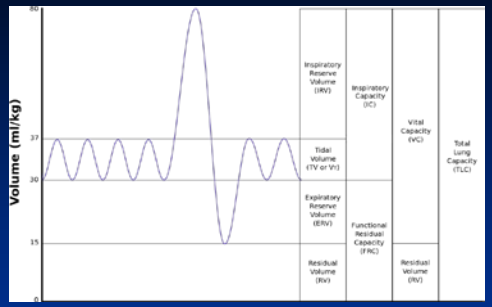
“How art thou out of breath when thou hast breath
To say to me that thou art out of breath?”

Romeo and Juliet, William Shakespeare



Management of Acute COPD Exacerbations

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Salem Pulmonary Associates
March 1, 2017

Outline

- COPD: Introduction & Overview
- Acute exacerbation of COPD (AECOPD): Update & Review
- Pharmacologic treatments that prevent AECOPD
- Non-pharmacologic treatments that prevent AECOPD
- Problem: COPD 30-day readmission rates
- Patient-centered COPD Care
- Final thoughts

Disclosure Slide

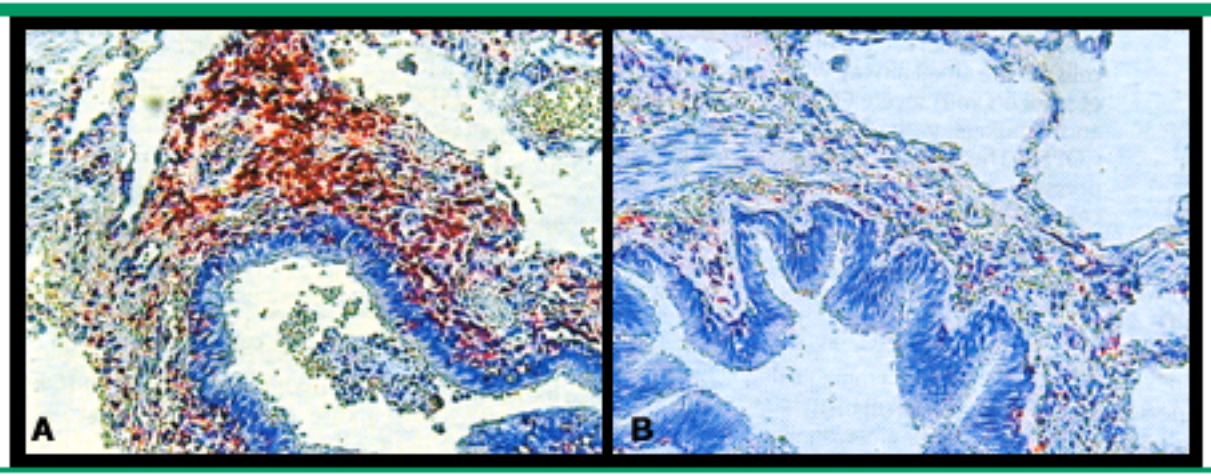
I have no specific *commercial* interests, nor have I received any outside financial compensation concerning this presentation

COPD Background

- Affects 32 million people in US and now 3rd leading cause of death worldwide (aging "boomers").
- Classic triad:
  - Emphysema
  - Chronic bronchitis
  - Reversible airways disease (varying degrees)
- Characterized by expiratory airflow limitation.
  - Not fully reversible
  - Usually progressive
  - Associated with abnormal lung inflammatory responses

COPD Pathology

Leukocyte infiltration in COPD



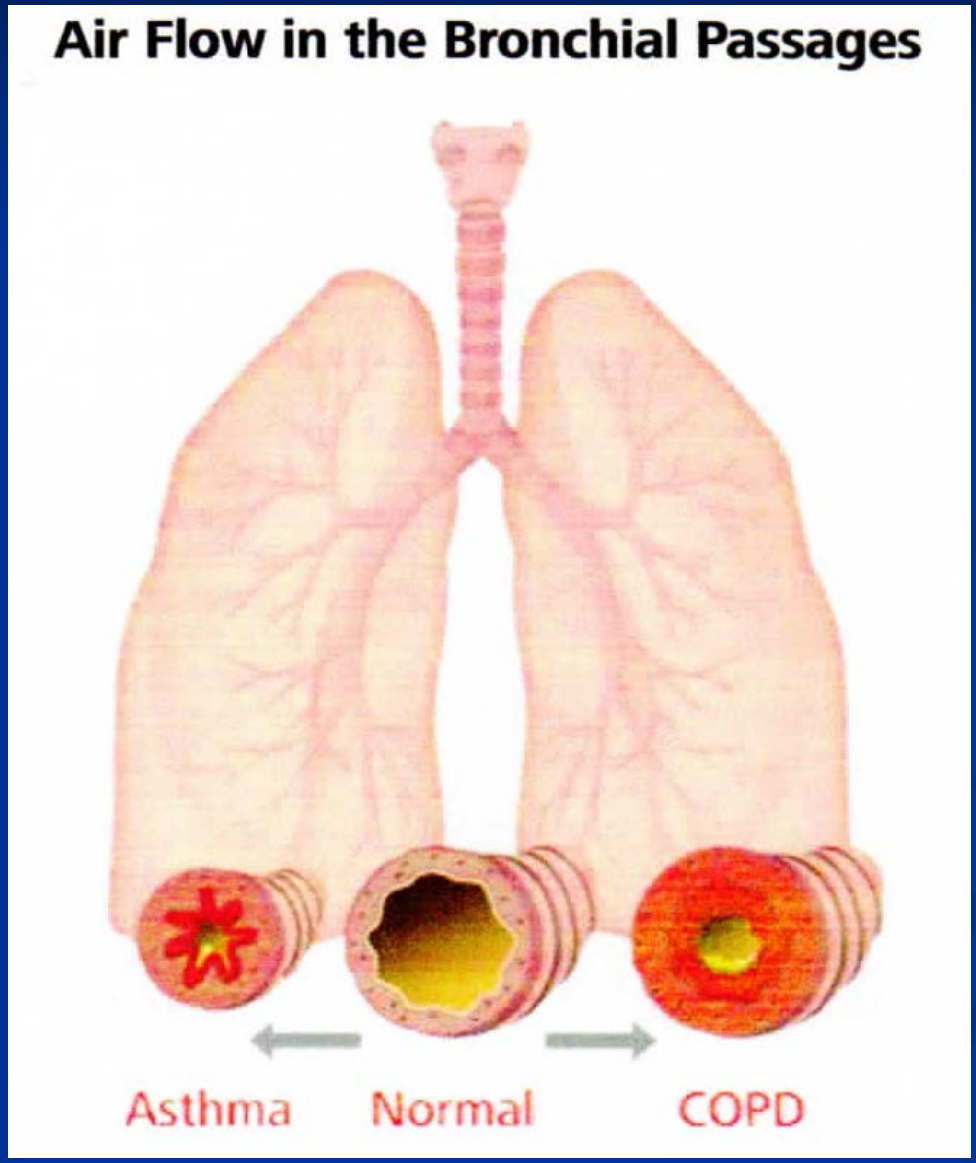
Photomicrograph showing leukocyte infiltration in a small airway of a smoker with severe COPD (A); and that of smoker with a mild COPD (B). Immunostaining with monoclonal antibody anti-CD45. Leukocytes are stained in red. Original magnification: X400.

Reproduced with permission from: Turato G, Zuin R Miniati M et al. Airway inflammation in severe chronic obstructive pulmonary disease: relationship with lung function and radiologic emphysema. Am J Respir Crit Care Med 2002;166:105. Copyright © 2002 American Thoracic Society.

COPD: Airflow Obstruction

- Mucous hypersecretion
  - Luminal obstruction
  - Chronic bronchitis
- Disrupted alveolar attachment
  - Dynamic airflow limitation
  - Emphysema
- Bronchial inflammation & fibrosis
  - Bronchospasm (reversible component)
  - Obliterative bronchiolitis (irreversible component)

COPD Pathology



COPD "Vicious Cycle" Paradigm

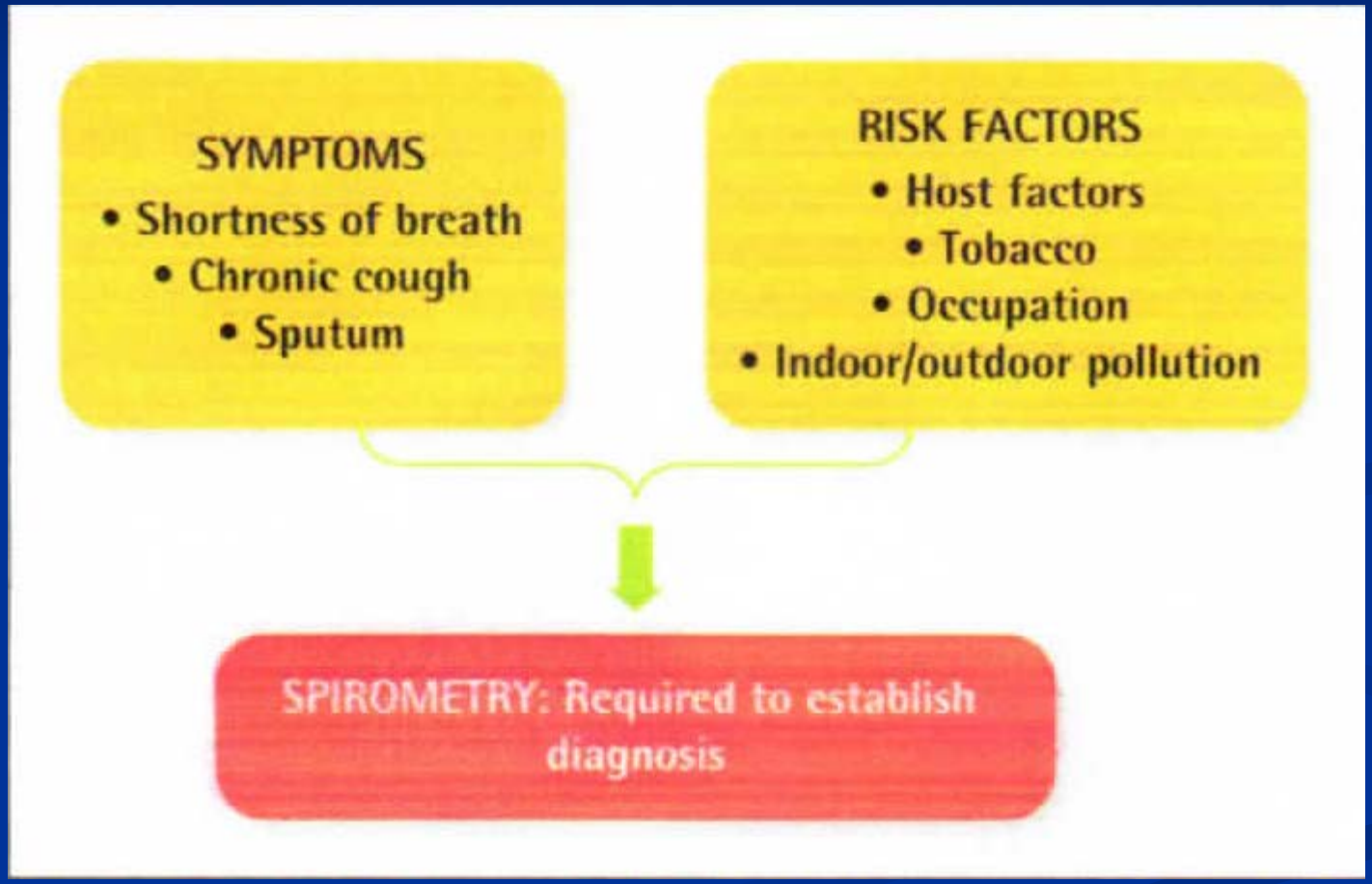
COPD Disease and Exacerbation Cascade

- Chronic
- Progressive
- Acute exacerbations of increasing frequency and intensity

Layers of COPD Disease Progression

- Lung deterioration
- Deconditioning
- Acute exacerbations

COPD Diagnosis



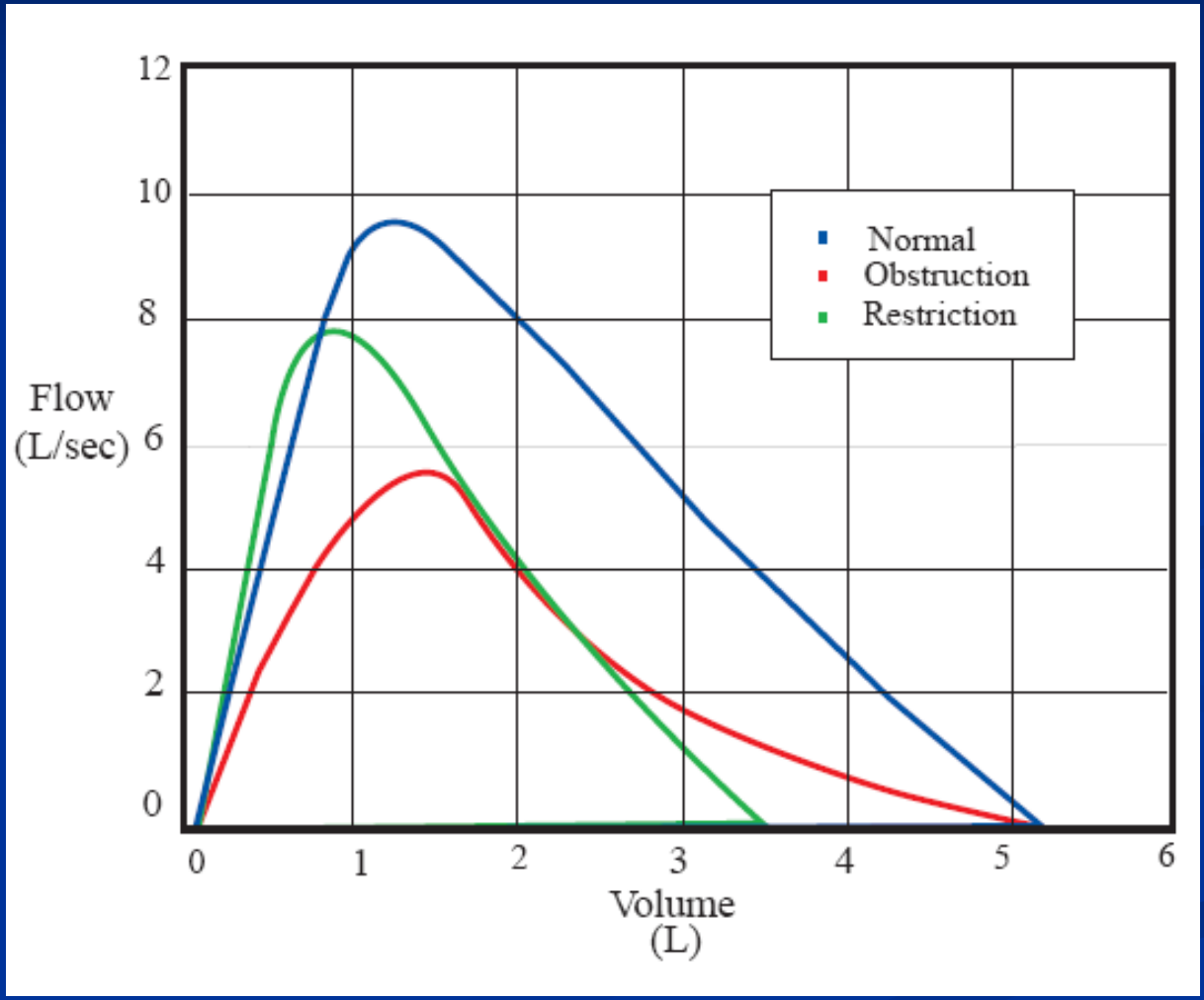
COPD Dx: Sxs & Risk Factors

Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD. Spirometry is required to establish a diagnosis of COPD.	
Dyspnea that is:	Progressive over time. Characteristically worse with exercise. Persistent.
Chronic cough:	May be intermittent and may be unproductive. Recurrent wheeze.
Chronic sputum production:	With any pattern.
Recurrent lower respiratory tract infections	
History of risk factors:	Host factors (such as genetic factors, congenital/developmental abnormalities etc.). Tobacco smoke. Smoke from home cooking and heating fuels. Occupational dusts, vapors, fumes, gases and other chemicals.
Family history of COPD and/or childhood factors:	For example low birthweight, childhood respiratory infections.

COPD Dx: Spirometry

- Spirometry is required!
  - Wheezing, dyspnea & coughing non-specific symptoms.
  - Perform post-BD spirometry to confirm presence of persistent (i.e., irreversible) airflow limitation.
  - Post-BD FEV1/FVC < 0.70 defines the disorder.
  - Consider performing FEV1/SVC maneuver for patients with suspected air-trapping and FEV1/FVC ≥ 0.70.

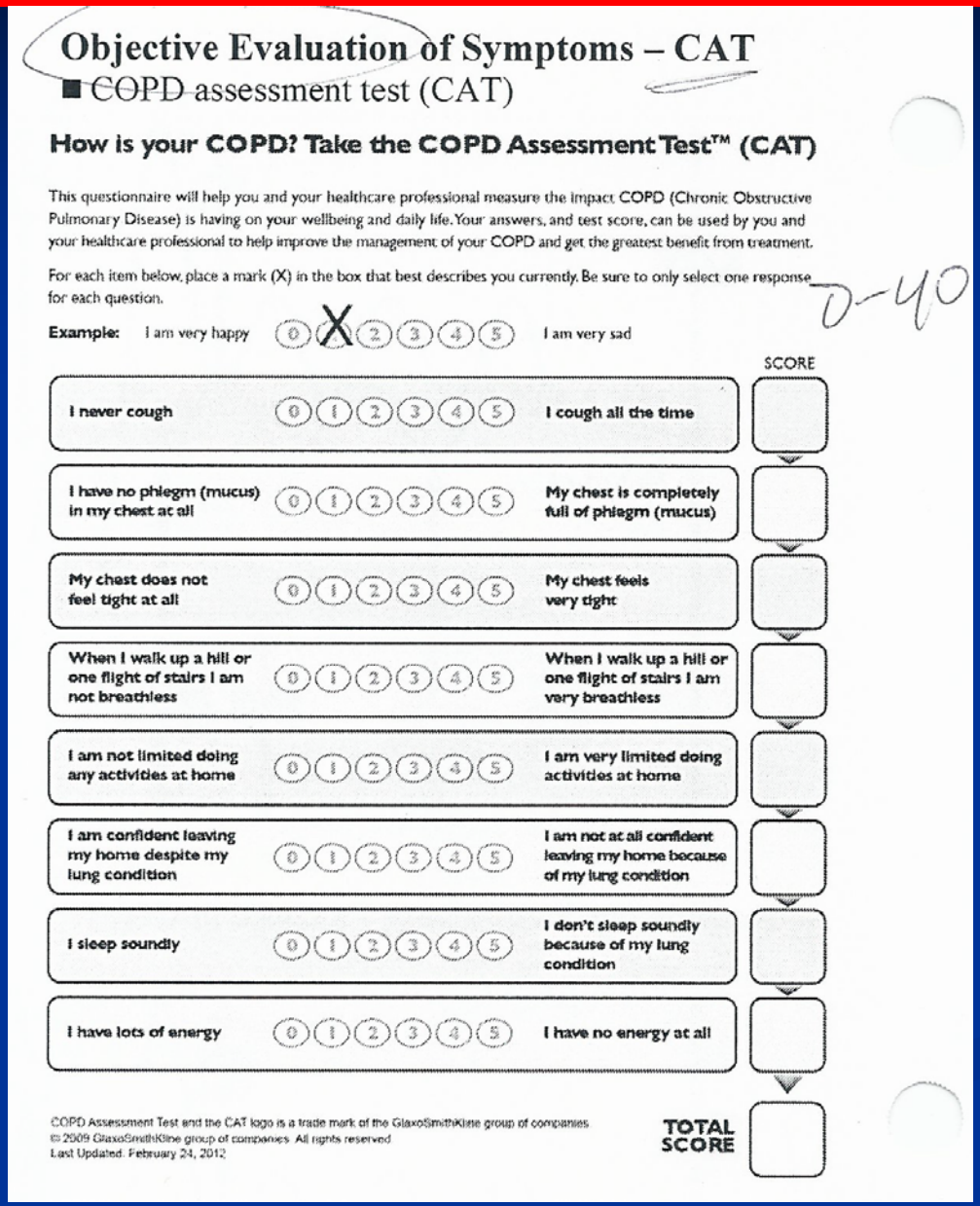
COPD Dx: Spirometry



COPD Assessment: 4 Elements

- Symptoms
  - Dyspnea, cough & sputum production
  - Use of validated questionnaires
- Degree of expiratory airflow limitation
  - Spirometry
- Risk of exacerbations
  - Based on history and severity of airflow limitation
- Comorbidities
  - CVD, CA, SRBD, DM, osteoporosis common co-diseases

COPD Assessment: Symptoms



Objective Evaluation of Symptoms – CAT

■ COPD assessment test (CAT)

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.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

0-40

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

		SCORE
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	
		TOTAL SCORE

Degree of negative QOL impact

- 0-10 Mild
- 11-20 Moderate
- 21-30 Severe
- 31-40 Very Severe

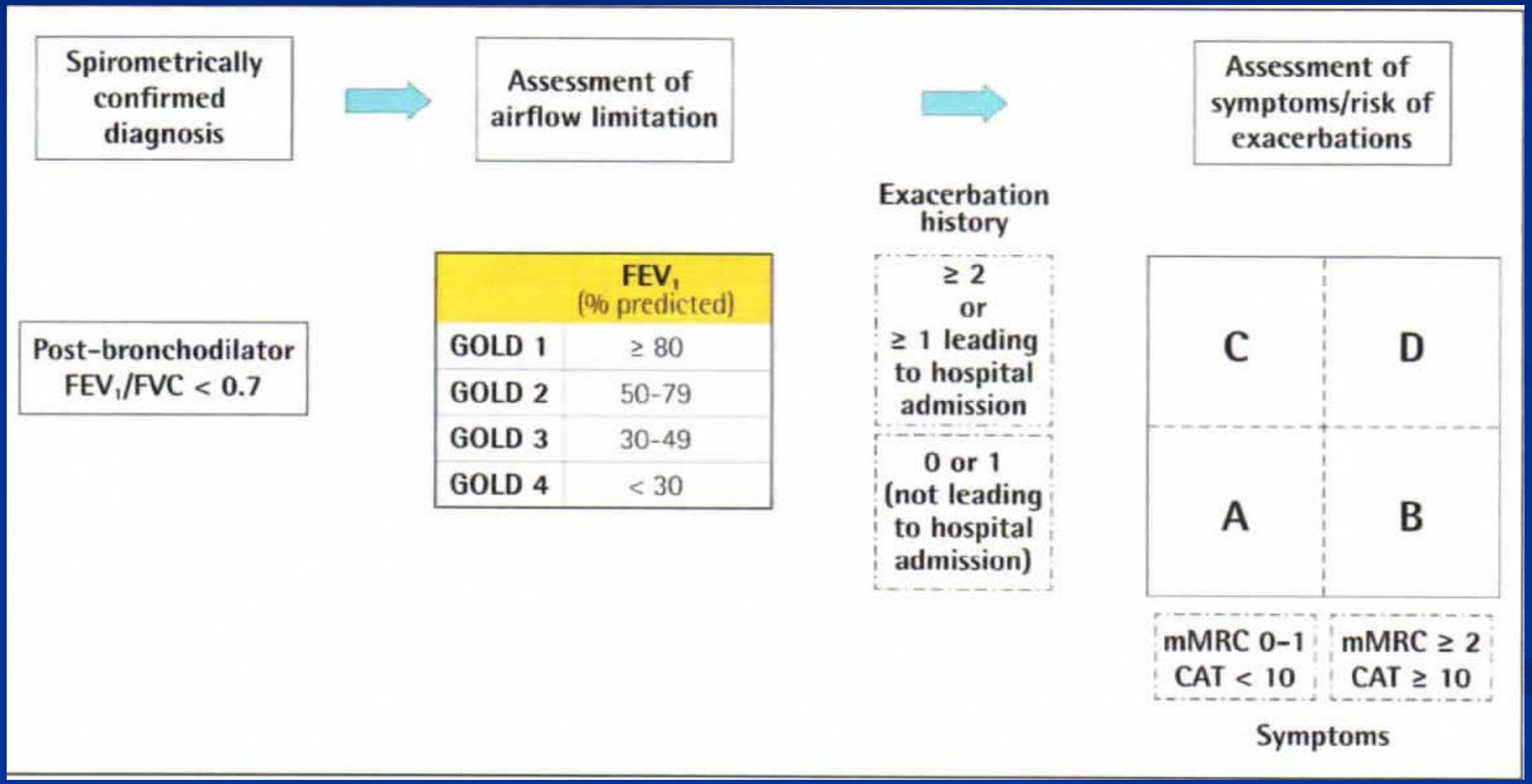
- Cough
- Phlegm
- Chest tightness
- DOE
- Activity limitation
- Functional confidence
- Sleep quality
- Energy level

COPD Assessment: Spiro Staging

Table 3. Classification of Severity of Airflow Limitation in COPD (Based on Post-Bronchodilator FEV_1)		
In patients with FEV1/FVC < 0.70:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

COPD Global Assessment

The refined ABCD assessment tool

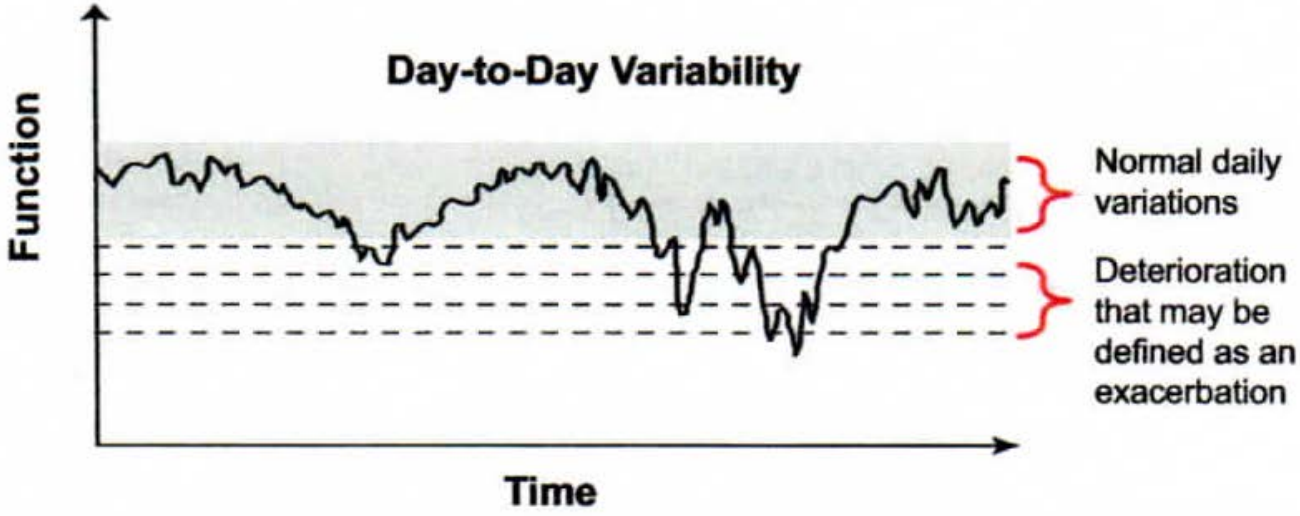


Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report

AECOPD Definition

What Is an AECOPD?

- The current definition of an acute exacerbation of COPD (AECOPD) in the GOLD Guidelines is as follows:
  - "An exacerbation of COPD is an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication."



AECOPD Causes

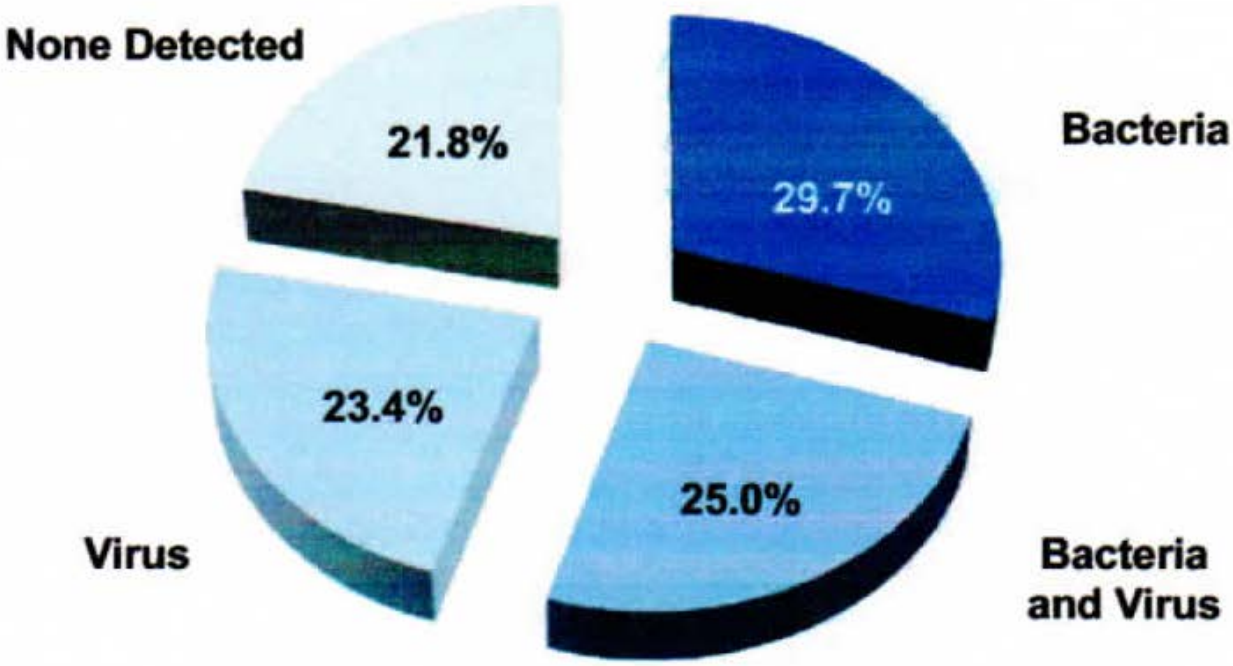
Potential Causes of Exacerbations

- Bacterial or viral infection
- Pollutants:
  - Nitrogen dioxide
  - Particulates (PM_{10})
  - Sulfur dioxide
  - Ozone
- Cold weather
- Interruption of regular treatment

AECOPD Causes

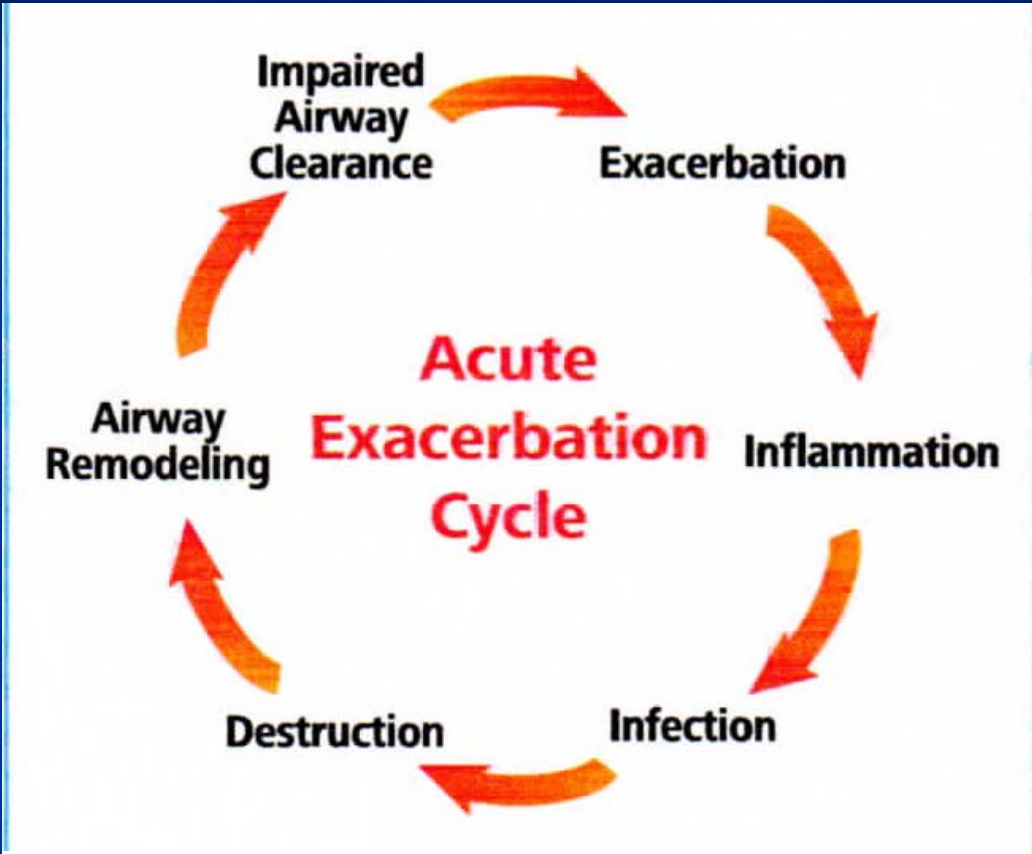
Etiology of AECOPD

Causes of exacerbations requiring hospitalization in patients (N = 64)



Papi A, et al. *Am J Respir Crit Care Med.* 2006;173:1114-1121.

AECOPD: "Vicious cycle" revisited



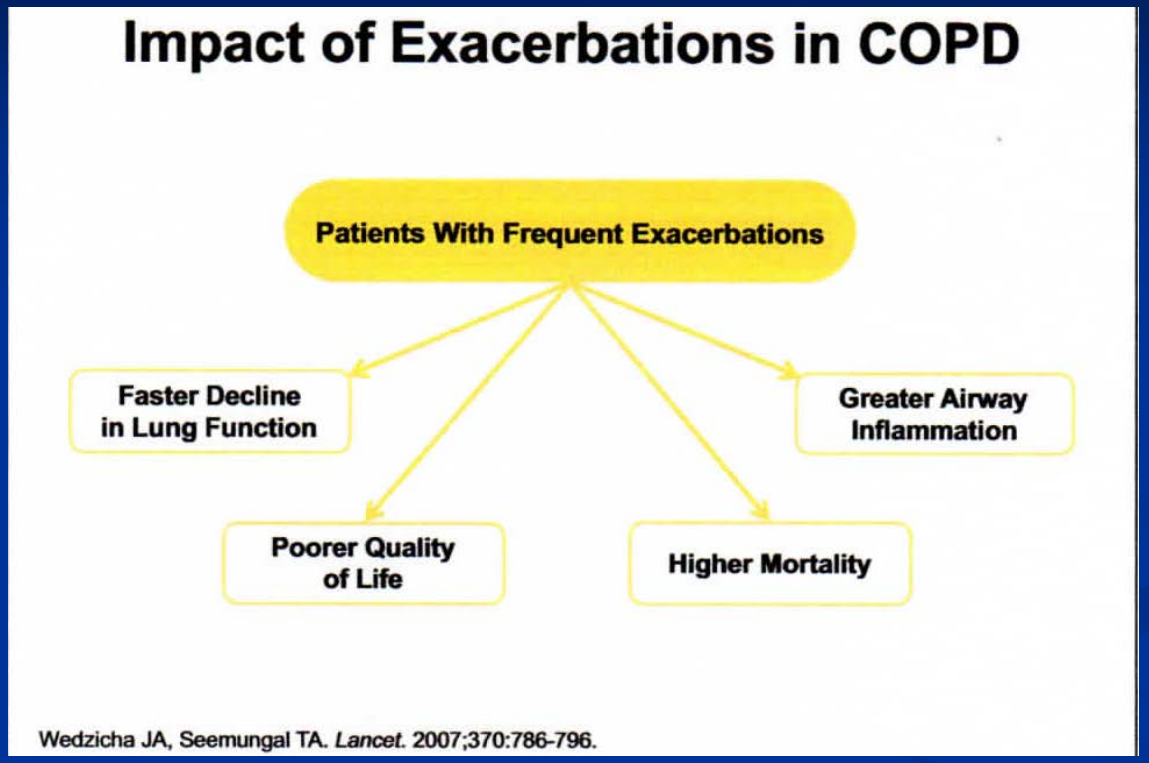
A COPD exacerbation is a dynamic process leading to destruction and airway remodeling. Thus it is time sensitive (time is tissue). When destruction occurs, repair takes longer and tissue may not fully repair. This can lower the baseline status, rendering a future exacerbation more likely.

AECOPD Risk Factors

Summary: Risk Factors for COPD Exacerbations

- Past exacerbation and/or admission for exacerbation
- Severe obstruction to airflow (FEV_1 < 50% of predicted)
- Low body mass index (< 20 kg/m^2)
- Pulmonary artery to aorta ratio (PA:A) > 1
- Elevated C-reactive protein, fibrinogen, and WBC count
- Long-term supplemental oxygen therapy
- Chronic oral corticosteroids
- Cardiovascular comorbidity
- Chronic sputum production/chronic bronchitis
- Gastroesophageal reflux disease (GERD)
- Older age

AECOPD Consequences



- Best Predictor = Hx of previous exacerbations
- Risk ↑ with ↑ airflow limitation (COPD severity)
- Treat with sense of urgency (*ala* AMI or CVA)!

AECOPD Consequences

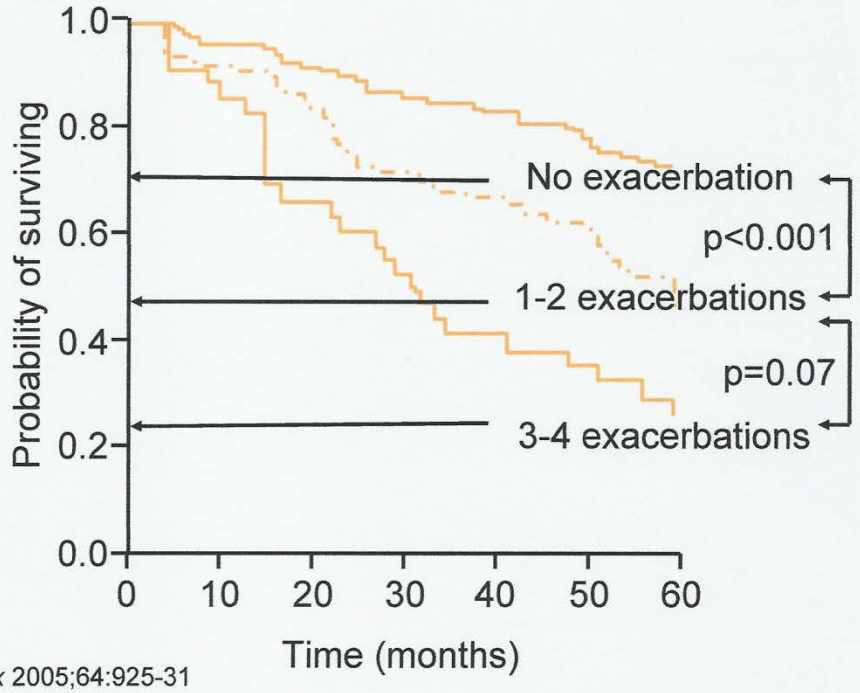
Effects of Repeated Exacerbations on Survival

Prospective study

Cohort of 304 males

Exacerbations requiring hospital treatment during the year

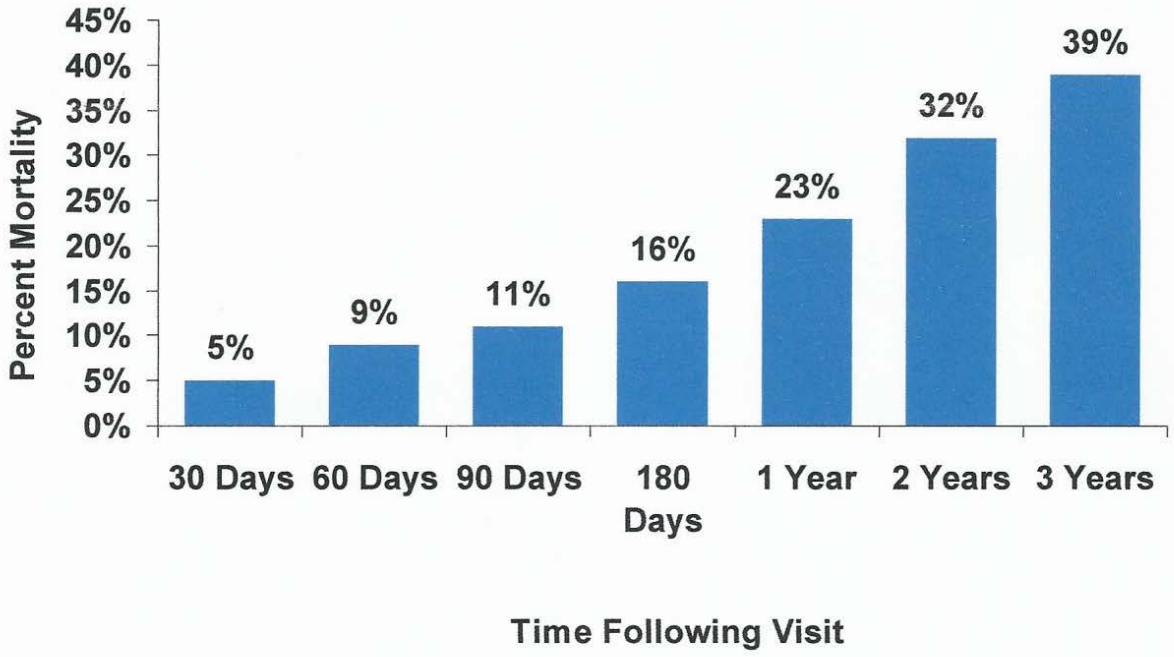
Follow-up over 5 years



Soler-Cataluña JJ et al. *Thorax* 2005;64:925-31

AECOPD Consequences

High Mortality Following Emergency Department Visit for COPD Exacerbation



Kim S, et al. *COPD*. 2006;3:75-81.

AECOPD Prevention

- Major principles/goals:
  - Reduce symptoms
  - Reduce frequency and severity of exacerbations
  - Improve overall health status
  - Improve exercise tolerance
  - Patient-specific:
    - Comorbidities
    - Side effects
    - Socioeconomic realities

AECOPD: Pharm Prevention

Pharmacologic Evidence-Based Measures That Reduce AECOPD

- Bronchodilators
- Inhaled corticosteroids
- PDE-4 inhibitors
- Prophylactic antibiotics

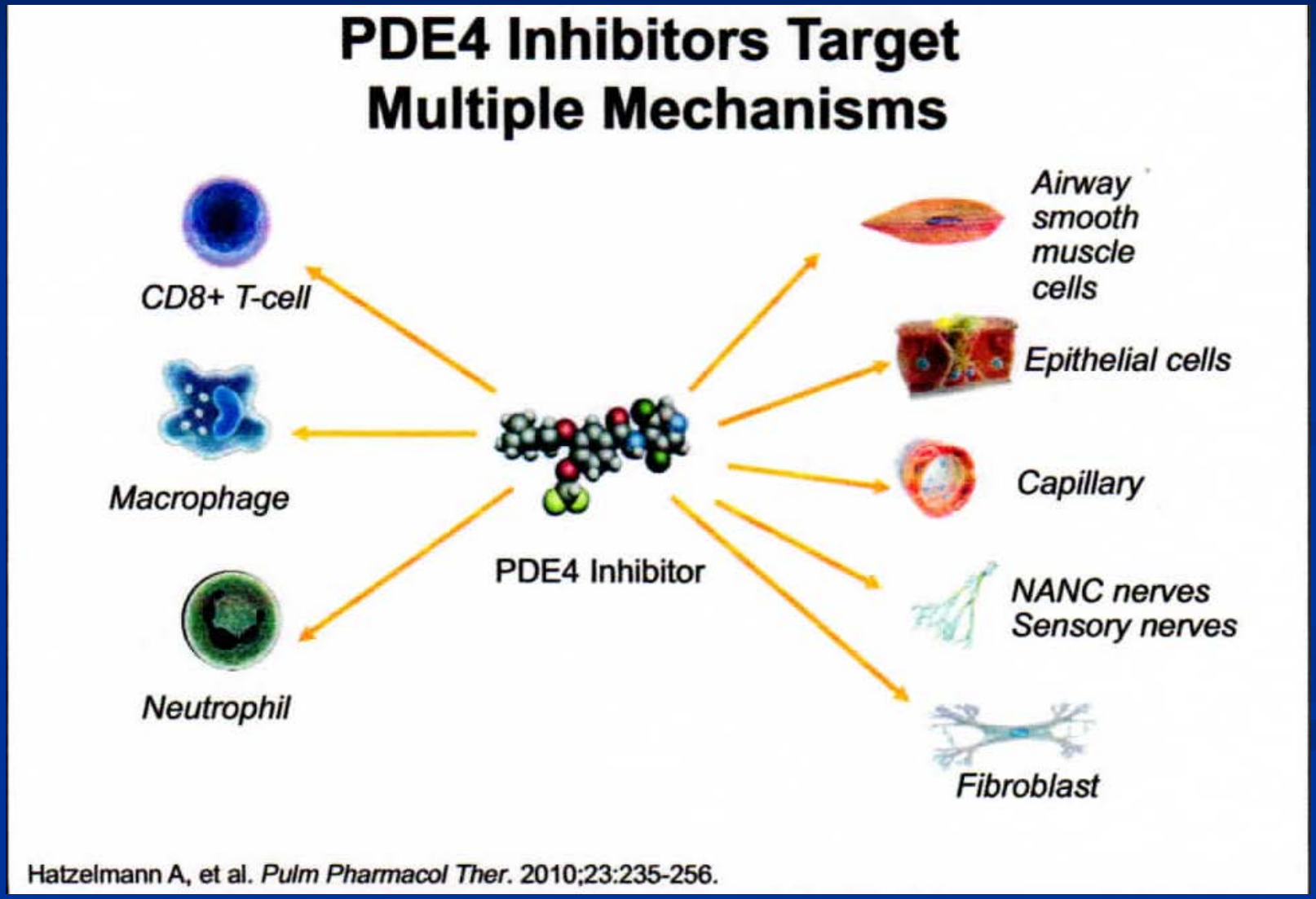
COPD: Bronchodilators

- Foundation for symptom management.
- Inhaled therapy preferred.
- Choice depends on availability, response & side effects.
- Long-acting > short-acting BDs re: convenience & sx relief.
- Long-acting BDs:
  - Beta-agonists (LABAs) & muscarinic antagonists (LAMAs).
  - LABA for “asthma overlap” & LAMA for smokers/chronic bronchitics.
  - Reduce exacerbations and hospitalizations (LAMA > LABA).
  - Improve symptoms and health status.
- Combining BDs of different classes:
  - Complementary improvement in efficacy.
  - Decrease risk of side effects vs higher dose of single BD class.

COPD: Corticosteroids

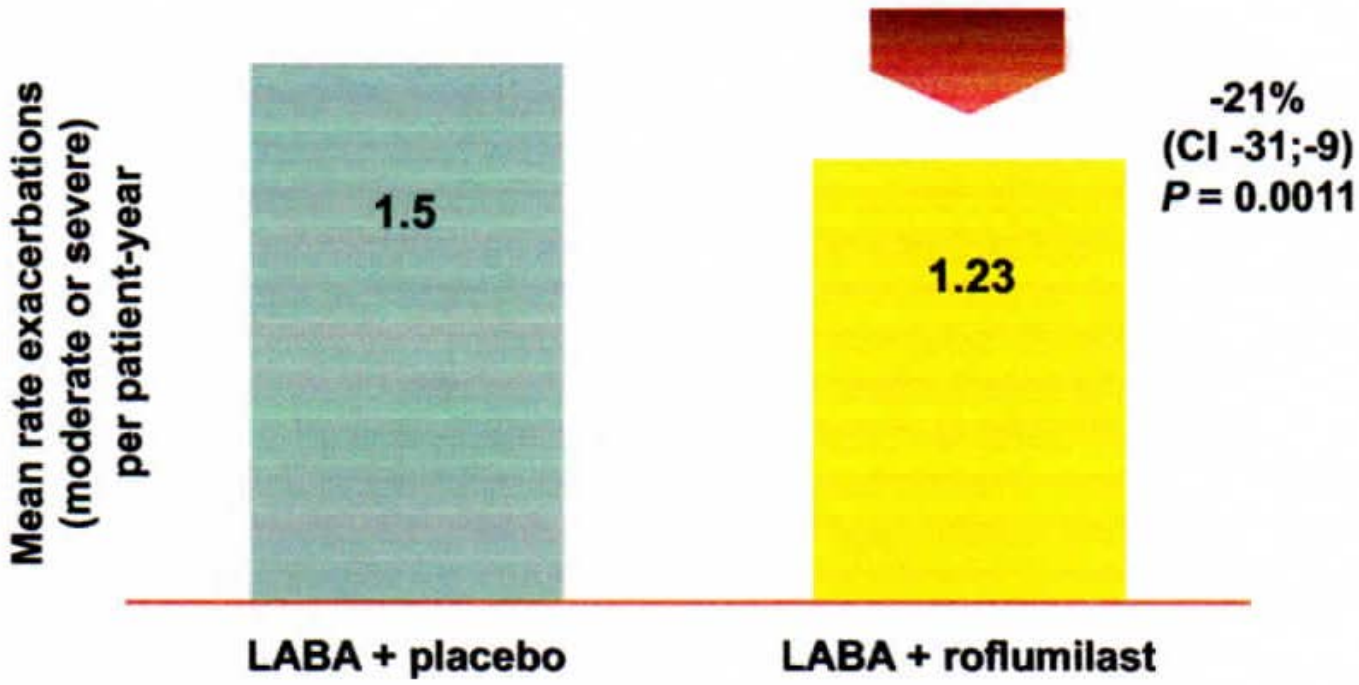
- Inhaled corticosteroids (ICS)
  - Consider adding to LABA for COPD pts with FEV1 < 60% predicted.
  - ICS ↓ symptoms & exacerbations and ↑ lung fxn & QOL.
  - May be associated with ↑ risk of pneumonia.
  - Long-term monotherapy not recommended.
- Combination ICS with long-acting BDs:
  - ICS + LABA: more effective than either therapy alone.
  - ICS + LABA + LAMA: most effective combination.
- Systemic corticosteroids (IV, IM and oral):
  - Long-term use not routinely recommended.
  - Reserved for acute exacerbations.

COPD: Roflumilast



COPD: Roflumilast

Roflumilast Significantly Reduced Exacerbations When Added to LABA

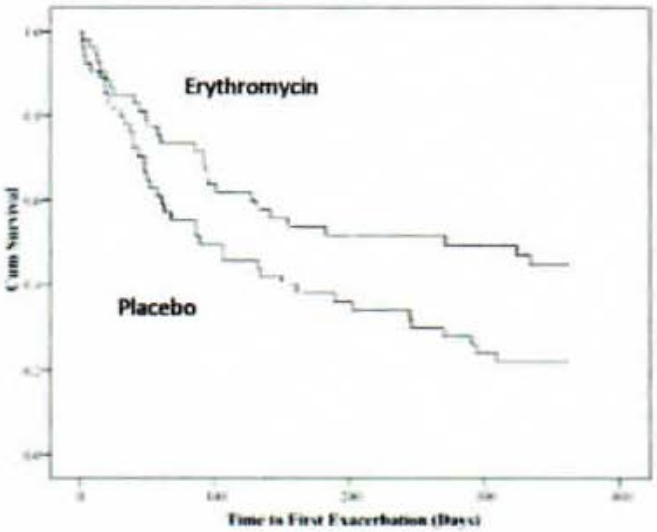


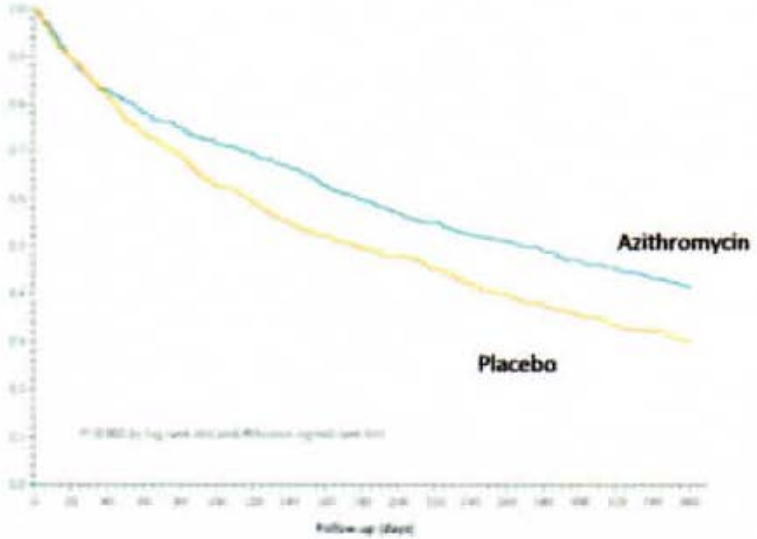
Pre-specified analysis of exacerbation rate in LABA subgroup

Hanania NA, et al. *Am J Respir Crit Care Med.* 2010 Abstract presentation.

COPD: Macrolides

Macrolides Prevent Exacerbations

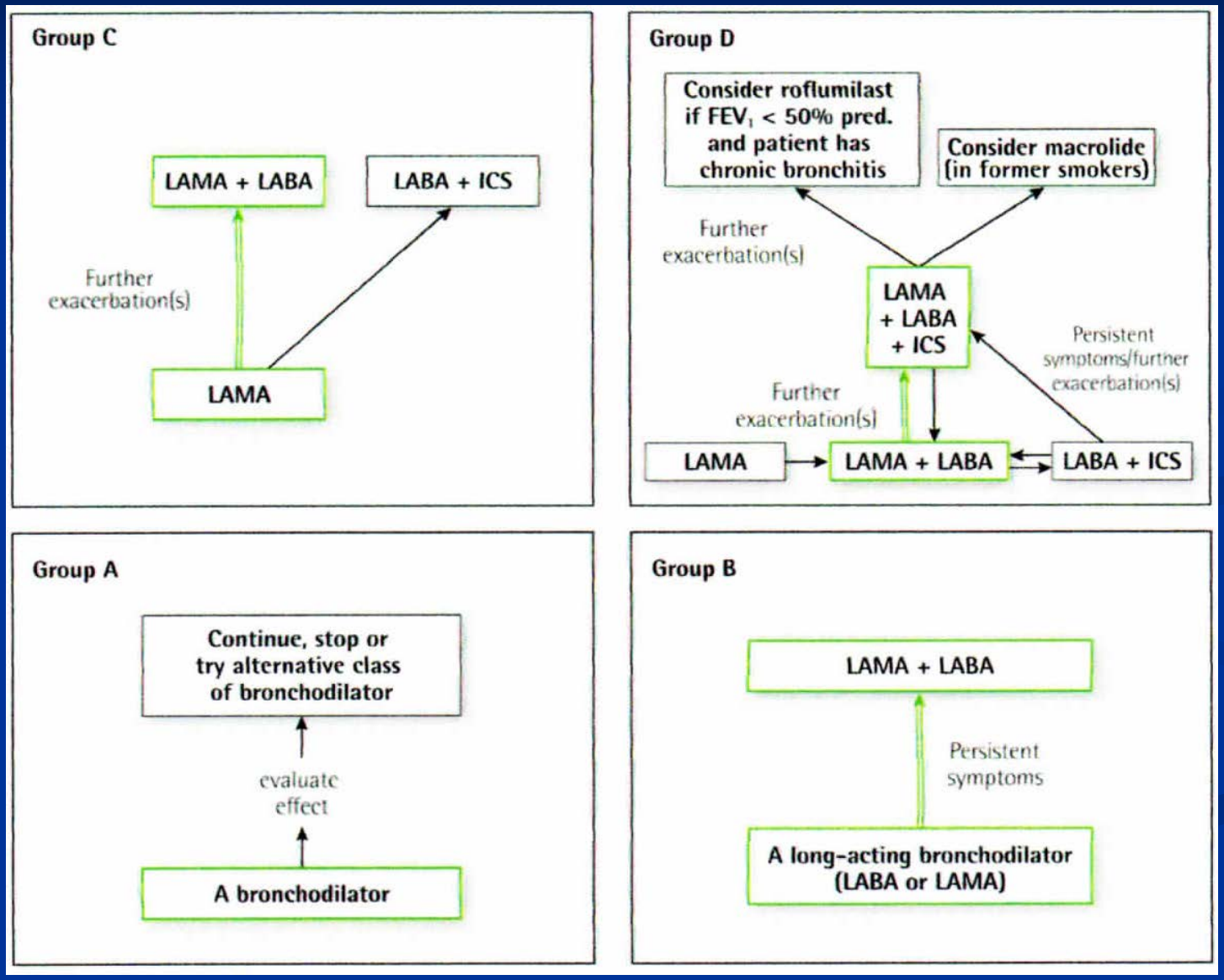




	Median Time to Exacerbation (days)	
	Erythromycin[1]	Azithromycin[2]
Macrolide	271	266
Placebo	89	174
P-value	0.020	< 0.001

1. Seemungal TA, et al. *Am J Respir Crit Care Med*. 2008;178(11):1139-1147.
2. Albert RK, et al. *N Engl J Med*. 2011;365(8):689-698.

COPD: Pharmacologic Algorithm



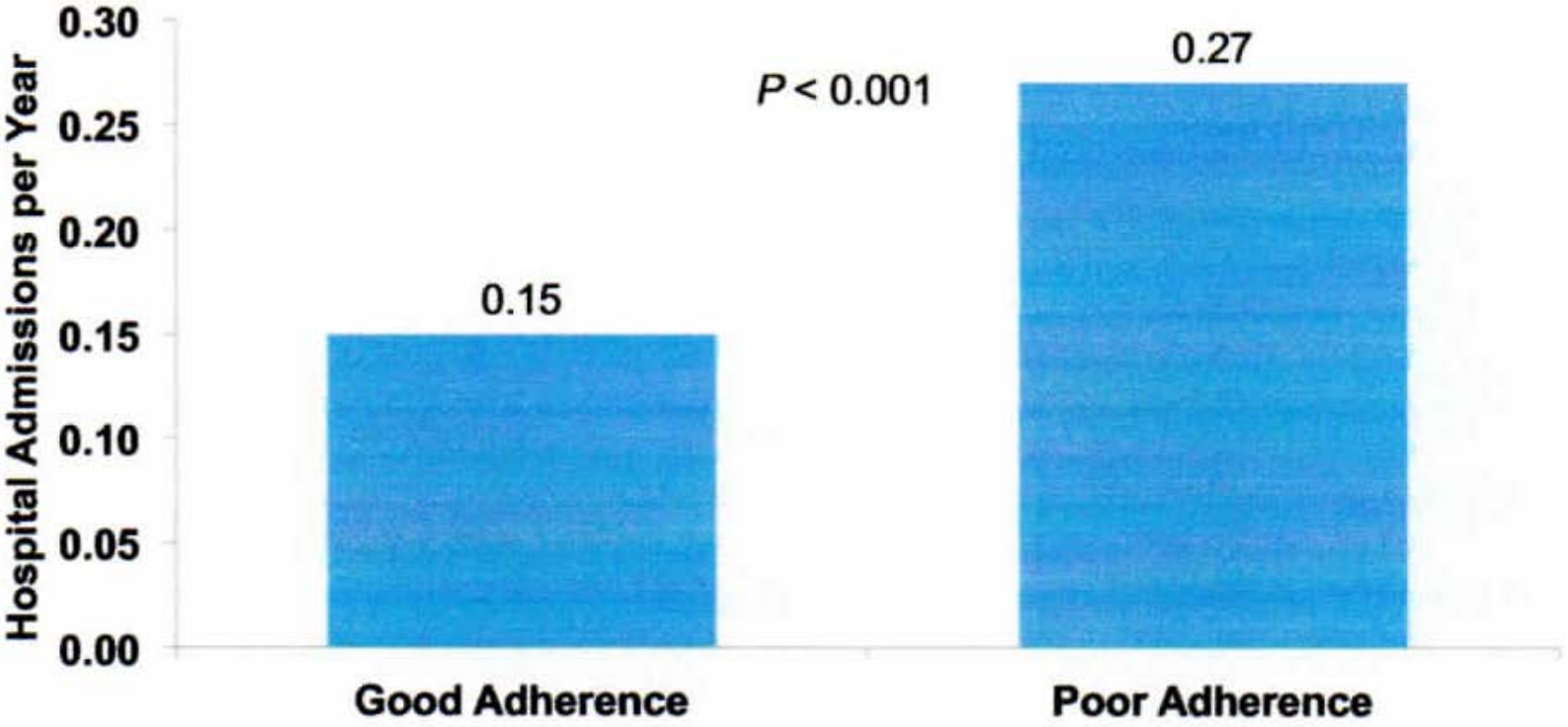
AECOPD: Non-pharm prevention

Nonpharmacologic Evidence-Based Measures That Reduce COPD Exacerbations

- Assess adherence
- Smoking cessation
- Immunizations
- Pulmonary rehabilitation
- Patient education

AECOPD: Non-pharm prevention

Higher Adherence to Therapy Is Associated with Decreased Risk for Severe COPD Exacerbations

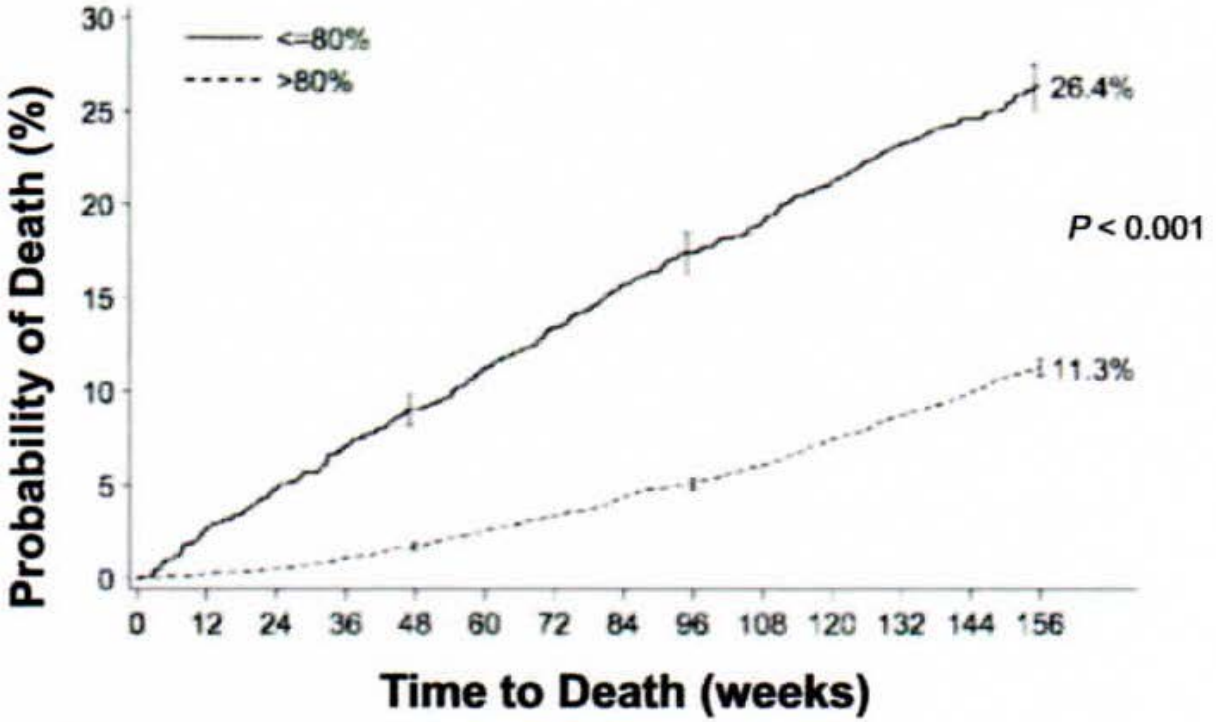


Good adherence was associated with a 44% reduction in risk for severe exacerbations requiring hospitalization

Vestbo J, et al. *Thorax*. 2009;64:939-943.

AECOPD: Non-pharm prevention

Higher Adherence to Therapy Is Associated with Decreased Mortality in COPD



Number at Risk				
≤ 80%	1232	1121	1018	894
> 80%	4880	4798	4633	4299

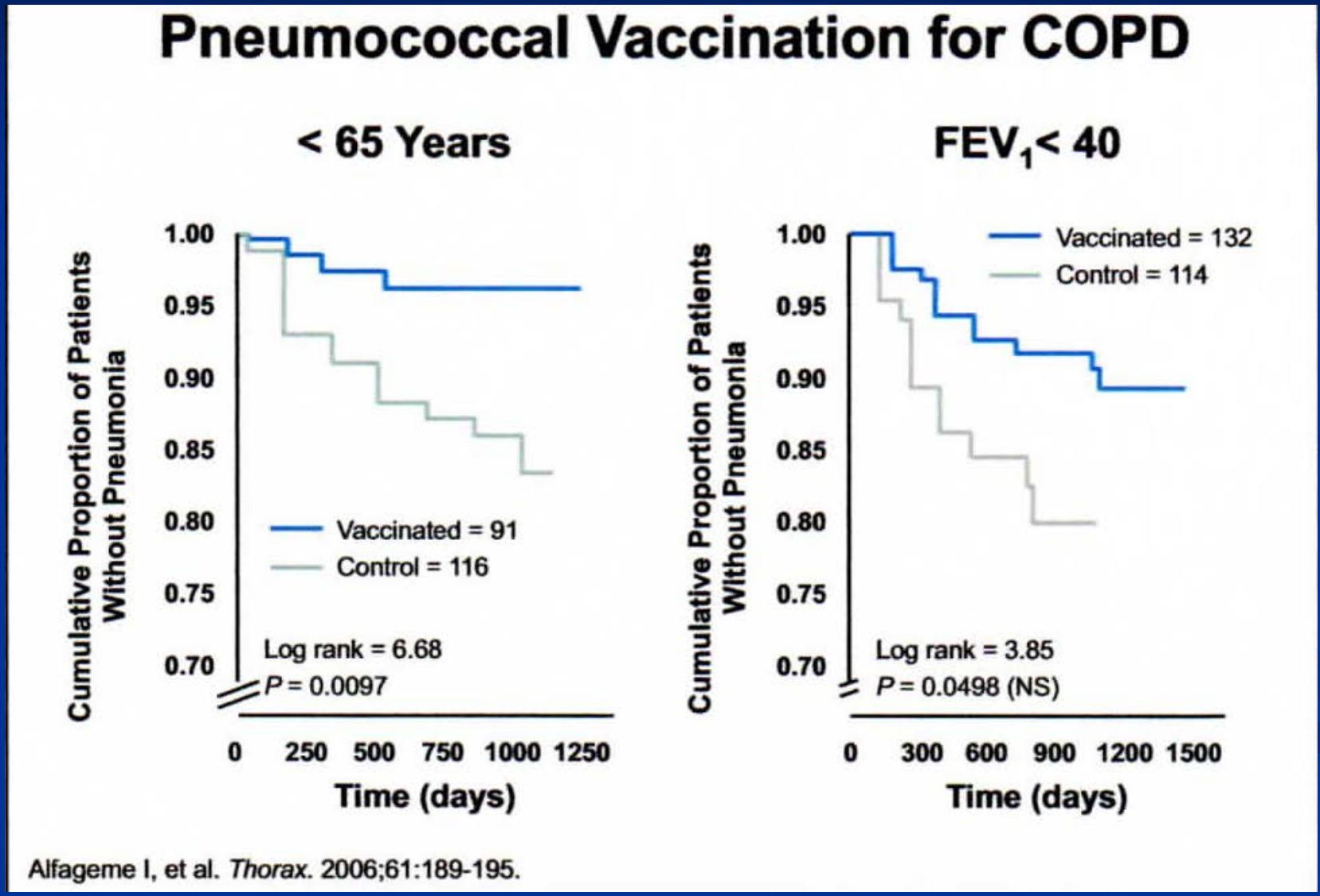
Good adherence was associated with a 60% mortality risk reduction independent of therapy

Vestbo J, et al. *Thorax*. 2009;64:939-943.

COPD: Smoking Cessation

- Intervention with greatest capacity to influence natural hx of COPD.
- Counseling: 3-minute talk = ↑ quit rate by 10%.
- Long-term quit rates of 25% possible with dedicated programs.
- Nicotine replacement protocols increase abstinence rates; E-cigarettes increasingly utilized but efficacy & safety controversial.
- Other pharmacotherapy (e.g., Varenicline, Bupropion, Nortriptyline)—best used as part of overall intervention program as opposed to sole intervention.
- Combination intervention with behavioral support provided by trained health professionals (e.g., 5 step programs with "5 A's" : Ask, Advise, Assess, Assist, Arrange) *plus* pharmacotherapy = highest success rates.

COPD: Pneumococcal Vaccines



Alfageme I, et al. *Thorax*. 2006;61:189-195.

AECOPD: Influenza Vaccines

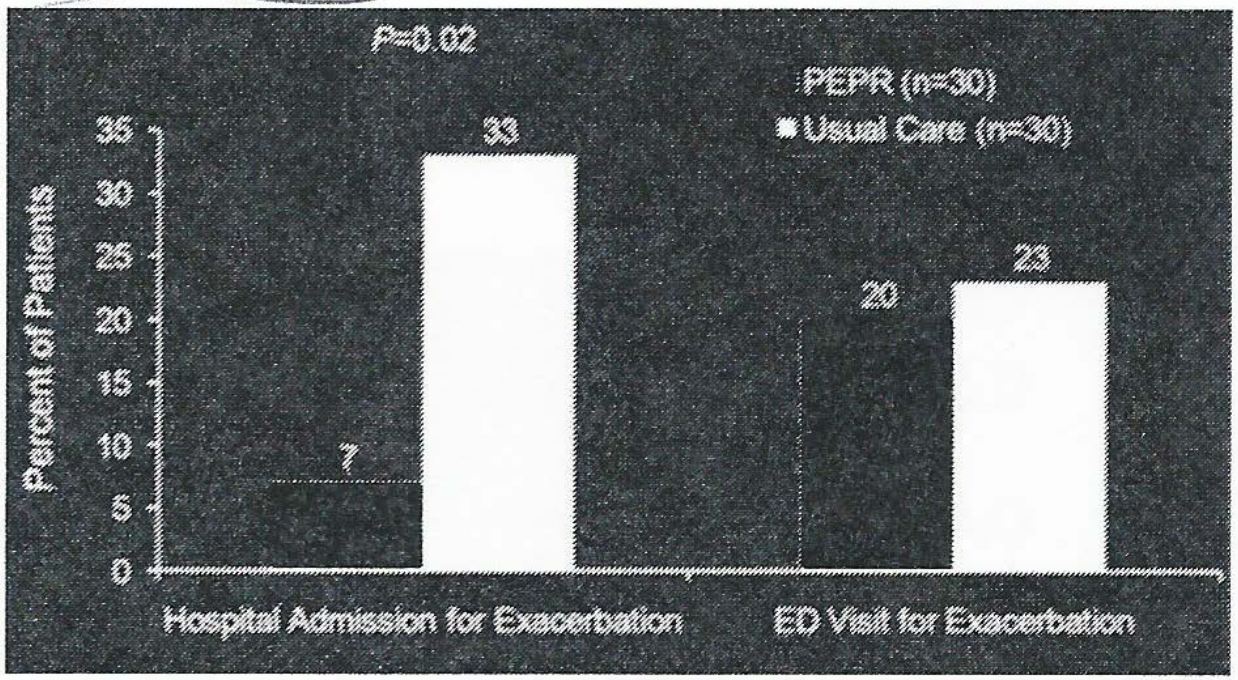
Influenza Vaccination: Risk for Any Exacerbation

- Evaluation of results from randomized clinical trials indicates that inactivated influenza vaccine reduces exacerbations in COPD patients
- The magnitude of this benefit is similar to that seen in large observational studies, and was due to a reduction in exacerbations occurring three or more weeks after vaccination, and due to influenza
- There is a mild increase in transient local adverse effects with vaccination, but no evidence of an increase in early exacerbations

Poole PJ, et al. *Cochrane Database Syst Rev*. 2006;CD002733.

AECOPD: Pulm Rehab

Pulmonary Rehab Reduces Severe Exacerbations



Source: Seymour JM, et al. *Thorax*. 2010;65:423-428.

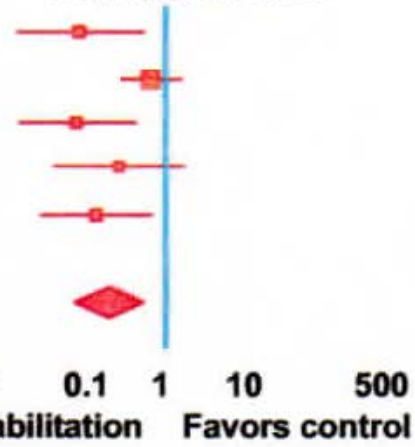
AECOPD: Pulm Rehab

Pulmonary Rehabilitation Following COPD Exacerbations: Hospitalization

	Experimental		Control			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Behnke 2000	3	14	9	12	16.7%	0.09 [0.01, 0.56]	
Eaton 2009	11	47	15	50	29.9%	0.71 [0.29, 1.77]	
Man 2004	2	20	12	21	18.1%	0.08 [0.02, 0.45]	
Murphy 2005	2	13	5	13	16.2%	0.29 [0.04, 1.90]	
Seymour 2010	2	30	10	30	19.0%	0.14 [0.03, 0.72]	
Total (95% CI)		**124**		**126**	**100.0%**	**0.22 [0.08, 0.58]**	
Total events	20		51				

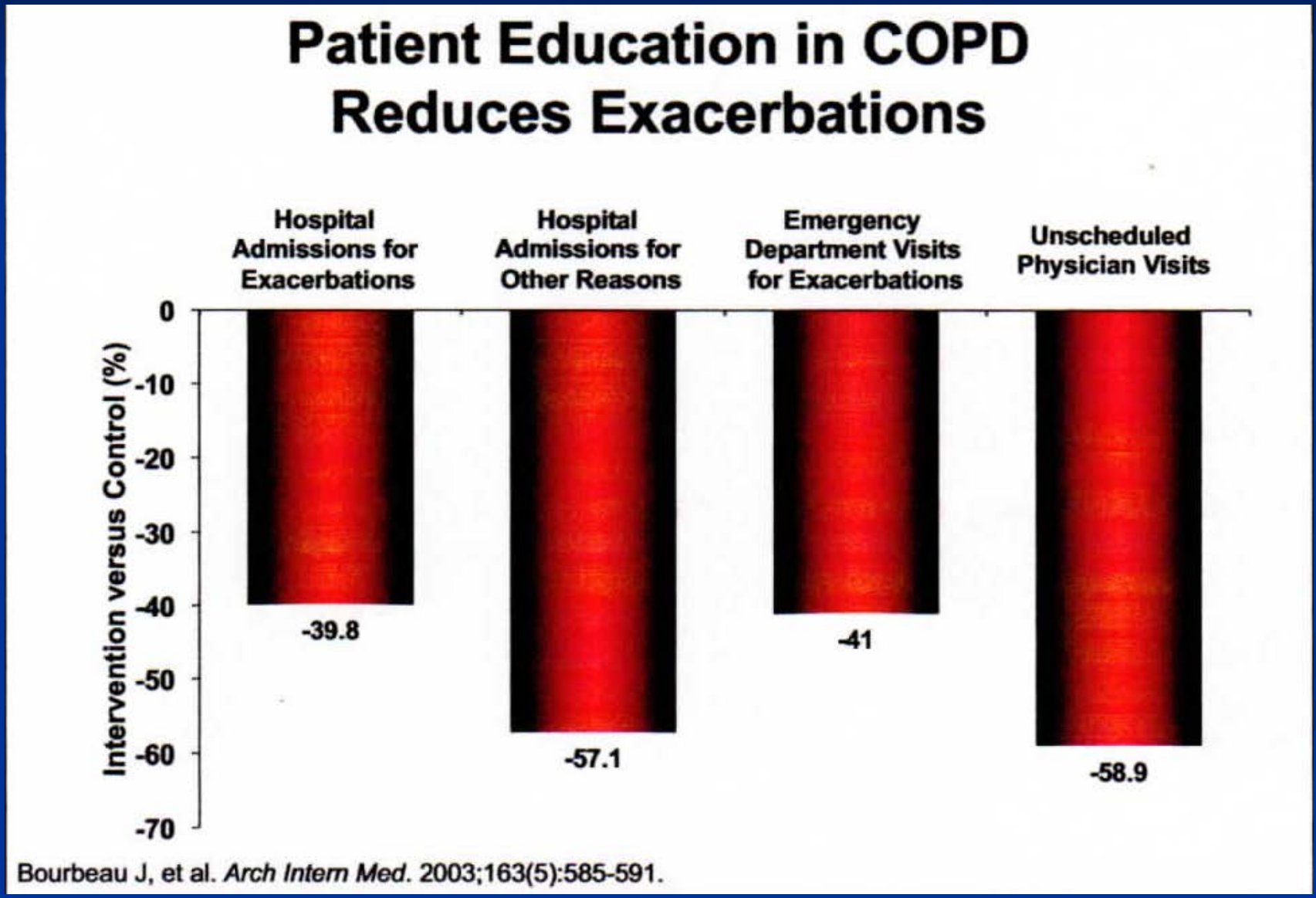
Heterogeneity: $Tau^2 = 0.61$; $Chi^2 = 8.15$, df = 4 ($P = 0.09$); $I^2 = 51\%$

Test for overall effect: $Z = 3.06$ ($P = 0.002$)

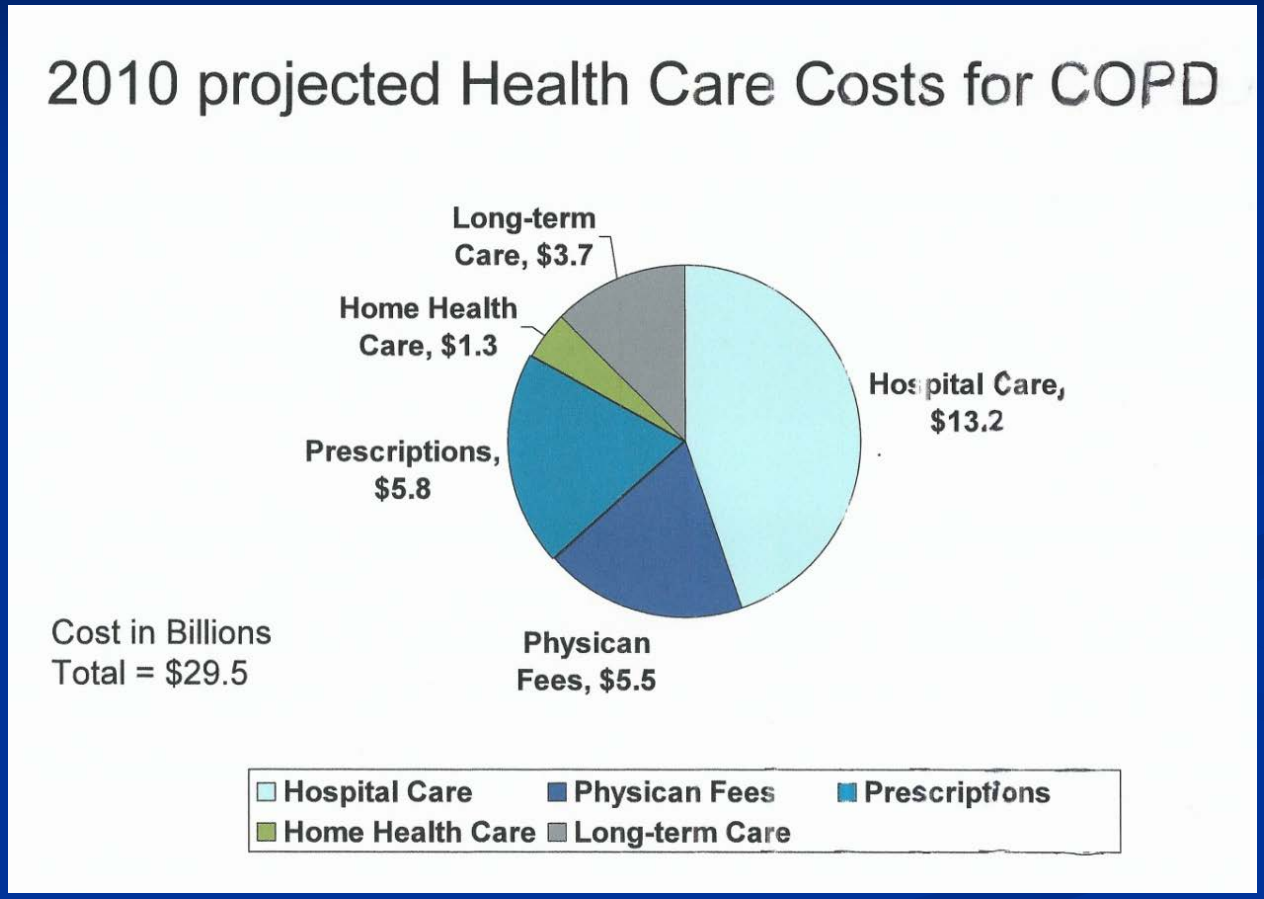


Puhan MA, et al. *Cochrane Database Syst Rev.* 2011;10:1-41.

AECOPD: Patient Education



COPD: Financial Costs



Projected total 2017 US costs > 60 billion dollars.

COPD Readmissions

Most Rehospitalizations after AECOPD Are Not For COPD

Condition at Index Discharge	30-Day Rehospitalization Rate (%)	Reasons for Rehospitalization (%)				
		Most Frequent	2nd Most Frequent	3rd Most Frequent	4th Most Frequent	5th to 10th Most Frequent
All	21.0	Heart failure (8.6)	Pneumonia (7.3)	Psychoses (4.3)	COPD (3.9)	GI problems, nutrition-related or metabolic issues, septicemia, GI bleeding, renal failure, urinary tract infection (17.0)
Heart failure	26.9	Heart failure (37.0)	Pneumonia (5.1)	Renal failure (3.9)	Nutrition-related or metabolic issues (3.1)	Acute MI, COPD, arrhythmias, circulatory disorders, GI bleeding, GI problems (14.0)
Pneumonia	20.1	Pneumonia (29.1)	Heart failure (7.4)	COPD (6.1)	Septicemia (3.6)	Nutrition-related or metabolic issues, GI problems, respiratory or ventilation problems, pulmonary edema, GI bleeding, urinary tract infection (14.9)
COPD	**22.6**	**COPD (36.2)**	**Pneumonia (11.4)**	**Heart failure (5.7)**	**Pulmonary edema (3.9)**	**Respiratory or ventilation problems, GI problems, nutrition-related or metabolic issues, arrhythmias, GI bleeding, acute MI (12.5)**
Psychoses	24.0	(67.3)		misuse (1.6)		depression, GI problems, COPD, organic mental conditions (7.0)
GI problems	19.2	GI problems (21.1)	Nutrition-related or metabolic issues (4.9)	Pneumonia (4.3)	Heart failure (4.2)	Major bowel surgery, urinary tract infection, septicemia, GI bleeding, COPD, chest pain (13.4)

COPD = chronic obstructive pulmonary disease; GI = gastrointestinal; MI = myocardial infarction

Jencks SF, et al. *New Eng J Med.* 2009;360:1418-1428.

COPD Care: Current Model

COPD TREATMENT CHALLENGES: PROBLEMS WITH USUAL CARE MANAGEMENT

Acute:

- Active treatment occurs only during acute exacerbation.
- Time-sensitive treatment is frequently delayed.

Chronic:

- The chronic component often is not addressed.
- Even when the patient gets pulmonary rehabilitation, it is a short-term solution for a problem that is lifelong, progressive and gets worse over time.
- How patients manage their care at home can make the greatest difference in disease control.

COPD Readmissions

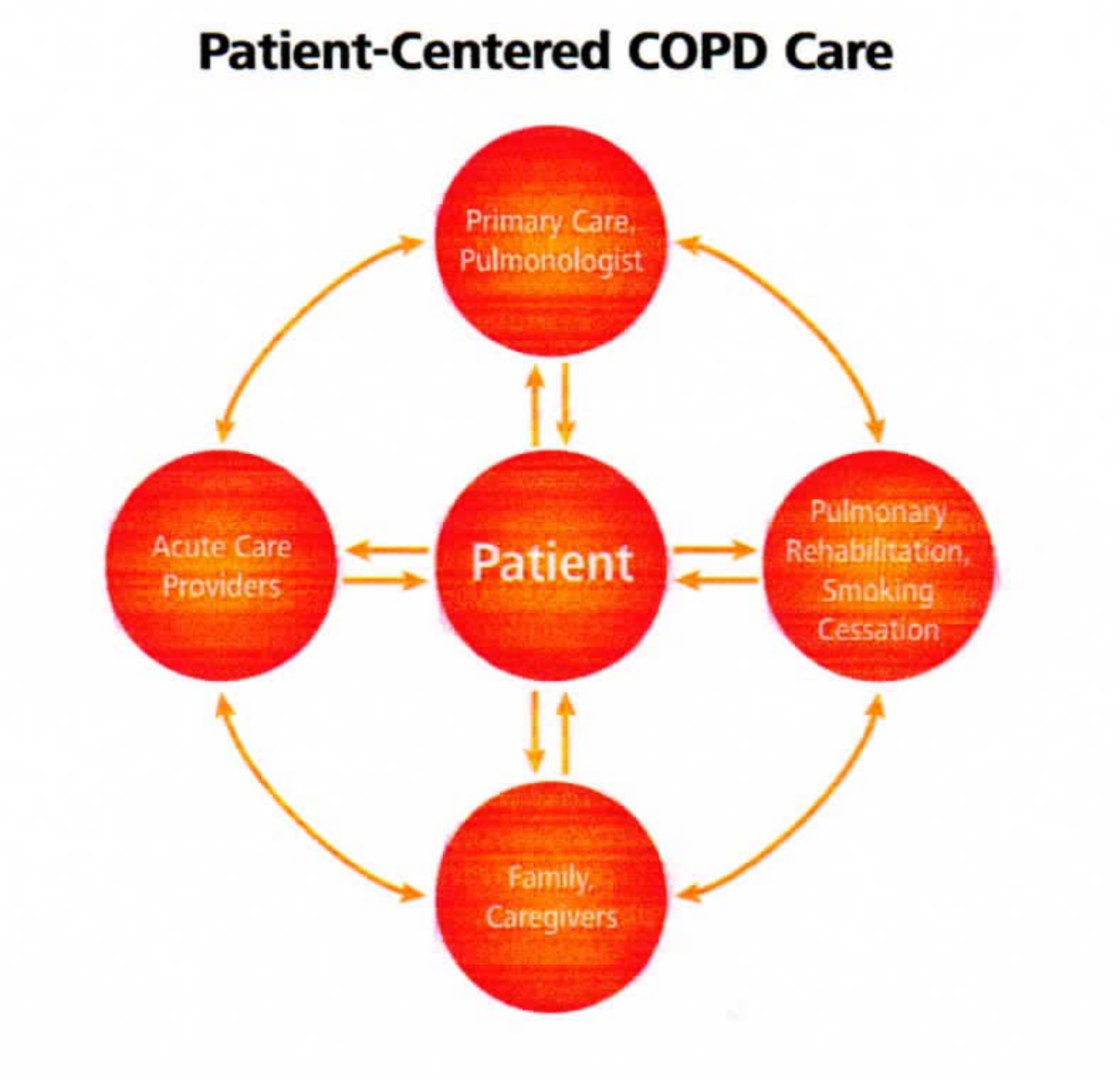
Causes of high COPD 30-day readmission rates

- Delayed and insufficient acute treatment.
- AECOPD *not* fully resolved at time of discharge.
- Disjointed patient management occurs across the continuum of care.
- Patient training is inadequate.
- Lack of health provider follow-up care post-discharge.
- Equipment in the home is inadequate.
- Lack of an AECOPD Rapid Action Plan

COPD: Better Care Model

- In 2014, CMS through ACA introduced 30-day readmission reimbursement penalties.
- Designed to move from “fee-for-service” to “patient-centric” disease management system.
- “Fee-for-service” = transition between acute and chronic disease states often disconnected and patients are often passive observers of their care.
- “Patient-centric” = coordinated care across the acute and chronic phases; patients are trained and supported to be active participants in the management of their disease.
- Healthcare “Triple Aim”:
  - Improved outcomes.
  - Per capita costs lowered.
  - Patients experience fuller, longer and more active lives.

COPD: Better Care Model



Patient-Centered COPD Care

1. Cross-continuum of care delivery

A. COPD coordinator function ("navigator")

1. First: educating & training patient and family to self-monitor & self-manage post-discharge (e.g., Pulmonary Rehabilitation RT).

2. Second: pulmonologist "extender" working across the continuum of care (particularly post-discharge) with goal of rapid response and relapse avoidance.

B. Efficient and effective communication between providers (PCP, pulmonologist, hospitalist and ED physicians).

C. Seamless discharge – no interruptions with medications nor care plan from the hospital to home.

C. Home visit – shortly after discharge to assess home environment

A. Proper equipment (home O2, mobility aids, nebulizers).

B. Medication reconciliation

C. Continued smoking cessation

D. Cognitive, family and financial considerations

Patient-Centered COPD Care

2. Patient and family involvement

A. Self-monitoring and self-management.
B. Early recognition and rapid response to AECOPD.
C. Facilitation of collaboration and communication with healthcare providers.

3. Active lifestyle

A. Inactivity is destructive – “shark analogy”.
B. Best predictor of COPD demise = % of time in bed/day.
C. Key role for pulmonary rehabilitation→home maintenance program.

4. Patient training

A. “Teach-back” method, inpatient-to-discharge reinforcement, checklists.
B. Proper administration of home meds (especially MDIs).
C. Mobility and exercise (walking).
D. Titration of home O2 (adjusted per home SpO2 monitoring).
E. Pursed-lips breathing.
F. Airway clearance (PEP devices).
G. Smoking cessation and avoidance of secondhand smoke.
H. Avoidance of exposure to toxic perfumes, dusts and chemicals.

Patient-Centered COPD Care

5. Proper equipment

A. Spacer for use with MDIs.
B. Appropriate O2 set-up (titrated, mobility).
C. Home pulse oximeters.
D. Airway clearance devices (PEP devices, vibrating vests).

6. AECOPD Rapid Action Plan

A. Early intervention is the key to successful exacerbation resolution and relapse avoidance.
B. Recognize early AECOPD signs (cough, sputum, dyspnea, rescue MDI use.
C. Checklist-procedures for patient and all providers.
D. Typical action plan: 1) call physician; 2) start Prednisone; 3) start antibiotic; 4) bronchodilators & fluids; 5) titrate supplemental O2; 6) pursed-lip breathing; 7) airway clearance protocol.

4. Pulmonary Rehabilitation & smoking cessation

A. Take advantage of AECOPD “teachable moment”.
B. Initiate during hospitalization prior to discharge.

COPD Readmissions Reduction

DASH Program

- Transition of care program (DASH)
  - Discharge, Assessment, and Summary at Home
- Face to face visits (days 1, 30)
- In home, respiratory therapist driven
- Coordinated with hospital discharge planner
- Patients receiving home oxygen therapy
- Phone call supplements (up to 12 per month)

Carlin B, et al. *Chest*. 2011;140(4_MeetingAbstracts):550A.

COPD Readmissions Reduction

DASH Program

- Provision and setup of oxygen equipment
- Clinical assessment (overall, education, therapy)
  - Patient
  - Home
  - Ancillary services, support
- Education
- Activity monitoring (ADLs)
- Medication reconciliation (direct)
- Data collection

Carlin B, et al. *Chest*. 2011;140(4_MeetingAbstracts):550A.

COPD Readmissions Reduction

DASH Results

(March 2010-May 2011)

• COPD	
– Discharges	301
– Overall 30 day readmission	26 (8.6%)
– Readmission with COPD exacerbation	8 (2.6%)
– Readmission for other cause	18 (6%)
➢ eg, fall, chest pain, surgery, etc	
• CHF	
– Discharges	57
– Overall 30 day readmission	3 (5.2%)

Carlin BW, et al. *Respir Care*. 2011 (Meeting abstracts).

Final Thoughts

- COPD = persistent airflow limitation that's common, preventable, progressive but very treatable; exacerbations & comorbidities contribute to overall severity.

- AECOPD episodes are major events that may be harbingers of continued deterioration and represent opportunities for improved care; a sense of urgency is warranted.

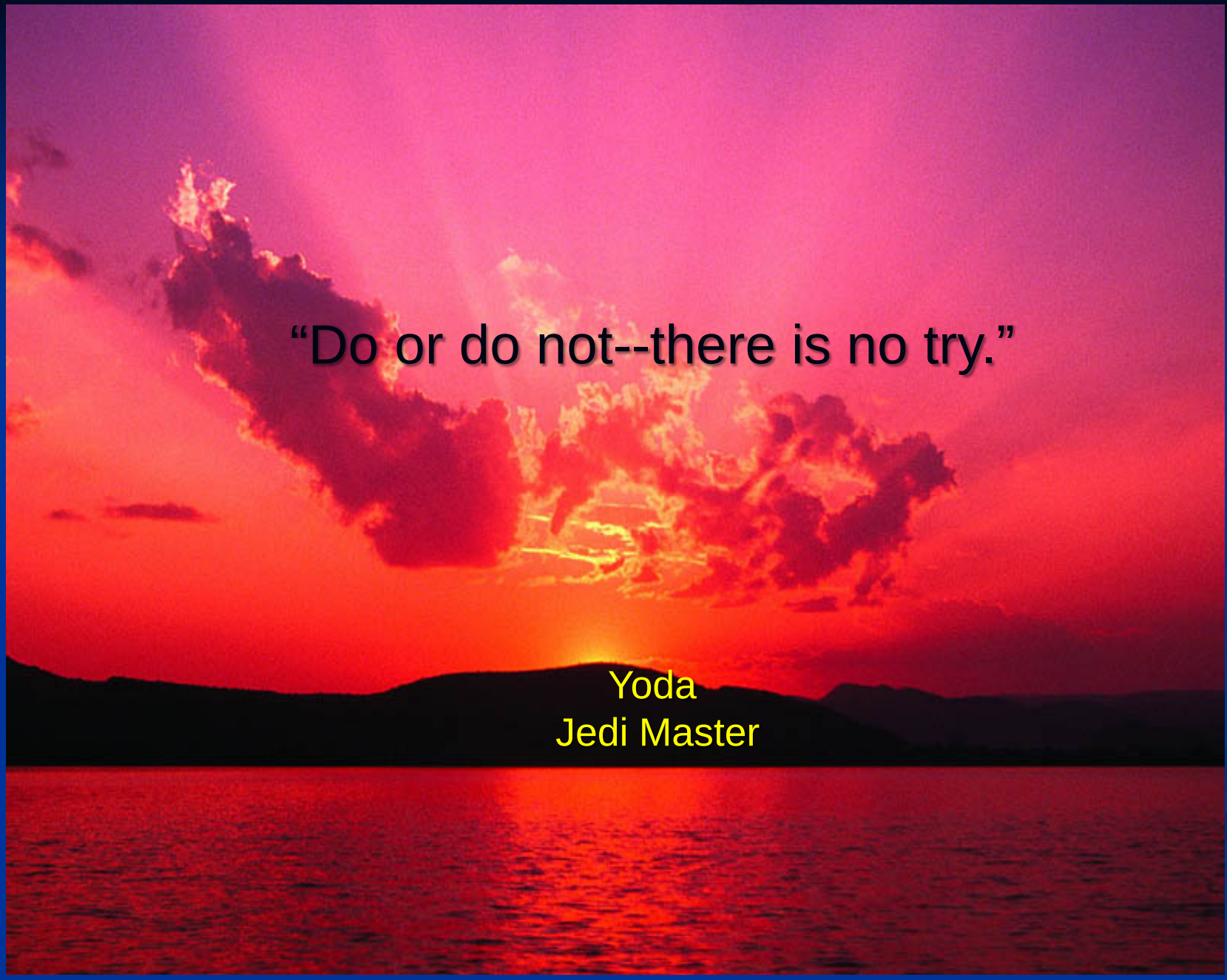
- COPD pharmacologic & non-pharmacologic therapy should be assessment-based and patient-centered with the overall aims to reduce symptoms, decrease exacerbations, improve general health status and maximize functional status.

- Patient-centered care offers the best opportunity to improve outcomes, costs and quality of life in COPD patients.

- Respiratory therapists are the key components to COPD patient-centered care as:
  - Early responders (e.g., emergency department, inpatient)
  - Independent practitioners providing continuity of care (physician extenders/navigators)
  - Patient educators
  - Provider educators (e.g., hospitalists, ER physicians)
  - Discharge planners/facilitators
  - Post-discharge care providers (e.g., pulmonary rehab, home visits, support groups)

Final Thoughts

As you develop your own COPD readmission reduction program, please keep in mind this inspirational (pun intended) thought…


“Do or do not--there is no try.”
Yoda
Jedi Master

COPD Exacerbation

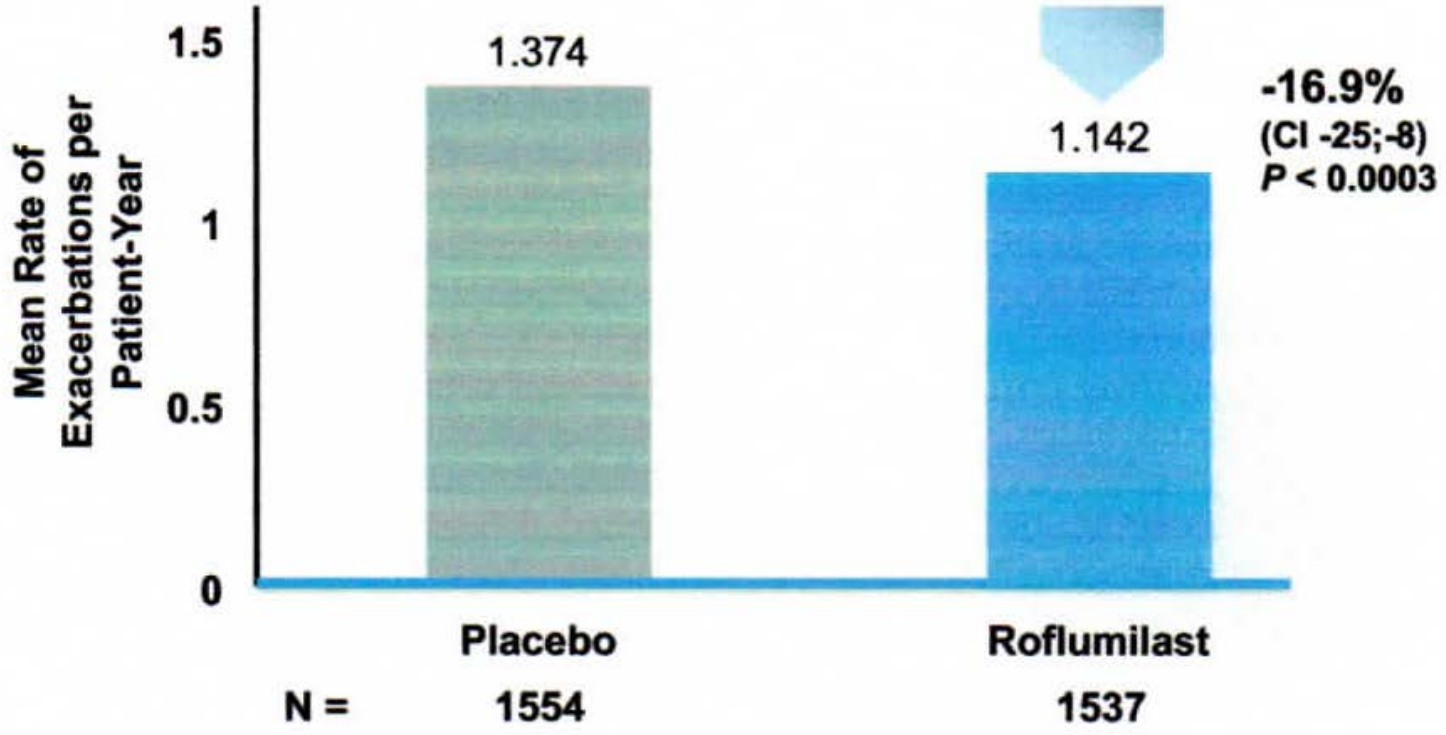
Summary

- COPD exacerbations may have a profound effect on patient outcomes; effective measures to reduce their frequency are available
- Viral, bacterial, and environmental conditions have been found to be causative agents
- Both pharmacologic and nonpharmacologic approaches can reduce COPD exacerbation rates
- Patient adherence to therapy needs to be assessed at each visit as nonadherence is common in COPD patients

COPD Exacerbation

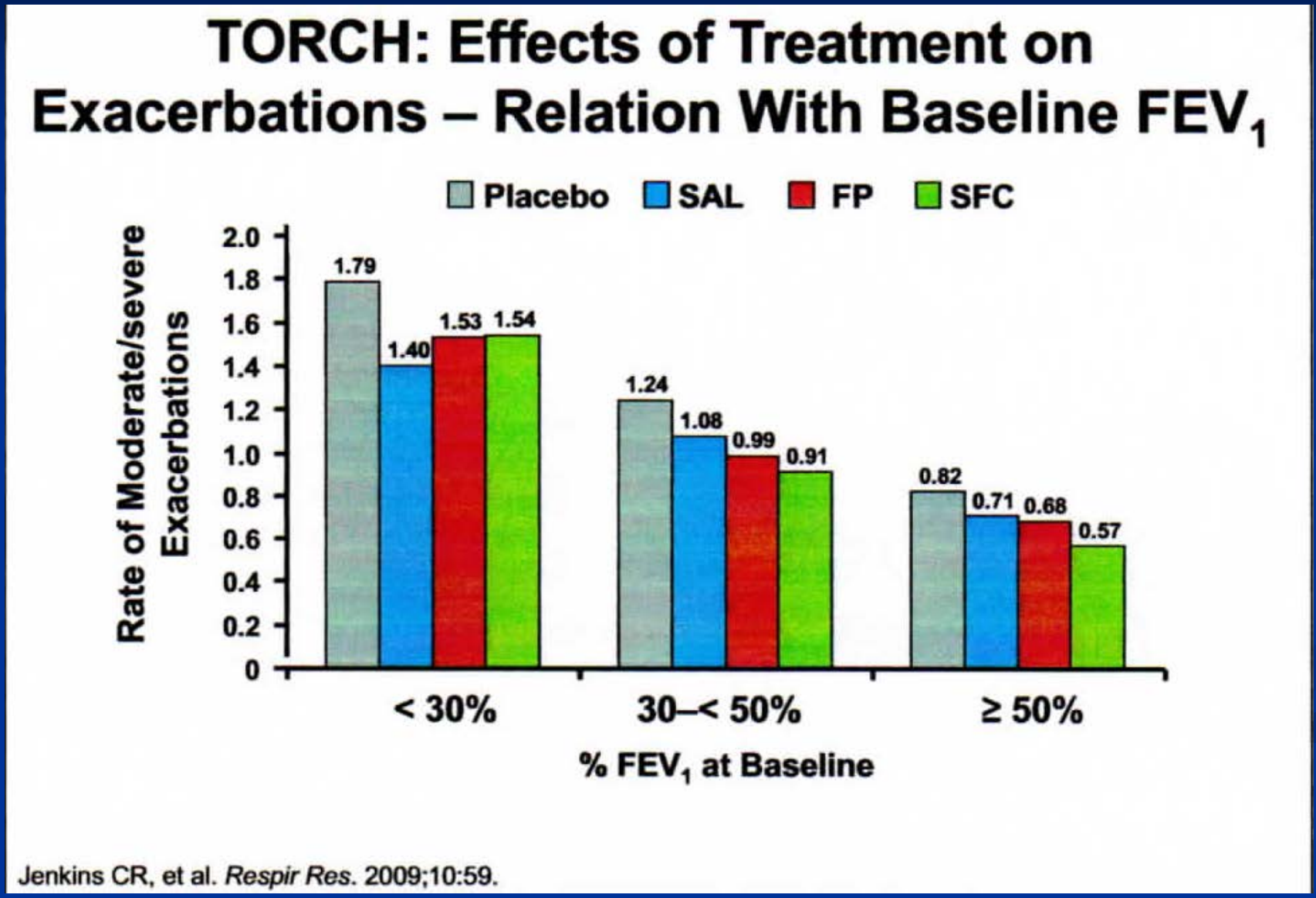
Effects of Roflumilast on the Rate of Moderate/Severe Exacerbations

Co-primary endpoint: Exacerbation rate



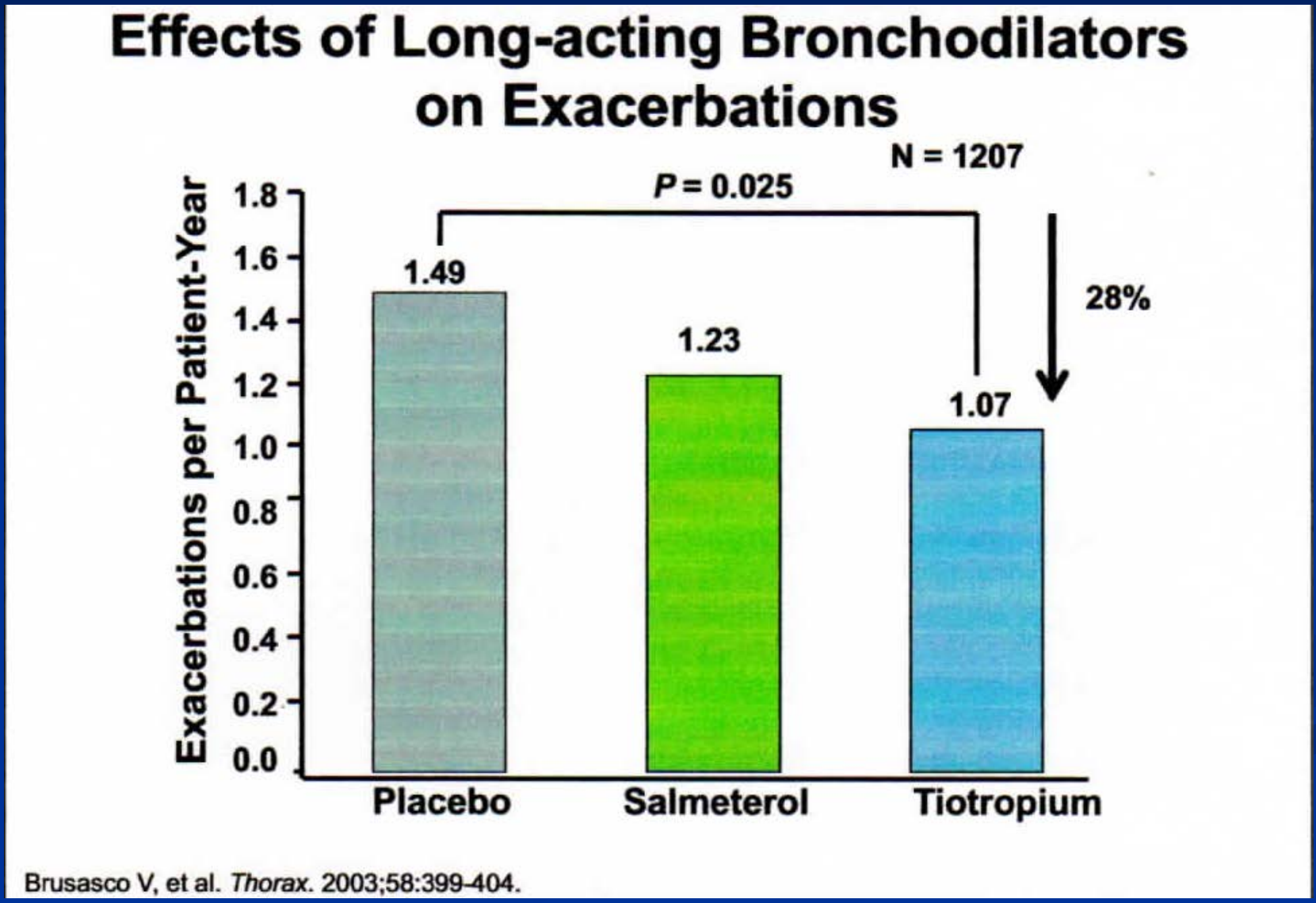
Calverley PM, et al. *Lancet*. 2009;374(9691):685-694.

COPD Exacerbation



Jenkins CR, et al. *Respir Res*. 2009;10:59.

COPD Exacerbation



COPD: BODE Index

Celli *et al* NEJM 2004

B – Body mass index (BMI)

O – degree of airflow Obstruction (FEV1)

D – degree of Dyspnea (mMRC)

E – Exercise tolerance (6 minute walk in meters)

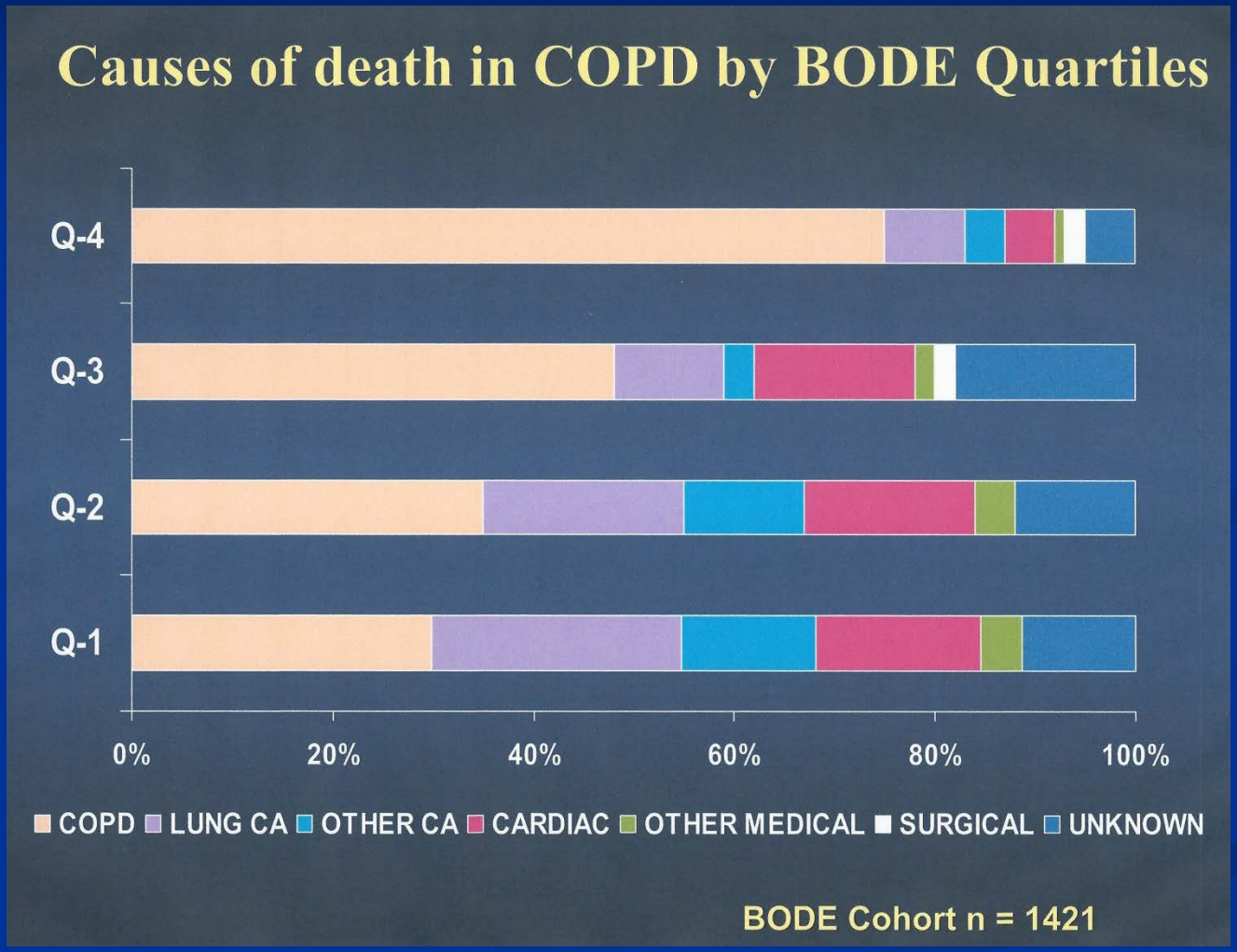
Variable	Points on BODE Index			
	0	1	2	3
FEV1 (% predicted)	≥65	50-64	36-49	≤35
Distance walked in 6 min (meters)	>350	250-349	150-249	≤149
MMRC dyspnea scale*	0-1	2	3	4
Body-mass index (BMI)	>21	≤21		

BODE Index Score	One year mortality	Two year mortality	52 month mortality
0-2	2%	6%	19%
3-4	2%	8%	32%
4-6	2%	14%	40%
7-10	5%	31%	80%

elp predict prognosis within six months of death.

Q1
Q2
Q3
Q4

COPD: BODE Index

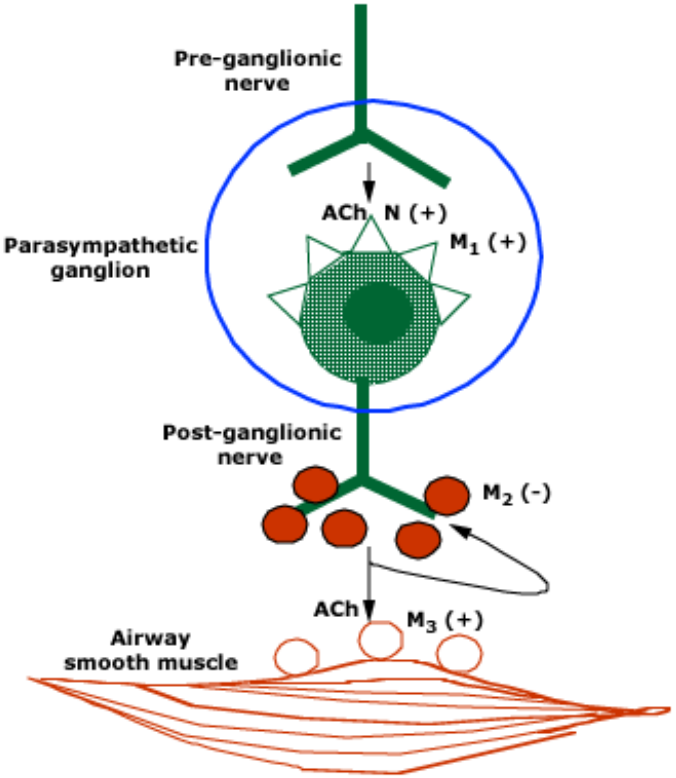


COPD: $Beta_2$-agonists

- Developed via modifications of Epinephrine molecule
- $Beta_2$-receptor specific: Bronchial smooth muscle relaxants
- Beta specificity lost at higher doses→CV and CNS side effects
- Examples: Albuterol, Levalbuterol, Salmeterol, Formoterol
- Other actions:
  - Decrease mast cell mediator release
  - Inhibit neutrophil, eosinophil and lymphocyte functional responses
  - Increase mucociliary transport
  - Affect vascular tone
  - Decrease pulmonary edema

COPD: Anticholinergics

Parasympathetic innervation of airways



Ganglionic transmission is mediated via nicotinic receptors (N), while the M_1 receptors may play a facilitatory role. M_2 receptors at the postganglionic terminal may inhibit release of acetylcholine (Ach), which acts on M_3 receptors on airway smooth muscle to cause bronchoconstriction.

Redrawn from Barnes, PJ, Life Sciences, 1993; 52:521.

COPD: Anticholinergics

Muscarinic receptors in the lung and the effect of selected anticholinergic medications

Type	Predominant location	Action	Atropine	Ipratropium Oxitropium Tiquizium	Tiotropium
M1	Peribronchial ganglion cells	Bronchoconstriction	Inhibits	Inhibits	Inhibits
		Increased secretion			
M2	Postganglionic nerves	Inhibit Ach release	Inhibits	Inhibits	Does not inhibit
		Bronchodilation			
M3	Smooth muscle mucous glands	Bronchoconstriction	Inhibits	Inhibits	Inhibits
		Increased secretion			

COPD: MX & PDE4i

- Methylxanthines (Theophylline)
  - Less effective and less well-tolerated than long-acting BDs.
  - May be option for nocturnal symptoms, less $.
  - May reduce exacerbations as single agent.
  - May improve lung function when added to LABA MDI.
- Phosphodiesterase-4 Inhibitors (Roflumilast)
  - ↓ exacerbations in GOLD 3 & 4 patients with chronic bronchitis.
  - Additive effect when added to LABA MDIs; no data with ICS yet.
  - No change in lung function.
  - Variable effects on perceived breathlessness.

COPD: Other Pharm

- Vaccines
  - Influenza vaccines yearly.
  - Pneumococcal vaccine: all patients ≥ 65 yrs & those < 65 yrs with FEV1 < 40% predicted.
- Alpha-1 Antitrypsin augmentation therapy
  - Only PiZZ, PiSZ, PiNN, PiNZ (functionally deficient homozygotes).
  - Screening for A1ATD indicated for all COPD pts.
- Antibiotics→Azithromycin
  - Immunomodulating & antiinflammatory effects
  - NEJM August 2011; 250 mg/day
  - COPD pts with previous exacerbation that yr or home O2.
  - 27% decrease in risk of exacerbation.
  - Beware: hearing loss, QTc prolongation, macrolide-resistant organisms.

COPD: Other Pharm

- Mucolytic agents (Carbocysteine, Dornase)
  - Patients with viscous sputum may benefit.
  - Reserve for use with chronic bronchitis patients.
  - Usually marginal functional improvement.
- Antitussives→not recommended.
- Vasodilators
  - Common coexistence of pulmonary HTN.
  - Nitric Oxide contraindicated in stable COPD.
  - PDE5i (Sildenafil) ↓ PA pressures but also ↓ PaO_2.

COPD: Pulm Rehab

Benefits of pulmonary rehabilitation in COPD

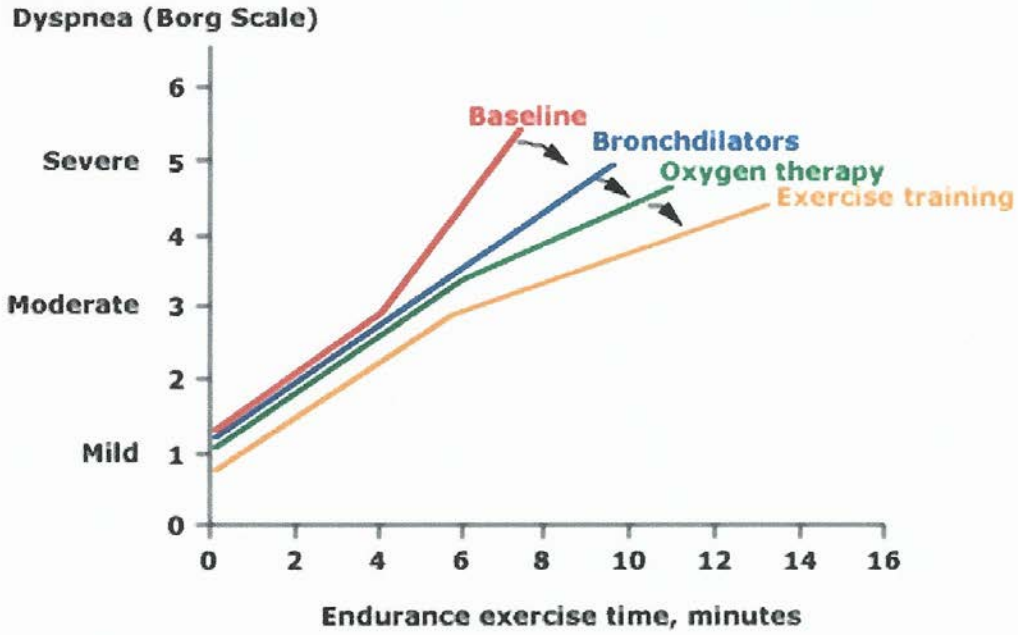
Improves exercise capacity (**Evidence A**)
Reduces the perceived intensity of breathlessness (**Evidence A**)
Improves health-related quality of life (**Evidence A**)
Reduces the number of hospitalizations and days in the hospital (**Evidence A**)
Reduces anxiety and depression associated with COPD (**Evidence A**)
Strength and endurance training of the upper limbs improves arm function (**Evidence B**)
Benefits extend well beyond the immediate period of training (**Evidence B**)
Improves survival (**Evidence B**)
Respiratory muscle training is beneficial, especially when combined with general exercise training (**Evidence C**)
Improves recovery after hospitalization for an exacerbation (**Evidence A**)[1]
Enhances the effect of long-acting bronchodilators (**Evidence B**)

References:

1. *Puhan MA, Gimeno-Santos E, Scharplatz M, et al. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2011.*

COPD: Pulm Rehab

Effect of pulmonary rehabilitation on dyspnea



Effect of exercise training on dyspnea compared with bronchodilators and oxygen.

Data from Am J Respir Crit Care Med 1999; 159:321.

COPD: Oxygen Therapy

- Long-term O2 therapy (> 15 hrs/day) for COPD with chronic respiratory failure (NOTT):
  - Improves mortality.
  - May improve QOL, CV morbidity, depression, cognitive function, exercise capacity and hospitalizations.

- Indications:
  - PaO2 $\leq$ 55 mmHg or SaO2 < 88%.
  - PaO2 55-60 mmHg or SaO2 $\geq$ 88% & evidence of pulm HTN, CHF or polycythemia (Hct > 55%).

COPD: PAP Therapy

- Non-invasive ventilation (e.g., BPAP)
  - Usually combined with O2 therapy.
  - May benefit some patients
    - Daytime hypercapnia.
    - Obstructive sleep apnea.
  - May improve survival but not overall QOL.
- Sleep-related breathing disorders
  - COPD + OSA ("Overlap Syndrome").
  - Two high-prevalence disorders.
    - 11% OSA patients with FEV1/FVC < 0.60.
    - 29% COPD with AHI > 5.
  - Treatment with CPAP = ↓ mortality, ↓hospitalizations & ↑QOL.

COPD: Surgical Treatments

Lung volume reduction surgery (LVRS) is more efficacious than medical therapy among patients with upper-lobe predominant emphysema and low exercise capacity.

LVRS is costly relative to health-care programs not including surgery.

In appropriately selected patients with very severe COPD, *lung transplantation* has been shown to improve quality of life and functional capacity.

COPD: Discharge Checklist

- Tobacco smoking cessation
- Vaccine administration
- ICS + LABA + LAMA MDIs (Category C & D patients)
- Inhaler instruction with actual device
- Oxygen titration, instruction, nocturnal screening and prescription
- CS taper instruction and monitoring
- Pulmonary rehabilitation referral and exercise prescription
- Self-management care plan
- Assess for drug affordability
- Follow-up care plan