Asthma and COPD: Are They a Spectr
Treatment Responses

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Pharmacological Treatments

Bronchodilators

- Inhaled short-acting β_2-Agonist (rescue)
- Inhaled short-acting anticholinergic
- Inhaled long-acting β_2-agonist
- Inhaled long-acting anticholinergic

Mild mod asthma	Severe asthma	COPD
+++	+++	+++
+	++	++
+	+++	+++
+	+++	+++

Controllers

- Oral steroid
- Inhaled corticosteroids
- Low dose theophylline
- Anti-leukotriene
- Anti-IgE

Mild – mod asthma	Severe asthma	COPD
+	+++	+
+++	++	(+)
+	+	+
+	+	+
+	+	+

Asthma	COPD
Allergen avoidance	Smoking cessation

First line treatment

Asthma

- Inhaled corticosteroid

COPD

- Inhaled long acting bronchodilators i.e. LAMA and LABA

First line treatment

Asthma

- Inhaled corticosteroid

COPD

- Inhaled long acting bronchodilators i.e. LAMA and LABA

Second line treatment

- LABA
- LAMA
- antileukotrienes

- Inhaled corticosteroid
- PDE4 inhibitor

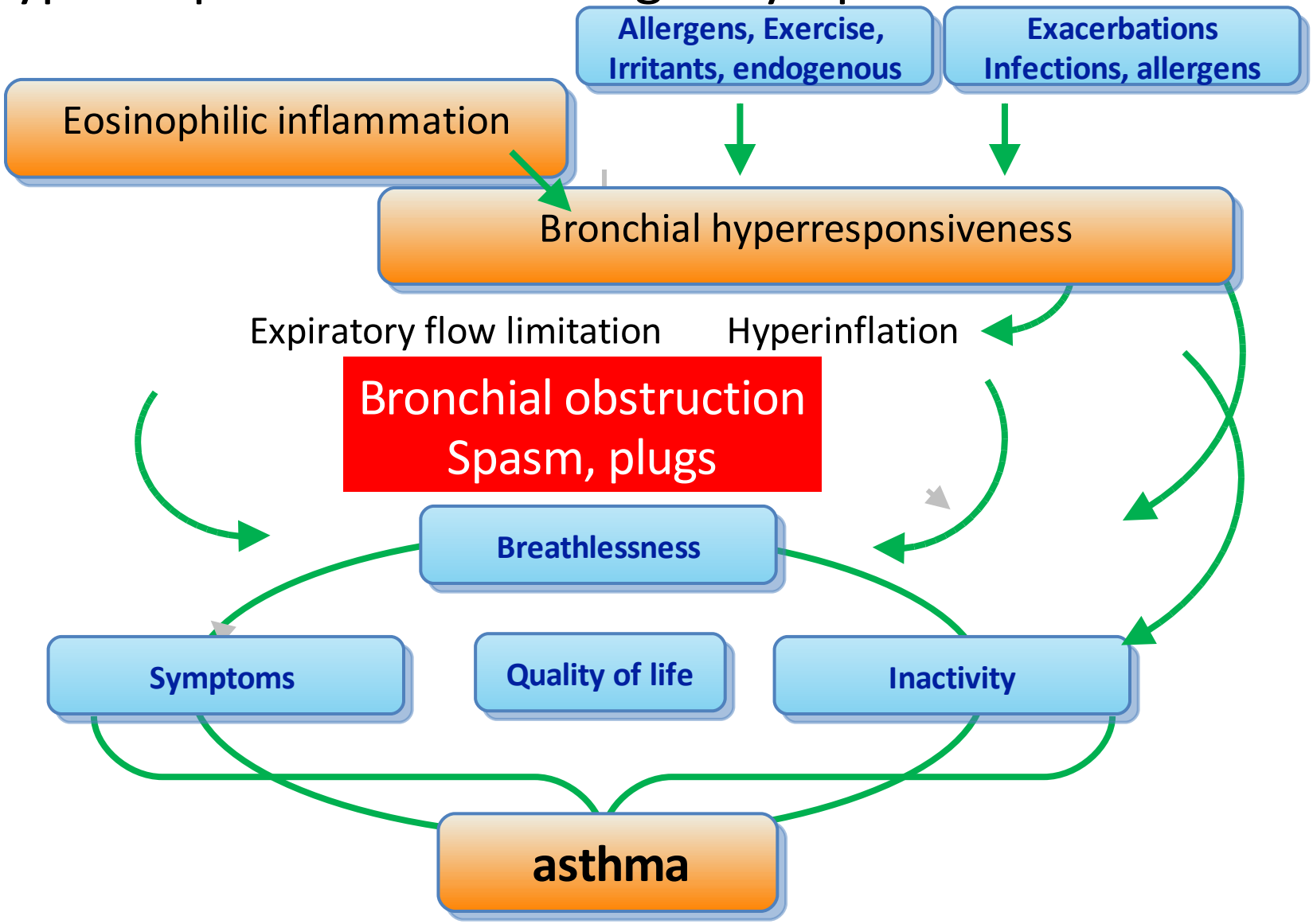
First line treatment

Asthma	COPD
Allergen avoidance	Smoking cessation
• Inhaled corticosteroid	• Inhaled long acting bronchodilators i.e. LAMA and LABA

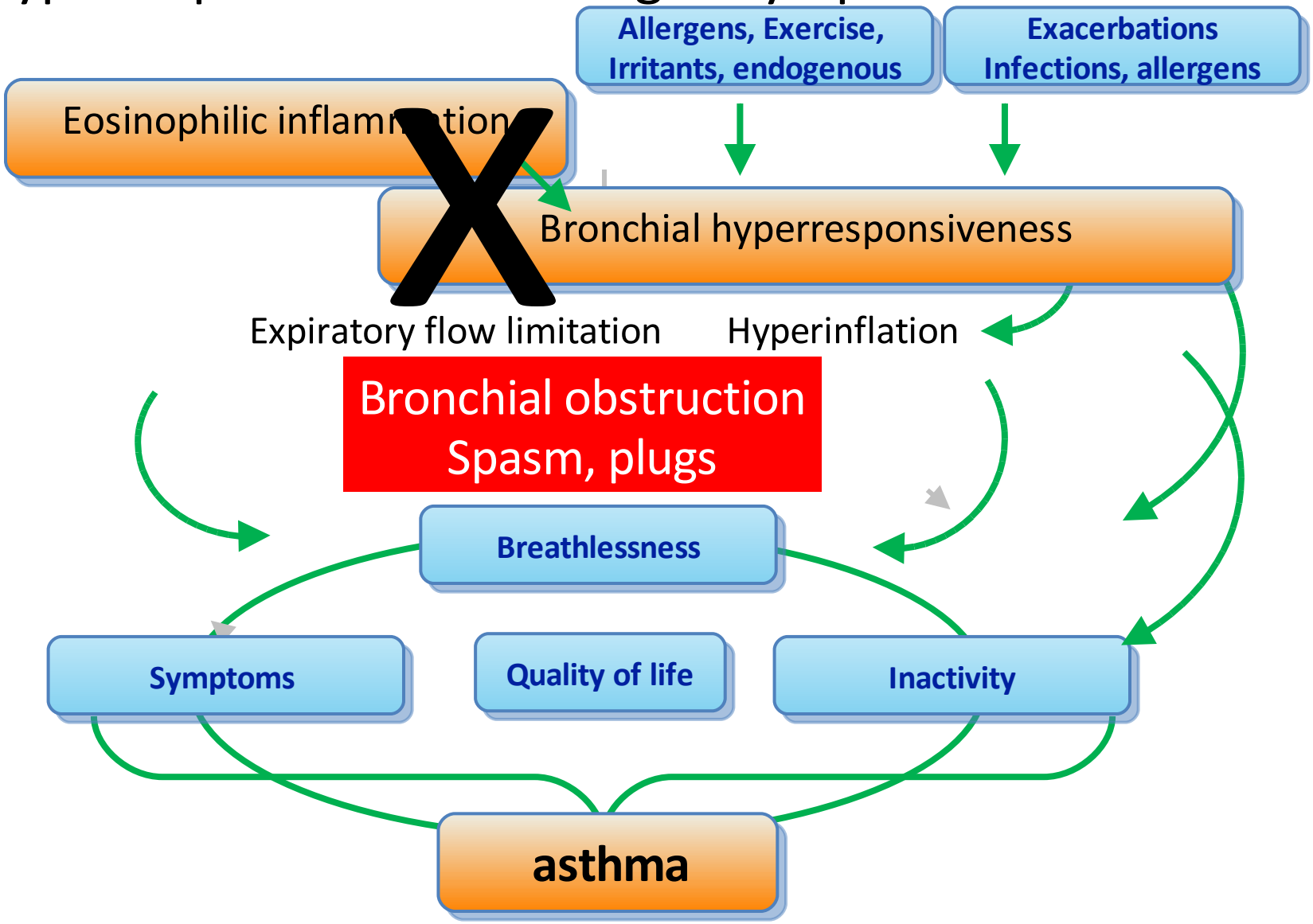
Second line treatment

• LABA • LAMA • antileukotrienes	• Inhaled corticosteroid • PDE4 inhibitor
Anti IgE Allergen immunotherapy	antibiotics

The central role of inflammation and bronchial hyperresponsiveness leading to symptoms in asthma



The central role of inflammation and bronchial hyperresponsiveness leading to symptoms in asthma



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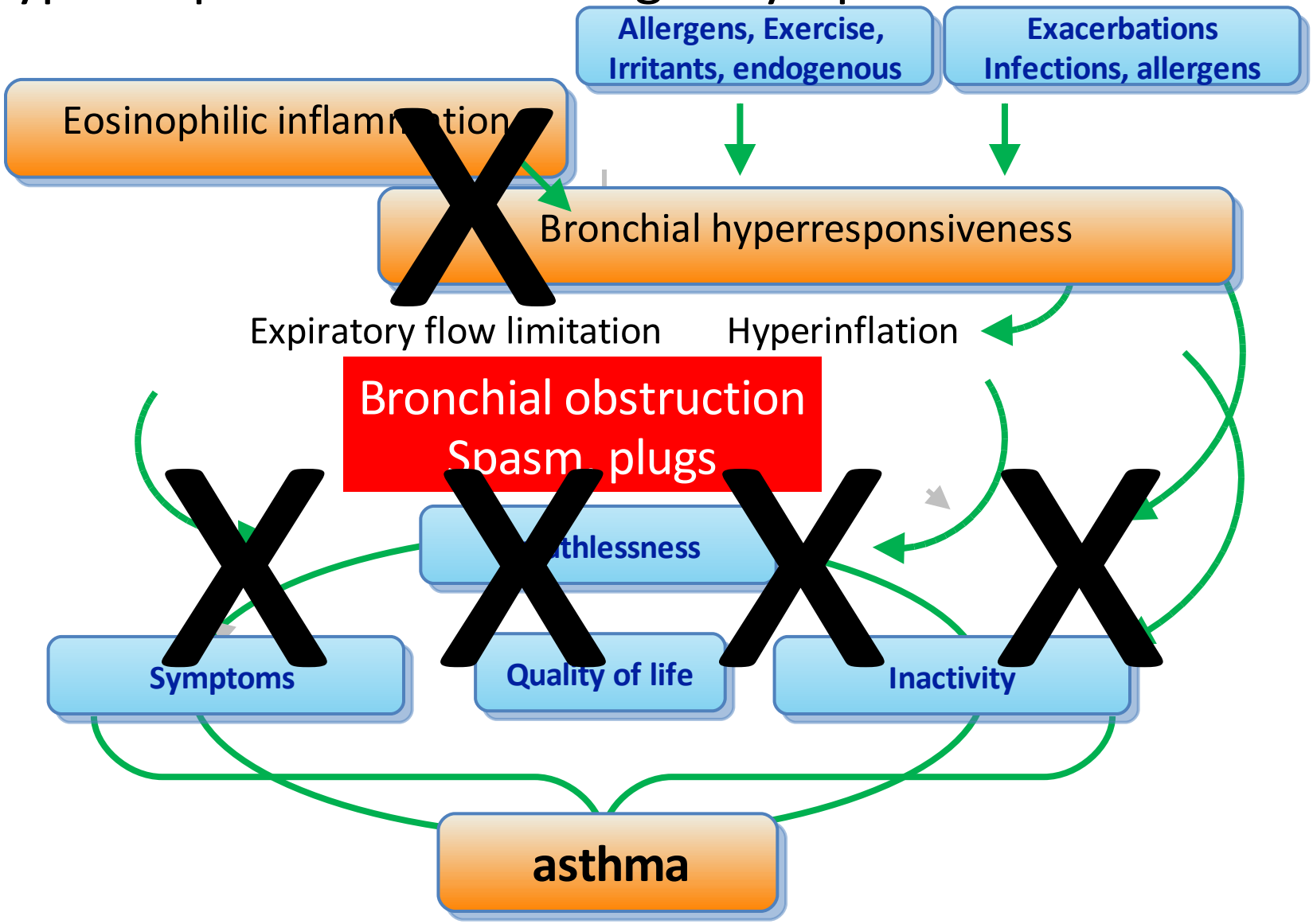


Levels of Asthma Control

(Assess patient impairment)

Characteristic	Controlled (All of the following)	Partly controlled (Any present in any week)	Uncontrolled
Daytime symptoms	Twice or less per week	More than twice per week	3 or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms / awakening	None	Any	
Need for rescue / "reliever" treatment	Twice or less per week	More than twice per week	
Lung function (PEF or FEV_1)	Normal	< 80% predicted or personal best (if known) on any day	

Assessment of Future Risk (risk of exacerbations, instability, rapid decline in lung function, side effects)

Gina 2010

REDUCE INCREASE

TREATMENT STEPS

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
	asthma education				
	environmental control				
	as needed rapid-acting ß2-agonist	as needed rapid-acting ß2-agonist			
CONTROLLER OPTIONS		SELECT ONE	SELECT ONE	TO STEP 3 TREATMENT, SELECT ONE OR MORE:	TO STEP 4 TREATMENT, ADD EITHER
		low-dose ICS*	low-dose ICS *plus* long-acting ß2-agonist	medium- *or* high-dose ICS *plus* long-acting ß2-agonist	oral glucocorticosteroid (lowest dose)
		leukotriene modifier**	medium- *or* high-dose ICS	leukotriene modifier	anti-IgE treatment
			low-dose ICS *plus* leukotriene modifier	sustained-release theophylline	
			low-dose ICS *plus* sustained-release theophylline	tiotropium	

*inhaled glucocorticosteroids
** receptor antagonist or synthesis inhibitors

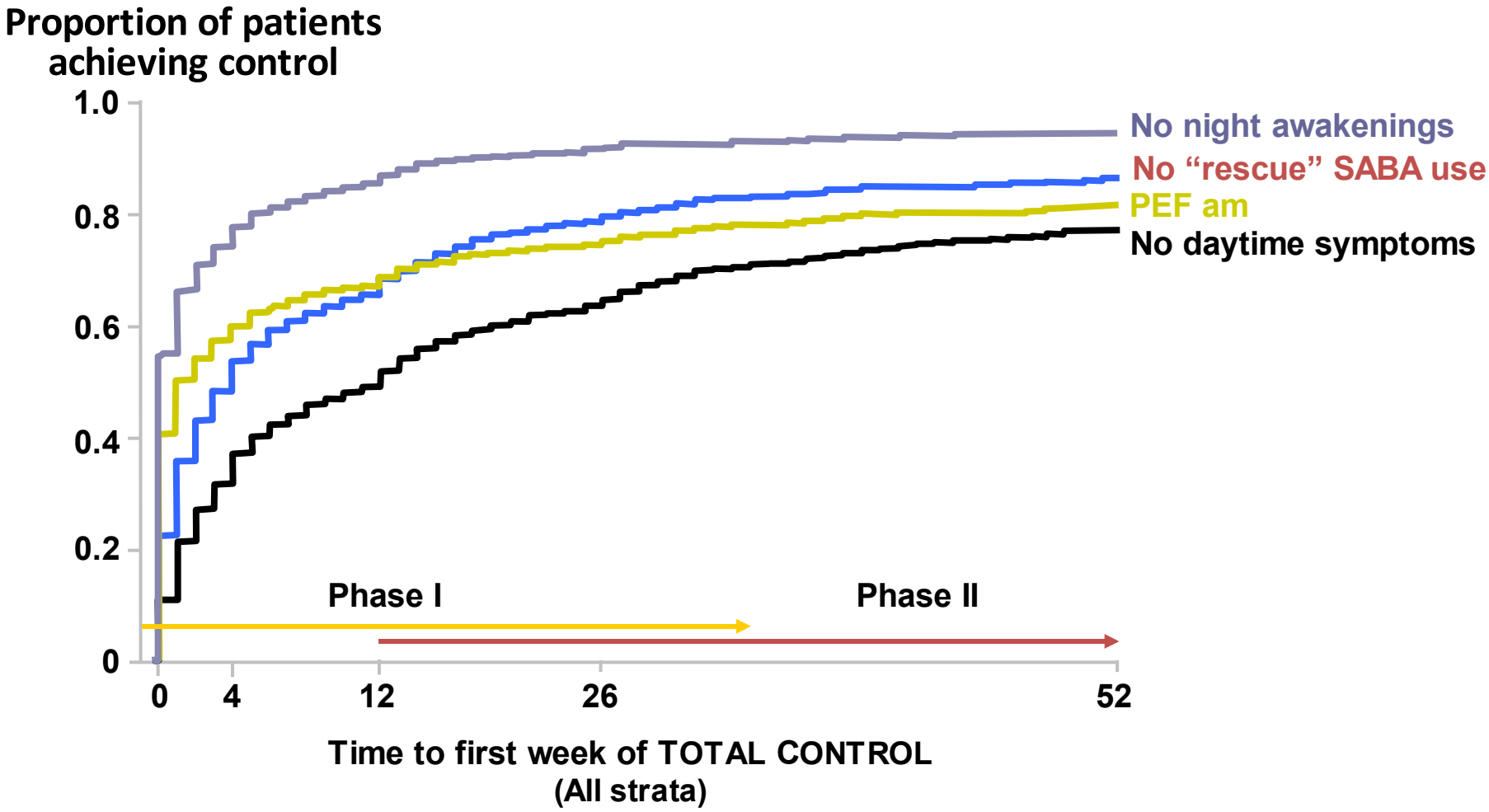
Shaded green - preferred controller options

Gina 2010

Clinical effects of inhaled corticosteorids in bronchial asthma

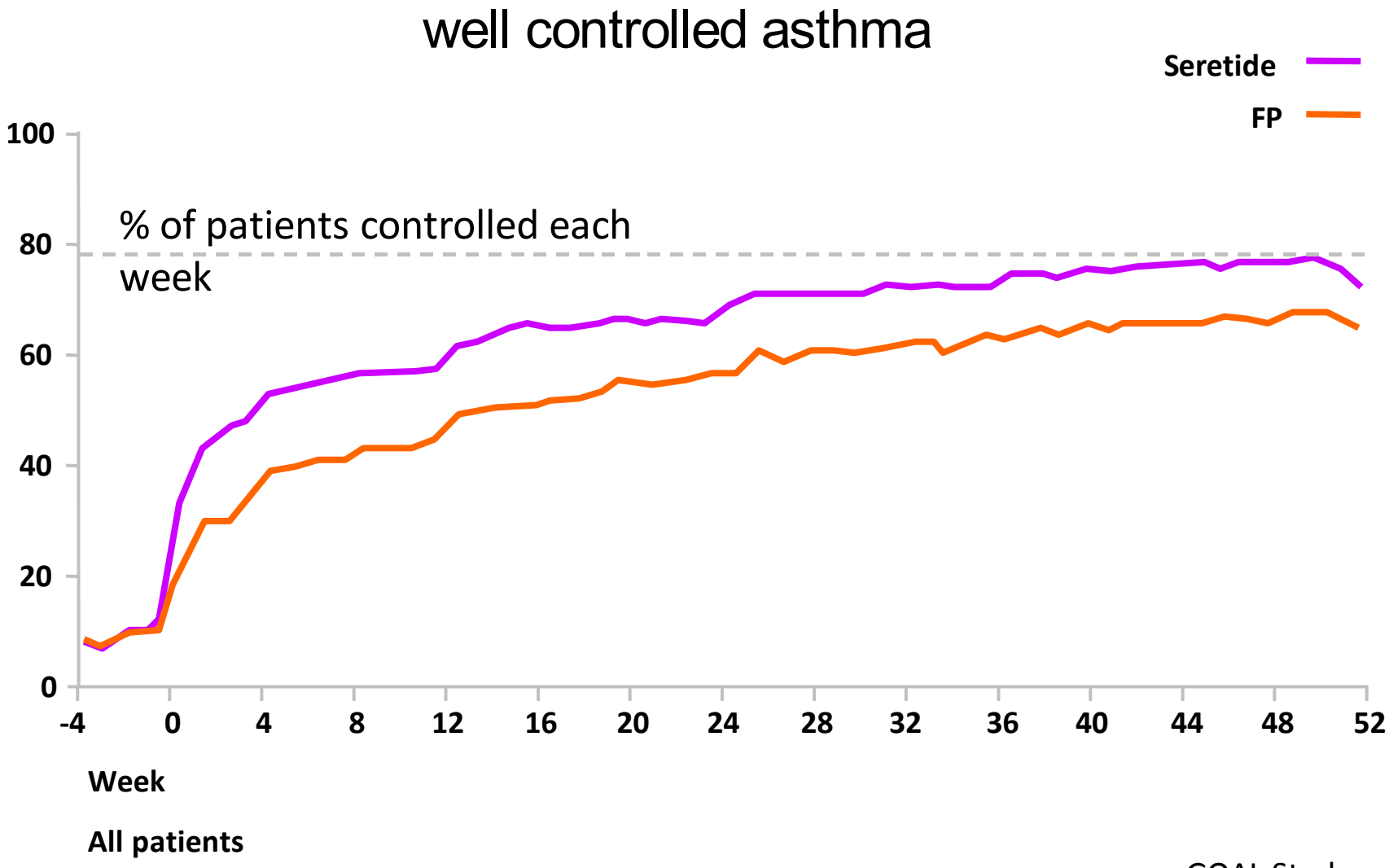
Certain	improve	quality of life, physical, social and psychical function
		lung function
	reduce	BHR = diurnal variation, EIA etc.
		symptoms day/night
		exacerbation/hospitalizations
		need for rescue medication
		need for oral corticosteroids
Probable	reduce	asthma deaths
		acc. decline in lung function
Possible		long term remission/cure

Time to TOTAL CONTROL for individual criteria in the GOAL study for Seretide treated patients



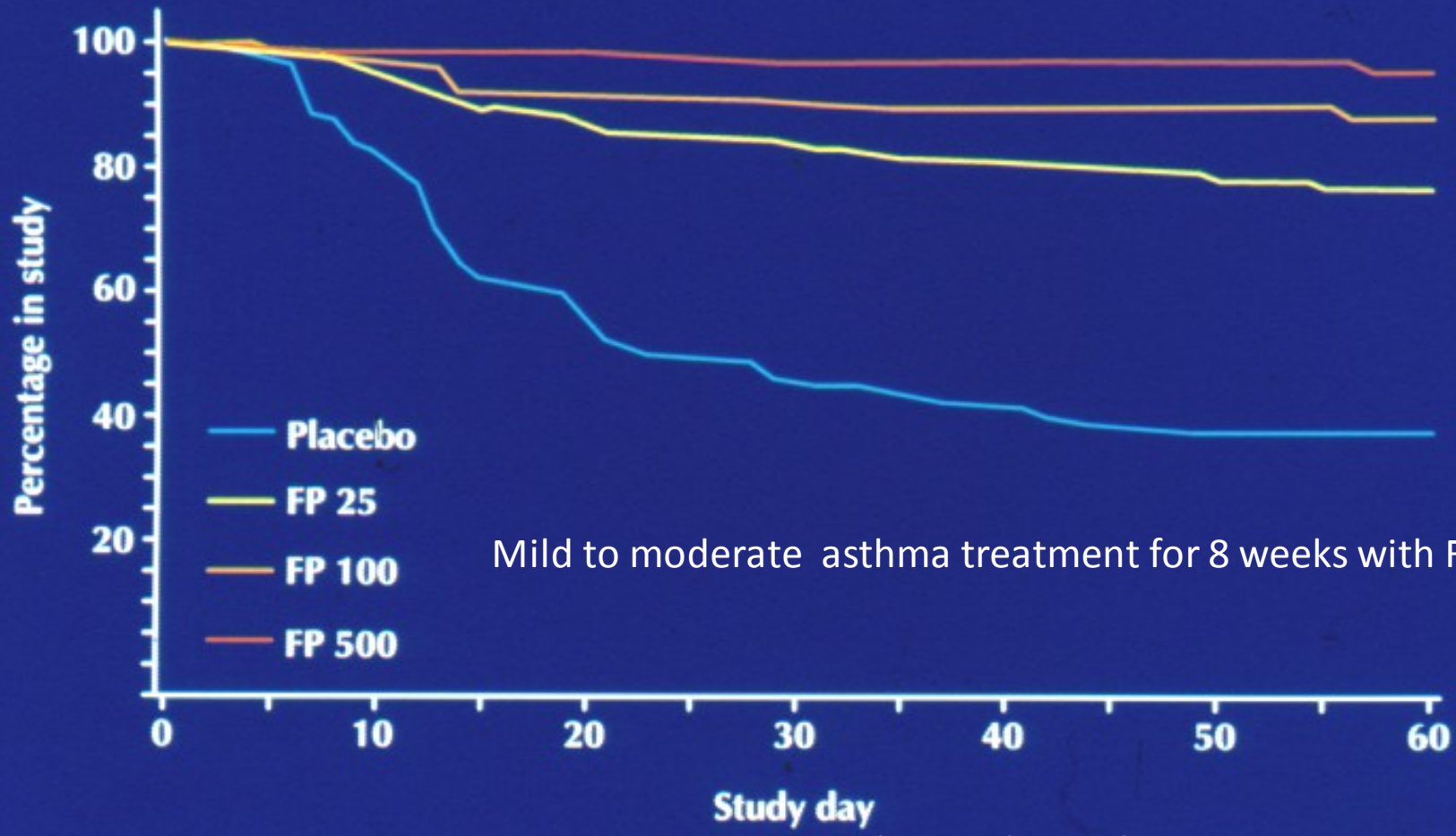
GOAL Study

Continued improvements with sustained treatment



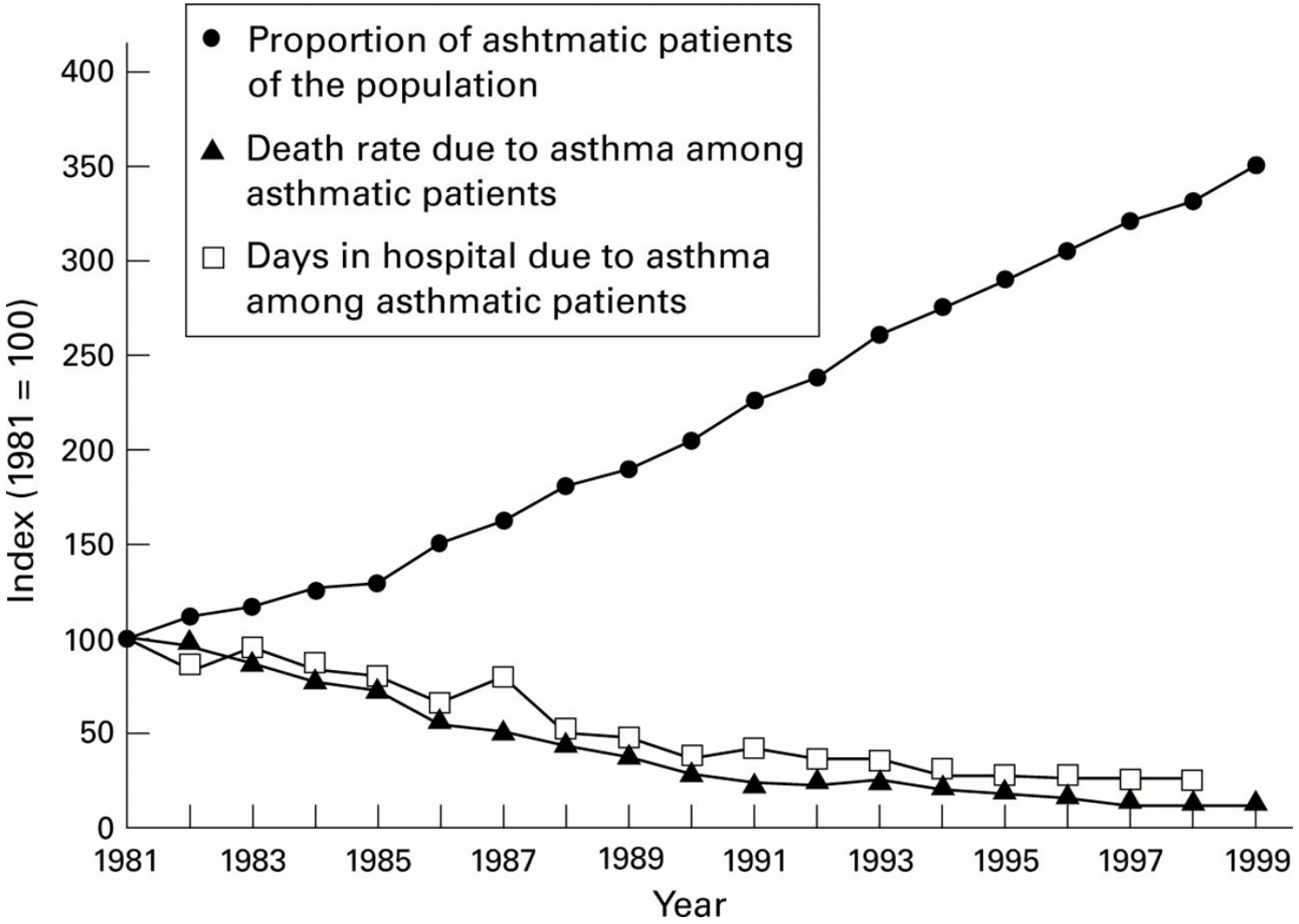
GOAL Study

PERCENT OF POPULATION REMAINING IN STUDY

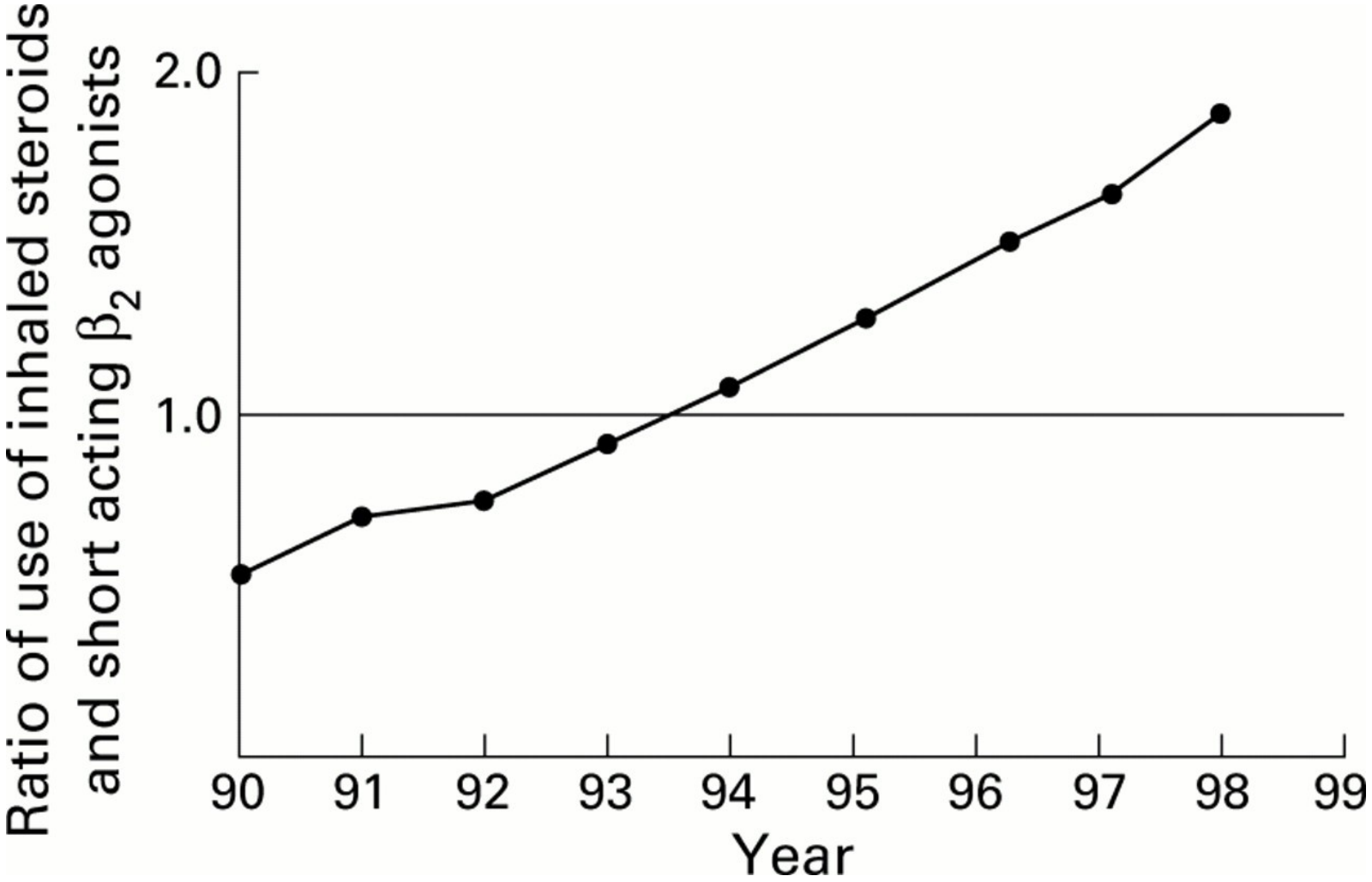


Mild to moderate asthma treatment for 8 weeks with FP

Chervinsky et al. JACI 1994, 94: 676-683

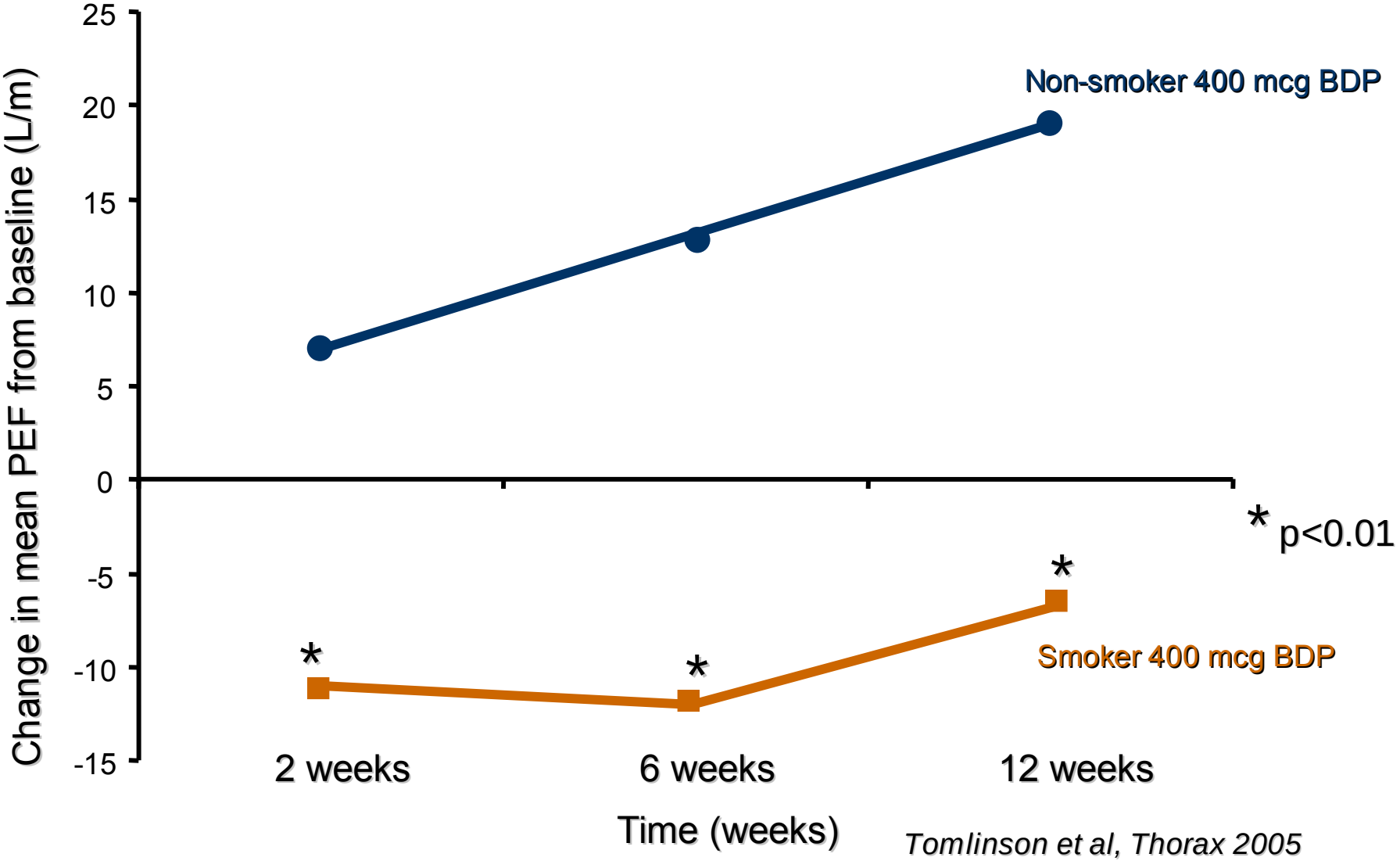


Relative increase in the number of asthmatic patients entitled to special reimbursement for their drug costs and decreases in death rate and days in hospital (index, 1981=100)



Ratio of the use of inhaled corticosteroids and short acting beta-2-agonists from 1994 to 1999

Change in mean PEF after inhaled beclomethasone (BDP) in asthma



Tomlinson et al, Thorax 2005

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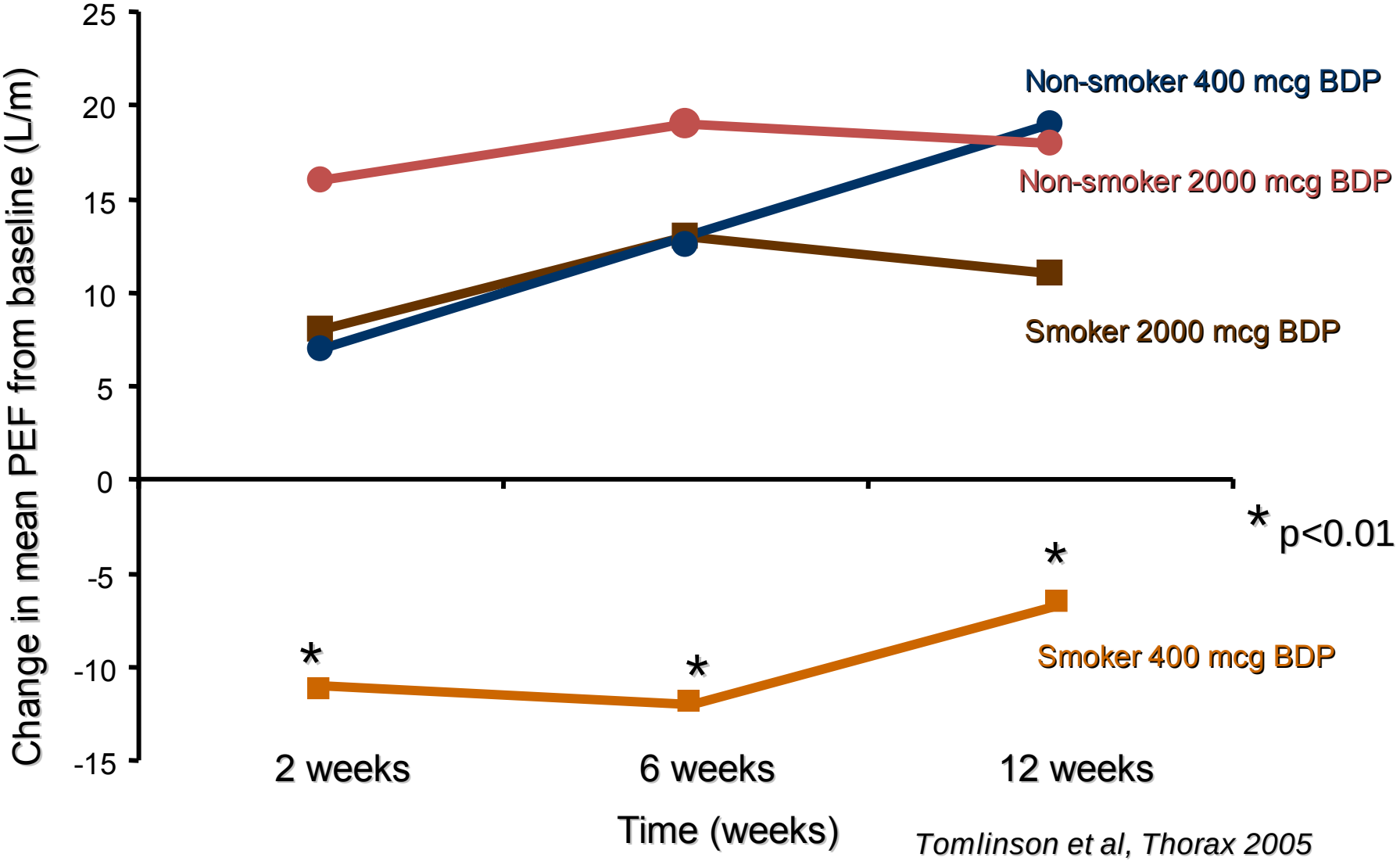


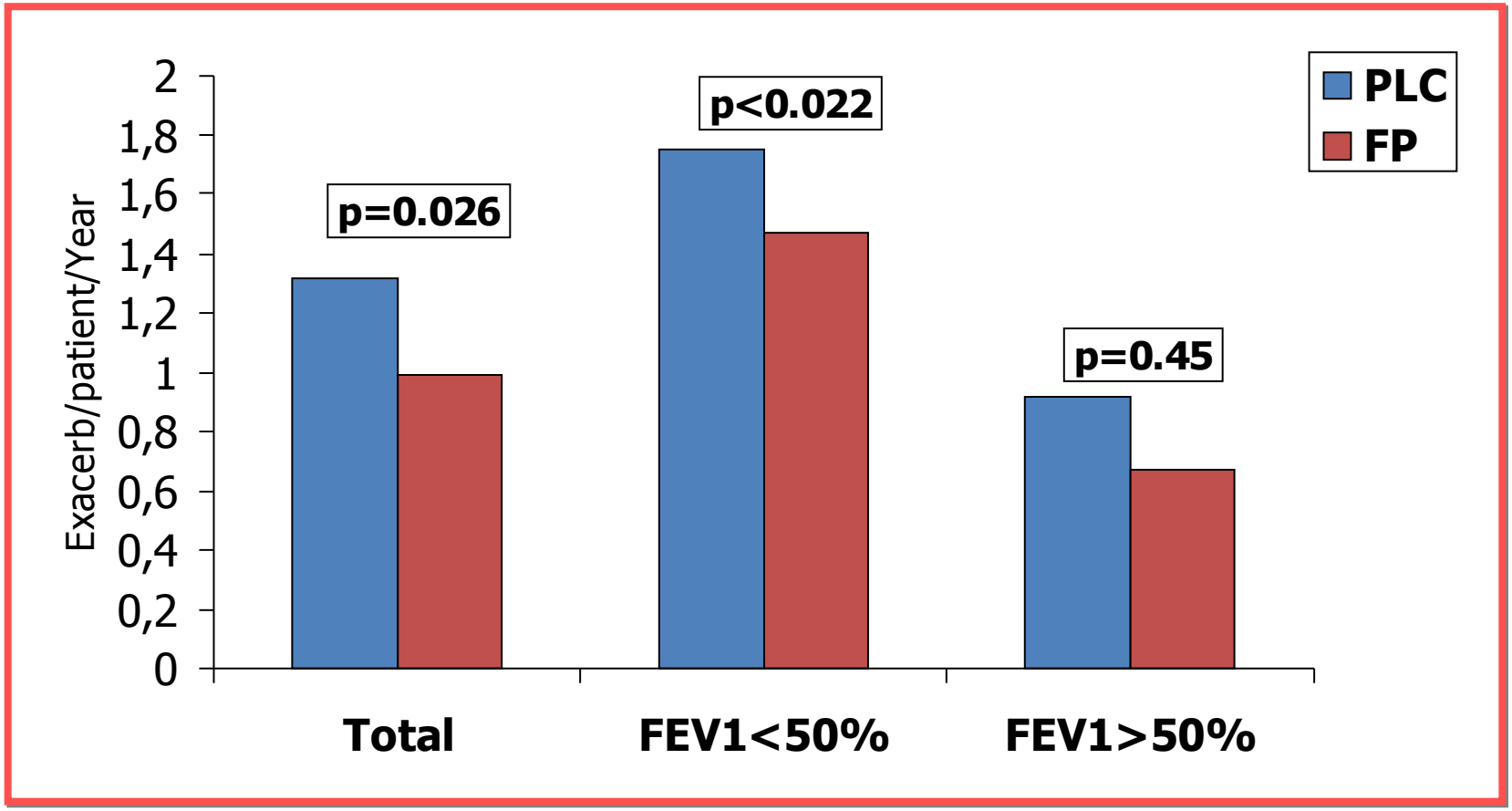
Tomlinson et al, Thorax 2005

Arguments for ICS in COPD

Pro	CON
Reduced rate of exacerbations Reduced decline in quality of life Reduced annual decline in spirometry	Local side effect in mouth and throught Horseness Pneumonia Suppression HPA axis Cost

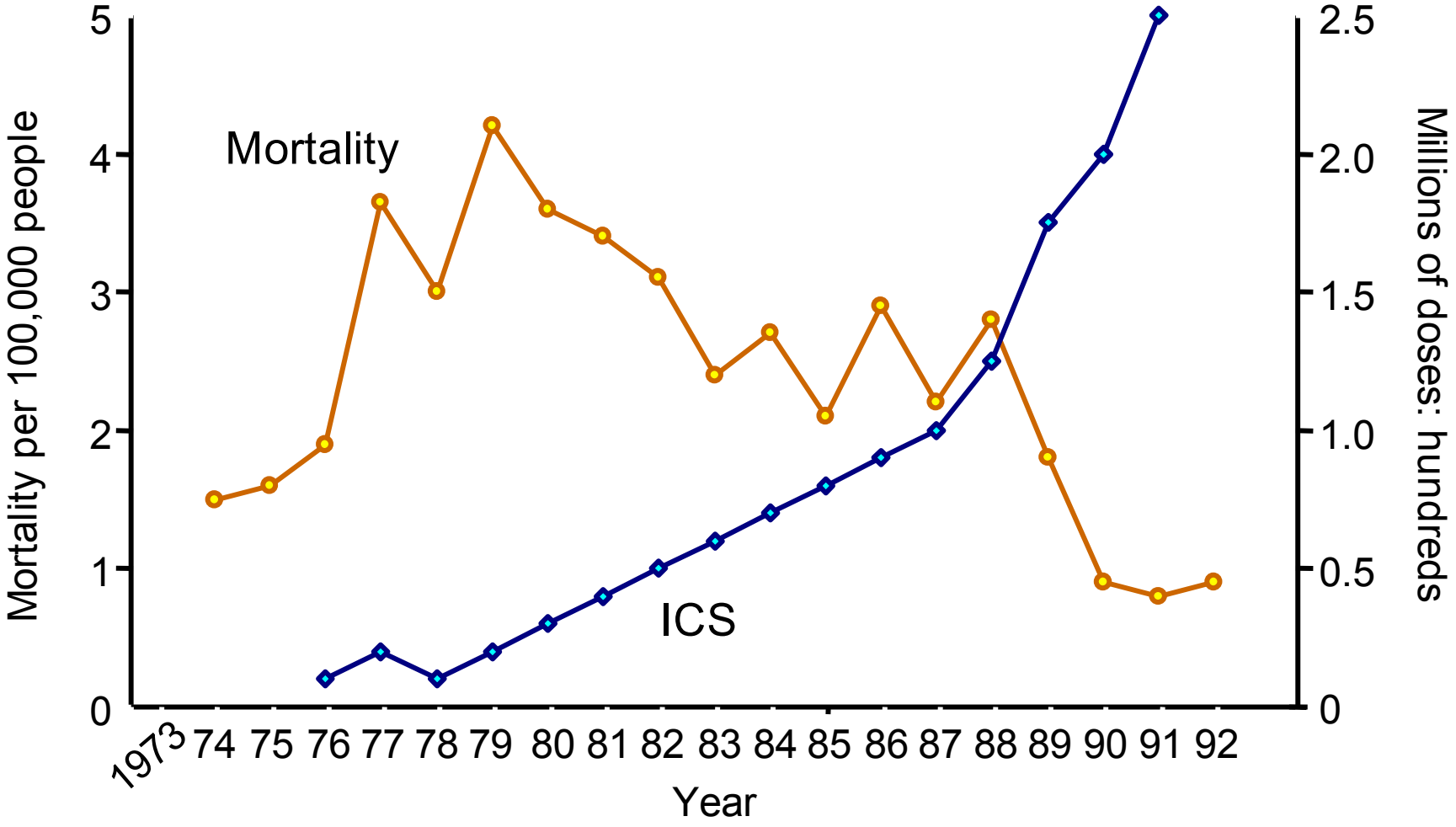
Cochrane Database of Systematic Reviews 2007

Background
- ICS on exacerbation rate



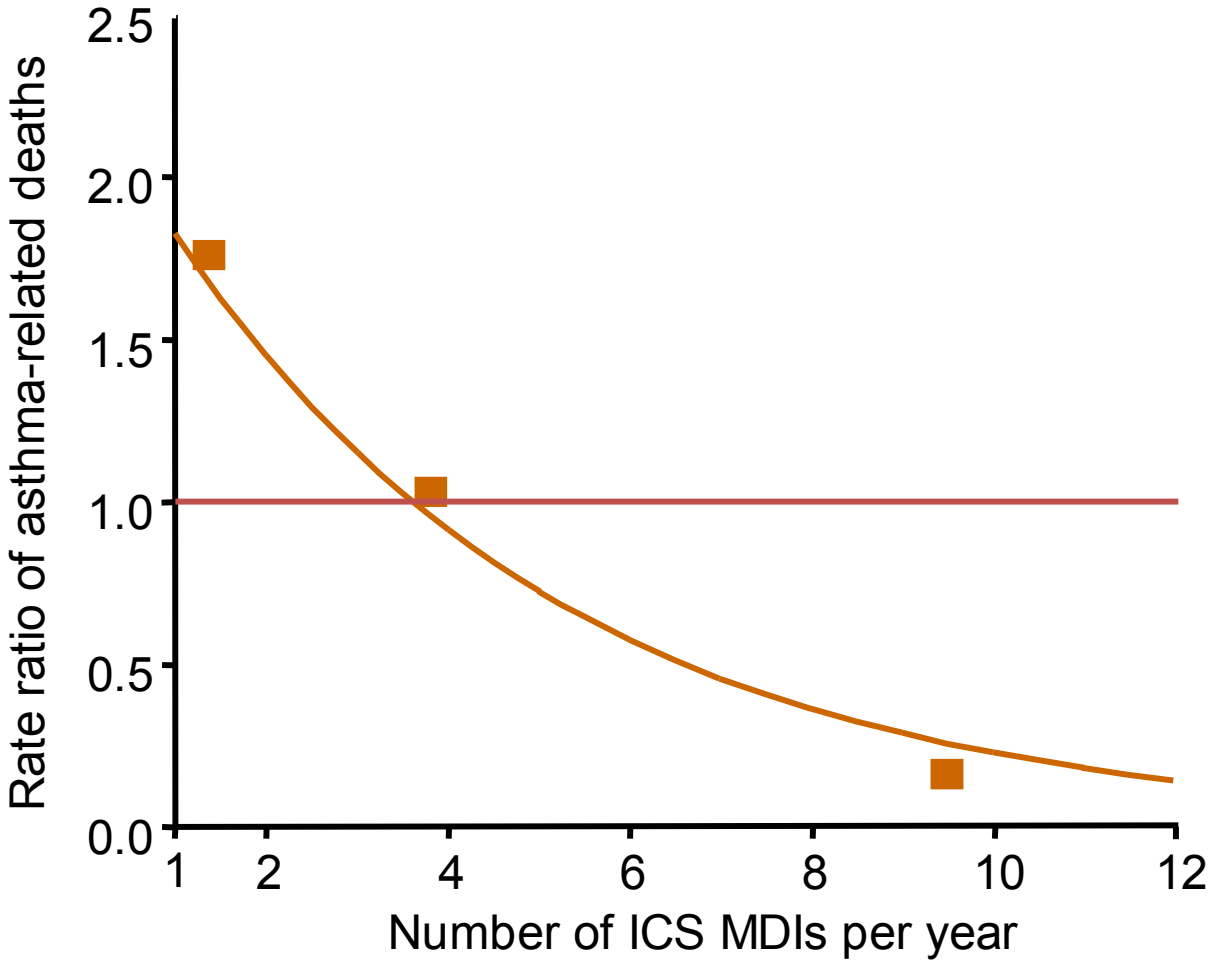
Eur Respir J 2003; 21: 68

Asthma-related mortality and ICS sales in New Zealand: 1974–1992



Suissa S, Ernst P. J Clin Epidemiol 1997;50:1079–88.

Rate ratio of asthma-related deaths by number of ICS MDIs per year



Adapted from Suissa S, et al. N Engl J Med 2000;334:332–6.

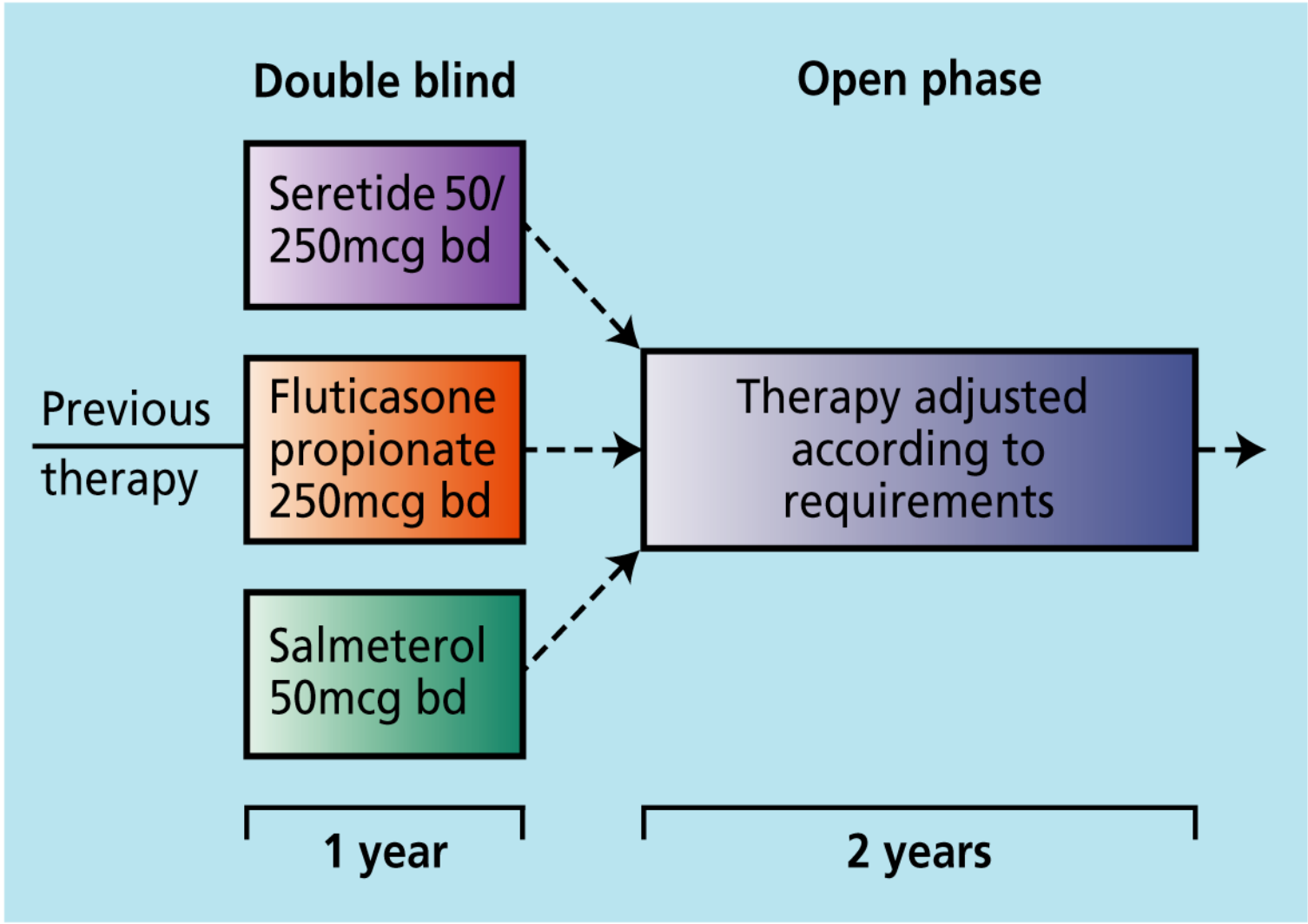
Addition of inhaled long-acting beta2-agonists to inhaled steroids as first line therapy for persistent asthma in steroid-naive adults

	ICS + LABA better than ICS alone
Asthma exacerbations	No
FEV-1	Yes - 210 ml
Symptom free days	Yes 11 % (CI 2 – 20)
Rescue beta-2 use	No
Adverse events, withdr… withdra…	No

insufficient evidence to recommend use of combination therapy rather than ICS alone as a first-line treatment

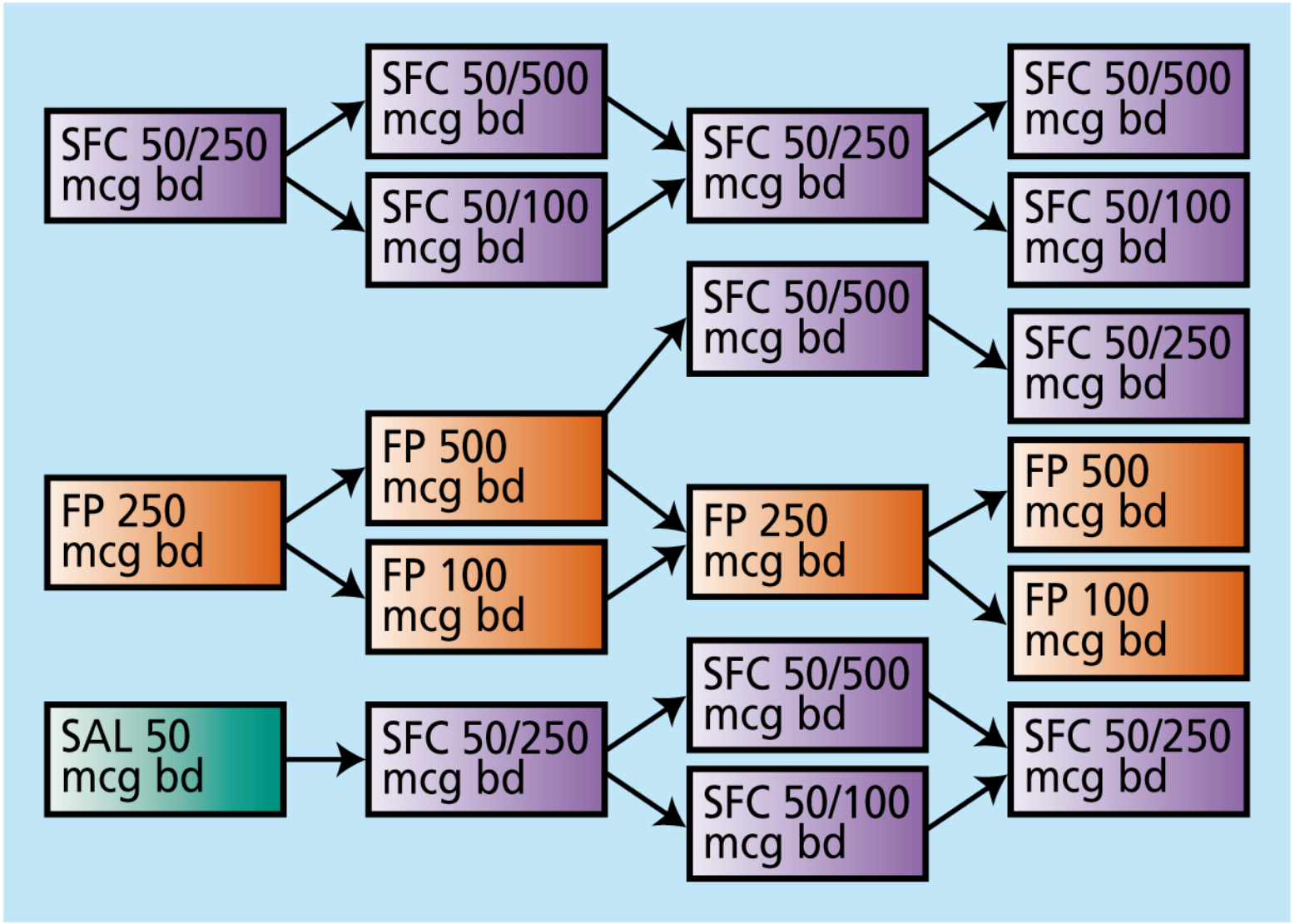
Chroin 2009 The Cochrane Collaboration

Study design



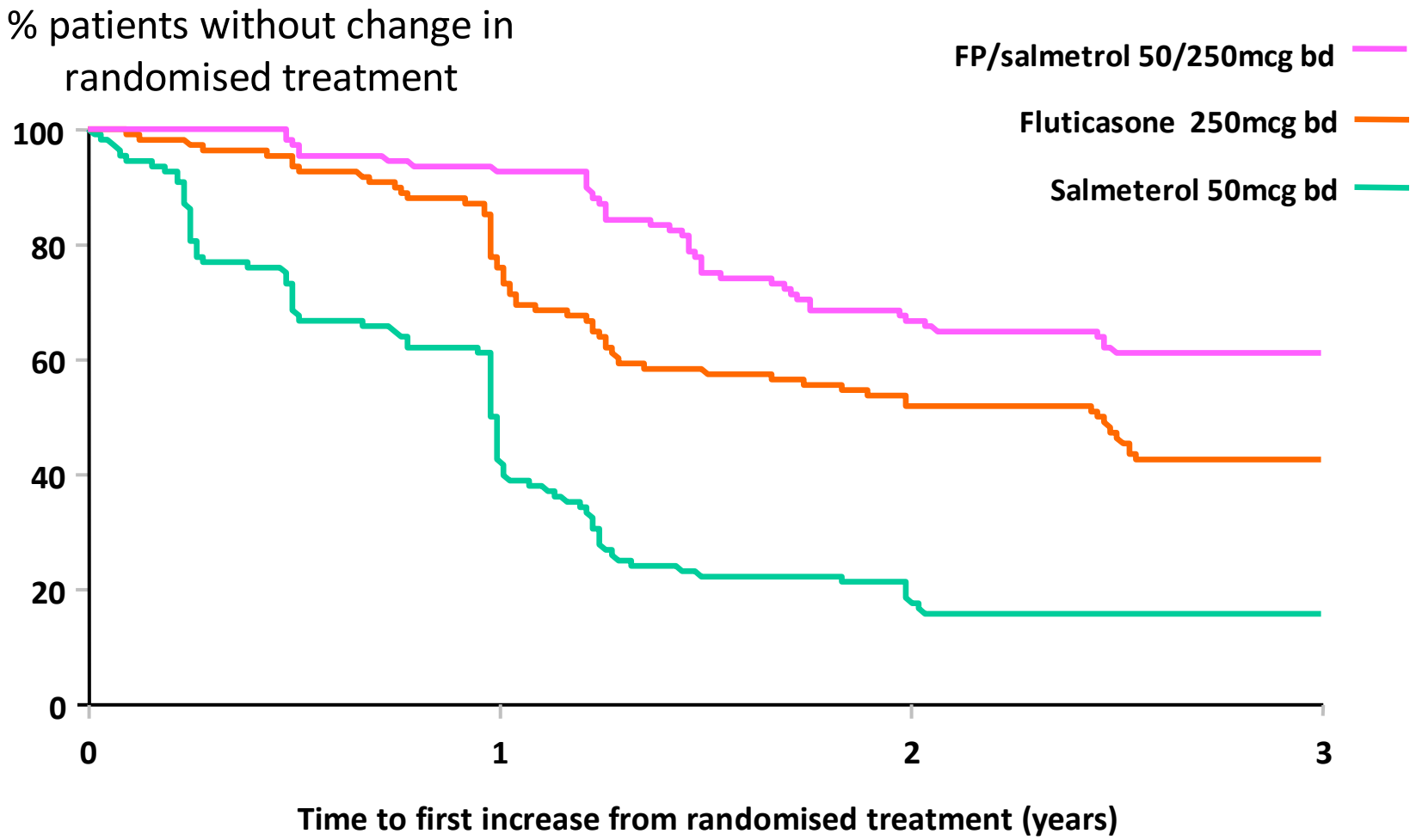
Lundback et al. *Respir Med* 2006

Treatment flow



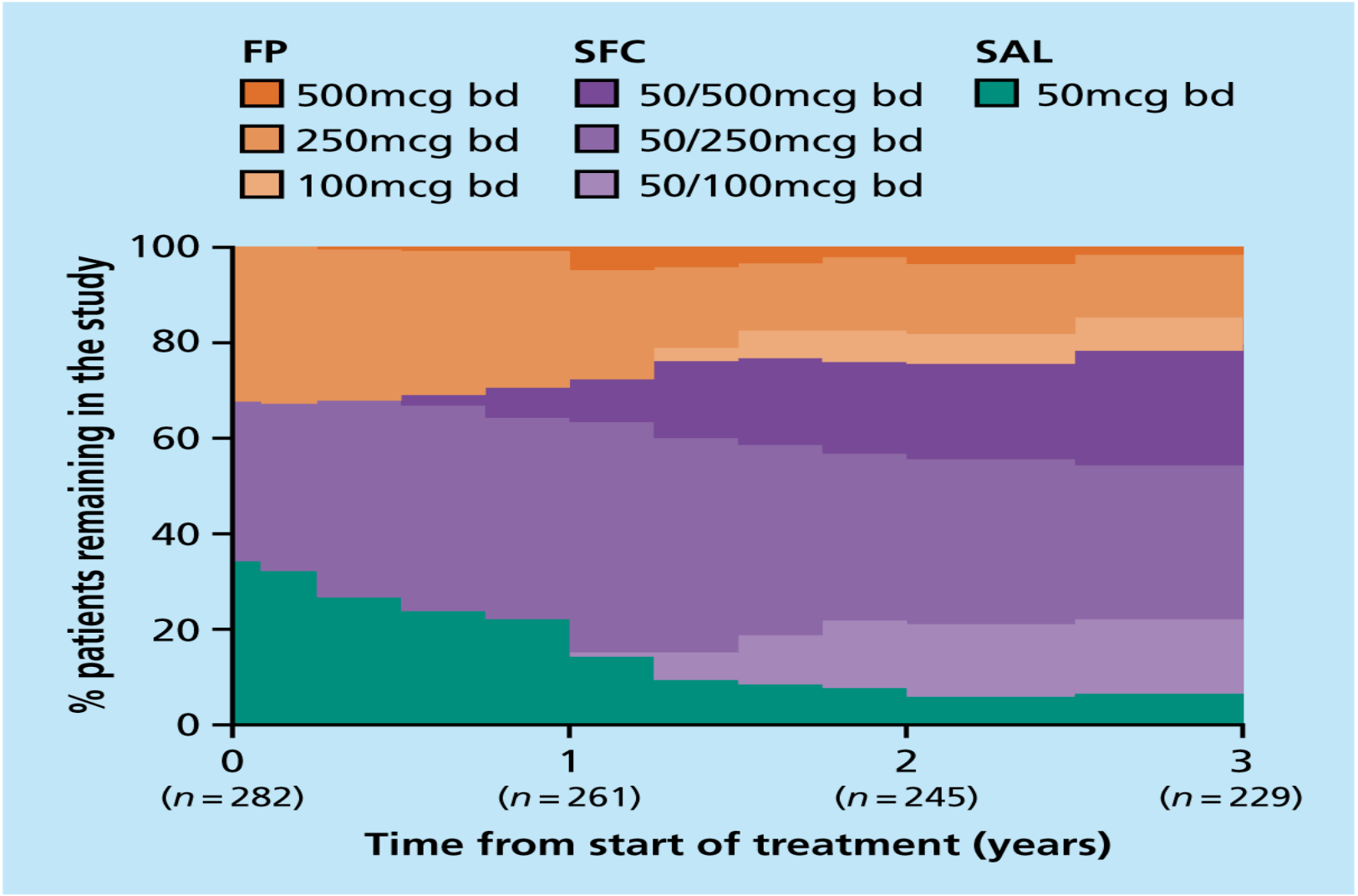
Lundbäck et al. Respir med 2006

Time to first increase from randomised treatment

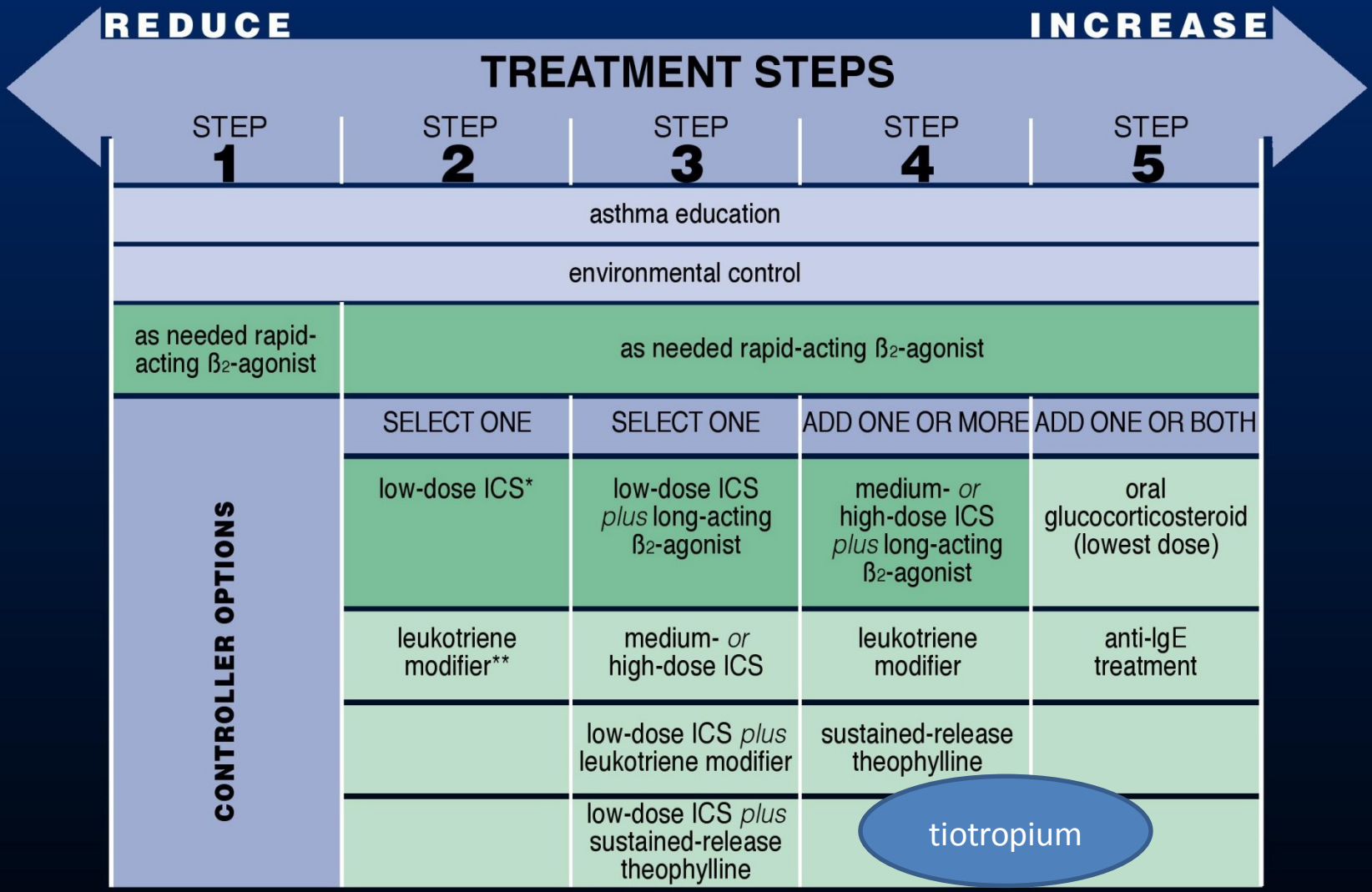


Lundbäck et al. Respir med 2006

Changes in treatment and dose throughout the study period

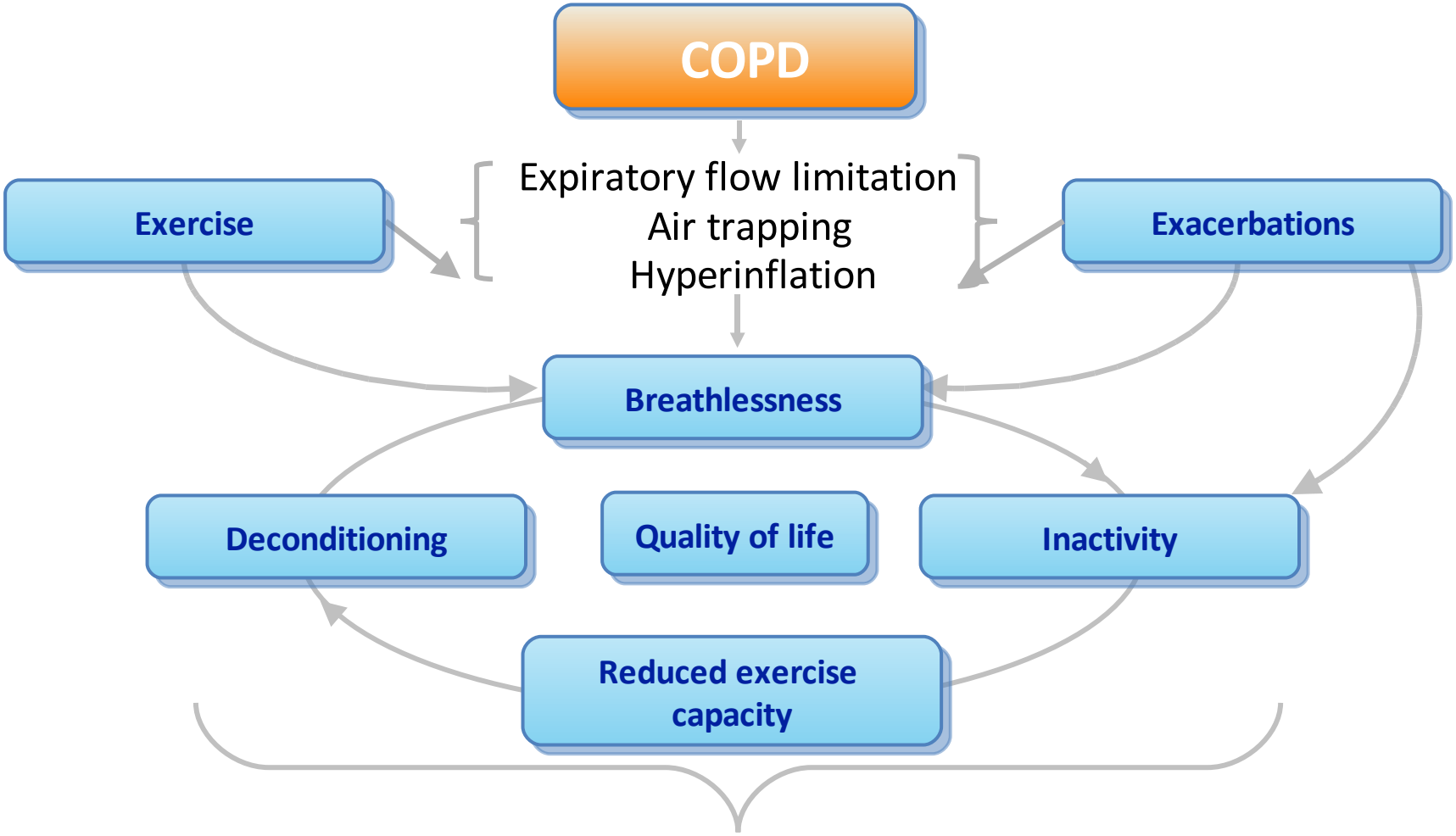


Lundback B et al, Respir Med 2006



*inhaled glucocorticosteroids
** receptor antagonist or synthesis inhibitors

The central role of airflow limitation leading to symptoms in COPD



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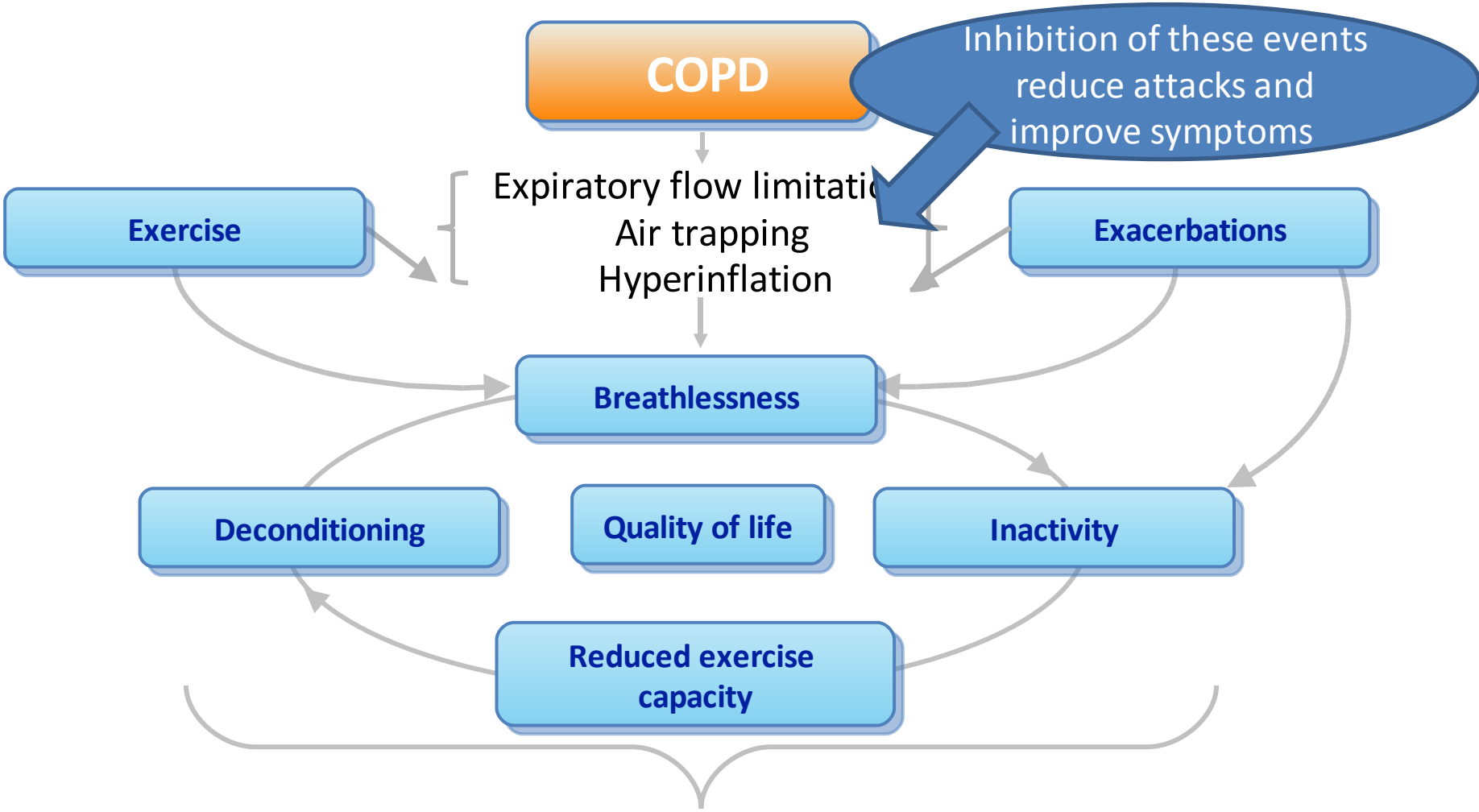


Outcomes are correlated with mean change from baseline in trough FEV_1

Average ΔFEV_1 (mL)	Category centred value of ΔFEV_1 (mL)	TDI (n=2,781)	ΔSGRQ (n=3,141)	Exacerbation rate/year (n=3,158)
–500, –50	–275	1.44	–3.15	0.63
–50, 50	0	1.31	–3.17	0.58
50, 150	100	1.79	–3.84	0.61
150, 250	200	2.12	–5.84	0.51
250, 500	375	2.68	–7.38	0.38

- TDI and ΔSGRQ at 12 weeks improved with increasing positive ΔFEV_1 (all $p<0.001$)
- Individual-level correlations: r=0.06–0.18
- Cohort-level correlations: r=0.79–0.95

As new bronchodilators are introduced there have been more consistent improvements in outcomes for patients with COPD

		Improvement in outcome				
	Duration of action (hours)[1]	Lung function[2–8]	Breathlessness[2–8]	Exercise endurance*[1,2]	Quality of life[1–14]	Exacerbations[1–3,5,7–14]
Albuterol	4–6	✓	✓	✓	NA	NA
Ipratropium bromide	6–8	✓	✓	✓	✓	✓
Salmeterol	≥12	✓✓	✓	✓	✓(✓‡)	✓✓
Formoterol	≥12	✓✓	✓✓	✓	✓✓	✓†
Tiotropium	24	✓✓✓	✓✓✓	✓	✓✓(✓‡)	✓✓(✓‡)

✓evidence of effectiveness; ✓✓evidence of effectiveness over SABA or SAMA; ✓✓✓evidence of effectiveness over LABA

*Outcome demonstrated by all bronchodilators, lack of evidence of significant differences between them
†Equivocal evidence depending on formulation;[5,10,11] ‡Evidence of numerical improvements over shorter acting comparator[4,8]
NA = evidence not available

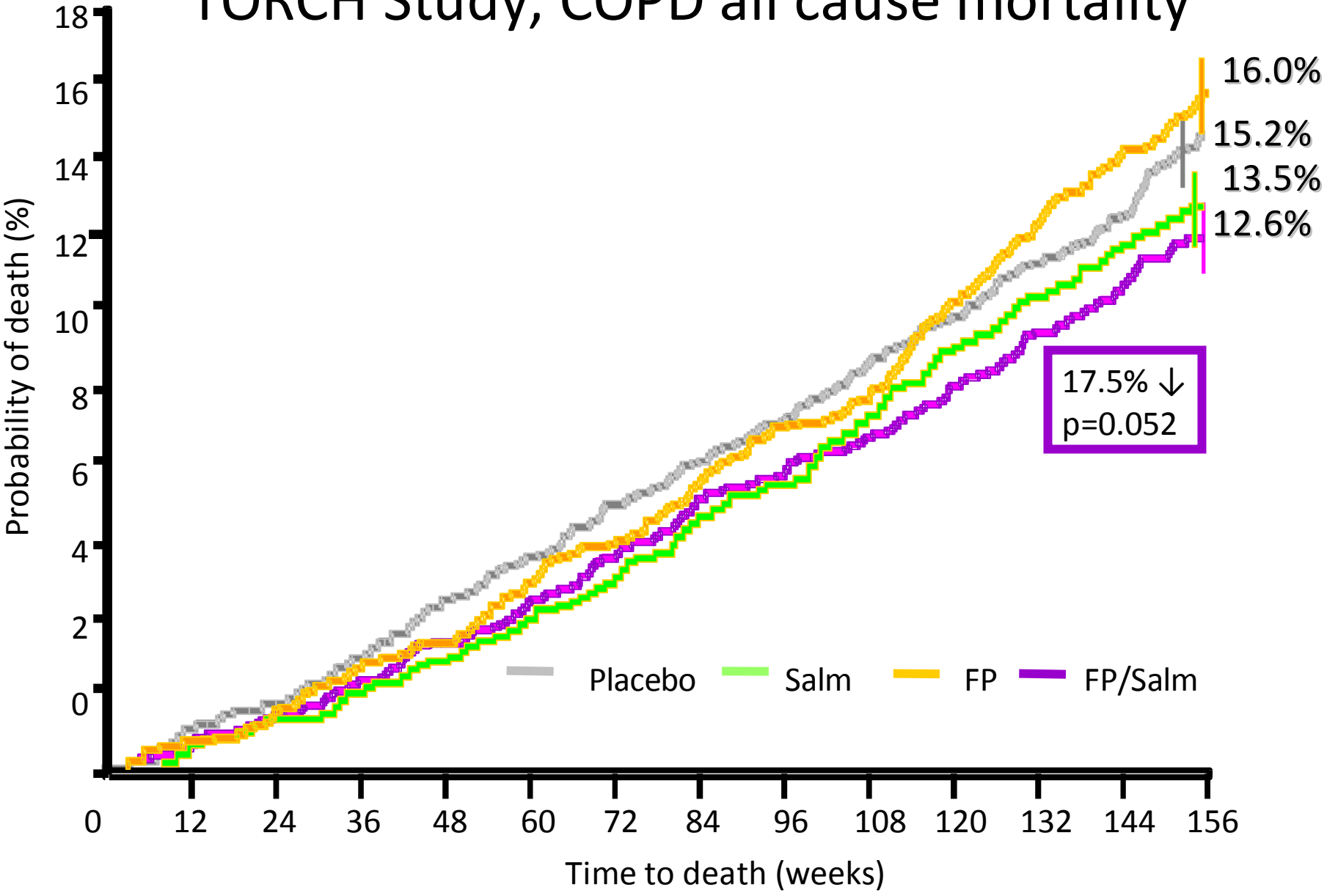
1. GOLD 2009; 2. Celli et al. ERJ 2004; 3. Mahler et al. Chest 1999; 4. Rennard et al. AJRCCM 2001
5. Dahl et al. AJRCCM 2001; 6. Wadbo et al. ERJ 2002; 7. Vincken et al. ERJ 2002; 8. Brusasco et al. Thorax 2003
9. Rutten van-Molken et al. Eur J Health Econ 2007; 10. Szafranski et al. ERJ 2003; 11. Calverley et al. ERJ 2003
12. Calverley et al. NEJM 2007; 13. Niewoehner et al. Ann Intern Med 2005; 14. Tashkin et al. NEJM 2008

Bronchodilators remain central to the symptomatic management of COPD

- Compared with placebo, existing long-acting bronchodilators[1]:
  - significantly improve and sustain lung function
  - significantly improve hyperinflation and symptoms of breathlessness
  - significantly improve quality of life
  - Significantly reduce exacerbations

1. GOLD 2009

TORCH Study, COPD all cause mortality



Calverley PA et al: NEJM 2007

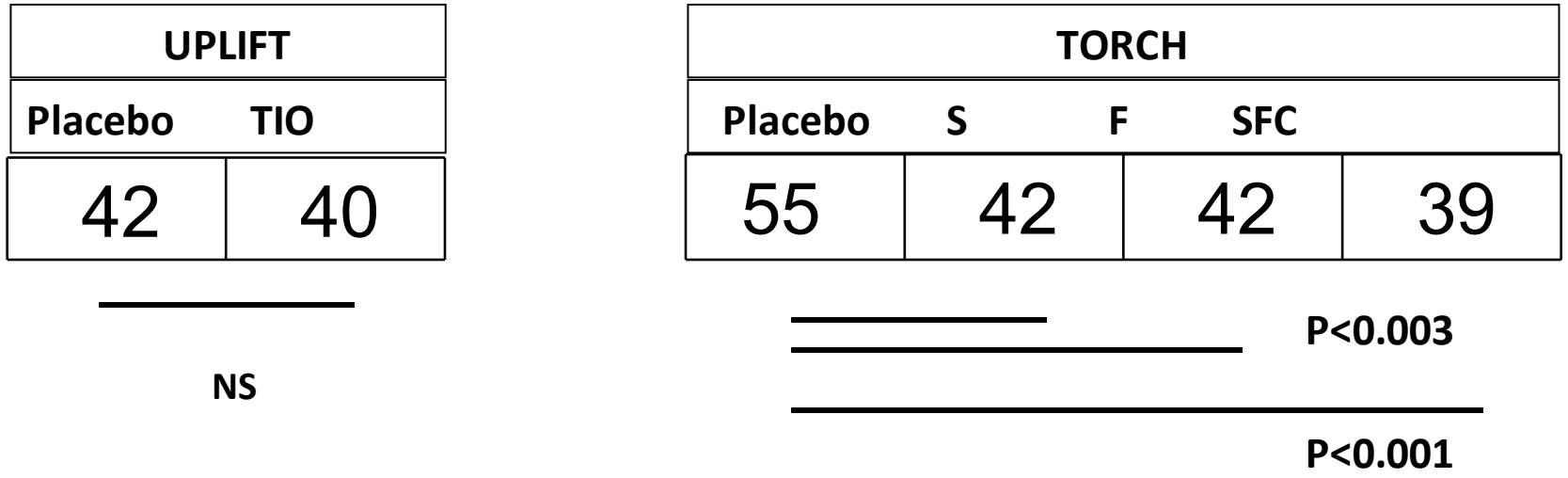
TORCH Study: 2x2 Factorial analysis

	Yes (deaths)	No (deaths)	Crude RR	Adjusted RR
Fluticasone	**439/3067**	**436/3045**	**1.00**	**1.00**
Salmeterol	**398/3054**	**477/3058**	**0.83**	**0.83 (p=0.0043)**

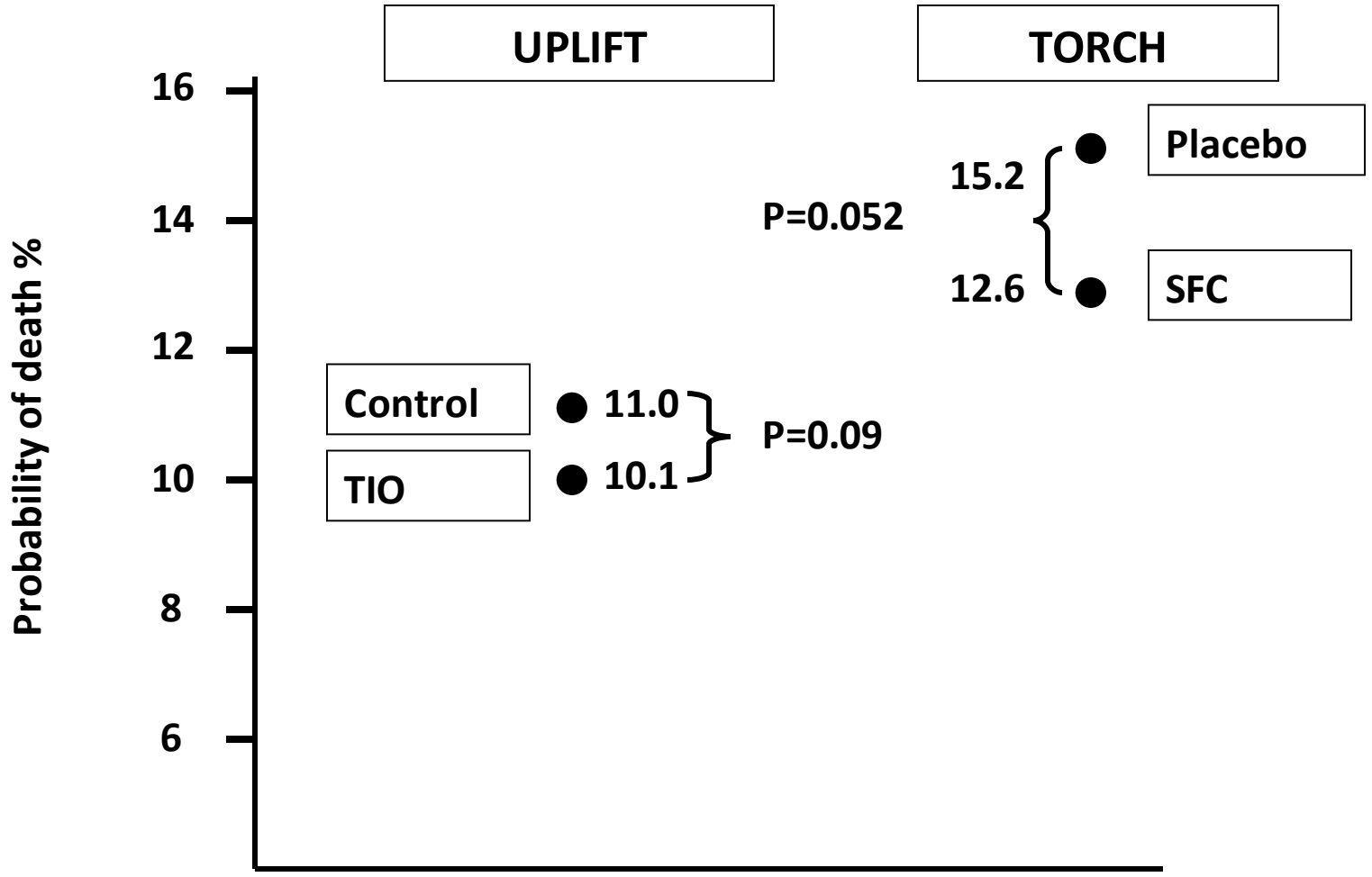
- No interaction between FP and salmeterol: p=0.32
- All of the benefit provided by salmeterol

Suissa S et al: ERJ 2008

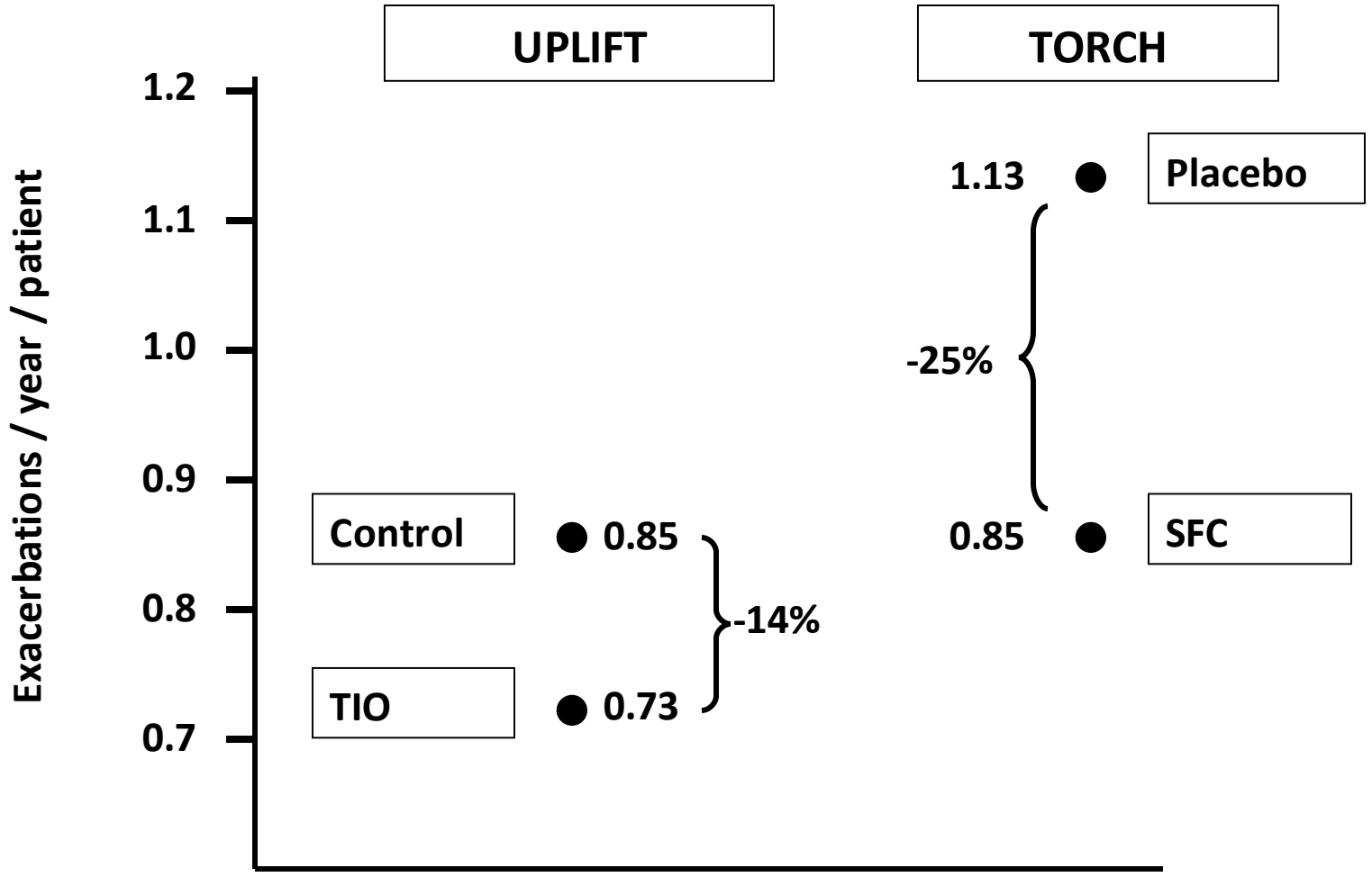
Annual decline in postbronchodilator FEV1 ml/year in the UPLIFT and TORCH studies



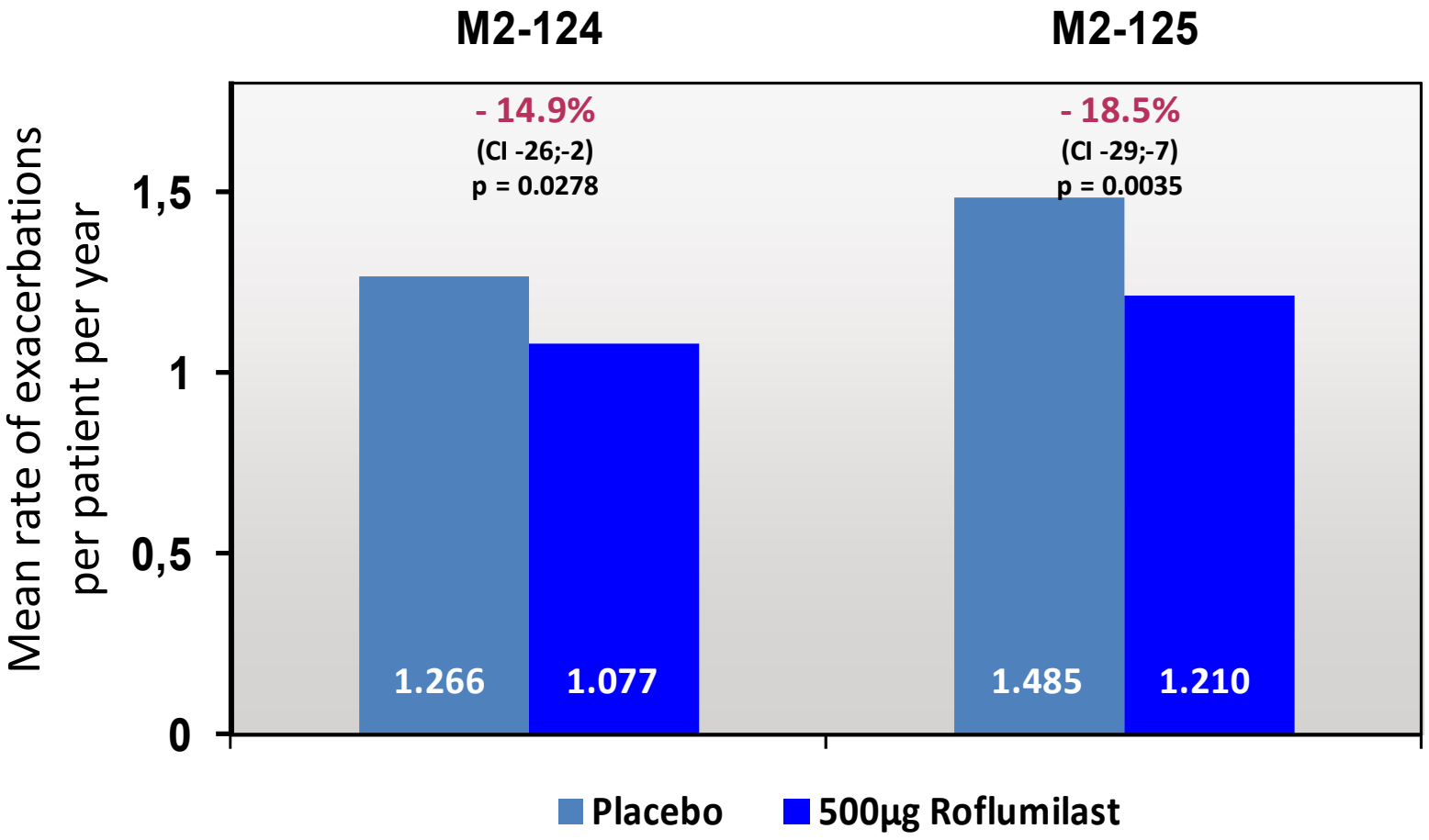
Probability of death (%) after 3 years observation in two large COPD trials



Exacerbation rates in two large COPD trials

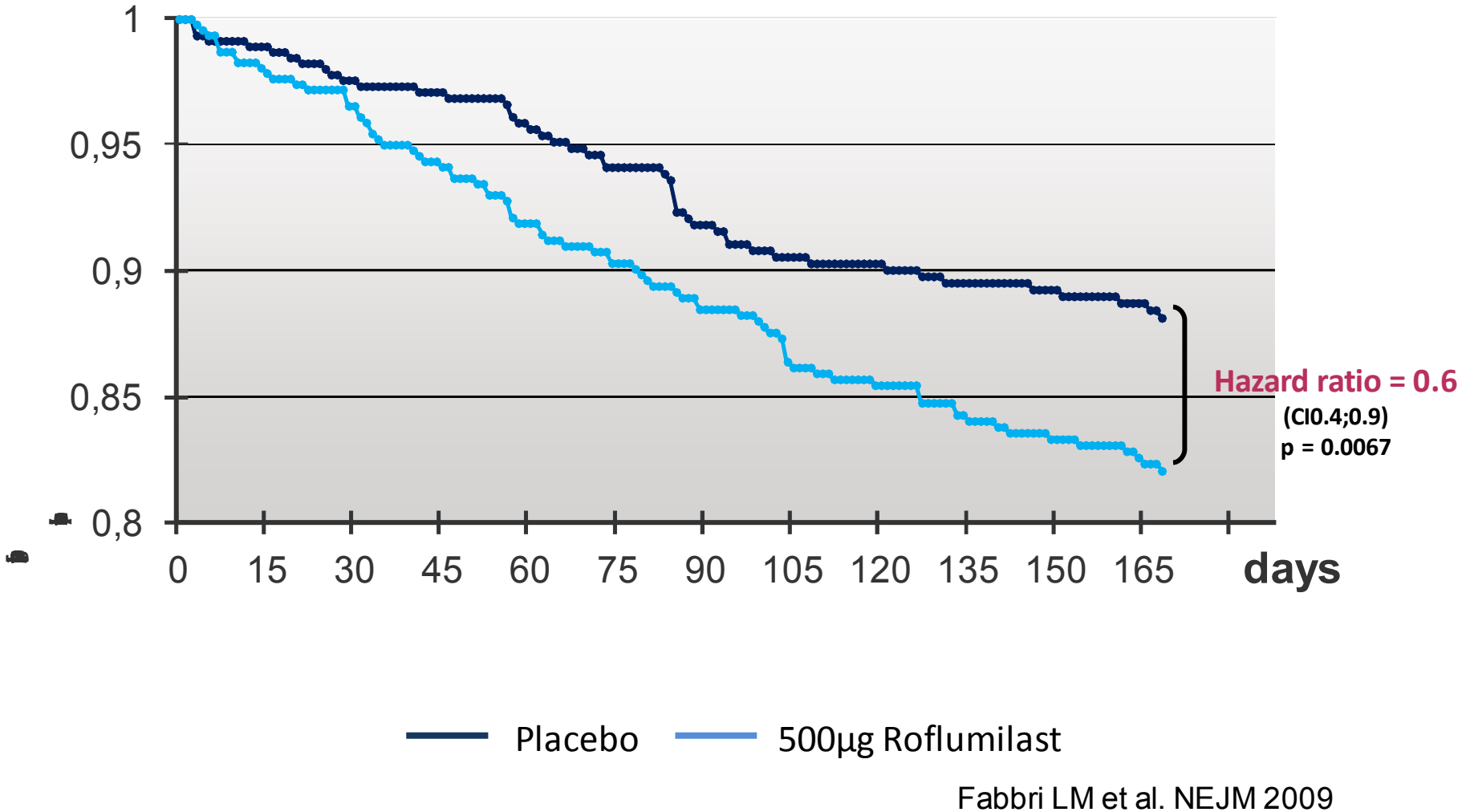


1 year studies - different maintenance treatments



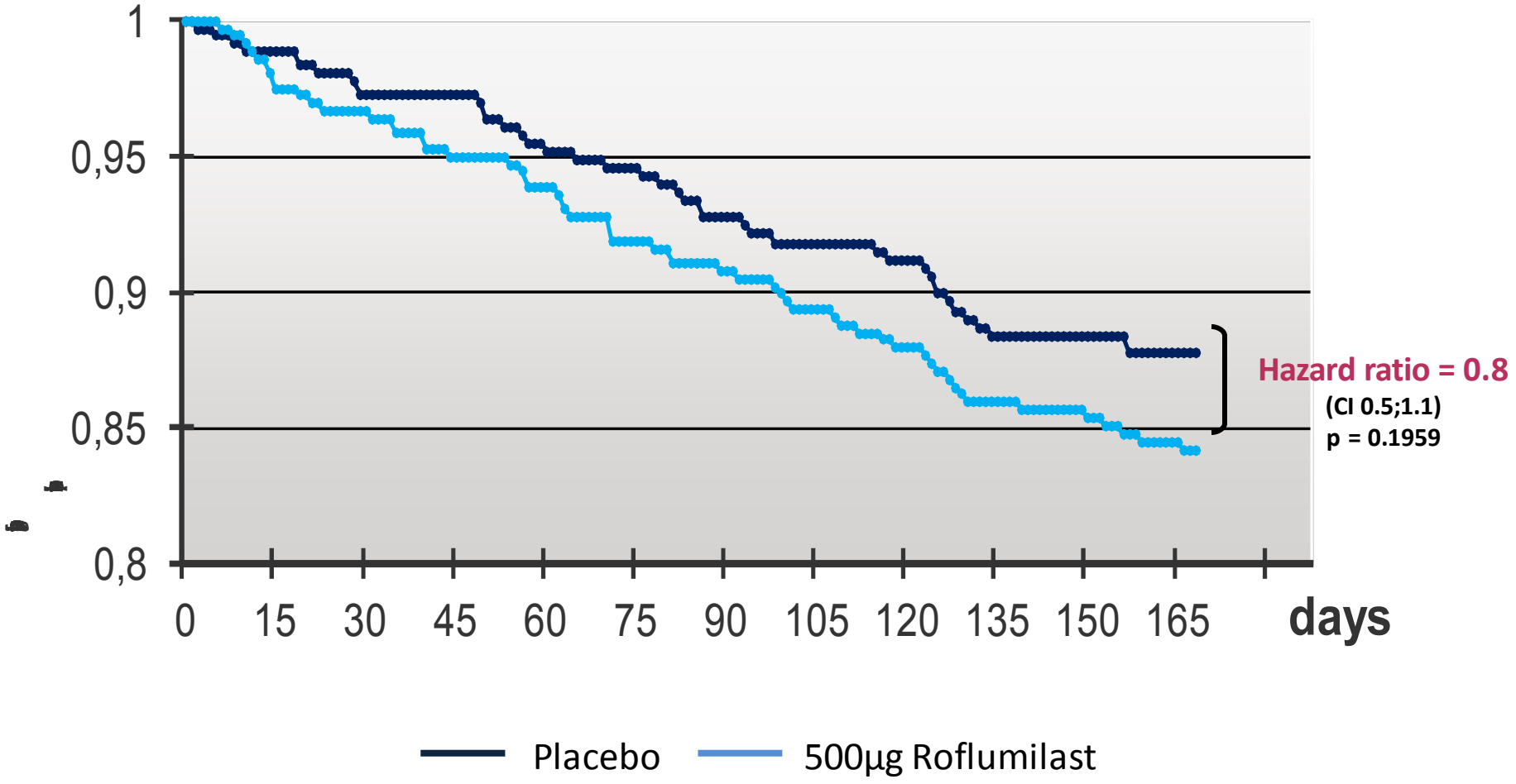
Calverley PM et al. Lancet 2009

6 months studies
Maintenance treatment with salmeterol



Fabbri LM et al. NEJM 2009

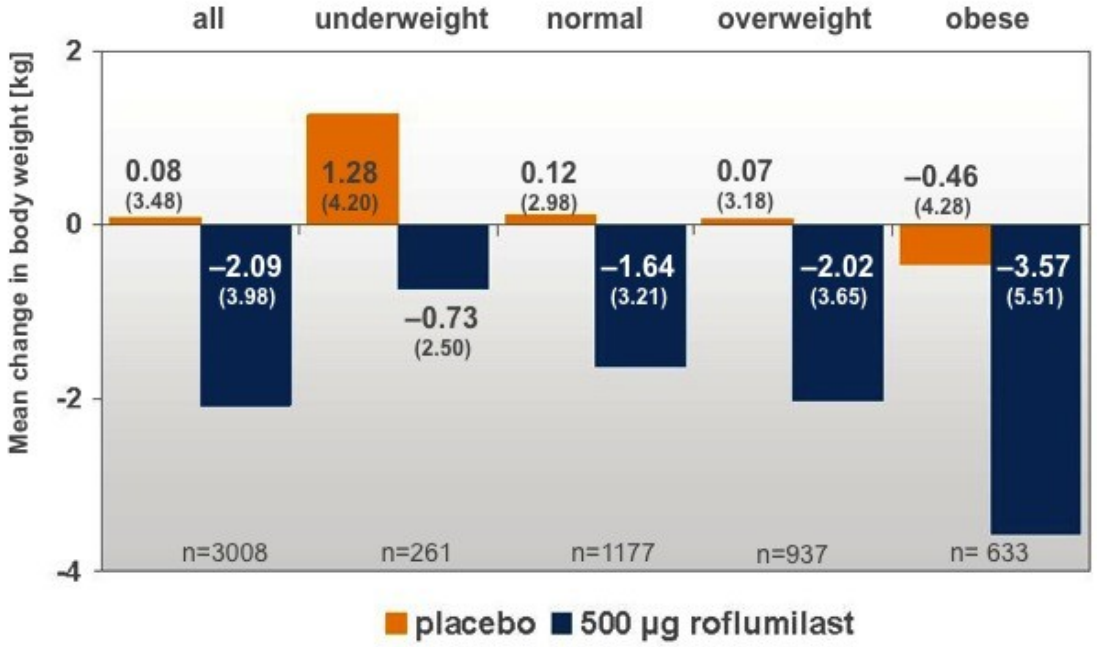
6 months studies
Maintenance treatment with tiotropium



Fabbri LM et al. NEJM 2009

Roflumilast– adverse effects

- GI symptoms
- Weight loss

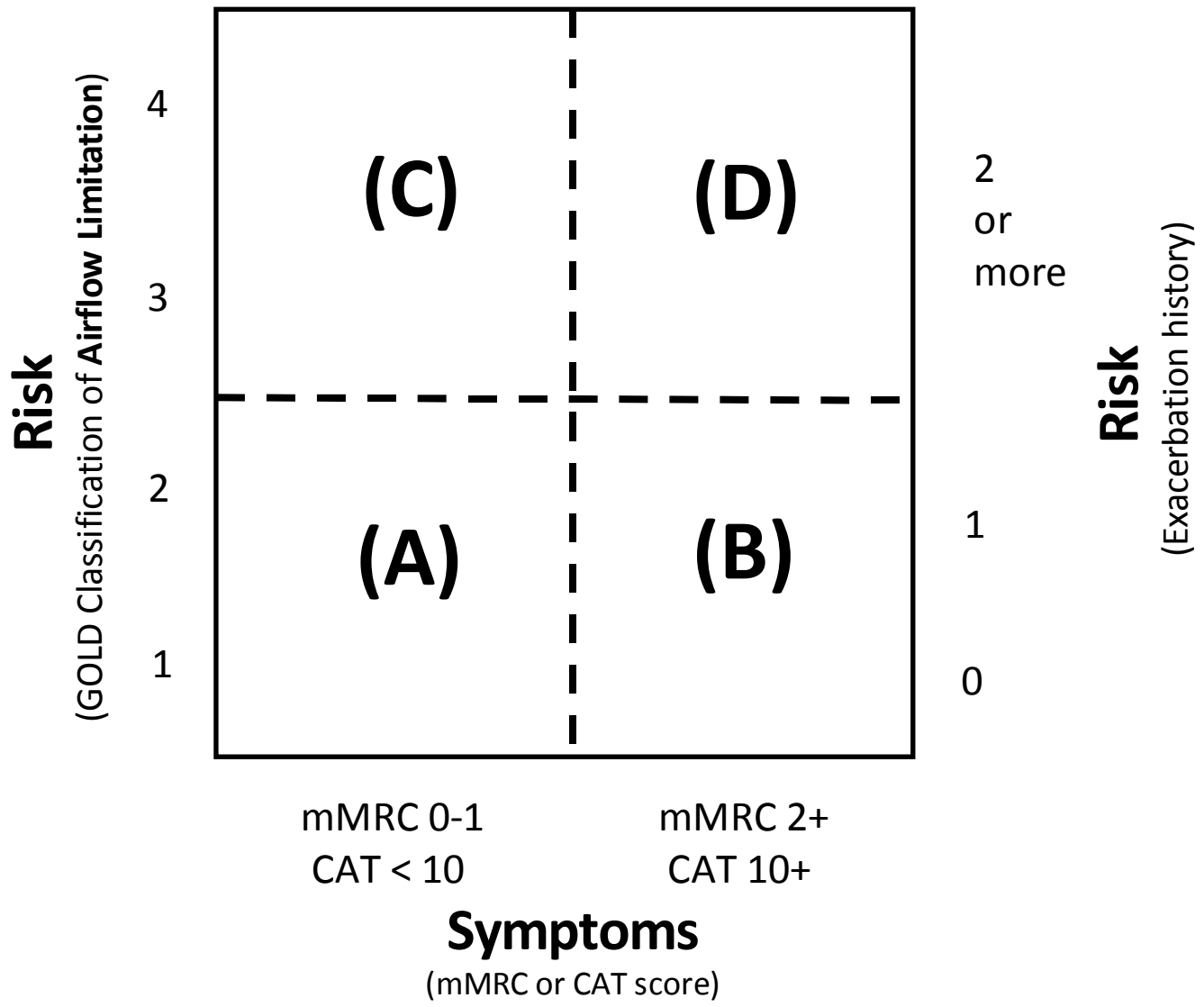


Combined assessment of COPD

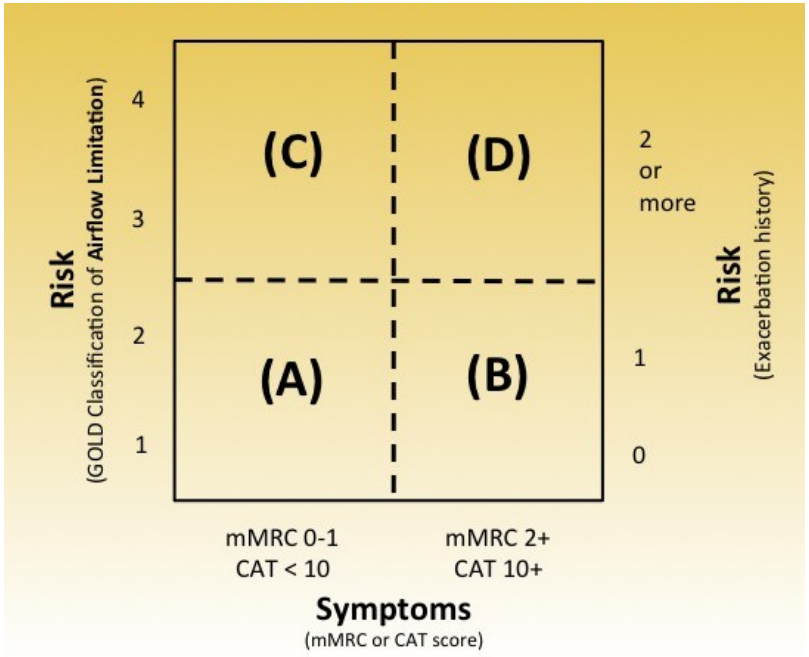
- Assess symptoms
- Assess degree of airflow limitation using spirometry
- Assess risk of exacerbations

An opportunity to combine these assessments for the purpose of improving management of COPD

Combined assessment of COPD



APSR 2011



Combined assessment of COPD

Patient	Characteristic	Spirometric Classification	Exacerbations per year	mMRC	CAT
A	Low Risk, Less Symptoms	GOLD1-2	≤ 1	0-1	< 10
B	Low Risk, More Symptoms	GOLD1-2	≤ 1	2+	≥ 10
C	High Risk, Less Symptoms	GOLD3-4	2+	0-1	< 10
D	High Risk, More Symptoms	GOLD3-4	2+	2+	≥ 10

Management of COPD – the aims

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

Management of COPD – the aims

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

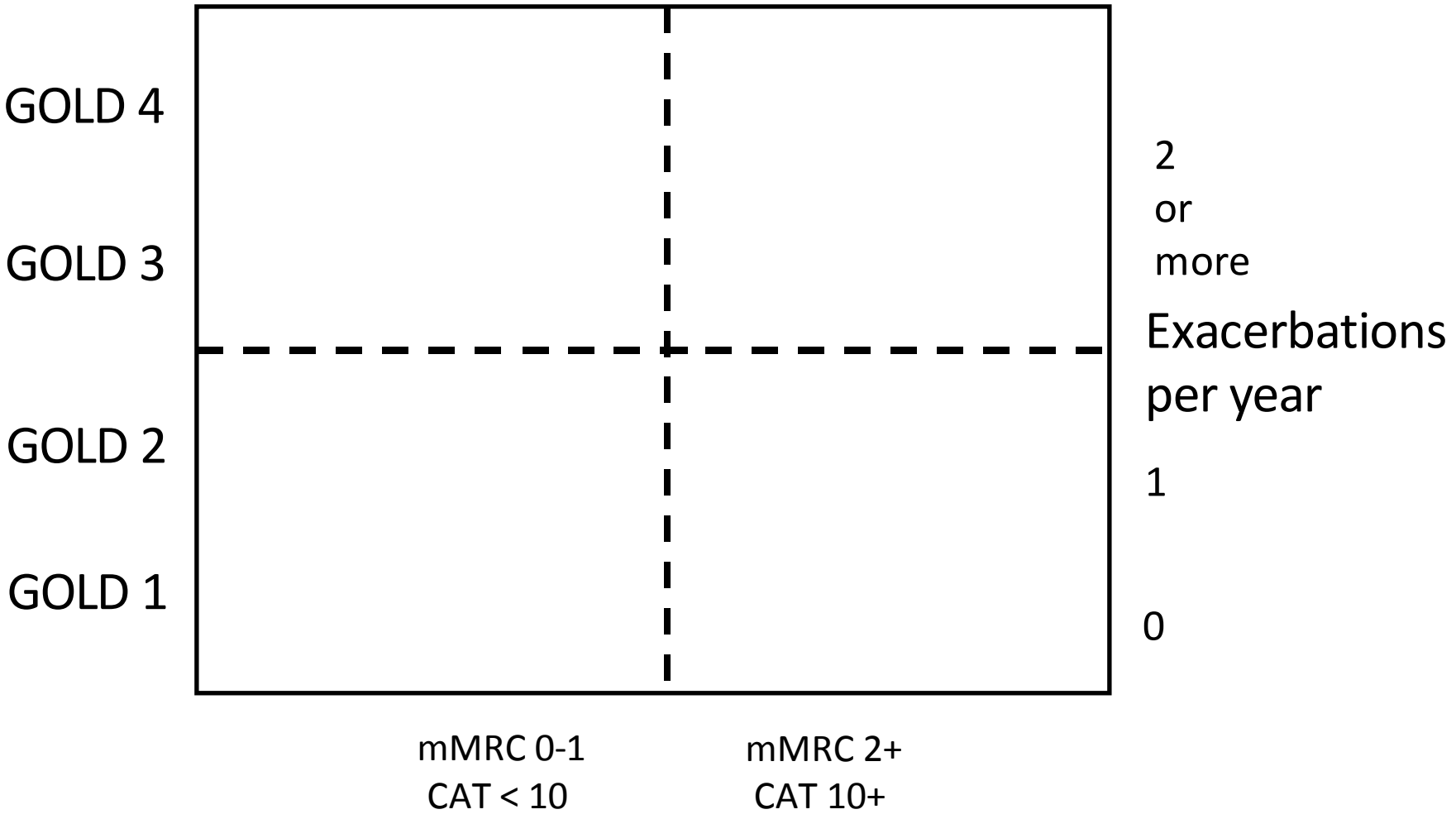
Reduce symptoms

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

Reduce risk

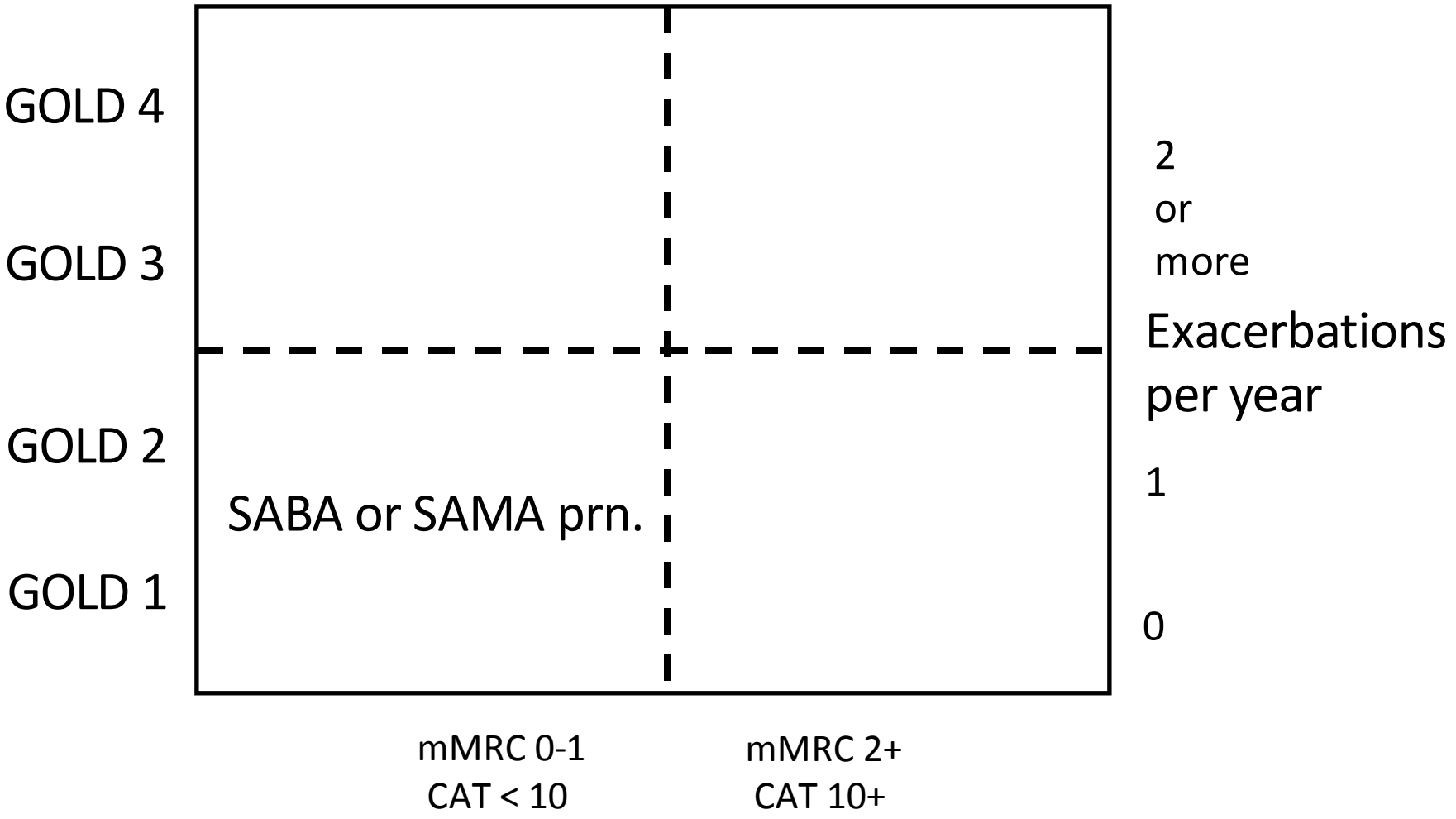
Management of COPD

Pharmacological **First choice**



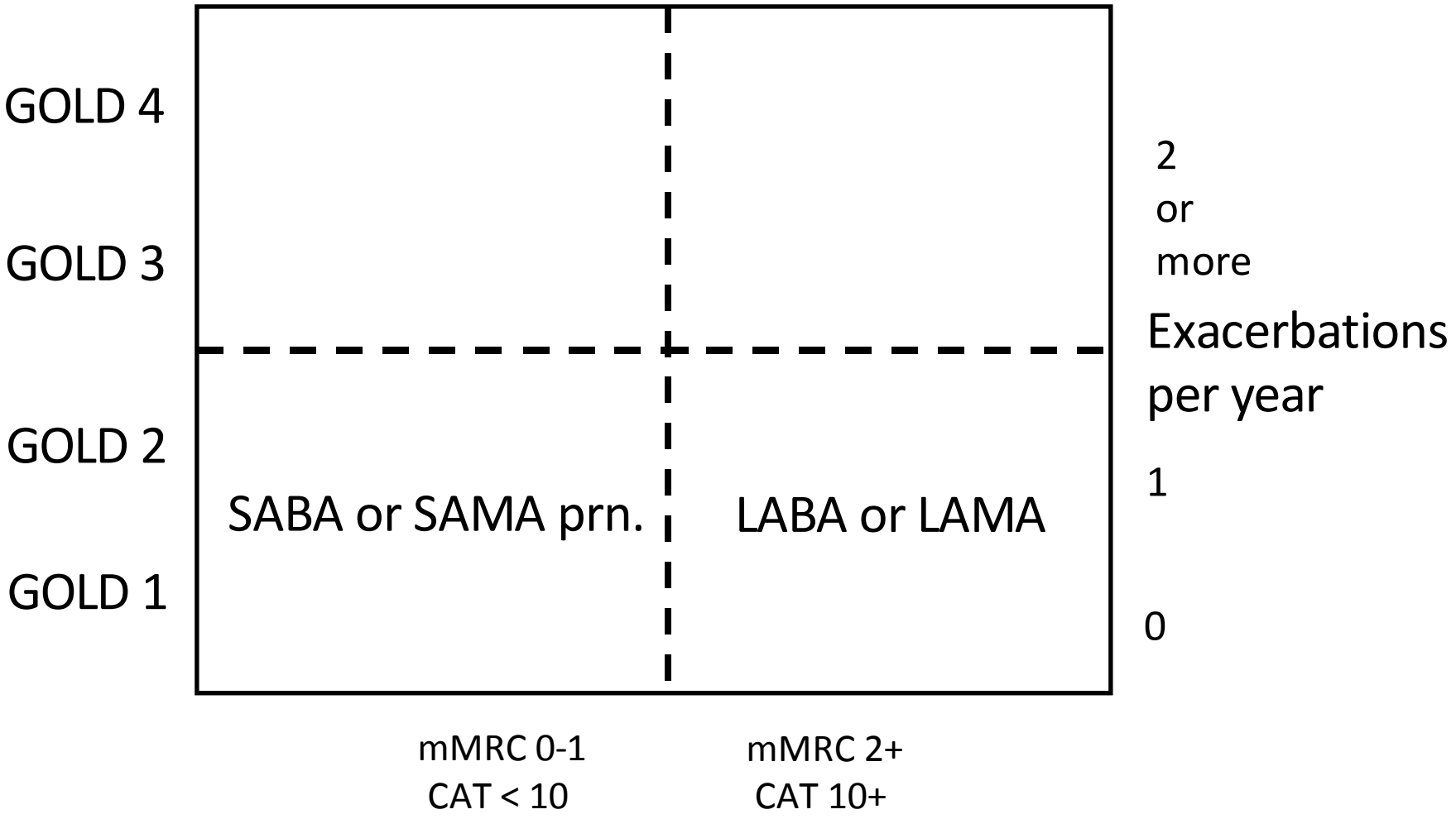
Management of COPD

Pharmacological **First choice**



Management of COPD

Pharmacological **First choice**



Management of COPD

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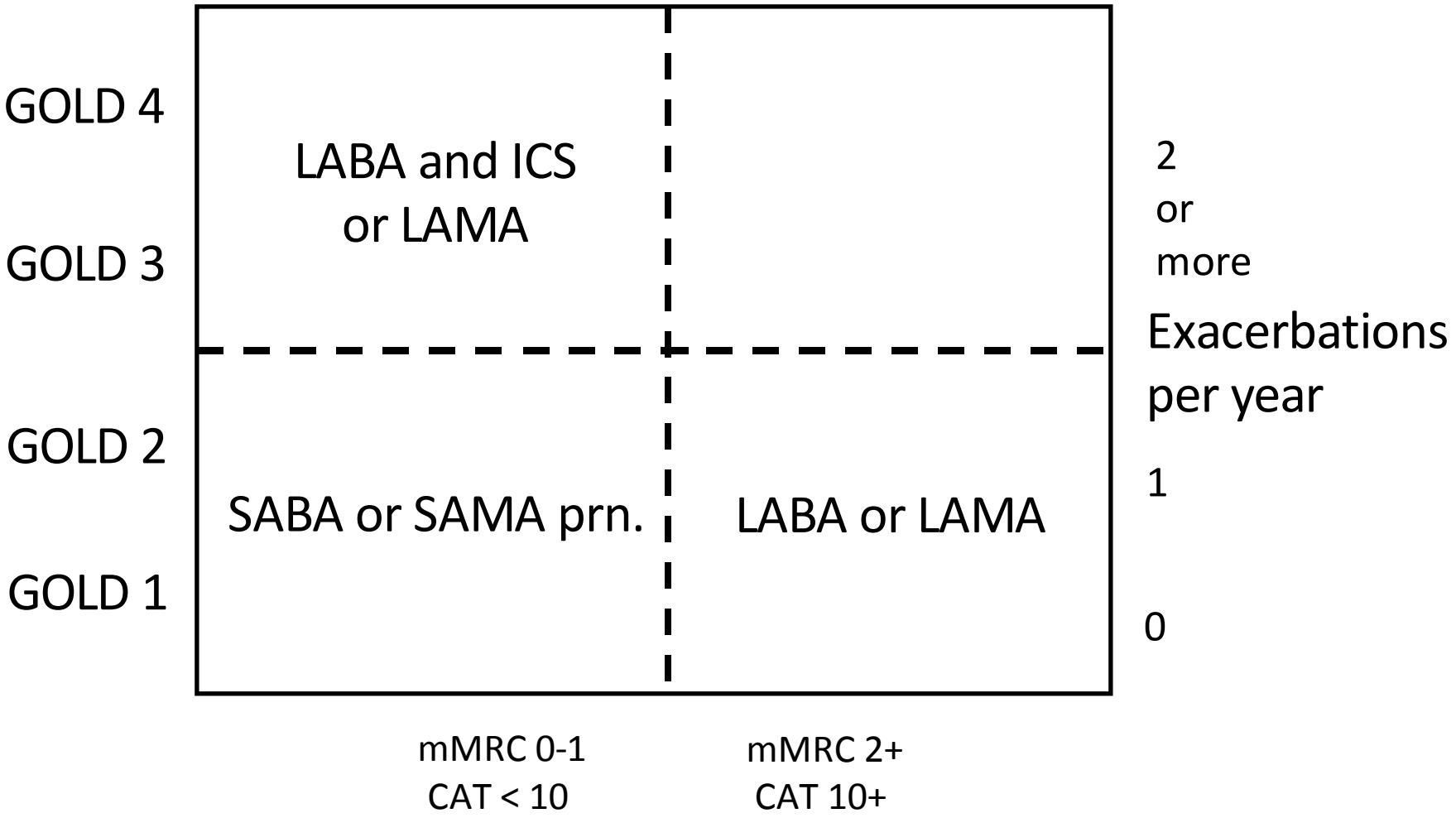
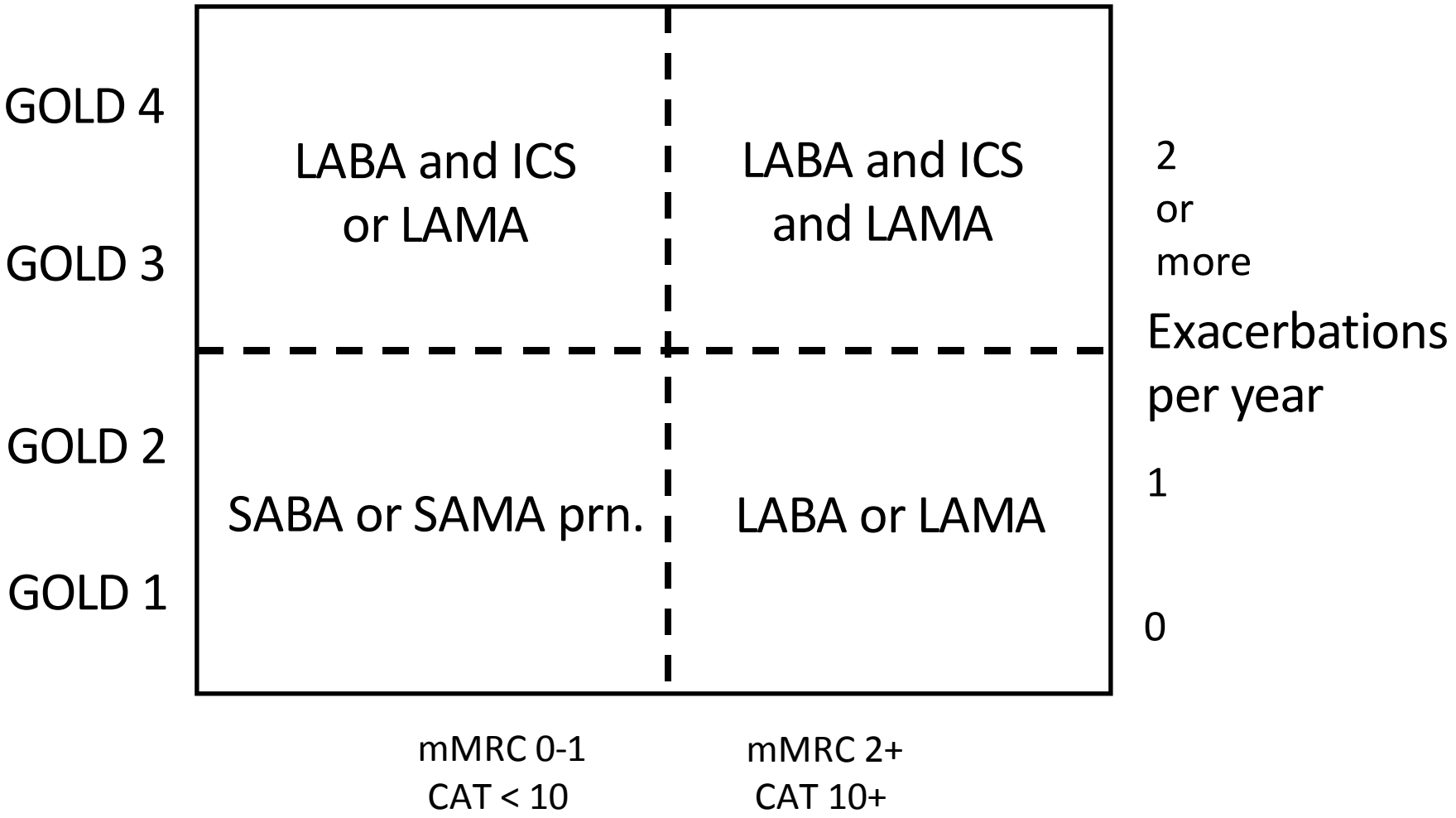


Management of COPD

Pharmacological **First choice**



Management of COPD

Pharmacological

Patient	First choice	First alternatives	Other alternatives
A	SABA or SAMA prn.	SABA and SAMA LABA or LAMA	Theophylline
B	LABA or LAMA	LABA and LAMA	Theophylline SABA or SAMA SABA and SAMA
C	LABA and ICS or LAMA	LABA and LAMA	Theophylline SABA and/or SAMA Consider PDE4-inh. LAMA and ICS
D	LABA and ICS and LAMA	ICS/LABA and LAMA ICS/LABA and PDE4-inh. LAMA and PDE4-inh.	Theophylline SABA and/or SAMA LAMA and ICS Carbocysteine

First line treatment

Asthma	COPD
Allergen avoidance	Smoking cessation
• Inhaled corticosteroid	• Inhaled long acting bronchodilators i.e. LAMA and LABA

Second line treatment

• LABA • LAMA • antileukotrienes	• Inhaled corticosteroid • PDE4 inhibitor
Anti IgE Allergen immunotherapy	antibiotics

Thank you for your attention