

REDUCE AND PREVENT EXACERBATION IN COPD PATIENTS:

IS IT EASY?

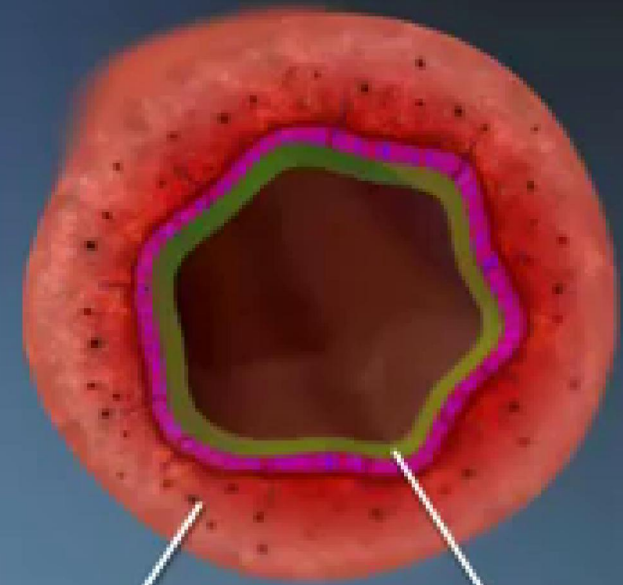
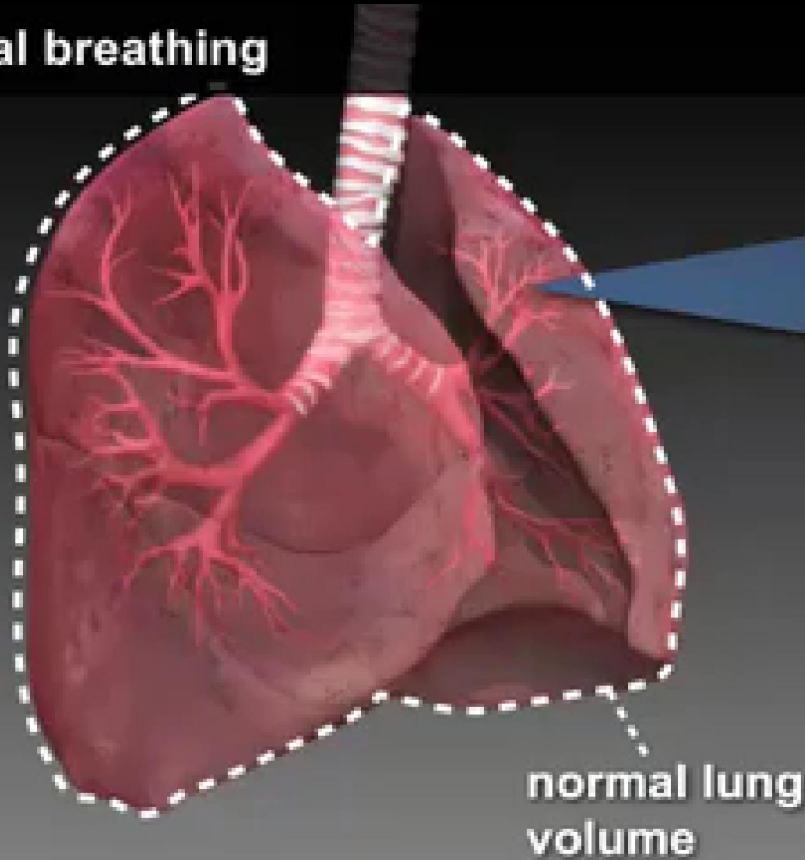
พ.ญ. ณ์ับผลิกา กองพลพรหม

สาขาวิชาโรคระบบทางเดินหายใจและเวชบำบัดวิกฤต

ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

How COPD Affects the Lungs

Normal breathing



bronchiole

mucus



Therapy at Each Stage of COPD

I: Mild

II: Moderate

III: Severe

IV: Very Severe

- $FEV_1/FVC < 70\%$
- $FEV_1 \geq 80\%$ predicted

- $FEV_1/FVC < 70\%$
- $50\% \leq FEV_1 < 80\%$ predicted

- $FEV_1/FVC < 70\%$
- $30\% \leq FEV_1 < 50\%$ predicted

- $FEV_1/FVC < 70\%$
- $FEV_1 < 30\%$ predicted
or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination →
Add short-acting bronchodilator (when needed) →

Add regular treatment with one or more long-acting bronchodilators (when needed); **Add** rehabilitation

Add inhaled glucocorticosteroids if repeated exacerbations

Add long term oxygen if chronic respiratory failure. **Consider** surgical treatments

Outline

Reduce and Prevent exacerbation in COPD patients: Is it easy?

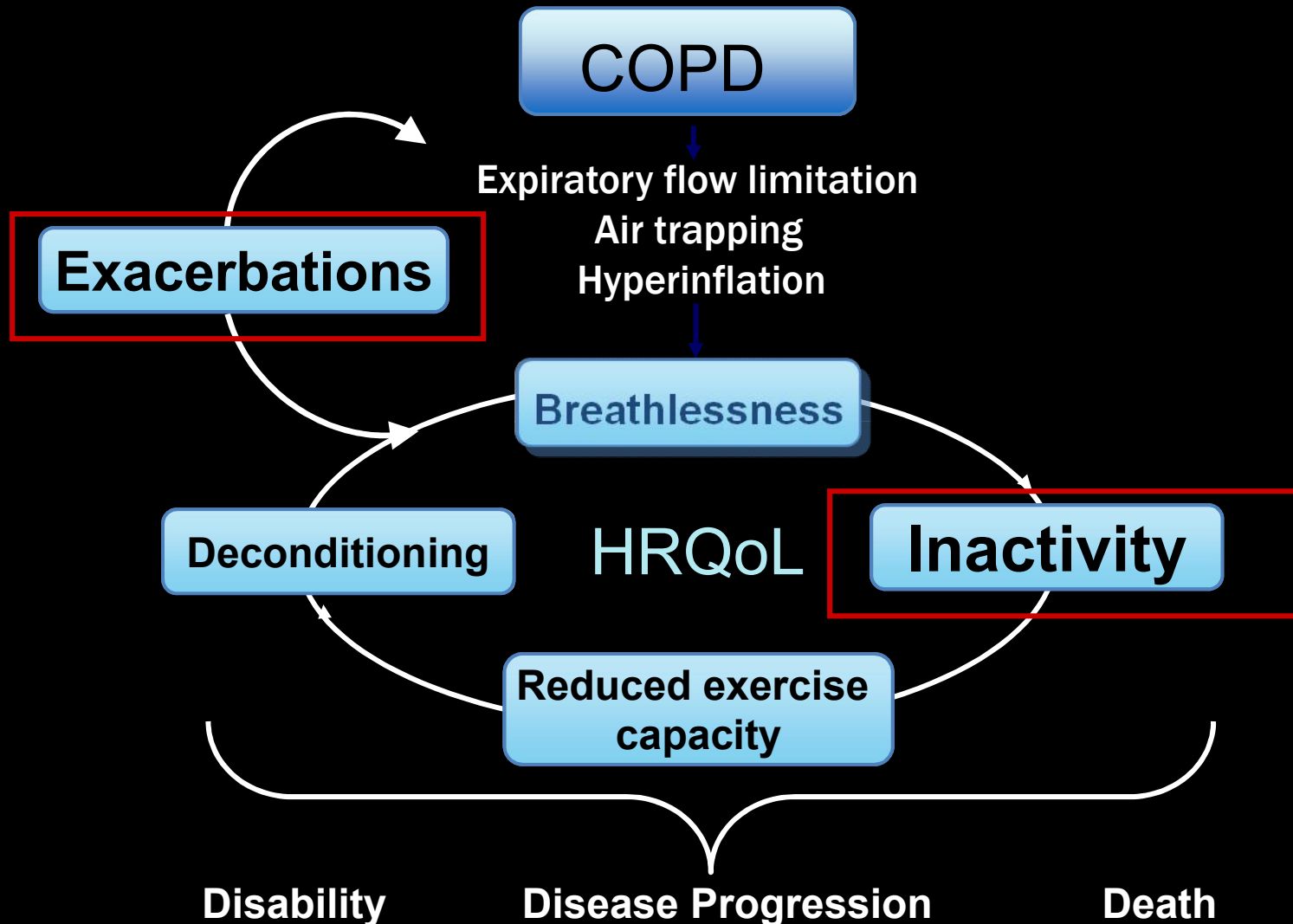
It isn't easy : Dr.Naplika (20 min)

- Challenge of reducing and preventing exacerbation
- Impact of Exacerbation (Journal data ex.ECLIPSE , Data admit)
- Exacerbation assessment, definition in practice -> it isn't clear
- Drug in practice -> available ,cost, start delay -> impact to outcome
- Non-Drug in practice Ex.Rehab -> limits of resource (HCP, place), outcome

It's easy : Dr.Watchara (20 min)

- Impact of Exacerbation -> We know. Prioritize to reduce & prevent exacerbation.
- Exacerbation definition in practice -> AE (ER, add antibiotic, add steroid)
- How to treat -> Follow by GOLD GL 1 hospitalization , 2 AE (ER, add antibiotic, add steroid)
- Drug in practice -> cost-effectiveness (price/efficacy)
- Non-Drug in practice Ex. Rehab -> together with drug

Clinical Course of COPD



REDUCE AND PREVENT
EXACERBATION IN COPD
PATIENTS: IS IT EASY?

Not

What are exacerbations?

Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2010 defines an exacerbation as:

“an event in the natural course of the disease characterized by a change in the patient’s baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset and may warrant a change in regular medication”¹

- May be mild, moderate or severe in nature. Severe exacerbations require hospitalisation and are associated with a prolonged recovery period²
- Commonly caused by bacterial/viral infections of the lungs and airways¹
- Associated with increases in markers of inflammation^{3,4}
- Distressing for patients and their loved ones

1. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2010. Available from www.goldcopd.org
2. Seemungal TA, Donaldson GC, Bhowmik A, et al. *Am J Respir Crit Care Med* 2000;161:1608-1613.
3. Perera W, Hurst JR, Wilkinson TM, et al. *Eur Respir J* 2007;29:527-534.
4. Papi A, Bellettato CM, Braccioni F, et al. *Am J Respir Crit Care Med* 2006;173:1114–1121.

Exacerbation

Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2014 defines an exacerbation as:

An acute event characterized by a worsening of patient's respiratory symptoms that is beyond normal day to day variations and leads to a change in medicine

Making this definition operational has been difficult.

- high degree of variability in the definition is due to different etiologies as well as studies/trials necessity of a particular definition

CHALLENGE OF REDUCING AND PREVENTING EXACERBATION

How important is it?

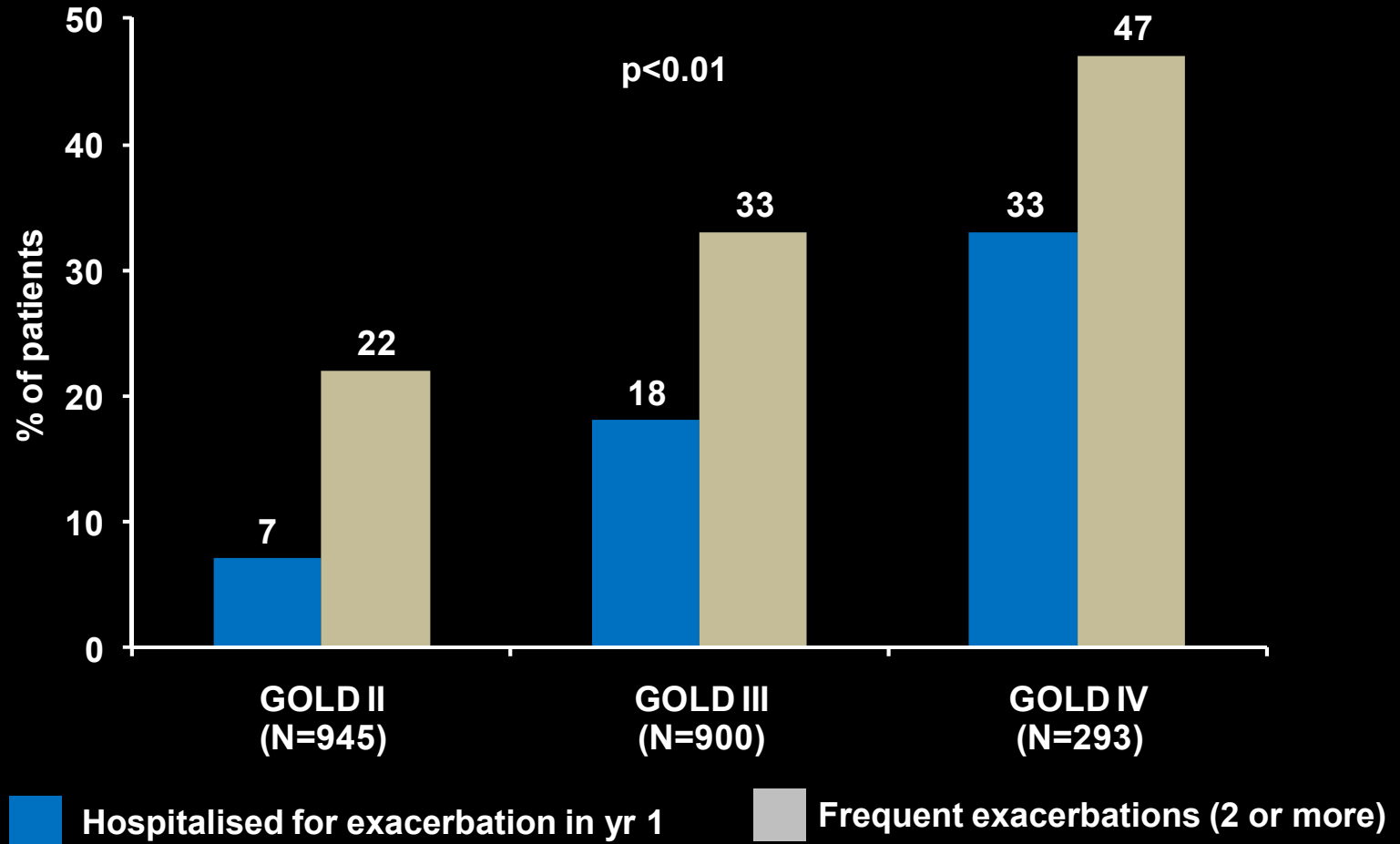
Rates of AECOPD and Severe AECOPD

- Annual rates of AECOPD varied from 0.8 to 3.8 per person with COPD

Johnston AK, Mannino DM. Informa Healthcare 2008: 15–26

- In population-based cohorts, hospitalization rates varied from 0.15 to 0.30 hospitalizations annually
- In hospital based cohorts (i.e., they were originally drawn from patients hospitalized with COPD) , annual hospitalization rates as high as 2.6 annually.

The 'frequent exacerbator phenotype': Frequency/severity by GOLD Category (1)



Exacerbation history: most powerful single predictor of exacerbations (independent of GOLD Stage)

Year 1

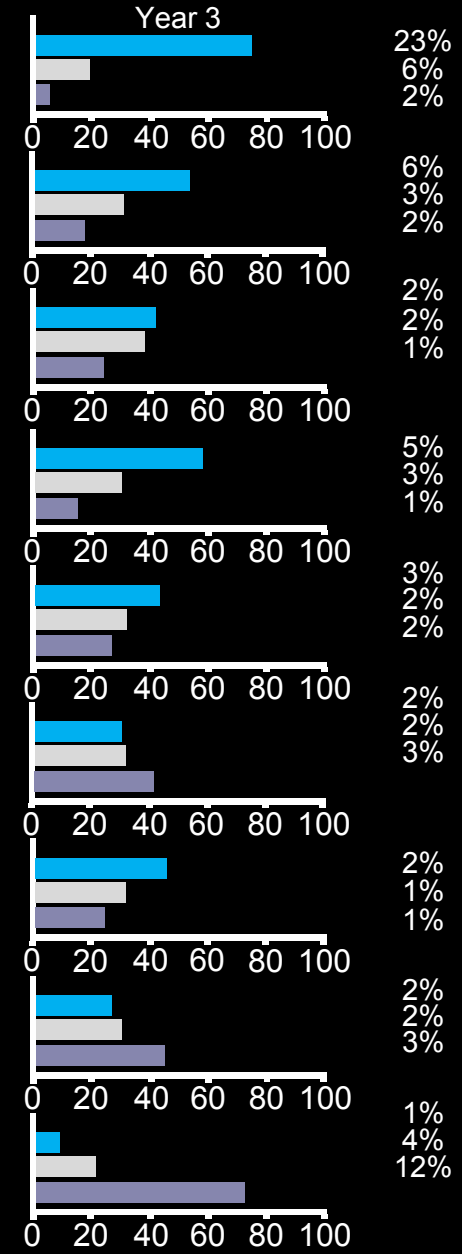
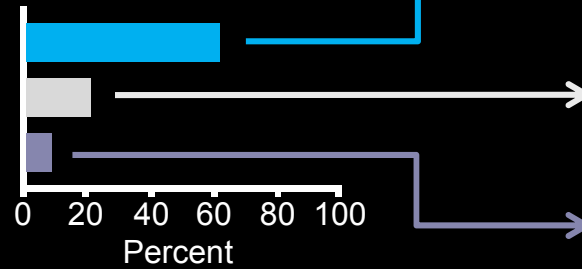
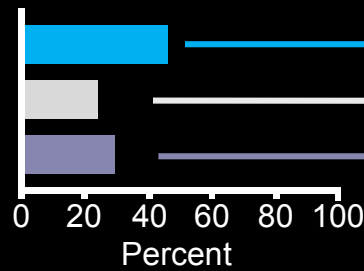
Year 2

Year 3

Exacerbations in the following year

- Patients with no exacerbation
- Patients with 1 exacerbation
- Patients with ≥ 2 exacerbations

**Patient-based
risk estimate**



N=1679 patients who completed the 3-year study

The percentages at right denote the proportions of all patients with no exacerbations, one exacerbation, or two or more exacerbations

Frequent exacerbators are found at all stages of COPD severity

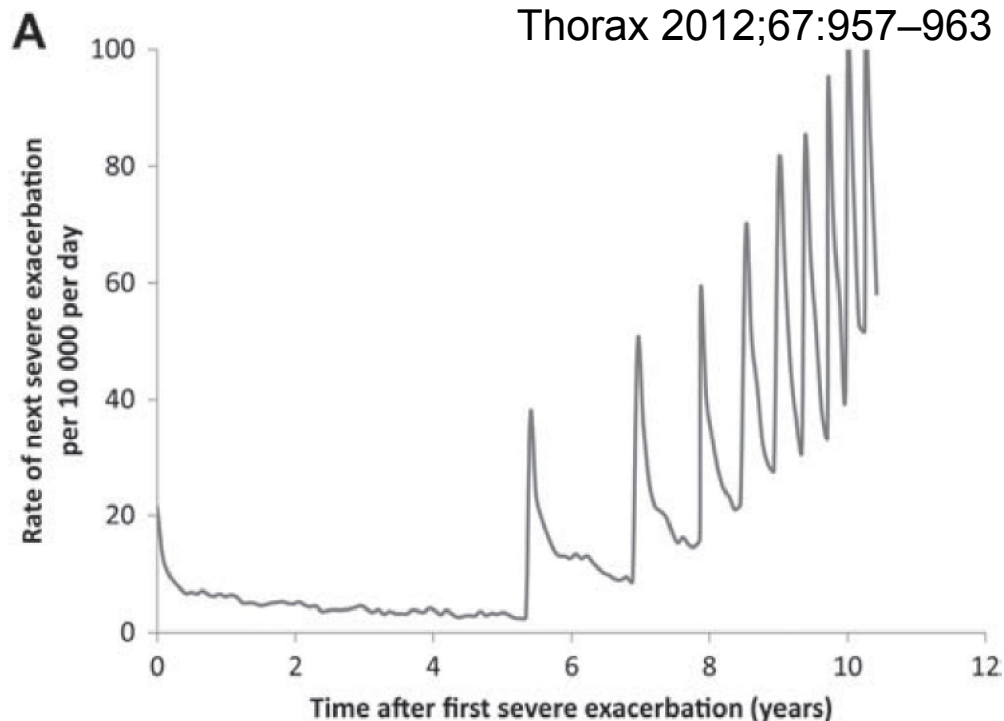
GOLD stage	Base-line therapy		Exacerbation rate in year 1 (number/patient)	% of patients who were 'Frequent exacerbators'
	% Patients on long-acting bronchodilators	% Patients on inhaled corticosteroids		
II	67	60	0.85	22
III	83	80	1.34	33
IV	86	86	2.00	47

Patients at increased risk can be identified based on patient recall of previous events

- Ask your patients for any exacerbation (flare-up) treated with antibiotics and/or oral steroids in the previous year
- Ask your patients about any hospitalizations due to exacerbations in the previous year

If your patient answers **YES** to either of these questions the risk is **5.72 times higher** that this patient will experience 2 or more exacerbations within the next year, compared with the patient answers NO (p<0.001)

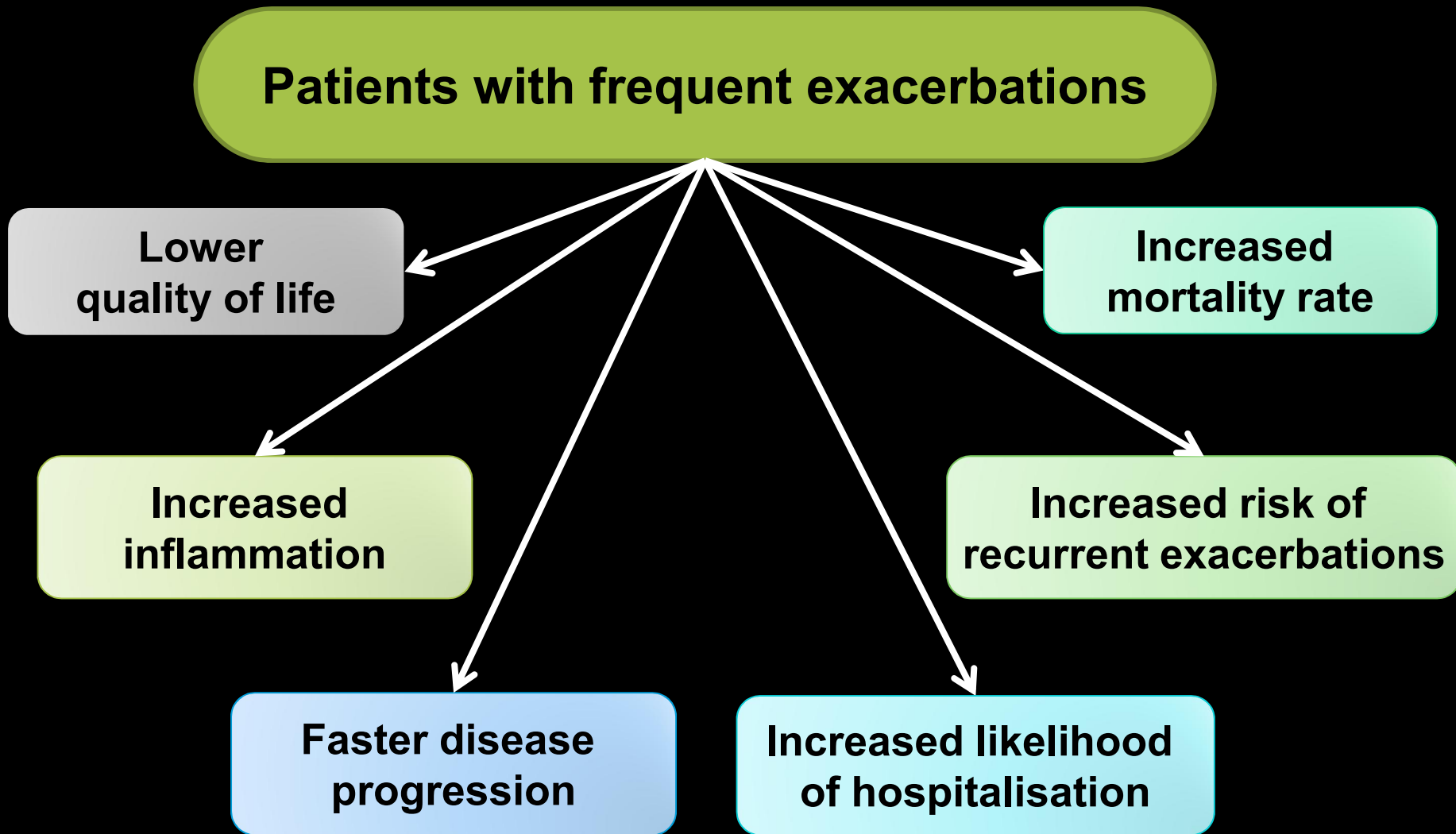
Thorax 2012;67:957–963



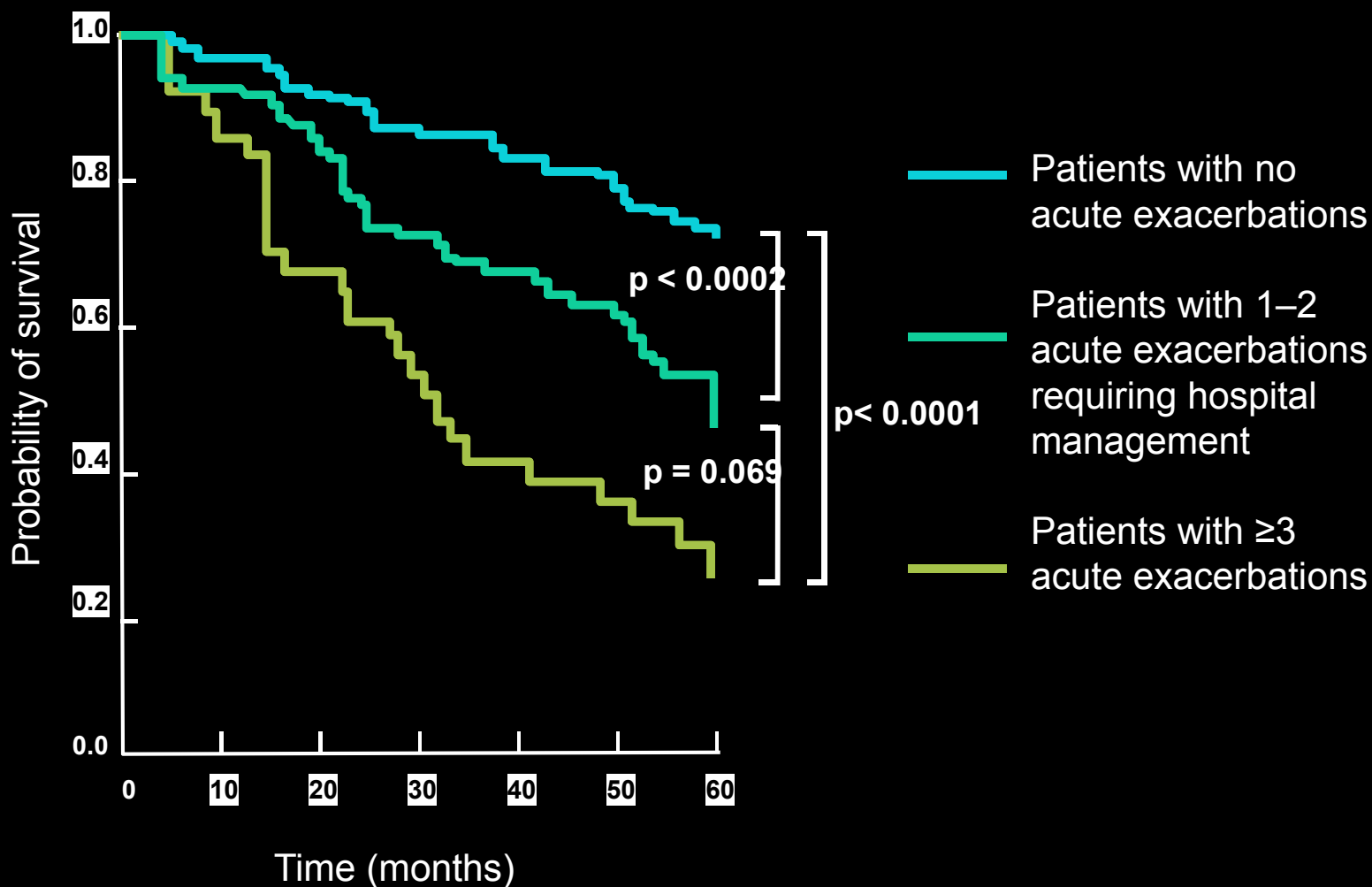
The cohort included 73,106 patients hospitalised for the first time for COPD, of whom 50,580 died during the 17-year follow-up.

- 50% and 75% mortality at 3.6 and 7.7 years respectively
- The median time from the first to the second hospitalised exacerbation was around 5 years and decreased to <4 months from the 9th to the 10th
- The risk of the subsequent severe exacerbation was increased threefold after the second severe exacerbation and 24-fold after the 10th, relative to the first
- Mortality after a severe exacerbation peaked to 40 deaths per 10 000 per day in the first week after admission, dropping gradually to 5 after 3 months

Frequent exacerbations drive disease progression



Exacerbation Frequency and Severity Both Increase Mortality Risk



- 12% of COPD patients followed at a specialized clinic presented repeated severe exacerbations (≥ 3.0 exacerbations per year)
 - responsible for 57% of all hospital admissions and for 61% of all emergency room visits

Arch Bronconeumol 2001; 37:375–381

- Frequent COPD exacerbators, ≥ 3.0 severe exacerbations per year, had a fourfold **increased risk of death** (95% CI, 1.80–9.45) compared with patients who did not have exacerbations at all

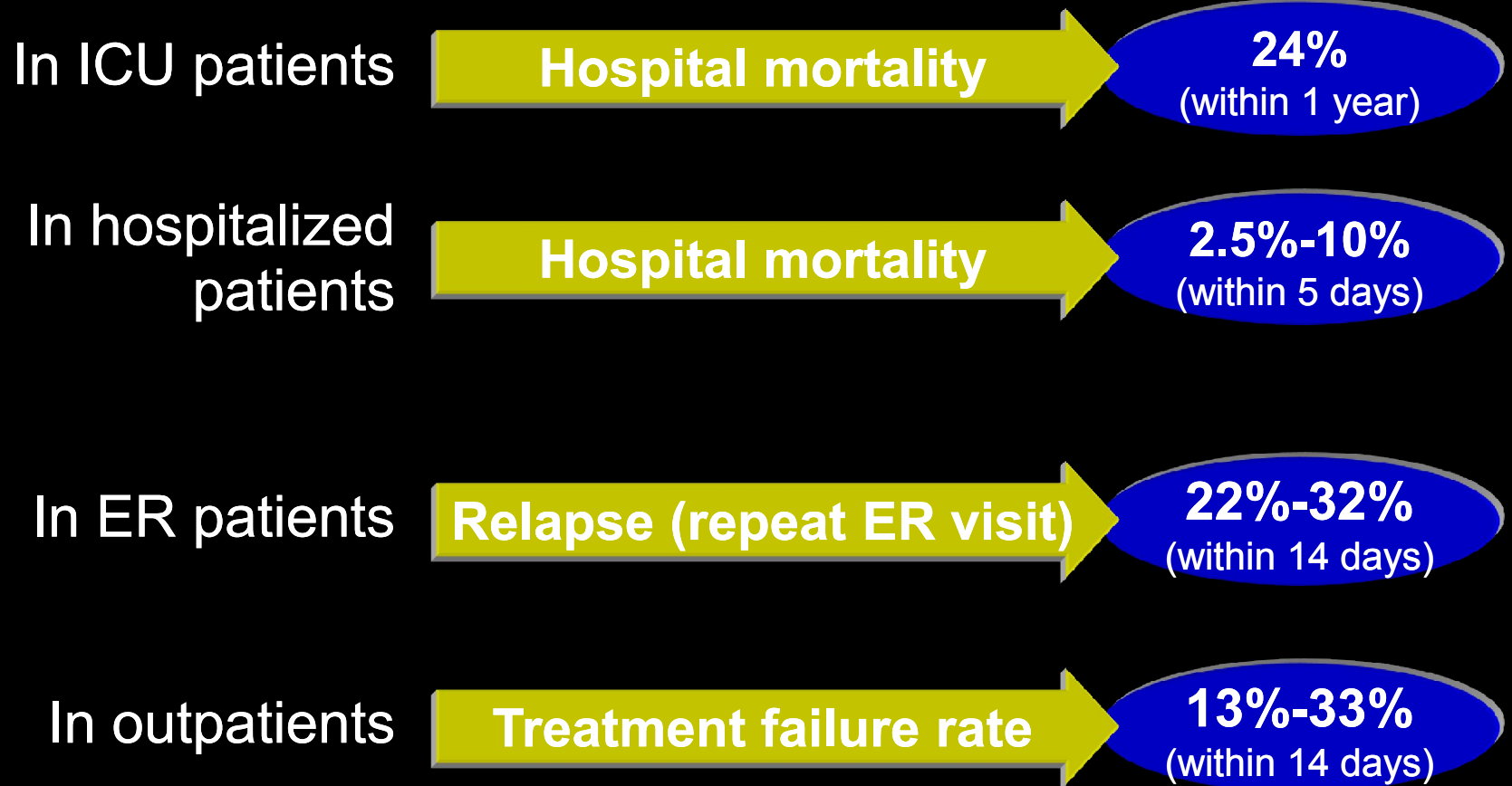
Thorax 2005; 60:925–931

- Hospitalization has emerged as the main cause of healthcare resource use costs related to COPD exacerbations
 - 73% of these costs are attributed to the 10% of COPD patients with repeated exacerbations alone

Chest 2000; 117:5S–9S

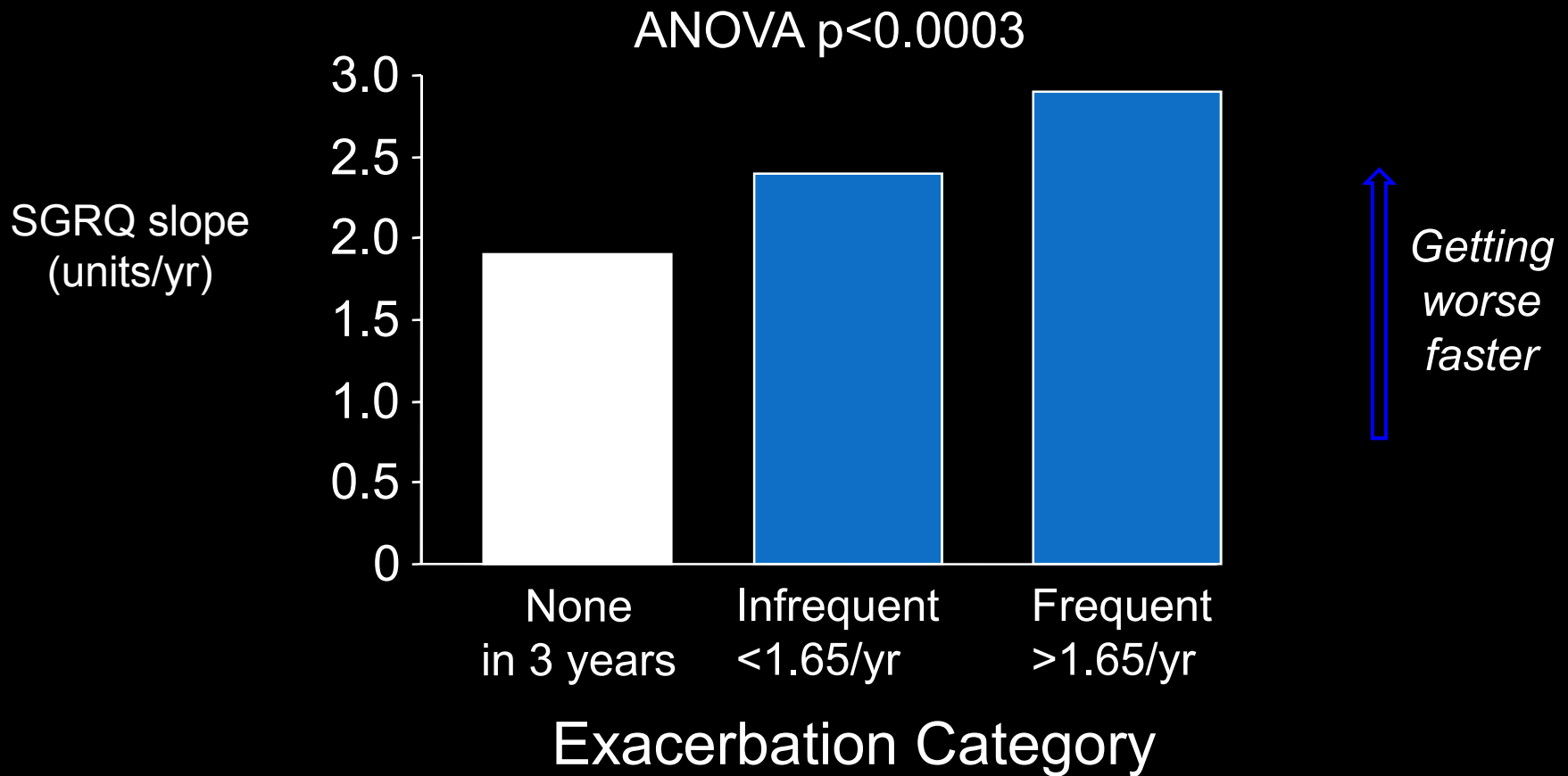
Outcome of COPD exacerbations

Percent of patients



Seneff et al. JAMA 1995
Murata et al. Ann Emerg Med 1991
Adams et al. Chest 2000
Patil et al. Arch Intern Med 2003

Exacerbations **and worsening** in health status over 3 years



Impact of frequent exacerbations on health related quality of life, using the St George's Respiratory Questionnaire (SGRQ)

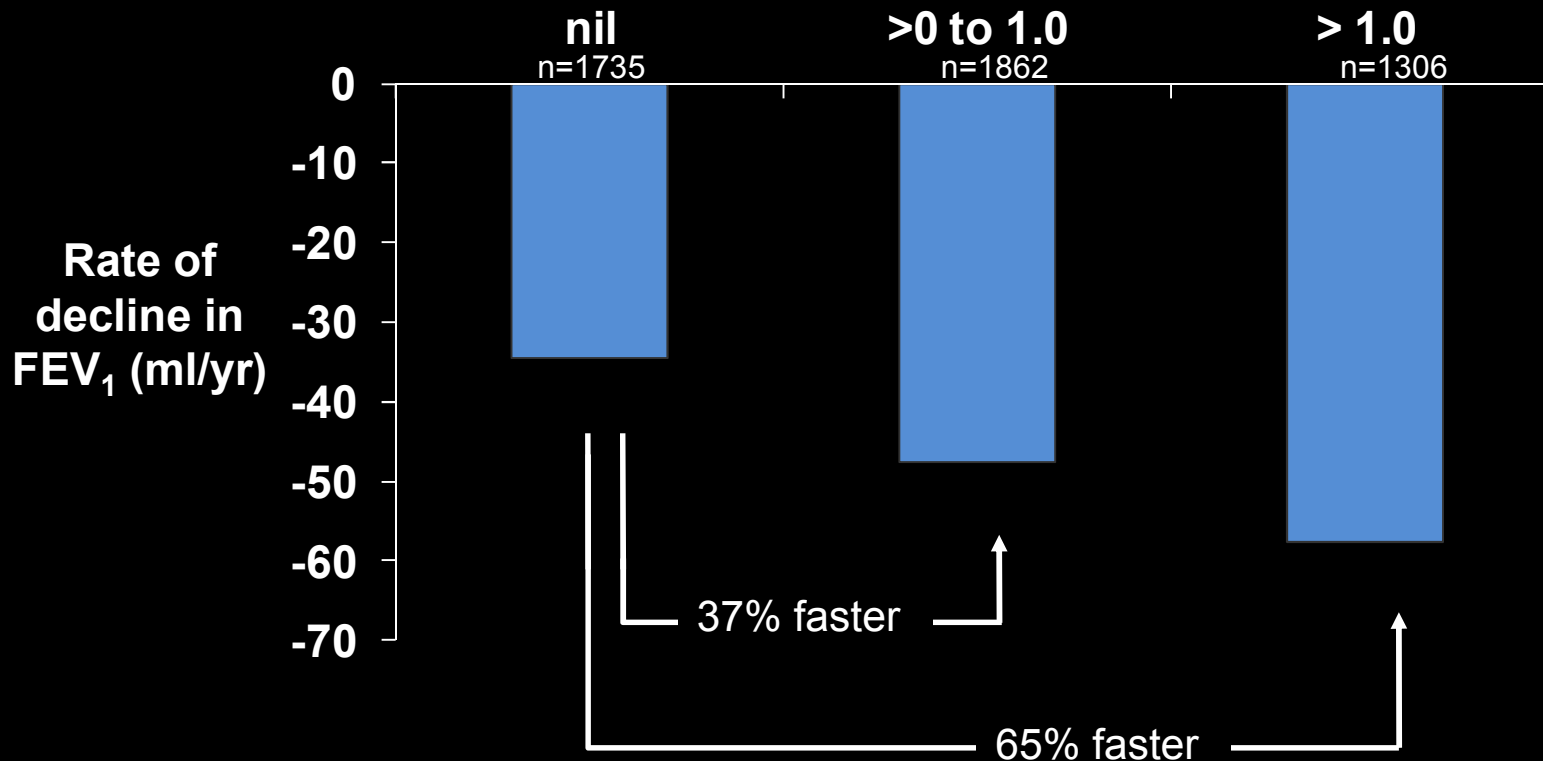
	No. of patients	Study design	Duration (years)	Threshold for frequent exacerbations	Impact of frequent exacerbations on HRQoL (differences between frequent and infrequent exacerbations, expressed as score units)	
					Baseline	End of study
Seemungal et al., 1998	70	Observational	1	≥3.0	NR	15.1
Miravittles et al., 2004	336	Observational	2	≥3.0	+7.2	+9.3
Soler et al., 2004	64	Case-control	1	≥3.0	+16.4	NR
Spencer et al., 2004	613	RCT	3	>1.65	+4.0	NR
Bourbeau et al., 2007	336	Observational	0.5	≥2.0	+4.0	+12.0

Strong association between increased exacerbation frequency and HRQoL deterioration

TORCH:

Exacerbation rate and FEV₁ decline

Exacerbations per year

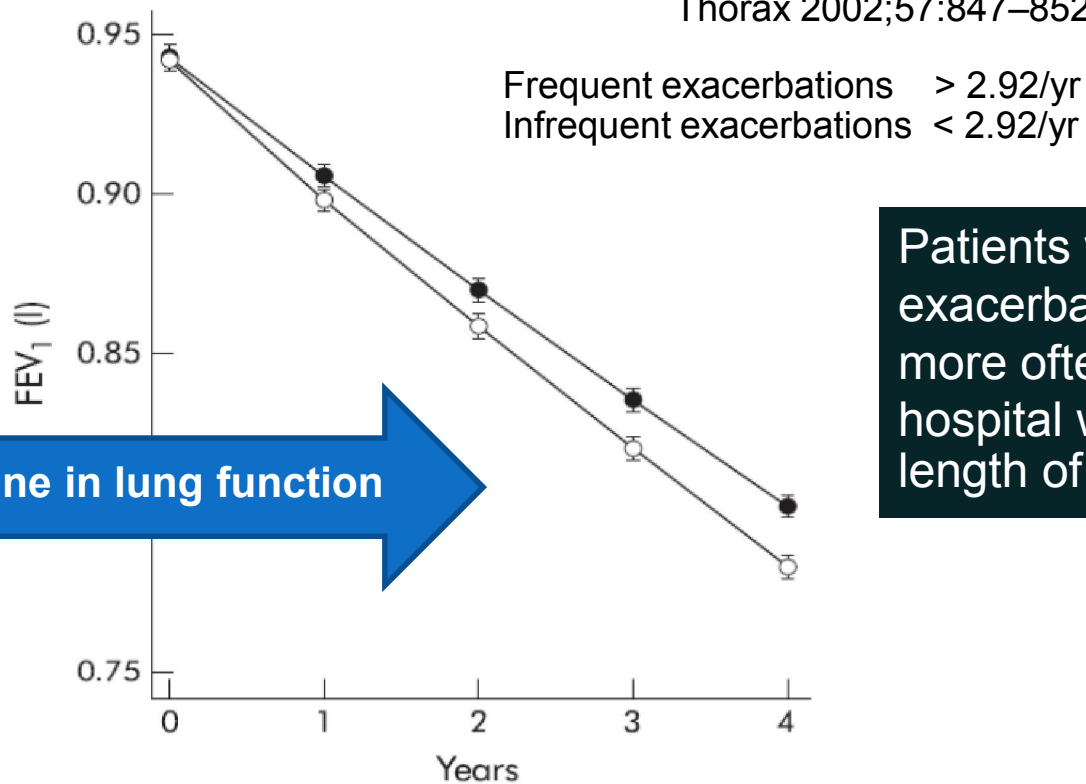


Adjusted for smoking status, gender, baseline FEV₁, region, BMI, prior exacerbations, treatment, time, time by treatment and covariate by time

Table 2. Impact of frequent exacerbators on FEV₁ decline

	Number of patients	Study design	Duration (in years)	Frequent exacerbator definition (<i>n</i> of exacerbations per year)	Rate of accelerated FEV ₁ decline		<i>p</i> values
					Infrequent exacerbations	Frequent exacerbations	
Kanner et al., 2001 (7)	5,887	Epidemiologic	5	≥1.50	Smoking status: Sustained quitter: –13.0 mL yr ⁻¹ Intermittent quitter: –32.6 mL yr ⁻¹ Continuous smoker: –55.4 mL yr ⁻¹	Smoking status: Sustained quitter: –12.0 mL yr ⁻¹ Intermittent quitter: –52.0 mL yr ⁻¹ Continued smoker: –69.4 mL yr ⁻¹	NS <.05 <.001
Donaldson et al., 2002 (8)	32	Observational	4	≥2.92	–32.1 mL yr ⁻¹	–40.1 mL yr ⁻¹	<.05
Miravittles et al., 2004 (3)	336	Observational	2	≥3.0	NR	NR	NS
Spencer et al., 2004 (5)	613	RCT	3	>1.65	–55 mL yr ⁻¹	–54 mL yr ⁻¹	NS
Cote et al., 2007 (15)	205	Observational	2	>2.0	NC	–4.0 (% predicted)	NS
Makris et al., 2007 (16)	102	Observational	3	>2.85	Smoking status: Ex-smokers: –0.85 (% predicted) Smokers: –3.15 (% predicted)	Smoking status: Ex-smokers: –2.80 (% predicted) Smokers: –4.10 (% predicted)	= .017

TORCH has demonstrated a negative association between exacerbation frequency and FEV₁ decline, with **higher rates of lung function deterioration in those patients experiencing more exacerbations**



25% decline in lung function

Patients with frequent exacerbations were more often admitted to hospital with longer length of stay

Figure 2 Percentage change in FEV₁ with standard errors over 4 years. Open circles represent infrequent exacerbators; closed circles represent frequent exacerbators.

Table 3 Initial and annual change in lung function in patients with infrequent and frequent exacerbations

	Starting value		Annual change	
	Infrequent	Frequent	Infrequent	Frequent
Exacerbations (reported and unreported)			<50% percentile, <2.92 per year (n=63)	> 50% percentile >2.92 per year (n=46)
PEF (l/min)	214	232	-0.72 (n=16)	-2.94*** (n=16)
FEV ₁ (ml)	893	950	-32.1	-40.1*

Outcome of COPD exacerbations

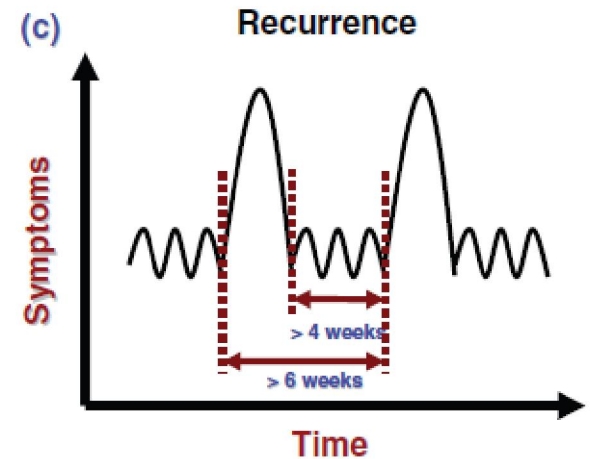
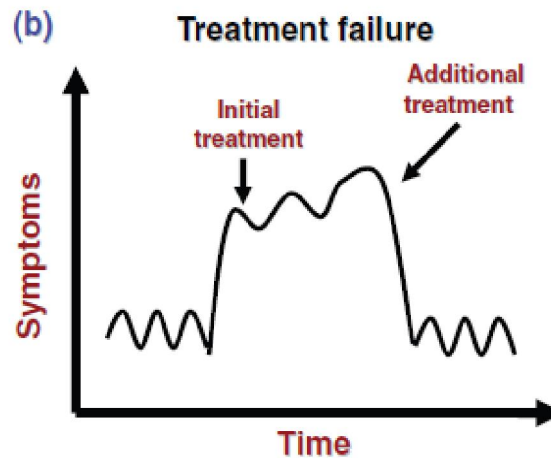
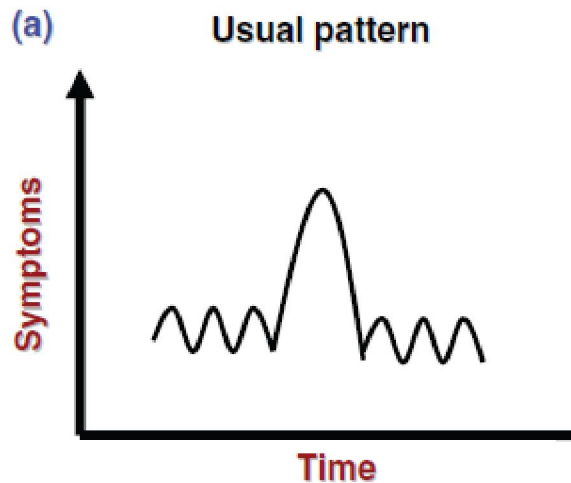
- Outcomes of AECOPD vary from the return to near baseline characteristics to respiratory failure and death.
- Patients hospitalized with AECOPD have outcomes that include
 - decreased quality of life
 - diminished lung function (FEV1)
 - increased incidence of readmission
 - shorter duration between subsequent admissions
 - poorer muscle functions/weakness
 - secondary life threatening disease processes
 - increased mortality

REDUCE AND PREVENT
EXACERBATION IN COPD
PATIENTS: IS IT EASY?

Not

HOW TO IDENTIFY AECOPD

WHO?



Usual pattern

Symptoms increase beyond the usual daily variation and can decrease with or without treatment to complete recovery

Treatment failure

Symptoms worsen during the exacerbation event such that further treatment is deemed

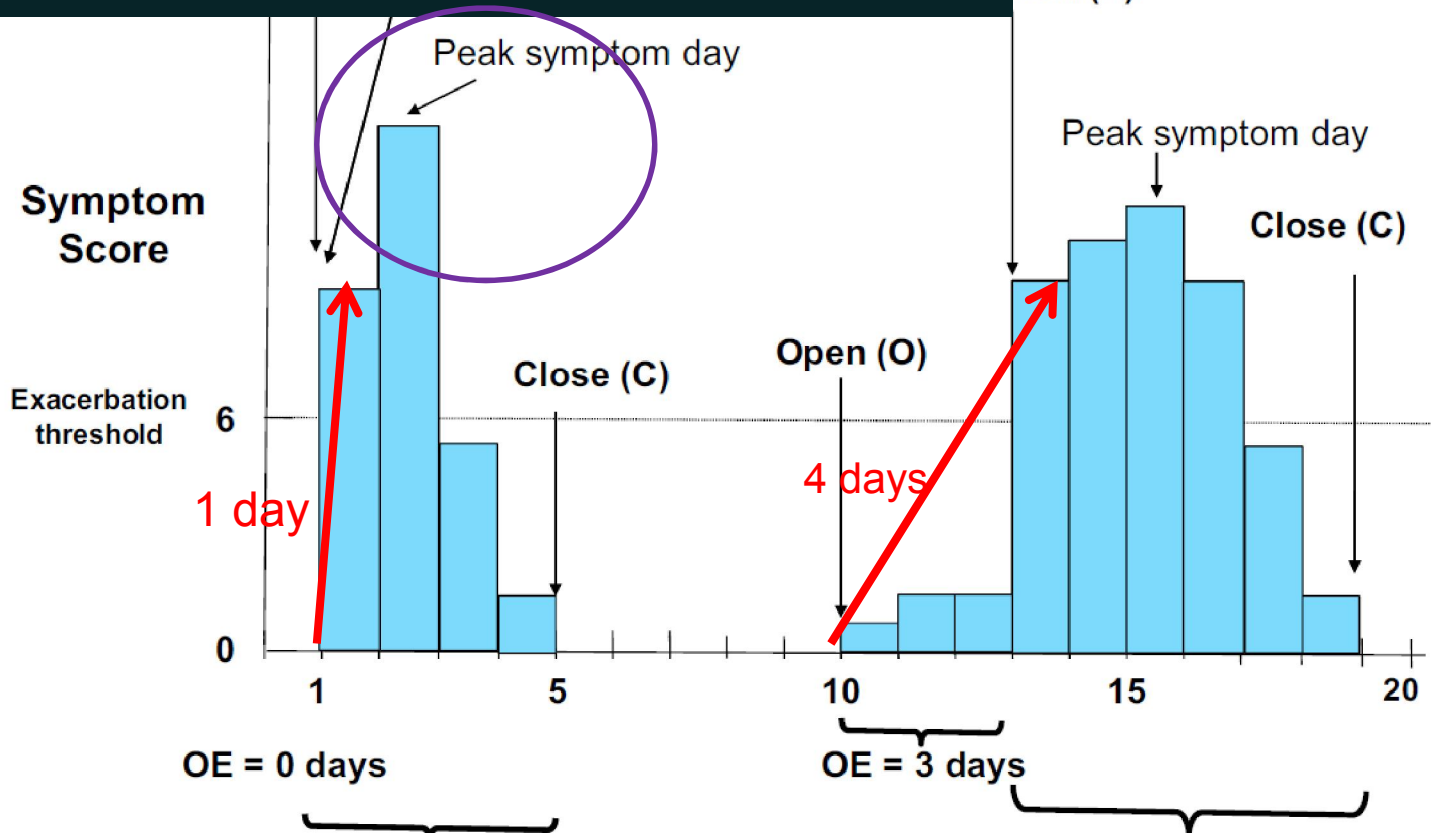
Recurrence

A new episode follows an earlier exacerbation with an interim period (more than 4 weeks) of usually relatively good health status

COPD exacerbations exhibit two distinct patterns - sudden and gradual onset

Sudden onset exacerbations associated with increased respiratory symptoms but shorter exacerbation recovery times

Thorax 2012;67:238e243

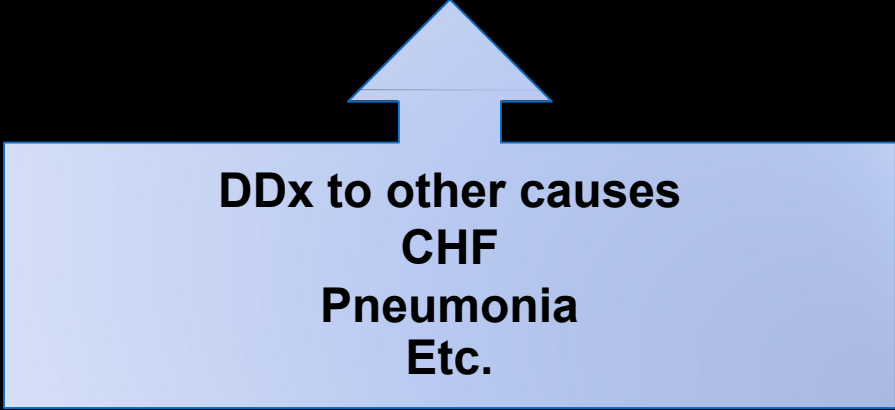


- Greater mean daily symptom scores (7.86 vs 6.55 points, $p < 0.001$)
- Greater peak symptom scores (10.7 vs 10.2 points, $p = 0.003$)
- Earlier peak symptoms (4.5 vs 8.0 days, $p < 0.001$)
- Shorter median recovery times back to baseline health status (11 vs 13 days)

Exacerbation Severity

- Level I : can be treated at home
- Level II : requires hospitalization
- Level III : leads to respiratory failure

Cannot detect



DDx to other causes
CHF
Pneumonia
Etc.

- Level I would be mild to moderate exacerbations
- Level II would be severe exacerbations
- Level III would be very severe exacerbations

HOW TO IDENTIFY HIGH RISK PATIENT

WHO?

Severity of COPD:

Increased baseline dyspnea

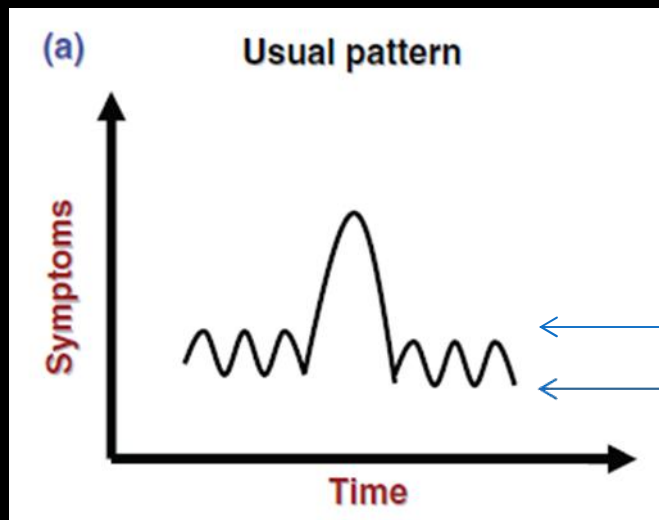
Low FEV1

Low PaO₂

- Eclipse study

- near a third of patients with very severe COPD were not associated with exacerbations at all, whereas others with less advanced disease may have repeated acute episodes

Hurst et al. N Engl J Med 2010

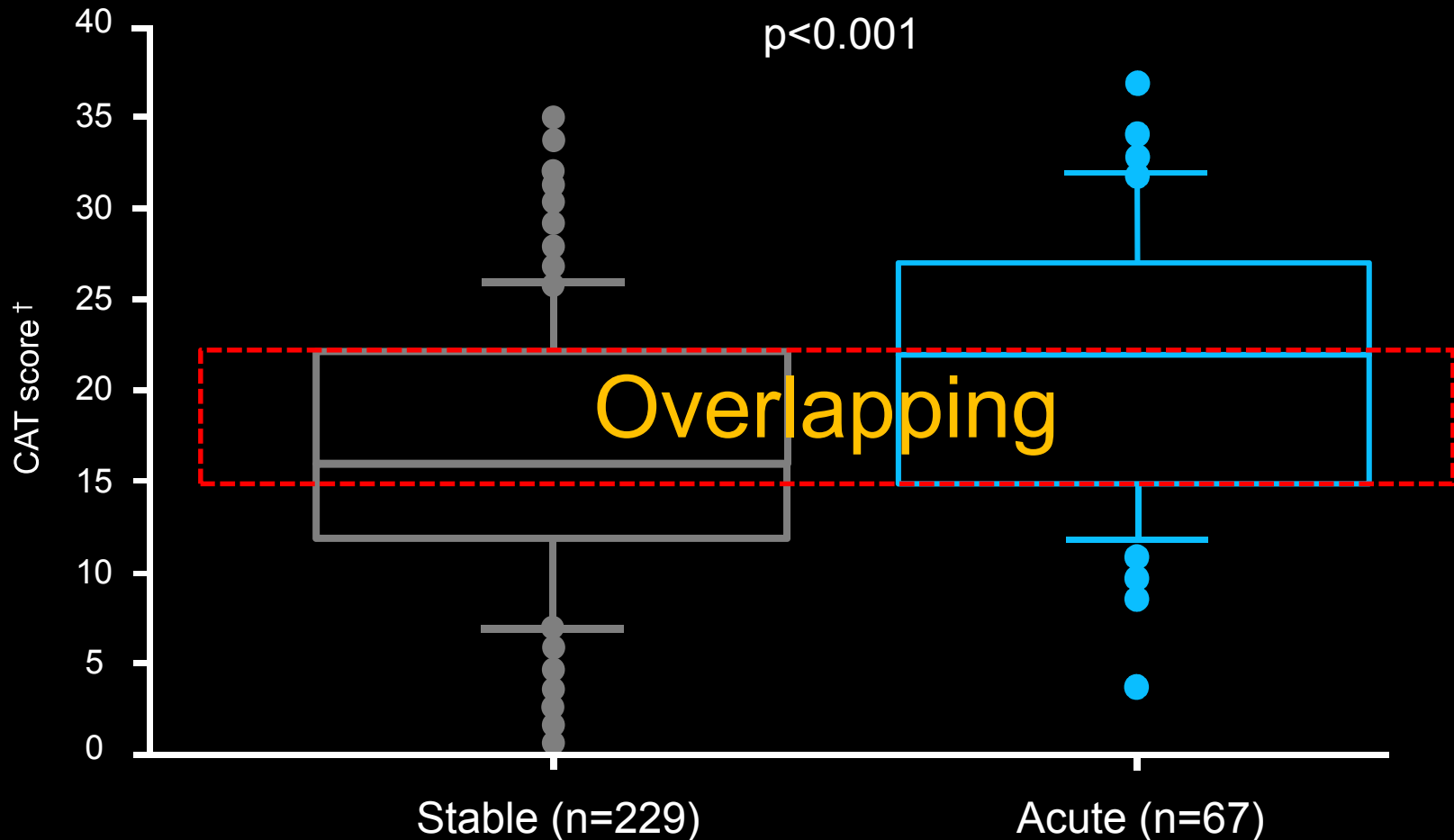


Increased baseline dyspnea

How to know the level
of diurnal variation

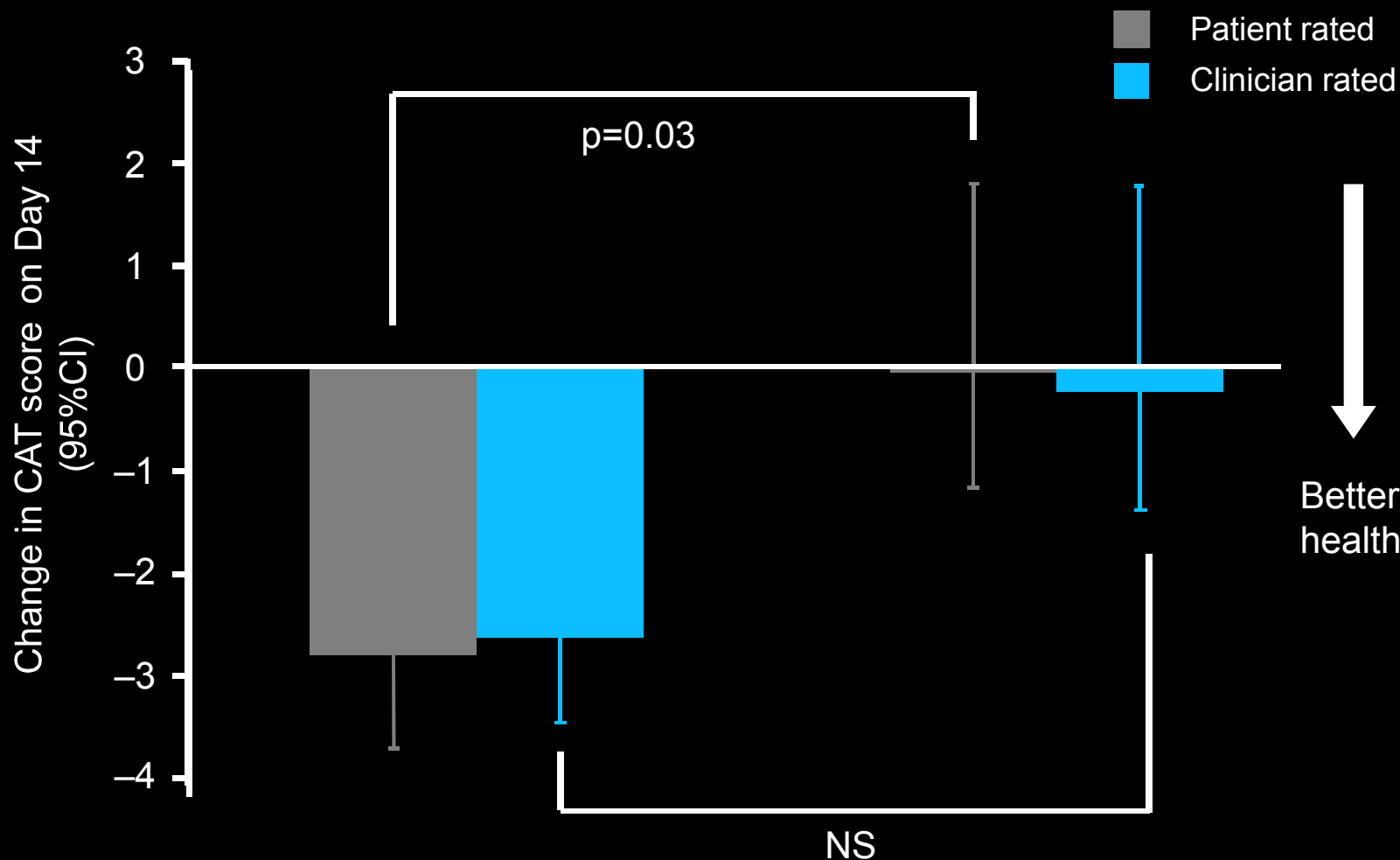
Monitor PEF? - not practical

CAT scores in stable and exacerbating patients



†CAT scaling range 0–40, higher score indicates poorer health; dots represent individuals who lie outside the 10% and 90% limits.

Change in CAT scores 14 days after treatment for an exacerbation



Data from 65 patients and their clinicians; subjective global response to treatment

Jones et al. ERS 2010

Risk factors

Older age

Severity of COPD:

- Increased baseline dyspnea

- Low FEV1

- Low PaO₂

Frequent past exacerbations

Chronic bronchial mucus hypersecretion

Inflammation:

- Higher airway inflammation

- Higher systemic inflammation

Bacterial load (stable phase)

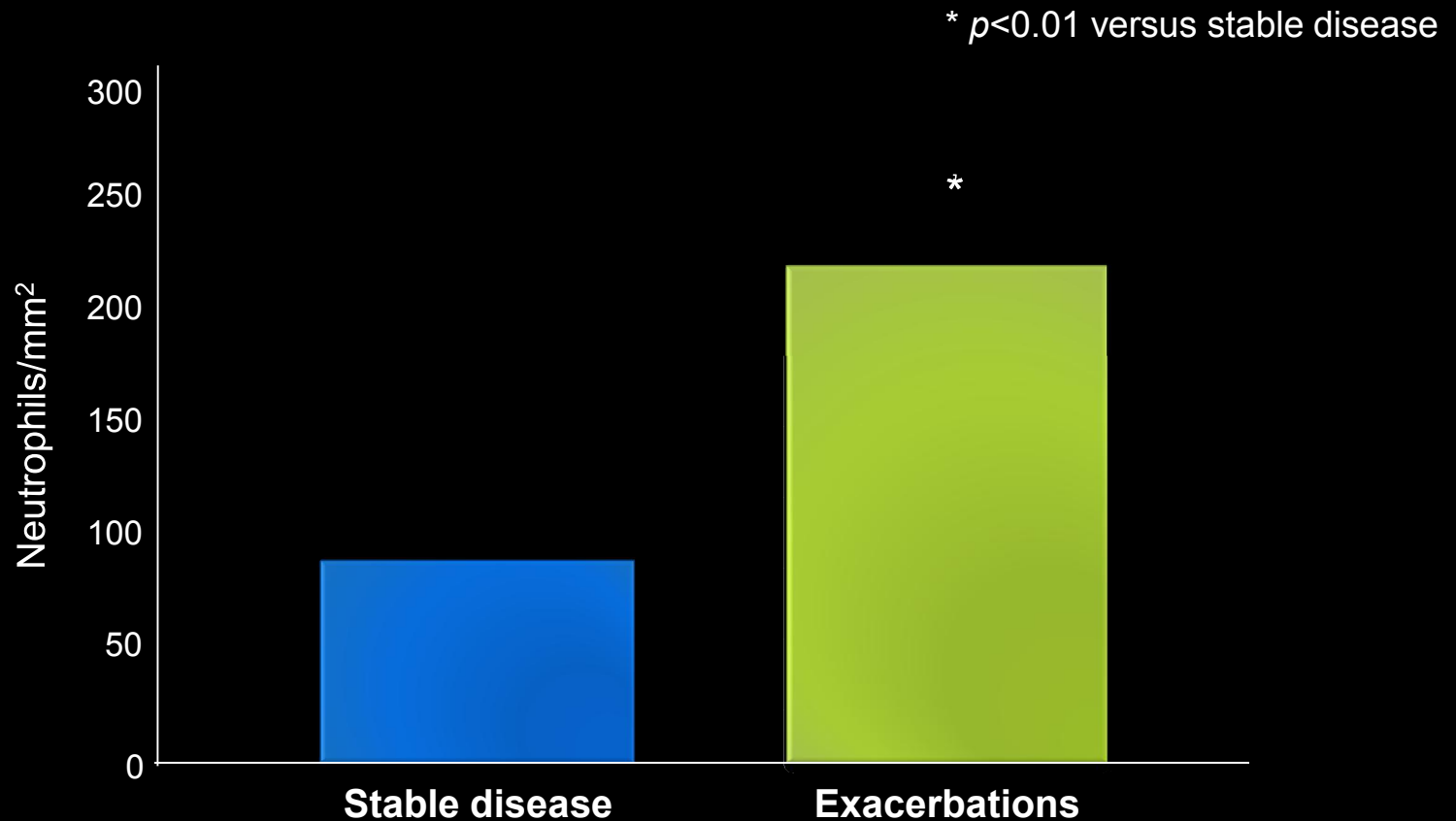
Comorbidities/systemic manifestations:

- Cardiovascular

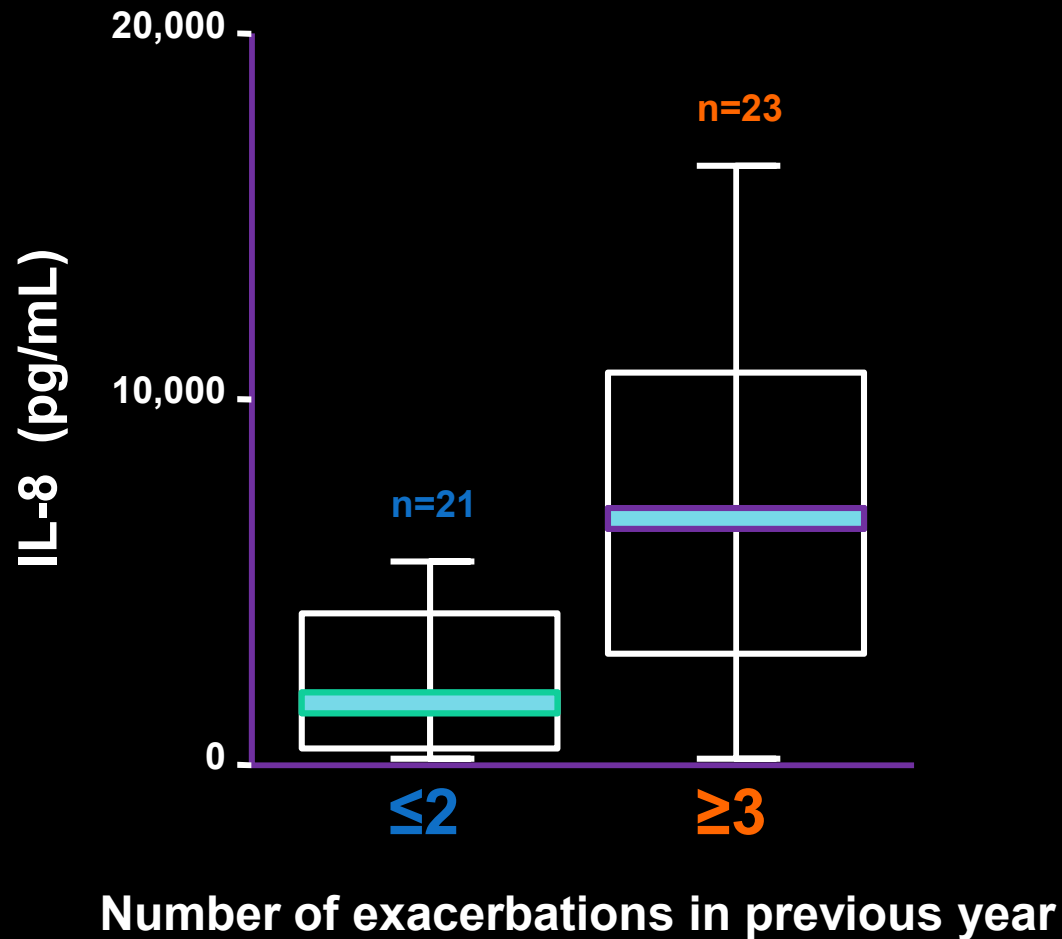
- Anxiety and depression

- Myopathy

Exacerbations are associated with increases in inflammatory cells



Inflammatory markers are increased at baseline in frequent exacerbators



HOW TO CHOOSE TREATMENT REGIMEN

Availability & Cost



Therapy at Each Stage of COPD

I: Mild

II: Moderate

III: Severe

IV: Very Severe

- $FEV_1/FVC < 70\%$
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- $FEV_1/FVC < 70\%$
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or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination →
Add short-acting bronchodilator (when needed) →

Add regular treatment with one or more long-acting bronchodilators (when needed); **Add** rehabilitation

Add inhaled glucocorticosteroids if repeated exacerbations

Add long term oxygen if chronic respiratory failure. **Consider** surgical treatments

Overview of Medications for stable COPD

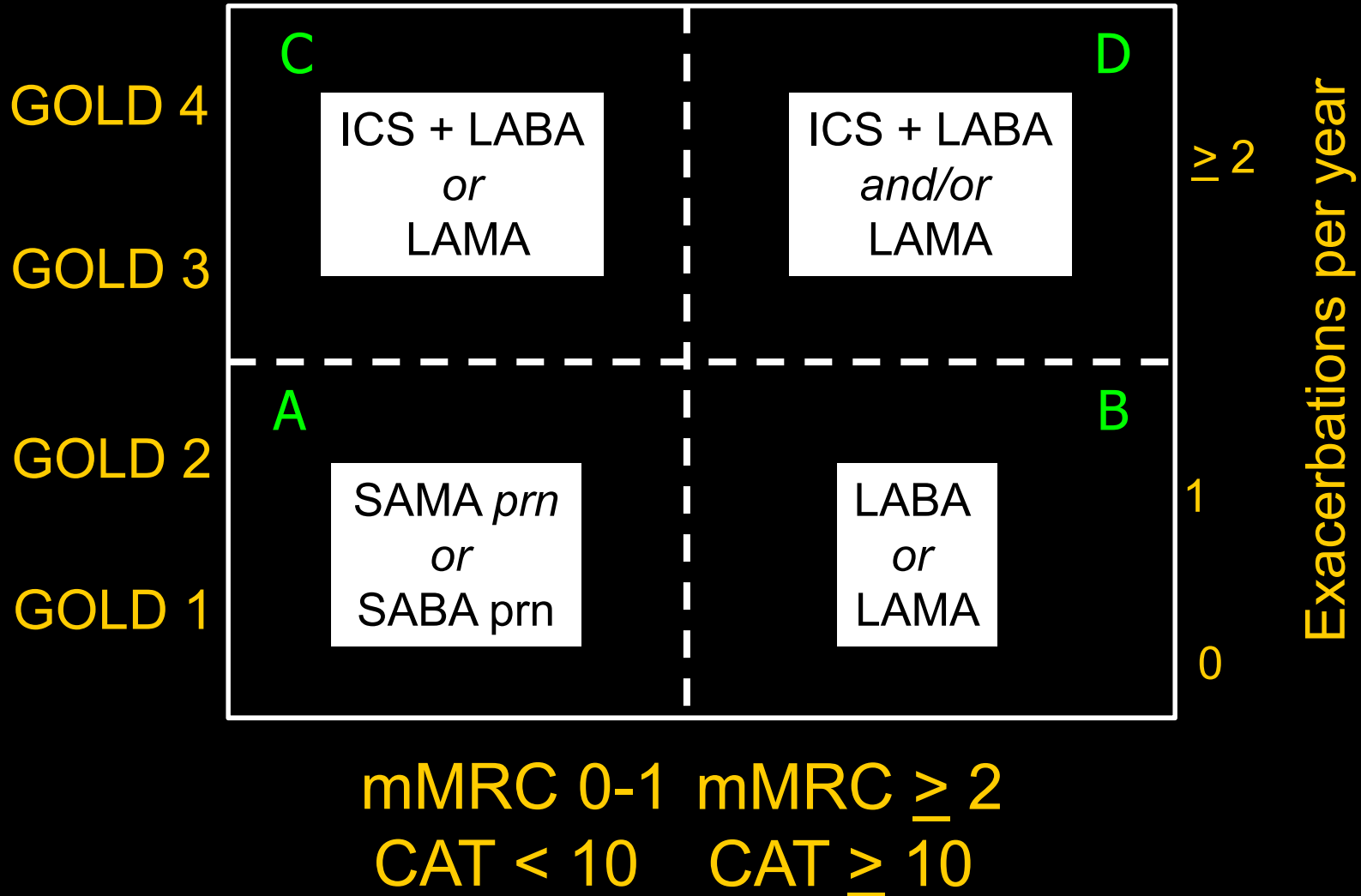
	SABA/SAMA				LAMA or LABA				ICS/LABA				PDE4			
<i>Symptom Reduction</i>	1	2	3	4	1	2	3	4	1	2*	3	4	1	2	3	4
Relieve symptoms	✓	✓	✓	✓	-	✓	✓	✓		✓	✓	✓	-	-	?	?
Improve exercise tolerance	-	-	-	-	-	✓	✓	✓		-	-	-	-	-	-	-
Improve health status	-	-	-	-	-	✓	✓	✓		✓	✓	✓	-	-	-	-
<i>Risk Reduction</i>	1	2	3	4	1	2	3	4	1	2*	3	4	1	2	3	4
Prevent disease progression	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Prevent and treat exacerbations	-	-	-	-	-	✓	✓	✓	-	✓	✓	✓	-	-	✓	✓
Reduce mortality	-	-	-	-	-	-	-	-	-	?	?	?	-	-	-	-

*Less than 60% FEV₁ (pre bronchodilator)

Not on a background of ICS

Manage Stable COPD: Pharmacologic Therapy

FIRST CHOICE



Population-based risk estimate
(i.e. probability-based)

Risk of future
events based
on spirometry

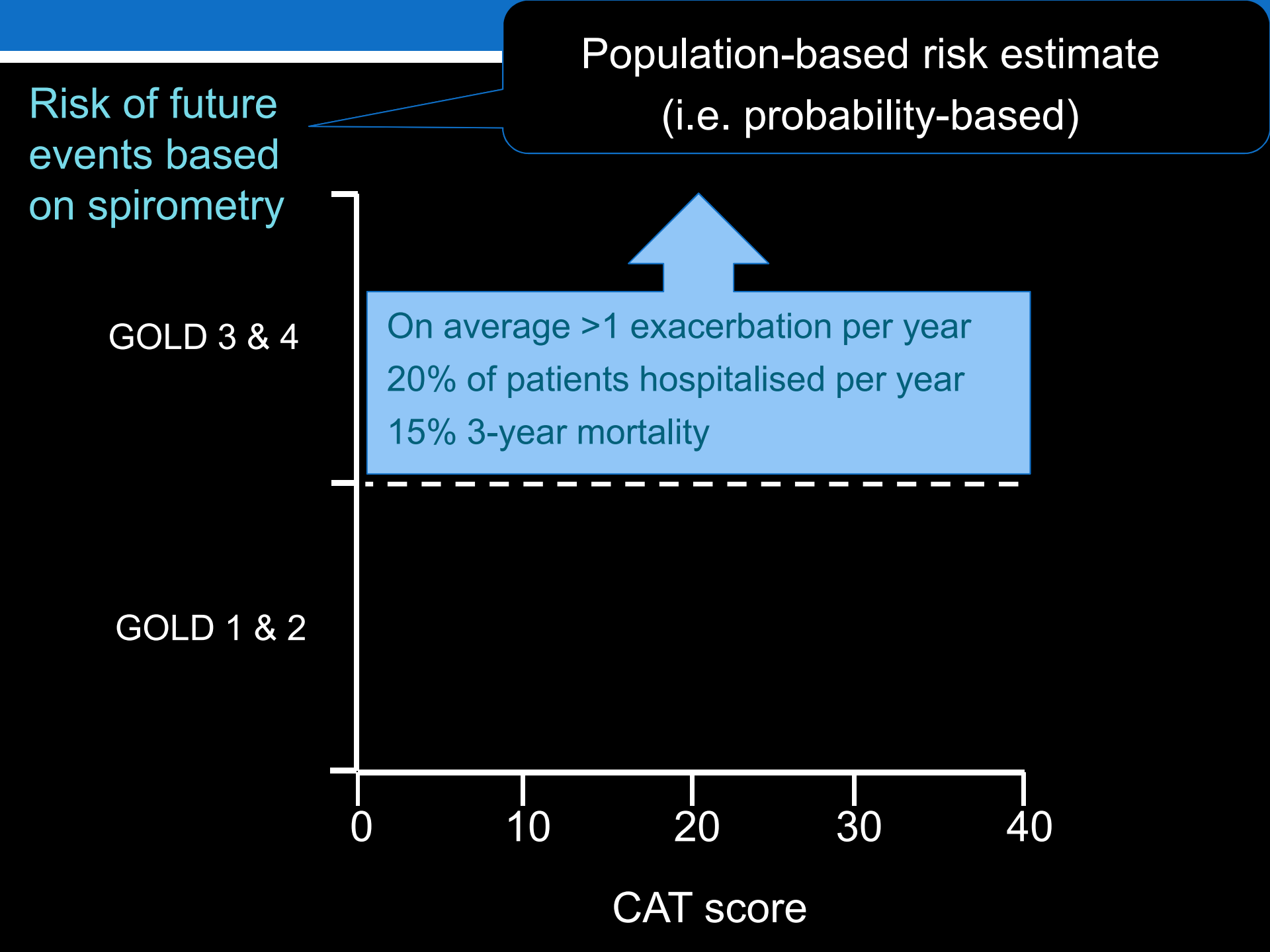
GOLD 3 & 4

On average >1 exacerbation per year
20% of patients hospitalised per year
15% 3-year mortality

GOLD 1 & 2

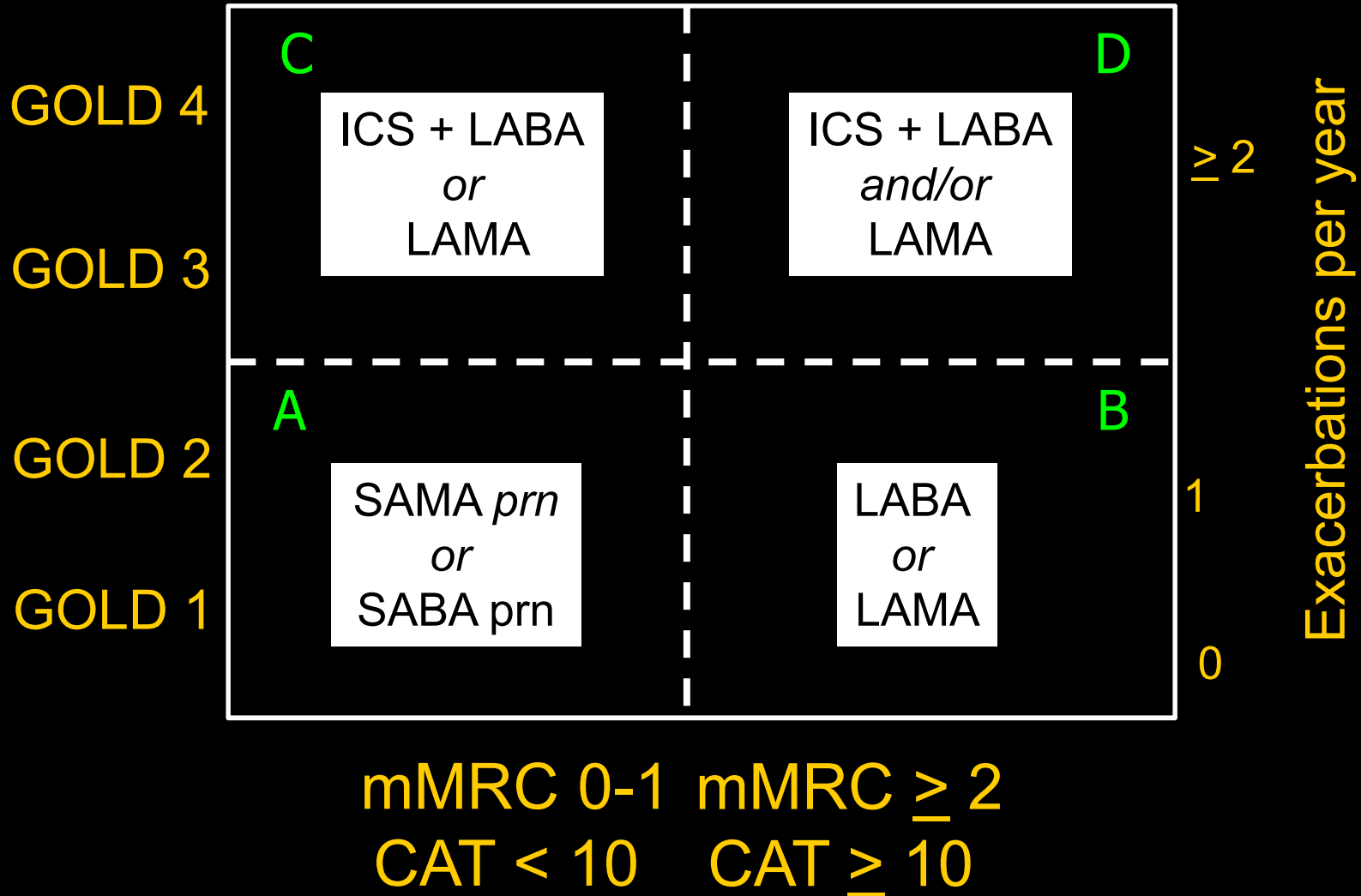
0 10 20 30 40

CAT score



Manage Stable COPD: Pharmacologic Therapy

FIRST CHOICE



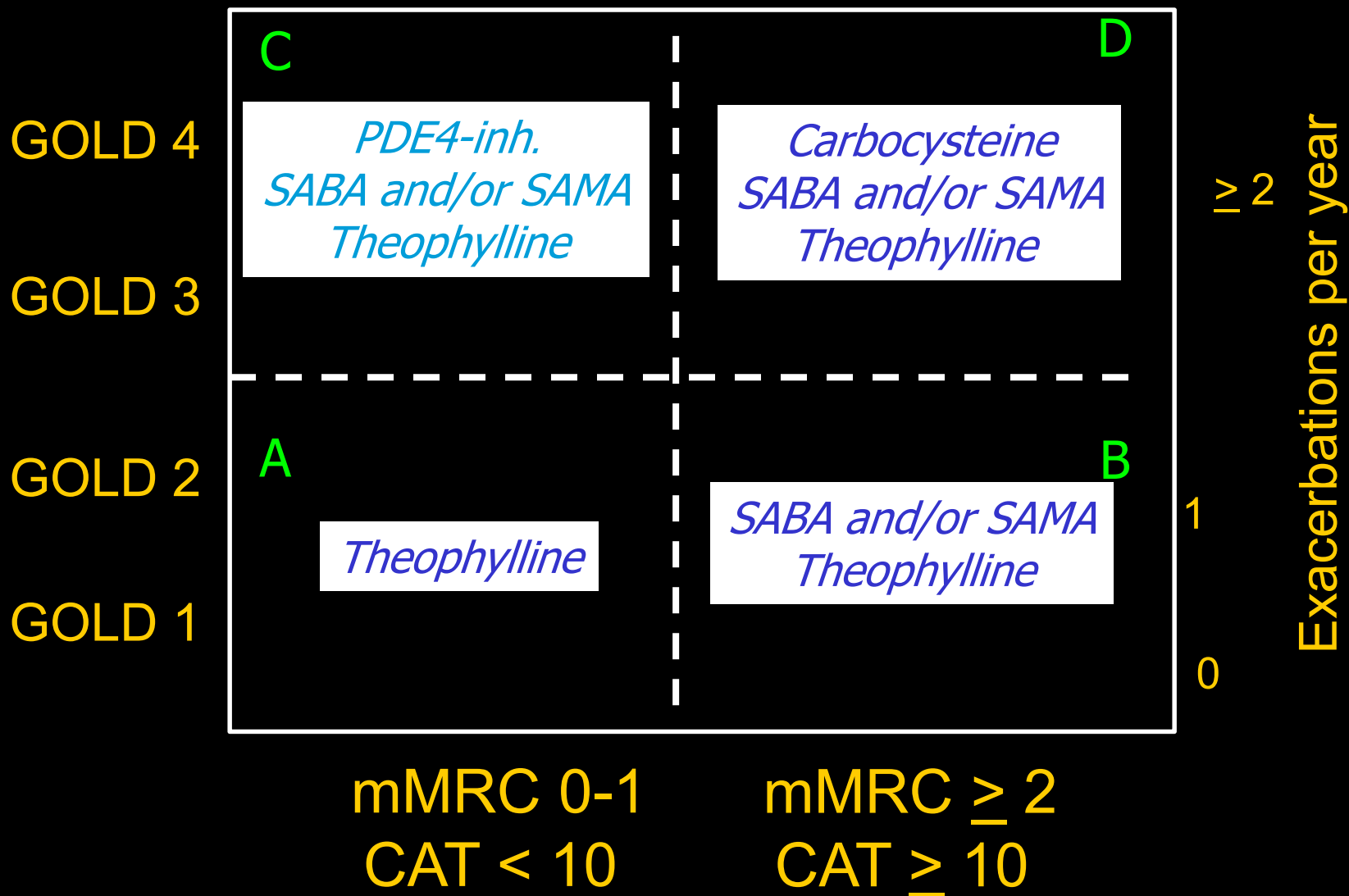
Manage Stable COPD: Pharmacologic Therapy

SECOND CHOICE

	C	D	
GOLD 4	LAMA and LABA	ICS and LAMA <i>or</i> ICS + LABA and LAMA <i>or</i> ICS + LABA and PDE4-inh <i>or</i> LAMA and LABA <i>or</i> LAMA and PDE4-inh.	Exacerbations per year ≥ 2 1 0
GOLD 3			
GOLD 2	A	B	
GOLD 1	LAMA <i>or</i> LABA <i>or</i> SABA and SAMA	LAMA and LABA	
	mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10	

Manage Stable COPD: Pharmacologic Therapy

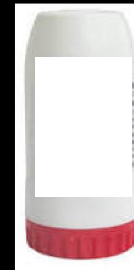
ALTERNATIVE CHOICES



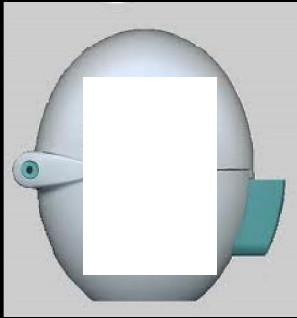
Cost / month



	Chula	Private
SFC ACC 50/500	749	NA
SFC ACC 50/250	577	1200
SFC evo 25/250	700	(25/125) 1050



	Chula	Private
B/F 320/9	737	NA
B/F 160/4.5	1118	1395



Chula	Private
1112	2220



Chula	Private
1297	1650



Chula	Private
356	NA



Chula	Private
120	390



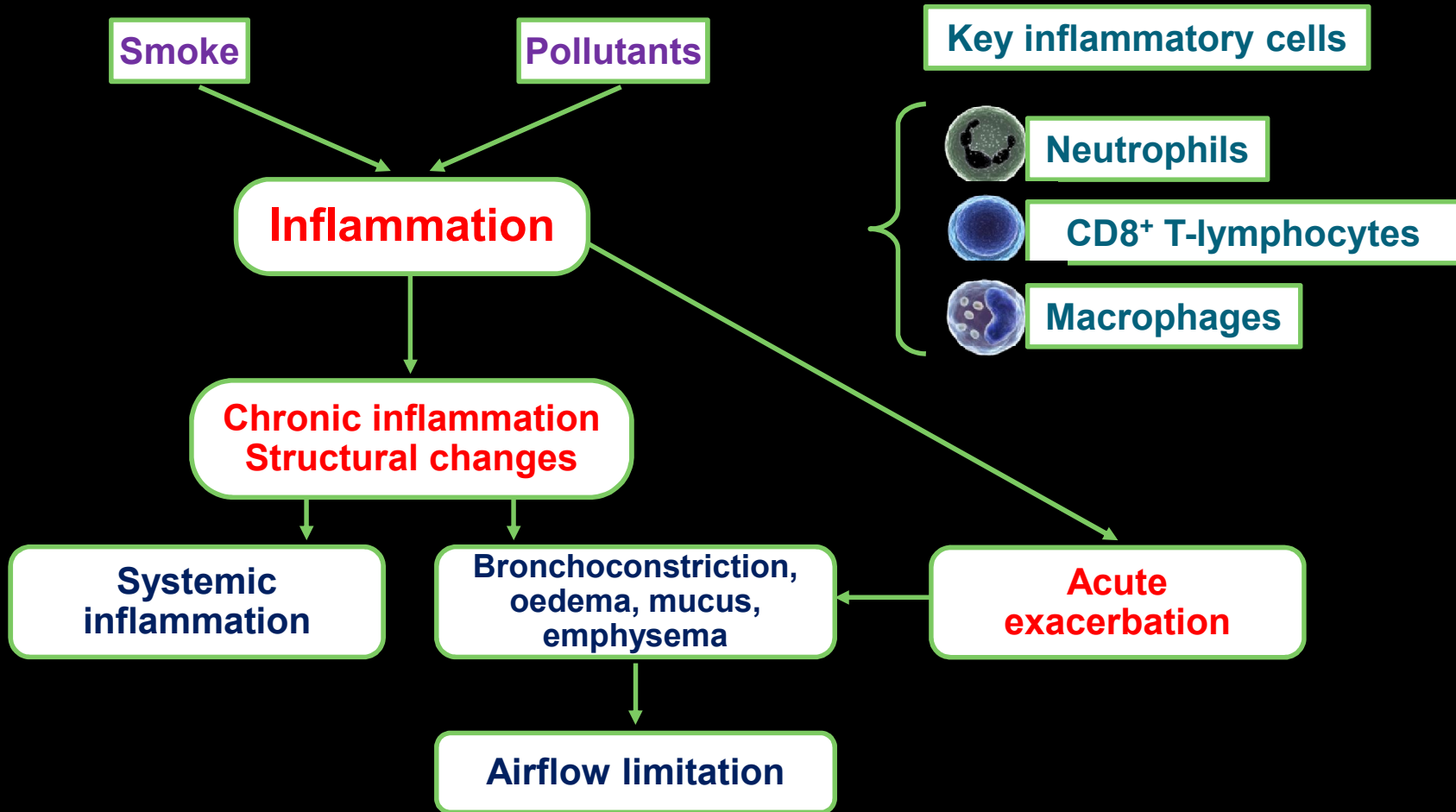
Chula	Private
1575	1740

Availability & Cost

COPD	B	C	D
1 st choice	LABA or LAMA	ICS+LABA or LAMA	ICS+LABA And/or LAMA
CU	1297 VS 1112	750 VS 1112	1900
Private	1650 VS 2220	1200 VS 2220	3420
2 nd choice	LABA and LAMA	LABA and LAMA	<ul style="list-style-type: none"> • ICS and LAMA • ICS + LABA and LAMA • ICS + LABA and PDE4-inh • LAMA and LABA • LAMA and PDE4-inh
CU	2400	2400	More than 1400
Private	3870	3870	More than 2700
3 rd choice	SAMA or SABA And theophylline	PDE4-inh. SABA and/or SAMA Theophylline	Carbocysteine SABA and/or SAMA Theophylline
CU	440	1900 VS 440	980
Private	760	2120 VS 760	1600

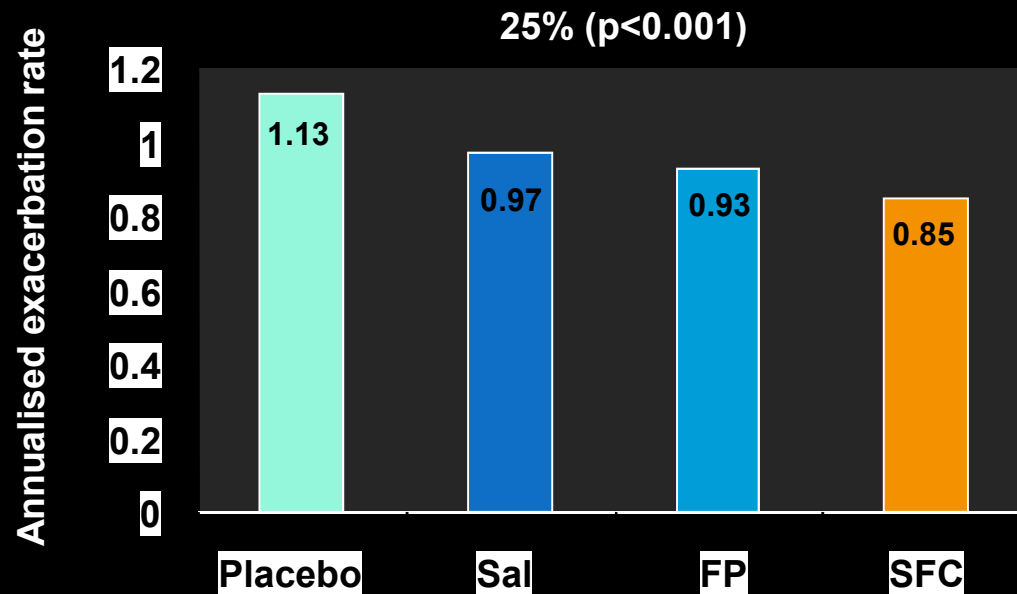
DRUG EFFICACY

Chronic Inflammation plays a central role in COPD



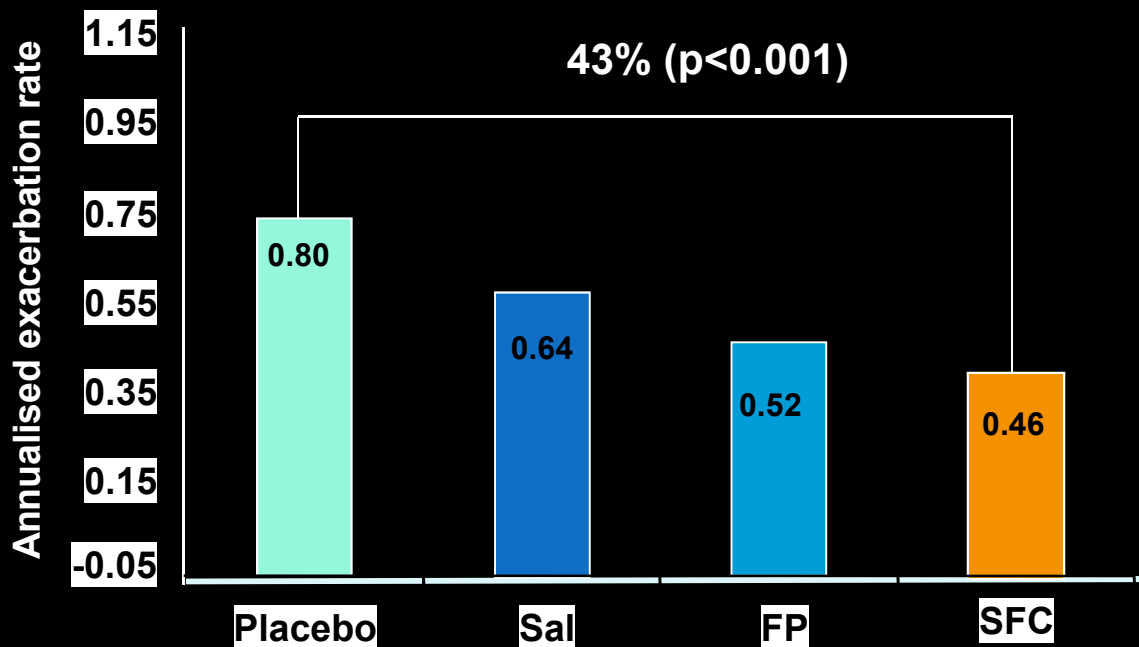
Exacerbation

SFC significantly reduces exacerbations over 3 years (TORCH)



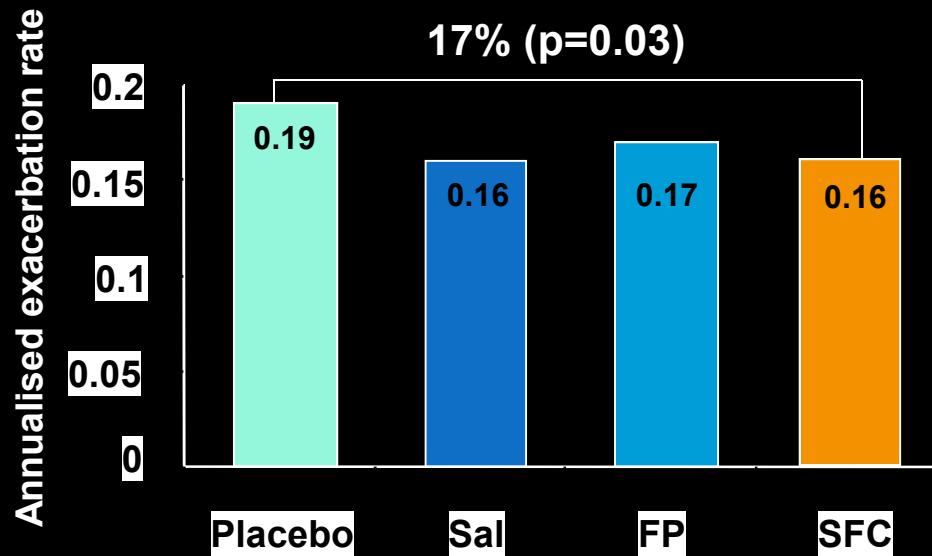
	Treatment effect	p-value
SFC vs placebo	25%	<0.001
SFC vs sal	12%	0.002
SFC vs FP	9%	0.02

SFC reduces the rate of exacerbations requiring systemic corticosteroids over 3 years (TORCH)



	Treatment effect	p-value
SFC vs placebo	43%	<0.001
SFC vs sal	29%	<0.001
SFC vs FP	13%	0.02

SFC reduces the rate of severe exacerbations requiring hospitalisation over 3 years (TORCH)



Treatment effect

p-value

SFC vs placebo

17%

0.03

SFC vs sal

-2%

0.79

SFC vs FP

5%

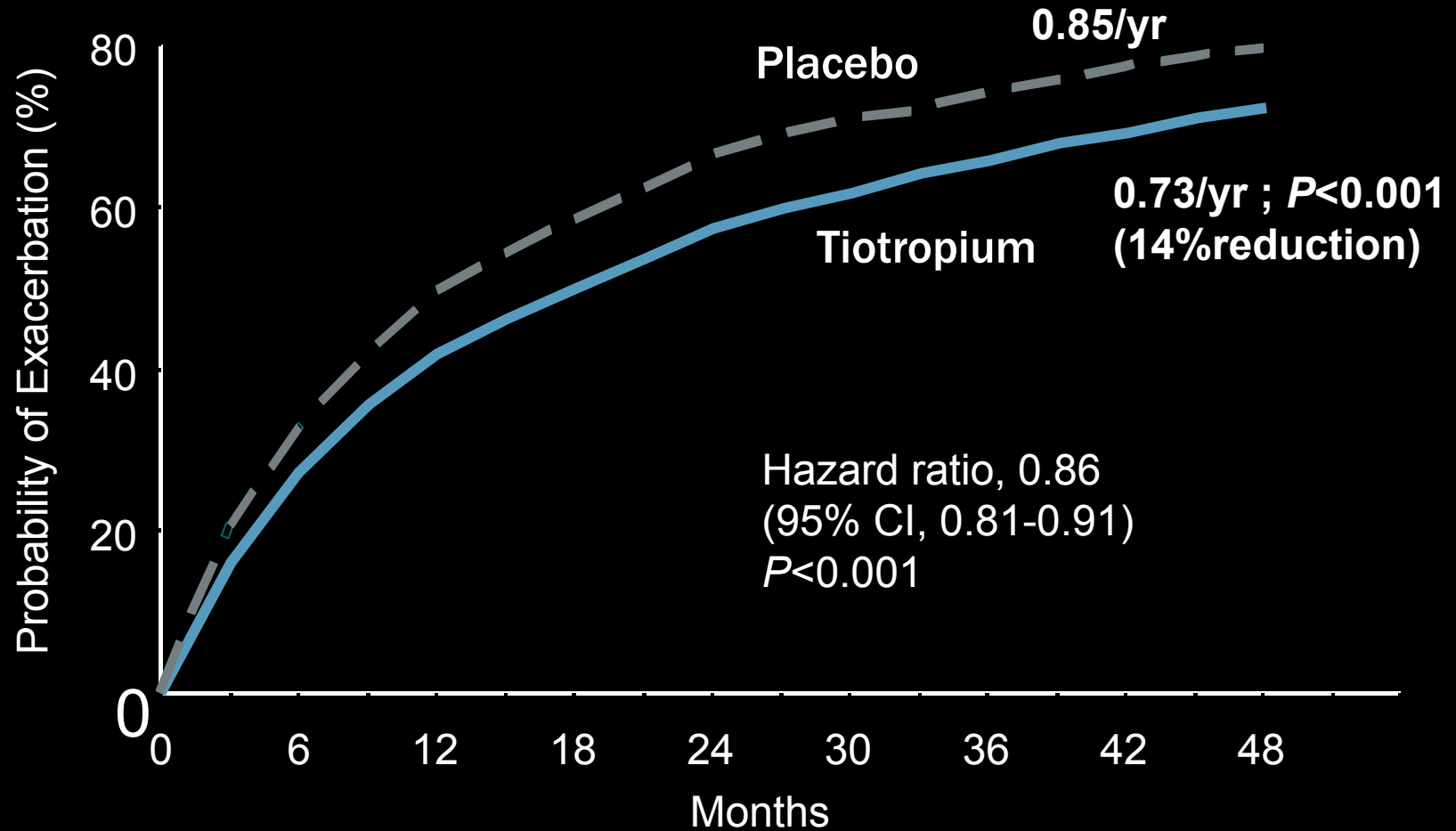
0.56

SFC: impact of exacerbation history (TORCH)¹

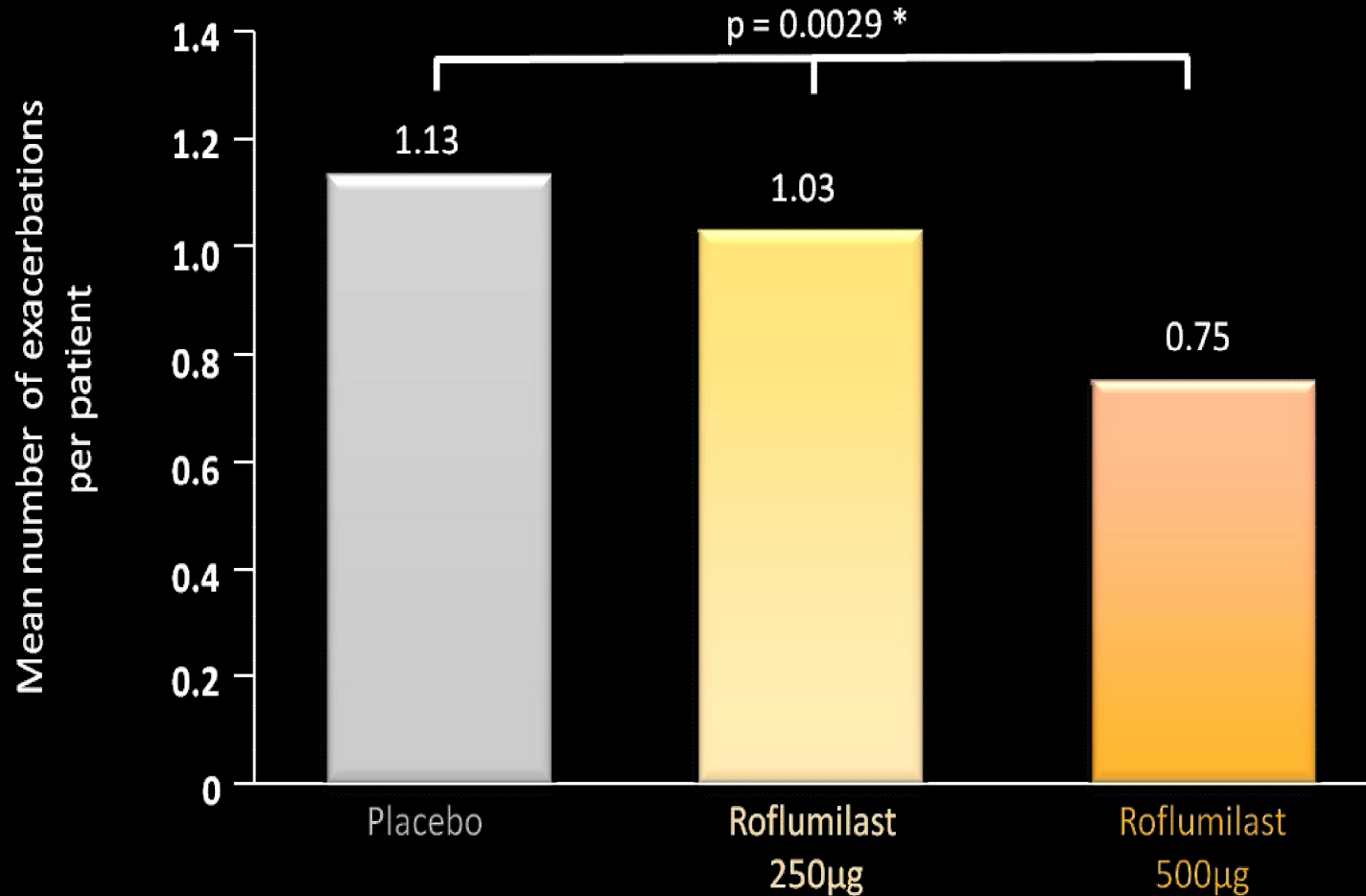
- In patients with a history of more frequent exacerbations, there were trends to higher rates overall, and a greater effect of treatment
- Reductions in exacerbation rates associated with treatment are not dependent on a history of frequent exacerbations, and the benefits of SFC on exacerbations are still seen in patients who had no history of an exacerbation in the previous 12 months

Exacerbation history: impact of SFC	% reduction
No recalled exacerbations	19
1 exacerbation in previous year	26
≥2 exacerbations in previous year	31

UPLIFT Study – Effects on Exacerbations

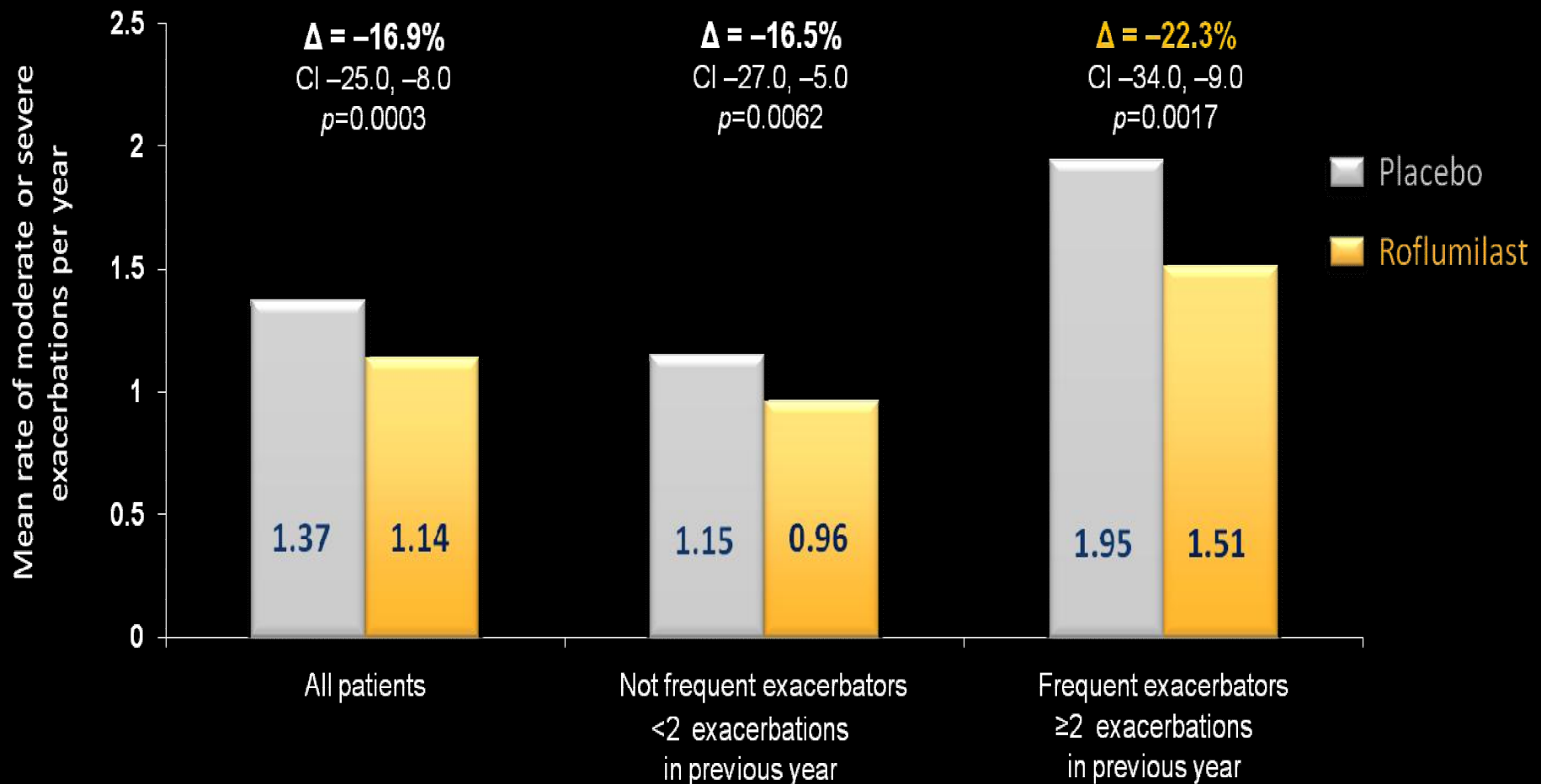


RECORD – ROFLUMILAST REDUCED EXACERBATIONS IN PATIENTS WITH MODERATE TO SEVERE COPD

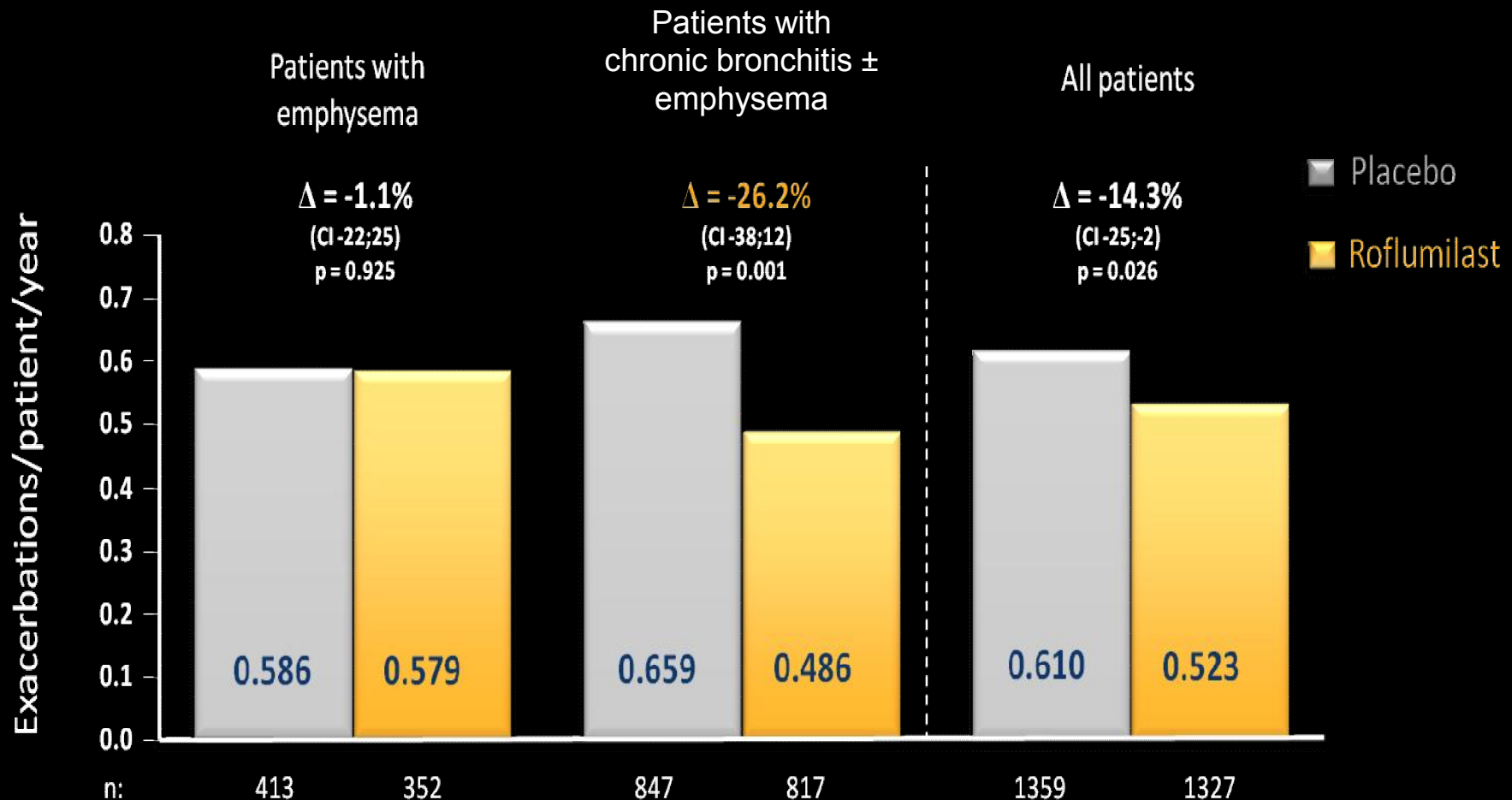


Greatest benefits of roflumilast were observed in PATIENTS WITH A HISTORY OF frequent exacerbations

► M2-124 and M2-125 pooled post hoc analysis

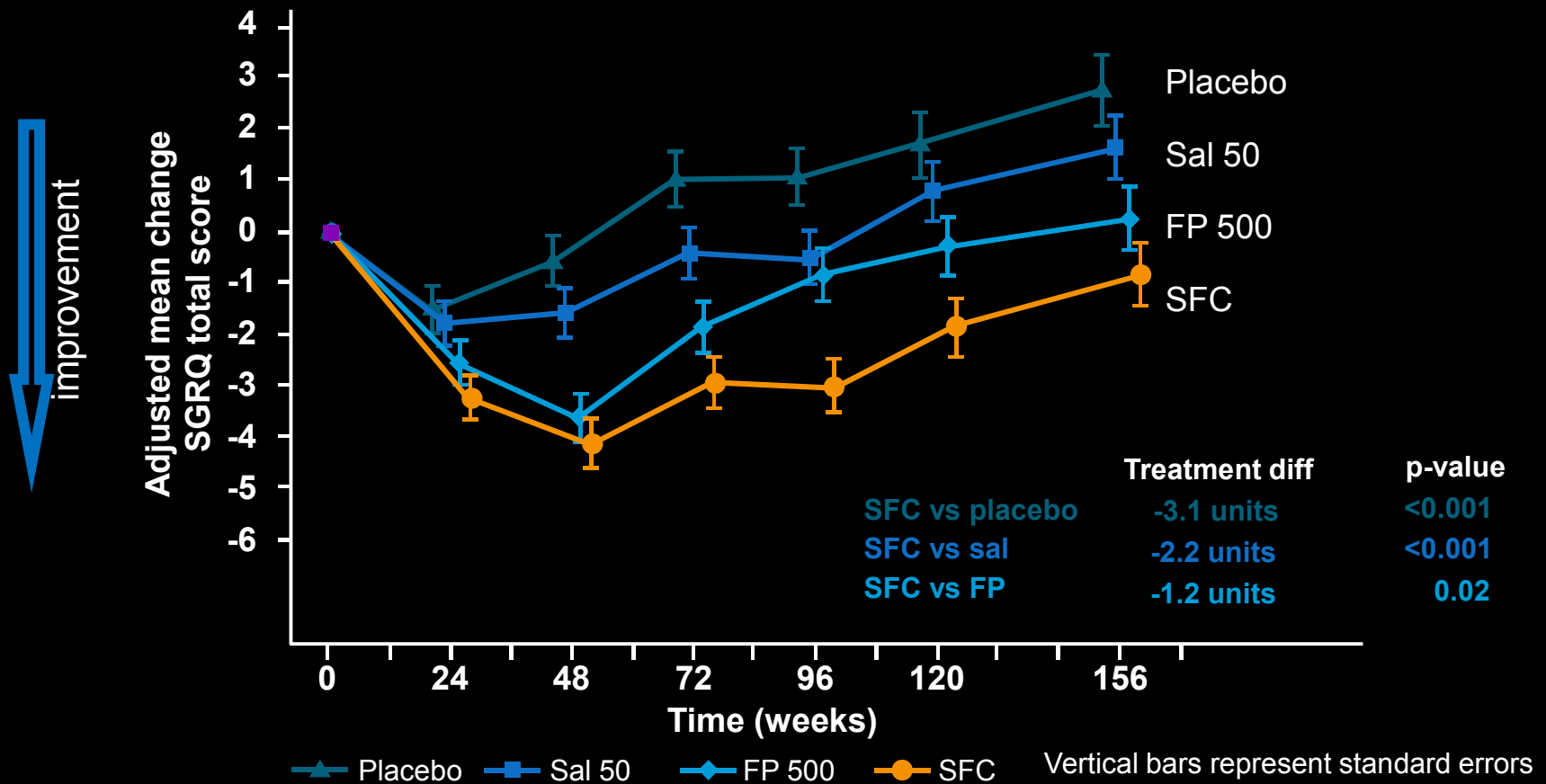


The effect of roflumilast on exacerbations was greatest in patients with chronic cough and sputum

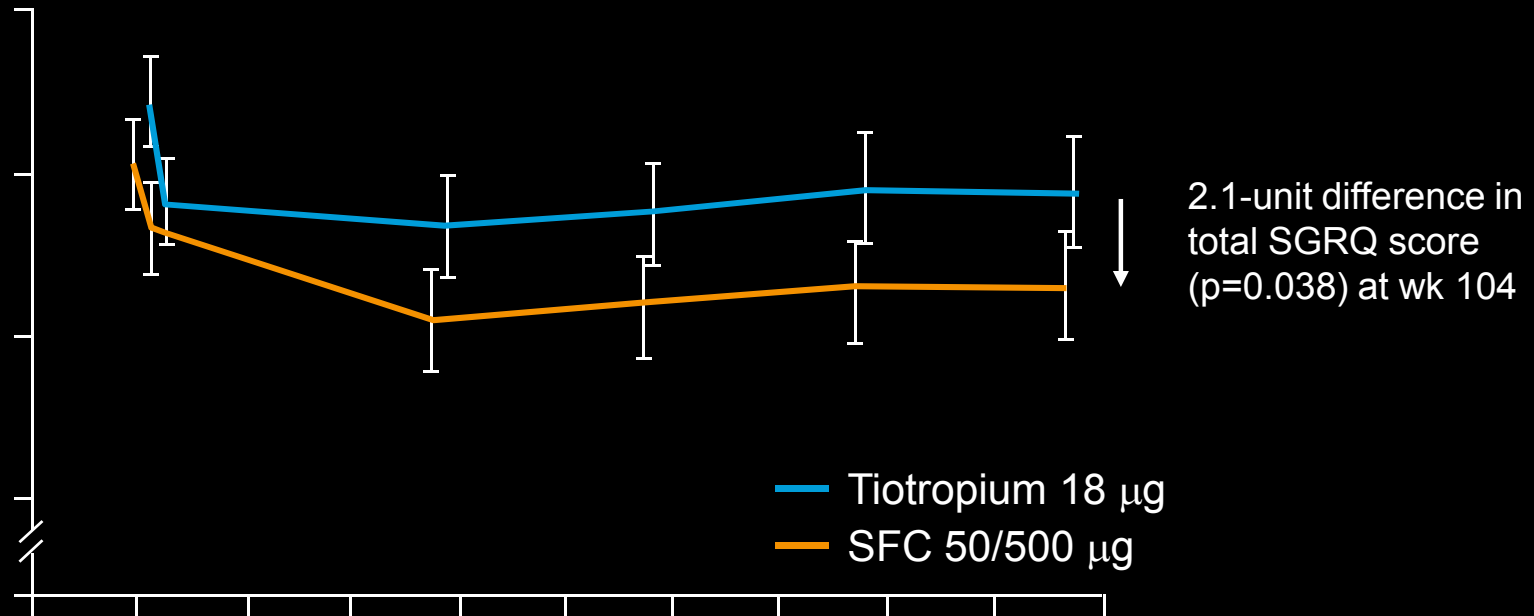


Quality of life

SFC significant improvements in **quality of life** (TORCH)

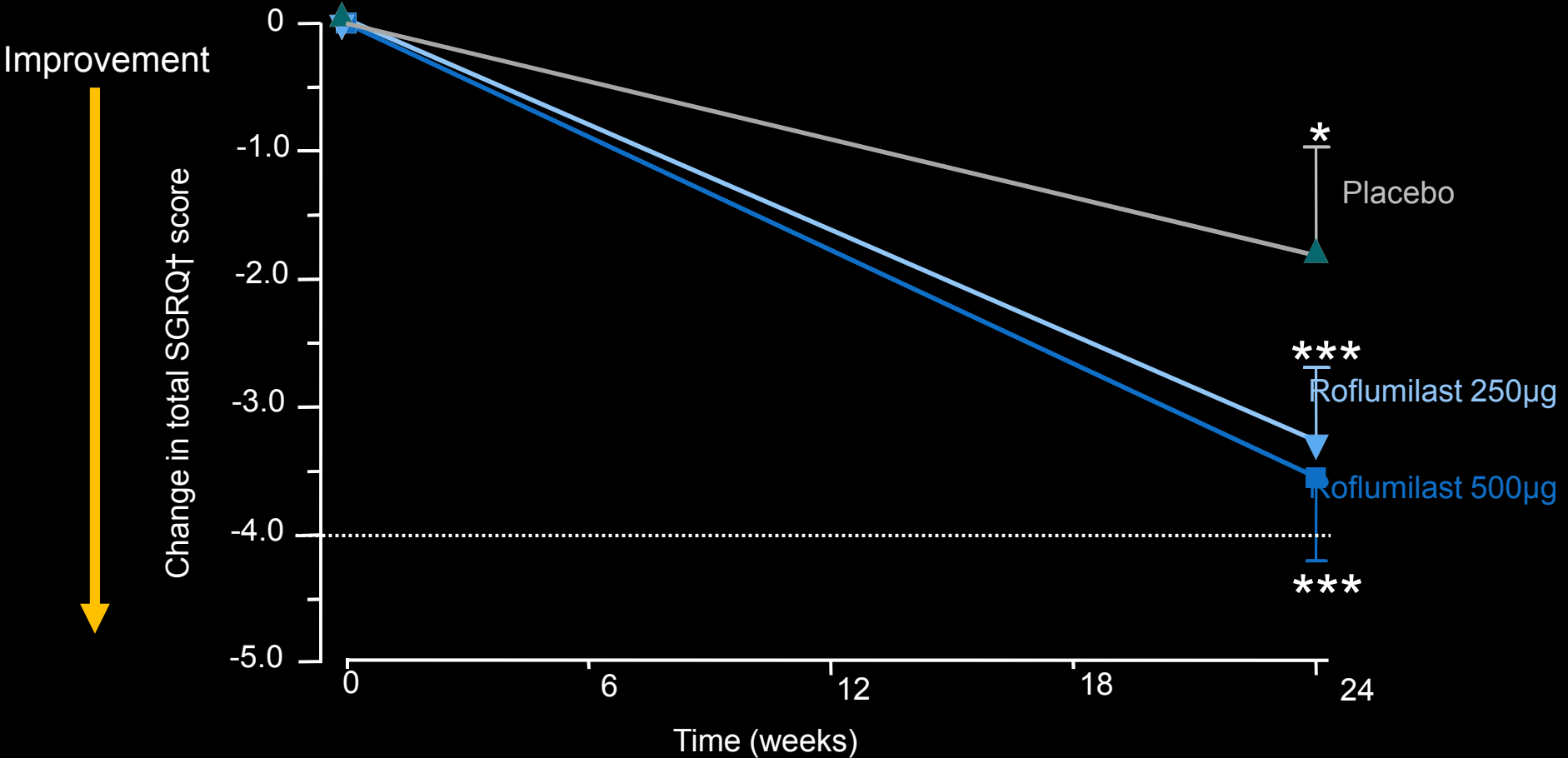


SFC: Significant and sustained improvements in **quality of life** (INSPIRE)



SFC vs Tio	Difference(SE)	95% CI	p-value
Visit 6 (wk 32)	-1.92 (0.832)	(-3.55, -0.29)	0.021
Visit 8 (wk 56)	-2.07 (0.883)	(-3.81, -0.34)	0.019
Visit 10 (wk 80)	-2.04 (0.936)	(-3.88, -0.20)	0.030
Visit 12 (wk 104)	-2.07 (0.994)	(-4.02, -0.12)	0.038

RECORD – roflumilast improved total SGRQ score in COPD patients



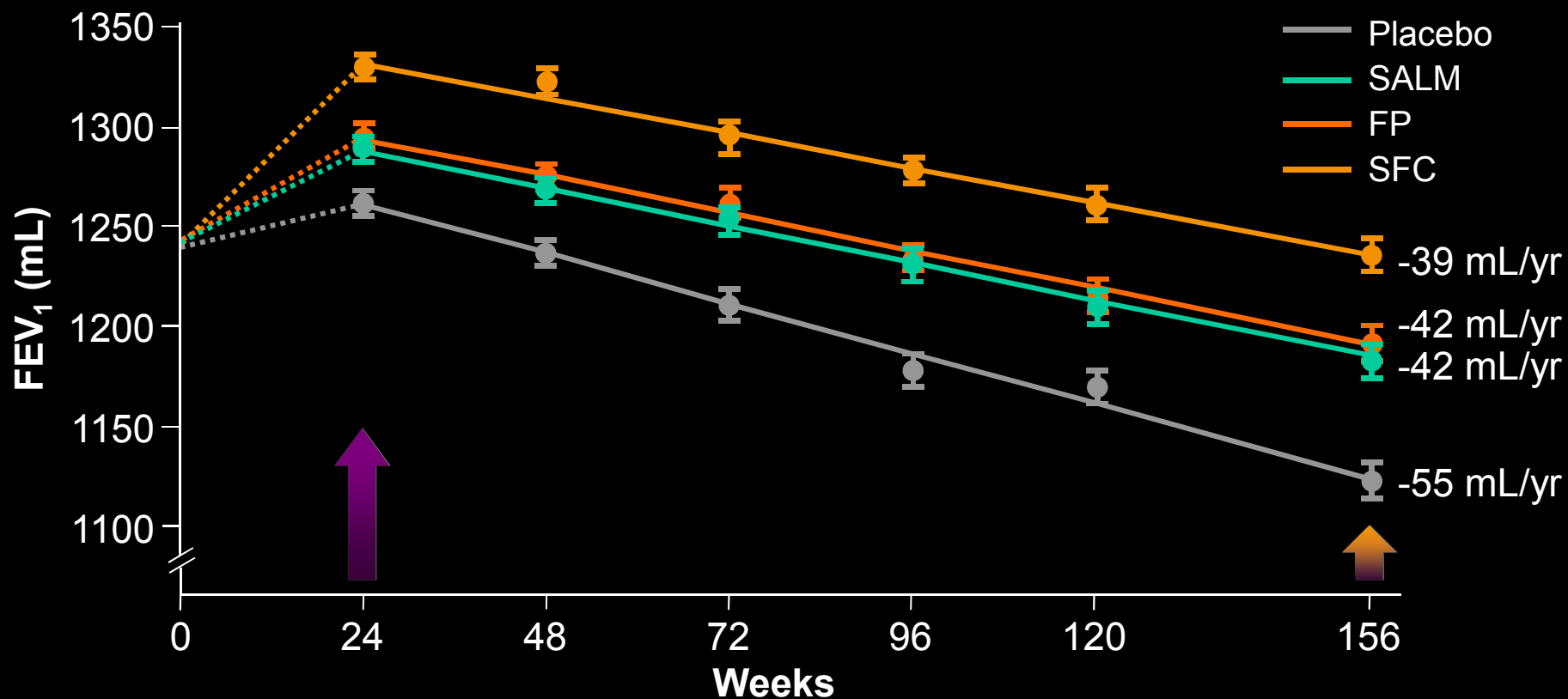
† SGRQ = St George's Respiratory Questionnaire

LS Mean and SEM

* p<0.05, *** p<0.0001 for change versus baseline

Lung function

SFC slows the rate of decline of lung function over 3 years (TORCH)

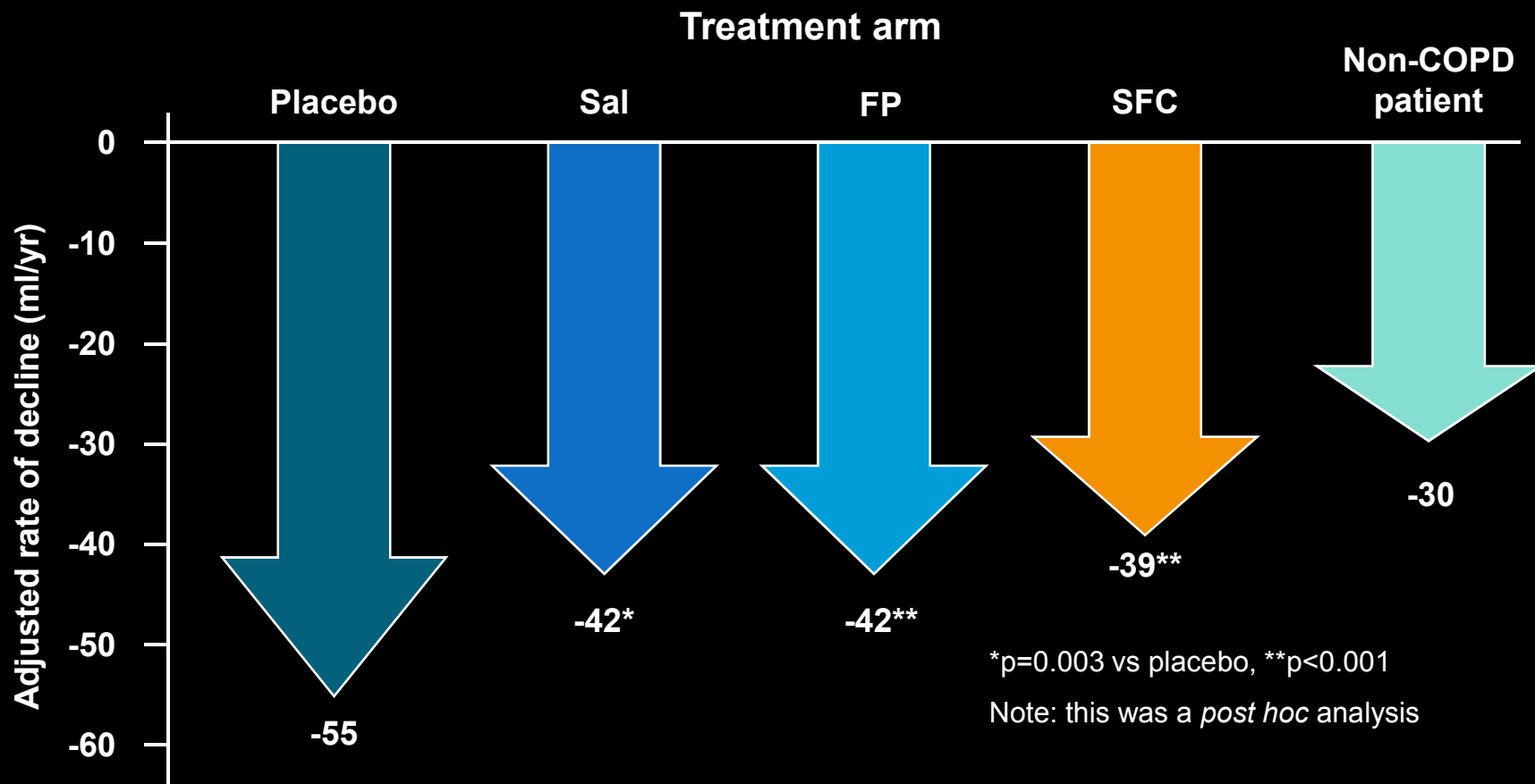


SFC versus placebo: 16 ml/year, $p < 0.001$

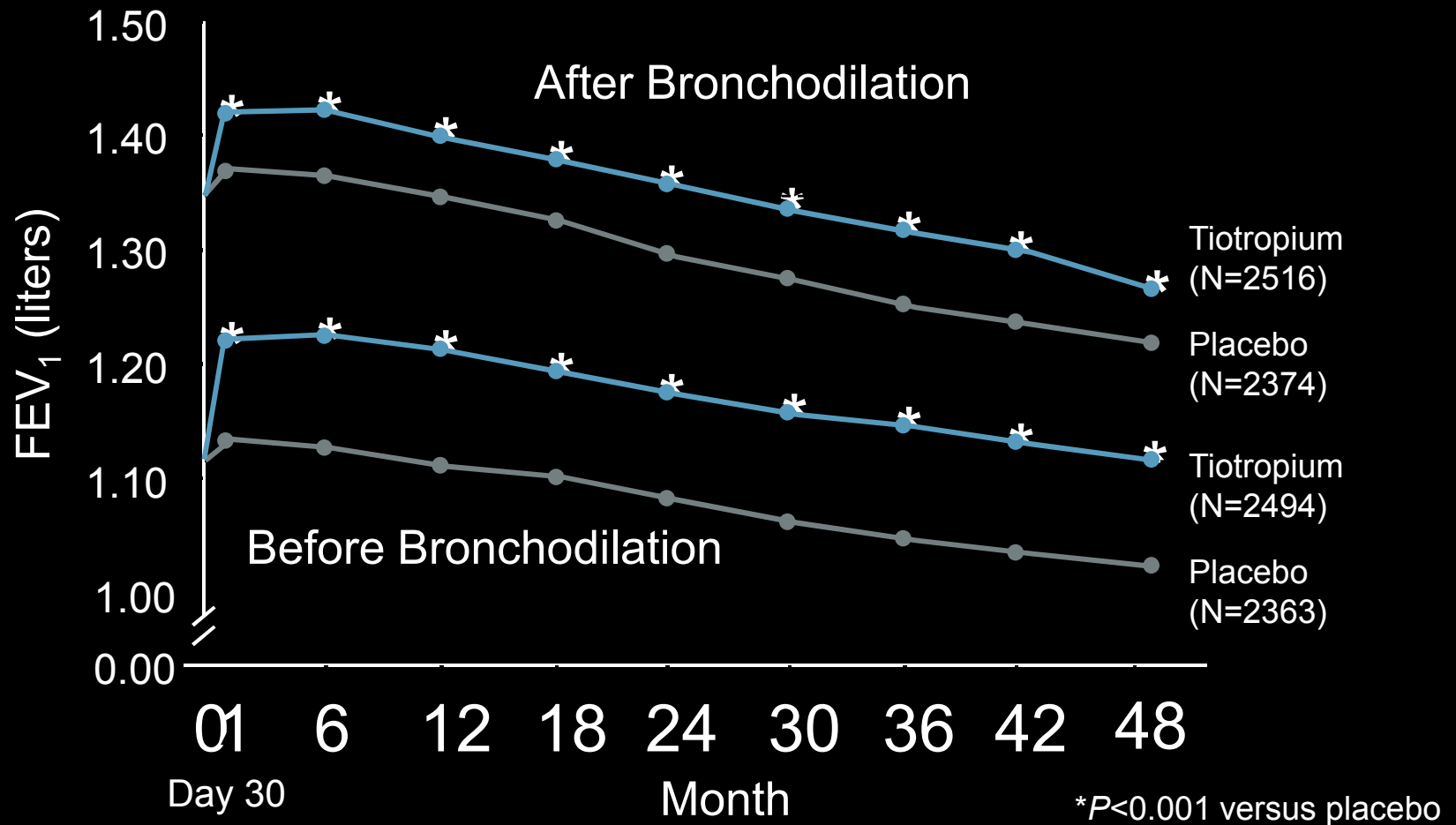
Salmeterol versus placebo: 13 ml/year, $p = 0.003$

FP versus placebo: 13 ml/year, $p = 0.003$

SFC slows the rate of decline of lung function over 3 years (TORCH)

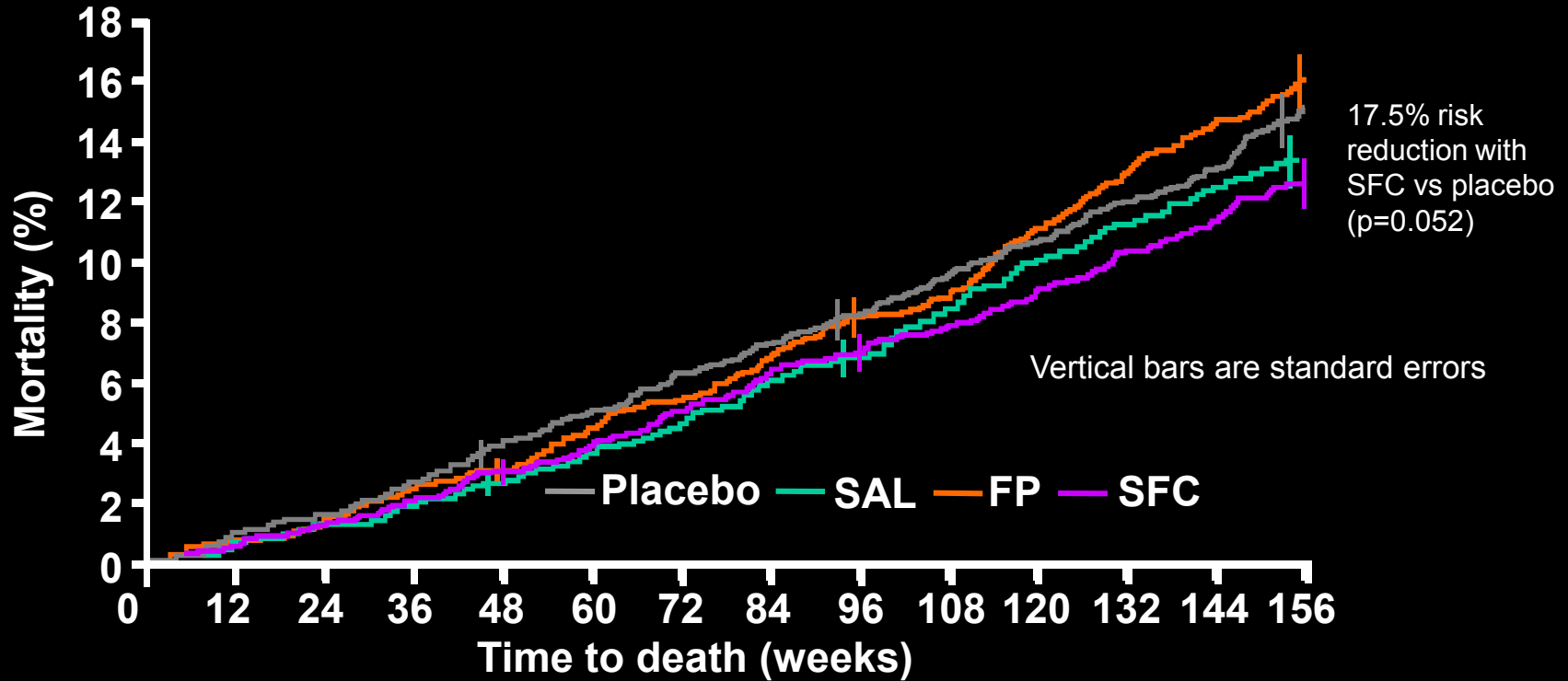


UPLIFT: Improvement of Lung Function Over 4 Years With Tiotropium



Survival

SFC all-cause mortality at 3 years (TORCH)



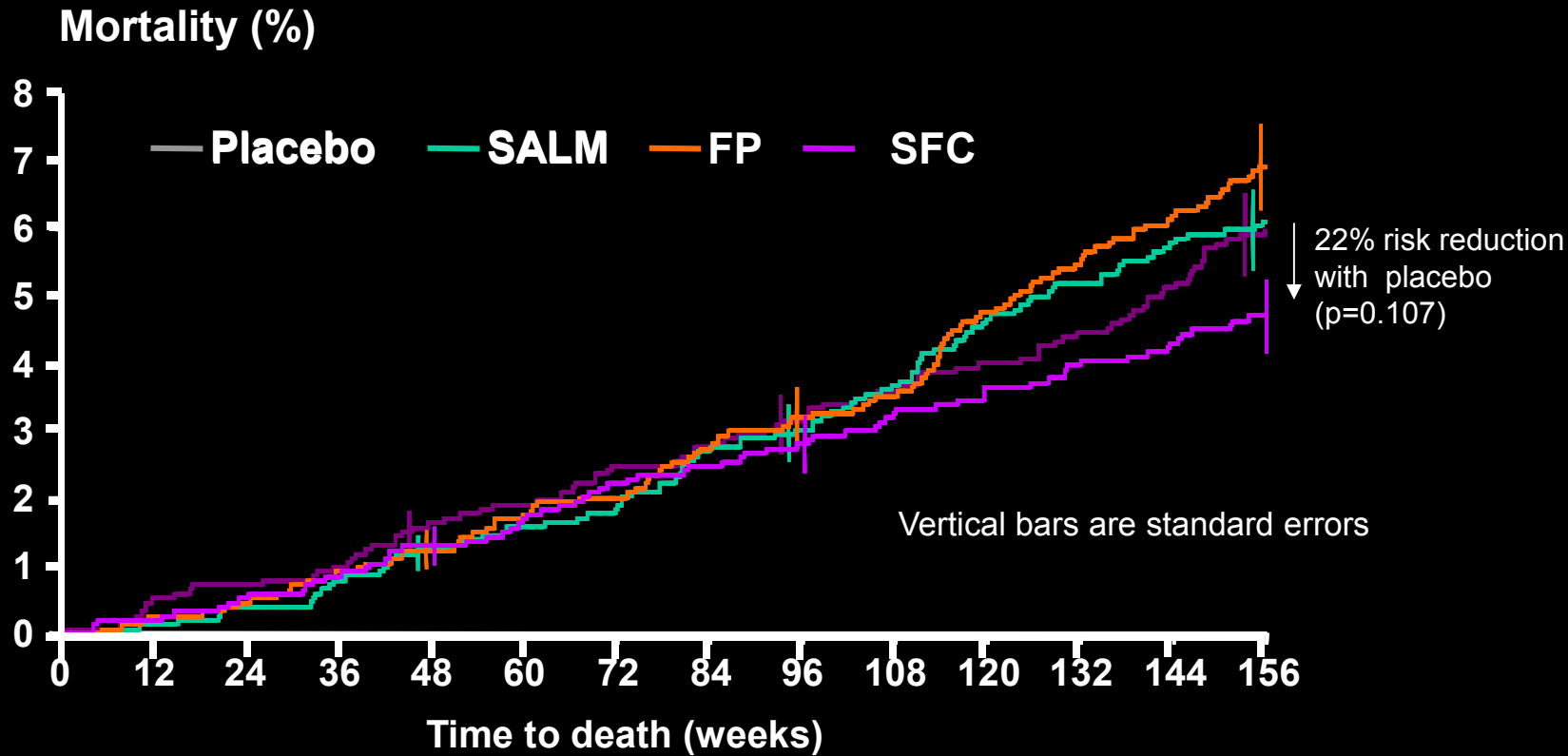
	0 weeks	48 weeks	96 weeks	156 weeks
Number	1524	1464	1399	1293
alive	1533	1487	1426	1339
	1521	1481	1417	1316
	1534	1487	1409	1288

SFC all-cause mortality at 3 years Cox's proportional hazards (TORCH)

	Placebo (n=1,524)	SFC (n=1,533)
Number of deaths	231	193
Percentage of deaths by 3 years	15.2	12.6
HR (95% CI) [†]	0.811 (0.670, 0.982)	
p-value [†]	0.031	

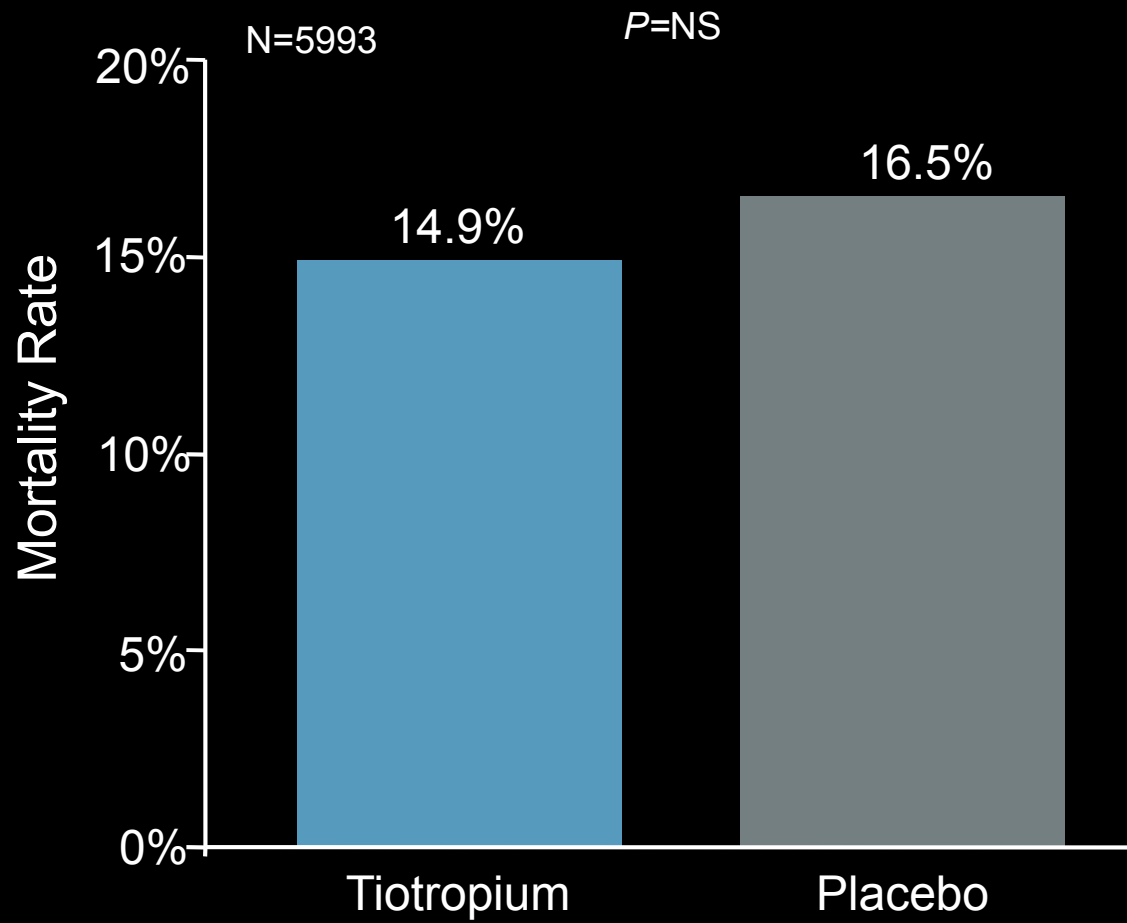
[†]Cox's proportional hazards model estimate at mean age, FEV₁, body mass index and proportional coefficients for smoking status, gender and region

SFC COPD-related mortality by 3 years (TORCH)



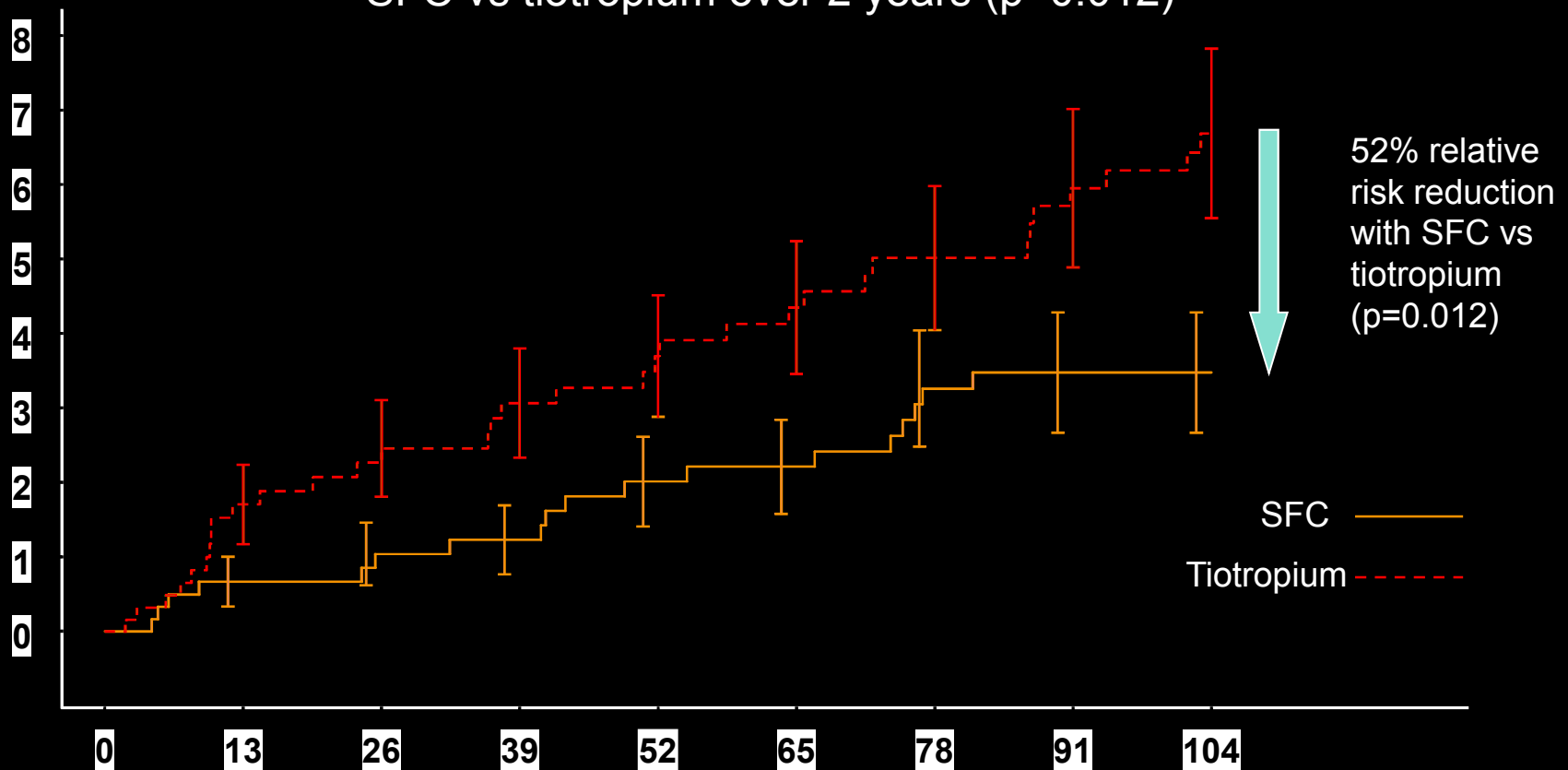
SFC reduced the rate of COPD-related mortality by 22% compared with placebo (Hazard ratio 0.78, 95% CI 0.570 to 1.057; p=0.107)

UPLIFT: 4-year Evaluation of Tiotropium – Mortality



SFC improved survival over 2 years vs tiotropium (INSPIRE)

INSPIRE showed a significant reduction in all-cause mortality with SFC vs tiotropium over 2 years ($p=0.012$)



PM&R

A COMBINATION OF PHYSICAL TRAINING, EDUCATION AND SUPPORT

Facility & Feasibility



Therapy at Each Stage of COPD

I: Mild

II: Moderate

III: Severe

IV: Very Severe

- $FEV_1/FVC < 70\%$
- $FEV_1 \geq 80\%$ predicted

- $FEV_1/FVC < 70\%$
- $50\% \leq FEV_1 < 80\%$ predicted

- $FEV_1/FVC < 70\%$
- $30\% \leq FEV_1 < 50\%$ predicted

- $FEV_1/FVC < 70\%$
- $FEV_1 < 30\%$ predicted
or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination

Add short-acting bronchodilator (when needed)

Add regular treatment with one or more long-acting bronchodilators (when needed); **Add** rehabilitation

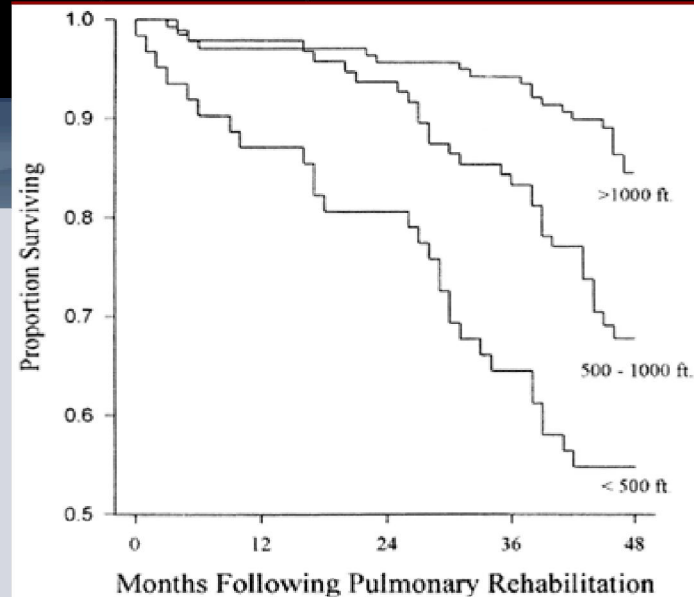
Add inhaled glucocorticosteroids if repeated exacerbations

Add long term oxygen if chronic respiratory failure. **Consider** surgical treatments

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**).
- Psychosocial intervention is helpful (**Evidence C**).

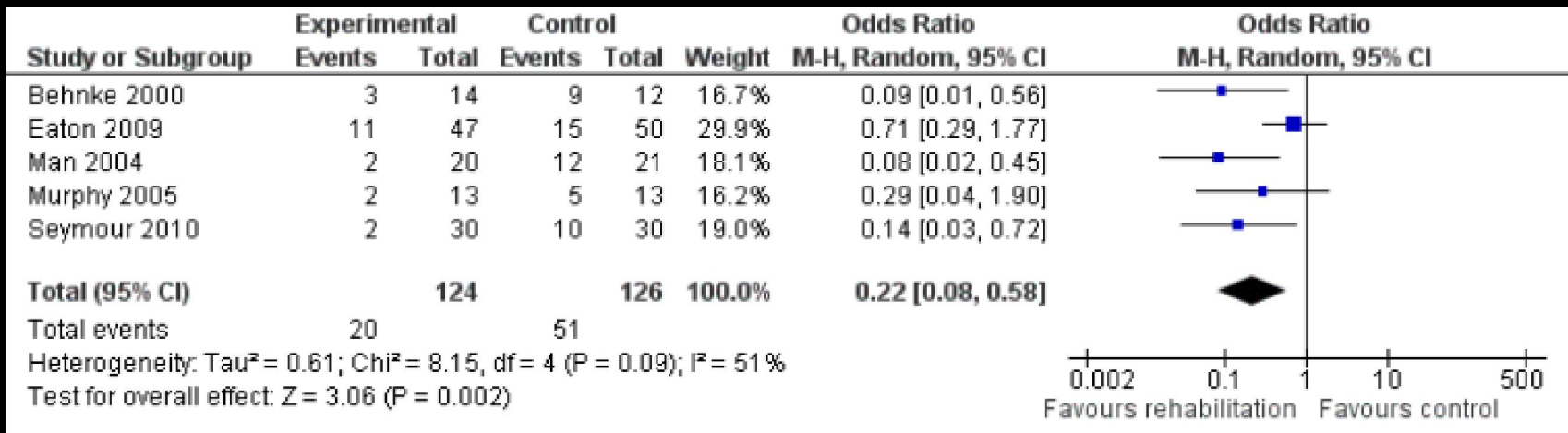
Medscape® www.medscape.com



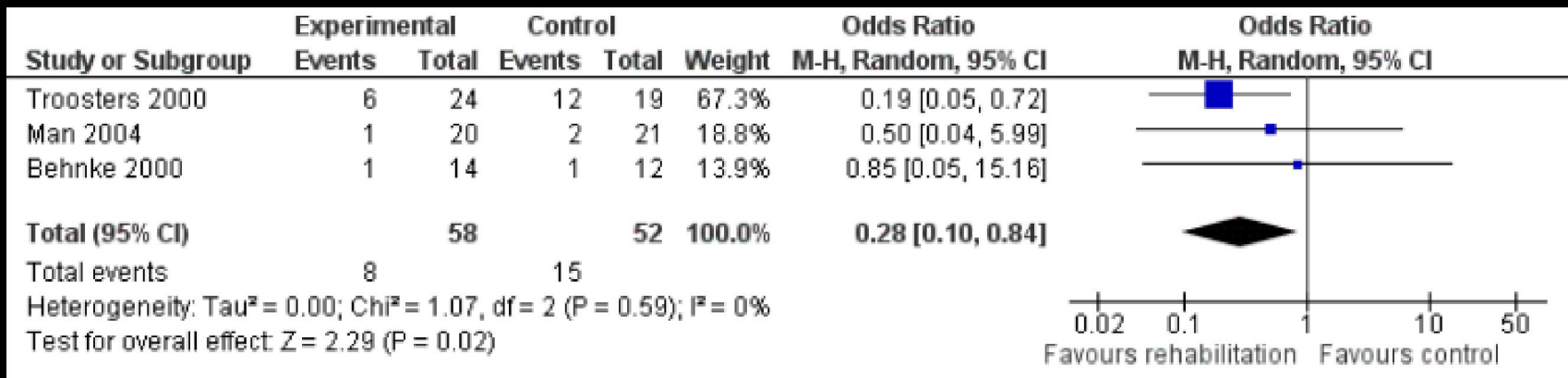
Relationship between the postrehabilitation 6-minute walk distance and survival following pulmonary rehabilitation in 149 patients with chronic lung disease (COPD in 133)

✓ For every 100-foot increase in exercise performance, estimated survival was increased by approximately 11%

Forest plot of comparison: Hospital admission



Forest plot of comparison: Mortality



Cochrane meta-analysis concluded that

- a significant reduction in odds of hospital admissions and death with pulmonary rehabilitation following acute exacerbations
- demonstrating consistent improvements in QoL and exercise capacity

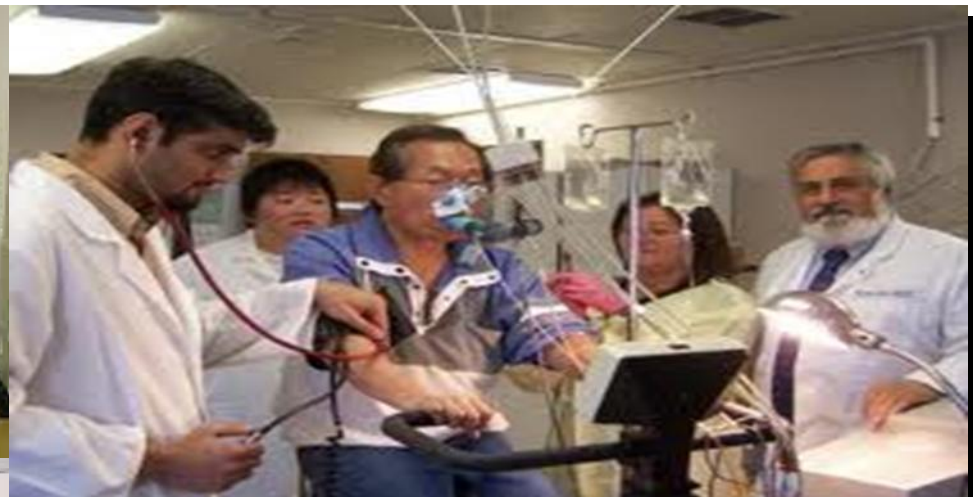


Fig. 2 : Diaphragmatic breathing: During inspiration diaphragm descends down and abdomen moves out. Patient exhales through nose with abdomen drawing in

Pulmonary rehabilitation programs

- Respiratory therapist
- Nurse
- Cardio-pulmonary physiotherapist

Medscape



Preferably it should be a large, quiet, and comfortable fitness facility in which all the people involved in the therapeutic process can be accommodated

Separate rooms should be available to offer discretion to patients who have undergone bronchial drainage procedures that may induce even copious expectoration



Summary

Reduce and Prevent exacerbation in COPD patients:

It isn't easy

- **Unclear definition of AECOPD**
- **It's hard to identify :**
 - **who has AECOPD → difficult to evaluate individual level of diurnal variation**
 - **who is at risk**
- **Drug : availability & cost**
- **Non-Drug : PM&R -> limits of resource (HCP, place), feasibility**

