MedStar Franklin Square Medical Center
Angelos Center for Lung Diseases

Knowledge and Compassion
Focused on You

December 3, 2015

Prevention of Acute COPD exacerbations

George Pyrgos MD

First Annual Symposium:
Successful Management of Lung Disease

Disclosures

- No funding received for this presentation
- I have previously conducted clinical trials with Boehringer Ingelheim.
- Principal Investigator in clinical trials with Astra Zeneca, Sanofi-Aventis and Pearl Therapeutics.

Goals

- Risk factors for AECOPD
- Importance of prevention of AECOPD
- Pharmacologic treatments
- Non pharmacologic treatments

What is an AECOPD?

- GOLD Guidelines :
- “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.”
  - Use of steroid antibiotic or both
  - Change in cough, sputum, but most importantly dyspnea

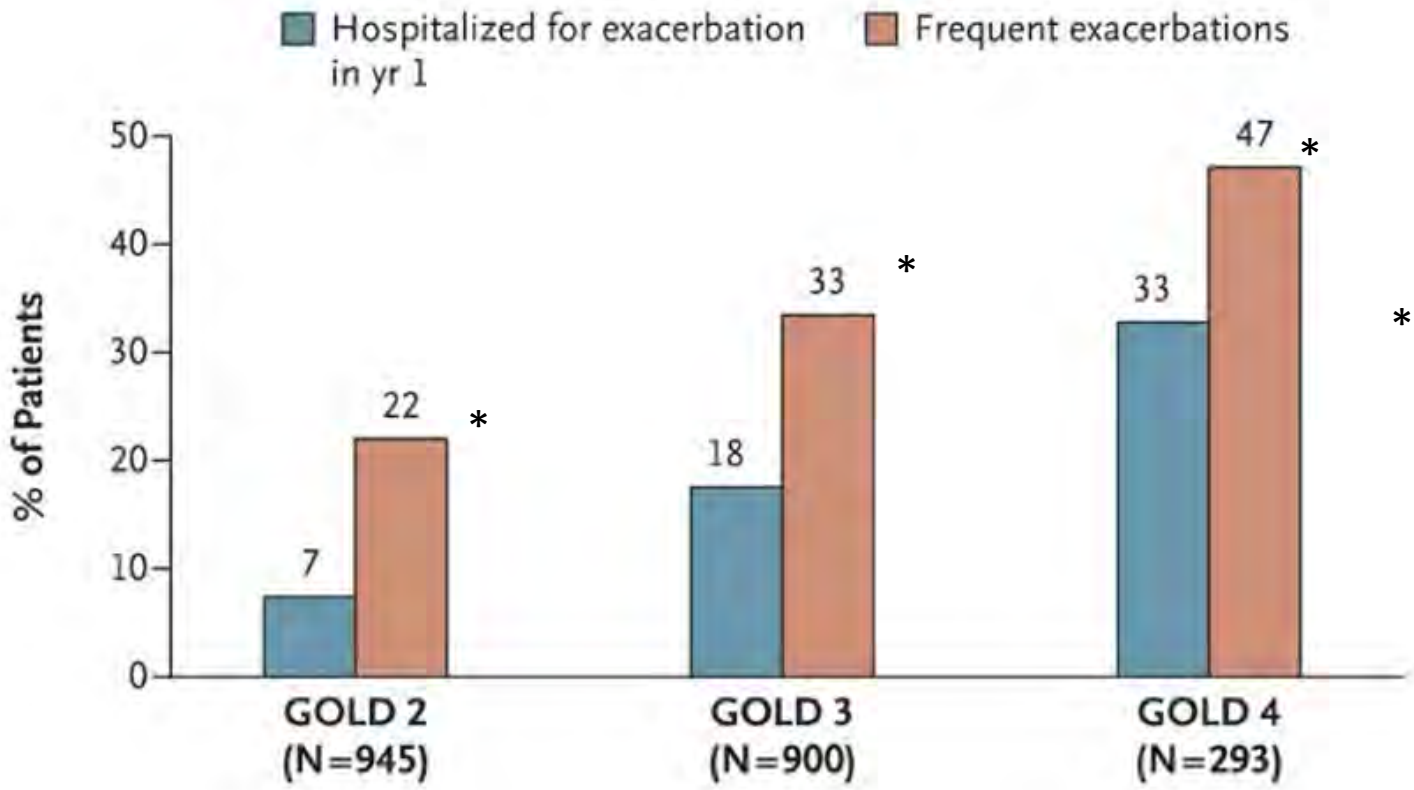
Confounders of AECOPD

- Heart Failure
- Pneumonia
- Pulmonary Embolism
- Bronchial Carcinoma
- Pneumothorax
- Rib fractures

Which patients have COPD exacerbations?

AECOPD RISK FACTORS

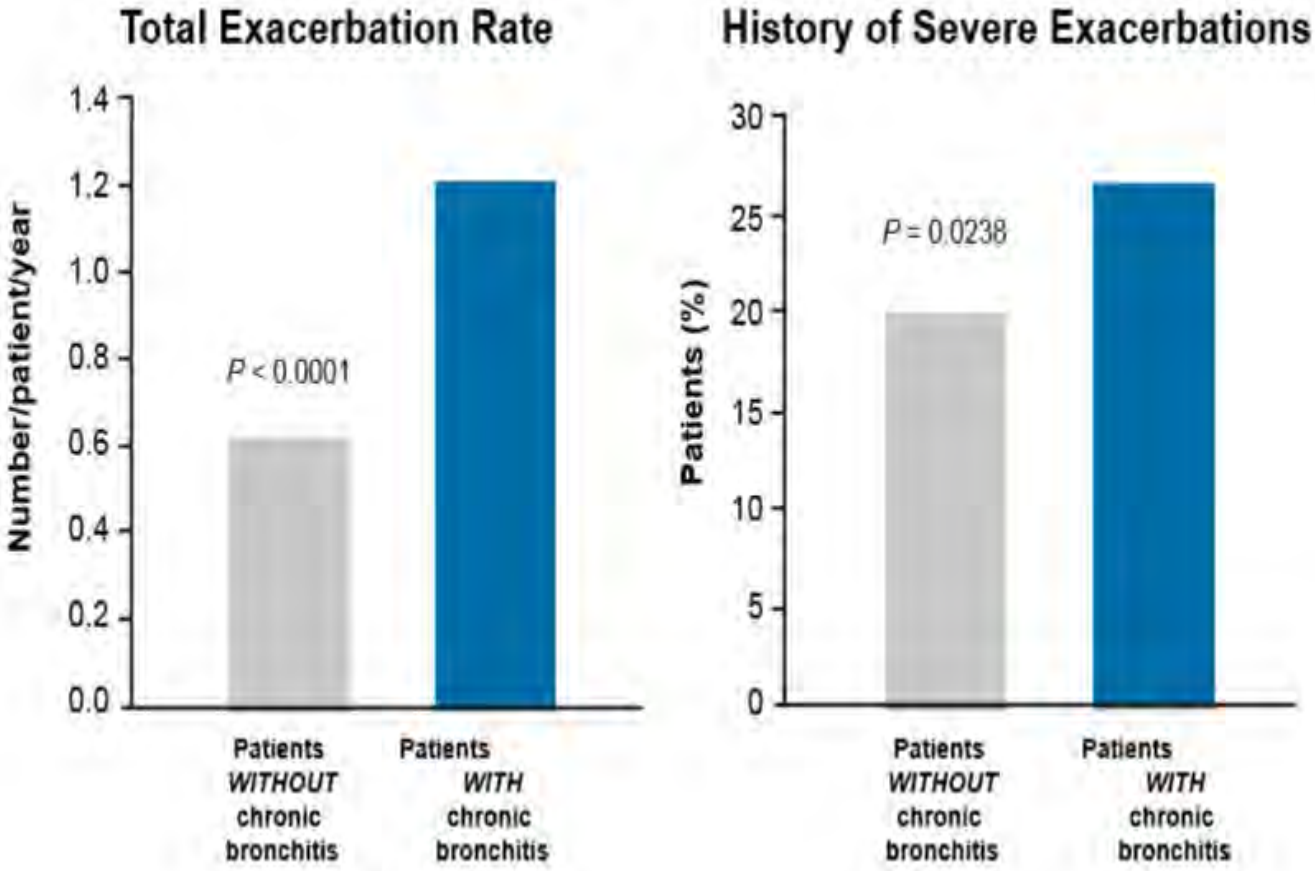
COPD Severity and Risk of Hospitalization



* p<0.001

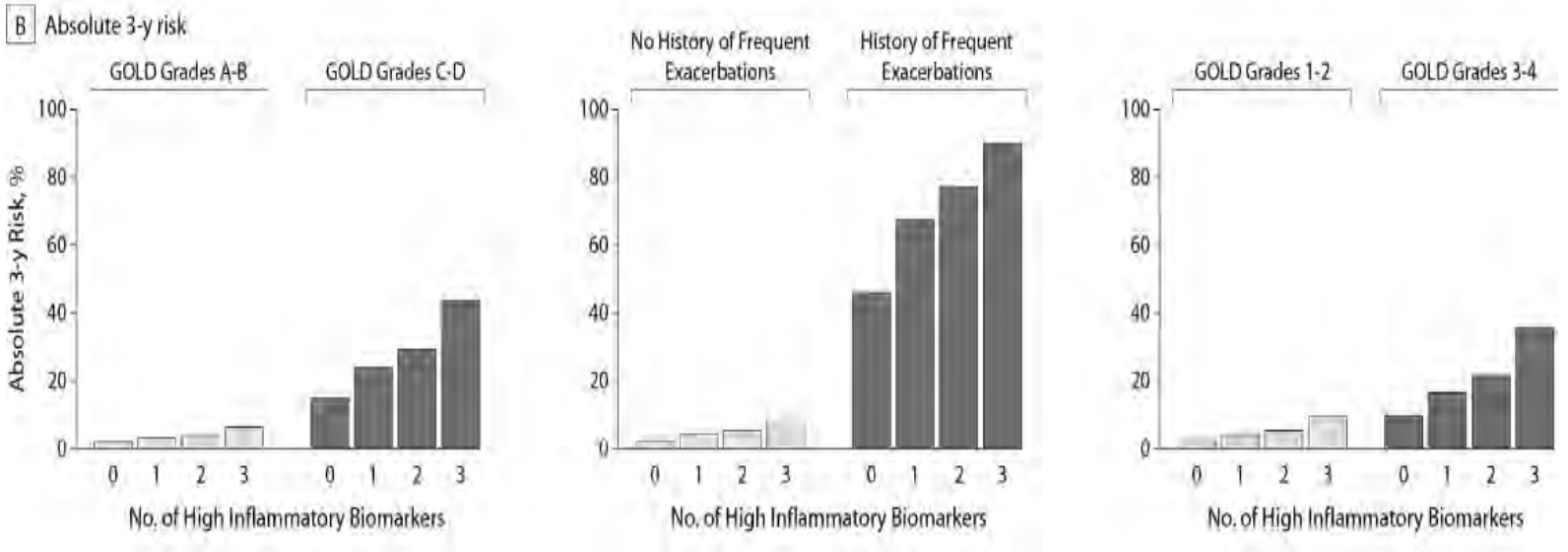
Wells MJ, et al. N Engl J Med. 2012;367(10):913-921.

Cough and Sputum Production Indicate Higher Rate of Severe Exacerbation



Kim V, et al. Chest. 2011;140:626-633.

Biological Markers for frequent exacerbations



Plasma C-reactive protein and fibrinogen and blood leukocyte count were defined as high or low according to cut points of 3 mg/L, 14 μmol/L, and 9 $\times 10^9$/L, respectively

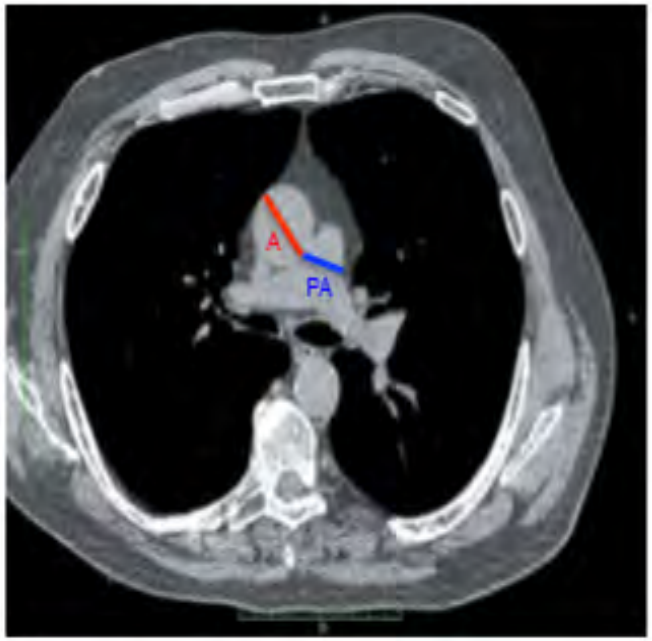
JAMA. 2013;309(22):2353-2361

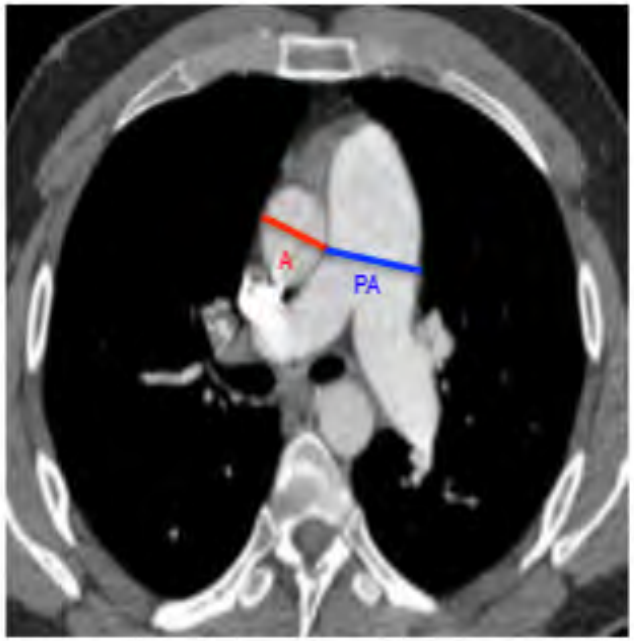
Pulmonary Artery to Aorta Ratio in the ECLIPSE Cohort

All Exacerbations (Data from Year 3)	Odds Ratio (95% CI)	*P* Value
Exacerbation in previous year	3.59 (2.76-4.67)	< 0.001
FEV_1 per percentage-point decrease	1.01 (1.01-1.02)	0.001
SGRQ, per 1-point increase	1.00 (0.99-1.01)	0.17
Gastroesophageal reflux disease	1.69 (1.27-2.23)	< 0.001
White-cell count, per $1x10^3/mm^3$ increase	1.01 (0.96-1.06)	0.85
Pulmonary artery to aorta ratio (PA:A) > 1	6.68 (4.47-9.96)	< 0.001

Wells MJ, et al. N Engl J Med. 2012;367(10):913-921.

Pulmonary Artery/ Aorta Ratio (PA:A)>1





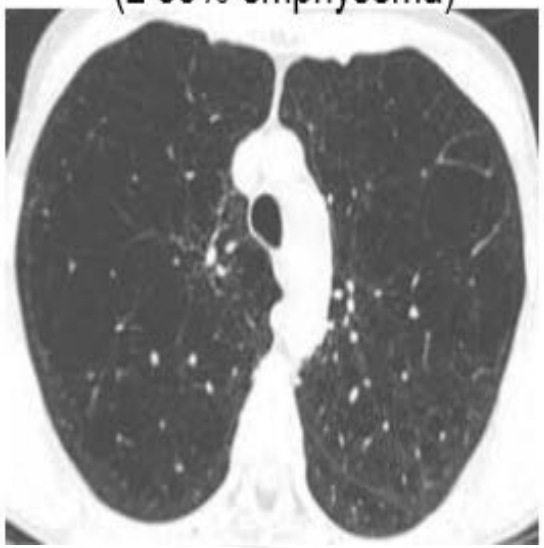
Odds Ratio for Admission:
6.68 (4.47-9.96) p<0.001

Wells MJ, et al. N Engl J Med. 2012;367(10):913-921.

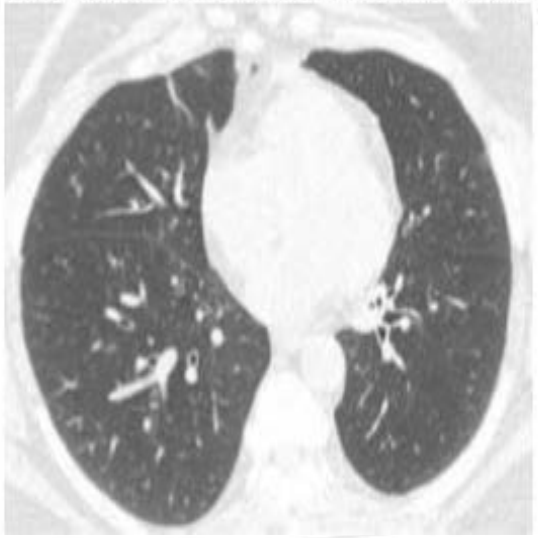
Radiologic Phenotypes:

- Bronchial wall thickness ≥ 1.75 mm has an increased exacerbation frequency: 1.84 fold change per 1 mm increase in wall thickness

Emphysema-predominant
(≥ 35% emphysema)

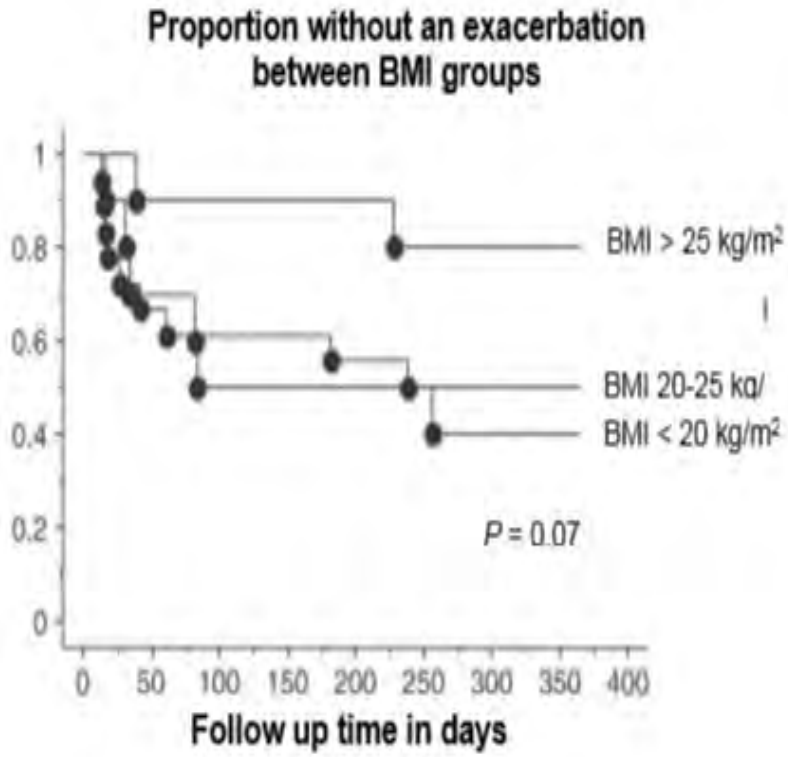


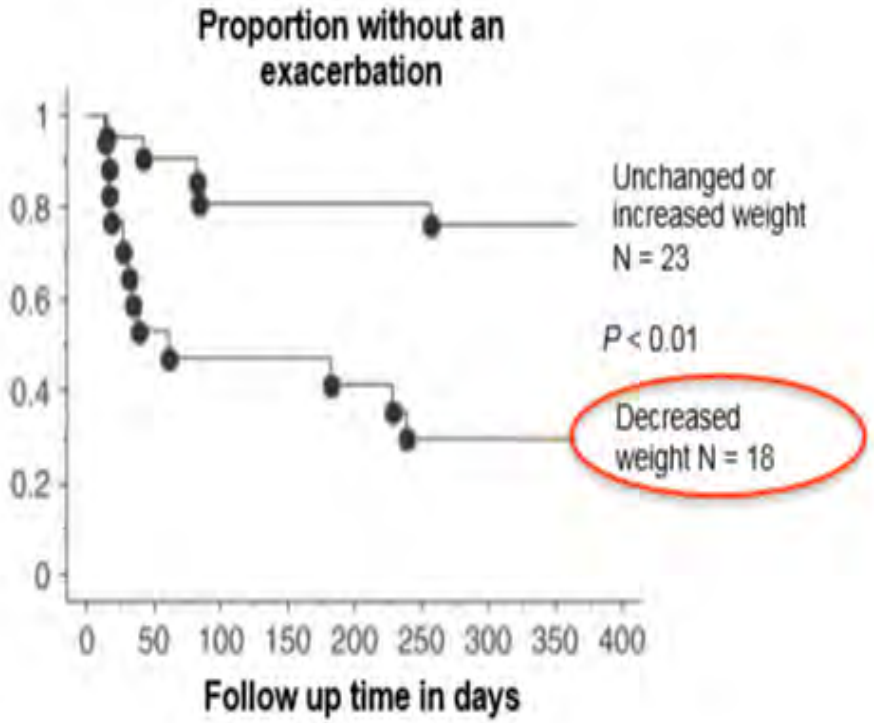
Airway-predominant
(≥ 1.75mm bronchial wall thickness)



Han MK, et al. Radiology. 2011;261(1):274-282

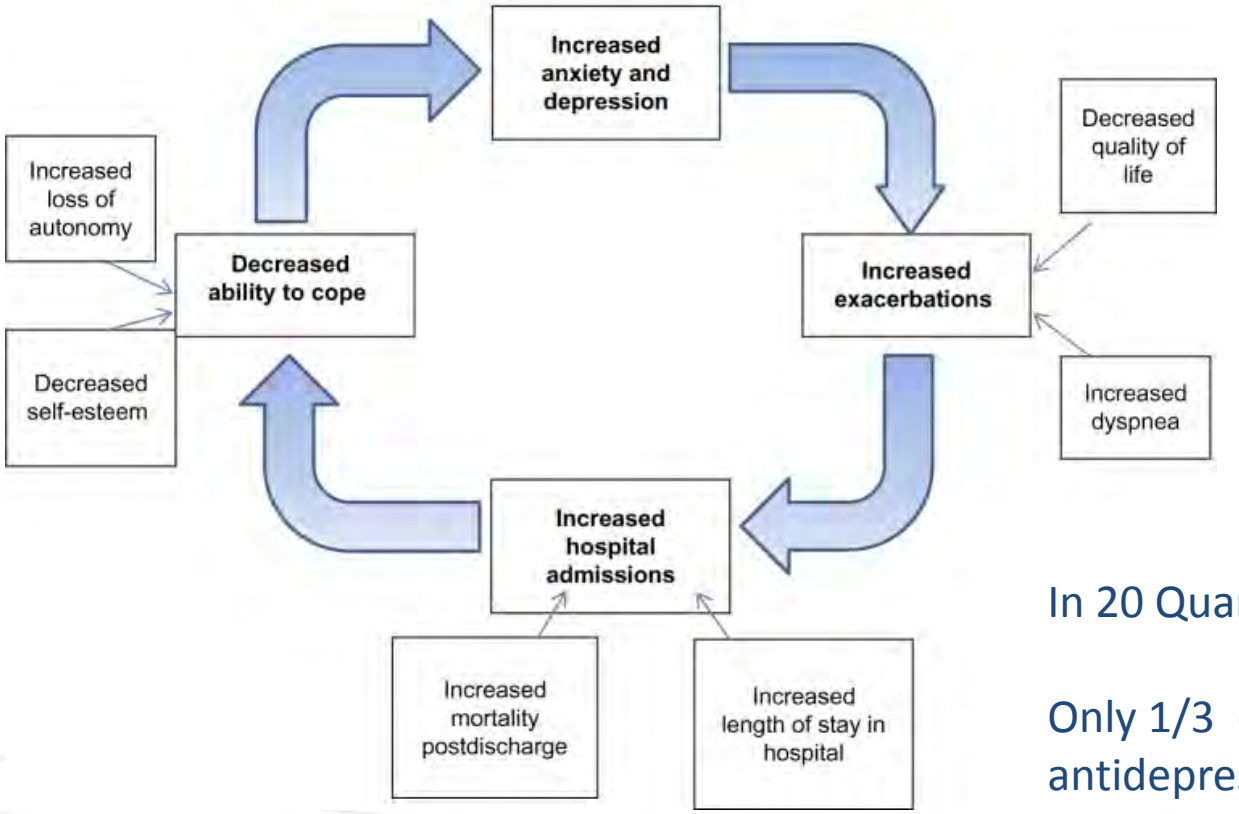
Poor nutritional status





Kessler R, et al. AJRCCM 1999;159:158-164,

Relationship between anxiety, depression and COPD



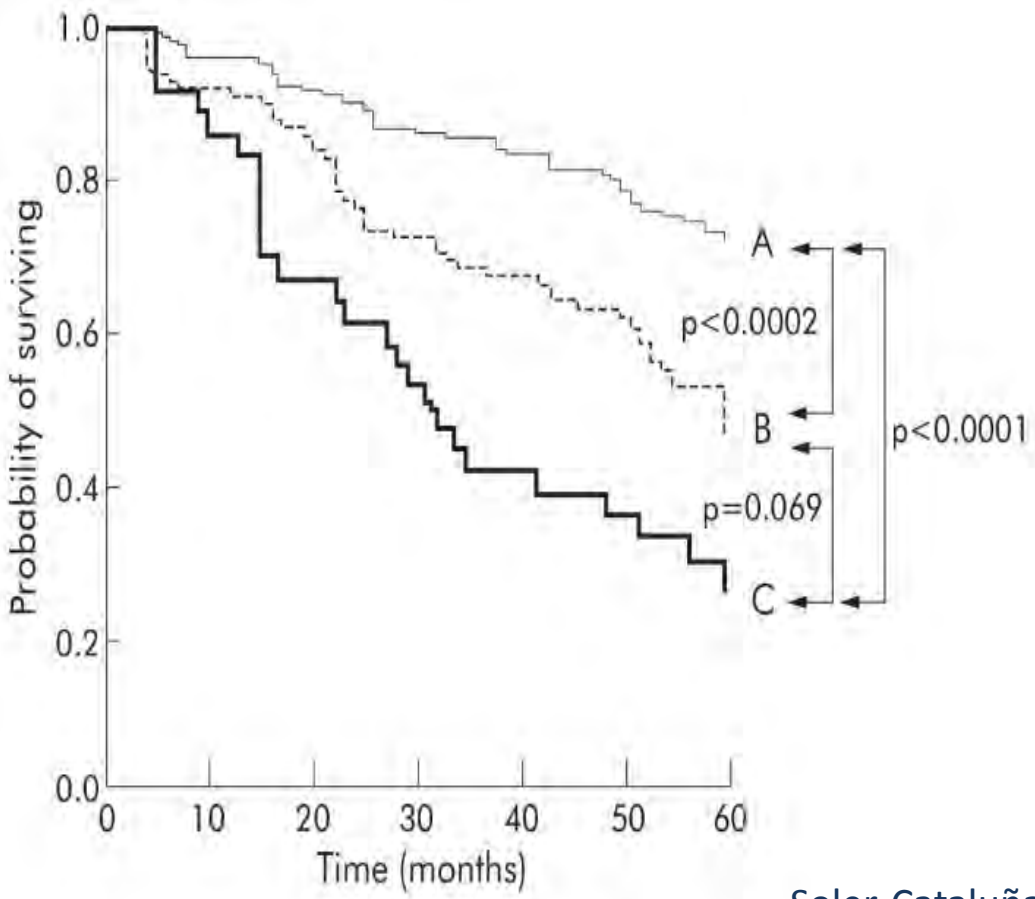
In 20 Quantitative COPD studies

Only 1/3 of patients treated with antidepressants

Int J Chron Obstruct Pulmon Dis. 2014; 9: 315–330.

WHY SHOULD WE CARE?

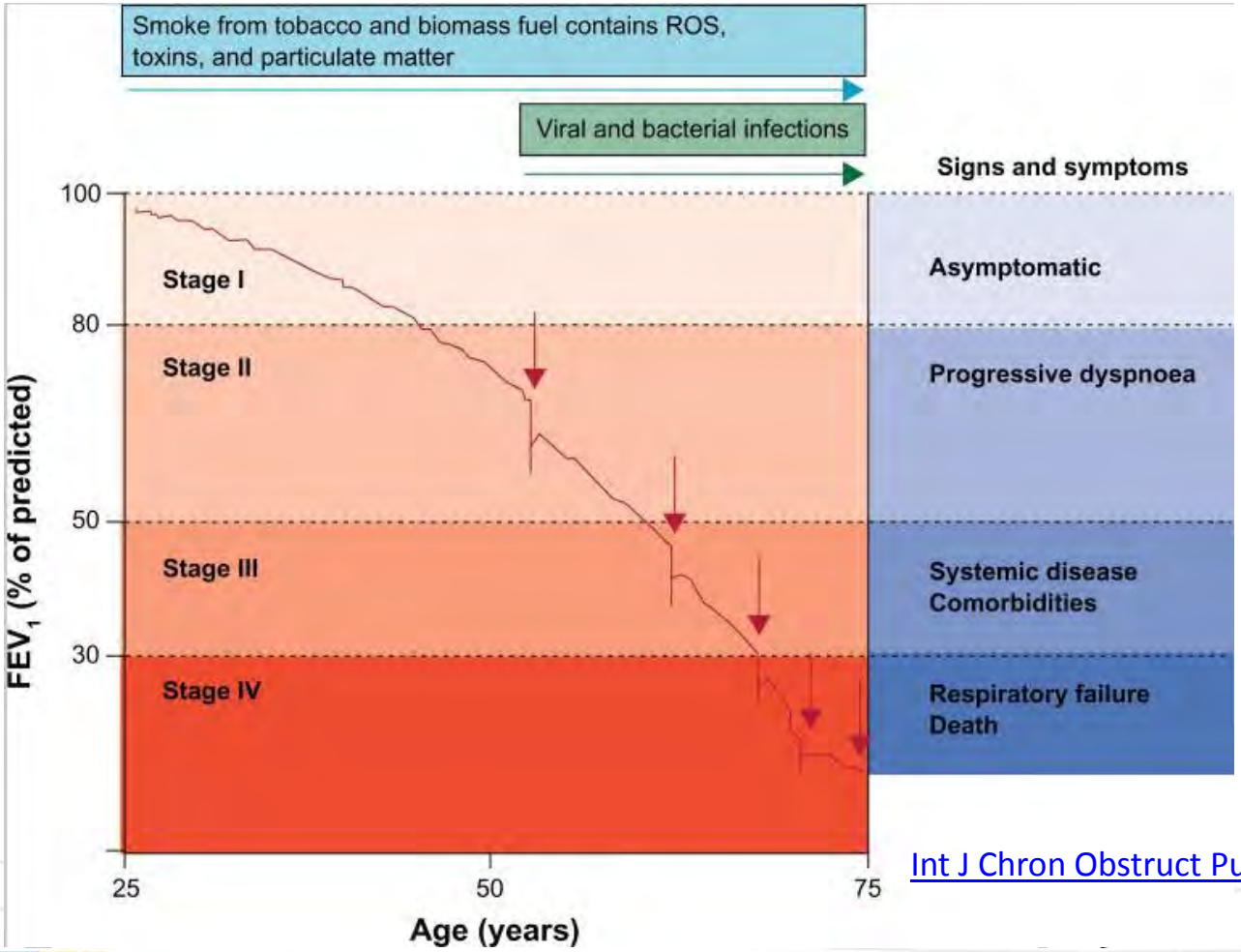
Patients with COPD Exacerbations have higher risk of Mortality



Group A: No hospital management
Group B: 1-2 exacerbations
Group C: ≥ 3 exacerbations

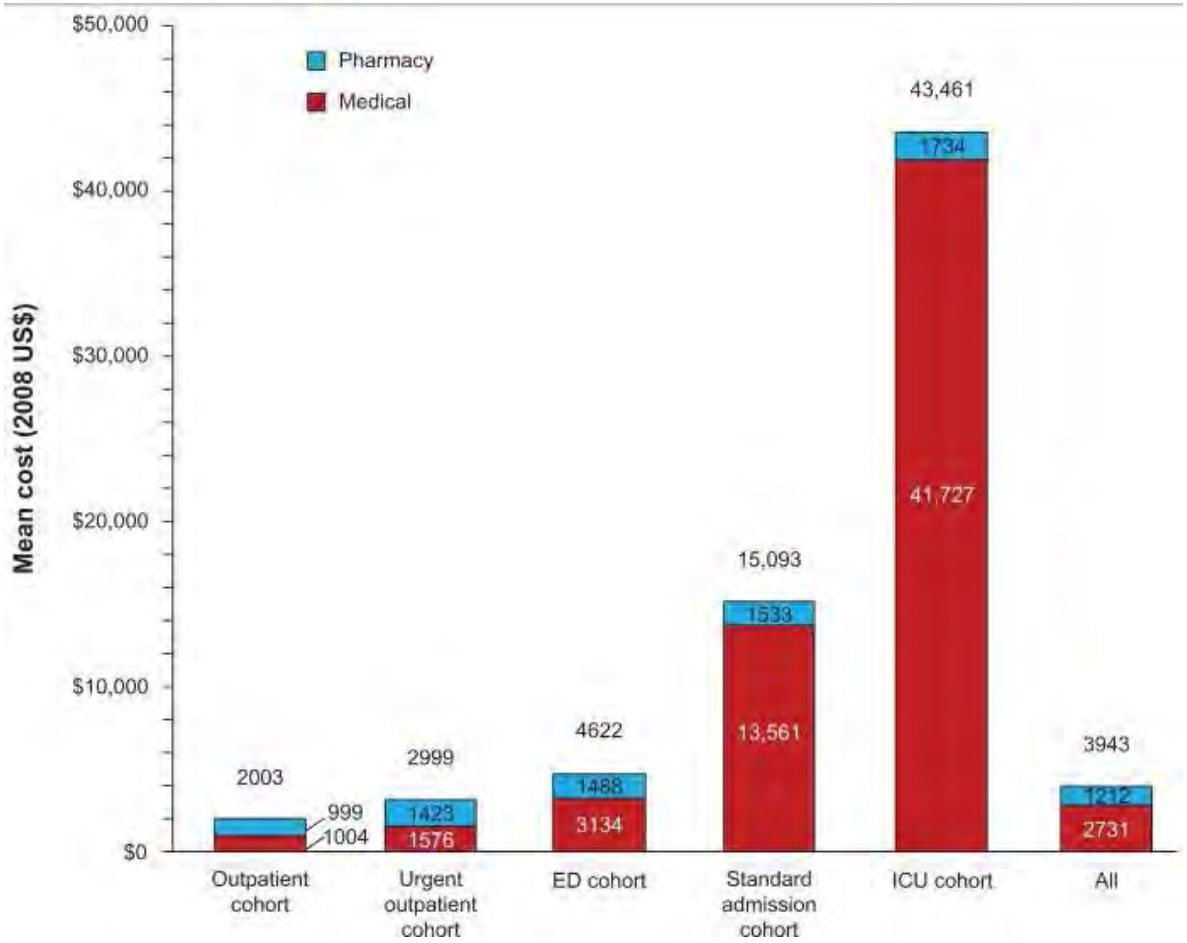
Soler-Cataluña JJ, et al. Thorax. 2005;60:925-931.

Patients with frequent COPD Exacerbations have higher rate of lung function decline



Int J Chron Obstruct Pulmon Dis. 2010; 5: 153–164.

Financial Cost of COPD management



Int J Chron Obstruct Pulmon Dis. 2010; 5: 341–349.

Pharmacologic Measures

PREVENTION OF AECOPD

Pharmacologic Agents Used for COPD

- LAMAs: tiotropium, aclidinium, umeclidinium,glycopyrronium
- LABAs: salmeterol, formoterol, olodaterol, vilanterol
- SABA: albuterol/salbutamol,
- SAMA: ipratropium
- ICS: fluticasone, mometasone, budesonide
- Phosphodiesterase Inhibitors: theophylline, roflumilast
- Antioxidants: N-acetylcysteine (NAC)
- Other drugs (TNF, statins, Vitamin D, p38 MAPK etc)

Which Drug?

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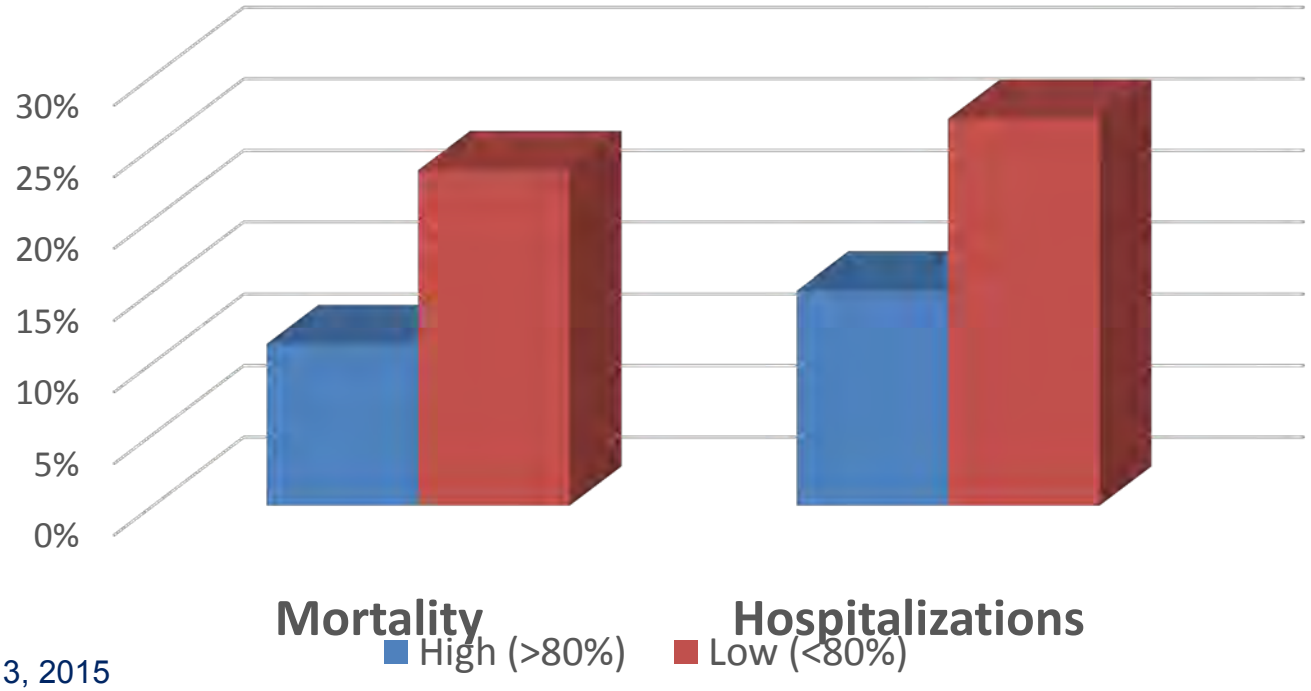
Best Drug for prevention of COPD exacerbations?

- The Drug that the patient will take!!!

Adherence is a major issue in COPD

- Overall adherence in COPD population is 50%



Thorax 2009;64:939-943
Int J Chron Obstruct Pulmon Dis. 2010

Recommended Pharmacologic Interventions

- LAMA vs. placebo : Grade 1A
- LABA vs. placebo : Grade 1B
- SAMA, SABA vs. placebo : Grade 2C
- SABA/SAMA > SABA : Grade 2B

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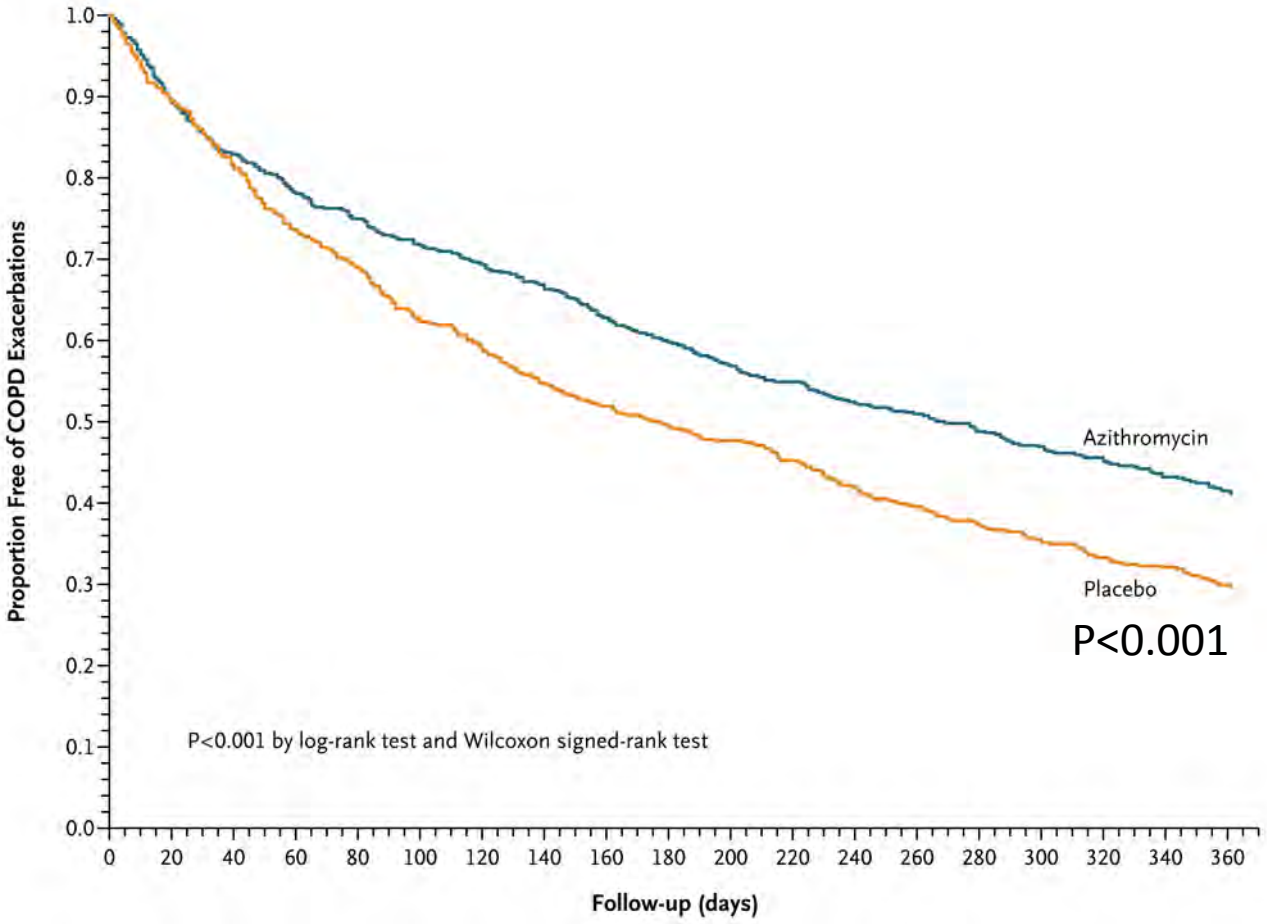
Chest. 2015;147(4):894-942

Recommended Interventions II

- Stable COPD: ICS/LABA vs. ICS : Grade 1B
- ICS/LABA vs. LAMA (no difference) Grade 1C
- Systemic steroids (inpatient or outpatient) within a month of an exacerbation : Grade 2B (not long term steroids)

Chest. 2015;147(4):894-942

Macrolide Therapy for Prevention of COPD Exacerbations



- 1 year
- 558 vs 559 pts
- 317 vs. 380 exacerbations

- NNT=2.86

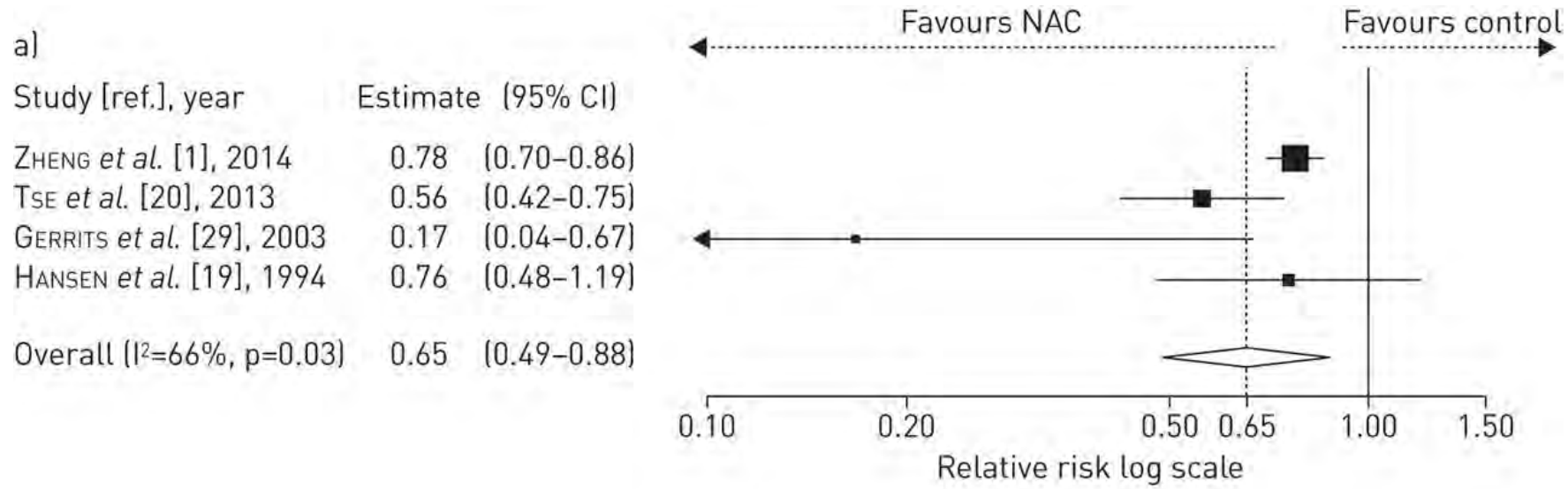
N Engl J Med. 2011 Aug 25; 365(8): 689–698.

Chronic Macrolide Therapy

- Grade 2A evidence (1 or more moderate to severe exacerbations) despite inhaler therapy

- Safety Concerns
  - QT prolongation
  - Hearing loss (p=0.04)
  - Colonization with resistant Bacteria

NAC Treatment in COPD



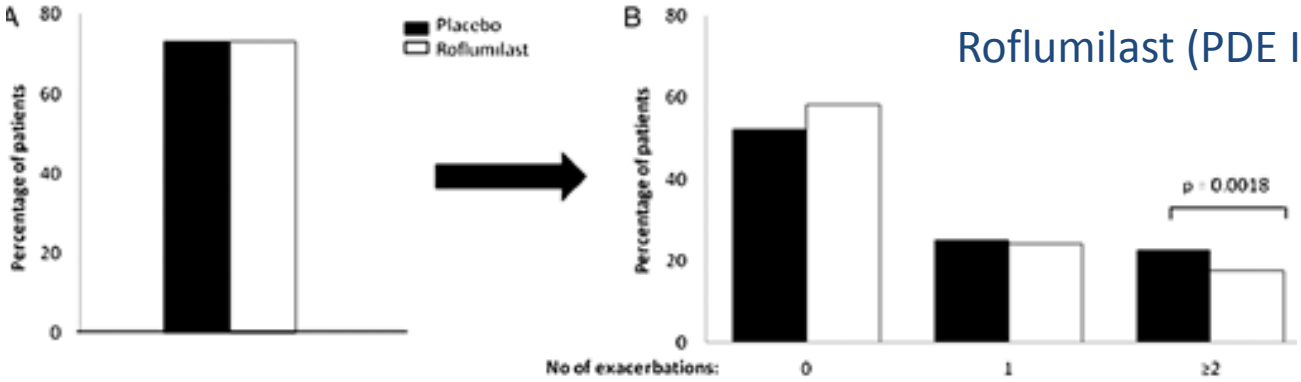
- Oral N acetylcysteine : Grade 2B (>2 AECOPD)

Eur Respir Rev. 2015 Sep;24(137):451-61

Efficacy of Roflumilast in the COPD Frequent Exacerbator Phenotype

Year 0

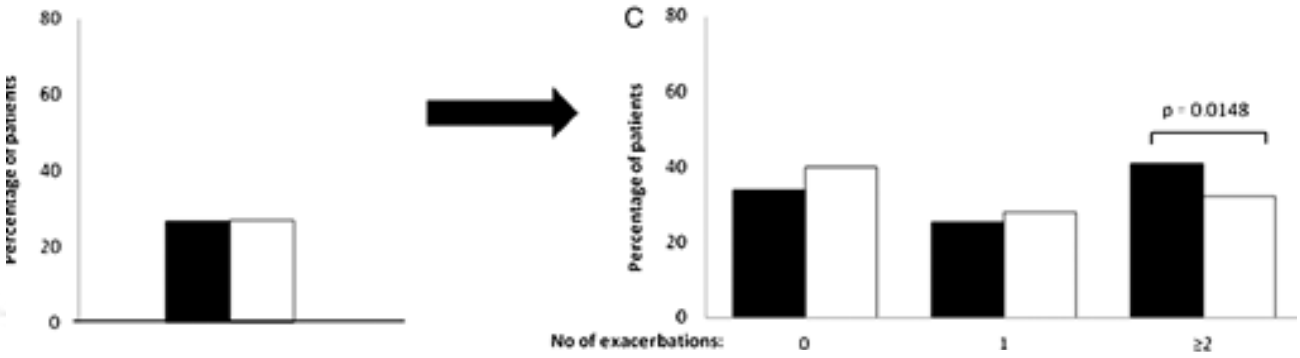
Year 1



Roflumilast (PDE IV inhibitor) (Grade 2A)

Infrequent exacerbators

Infrequent exacerbators >2 exacerbations



>2 exacerbations

Infrequent exacerbators >2 exacerbations

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Chest. 2013;143(5):1302-1311

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Other Oral Drugs

- Theophylline ER bid (Grade 2B)
- Use lowest effective dose
- Monitor for side effects

Non-Pharmacologic Measures

PREVENTION OF AECOPD

Non-pharmacologic Evidence Based Measures that reduce COPD exacerbations

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

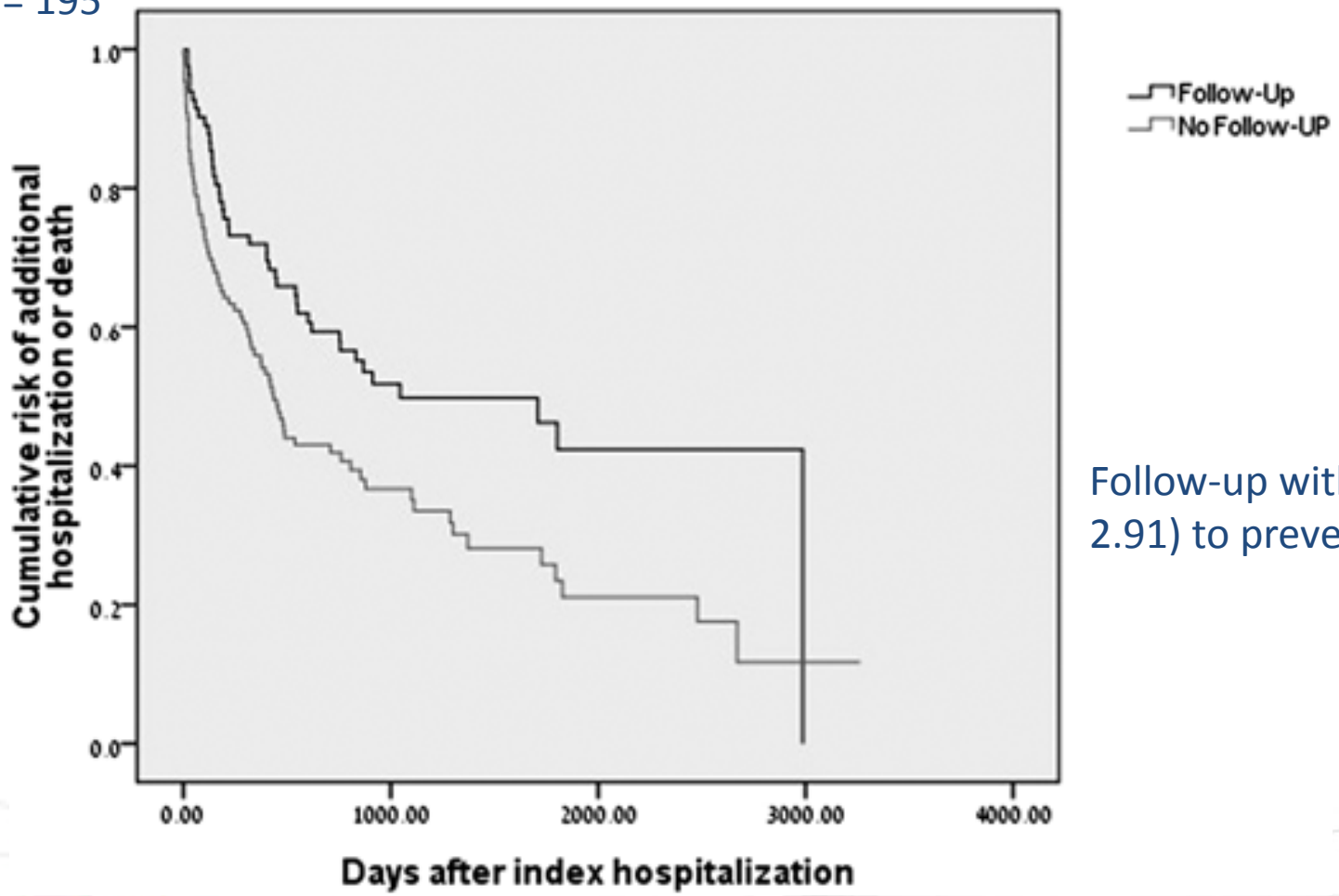
Adapted from Global Initiative for Chronic Obstructive Lung Disease.

Likely ineffective measures for prevention of AECOPD

- Telemedicine Programs
- Pulmonary Rehabilitation > 4 weeks after Hospitalization (still improves SOB, QALY, etc.)
- Pneumococcal / Influenza (?) vaccination
- COPD Action Plans alone
- Statins (Grade 1B), TNF inhibitors

Cumulative risk of additional hospitalization or death and pulmonary follow-up

N= 195



Follow-up within 30 days (RR: 2.91) to prevent readmission

Conclusion

- Identify patients at risk for AECOPD
- Pulmonary consultation for AECOPD
- Assess adherence to bronchodilator therapy
- Consider treatment best suited for your patient
- Consider adjuvant oral therapies if bronchodilators insufficient

Lung Health Awareness Month

WORLD COPD DAY: November 18, 2015

http://tinyurl.com/copd-angelos (NIHLBI)

#COPDChat

http://www.lungforce.org/

http://www.copdfoundation.org/

www.lung.org

https://www.chestnet.org/Foundation/Patient-Education-Resources/COPD

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