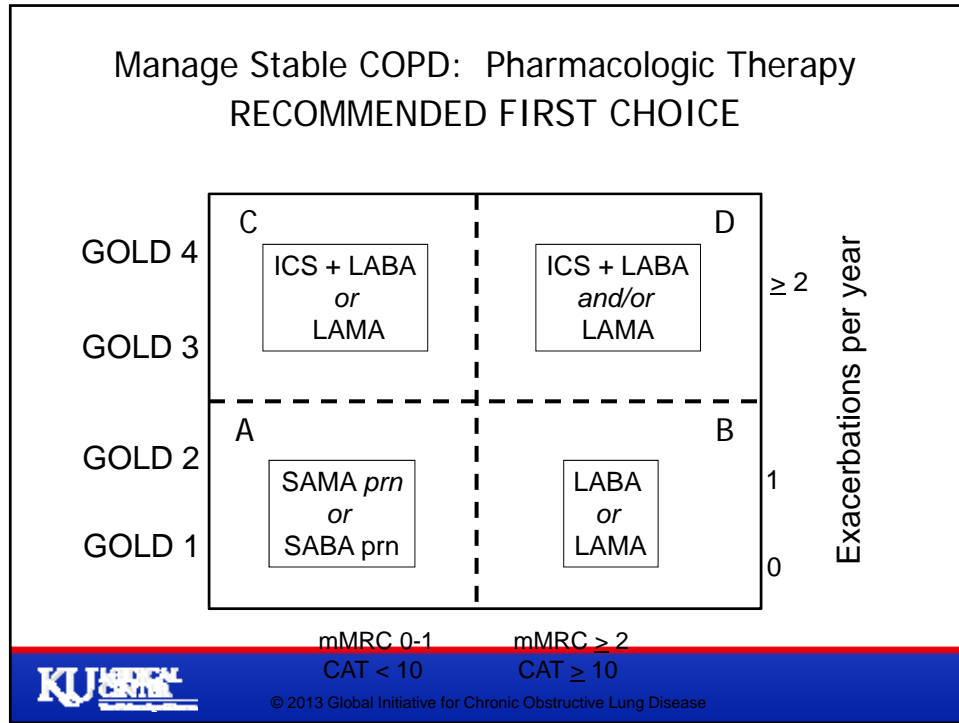
Lancet 2009; 374: 695-703



## Treatment of COPD

- Azithromycin (N Engl J Med 2011;365:689-98.)
  - 1500 patients, 1 year trial
  - Azithromycin vs placebo
  - Primary endpoint:
    - Frequency of exacerbations
  - Reduced:
    - Time to first exacerbation
    - Frequency of exacerbation
  - Improved QoL
  - Hearing decrement was noted
  - Remember Azithro's Black Box Warning





- A 64 yo male with COPD presents to the ER with progressive dyspnea, cough, chest pain, and altered mental status. He is afebrile, HR: 115, BP 165/90, RR 32 and using accessory muscles. He is wheezing on exam and CXR is unremarkable. A duoneb is given with improved RR to 26. His post-bronchodilator ABG is 7.30/50/62 on room air. Your next best step is?
  - A. Admit to the floor with steroids, nebs, and abx
  - B. Admit to the floor with steroids and nebs
  - C. Initiate NIPPV, steroids, nebs, and abx
  - D. D/C home with steroids and abx

## Treatment of COPD

- Acute Exacerbation (Inpatient)
  - Corticosteroids (SCCOPE Trial)
    - Large VA Study Compared 2 wks vs. 8 wks vs. placebo
    - Steroids:
      - Reduced Length of Stay
      - Improved FEV1
      - Less Treatment Failure
    - No Difference in Duration of Steroids
  - Taper:
    - Solumedrol 125mg q 6hr x 72hr
    - Prednisone 60mg→40mg→20mg x3 Days Each

Niewoehner D, et al. NEJM. 1999;340:1941.



## Treatment of COPD

- REDUCE Trial
  - Non-ICU Admissions
  - 40mg Steroids x 5 days vs 2 week taper
  - No change in outcomes
- GOLD
  - Grade B Recommendation

Leuppi J, et al. JAMA. 2013;309:2223-31.



## Treatment of COPD

- Acute Exacerbation
  - Increase Bronchodilator
  - Beta-agonist plus Anticholinergic Better
  - Resume Home Inhalers
  - Oxygen if Hypoxic
  - Chest Physiotherapy NOT Beneficial



## Treatment of COPD

- Non-Invasive Ventilation in Acute Exacerbation
  - Improves Resp Acidosis
  - Decreases Resp Rate
  - Decreases Length of Stay
  - Improves Mortality
  - Reduces Intubations

International Consensus Conf in Intensive Care Medicine: NIPPV in acute resp failure. Am J Resp Crit Care Med. 2001;163:283.



## NIPPV for COPD

- Indications
  - Dyspnea w/ Accessory Muscle Motion
  - Moderate to Severe Acidosis (pH <7.35)
  - Respiratory Rate >25
- Contraindications
  - Shock/MI
  - Altered Mental Status
  - Copious Secretions
  - Inability to Fit/Tolerate Mask

International Consensus Conf in Intensive Care Medicine: NIPPV in acute resp failure. Am J Resp Crit Care Med. 2001;163:283.



## NIPPV for COPD

- Consideration for Outpatient
  - Hypoxemia at Baseline
  - Baseline PaCO<sub>2</sub> > 54
  - Repeated Admissions
- Outcomes Data
  - ? Improved Mortality
  - May Reduce Exacerbations
  - No Effect on QoL

McEvoy R, et al. Thorax. 2009;64:561-66.



## Oxygen in COPD

- Supplemental O<sub>2</sub> vs. no supp O<sub>2</sub>
- Endpoints
  - Death rates significantly lower
    - Except in patients with nocturnal or moderate hypoxemia
  - Indices measuring quality of life were significantly improved.
  - With >15 hours per day PAP decreased
  - Cardiac output was increased as well

NOTT and MRC Oxygen vs. no supplemental oxygen trials



## Summary

- COPD Prevalence is Increasing
- COPD is Treatable and Preventable
- Spirometry is Key to Diagnosis & Early Intervention
- Smoking Cessation is Only Intervention to Halt Progressive Decline of Lung Function
- Bronchodilators are Beneficial
- ICS Reduce Acute Exacerbations
- Rx Systemic Steroids and Antibiotics by the Data
- Oxygen is Only Drug Shown to Improve Mortality

