COPD 환자
외래에서 진료하기

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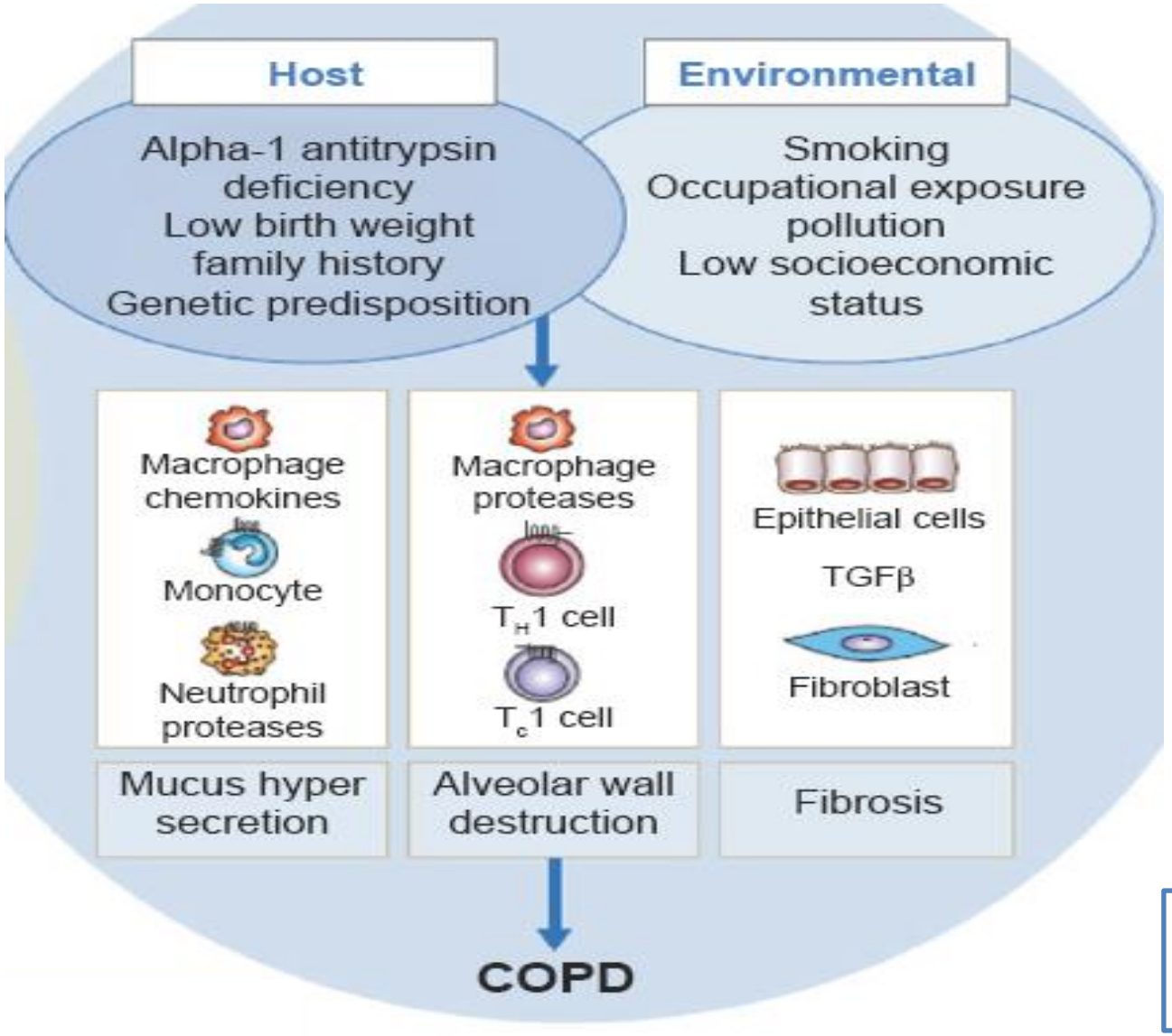
Definition of COPD

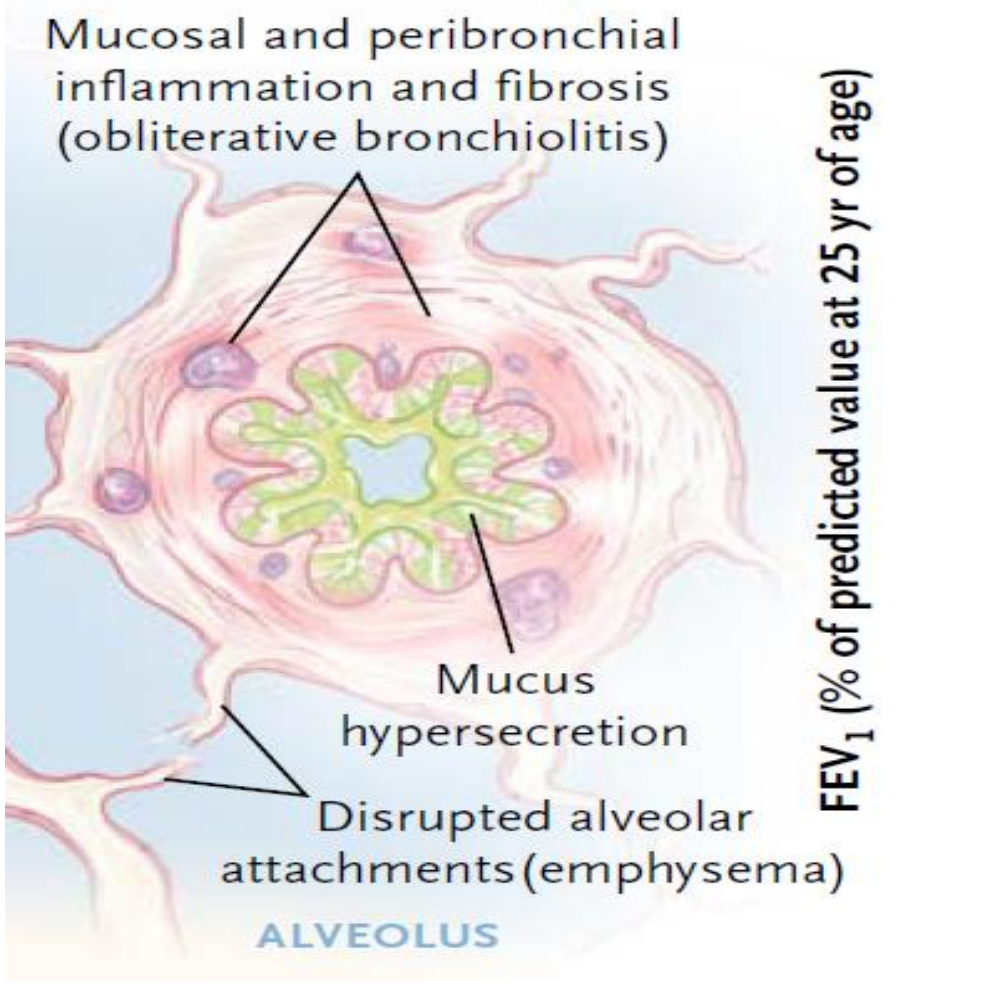
Chronic obstructive pulmonary disease (COPD)

- Common, preventable and treatable disease that is characterized by
  - ✓ Persistent respiratory symptoms and airflow limitation
  - ✓ Due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases
  - ✓ Influenced by host factors including abnormal lung development

GOLD 2022.

Pathophysiology of COPD



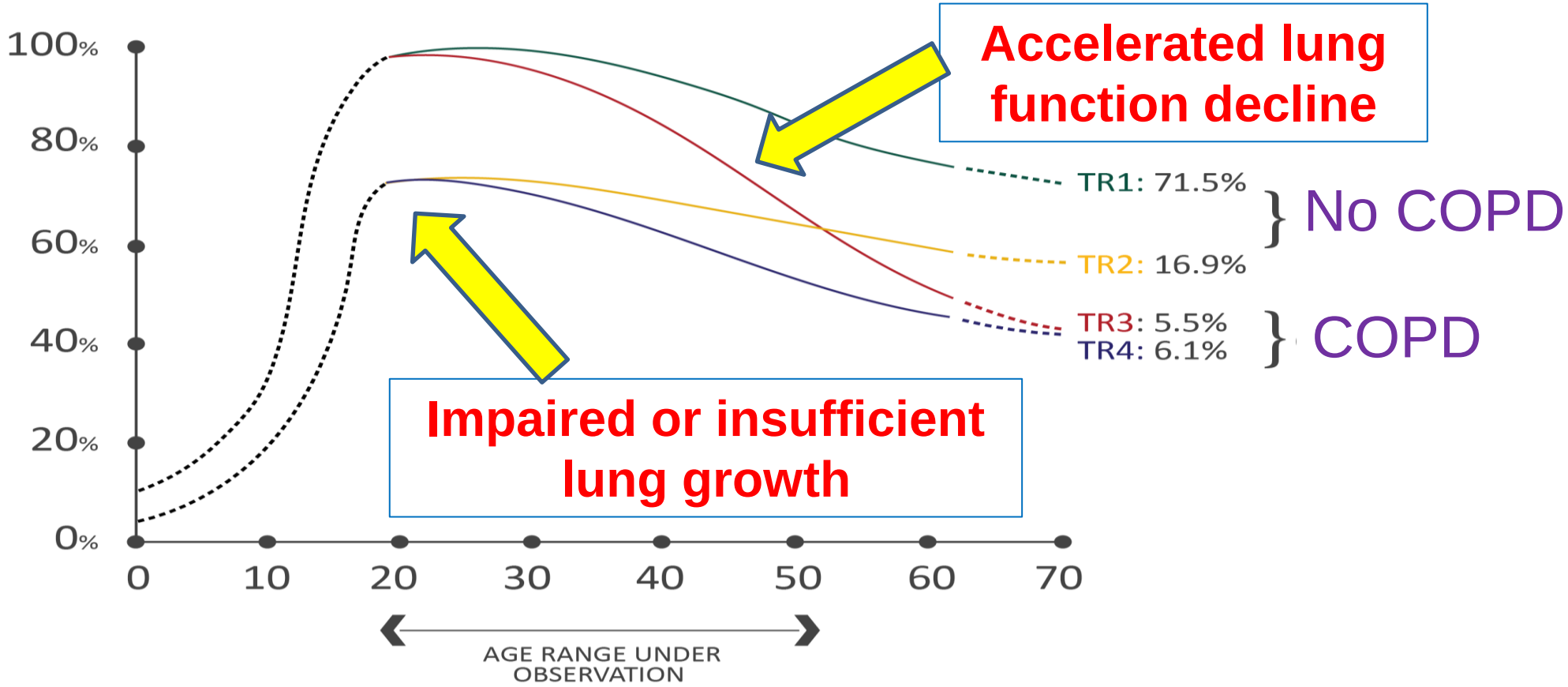


Predominant parenchymal destructive or predominant airflow limitation

Kostikas K, et al. Int J Chron Obsruct Pulmon Dis 2016;11:1297-306.

Lung function change over time

FEV1 in % of predicted maximally attained value



- TR1: Normal
- TR2: Small lungs but no COPD
- TR3: Normal initial FEV1 with rapid decline leading to COPD
- TR4: Small lungs leading to COPD

Lange P, et al. N Engl J Med 2015;373;111-22.

COPD risk factors in young adults

Male sex

Low BMI

Smoking

Airway hyper-responsiveness

Respiratory infections in childhood

Family history of asthma

TABLE 2. MUTUALLY ADJUSTED INCIDENCE RATE RATIOS FOR THE ASSOCIATION BETWEEN EACH POTENTIAL PREDICTOR AND THE INCIDENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS DEFINED BY THE THREE SPIROMETRIC CRITERIA

	IRR (95% CI)		
	GOLD	LLN (Quanjer)	LLN (LuftiBus)
Female	0.53 (0.32, 0.86)*	0.95 (0.52, 1.75)	1.68 (0.99, 2.86)
Age (⩾ 35 vs. < 35 yr)	2.24 (1.48, 3.39)†	1.25 (0.65, 2.39)	0.92 (0.53, 1.60)
BMI (vs. normal)			
Underweight	3.55 (1.59, 7.93)*	2.35 (0.72, 7.64)	1.14 (0.31, 4.22)
Overweight/obese	0.62 (0.42, 0.91)*	0.78 (0.30, 2.00)	1.03 (0.55, 1.94)
Low socioeconomic class	1.02 (0.56, 1.83)	0.63 (0.27, 1.50)	0.83 (0.45, 1.54)
Smoking habits (vs. nonsmoker)			
Quitter/sustained quitter	2.08 (1.34, 3.21)*	1.69 (0.92, 3.10)	1.30 (0.81, 2.09)
Persistent smoker/new smoker/restarter	2.61 (1.62, 4.20)†	2.42 (1.35, 4.33)*	2.43 (1.25, 4.73)*
ETS	1.08 (0.71, 1.66)	1.09 (0.68, 1.76)	1.10 (0.62, 1.93)
Biomass exposure	1.17 (0.69, 1.97)	1.25 (0.57, 2.74)	0.95 (0.53, 1.70)
Occupational exposures	1.01 (0.69, 1.47)	1.02 (0.59, 1.77)	1.19 (0.86, 1.66)
AHR	3.97 (2.07, 7.65)†	3.89 (1.78, 8.53)†	3.39 (1.72, 6.70)†
IgE sensitization	0.69 (0.44, 1.10)	0.86 (0.46, 1.60)	1.11 (0.68, 1.79)
Respiratory infections in childhood	1.88 (1.02, 3.46)*	1.97 (0.86, 4.54)	2.23 (1.64, 3.04)†
Family history of asthma	1.95 (1.25, 3.04)*	2.24 (1.12, 4.48)*	2.09 (1.26, 3.47)*

Marco R, et al. Am J Respir Crit Care Med 2011;183(7):891-7.

COPD risk factors in asthma

- 68,211 asthma patients, mean age 48.2 yrs, 18-yr follow-up

Variables	aFTR*	95% CI	P-value
Male sex	0.62	(0.56, 0.68)	<0.001
Age, years			
< 30 years	Ref		
30-39 years	0.34	(0.23, 0.50)	<0.001
≥ 40 years	0.03	(0.02, 0.04)	<0.001
Asthma exacerbation	0.81	(0.17, 0.25)	<0.007
Asthma severity			
Mild	Ref		
Moderate	0.23	(0.21, 0.26)	<0.001
Severe	0.10	(0.08, 0.12)	<0.001
SABA overuse (>2 canisters)	0.61	(0.44, 0.84)	0.003
Medication adherence (PDC ≥ 80%)	1.83	(1.54, 2.17)	<0.001

*aFTR, adusted failure time ratio

Asamoah-Boaheng M, et al. COPD 2022 Jan 10;1-10.

Proposed definitions in GOLD 2022 update

- **Early COPD**
  - ✓ Biological “early” > clinical “early”
  - ✓ Initial biological mechanism that eventually lead to the disease rather than the initial perception of symptoms

- **Mild COPD**
  - ✓ Mild severity of airflow limitation (at any age, with or without progression)

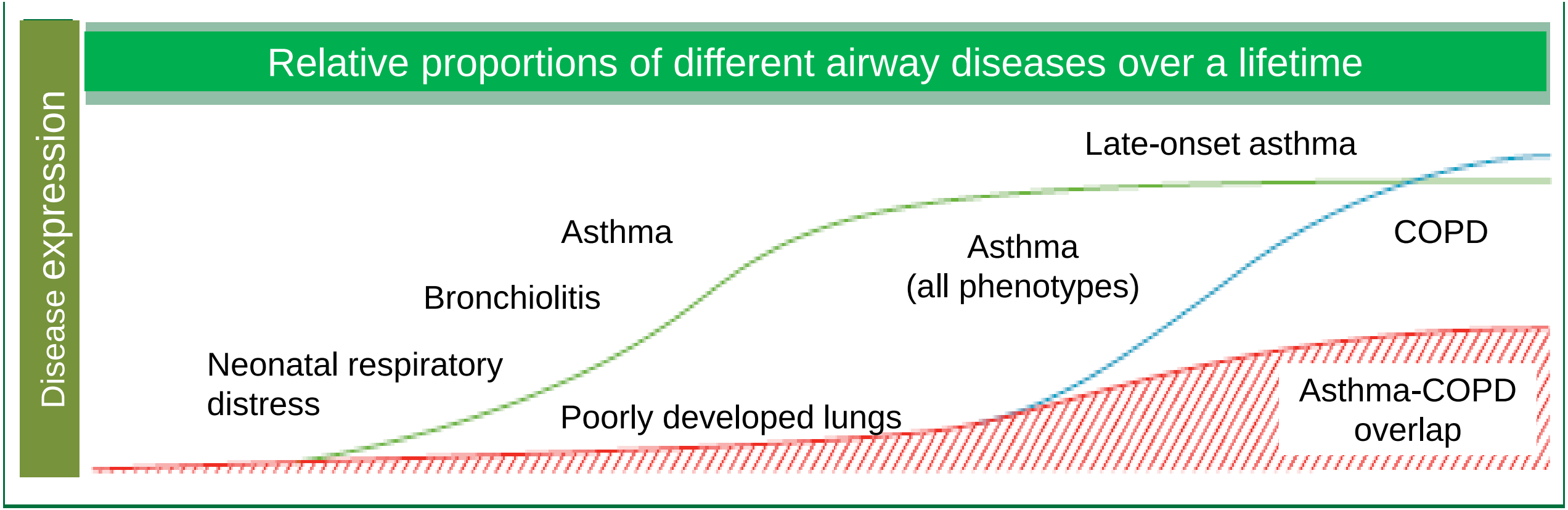
- **COPD in young people**
  - ✓ Patients aged 20-50 years
  - ✓ Possibility of a family history of respiratory diseases and/or early-life events (early-life origins of COPD)

- **Pre-COPD**
  - ✓ Patients who have respiratory symptoms with or without detectable structural and/or functional abnormalities, in the absence of airflow limitation

GOLD 2022.

Natural course of chronic airway disease

- Interplay of genetic and environmental factors of airway diseases



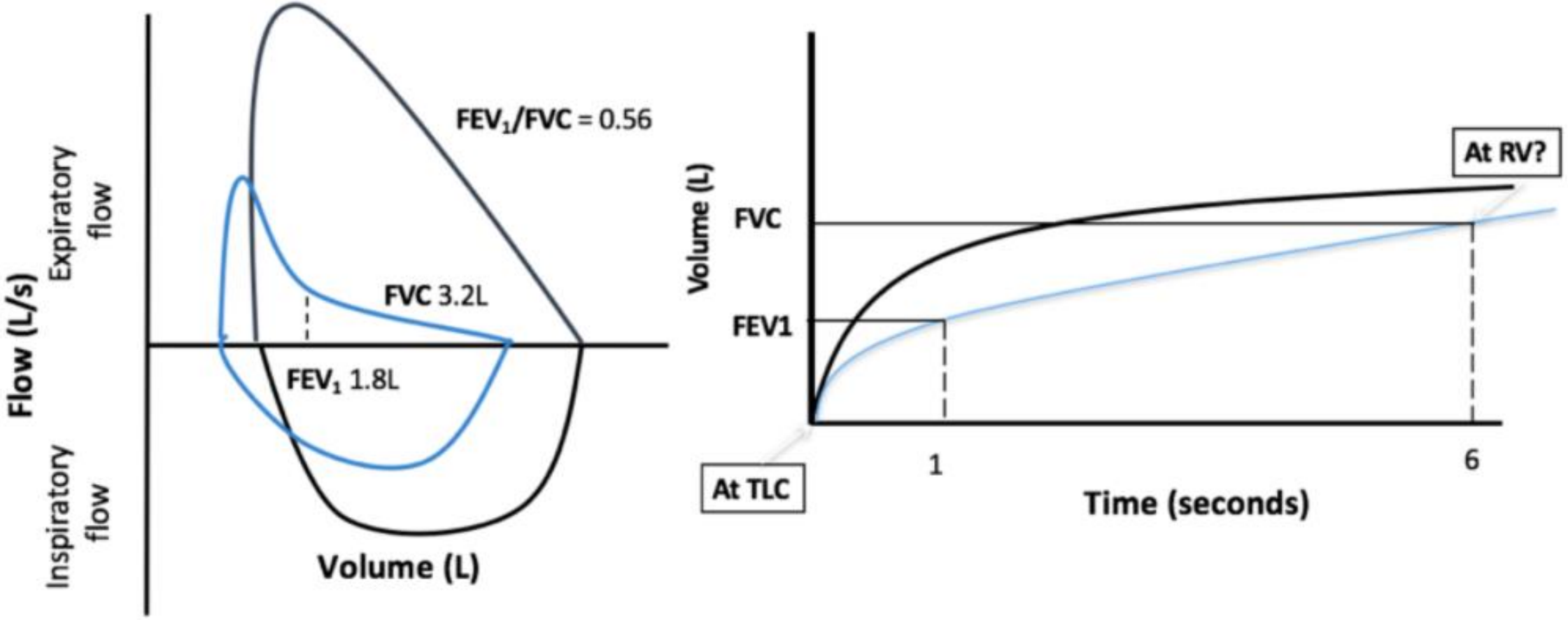
Bateman ED, et al. Lancet Respir Med 2015;3(9):719-728.

Key indicators for considering a diagnosis of COPD

40세 이상 환자가 아래와 같은 지표가 있으면 COPD를 의심하고 폐활량측정법을 시행하여 진단한다.	
증상	
호흡곤란	운동시 심해짐, 움직이지 않으면 덜하거나 없음
기침	있기도 하고 없기도 함
가래	있기도 하고 없기도 함
위험인자	
흡연	현재 흡연력 또는 과거 흡연력
분진, 가스 노출력	직업력(분진 및 화학물질); 집안 연기(취사/난방)
COPD 가족력	특히 COPD 형제력
소아기 병력	출생 시 저체중, 소아기 호흡기 감염

KATRD 2018

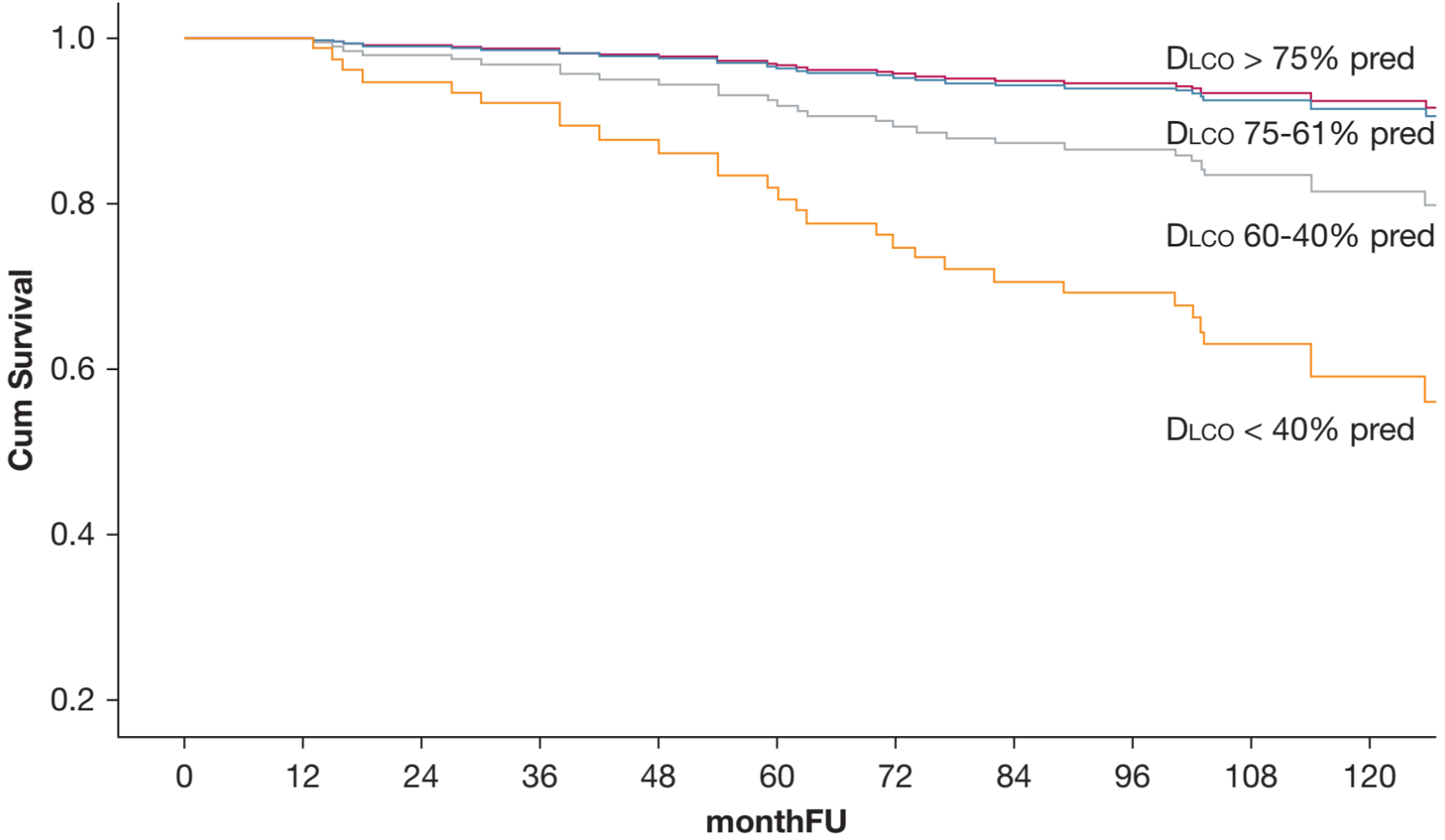
Spirometry: Airflow limitation



* 기관지확장제 투여 후 FEV1/FVC<0.7이면 기류제한이 있다고 판단 (또는 FEV1/FEV6 <0.73)

DLCO as a prognostic factor

- GOLD stage I COPD patients (n=360), 9-yr follow up

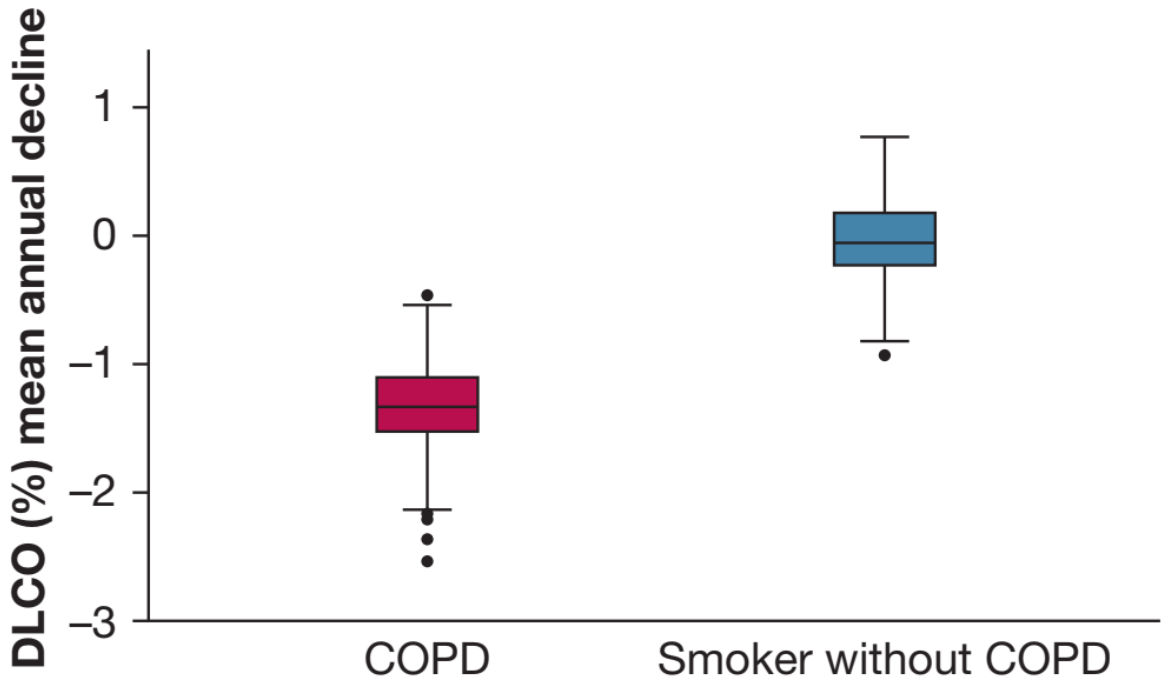


de-Toress JP et al. CHEST 2021;160(3):872-878.

DLCO as a prognostic factor

TABLE 3] Cox Proportional Analysis of the Baseline Variables Associated With All-Cause Mortality

Variable	Hazard Ratio (95% CI)	*P*
Age	1.05 (1.00-1.10)	.04
Sex	1.16 (0.41-3.32)	.77
BMI	0.97 (0.88-1.07)	.55
Pack-years	1.00 (0.99-1.01)	.23
Smoking status	1.55 (0.99-3.60)	.36
$D_{LCO} < 60\%$	3.37 (1.35-8.39)	.009



➔ PFT follow-up with spirometry + BDR + DLCO (+ TLC + RV)

de-Toress JP et al. CHEST 2021;160(3):872-878.
Casanova C, et al. CHEST 2021;160(2):481-490.

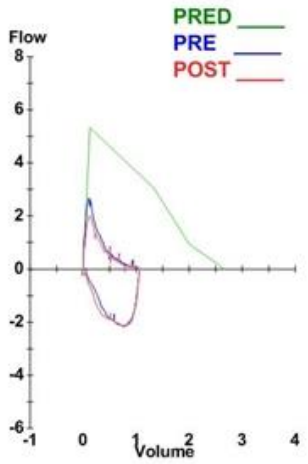
Pitfall of PFT interpretation

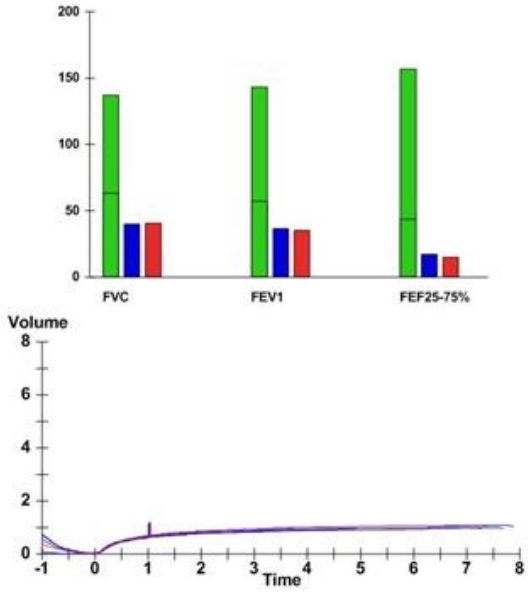
Age: 62 Gender: Female
Race: Asian
Height(cm): 155 Weight(kg): 59.0
Any Info:

Room: 45 Date: 10/18/17
Temp: 24 PBar: 767
Physician:
Technician:

Spirometry (BTPS)

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	2.68	1.07	40	1.07	40	0
FEV1	Liters	1.95	0.71	36	0.68	35	-4
FEV1/FVC	%	73	66		63		
FEF25-75%	L/sec	2.35	0.40	17	0.34	15	-13
FEF25%	L/sec		2.21		1.38		-38
FEF50%	L/sec	3.05	0.54	18	0.48	16	-11
FEF75%	L/sec	0.94	0.19	20	0.14	15	-25
PEF	L/sec	5.30	2.66	50	2.01	38	-25
FVL ECode			_ 000		111000		
DLCO	mL/mmHg/min	17.6	1.2	7			
DLCO/VA	mL/mHg/min/L	3.87	0.84	22			
VA	Liters		1.43				
CO T.C.	Sec	17.5	82.8	473			
IVC	Liters		1.08				





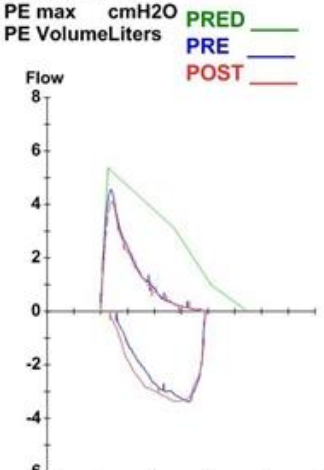
Comments:

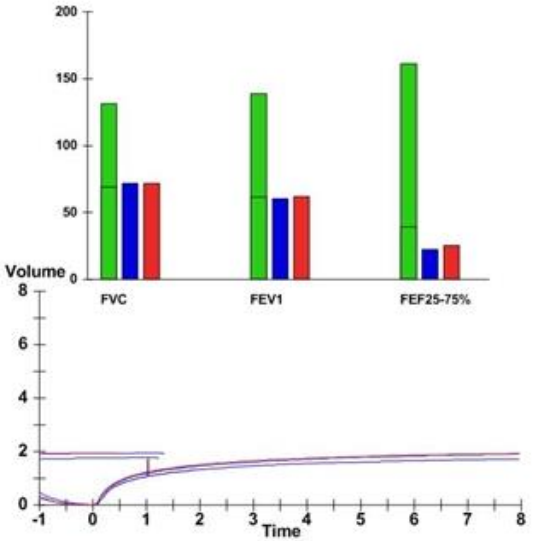
Age: 61 Gender: Female
Race: Asian
Height(cm): 156 Weight(kg): 54.0
Any Info:

Room: IM Date: 02/01/17
Temp: 25 PBar: 772
Physician:
Technician:

Spirometry (BTPS)

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	2.74	1.96	71	1.96	71	0
FEV1	Liters	2.01	1.21	60	1.24	62	3
FEV1/FVC	%	73	62		63		
FEF25-75%	L/sec	2.40	0.54	22	0.60	25	12
FEF25%	L/sec		2.49		2.55		2
FEF50%	L/sec	3.11	0.86	28	0.83	27	-4
FEF75%	L/sec	0.98	0.18	18	0.23	23	27
PEF	L/sec	5.38	4.54	84	4.14	77	-9
FVL ECode			101000		111000		
DLCO	mL/mmHg/min	16.9	14.5	86			
DLCO/VA	mL/mHg/min/L	3.93	4.50	115			
VA	Liters		3.22				
CO T.C.	Sec	17.3	15.4	89			
IVC	Liters		1.68				
PI max	cmH2O	73					
PI Volume	Liters						
PE max	cmH2O	138					
PE Volume	Liters						





Comments:

Pitfall of PFT interpretation

Age: 84 Gender: Female
Race: Asian
Height(cm): 148 Weight(kg): 34.0
Any Info:

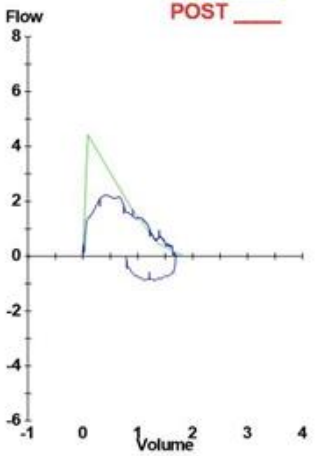
Room: OS
Temp: 24
Physician:
Technician:

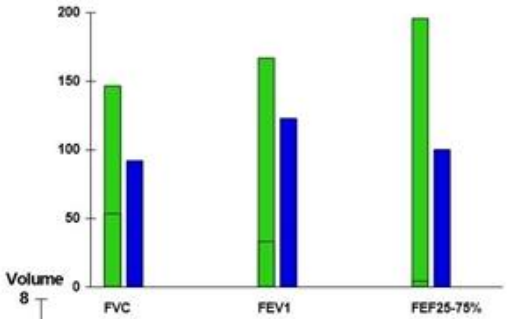
Date: 02/09/22
PBar: 772

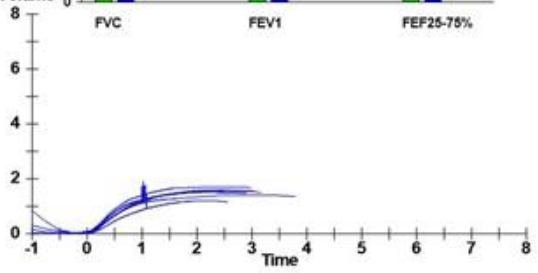
Spirometry (BTPS)

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	1.84	1.70	92			
FEV1	Liters	1.16	1.43	123			
FEV1/FVC	%	69	84				
FEF25-75%	L/sec	1.53	1.53	100			
FEF25%	L/sec		2.16				
FEF50%	L/sec	1.64	1.60	97			
FEF75%	L/sec	0.45	0.88	194			
PEF	L/sec	4.42	2.23	50			
FVL ECode			001011				
DLCO	mL/mmHg/min	9.3					
DLCO/VA	mL/mHg/min/L	3.35					
VA	Liters						
CO T.C.	Sec	23.2					
IVC	Liters						
PI max	cmH2O	61					
PI Volume	Liters						
PE max	cmH2O	125					
PE Volume	Liters						

PRED
PRE
POST

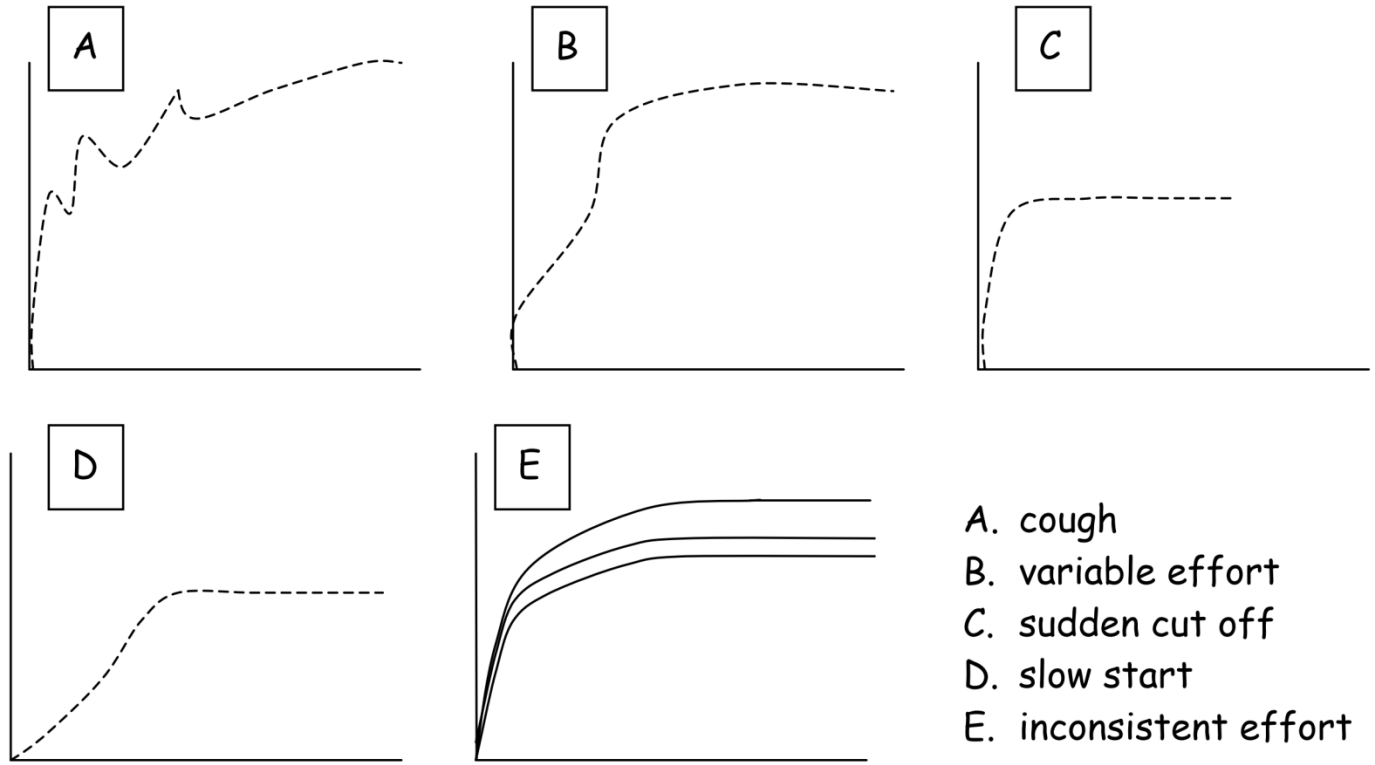






Comments:

Figure 7. EXAMPLES: POORLY PERFORMED CURVES



A. cough
B. variable effort
C. sudden cut off
D. slow start
E. inconsistent effort

GOLD 2010.

Assessment of COPD

- 질병의 중증도, 환자의 건강상태 및 향후 위험에 대한 영향을 결정하기 위해 다음의 요소를 고려
  - ✓ 환자 증상의 현재 정도
  - ✓ 폐기능 이상의 중증도
  - ✓ 급성 악화의 빈도
  - ✓ 동반질환의 존재

Assessment of symptoms: Dyspnea

➢ Modified Medical Research Council (mMRC) scale

Grade	호흡곤란 내용
0	힘든 운동을 할 때 숨찬 것을 제외하면 숨차서 고생한 적이 없다
1	평지를 빨리 걷거나, 약간 오르막을 걸을 때 숨차서 힘들다
2	숨차서 평지를 동년배보다 늦게 걷거나 평지를 자신의 속도로 걸을 때 숨차서 멈추어 쉰다
3	평지를 약 100m 또는 몇 분 동안 걷고 나서 숨차서 멈추어 쉰다
4	너무 숨차서 집 바깥에 못 나가거나 옷을 입거나 벗을 때 숨이 차다

Fletcher CM. BMJ 1960;2:1662.

Assessment of symtoms: Quality of life

➢ COPD Assessment Test (CAT)

나는 전혀 기침을 하지 않는다	0 1 2 3 4 5	나는 항상 기침을 한다
나는 가슴에 전혀 가래가 없다	0 1 2 3 4 5	나는 가슴에 가래가 가득 차 있다
나는 전혀 가슴이 답답함을 느끼지 않는다	0 1 2 3 4 5	나는 가슴이 아주 답답함을 느낀다
나는 언덕이나 계단을 오를 때 전혀 숨이 차지 않는다	0 1 2 3 4 5	나는 언덕이나 계단을 오를 때 아주 숨이 차다
나는 집에서 활동하는 데 전혀 제약을 받지 않는다	0 1 2 3 4 5	나는 집에서 활동하는 데 많은 제약을 받는다
폐질환에도 불구하고 나는 외출하는 데 자신이 있다	0 1 2 3 4 5	폐질환으로 인하여 나는 외출하는 데 전혀 자신이 없다
나는 잠을 깊이 잔다	0 1 2 3 4 5	폐질환으로 인하여 나는 잠을 깊이 자지 못한다
나는 기운이 왕성하다	0 1 2 3 4 5	나는 전혀 기운이 없다

평가영역

- ➢ 호흡기증상
- ➢ 활동정도
- ➢ 수면
- ➢ 자신감

CAT score: 0~40
- Normal: 0~9

Jones PW, et al. Eur Repir J 2009;34(3):648-54.

Classification of airflow limitation severity

Fixed airfow limitation : Post-bronchodilator FEV1/FVC raio < 0.7		
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

Acute exacerbation and lung function

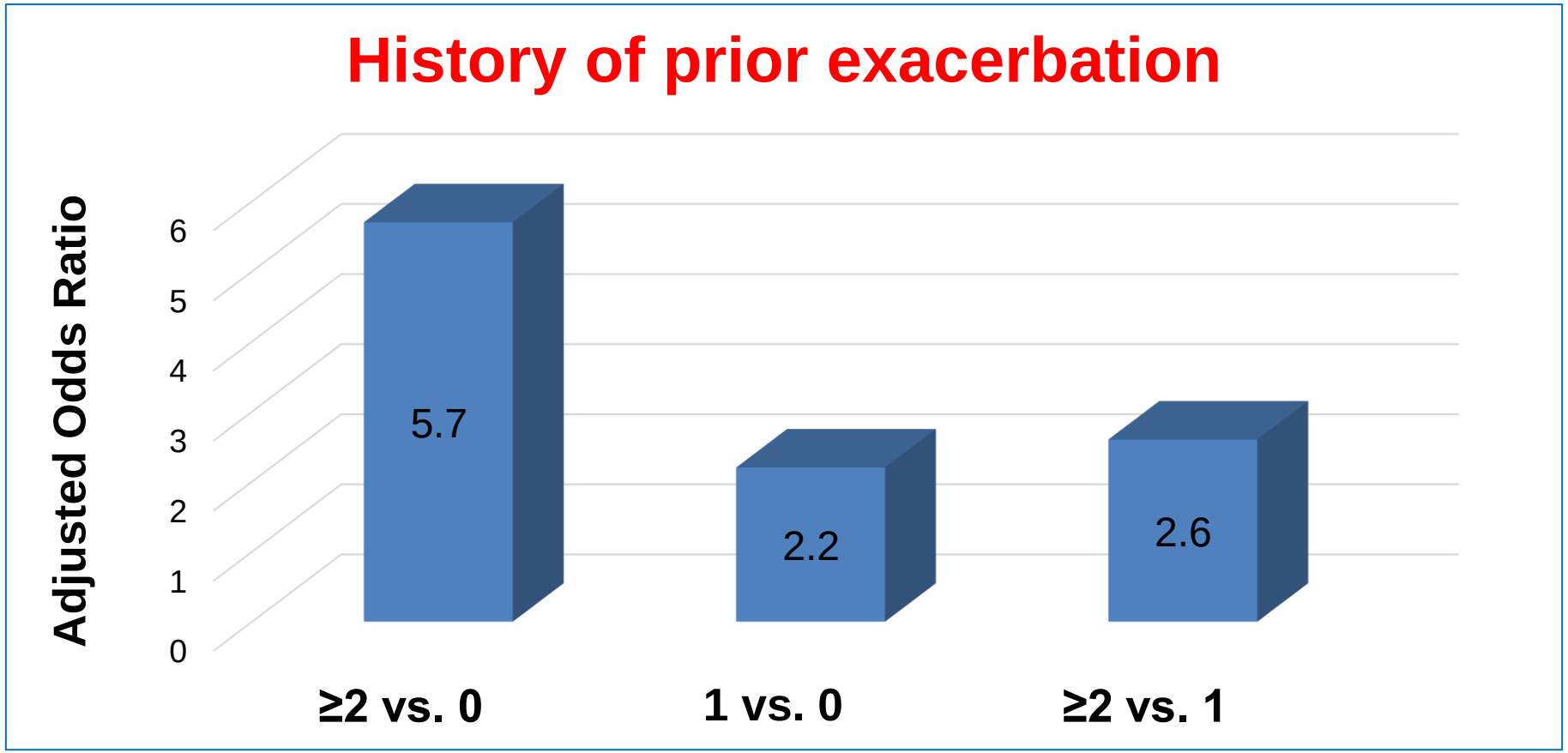
- 109 COPD patients, 757 exacerbation
- Lung function follow-up over 4 years

	Annual change		
	Infrequent AE	Frequent AE	P value
Exacerbations	<50% percentile <2.92 per year	>50% percentile >2.92 per year	
PEF (L/min)	-0.72	-2.94	<0.05
FEV1 (mL)	-32.1	-40.1	<0.001

Donaldson GC, et al. Thorax 2002;57(10):847-52.

Predictor of acute exacerbation

- 2,138 COPD patients enrolled in ECLIPSE study, 40~75yrs, ≥10PYs, FEV1 <80%
- Follow-up for 3 years



Papi A, et al. Lancet 2018;391:1076-84.

Combined assessment of COPD

Spirometrically Confirmed Diagnosis

Assessment of airflow limitation

Assessment of symptoms/risk of exacerbations

Post-bronchodilator $FEV_1/FVC < 0.7$

Grade	FEV_1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

Moderate or Severe Exacerbation History

≥2 or ≥ 1 leading to hospital admission

0 or 1 (not leading to hospital admission)

C	D
A	B

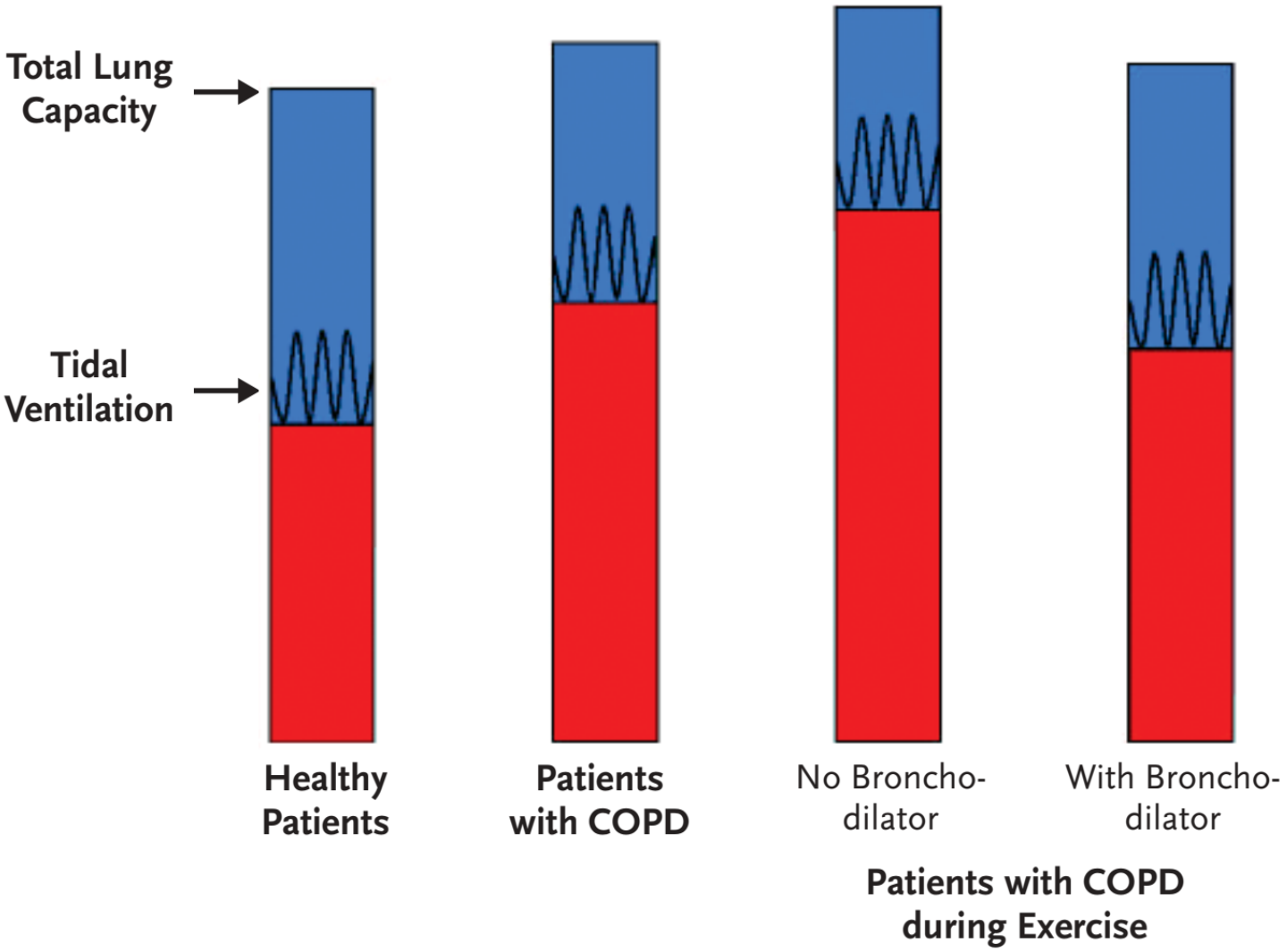
mMRC 0-1 CAT < 10

mMRC ≥ 2 CAT ≥ 10

Symptoms

GOLD 2022.

Pulmonary hyperinflation and bronchodilator



- Inspiratory capacity ↓
- Functional residual capacity ↑

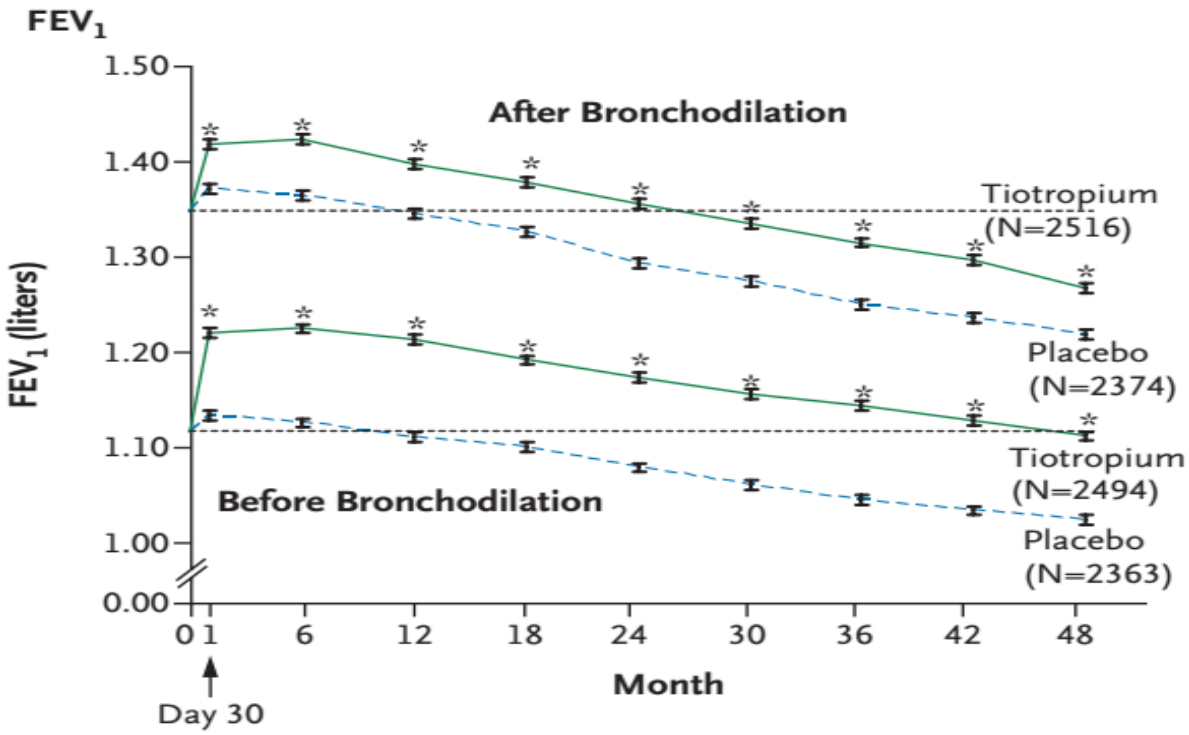
- Dynamic hyperinflation during exercise

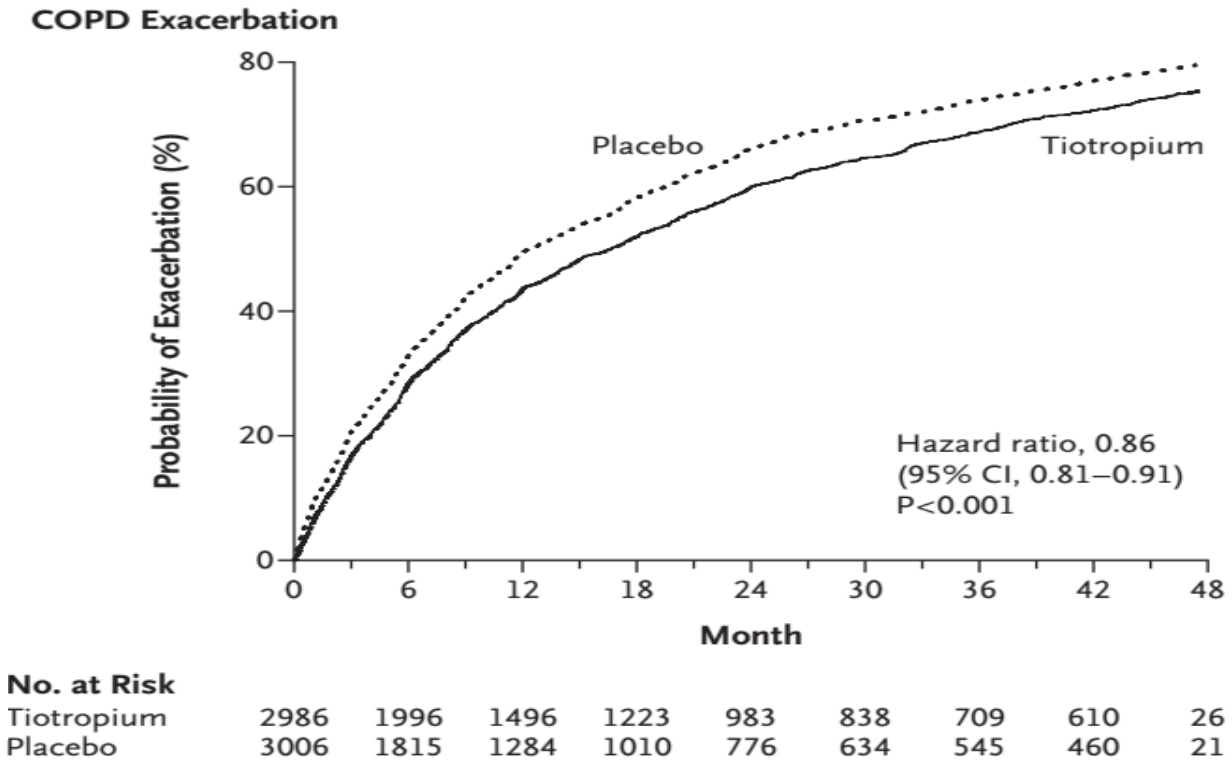
- **Inhaled bronchodiltor**
  - ✓ Work of breathing ↓
  - ✓ Exercise tolerance ↑

Sutherland ER, et al. N Engl J Med 2004;350:2689-97.

Bronchodilator: Lung function and acute exacerbation

- COPD patients, FEV1 ≤70% (GOLD II,46%; III, 46%; IV, 8%)
- **Tiotropium** (n=1887) vs. placebo (n=1648)
- Duration 4 years (UPLIFT study)

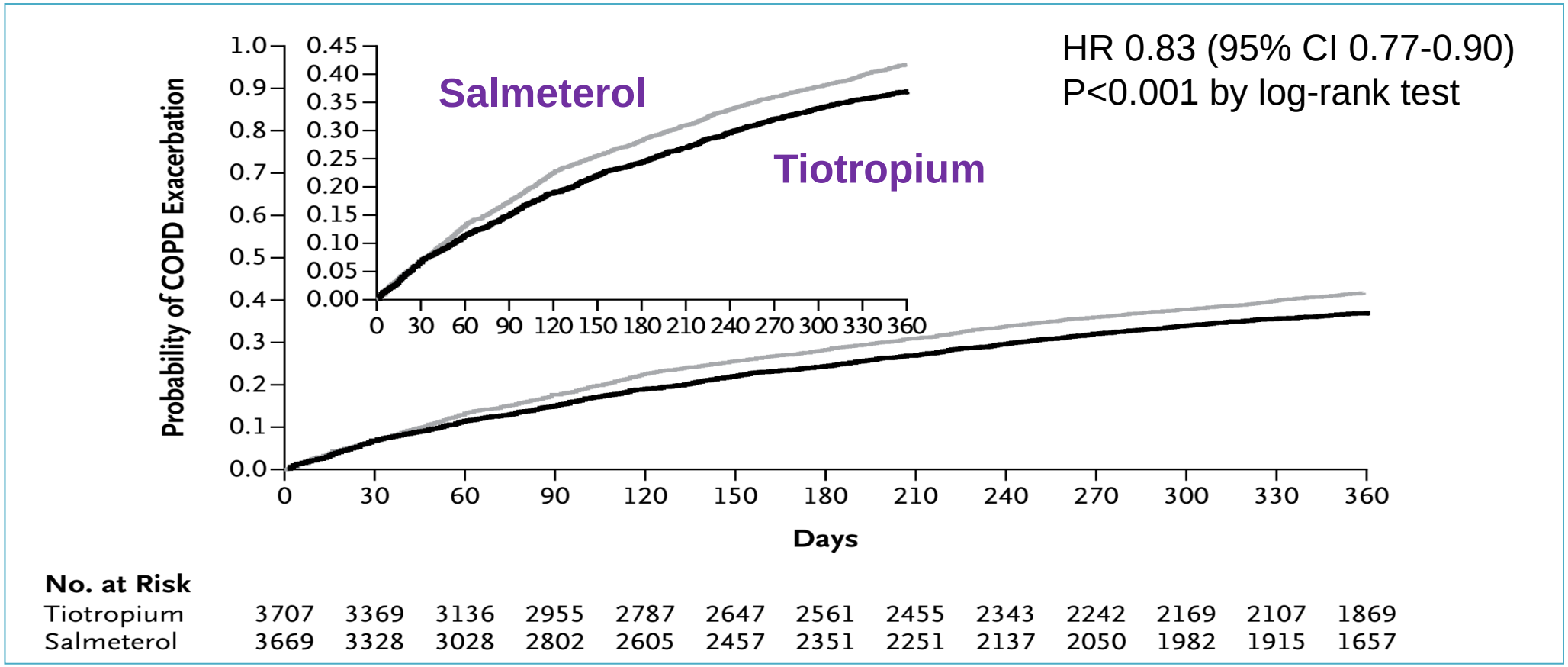




Tashkin DP, et al. Eur Respir J 2008;31(4):742-750.

Acute exacerbation: LAMA vs LABA

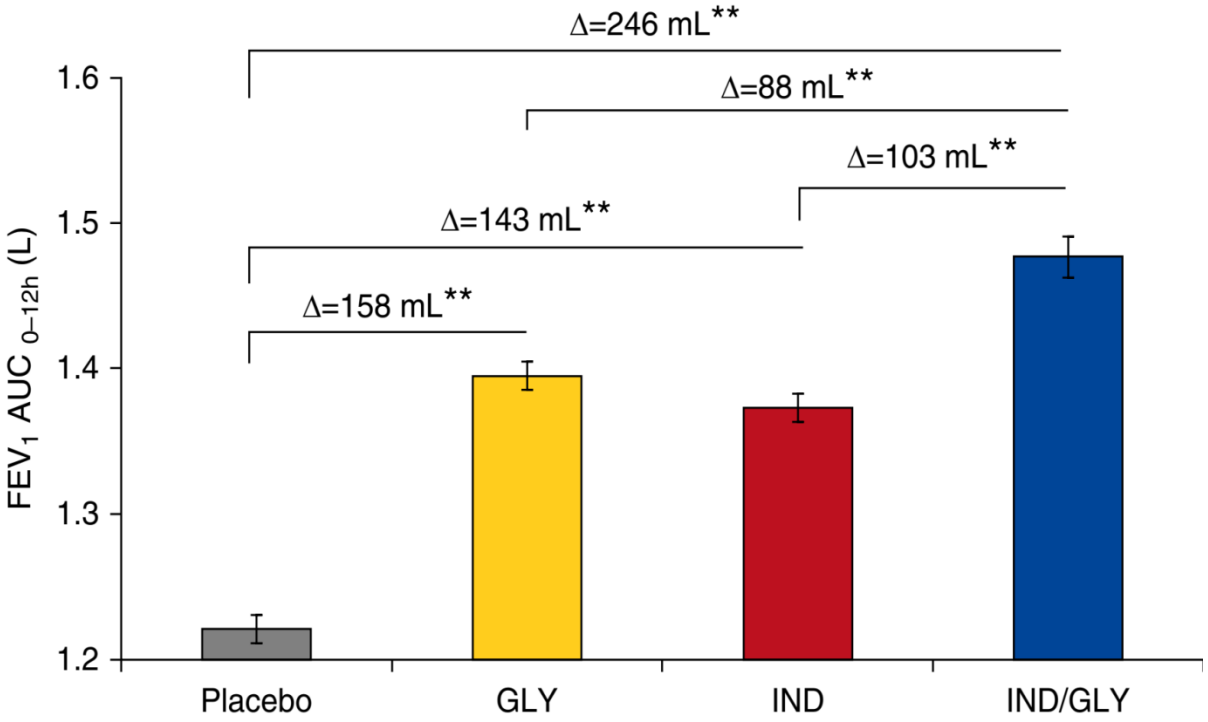
- 52-week, RCT, moderate-to-very severe COPD patients with ≥1 exacerbation (POET-COPD study)

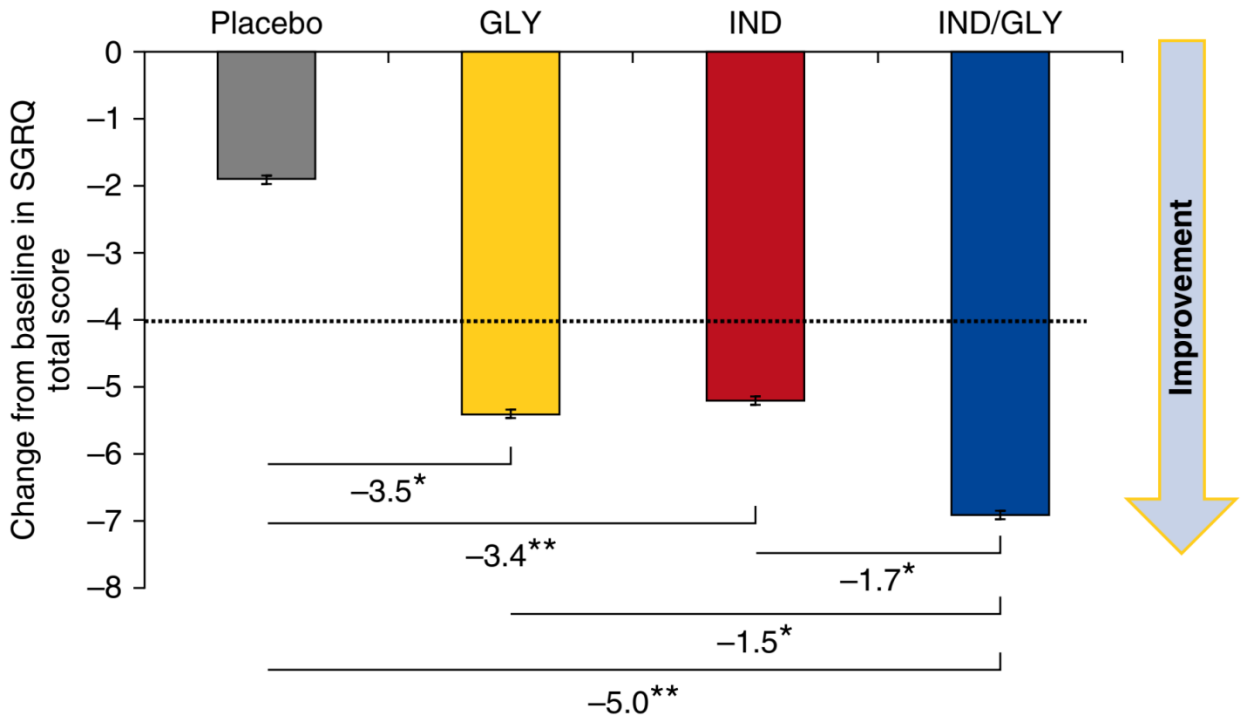


Vogelmeier C, et al. N Engl J Med 2011;364:1093-103.

Lung function and symptom: LAMA/LABA vs mono

- 12-week RCT, moderate-to-severe COPD (FLIGHT1/2)
- Indacaterol/glycopyrrolate vs. indacaterol vs. glycopyrrolate vs. placebo

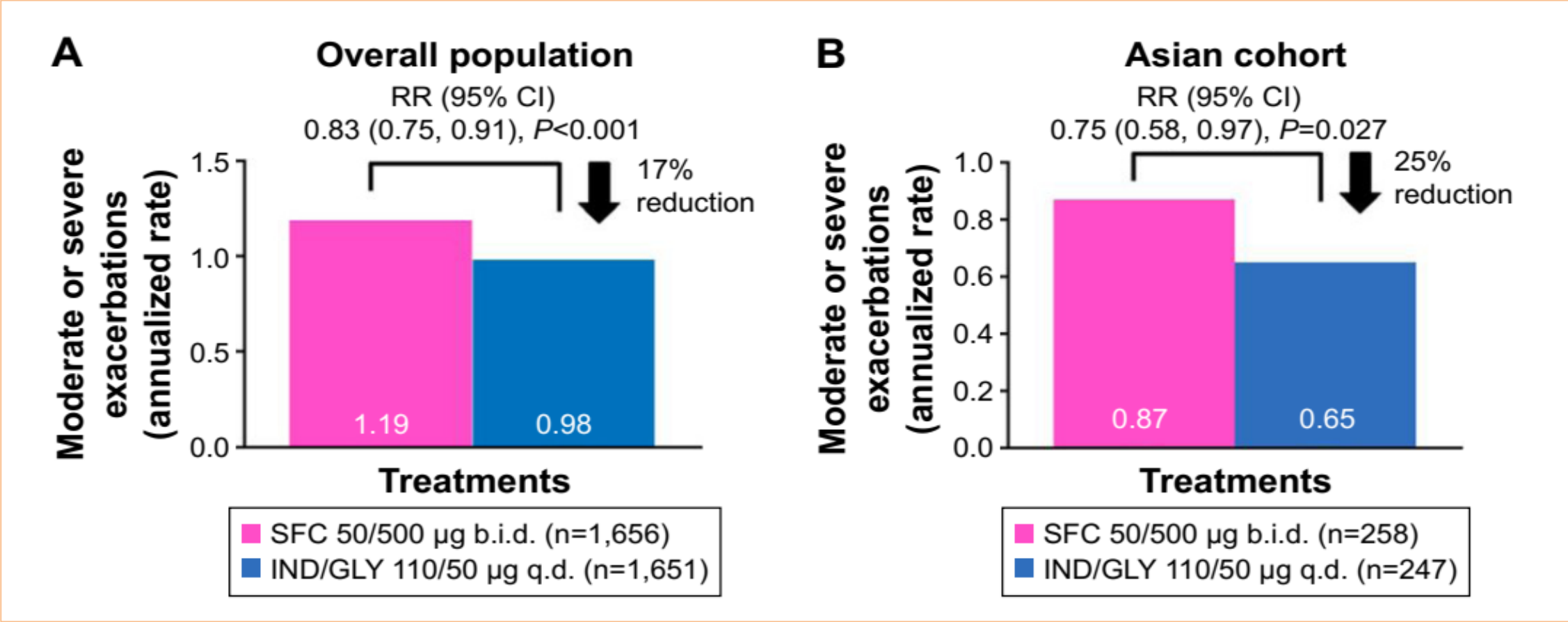




Mahler DA, et al. Am J Repir Crit Care 2015;192(9):1068-79.

Acute exacerbation: LAMA/LABA vs ICS/LABA

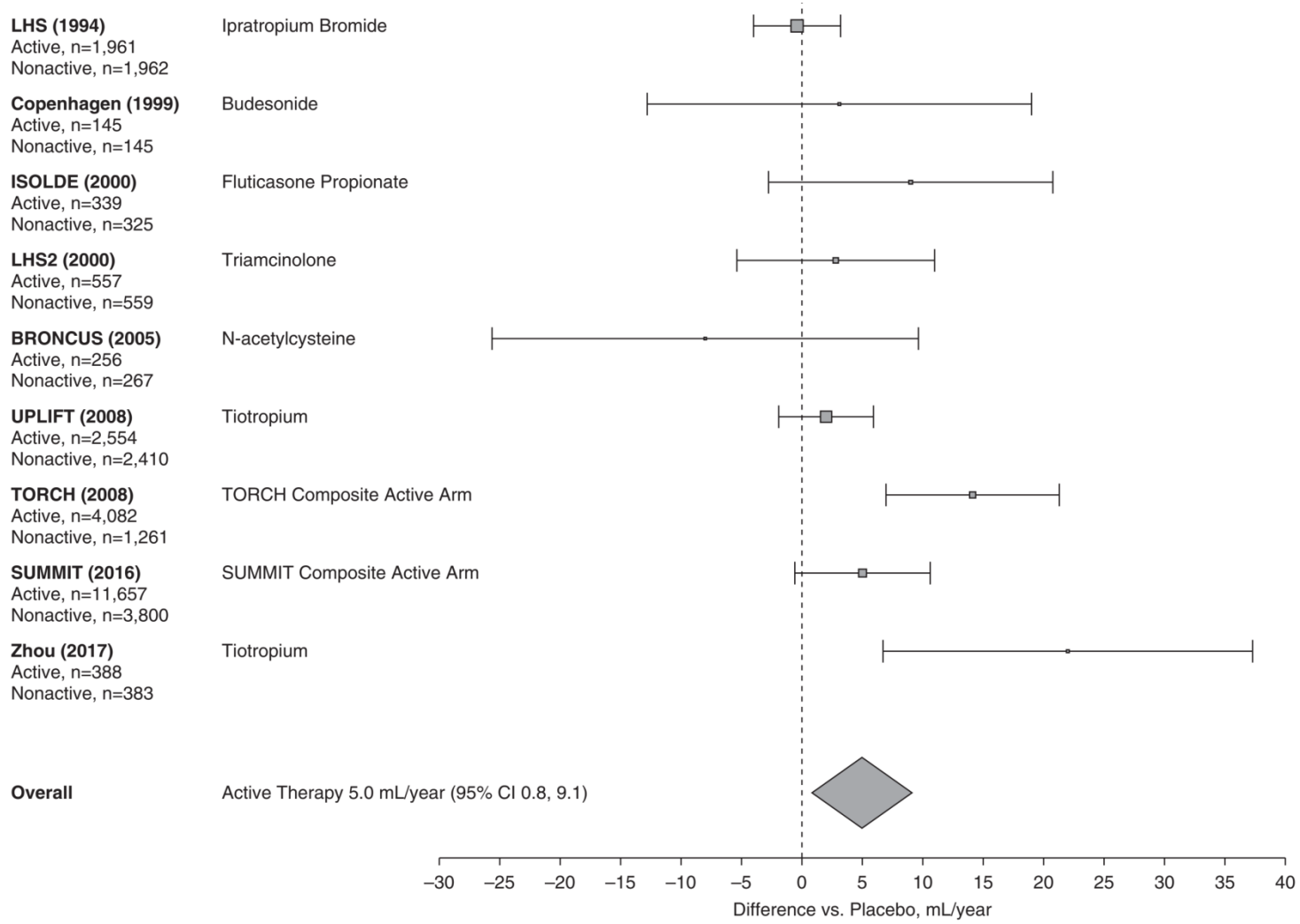
- 52-week, RCT, COPD patients with FEV1 25~60%, ≥2 mMRC, ≥1 exacerbation, FLAME
- LAMA/LABA (glycopyrronium/indacaterol) qd vs ICS/LABA (fluticasone/salmeterol) bid



Wedzicha JA, et al. N Engl J Med 2016;34(23):2222-34.
Wedzicha JA, et al. Int J Chron Obstruct Pulmon Dis 2017;12:339-349.

Lung function decline

- 33,051 COPD patients with active treatment vs. placebo, systematic review

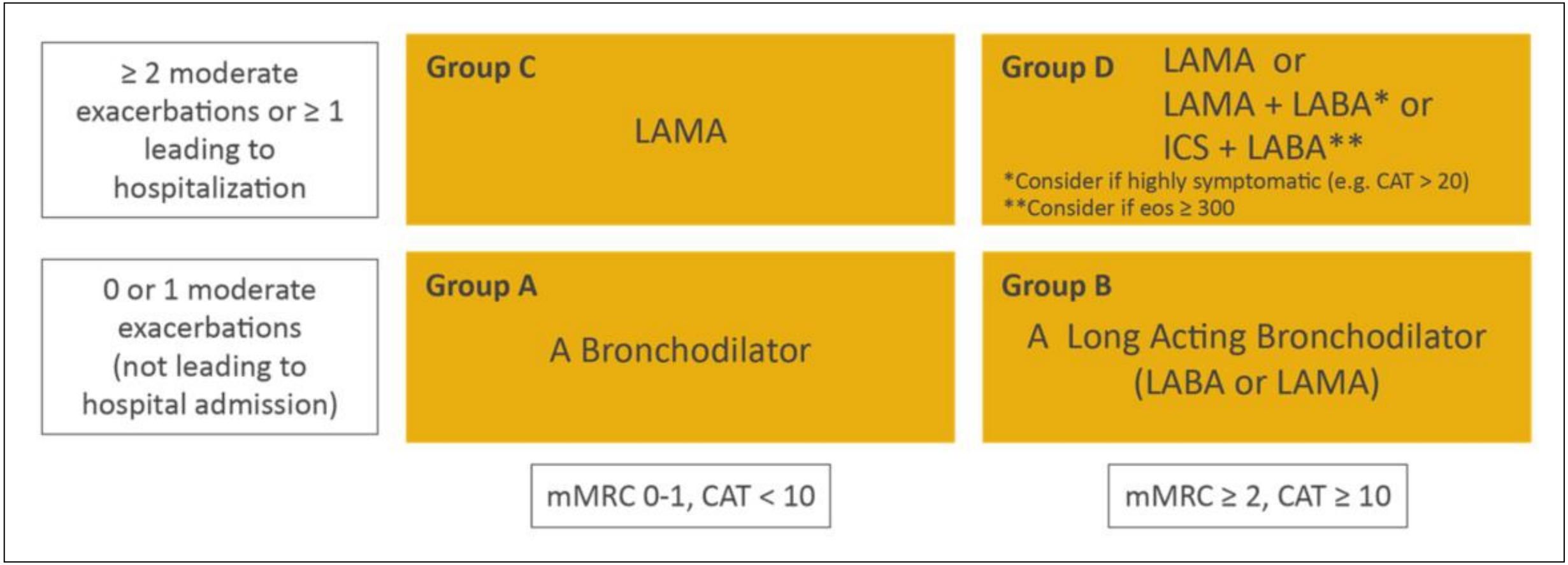


✓ Effect of all active therapies on the rate of decline in FEV1

→ **5.0 mL/year**

Celli BR, et al. Am J Respir Crit Care Med 2021;203:689-98.

Initial phamacotherapy of COPD



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Indication of ICS treatment

- Factors to consider when initiating ICS treatment in combination with one or two long-acting bronchodilators

Strong support	Consider use	Avoid use
History of hospitalization(s) for exacerbations of COPD[#] ≥2 moderate exacerbations of COPD per year[#] Blood eosinophils ≥300 cells/μL History of, or concomitant, asthma	1 moderate exacerbation of COPD per year[#] Blood eosinophils ≥100 to <300 cells/μL	Repeated pneumonia events Blood eosinophils <100 cells/μL History of mycobacterial infection

[#]despite appropriate long-acting bronchodilator maintenance therapy
*note that blood eosinophil should be seen as a continuum, quoted values respresent approximate cut-points; eosinophil counts are likely to fluctuate

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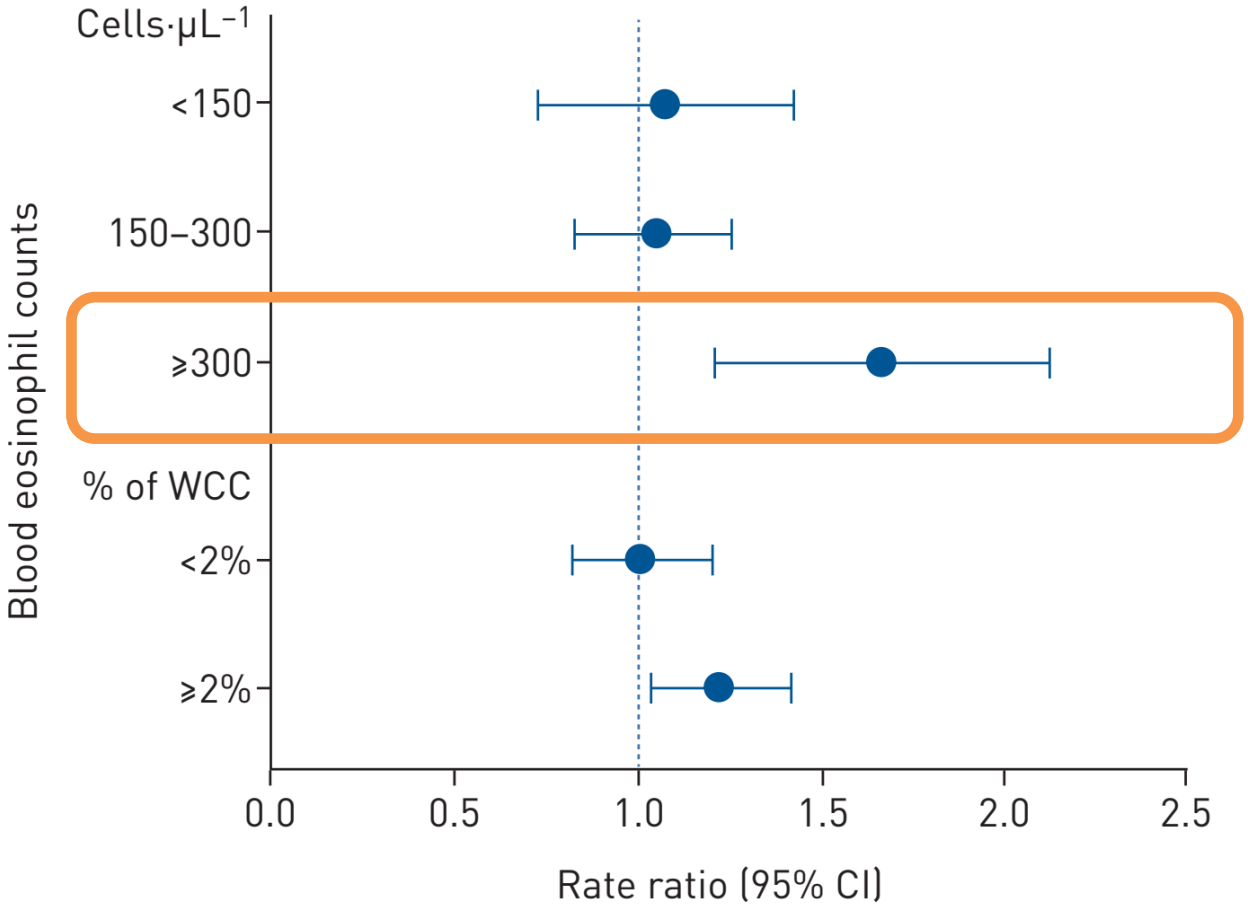
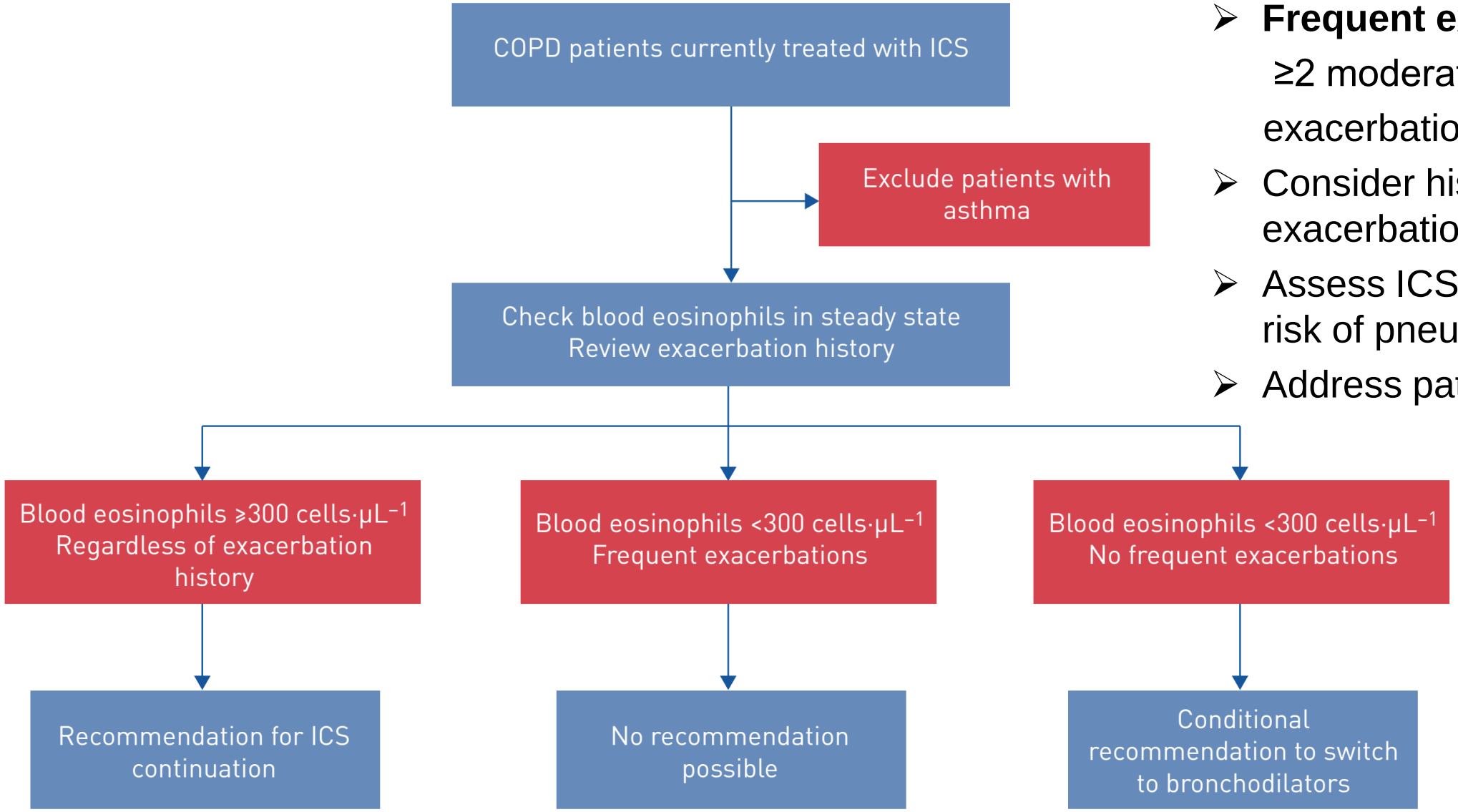
Exacerbation risk after ICS withdrawal

- Frequency of moderate and severe exacerbations after ICS withdrawal stratified by baseline blood eosinophil



Chalmers JD, et al. Eur Respir J 2020;55(6):2000351.

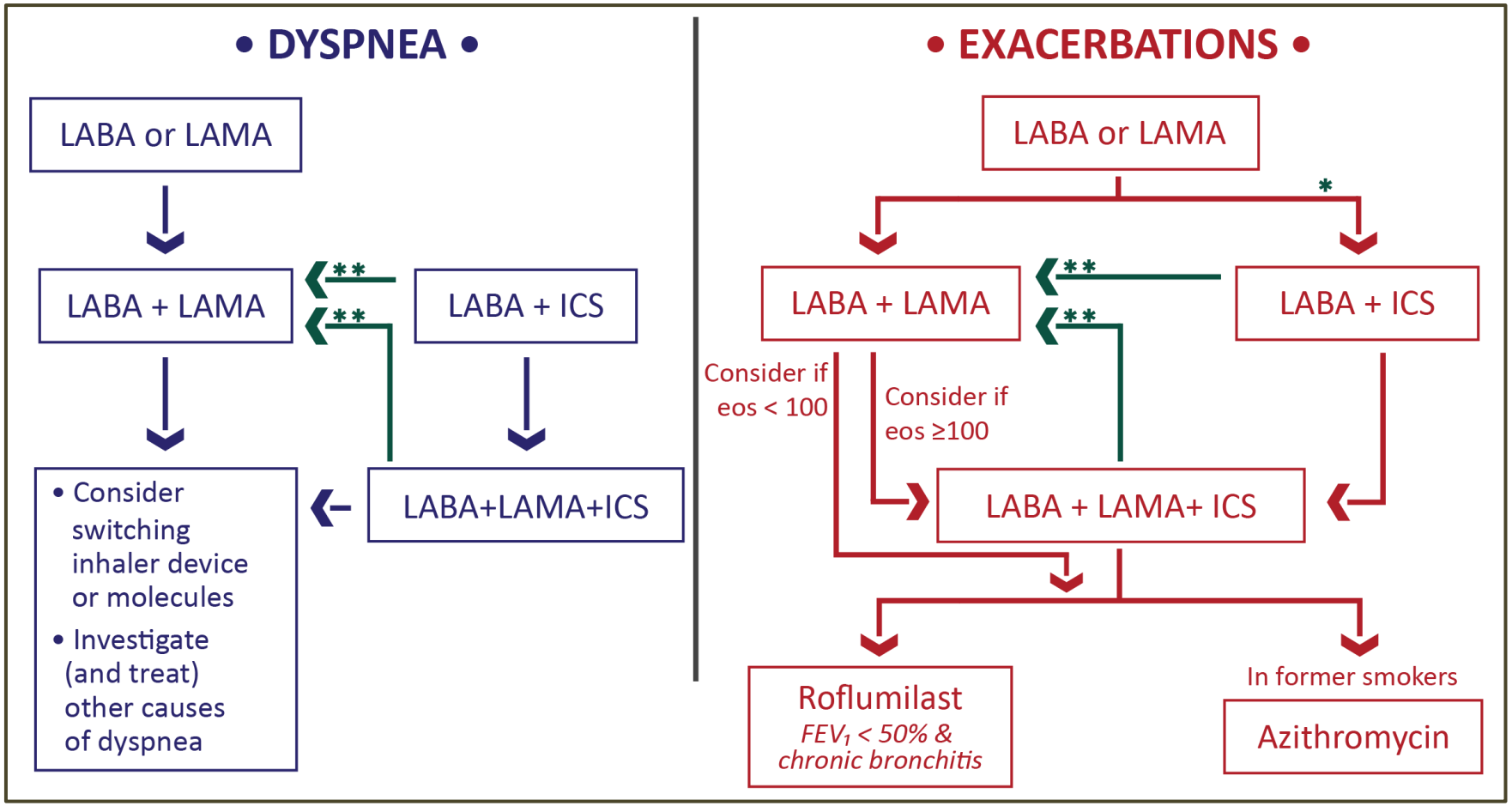
ICS withdrawal algorithm (ERS guideline)



- **Frequent exacerbation**: ≥2 moderate or 1 severe exacerbation per year
- Consider history of exacerbations prior to ICS
- Assess ICS side-effect and risk of pneumonia
- Address patient preferences

Chalmers JD, et al. Eur Respir J 2020;55(6):2000351.

Follow-up phamacological treatment



* Consider if blood eosinophil count ≥ 300 cells/uL or blood eosinophil count ≥ 100 cells/uL AND ≥ 2 moderate exacerbation/1 hospitalization

** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS

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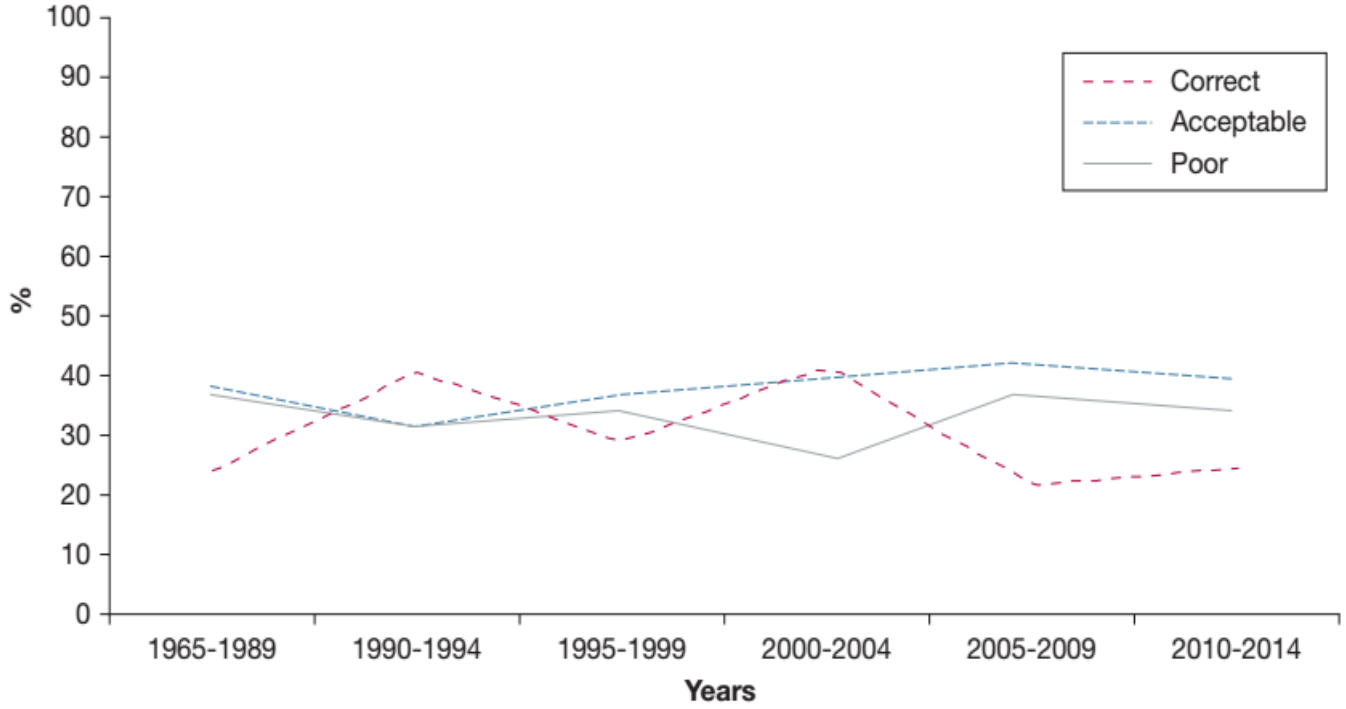
Errors in inhaler use: Systematic review

- 144 articles reporting direct observation of inhaler technique
- By trained personnel, 1975-2014

TABLE 5] Frequencies of Errors in Studies Reporting Data for All Steps

Step	Percentage	95% CI
MDI and BAMDI (n = 56 groups)		
Preparation	22	18-26
Full expiration	42	38-46
Coordination (inspire and actuate)	34	29-39
Slow deep inspiration	41	37-44
Breath-hold	41	38-45
DPI (n = 52 groups)		
Preparation	25	21-30
Full expiration	45	40-51
Lips on mouthpiece	8	6-11
Brisk, accelerated deep inspiration	16	13-20
Breath-hold	35	31-39

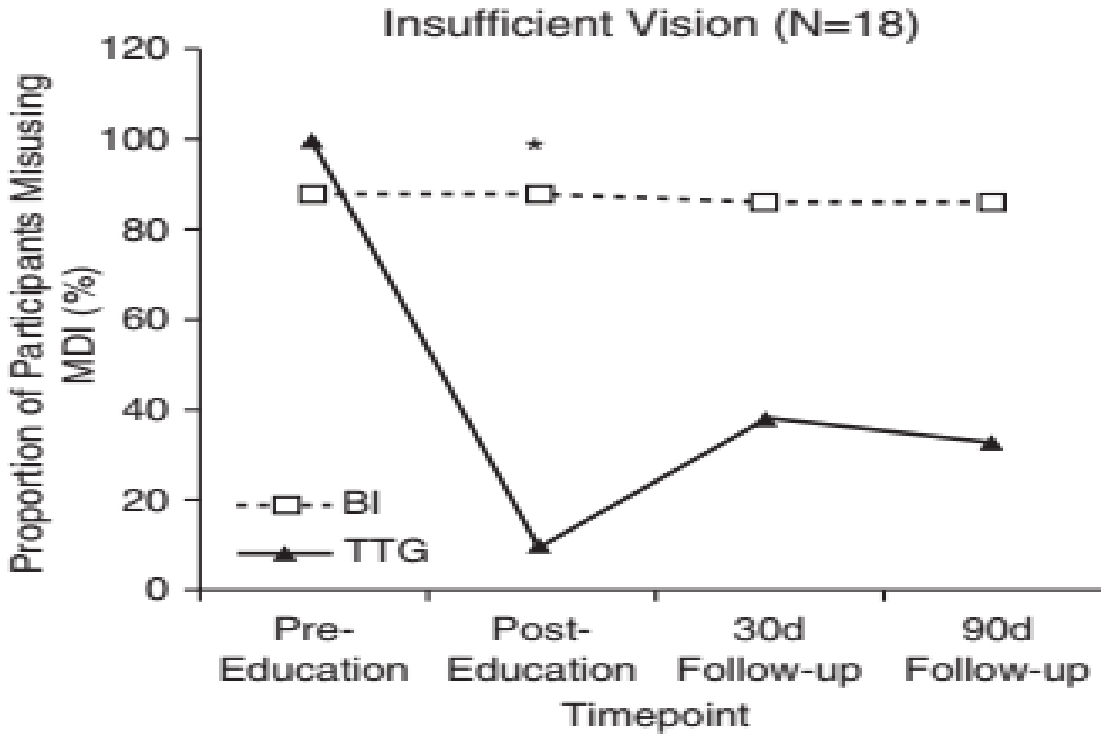


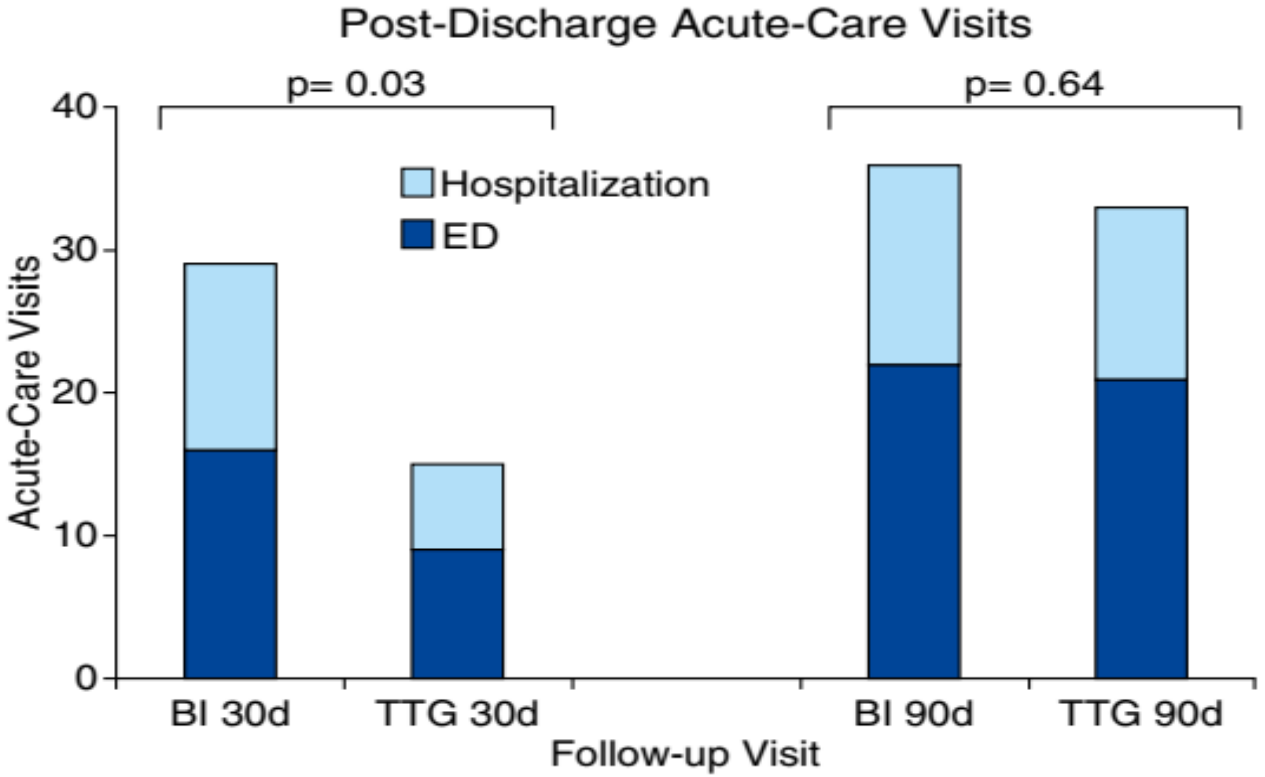
✓ CONCLUSIONS: Incorrect inhaler technique is unacceptably frequent and has not improved over the past 40 years.

Sanchis J, et al. Chest 2016;150(2);394-406.

Interventions to teach inhaler techniques

- 120 patients hospitalized with asthma or COPD
- RCT, brief verbal step-by-step inhaler directions vs. iterative teach-back education (teach-to-goal)





Press VG, et al. Ann Am Thorac Soc 2016;13(6):816-24.

Unintentional discontinuation of medications

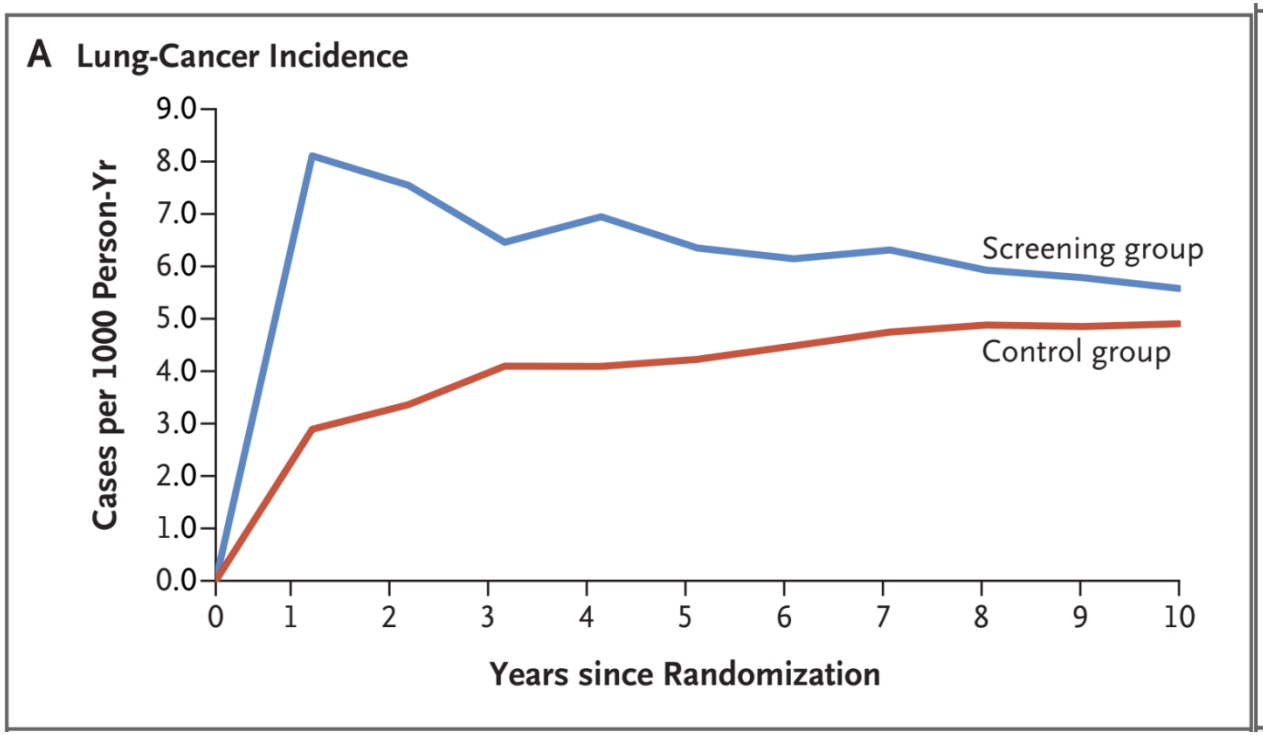
- Risk for unintentional discontinuation of medications prescribed for chronic diseases after hospitalization

Medication discontinuation	No (%) of patients			ICU stay	
	Control	Hospitalized	AOR (95% CI)	No (%)	AOR (95% CI)
Statins	11627 (10.7)	13277 (13.6)	1.33 (1.29-1.37)	1484 (14.6)	1.48 (1.39-1.57)
Antiplatelet/ anticoagulants	2535 (11.8)	5564 (19.4)	1.86 (1.77-1.97)	522 (22.8)	2.31 (2.07-2.57)
Levothyroxine	7114 (11.0)	6831 (12.3)	1.18 (1.14-1.23)	614 (15)	1.51 (1.38-1.66)
Respiratory inhalers	79 (3.0)	231 (4.5)	1.50 (1.15-1.97)	20 (5.4)	1.84 (1.10-3.08)
Gastric acid suppressors	4330 (9.4)	7394 (12.4)	1.50 (1.43-1.56)	670 (15.4)	1.87 (1.71-2.05)

Bell CM, et al. JAMA. 2011;306(8):840-7.

Lung cancer screening

- 13,195 male and 2,594 female, current or former smokers aged 50-74 years, NELSON study
- Low-dose CT screening vs. no screening



Koning HJ et al. N Engl J Med 2020;382(6):503-513.

Annual LDCT for lung cancer screening

- Recommended in patients with COPD due to smoking
  - ✓ According to recommendations for the general population

- Not recommended in patients with COPD not due to smoking
  - ✓ Due to insufficient data to establish benefit over harm

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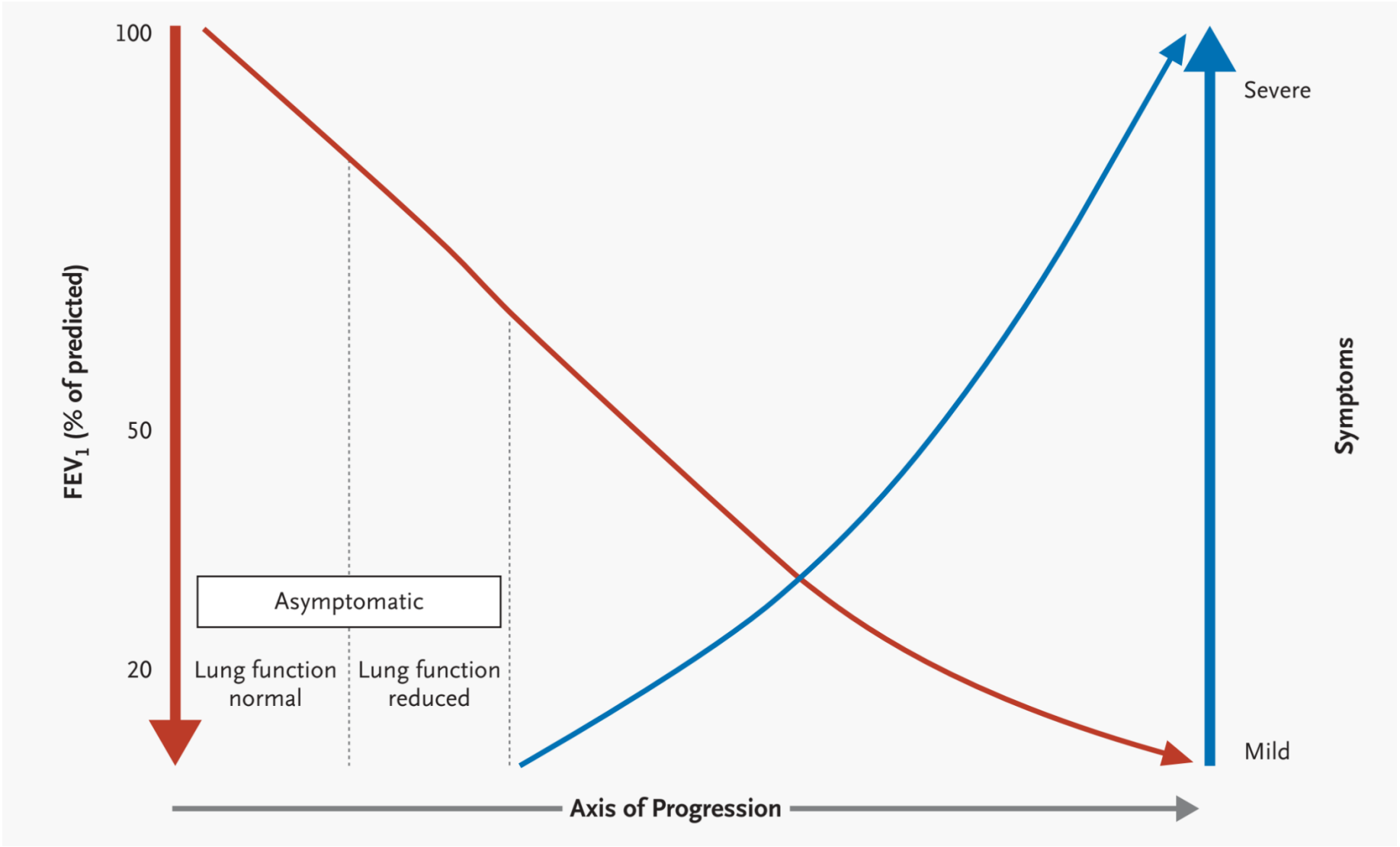
Disease progression of COPD



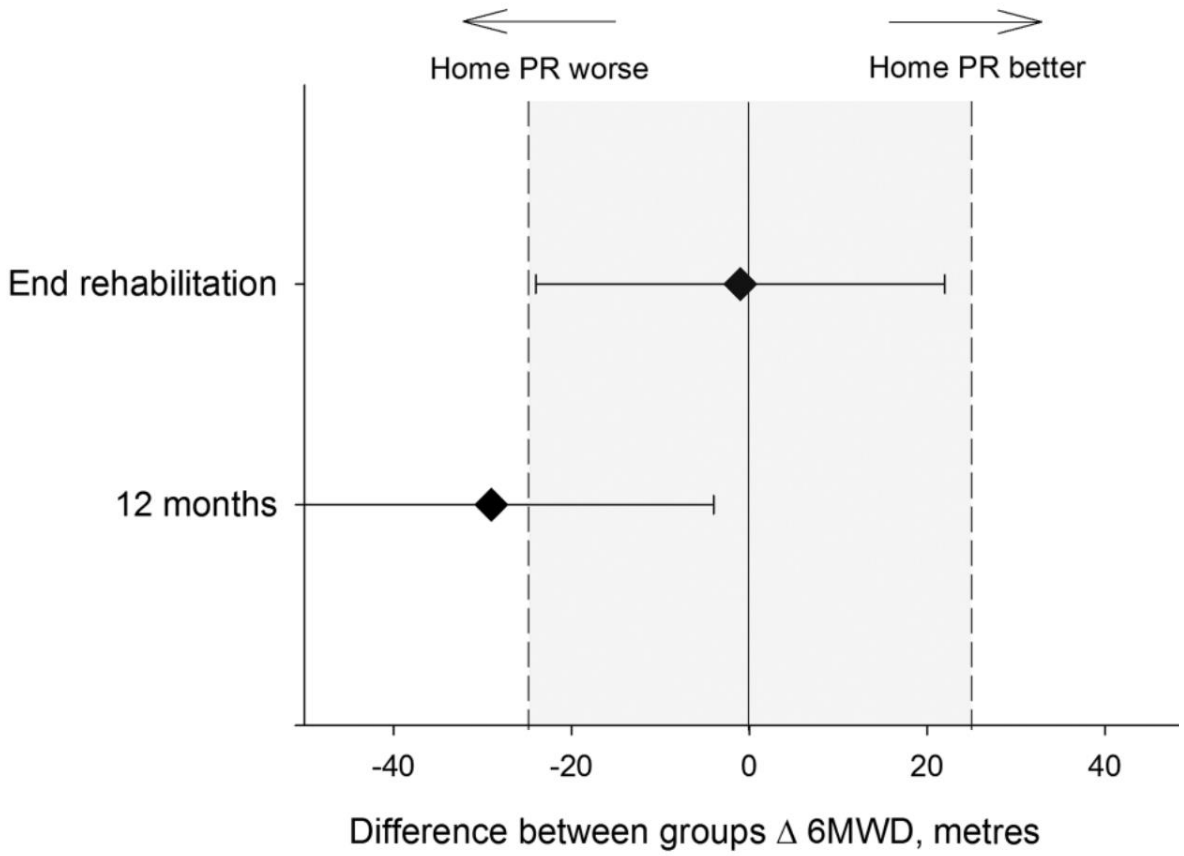
Sutherland ER, et al. N Engl J Med 2004;350:2689-97.

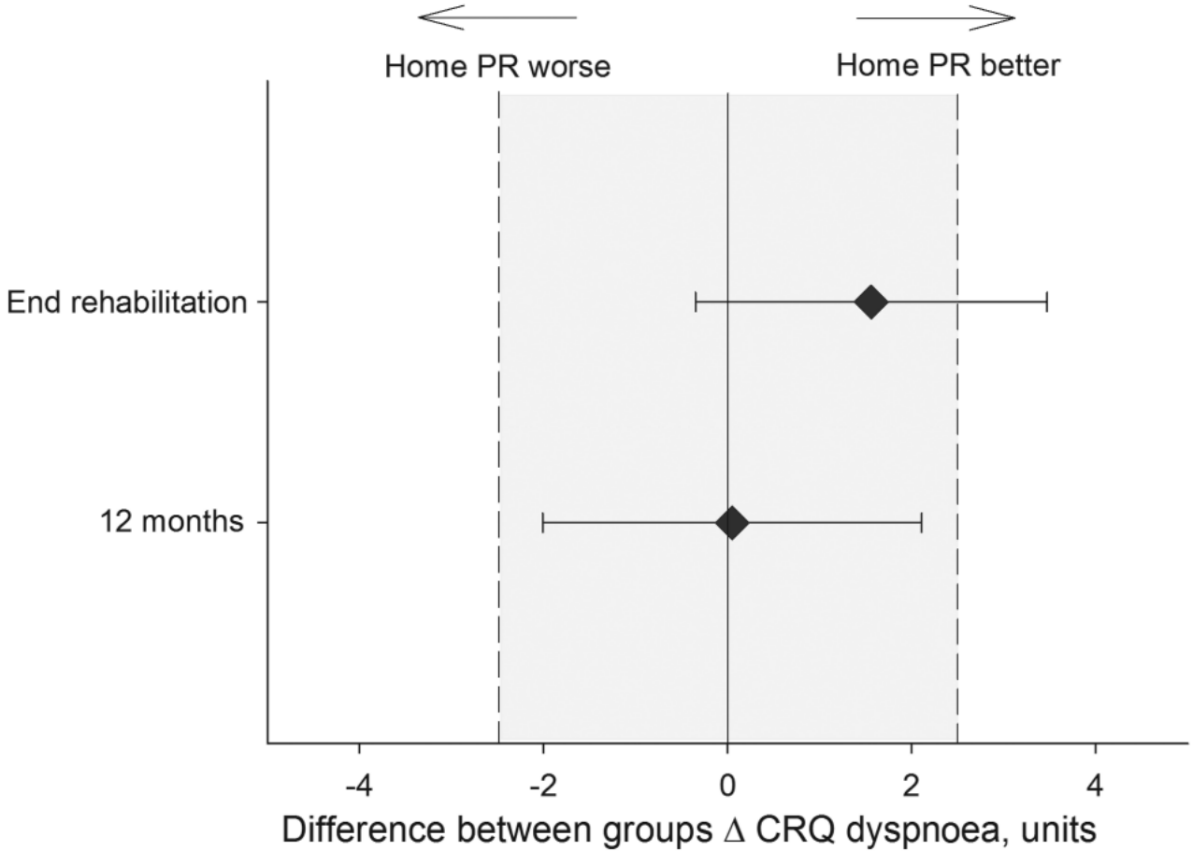
Effect of pulmonary rehabilitation

- 운동능력 향상
- 호흡곤란 감소
- 건강과 관련된 삶의 질 향상
- 병원 입원 횟수와 입원기간 감소
- COPD와 관련된 불안과 우울증 감소
- 상지근력과 지구력 훈련으로 상지기능 호전
- 재활치료의 효과가 치료 후에 지속
- 생존율 증가
- 일반적인 운동훈련과 병행하였을 때 호흡근육 훈련이 효과적
- 급성악화로 입원 후 회복율 향상
- 지속성 β2-작용제 효과증대

Home-based rehabilitation

- Stable COPD, 12 wks home-based rehabilitation with minimal resource (aerobic/resistance training and self-management education) vs. center-based

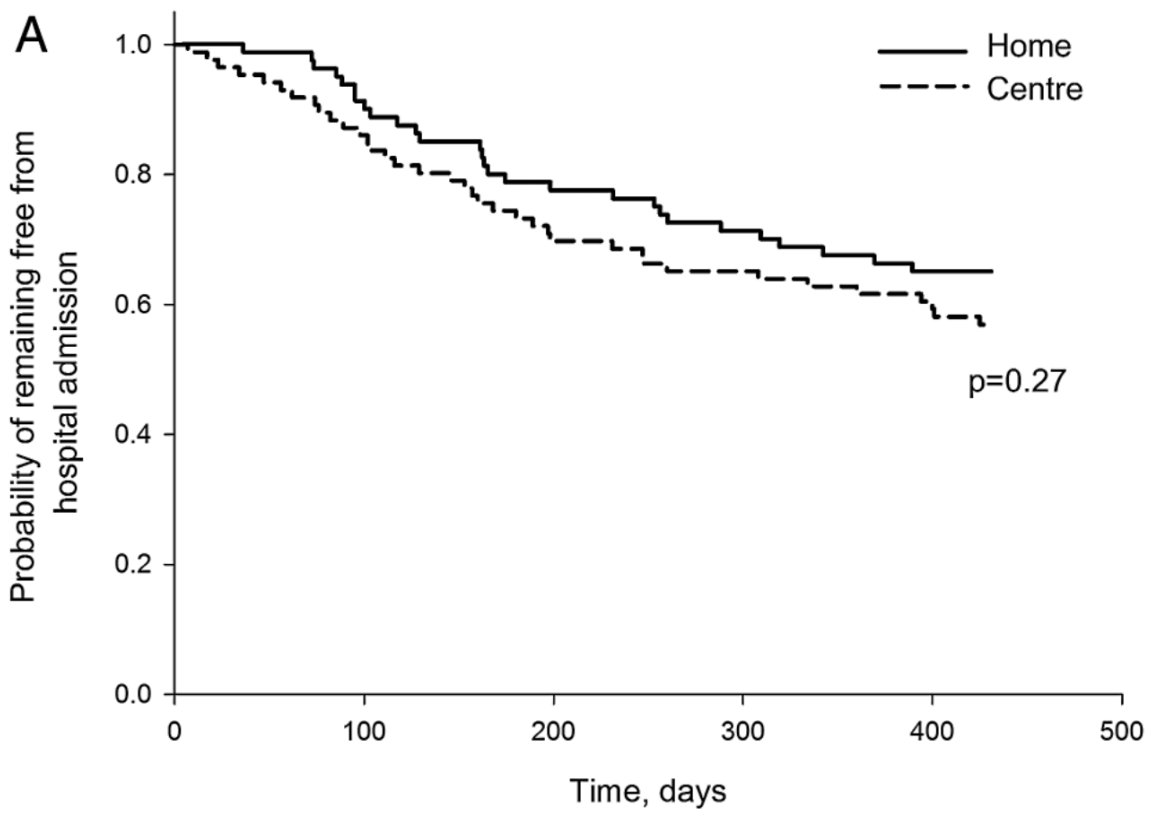


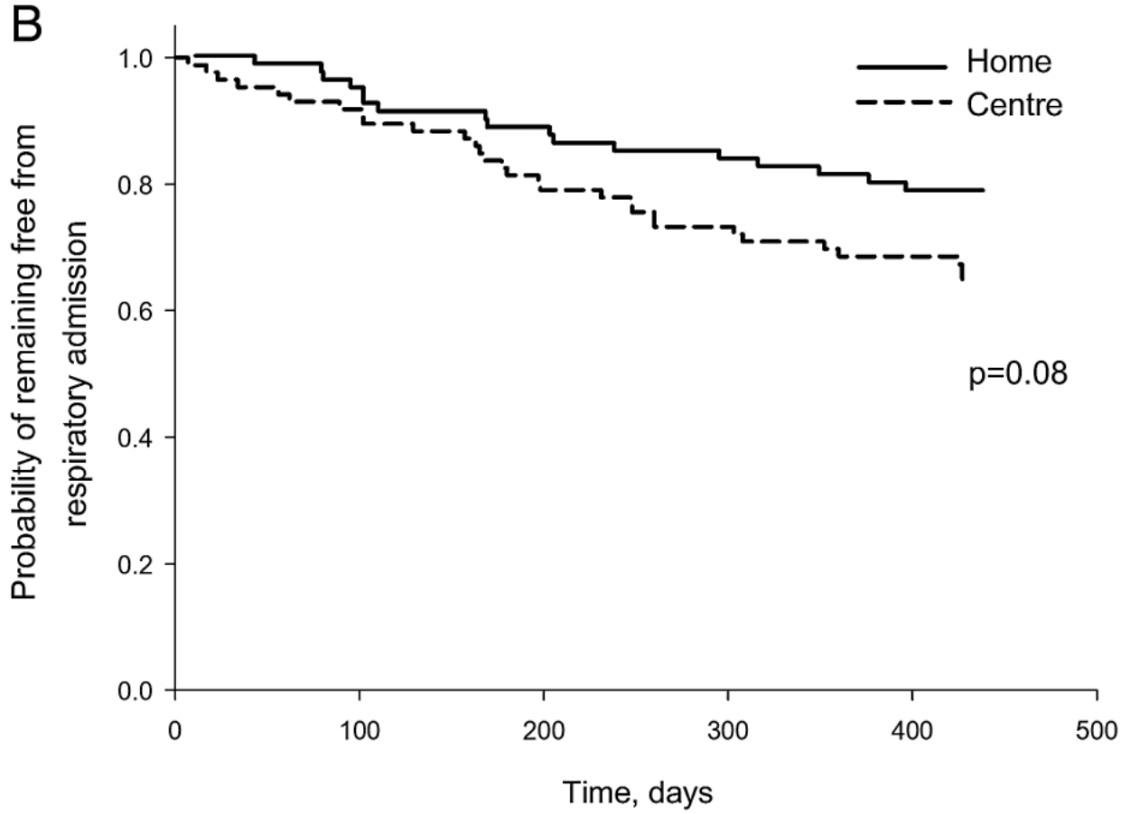


Holland AE, et al. Thorax 2017;72:57-65.

Home-based rehabilitation

- Stable COPD, 12 wks home-based rehabilitation with minimal resource (aerobic/resistance training and self-management education) vs. center-based





Holland AE, et al. Thorax 2017;72:57-65.

Nutritional status and mortality

- Low BMI and fat-free mass: worse outcome in COPD

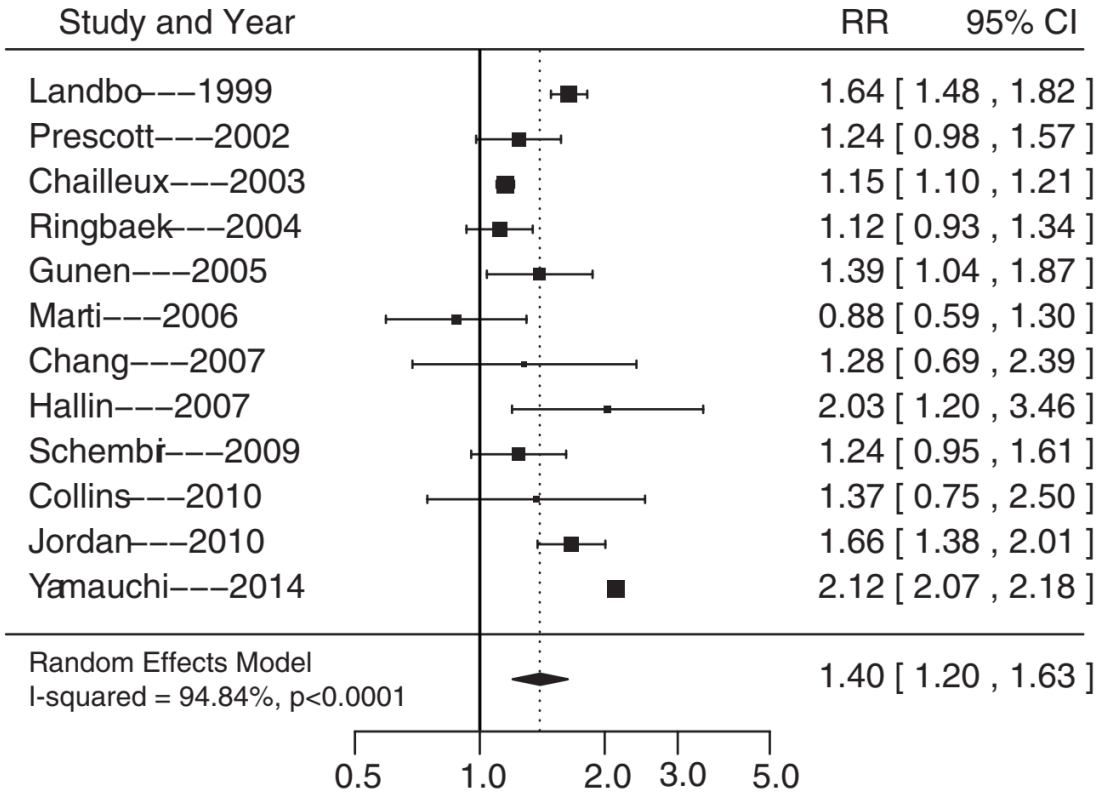


Figure 2. Summary of relative risks of all-cause mortality in underweight COPD patients. COPD = chronic obstructive pulmonary disease.

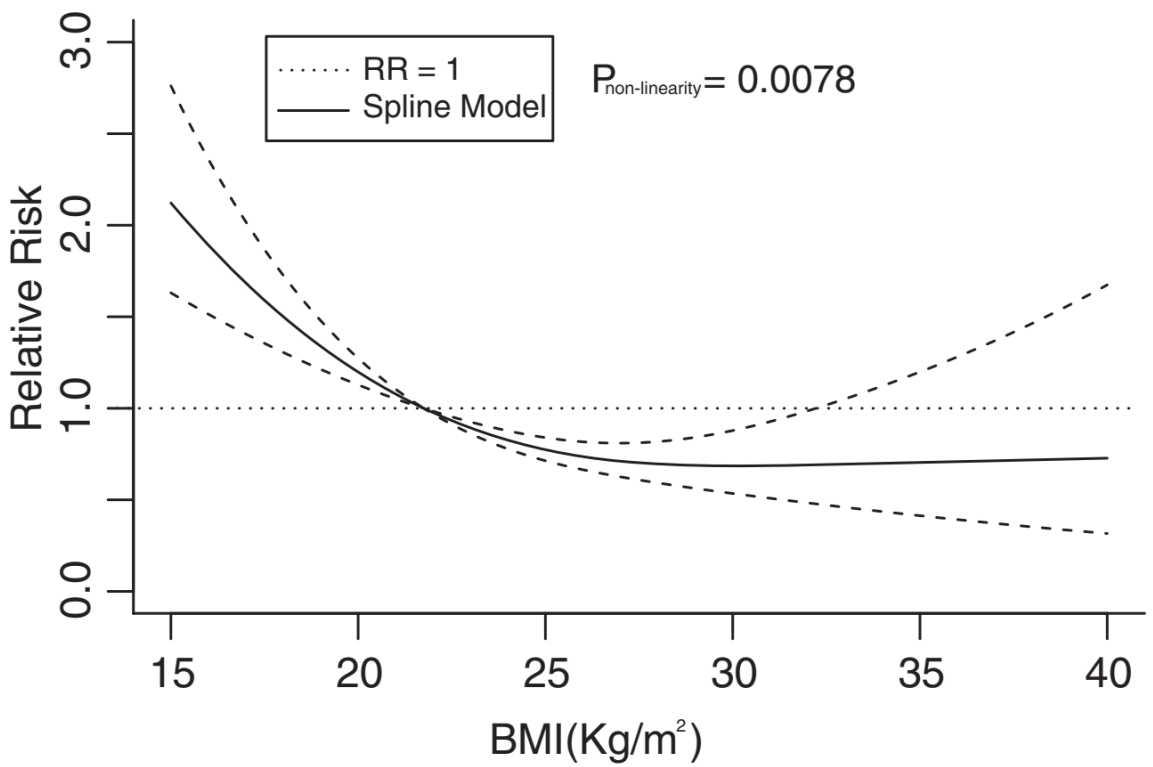
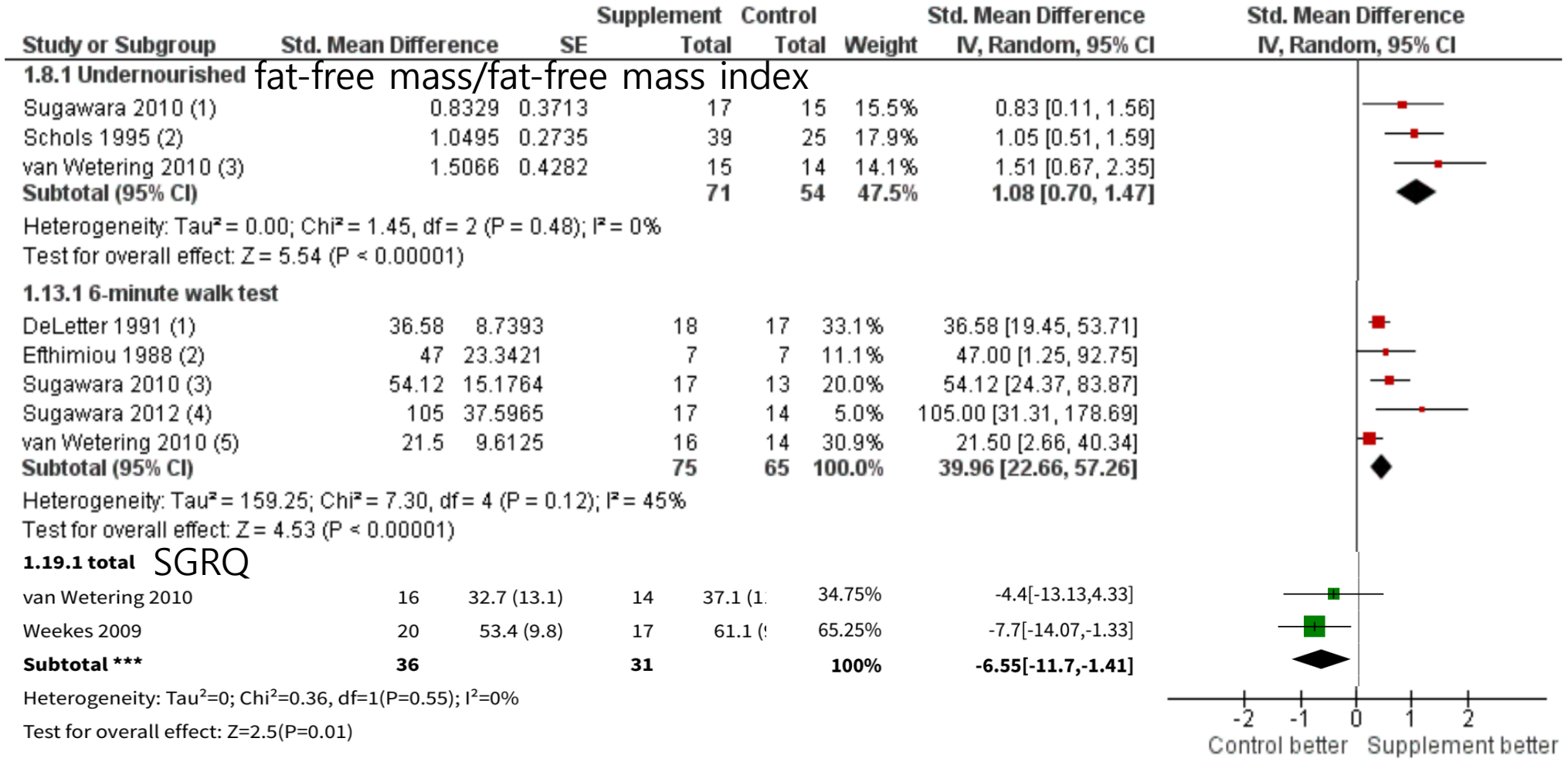


Figure 5. Dose–response relationship between BMI score and risk of all-cause mortality. BMI = body mass index.

Guo Y, et al. Medicine (Baltimore) 2016;95(28):e4225.

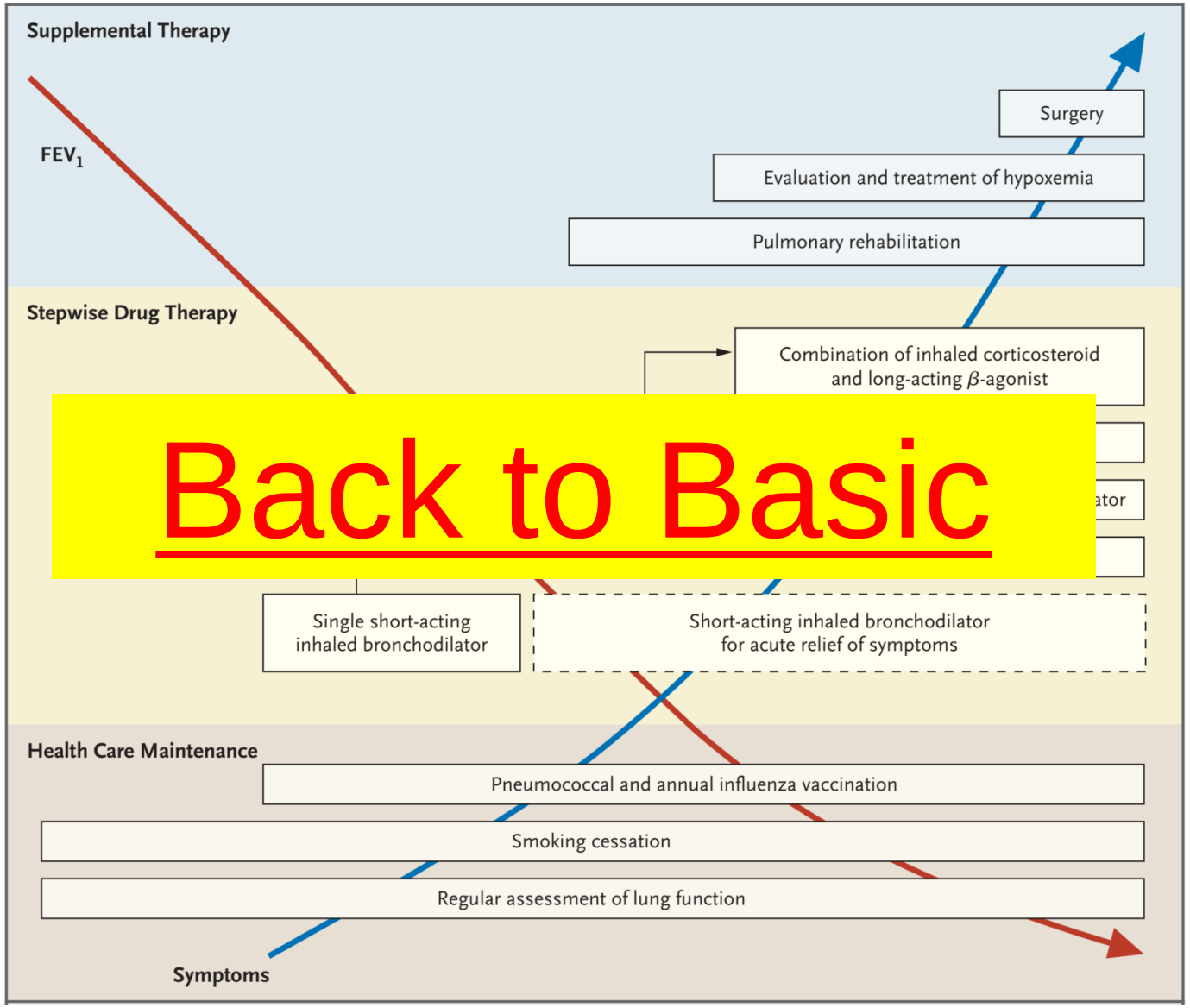
Nutritional supplementation

- Nutritional supplementation vs. placebo or usual diet



Ferreira IM, et al. Cochrane Database Syst Rev 2012;12:CD000998.

Algorithm for treatment of COPD



Sutherland ER, et al. N Engl J Med 2004;350:2689-97.

Thank You for Your Attention