

COPD 2019: Current Guidelines

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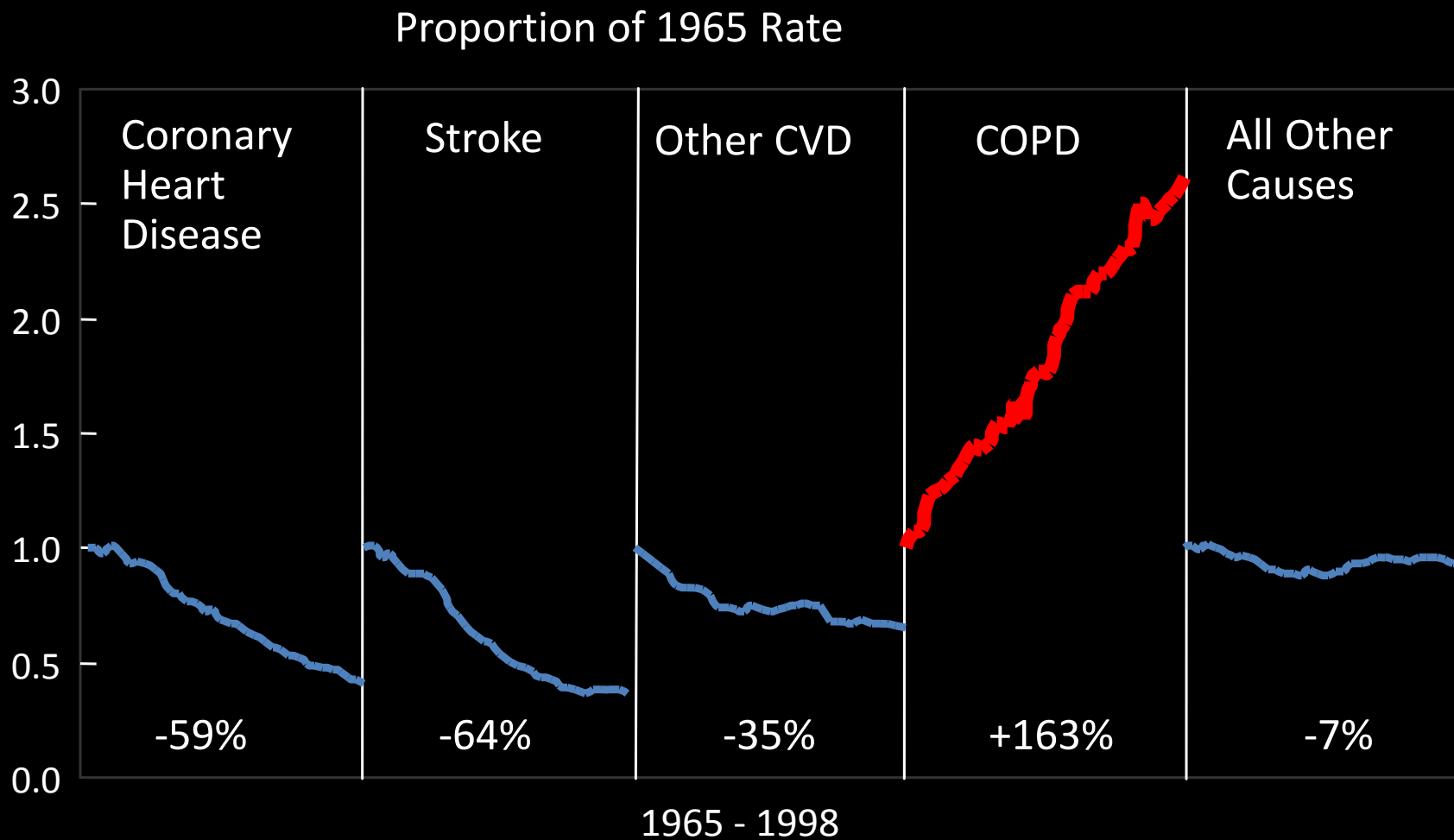
Disclosures

- Non-promotional lectures on lung inflammation- Genentech
- Consultant on research directions- AstraZeneca/Sunovion/Boehringer Ingeheim

Learning Objectives

1. Outline the changes on the 2017-18 GOLD COPD Guideline
2. Assess the implications of a new definition of COPD
3. Apply guideline-approved practice strategies to stage and treat COPD
4. Recognize effects of the COPD exacerbation and the measures that have been shown to prevent them

Percent Change in Age-adjusted U.S. Death Rates



PINK PUFFER

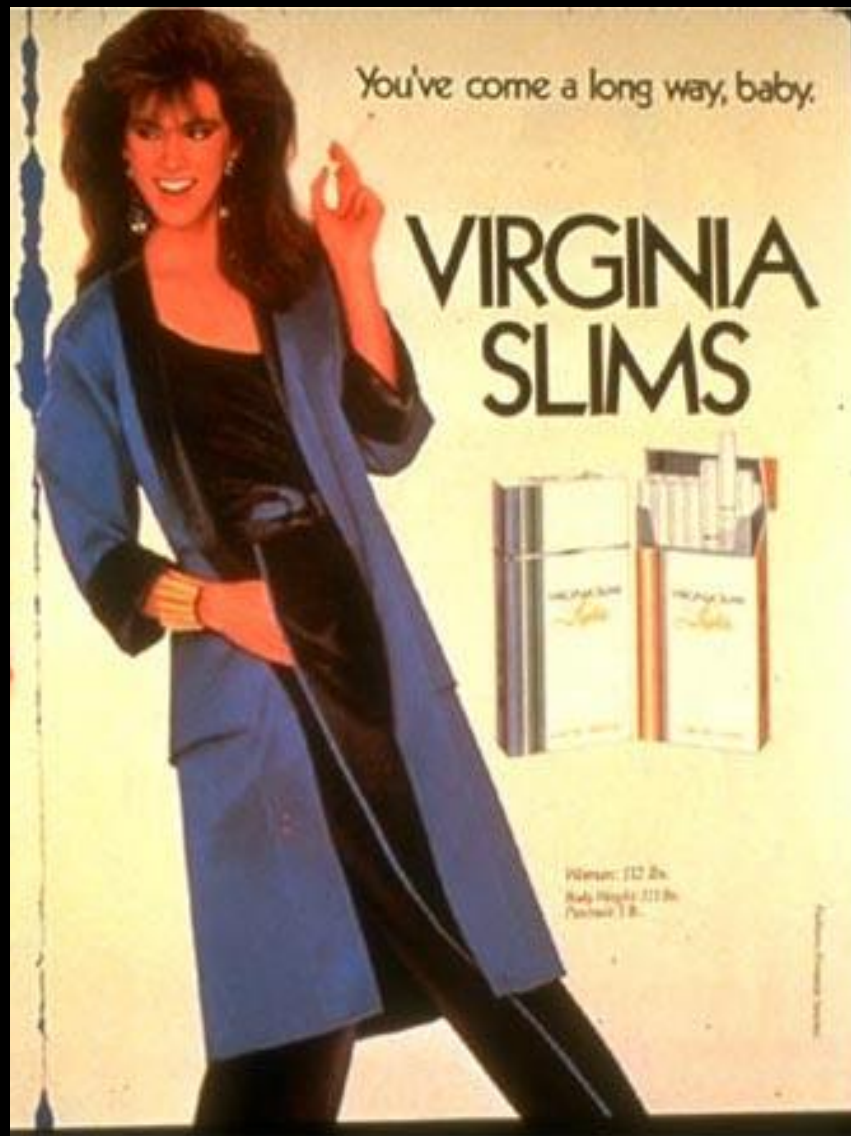


BLUE BLOATER



You've come a long way, baby.

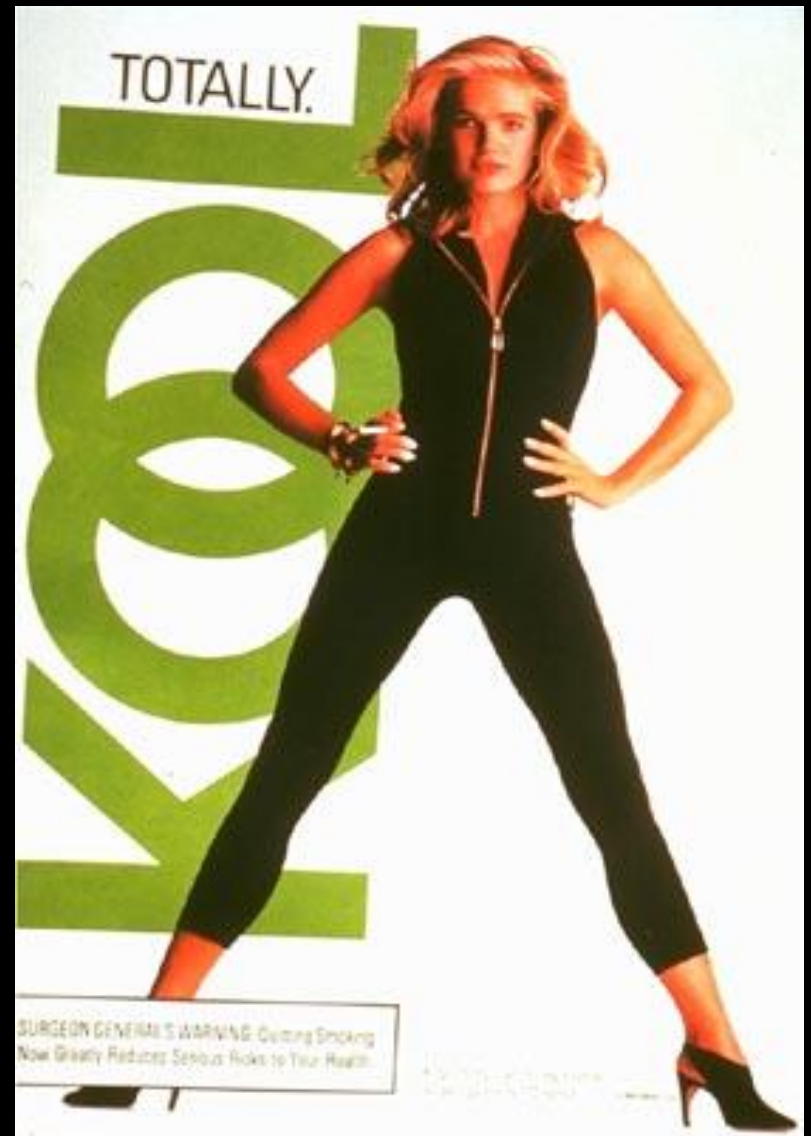
VIRGINIA SLIMS



Winston: 112 20s
 Ruby Lights: 112 20s
 Perfect 10s

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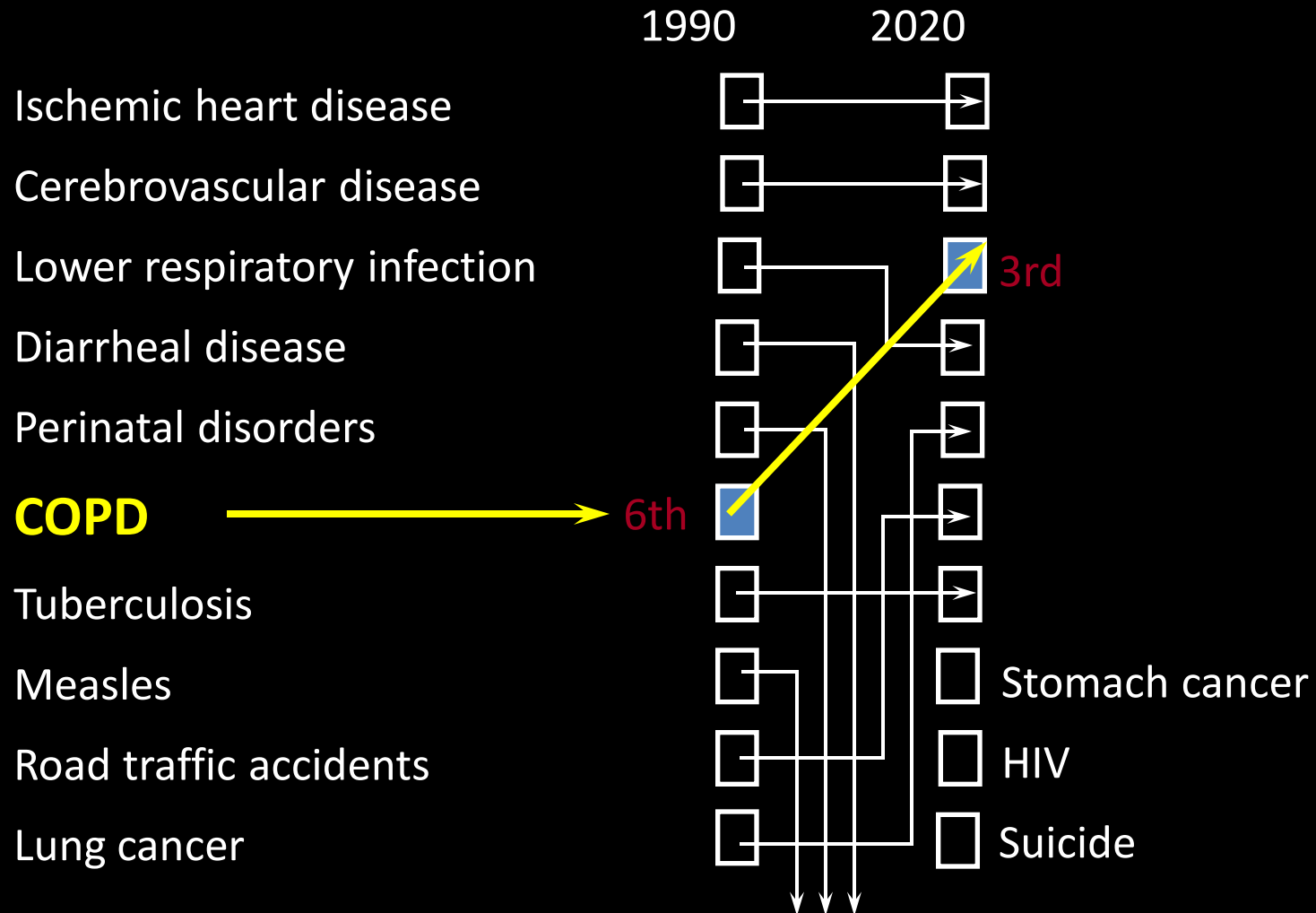
TOTALLY.



SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.

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Future Global Mortality



Global Initiative for Chronic Obstructive Lung Disease



**GLOBAL STRATEGY FOR THE DIAGNOSIS,
MANAGEMENT, AND PREVENTION OF
CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

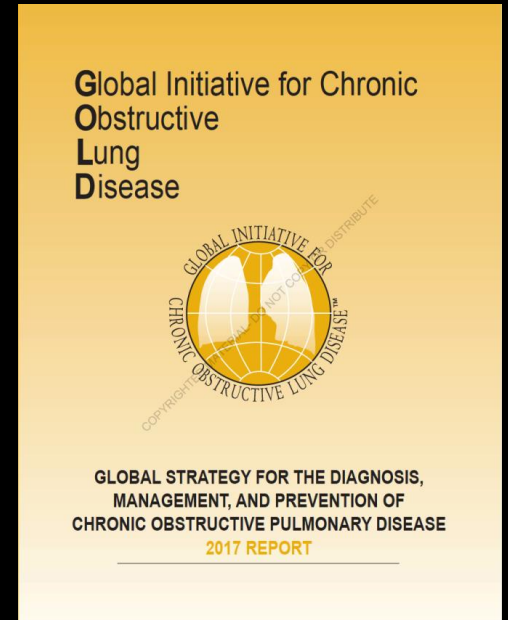
2017 REPORT

COPD: The Epidemic

- **15 million** patients have COPD¹
- **64%** diagnosed by a PCP **and 28%** diagnosed by a specialist
- **7%** diagnosed by other HCP
- **31%-43%** receive spirometry-confirmed diagnosis²
- **12 million** patients remain undiagnosed³
- **<50% of PCPs** are aware of the existence of GOLD guidelines and even fewer have read them⁴

Outline

- Definition of COPD
- Staging of COPD
- Treatment algorithms
- Delivery Devices
- Oxygen therapy for COPD
- “De-escalation”
- Acute Exacerbation of COPD





GOLD Definition of COPD

- n COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced *chronic inflammatory response* in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients

GOLD 2015



**.....an abnormal inflammatory response
of the lungs to noxious particles or gases**



GOLD Definition of COPD-Changed

- n COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced *chronic inflammatory response* in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients

GOLD 2015

- n “COPD is a common, preventable and treatable disease that is characterized by persistent *respiratory symptoms* and airflow limitation that is due to airway and/or alveolar abnormalities *usually* caused by significant exposure to noxious particles or gases.”

GOLD 2017/2018

COPD: Pathophysiology



Tobacco Smoke



Occupational Dust
& Air Pollution

Inflammation

Small Airway Disease
Airway Inflammation
Airway Remodeling



Parenchymal Destruction
Loss of alveolar attachments
Decrease of elastic recoil

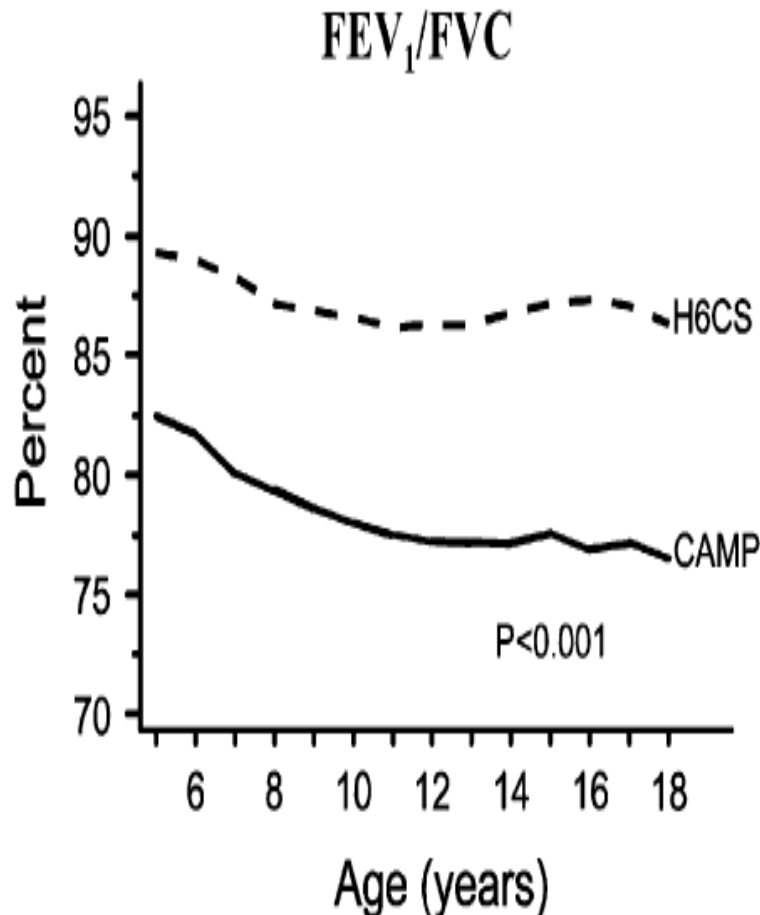
Airflow Limitation

Childhood Asthma

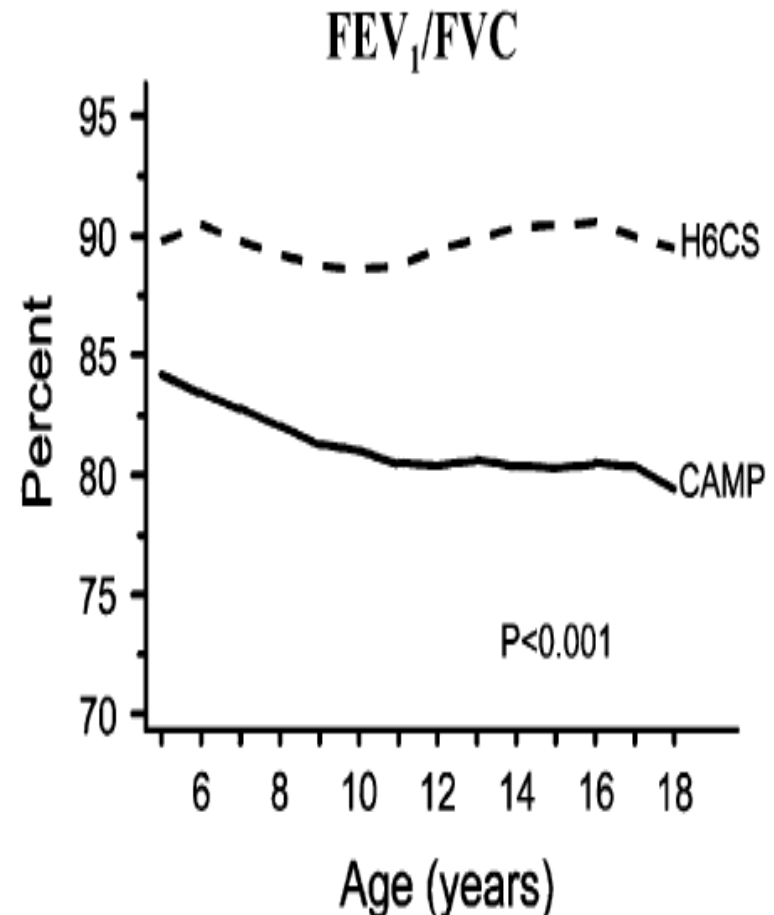


Progression of Asthma Measured by Lung Function in the Childhood Asthma Management Program

Boys

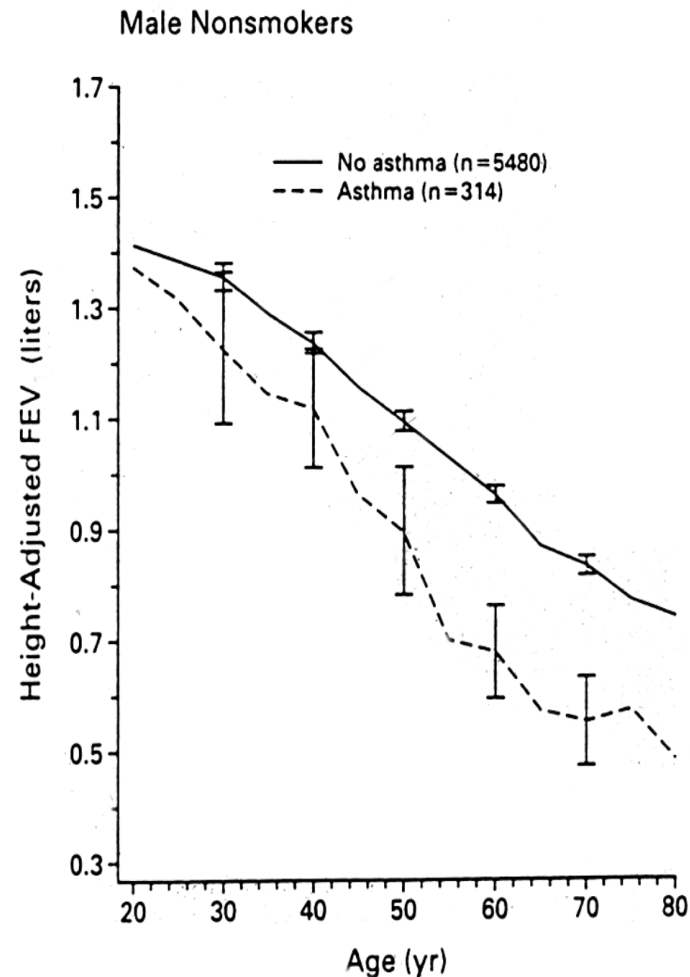


Girls



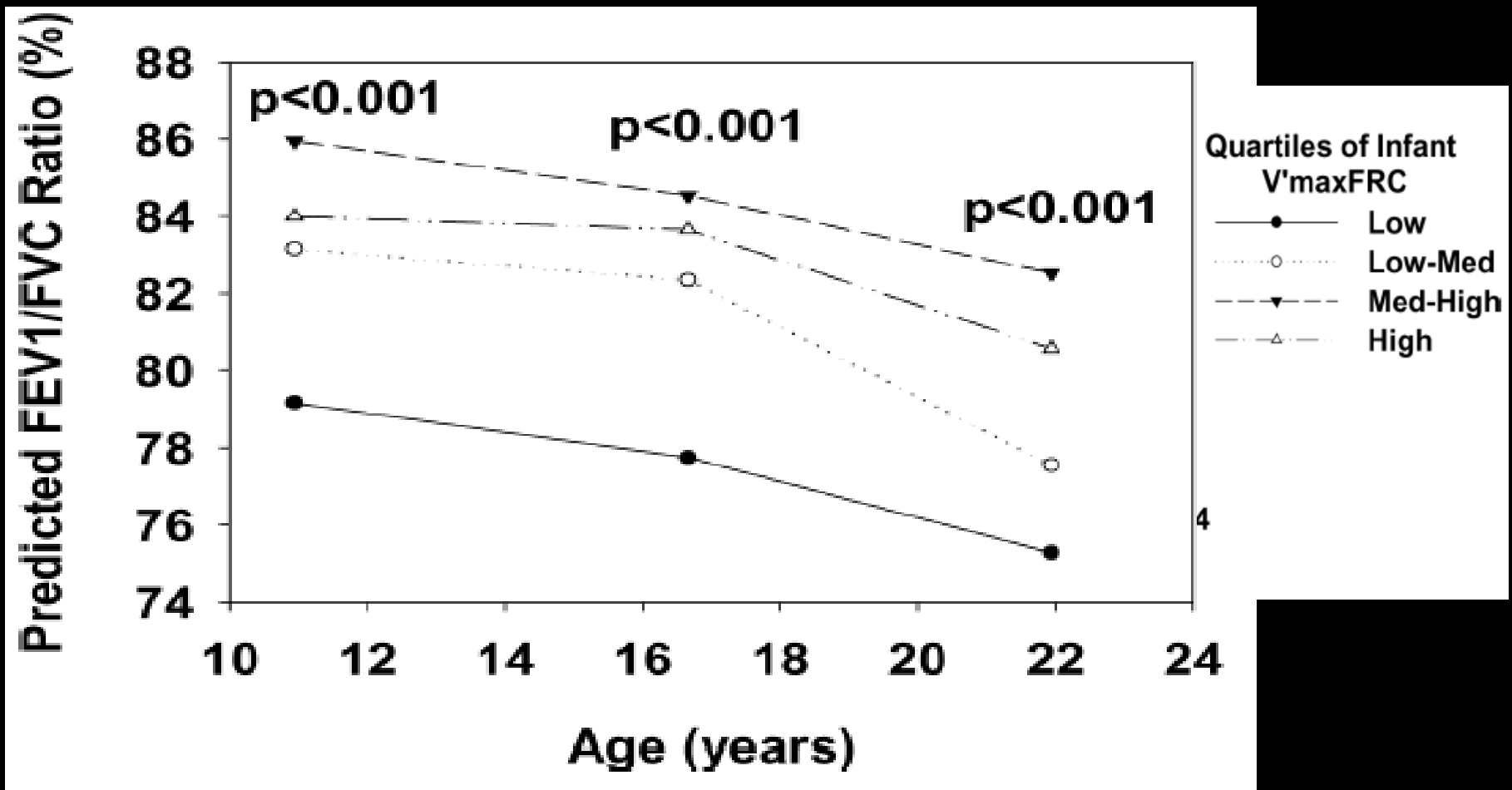
A 15-Year follow-up Study of Ventilatory Function in Adults With Asthma

- Analyzed FEV1 over 15 years in the Copenhagen Heart Study in 17,506 pts.
- Greater decline in subjects with asthma (38ml/yr vs. 22 ml/year)
- A 60 y.o. 175 cm tall non-smoking male had an FEV1 of 3.05 vs. 1.99 for a similar asthmatic



Poor airway function in early infancy and lung function by age 22 years: a non-selective longitudinal cohort study

123 babies born in Tucson . Lung function at 2 months and 11, 16, 22

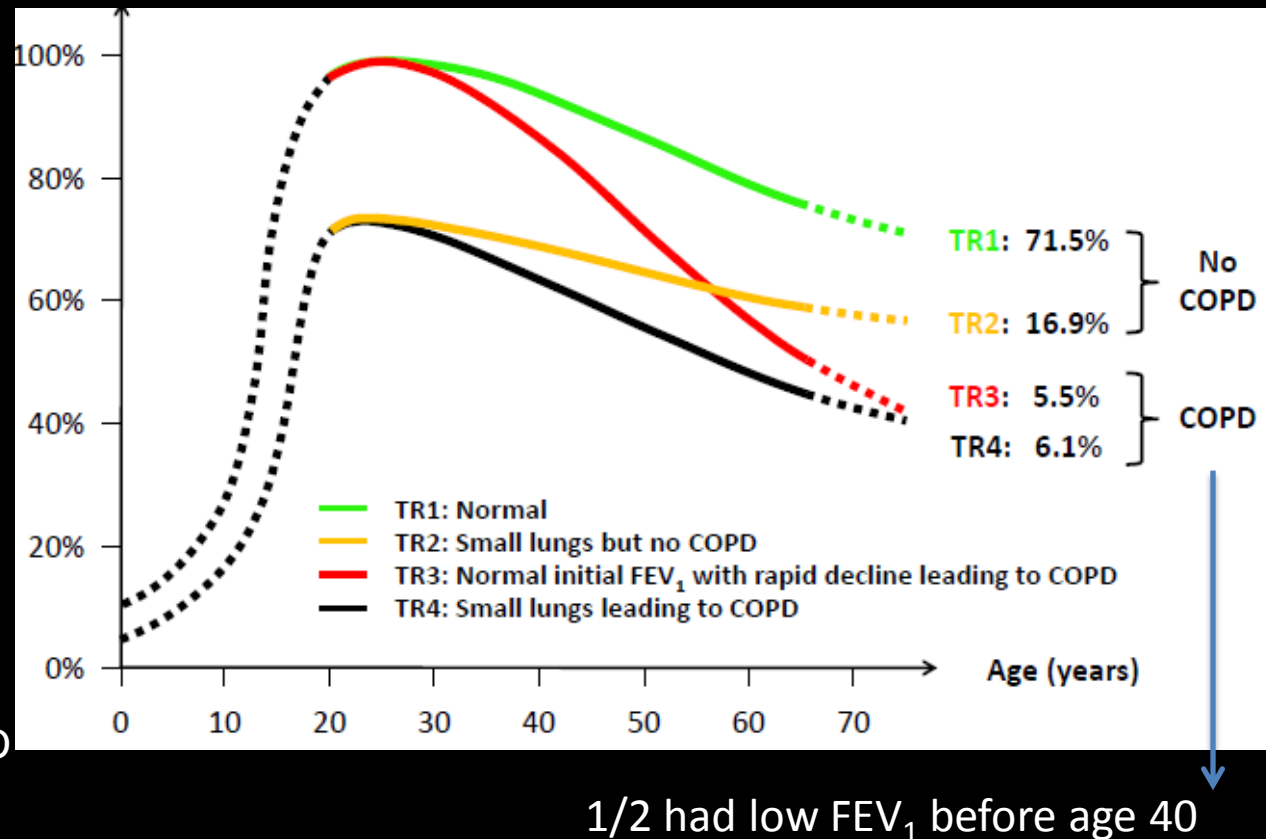




Poorer lung function in early adulthood may predispose to COPD

Incidence of COPD higher when FEV₁ was <80% predicted before age 40 (26% vs 7%; $P < 0.001$)

Accelerated decline in FEV₁ not an obligate feature of COPD



Conclusions

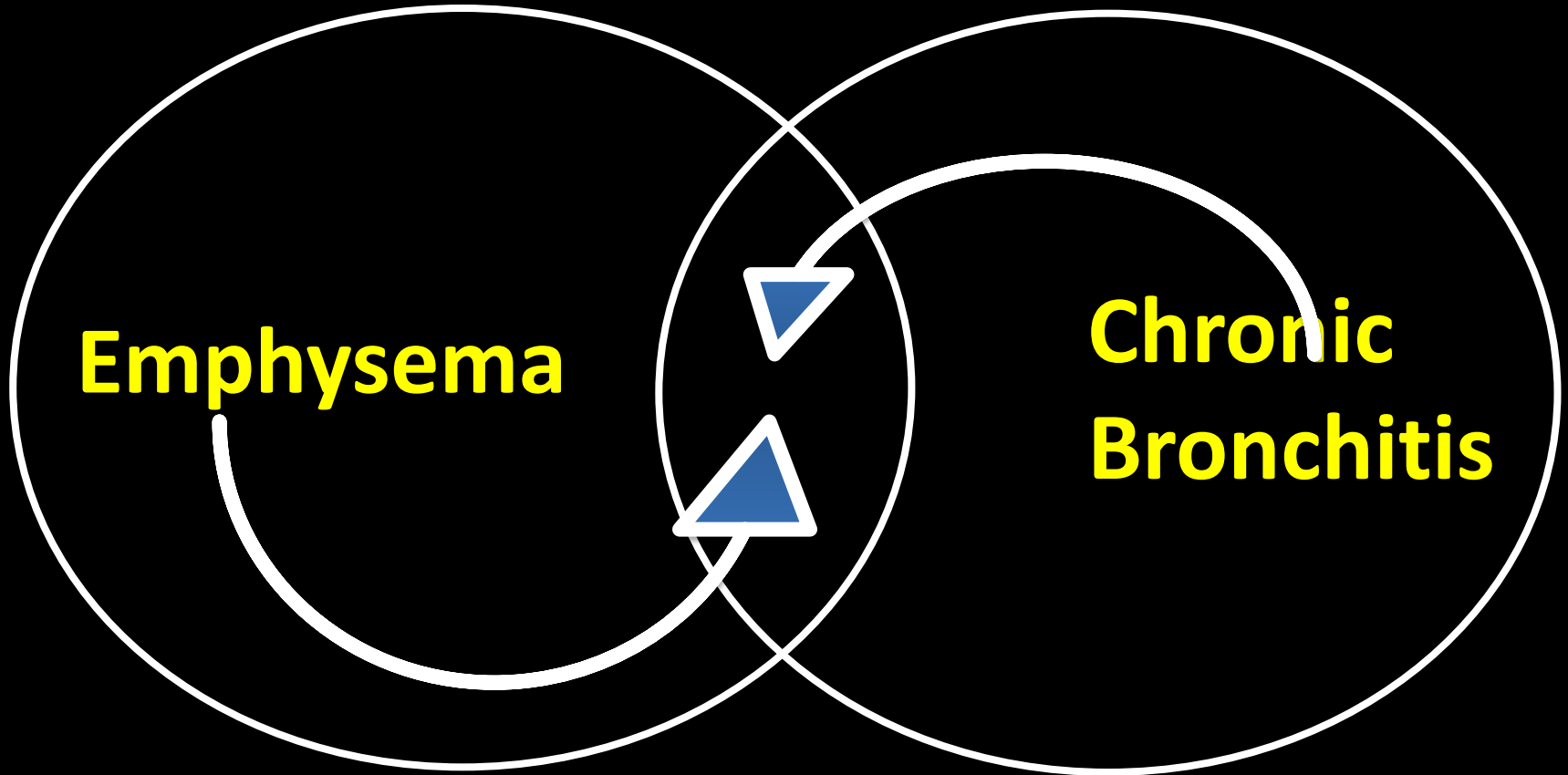
- Low lung function “Early” in life is as important a risk for COPD development
- A combination of a rapid COPD decline starting at low lung function is even worse
- Asthma at an early age may be associated with a rapid decline in lung function and a combination of asthma and starting at low lung function may lead to severe fixed airflow obstruction.

No known risk factors and...

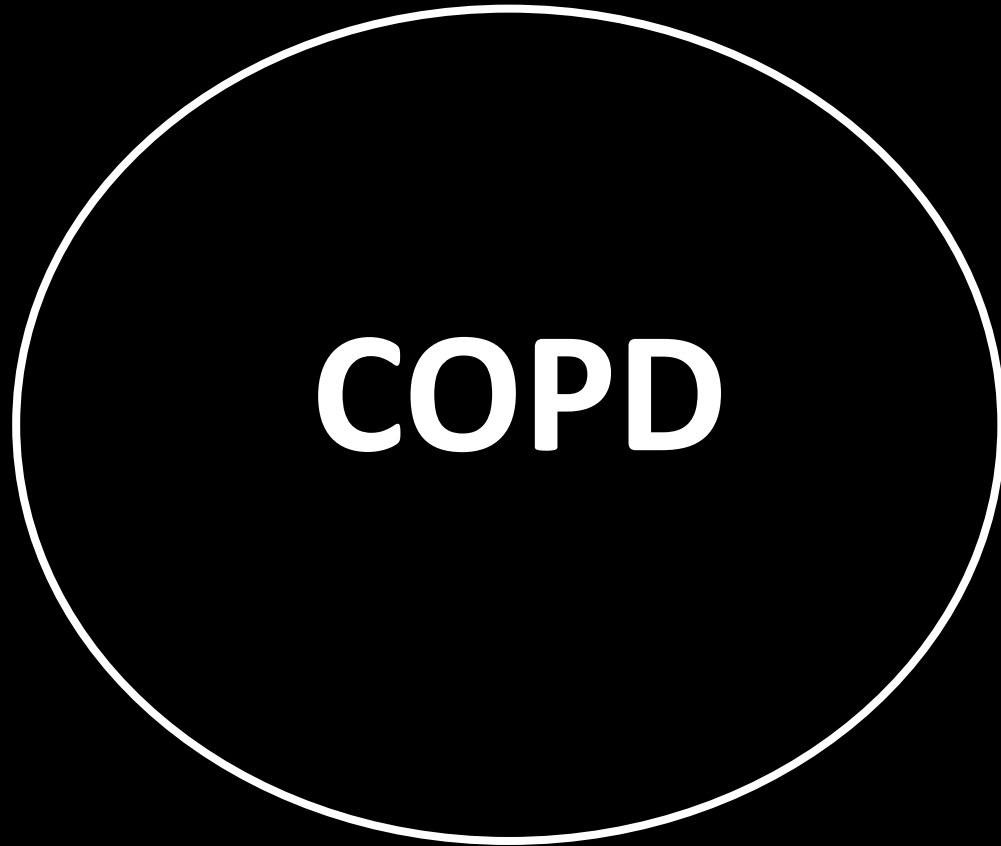
1. low lung function starting early in life resulting in fixed airflow obstruction later in life.
2. asthma resulting in fixed airflow obstruction later in life.

Is this COPD?

Current View



Current View



A Single Disease

COPD 2017

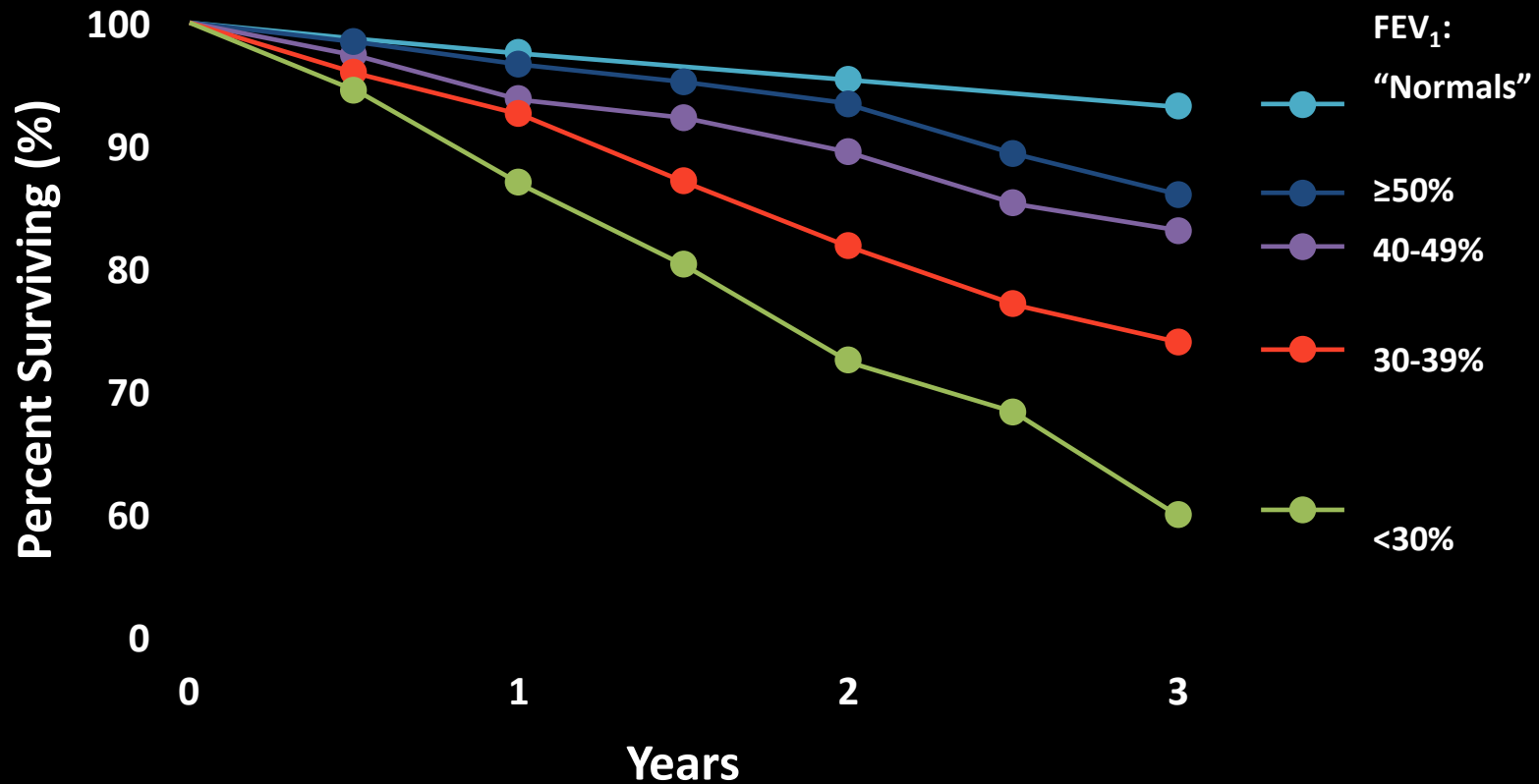
Staging

GOLD Classification of COPD

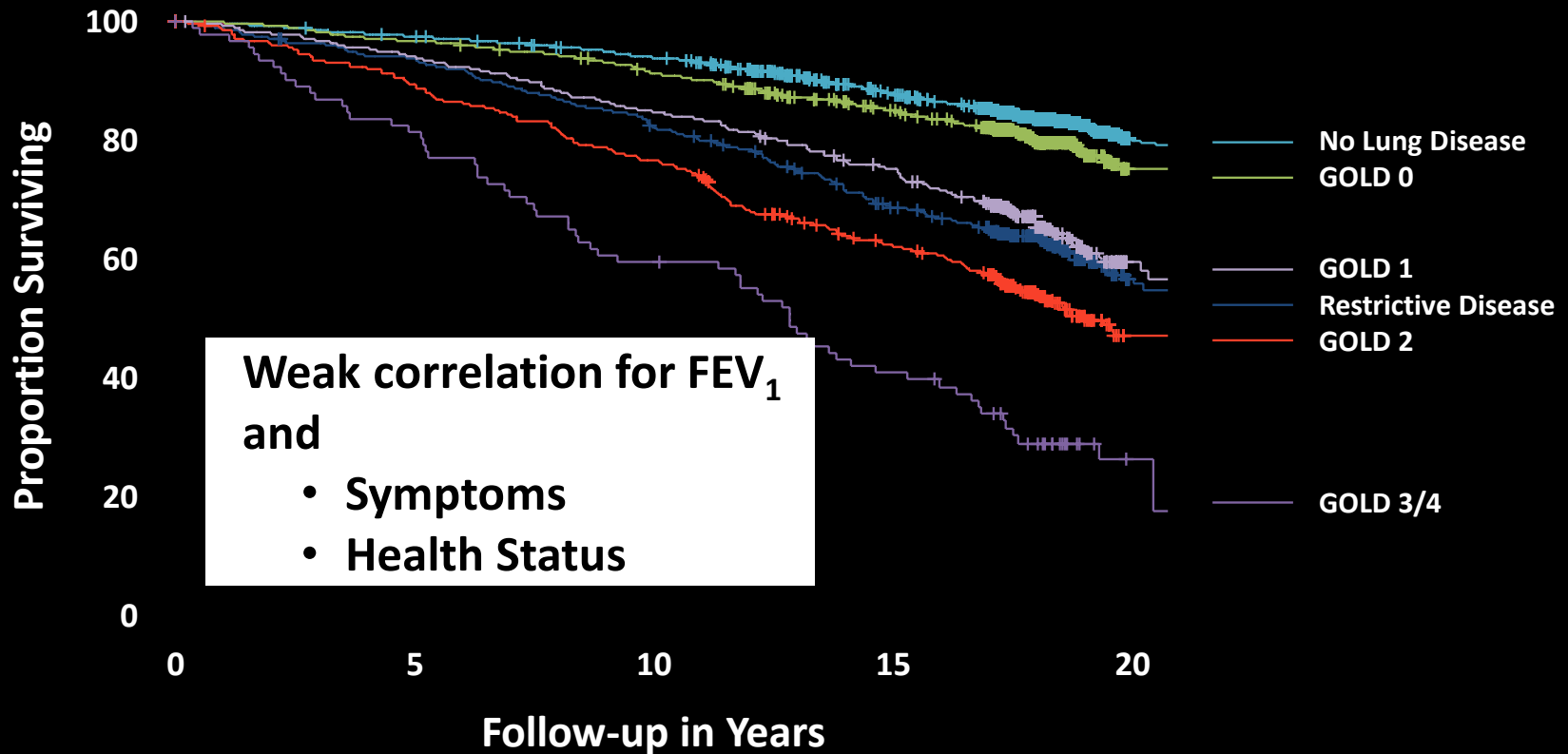
Staging by Spirometry

Stage I: Mild	$FEV_1/FVC < 0.70$ $FEV_1 \geq 80\%$ predicted
Stage II: Moderate	$FEV_1/FVC < 0.70$ $50\% \leq FEV_1 < 80\%$ predicted
Stage III: Severe	$FEV_1/FVC < 0.70$ $30\% \leq FEV_1 < 50\%$ predicted
Stage IV: Very Severe	$FEV_1/FVC < 0.70$ $FEV_1 < 30\%$ predicted <i>or</i> $FEV_1 < 50\%$ predicted <i>plus</i> chronic respiratory failure

Relationship between Lung Function and Mortality



Survival by Lung Function Impairment



GOLD Assessment of Severity

C	D	2 IV
A	B	1 Risk Exacerbation history
		0
mMRC 0-1 CAT <10	mMRC ≥2 CAT ≥ 10	
Symptoms mMRC or CAT Score		

mMRC Breathlessness Scale

Grade	Description of Breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

Chris Stenton. The MRC breathlessness scale. *Occup Med (Lond)*(2008);58(3): 226-227 doi:10.1093/occmed/kqn162, Table 1.
By permission of Oxford University Press on behalf of the Society of Occupational Medicine.
A mMRC score of 1 or more suggests significant symptoms.

Case

- A 55 yo Male has a 40 pack year history of smoking
- Has a daily “smokers cough” and has needed antibiotics two times in the past year for a winter and spring chest cold
- Has to stop walking because of breathlessness after a few minutes on level ground

Current studies	Pre-bronchodilator	Post-bronchodilator
FEV ₁	2.44 L (82% predicted)	2.52 L (85% predicted)
FEV ₁ /FVC (%)	71%	72%

55 yo Male

- COPD risk factor
- Chronic bronchitis by history
- Exacerbation 2 mMRC=Grade 3
- His GOLD Stage=?

NO Airflow Obstruction!
No COPD!

$FEV_1/FVC (\%)=73\%$

Risk Exacerbation history	2 IV	C	D
	1	A	B
0			
		mMRC 0-1 CAT <10	mMRC ≥2 CAT ≥ 10
		Symptoms mMRC or CAT SCORE	

Clinical and Radiologic Disease in Smokers With Normal Spirometry

- COPDGene study “GOLD 0”
- Findings:
 - worse quality of life
 - lower 6-minute walk distance
 - half had CT evidence of emphysema or airway thickening

“There are 35 million current and former smokers older than 55 years in the United States who may have unrecognized disease or impairment”.

Smokers with a normal FEV₁

Spiromics Study

- Ever- or former smokers compared to never smokers with normal FEV₁/FVC,%
- CAT cutoff score of 10 or greater, was observed in 50% of smokers; prevalence of CMH* 33% in symptomatic smokers
- They had significantly less physical activity, slightly lower lung function, more respiratory exacerbations, and HRCT** findings consistent with greater airway wall thickening and low percentage emphysema.

*CMH=chronic mucus hypesecretion **HRCT Hi Resolution CT scan

COPD 2017

Therapeutics

GOLD 2017 Guidance on the Importance of Delivery

The choice of inhaler device will depend on availability, cost, the prescribing physician, and the skills and ability of the patient....

....It is essential to ensure that inhaler technique is correct and to re-check this at each visit.¹

**Inhalation delivery barriers can lead to under treatment
or unintentional overtreatment**

GOLD 2017

GOLD COPD 2017

Therapeutics

- The importance of using inhaler devices correctly and how to deal with poor adherence is now emphasized**

Up to 68% of patients do not use their inhaler well enough to benefit from the prescribed medication¹

~50% of internal medicine specialist residents did Not know the correct order of steps when using most common rescue inhaler device²

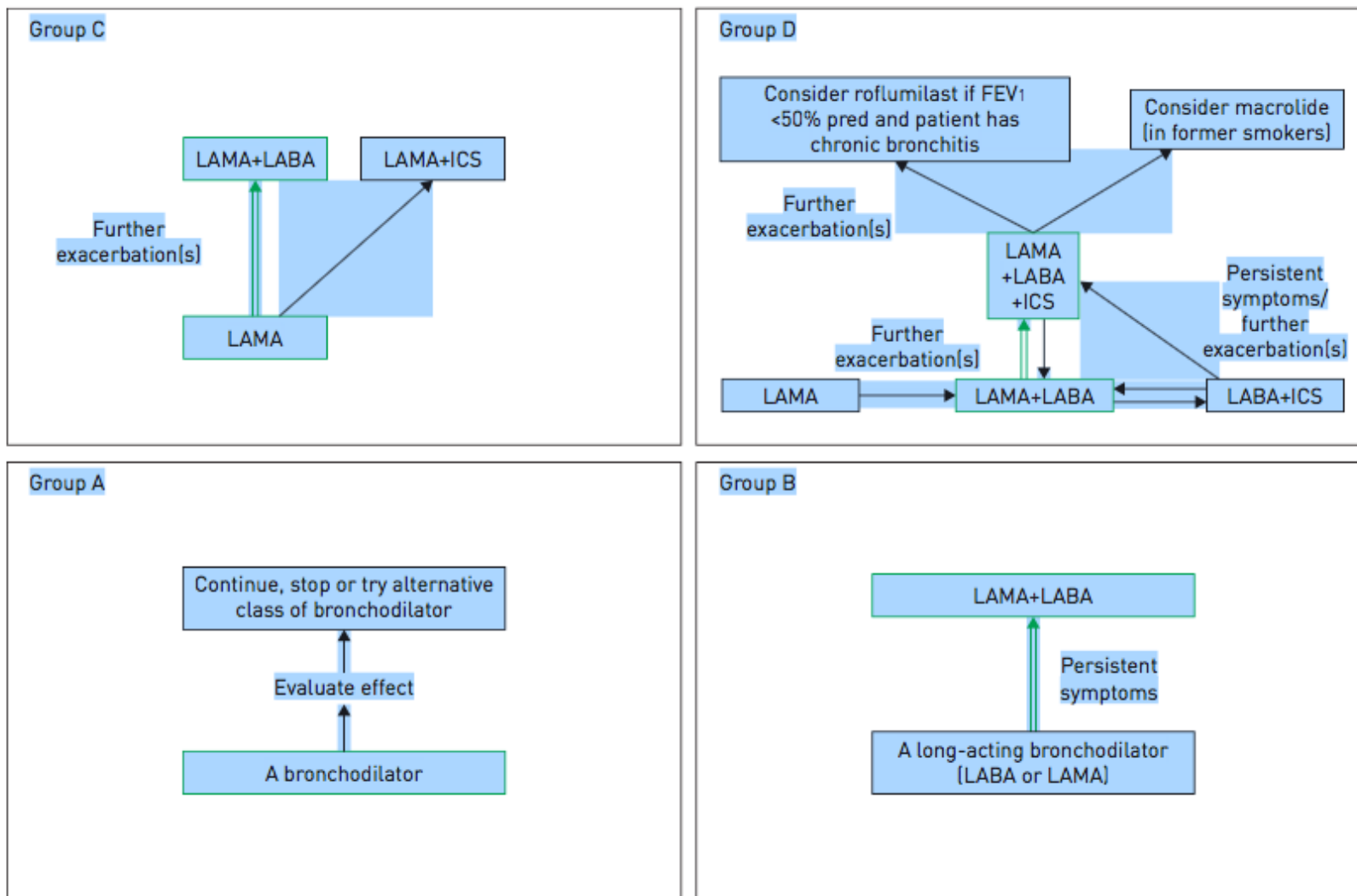
1. Fink JB, et al. *Respir Care*. 2005;50(10):1360-1375

2. Han MK, et al. *Lancet Respir Med*. 2016;4(6):473-526.

COPD

Treatment algorithms

Manage Stable COPD: Pharmacologic Therapy



⇒: preferred treatment

Oxygen Therapy

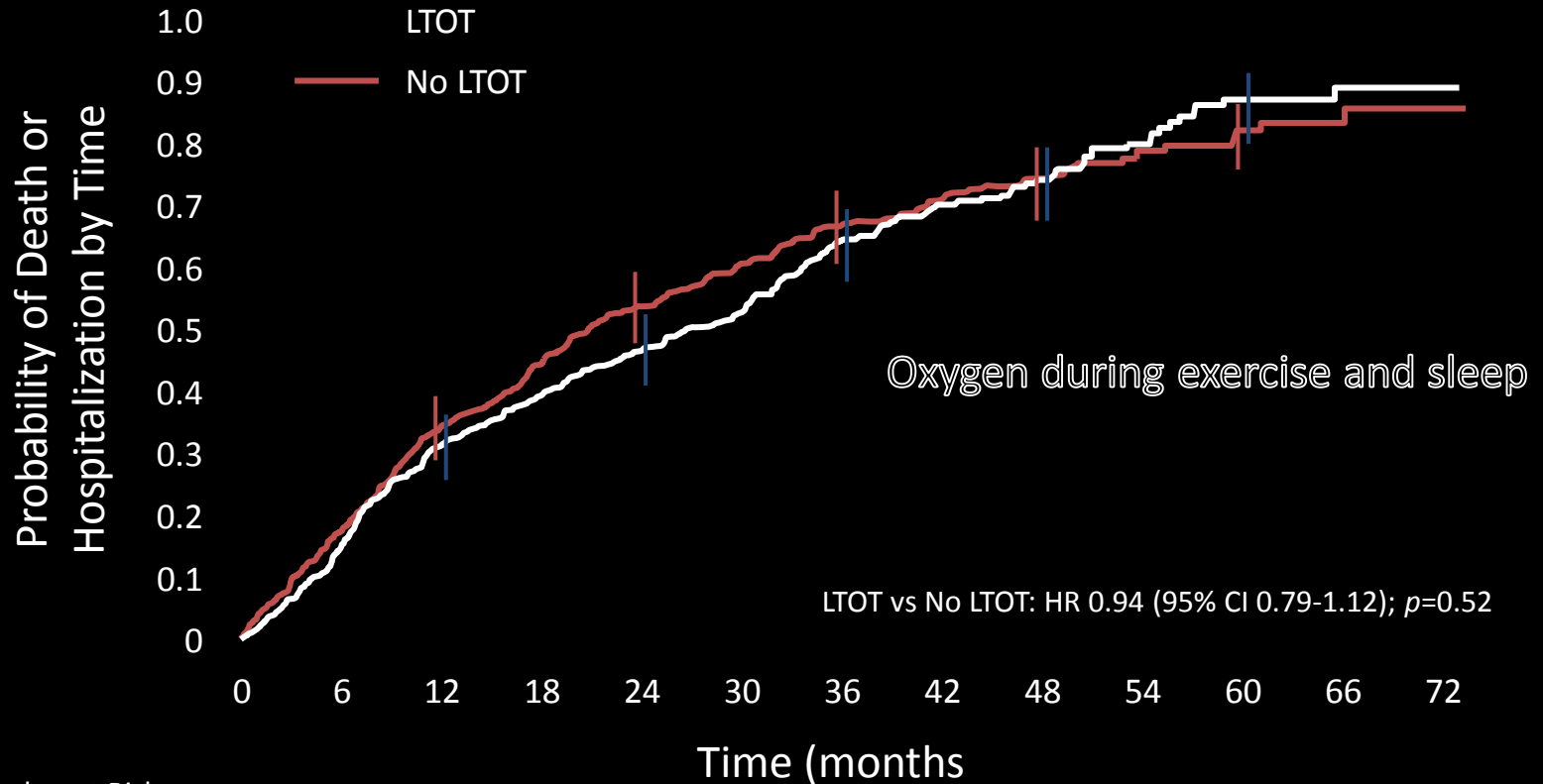
- Long-term oxygen therapy is recommended in stable patients who have:
- PaO₂ at or below 7.3 kPa (55 mm Hg) or SaO₂ at or below 88%, with or without hypercapnia confirmed twice over a 3-week period or
- PaO₂ between 7.3 kPa (55 mm Hg) and 8.0 kPa (60 mm Hg), or SaO₂ of 88%, if there is evidence of pulmonary hypertension, peripheral edema suggesting congestive cardiac failure, or polycythemia (hematocrit >55%)

Oxygen for exercise hypoxemia?

kPa = kilopascal; PaO₂ = partial pressure of oxygen dissolved in the blood; SaO₂ = saturation of oxygen bound to hemoglobin.

Global Initiative for Chronic Obstructive Pulmonary Disease (Revised 2017). GOLD website. www.goldcopd.org. Accessed April 27, 2017.

LOTT Primary Outcome: Death or 1st Hospitalization



Number at Risk

No LTOT	370	304	232	181	139	102	76	59	43	29	21	7	1
LTOT	368	314	243	198	158	125	86	61	44	24	13	6	1

CI = confidence interval; HR = hazard ratio; LTOT = long-term oxygen therapy; no. = number.

Long-Term Oxygen Treatment Trial Research Group. *N Engl J Med.* 2016;375:1617-1627.

GOLD 2017

“We now suggest escalation and *de-escalation* strategies.....with resolution of some symptoms that may subsequently require less therapy.”

“We acknowledge that treatment escalation has not been systematically tested; trials of de-escalation are also limited and only include ICSs”

The WISDOM Trial¹

- 12 month study; Severe COPD with exacerbations on triple therapy (LABA/ICS/LAMA). ICS withdrawn
LABA/LAMA vs Triple Therapy
- Withdrawal did not increase exacerbations of COPD; some decrease in lung function
- In WISDOM the chance of exacerbating off ICS greater when eosinophil count >300 cells/mcL

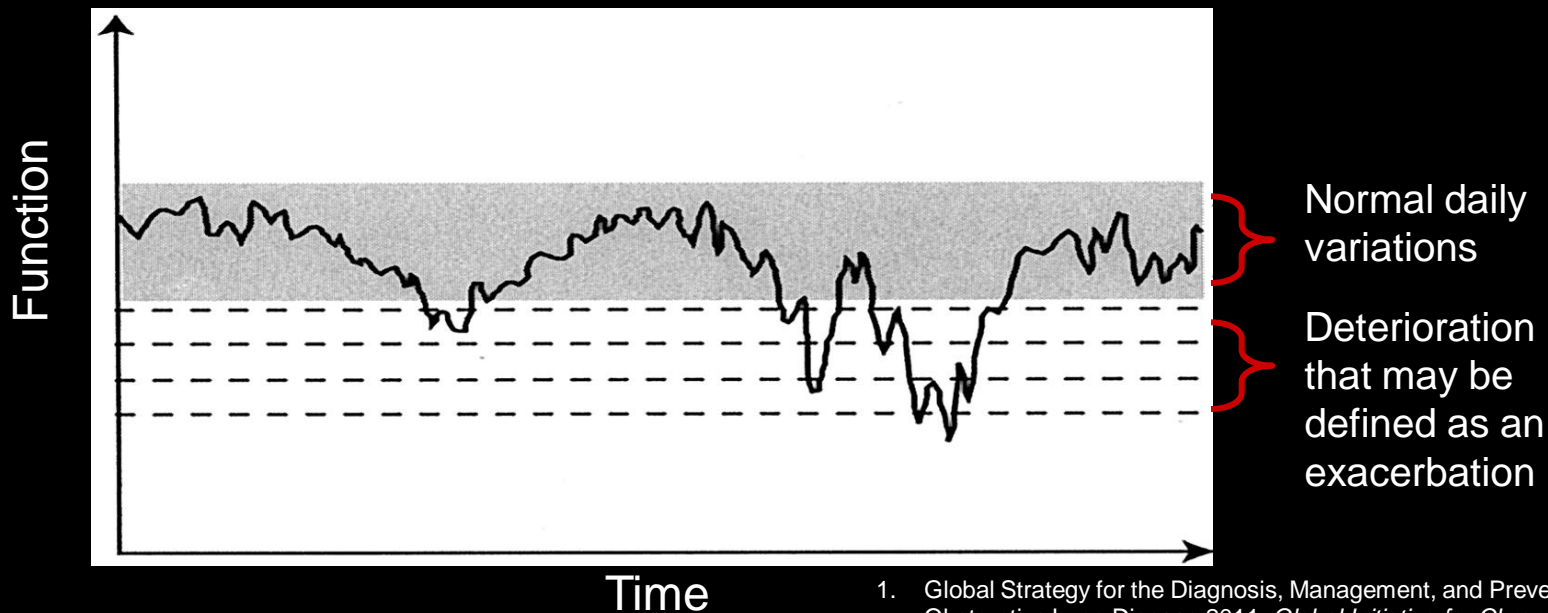
Therapeutics

Corticosteroids for COPD

- Blood eosinophil counts may predict the efficacy of ICS in preventing exacerbations in patients with COPD, but prospective studies are needed.
- In patients with lower blood eosinophil counts ($< 2\%$) there is evidence for a poor response to ICS and an increased risk of pneumonia.

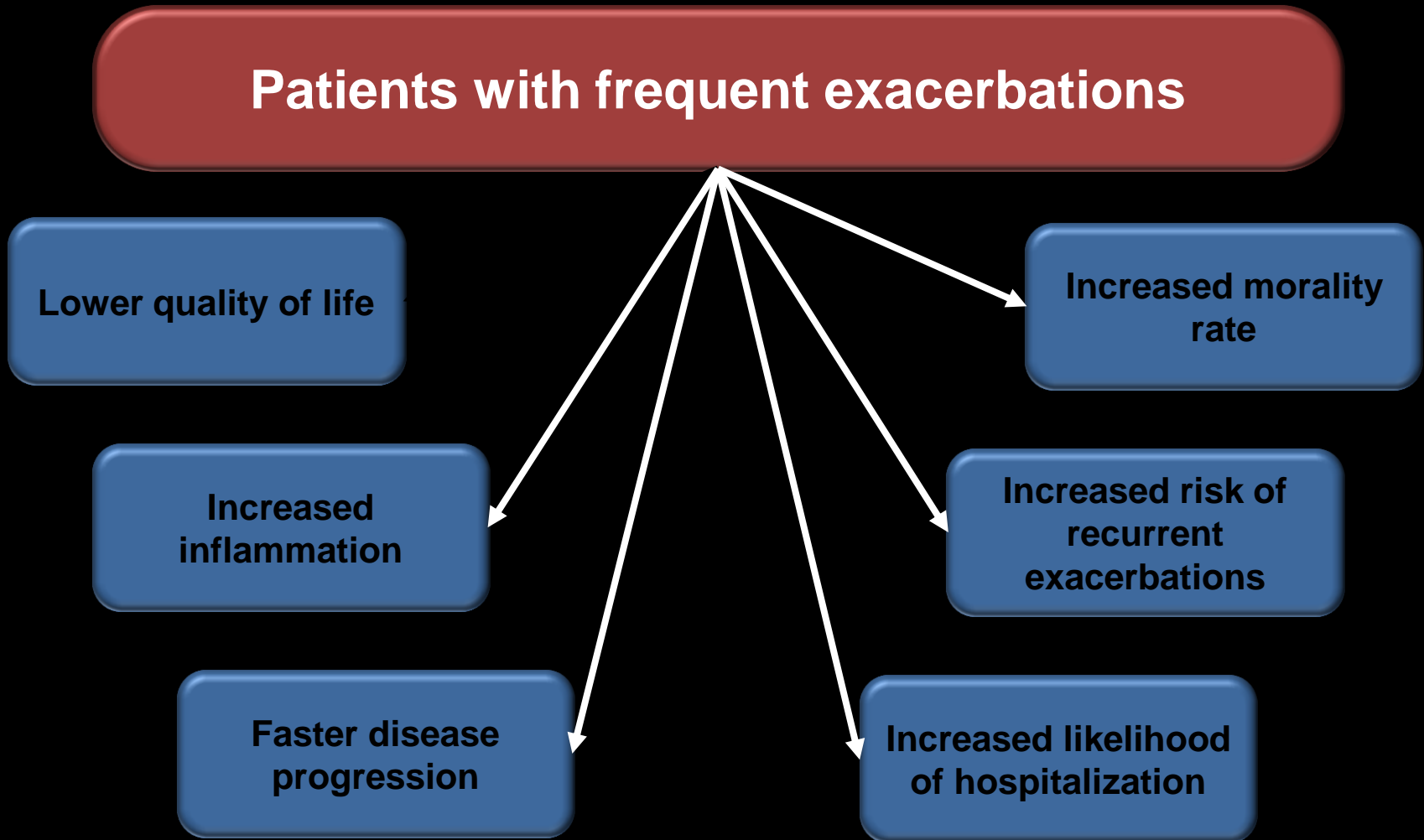
What is an AECOPD?

- 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.”

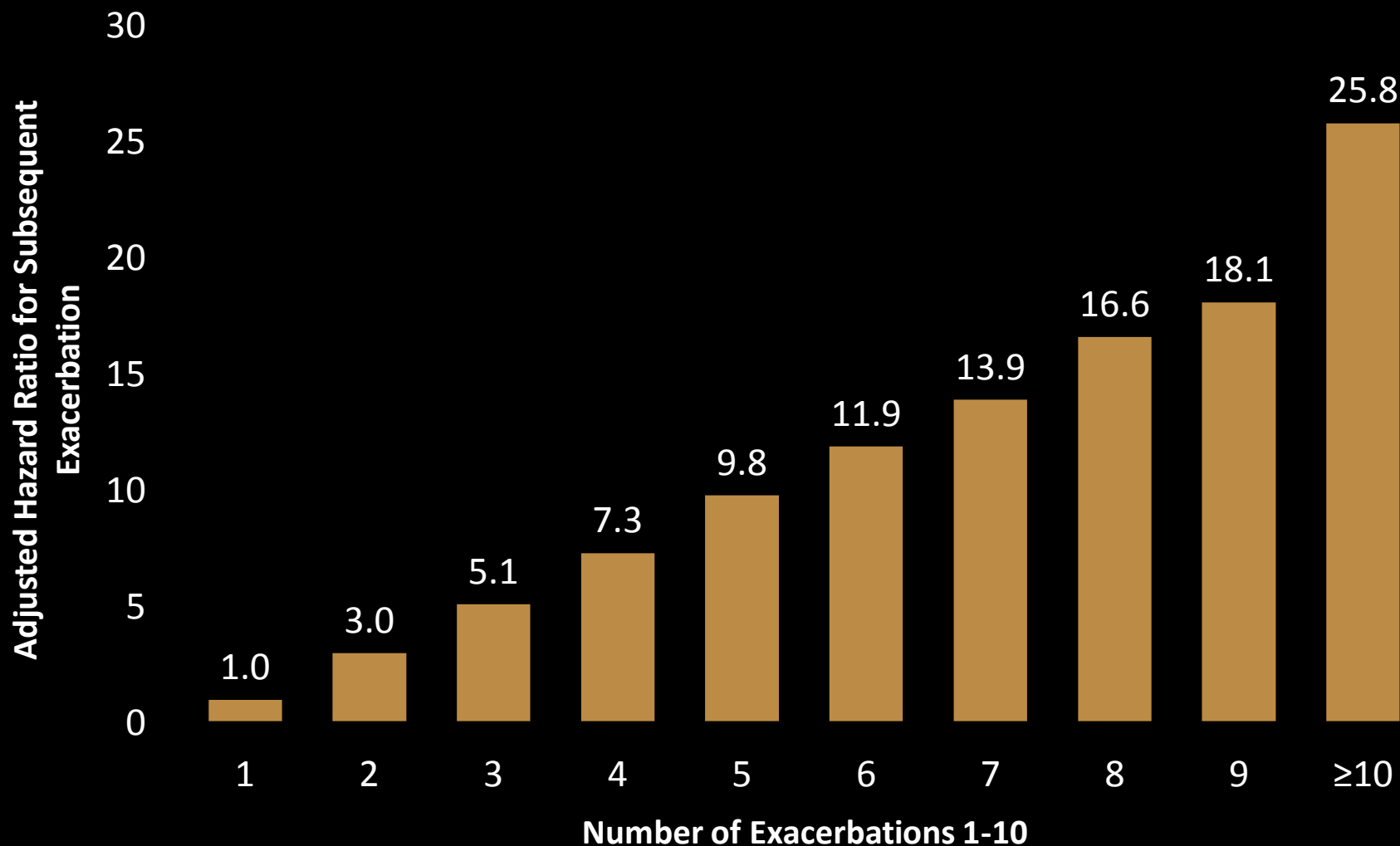


1. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2011. *Global Initiative for Chronic Obstructive Lung Disease*. www.goldcopd.org. Accessed March 30, 2012.
2. Rodriguez-Roisin R. *CHEST*. 2000;117:398S-401S.
3. Celli BR, et al. *Eur Resp J*. 2004;23:932-46.

Impact of Frequent COPD Exacerbations

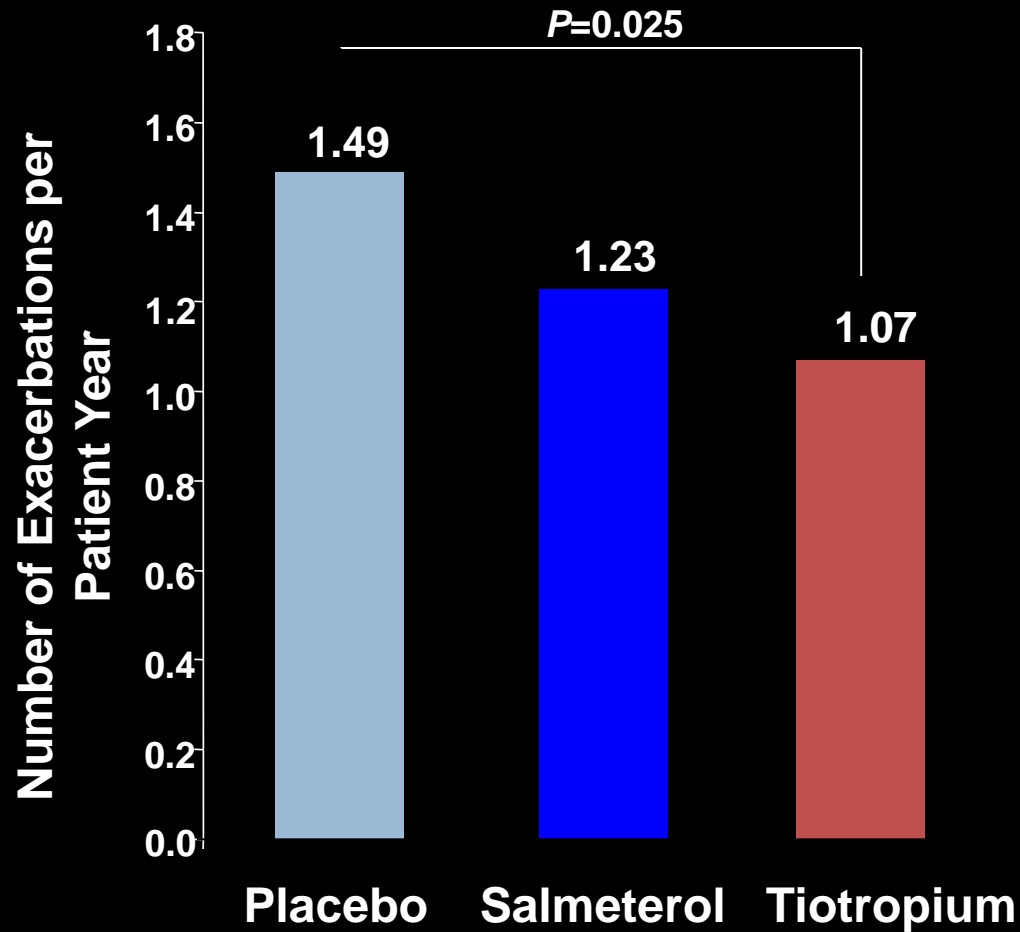


Risk for Subsequent COPD Exacerbation

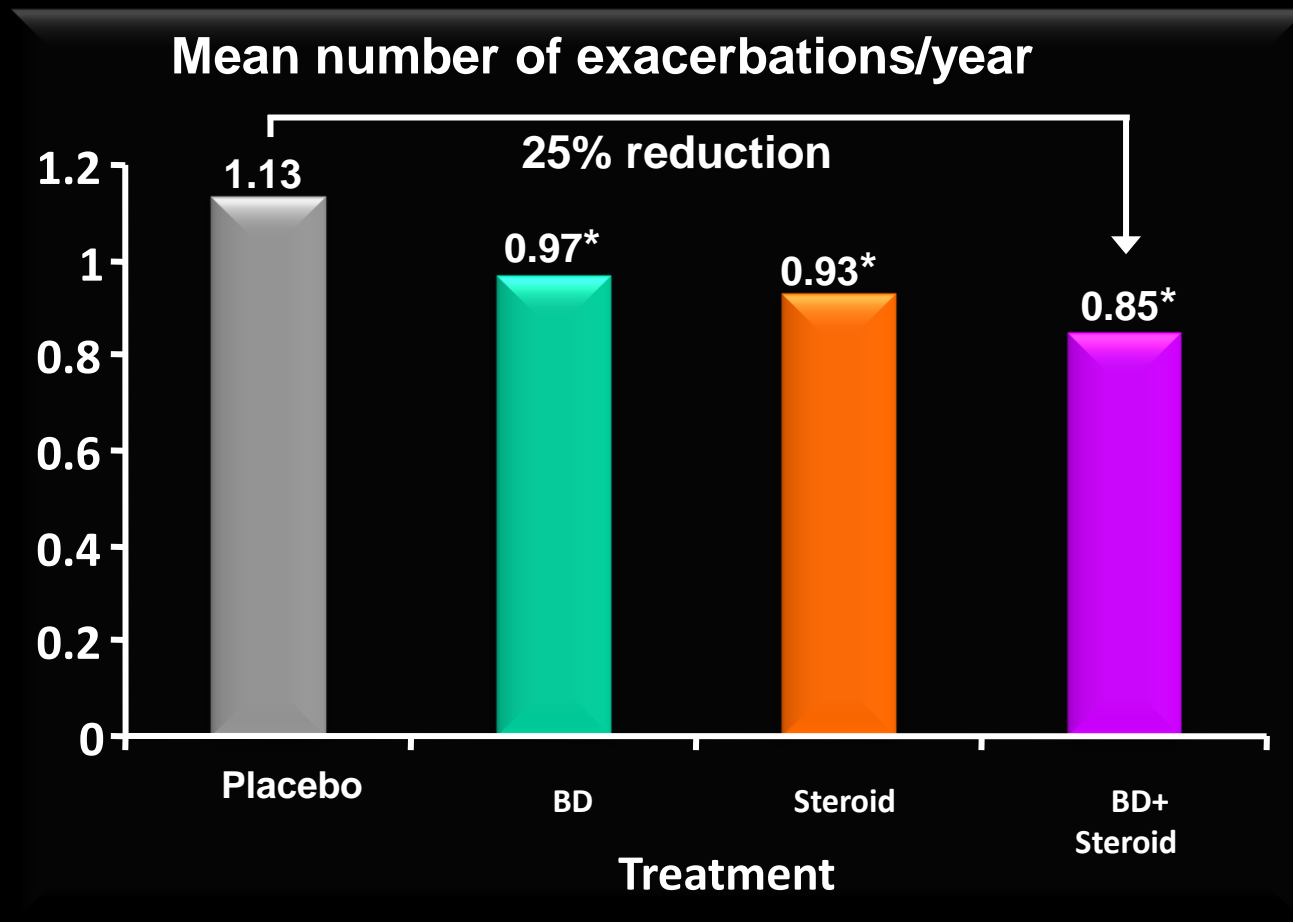


Suissa S, et al. *Thorax*. 2012; 67: 957-963.

Long-acting Bronchodilators Reduce Exacerbation Frequency



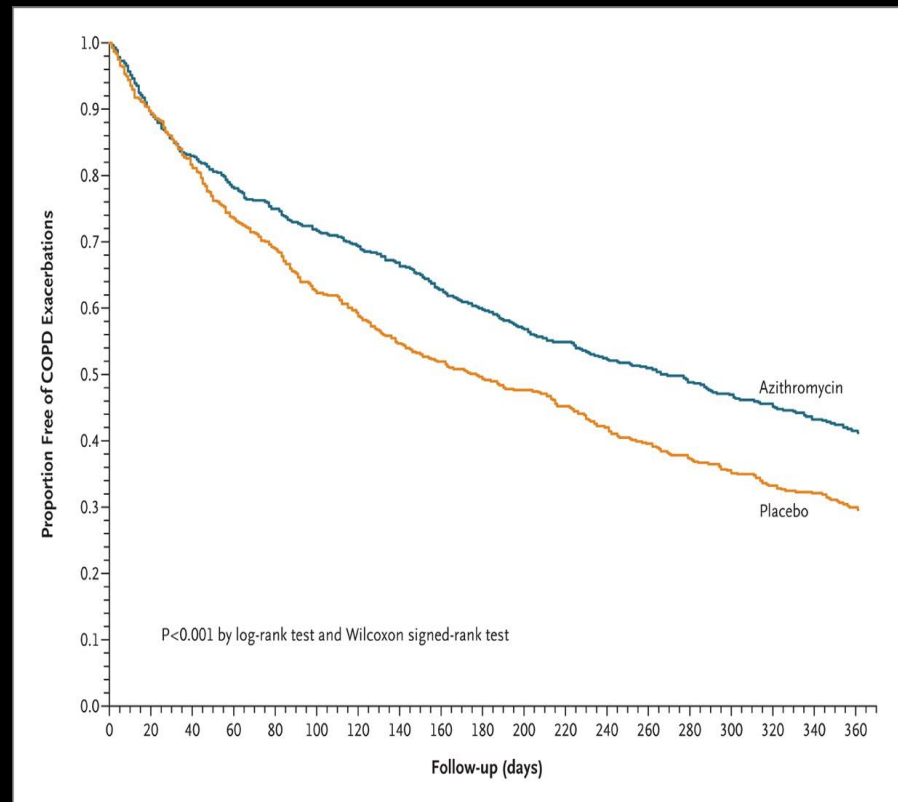
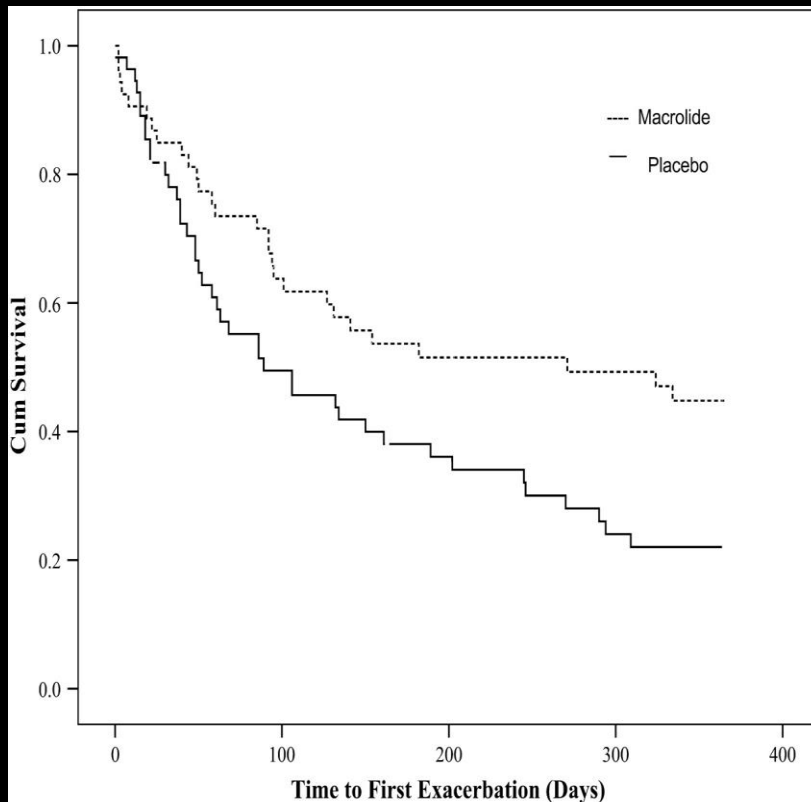
Moderate and Severe exacerbations are Reduced with Bronchodilator Plus Inhaled Steroid¹⁷



*p < 0.001 vs placebo BD= bronchodilator

Macrolides Prevent COPD Exacerbations

Median time to exacerbation
266 Azithro 174 Placebo

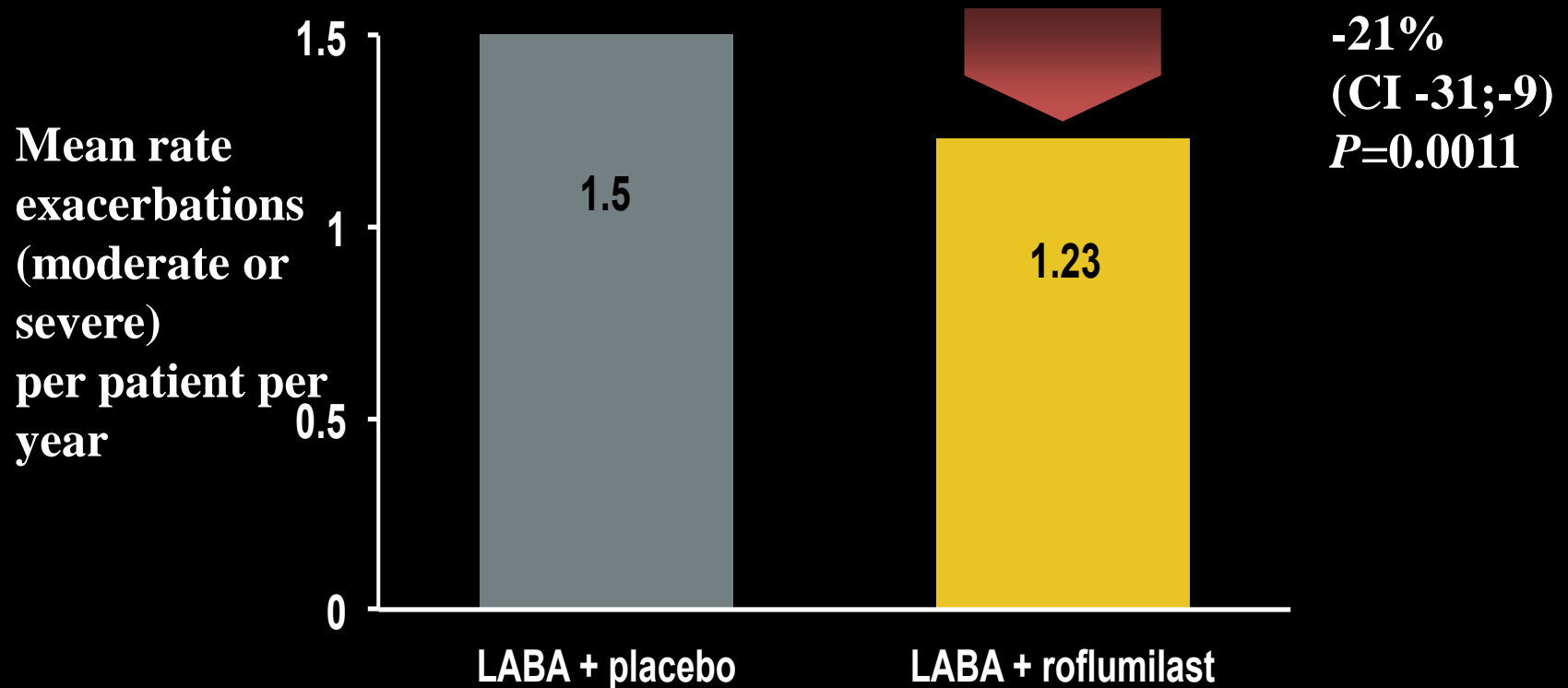


Median time to 1st exacerbation
271 days Macrolide; 89 days Placebo

Proportion of Participants Free from
Acute Exacerbations of COPD for 1 Year

Roflumilast and Exacerbations

Significant Reduction in Exacerbations When Added to LABA



REACT Trial= 13% Reduction with LABA/ICS

Fabbri et al *Lancet* 2009;374:695-703. Martinez et al *Lancet* 2015;385:857-85

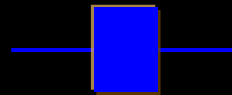
Pulmonary Rehabilitation Reduces Risk of Unplanned Admission

Study
(in rehabilitation/
usual care group)

Risk ratio (95%
Ci)

Weight in %

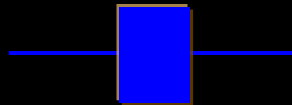
Behnke



0.29 (0.10 to
0.82)

37%

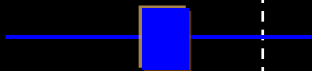
Man



0.17 (0.04 to
0.69)

44%

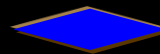
Murphy



0.40 (0.09 to
1.70)

19%

Overall



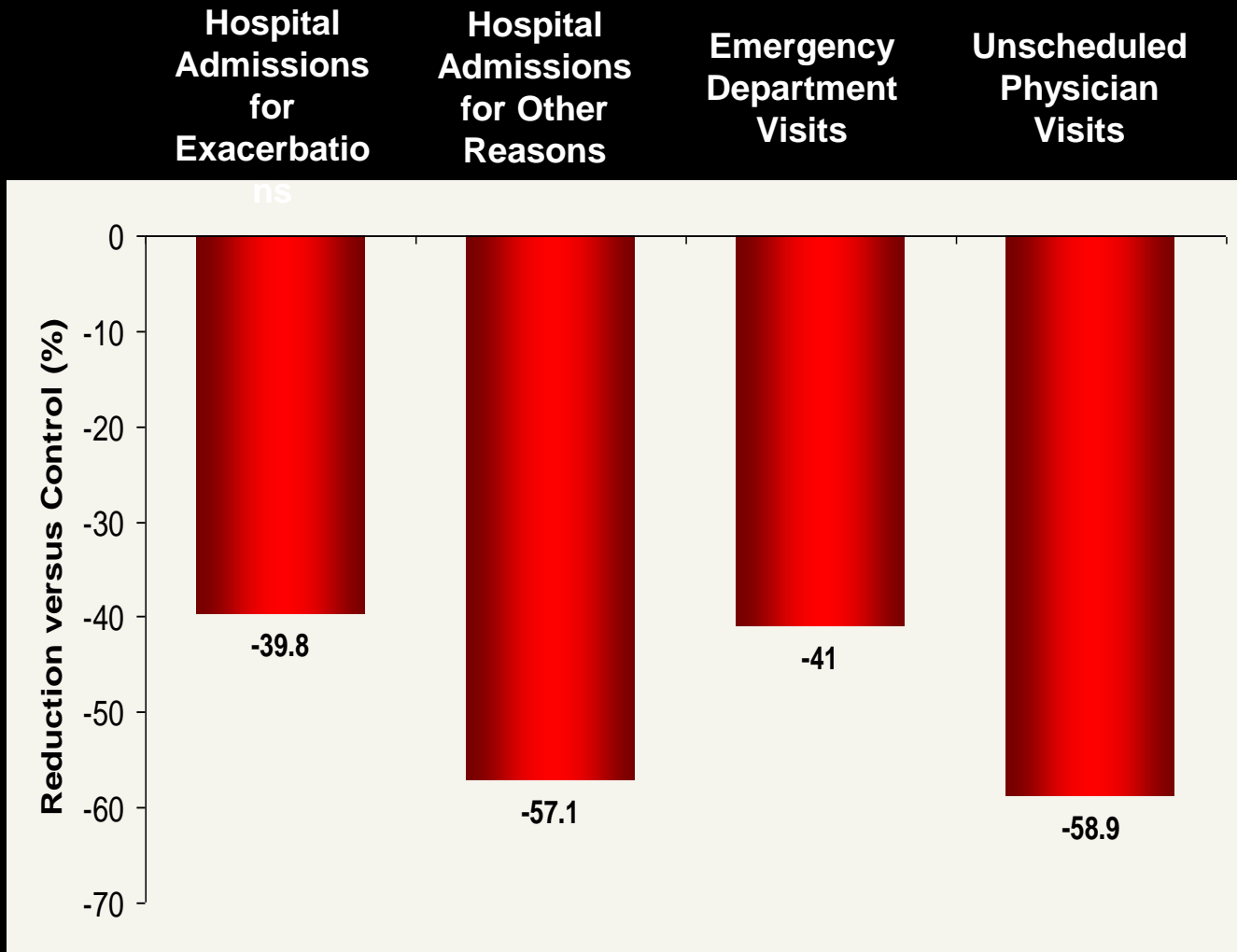
0.26 (0.12 to 0.54)
Chi-Squared 0.70,
p=0.71

Favors
rehabilitation

Favors usual
care

Risk of unplanned
hospital admission

Patient Education in COPD Reduces Exacerbations

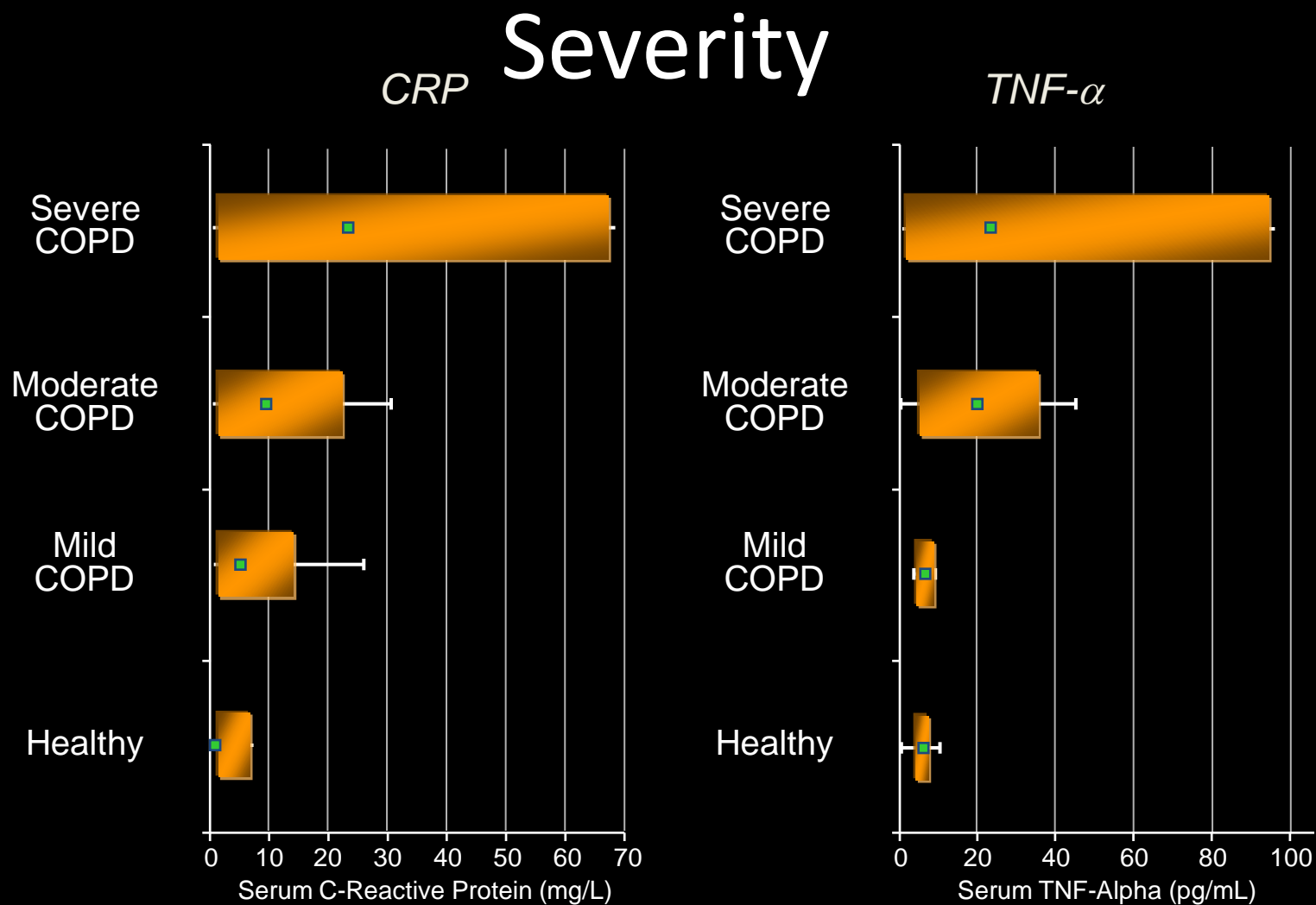


COPD Care in the 21st Century: A Public Health Priority.

- Numerous strategies have been proposed to combat these high rates, including the use of discharge bundles, hospital at-home programs, telemedicine, and tele-rehabilitation, but no single best strategy has emerged.

Criner RN, Han MK. Respir Care. 2018 May;63(5):591-600

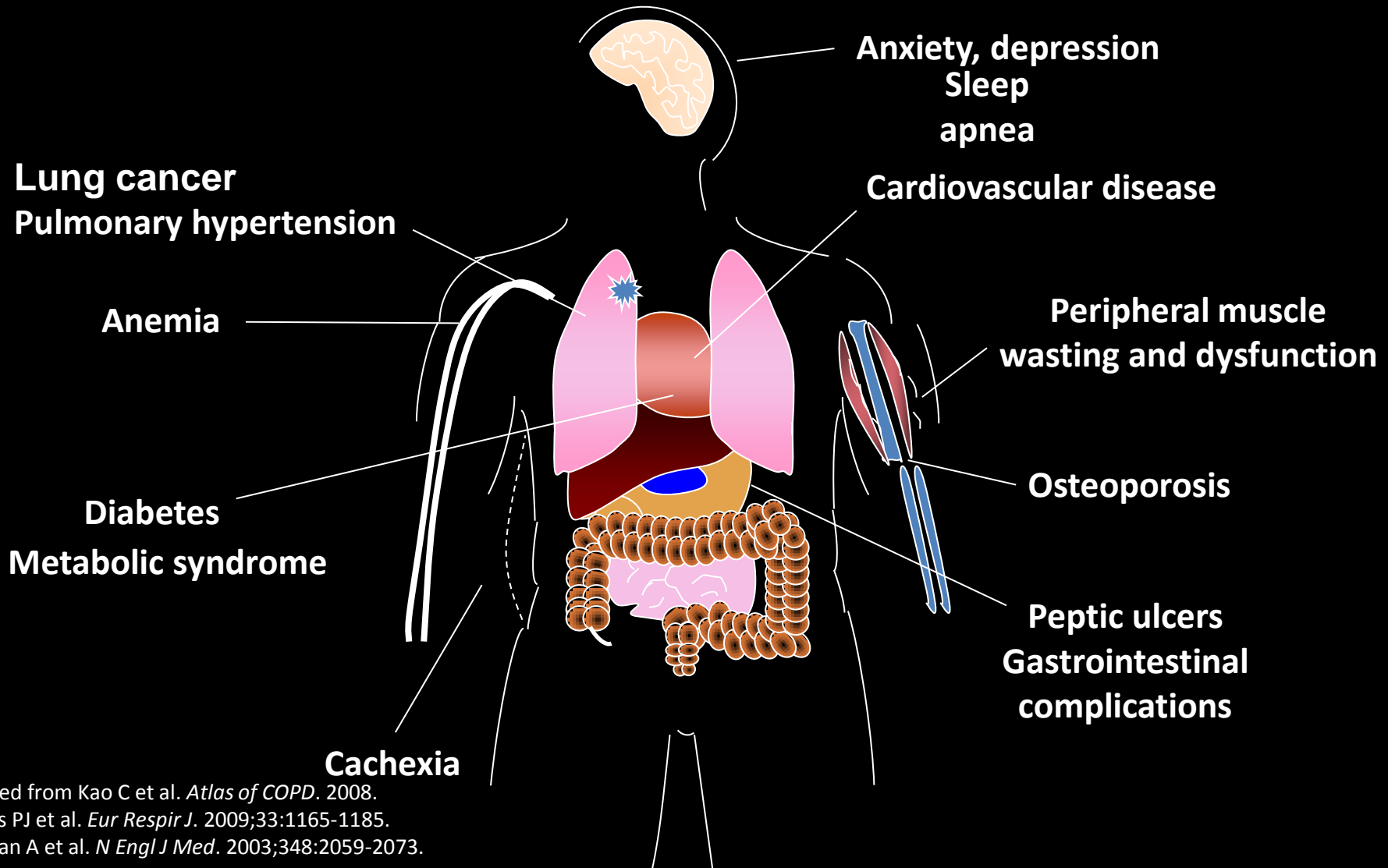
Systemic Inflammation Rises with COPD



COPD Comorbidities

Are Common

Levels of CRP, IL-6 Fibrinogen, TNF α WBCs rise with COPD Severity
and relate to co-morbidities of COPD

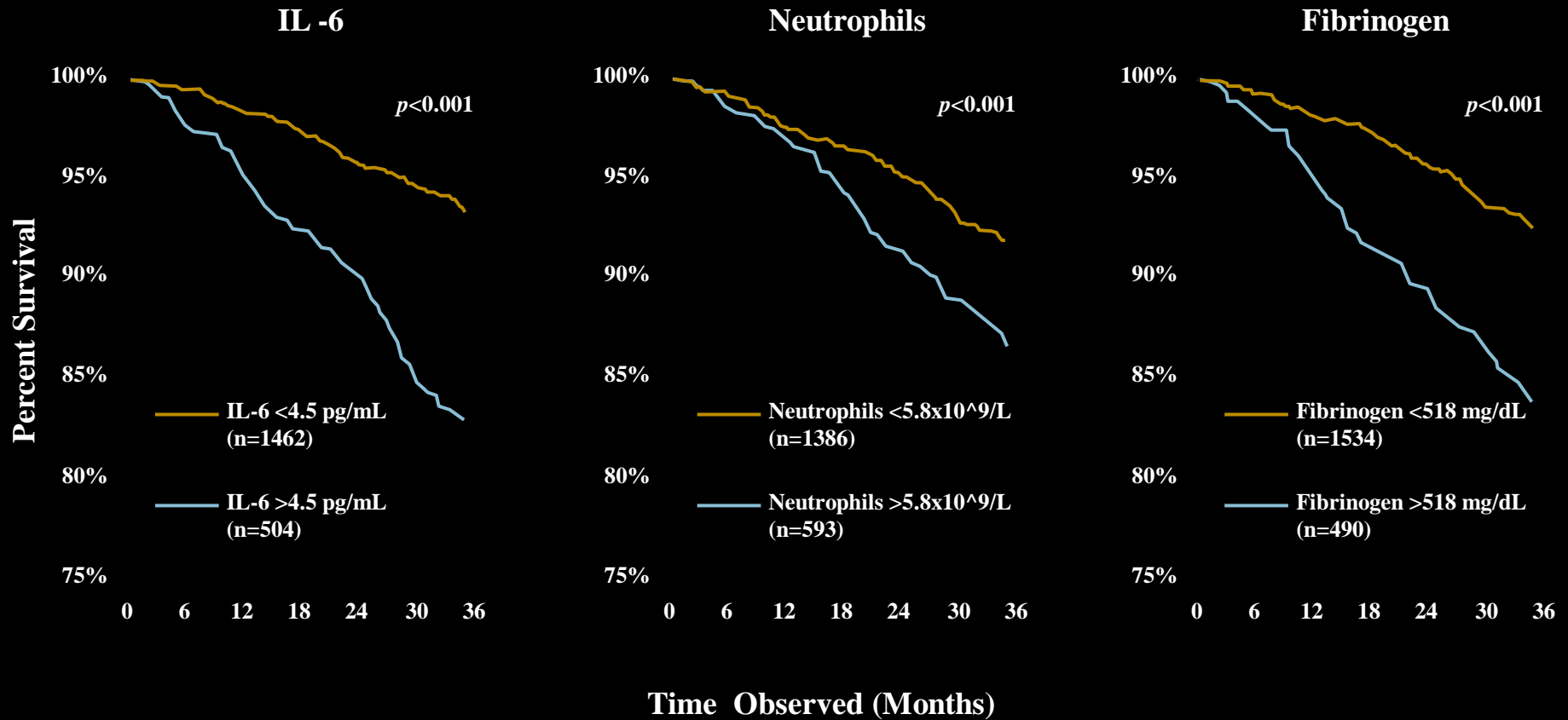


COPD and Comorbidities

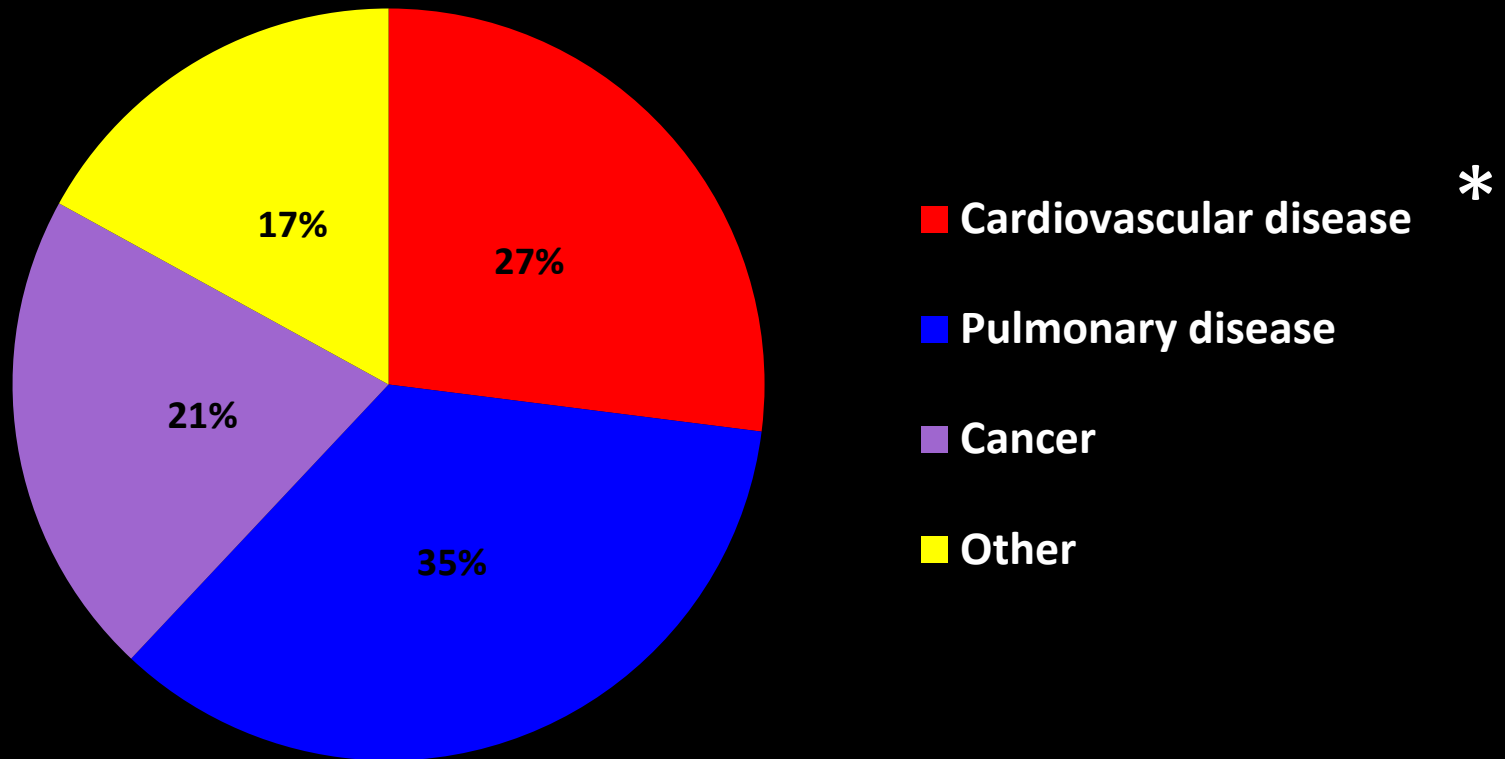
Some common comorbidities occurring in patients with COPD with stable disease include:

- ▶ Cardiovascular disease (CVD)
- ▶ Heart failure
- ▶ Ischaemic heart disease (IHD)
- ▶ Arrhythmias
- ▶ Peripheral vascular disease
- ▶ Hypertension
- ▶ Osteoporosis
- ▶ Anxiety and depression
- ▶ COPD and lung cancer
- ▶ Metabolic syndrome and diabetes
- ▶ Gastroesophageal reflux (GERD)
- ▶ Bronchiectasis
- ▶ Obstructive sleep apnea

Inflammation Predicts Mortality in COPD

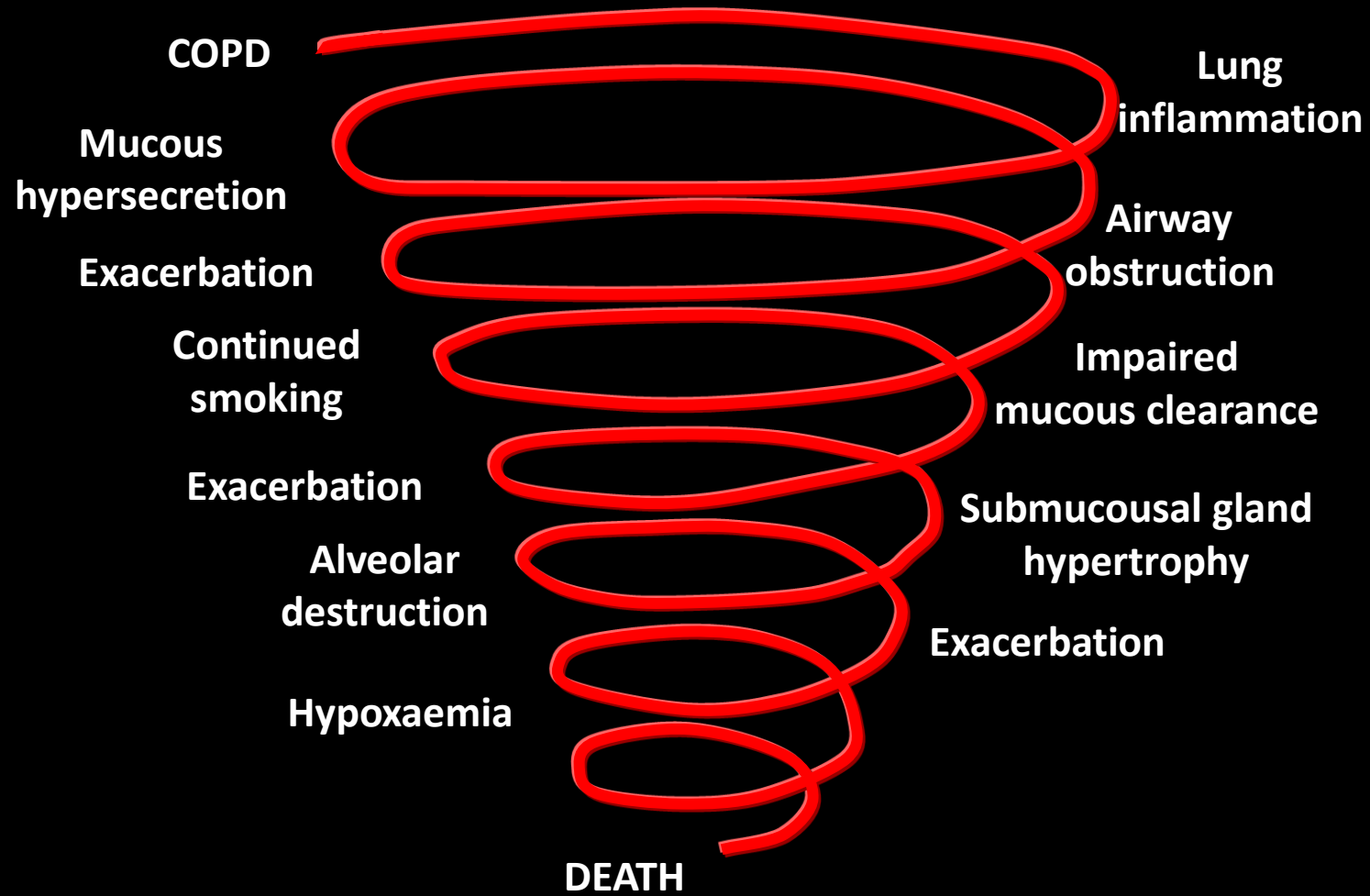


Causes of Death in COPD: TORCH Study



***For every 10% decrease in FEV₁ Cardiovascular mortality increases by about 28%**

The Downward Spiral in COPD



Summary

GOLD 2017

- New grading for COPD severity A-D
- GOLD Treatment Protocol driven by severity
- Emphasis on inhaler technique/recognition of advantages/disadvantages of each devices
- Oxygen for resting hypoxemia
- De-escalate ICS in A-C patients except with eosinophilia?
- Exacerbations can be prevented: meds, rehab, patient education