Is it essential to remove the FEV_1 severity in revised combined COPD assessment?

YES!

동아대학교 호흡기 내과
엄수정

Contents

1. Background of Combined Assessment
2. Predictive role of GOLD classifications
3. 2017 GOLD- Revised Assessment tool
   1) Treatment goal and FEV_1
   2) Benefit of Revised Assessment tool
4. Summary

Contents

1. **Background of Combined Assessment**
2. Predictive role of GOLD classifications
3. 2017 GOLD- Revised Assessment tool
   1) Treatment goal and FEV_1
   2) Benefit of Revised Assessment tool
4. Summary

GOLD 2006

I: Mild	II: Moderate	III: Severe	IV: Very Severe
$FEV_1 \geq 80\%$ pred	**$FEV_1 < 80\% \geq 50\%$**	**$FEV_1 < 50\% \geq 30\%$**	**$FEV_1 < 30\%$ pred** ***or*** **$FEV_1 < 50\%$ pred plus chronic respiratory failure**

Staging by FEV1

GOLD 2006

I: Mild	II: Moderate	III: Severe	IV: Very Severe
FEV_1 ≥ 80% pred	**FEV_1 < 80% ≥ 50%**	**FEV_1 < 50% ≥ 30%**	**FEV_1 < 30% pred** ***or*** **FEV_1 < 50% pred plus chronic respiratory failure**

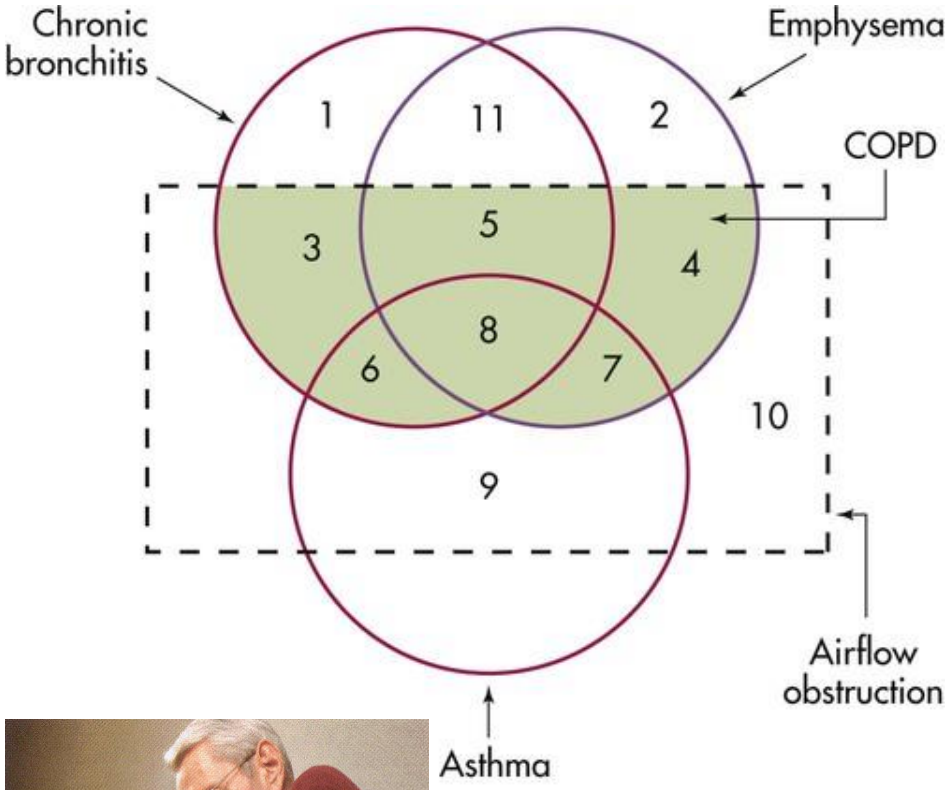
Active reduction of risk factor(s); influenza vaccination →

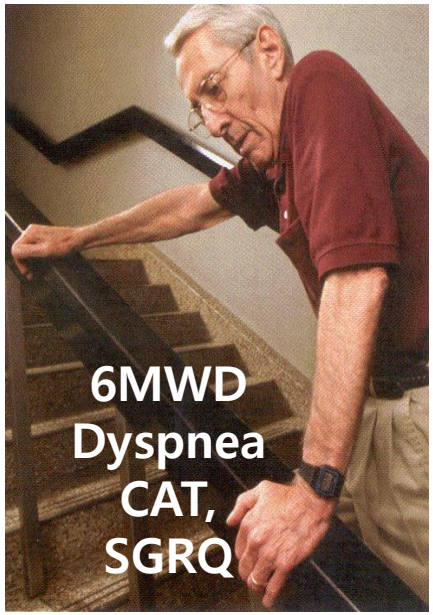
Add short-acting bronchodilator (when needed) →

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

Add inhaled glucocorticosteroids if repeated exacerbations

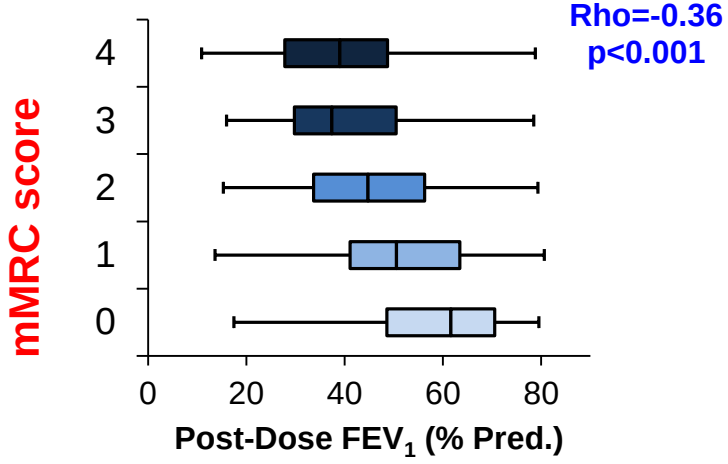
Add long term oxygen if chronic respiratory failure. ***Consider*** surgical treatments

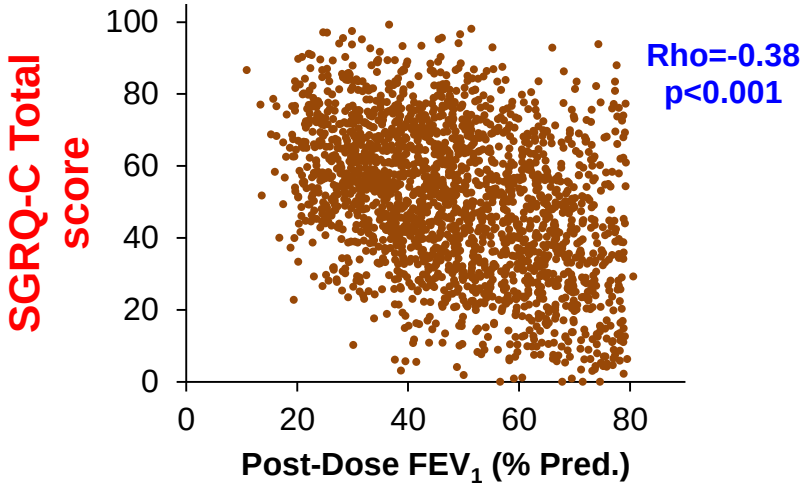

Chronic bronchitis
Emphysema
COPD
Airflow obstruction
Asthma
1
11
2
3
5
4
8
6
7
10
9

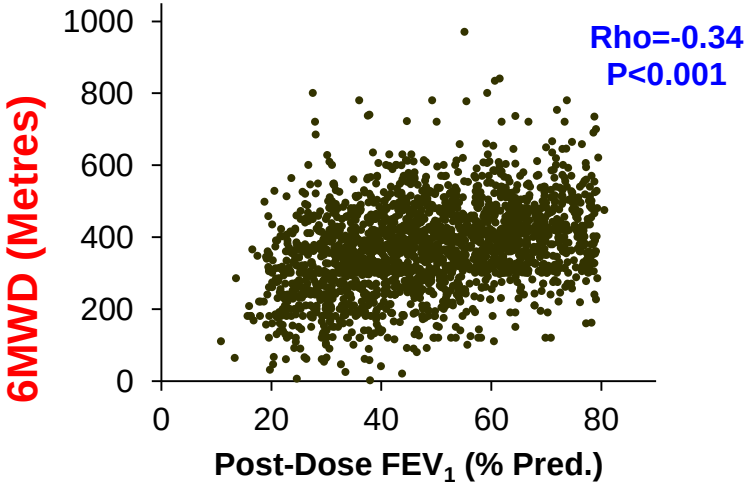

6MWD
Dyspnea
CAT,
SGRQ

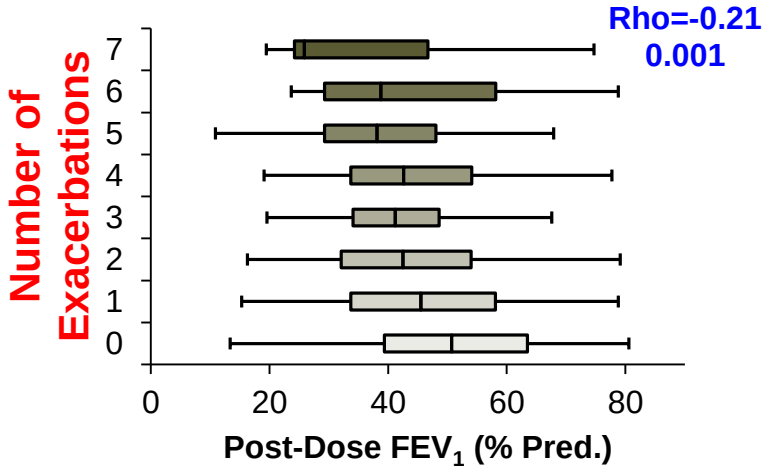
Disease Outcome Parameters & FEV_1

ECLIPSE



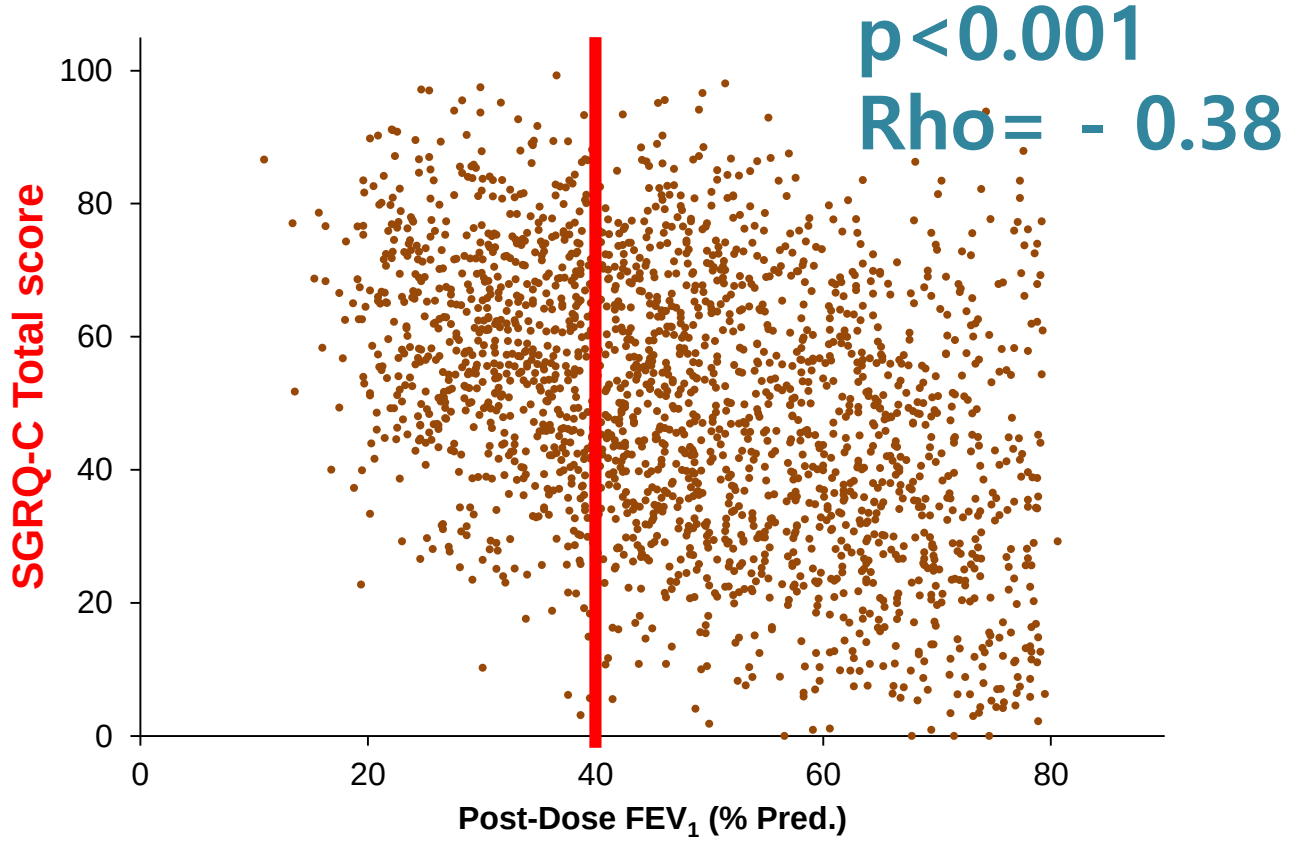






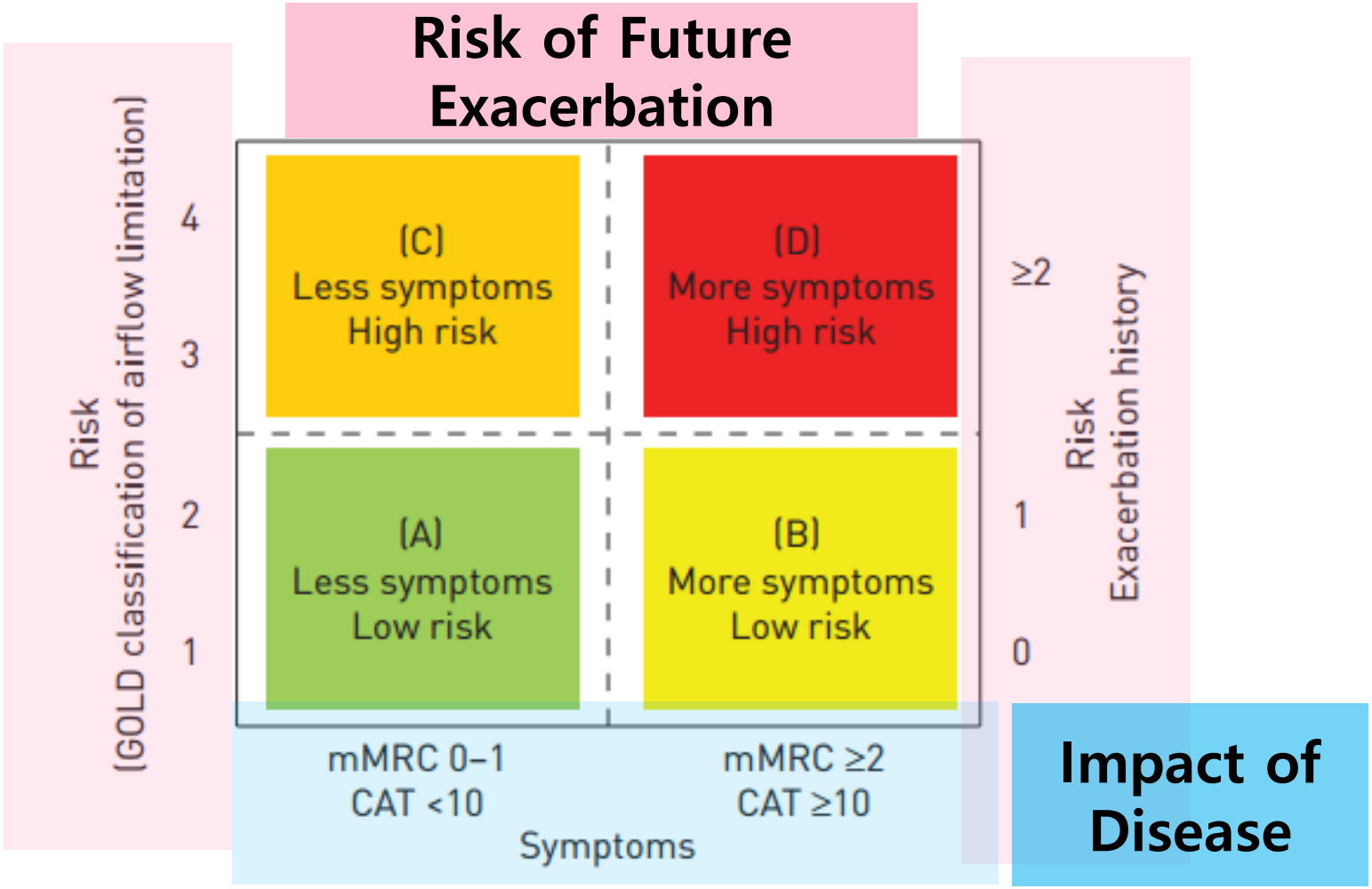
Agusti A, et al. Respir Res 2010; 11: 122.

Individual state and FEV1



Agusti A, et al. Respir Res 2010; 11: 122.

GOLD 2011


Risk of Future Exacerbation
Risk (GOLD classification of airflow limitation)
4
3
2
1
(C) Less symptoms High risk
(D) More symptoms High risk
(A) Less symptoms Low risk
(B) More symptoms Low risk
≥2
1
0
Risk Exacerbation history
mMRC 0–1 CAT <10
mMRC ≥2 CAT ≥10
Symptoms
Impact of Disease

Distribution of the patient groups

GOLD 2007(stage) vs 2011(group)

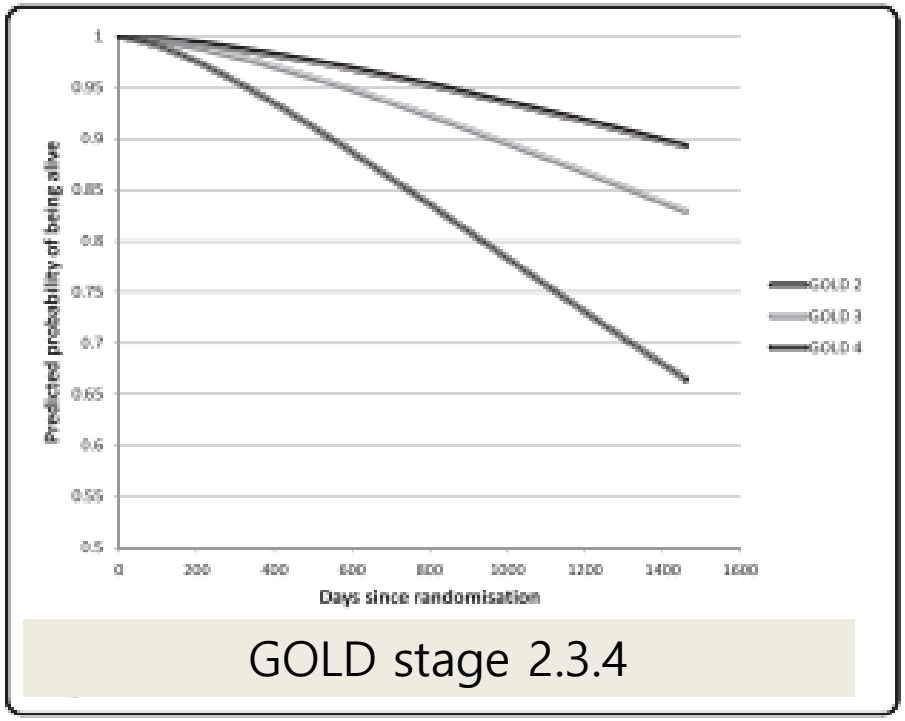
ECLIPSE

Agusti et al. Eur Respir J 2013; 42: 636–646

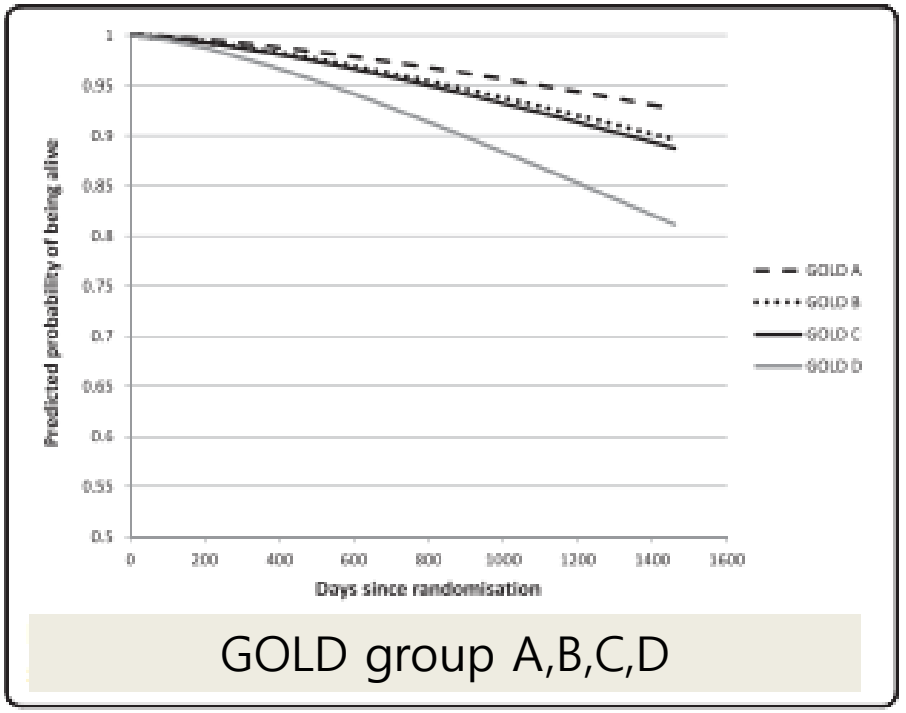
Contents

Survival Prediction

UPLIFT



GOLD stage 2.3.4

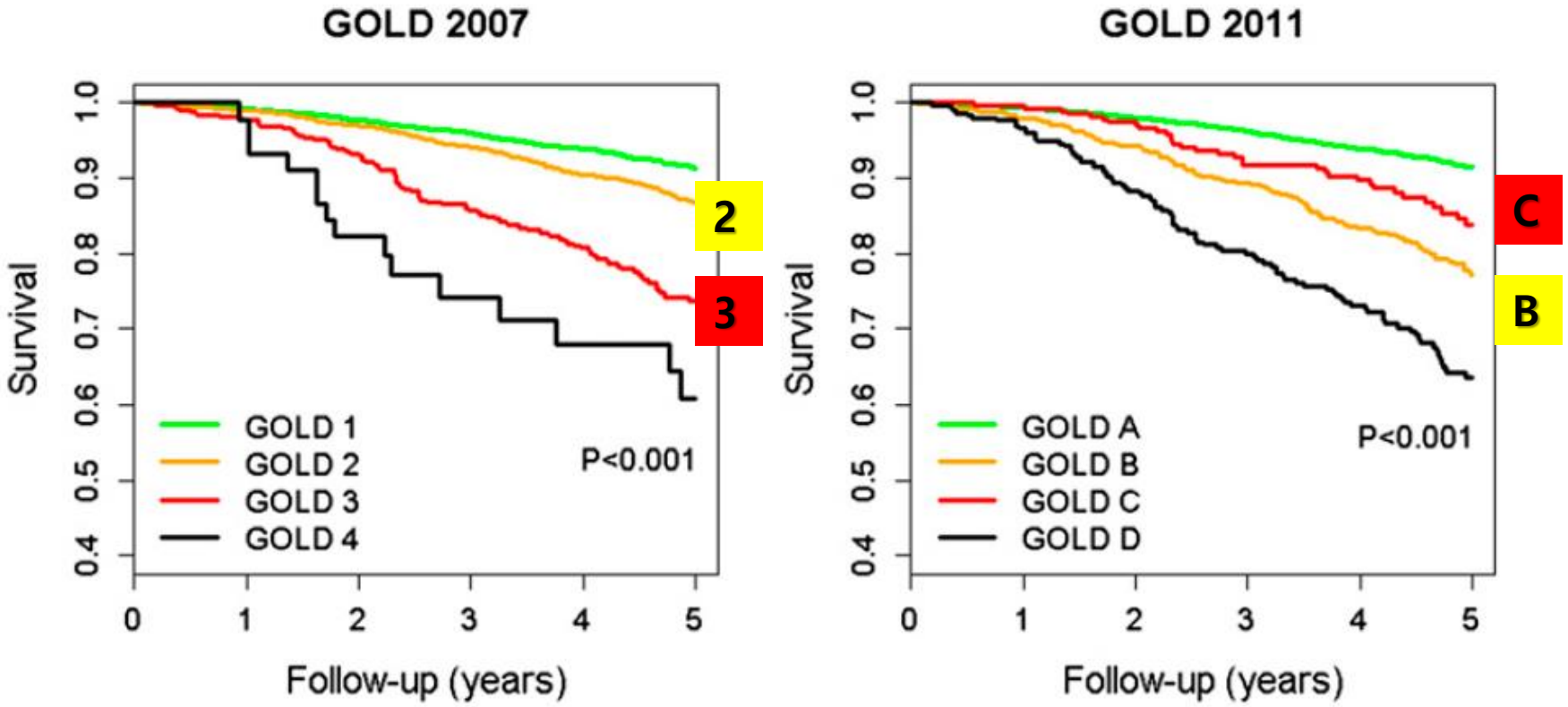


GOLD group A,B,C,D

. Goossens LM, et al. BMC Pulm Med. 2014;14:163.

Survival Prediction

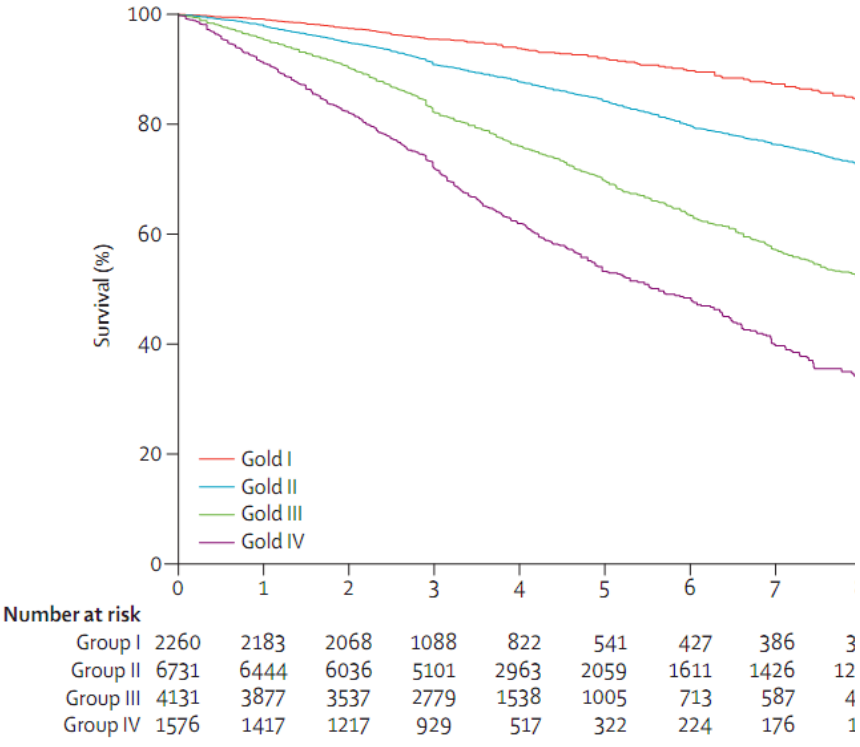
CCHS (Copenhagen City Heart Study) cohort



Lange P, et al. Am J Respir Crit Care Med 2012; 186: 975-981.

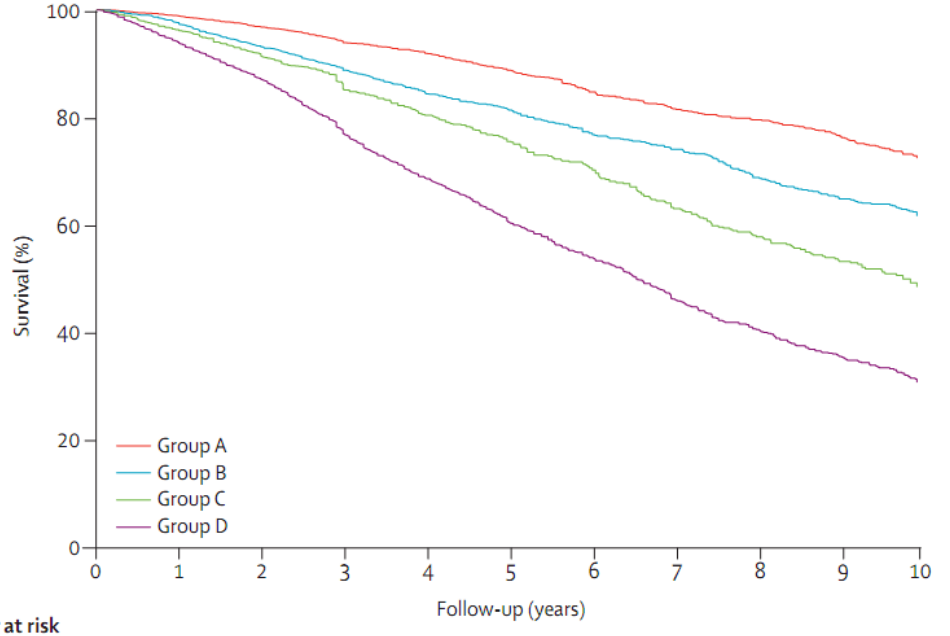
Mortality Prediction
GOLD 2007 vs GOLD 2011

15632 patients from 22 COPD cohorts from seven countries



Number at risk

Group I	2260	2183	2068	1088	822	541	427	386	3
Group II	6731	6444	6036	5101	2963	2059	1611	1426	12
Group III	4131	3877	3537	2779	1538	1005	713	587	4
Group IV	1576	1417	1217	929	517	322	224	176	1



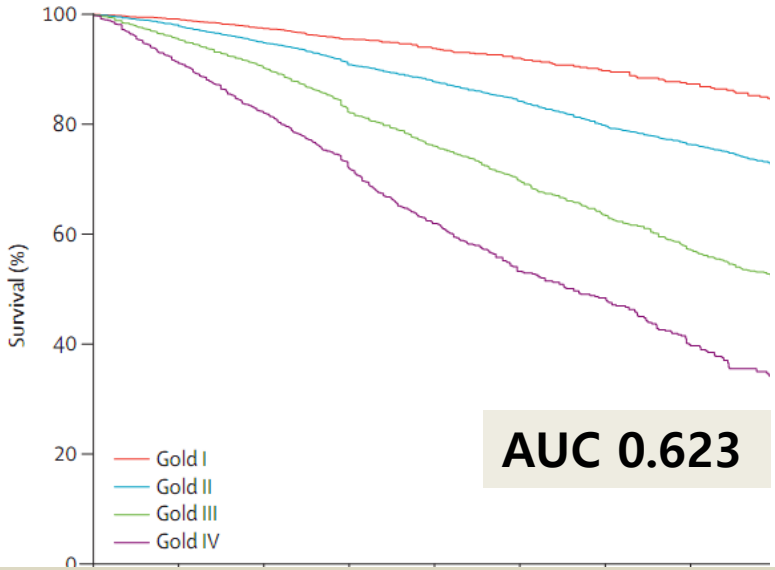
Number at risk

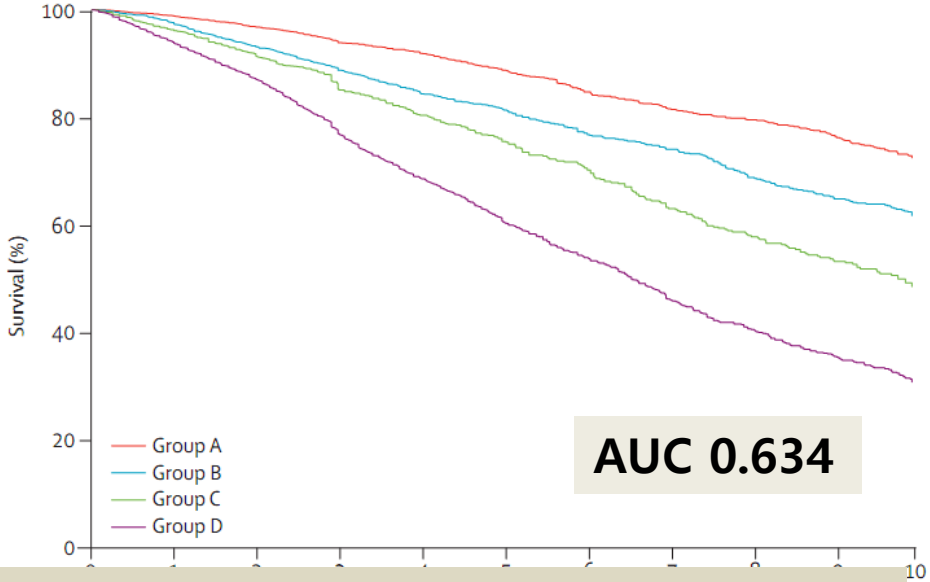
Group A	5273	5092	4841	4221	2006	1282	994	887	800	741	448
Group B	2530	2412	2218	1877	1095	769	608	552	478	443	383
Group C	1746	1644	1516	1204	676	481	390	322	263	228	145
Group D	4267	3934	3522	2664	1412	821	544	425	315	267	189

Lancet Respir Med 2015;3:443-50

Mortality Prediction in individual level GOLD 2007 vs GOLD 2011

15632 patients from 22 COPD cohorts from seven countries





Both systems Failed to Predict Individual Mortality

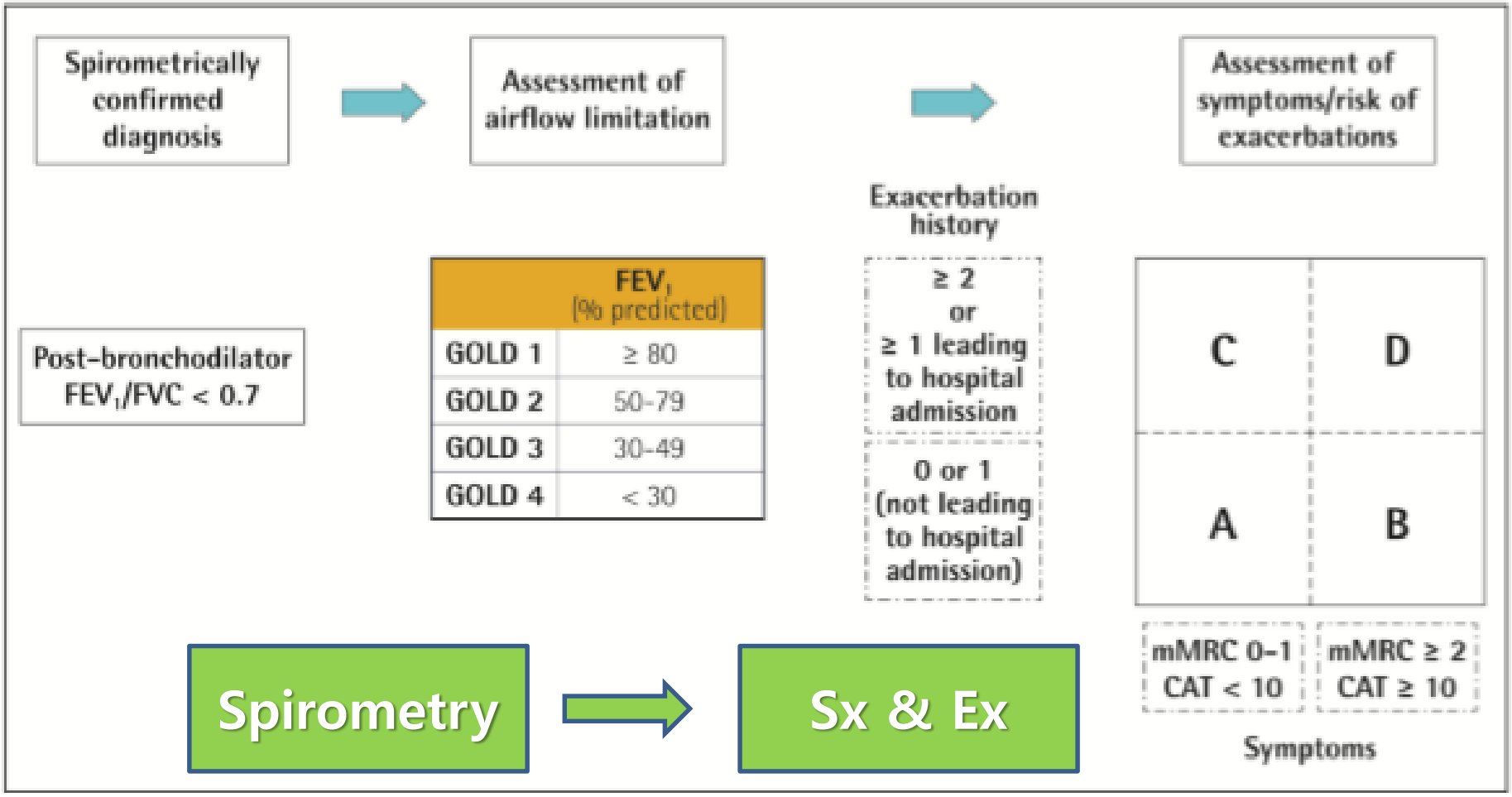
Lancet Respir Med 2015;3:443-50

Contents

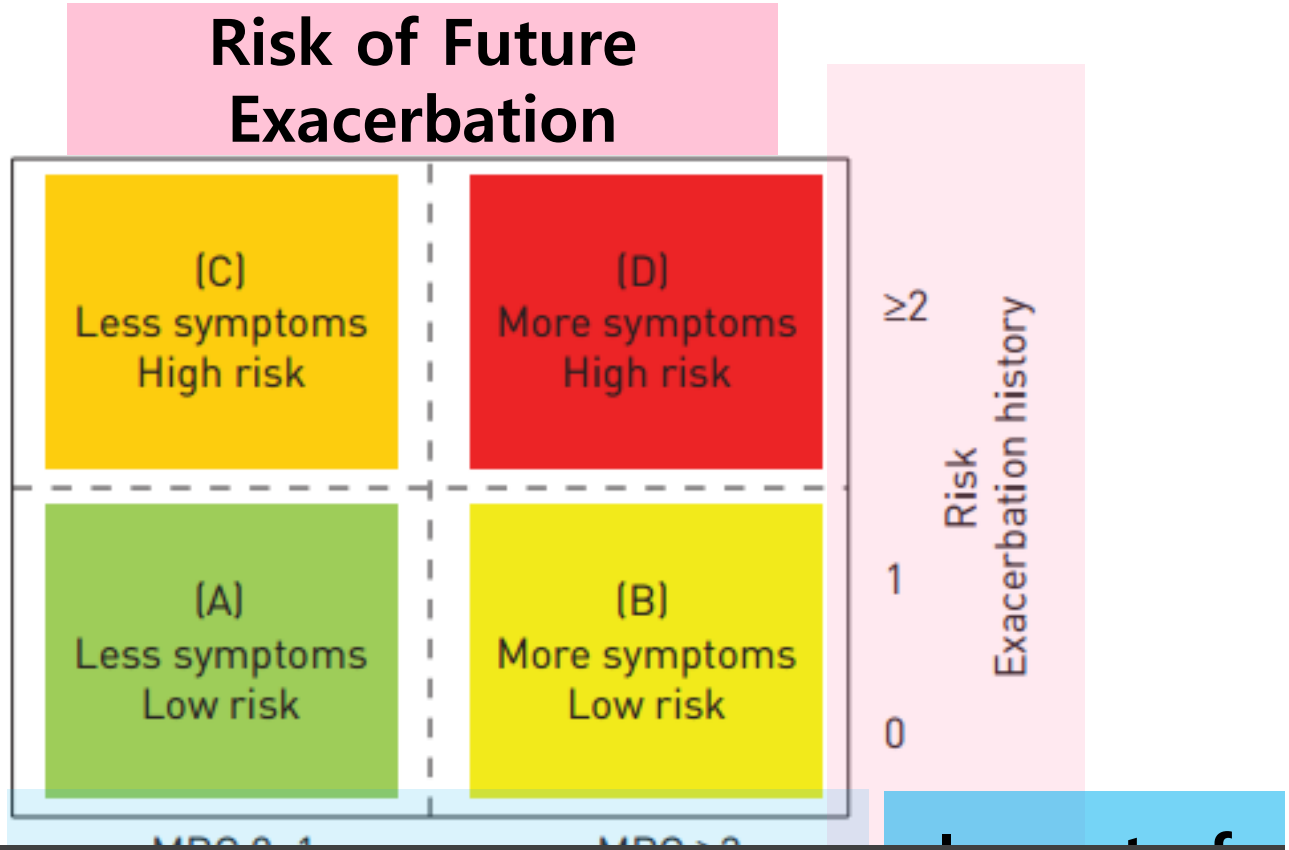
Is it essential to remove the FEV_1 severity in revised combined COPD assessment?

NO!

2017 GOLD ASSESSMENT



GOLD 2017



empirical proposal mostly based on expert opinion

GOLD 2017

Revised combined COPD assessment

An understanding of the impact of COPD on an individual patient combines the symptomatic assessment with the patient's spirometric classification and/or risk of exacerbations. The "ABCD" assessment tool of the 2011 GOLD update was a major step forward from the simple spirometric grading system of the earlier versions of GOLD because it incorporated patient-reported outcomes

FEV_1 , for Patient Asessment ,
NOT FOR PHAMACOLOGIC MANAGEMENT

Spirometry, in conjunction with patient symptoms and exacerbation history, remains vital for the diagnosis, prognostication and consideration of other important therapeutic approaches.

exacerbation history, remains vital for the diagnosis, prognostication and consideration of other important therapeutic approaches. This new approach to assessment is illustrated in **Figure 2.4**.

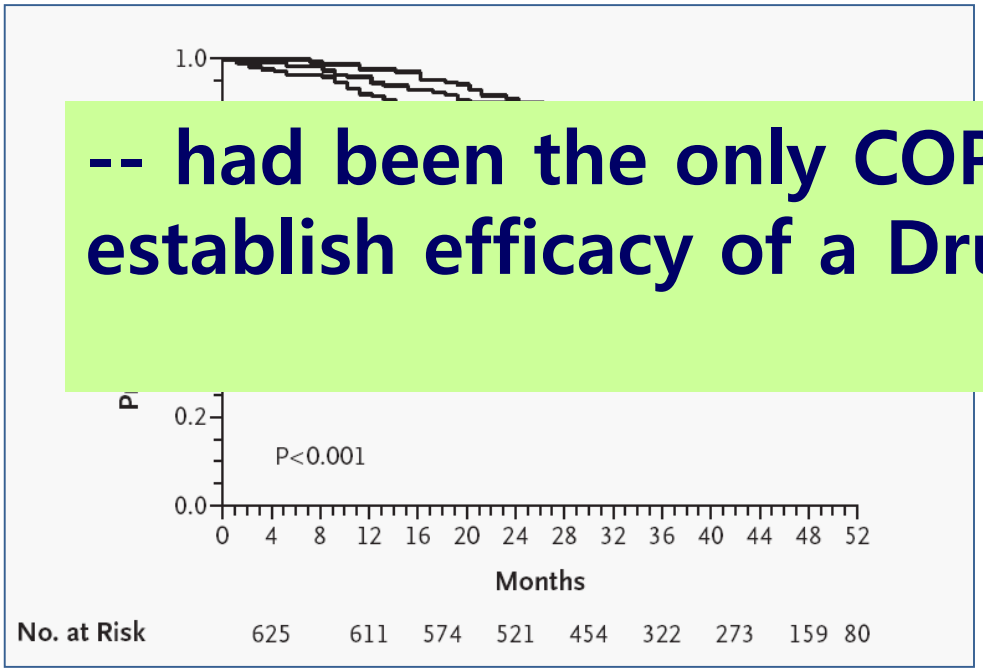
Spirometry Role

- Diagnosis
- Assessment of severity of airflow obstruction (for prognosis)
- Follow-up assessment
  - Therapeutic decisions
    - Pharmacological in selected circumstances
    - Consider alternative diagnoses
    - Non-pharmacological (e.g., interventional procedures)
  - Identification of rapid decline

Contents

FEV_1

- Define the disease
- Characterize the severity of the disease
- Predictor of mortality
- Indicator of future exacerbation
- Response to therapy



-- had been the only COPD biomarker to establish efficacy of a Drug for COPD

- US FDA-

Very Severe

< 30% pred

FEV_1 < 50% pred

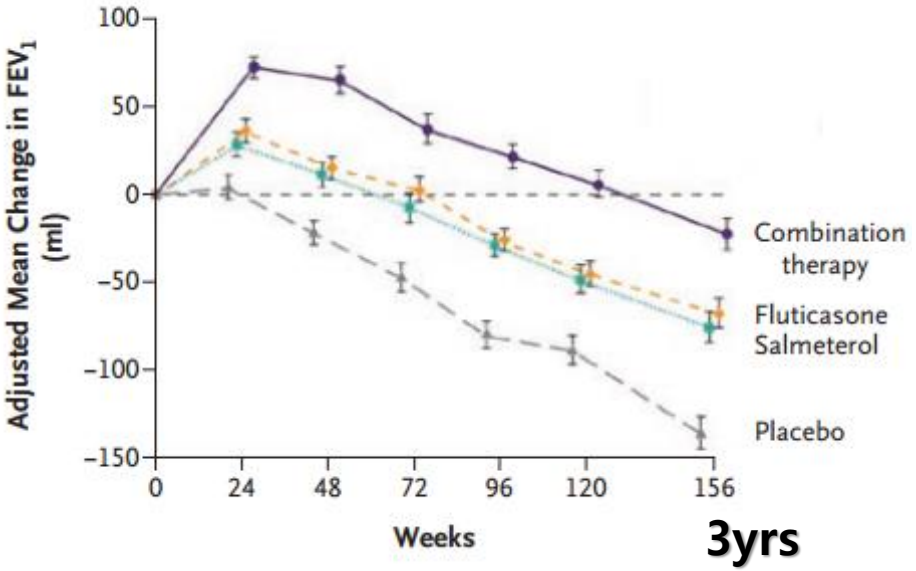
is chronic

spiratory failure

Previous GOLD stage

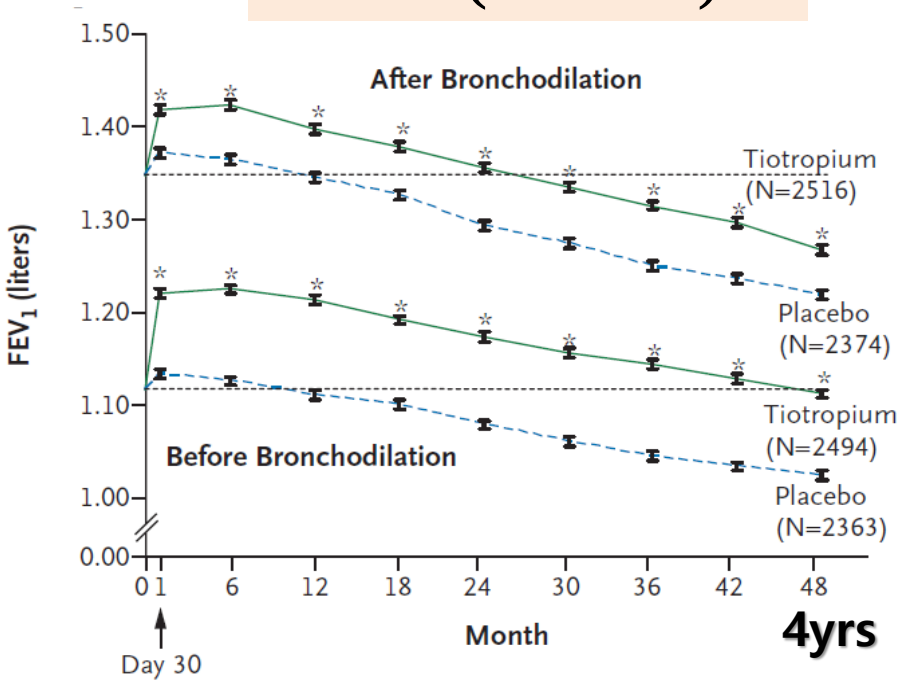
Celli BR. NEJM 2004;350:1005
Cote CG Am J Med 2006;119:s54
Donaldson GC Thorax 2006;61:164

ICS/LABA (TORCH)



3yrs

LAMA (UPLIFT)



4yrs

No Proved <u>Pharmacologic Option</u> to Alter Disease Progression

Calverley et al. N Engl J Med 2007;356:775-89.
Tashkin DP et al. N Engl J Med 2008;359:1543-54.

Manage Stable COPD: Goals of Therapy

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

Reduce symptoms

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

Reduce risk

Manage Stable COPD: Goals of Therapy

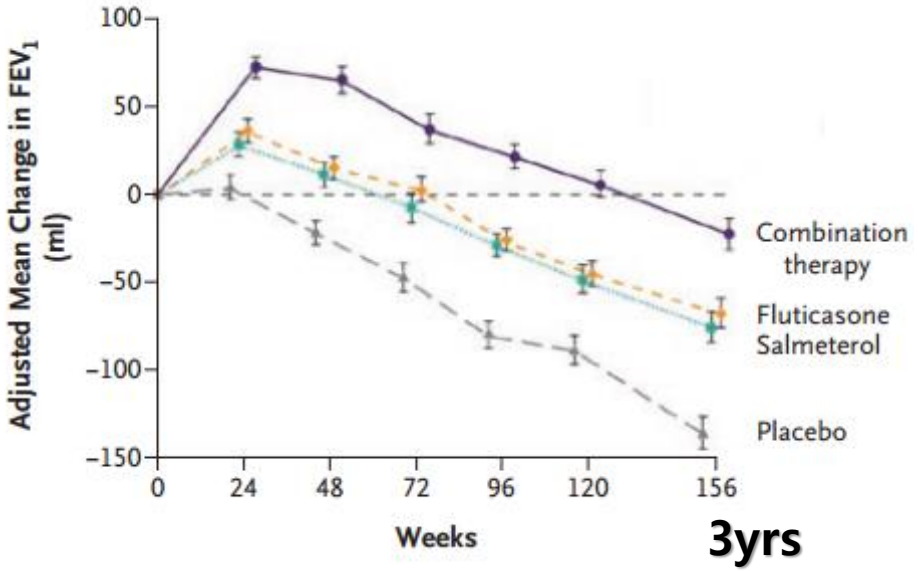
- Relieve symptoms
- Improve exercise tolerance
- Improve health status

Reduce symptoms

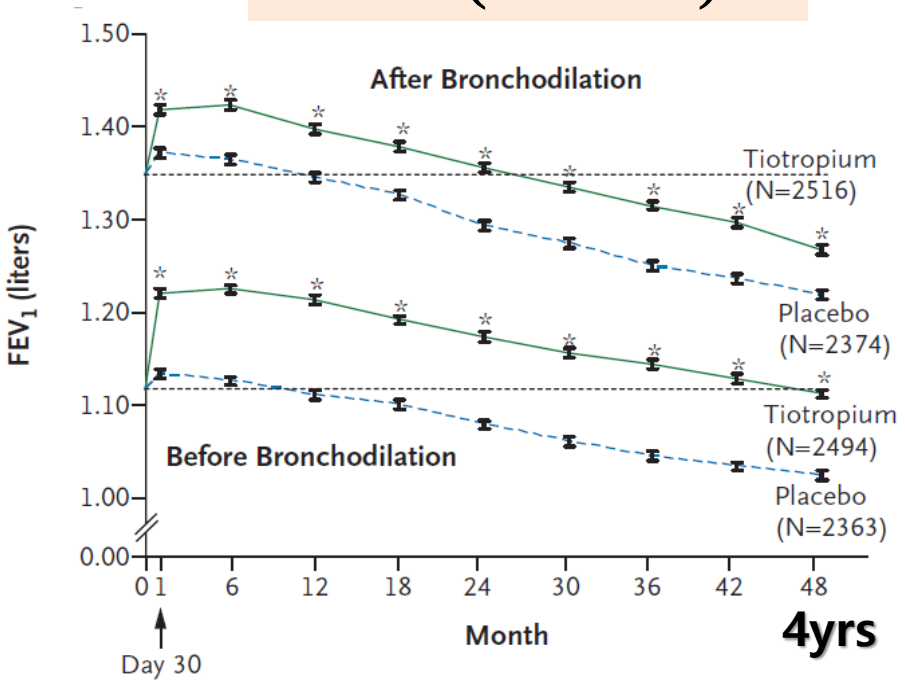
- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

Reduce risk

ICS/LABA (TORCH)



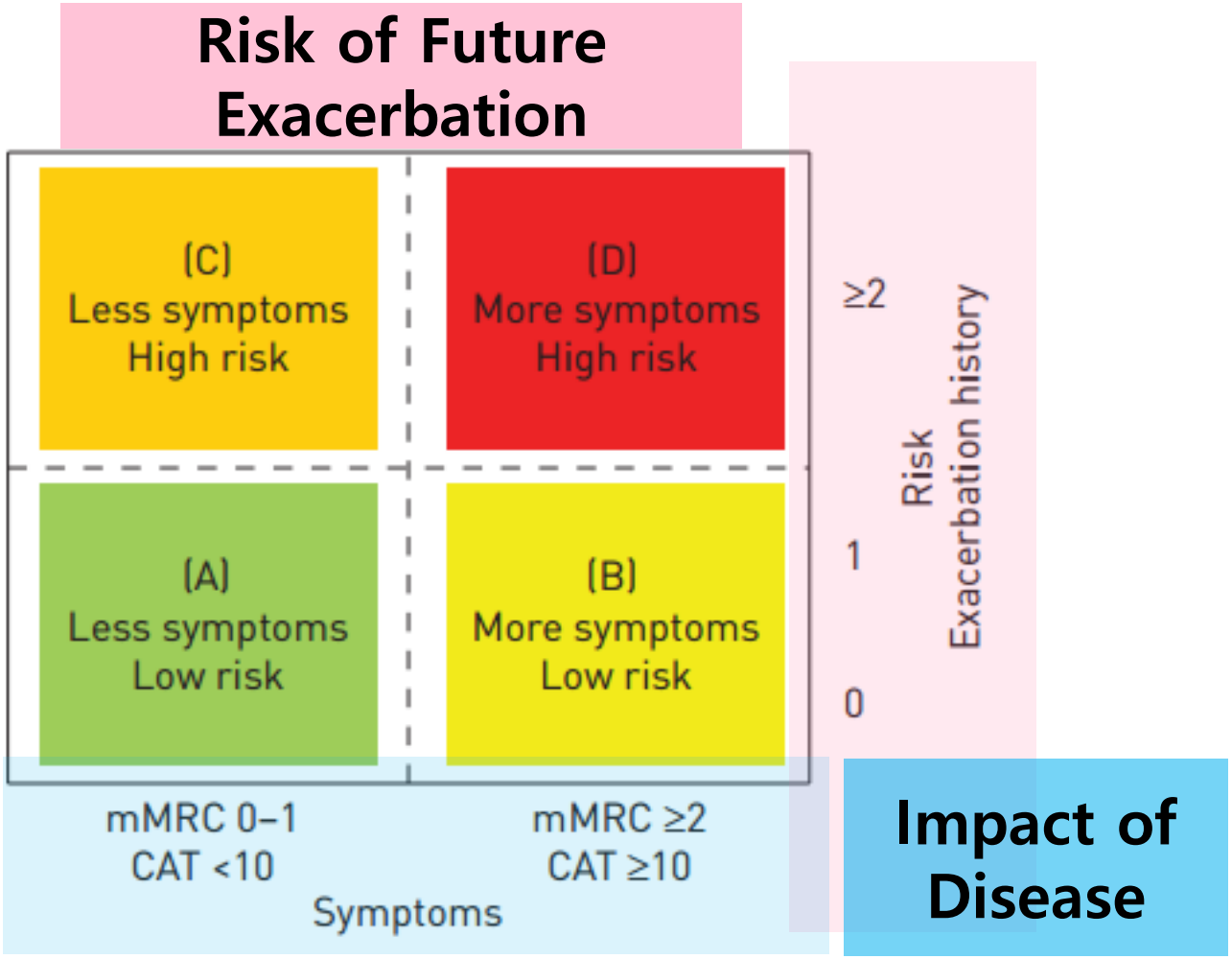
LAMA (UPLIFT)

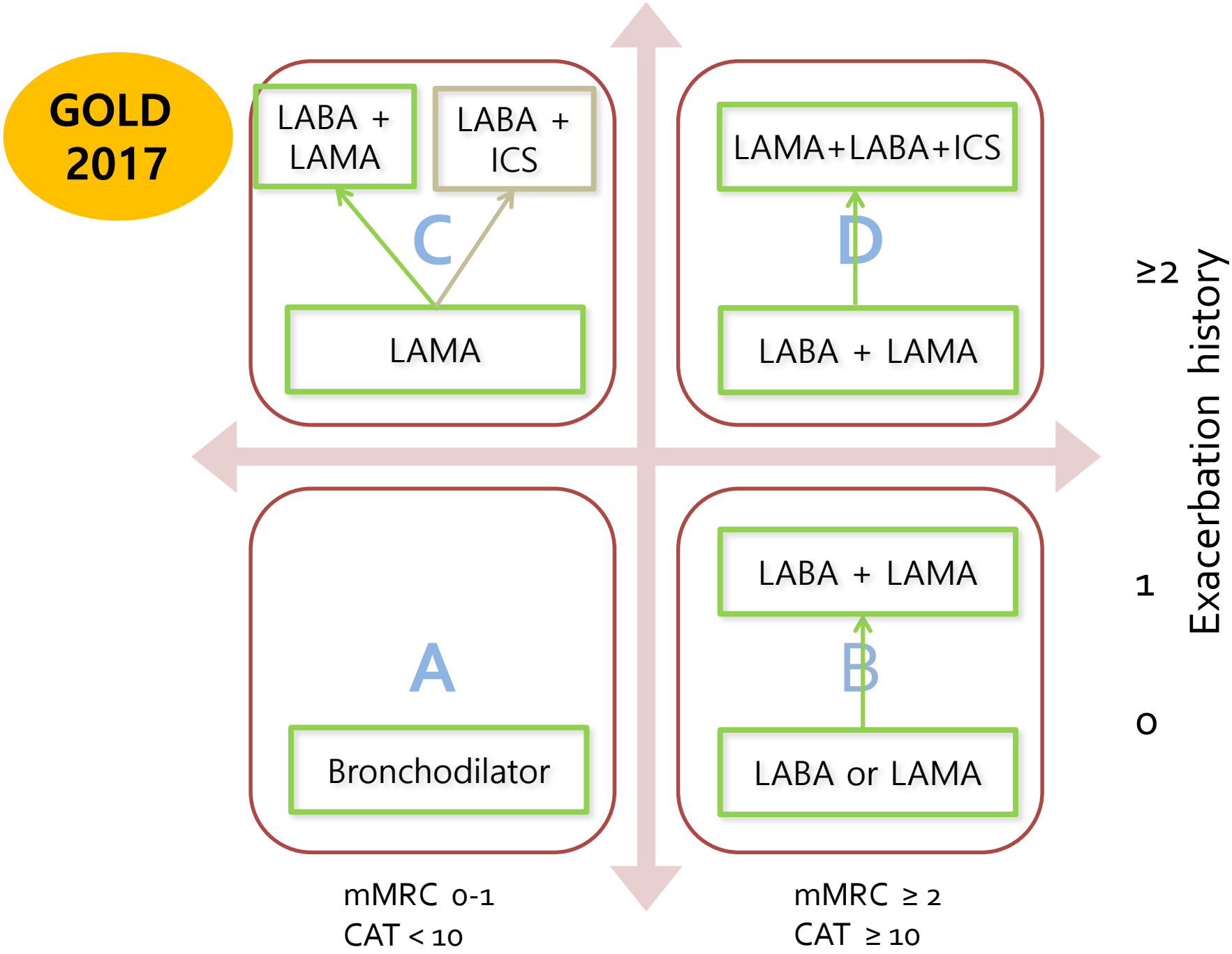


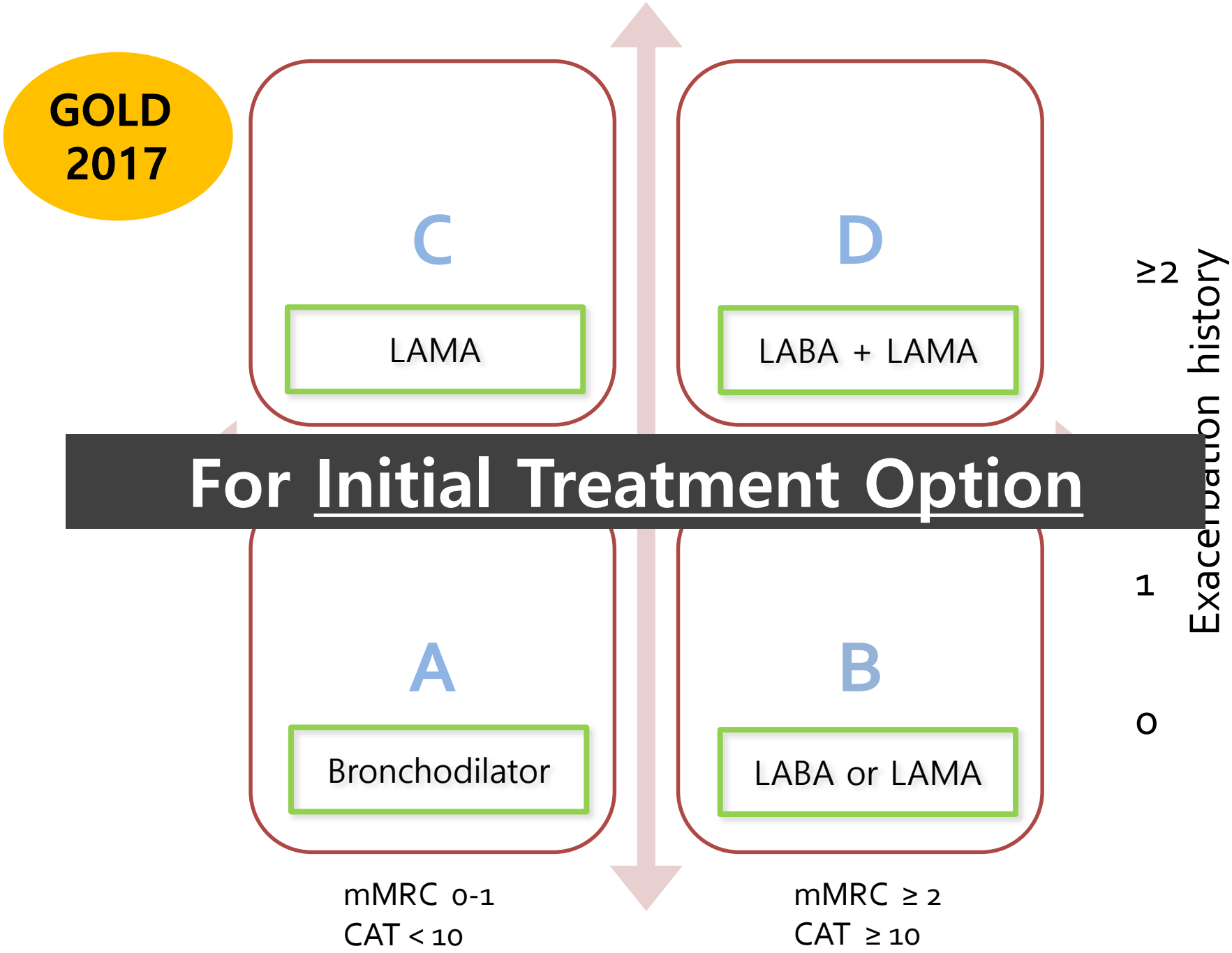
No Proved <u>Pharmacologic Option</u> to Alter Disease Progression

Proved <u>Pharmacologic Option</u> to Reduce Disease Exacerbations and Improve symptom

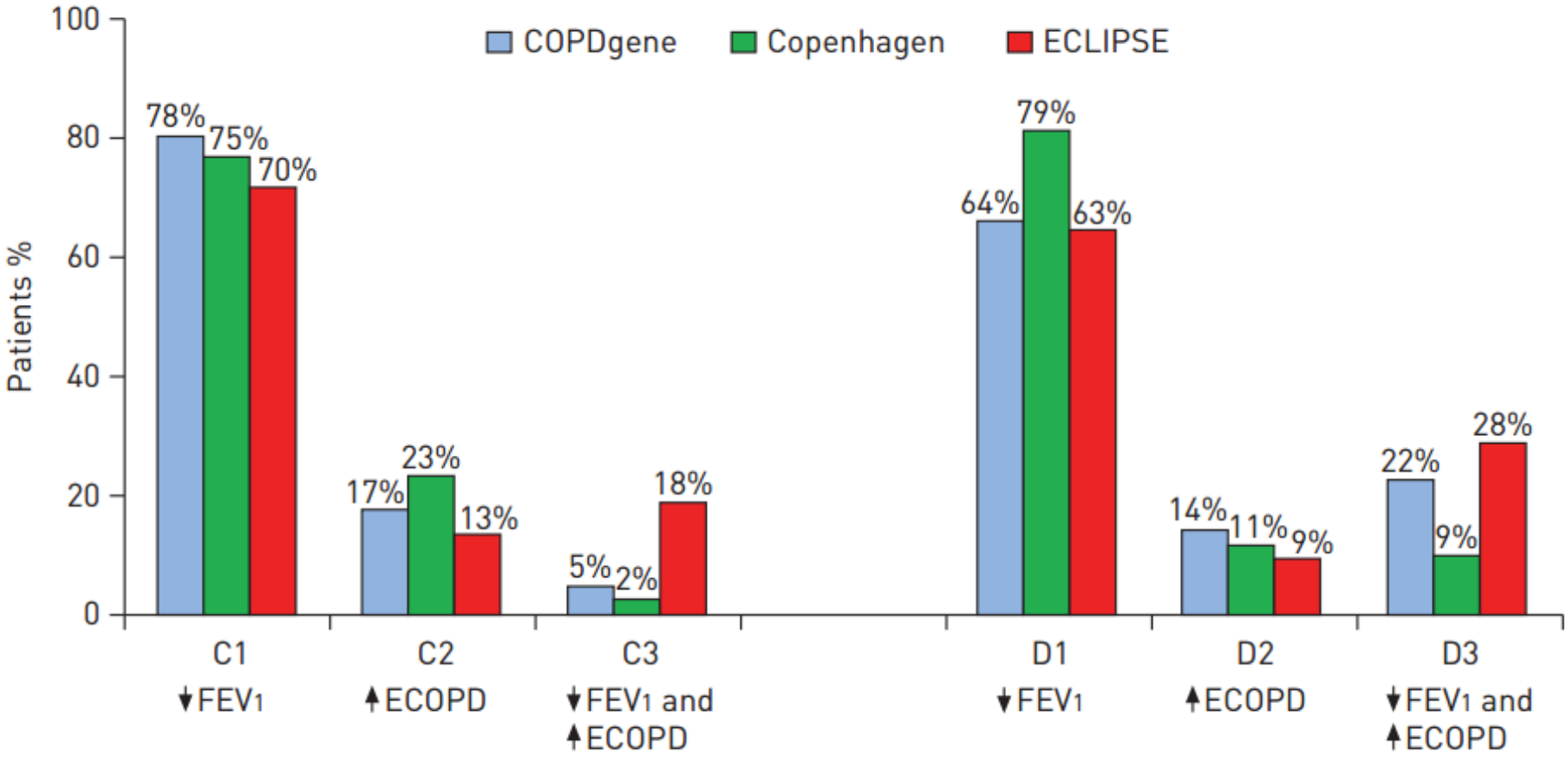
GOLD 2017


Risk of Future Exacerbation
(C)
Less symptoms
High risk
(D)
More symptoms
High risk
(A)
Less symptoms
Low risk
(B)
More symptoms
Low risk
≥2
1
0
Risk
Exacerbation history
mMRC 0–1
CAT <10
mMRC ≥2
CAT ≥10
Symptoms
Impact of Disease


GOLD 2017
LABA + LAMA
LABA + ICS
C
LAMA
LAMA+LABA+ICS
D
LABA + LAMA
A
Bronchodilator
LABA + LAMA
B
LABA or LAMA
mMRC 0-1
CAT < 10
mMRC ≥ 2
CAT ≥ 10
≥ 2
1
0
Exacerbation history

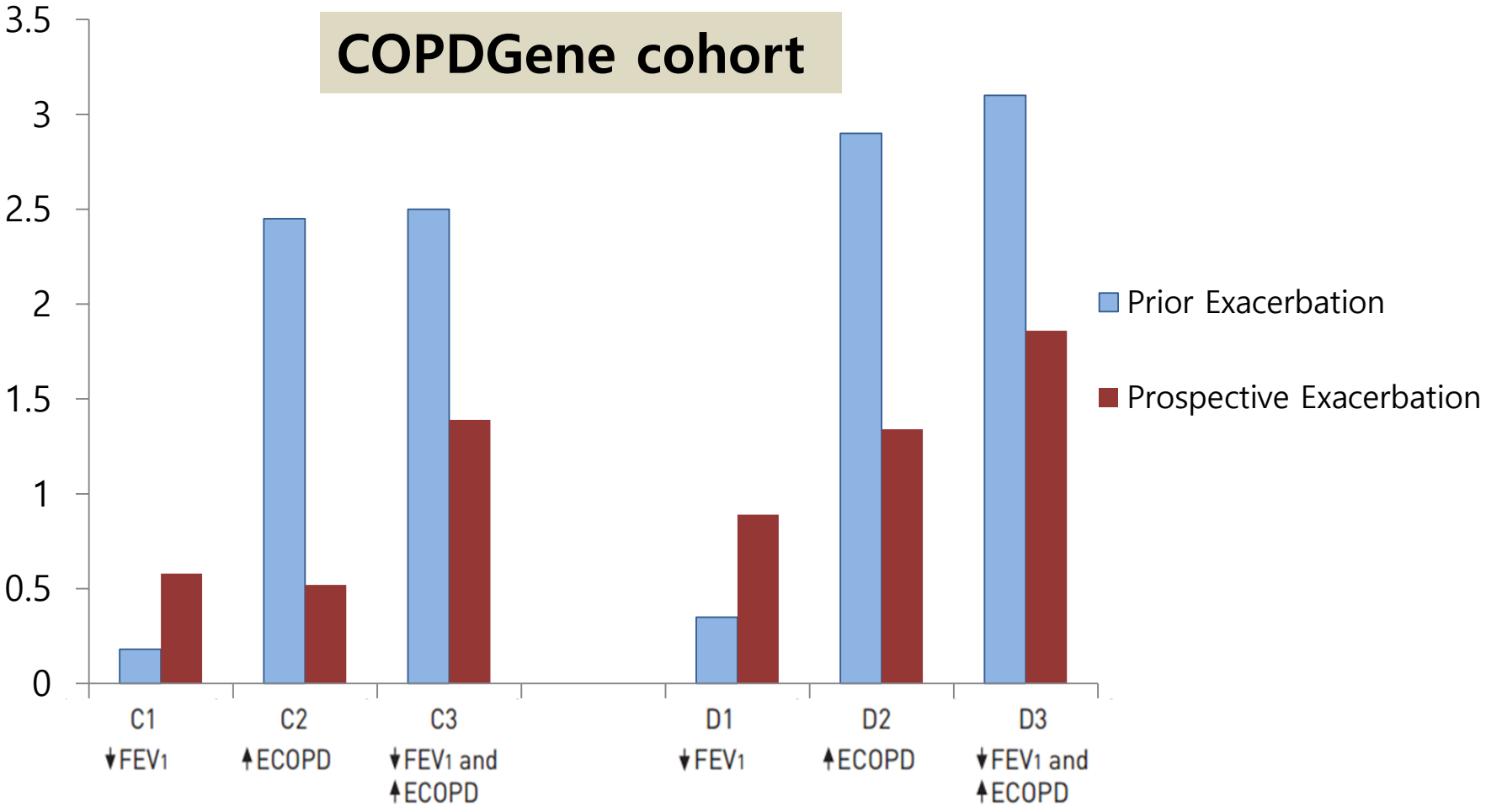

GOLD 2017
C
LAMA
D
LABA + LAMA
For Initial Treatment Option
A
Bronchodilator
B
LABA or LAMA
≥2
1
0
Exacerbation history
mMRC 0-1
CAT < 10
mMRC ≥ 2
CAT ≥ 10

Heterogeneity of previous GOLD categorization



Agusti A, et al. Eur Respir J 2013; 42: 1391–1401.

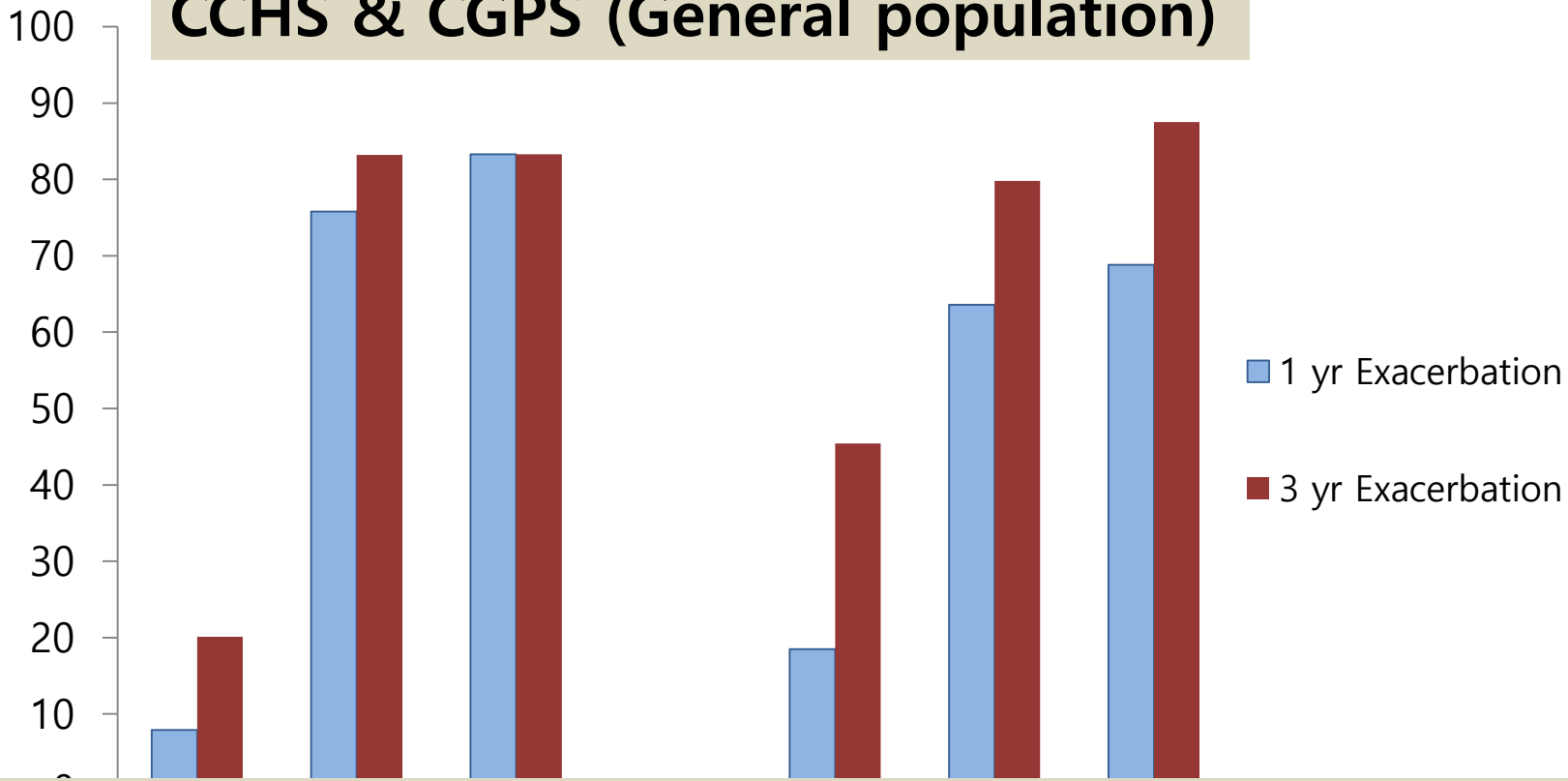
Prospective Exacerbation Prediction



Han MK, et al. Lancet Respir Med 2013; 1: 43–50.

Prospective Exacerbation

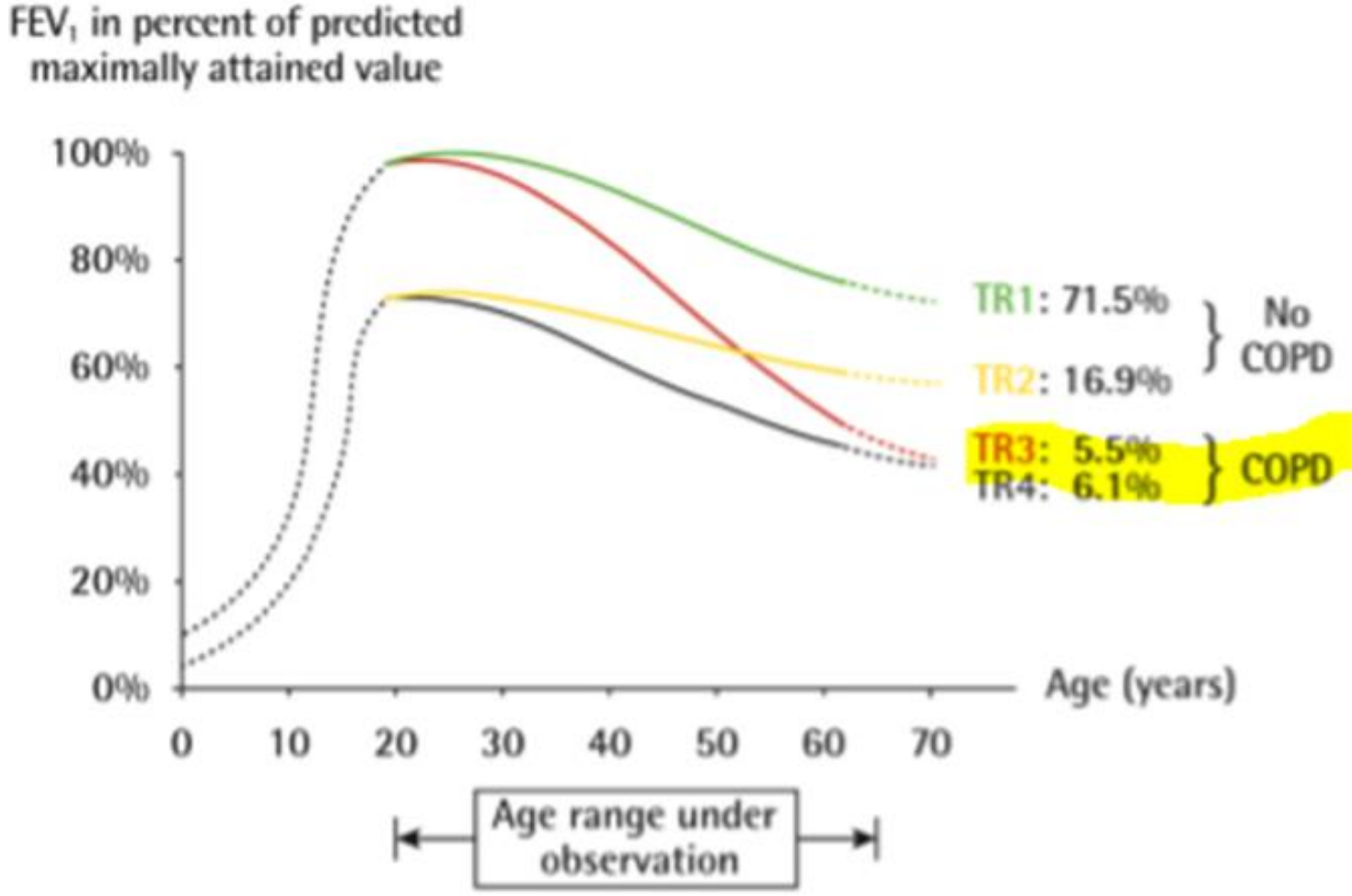
CCHS & CGPS (General population)



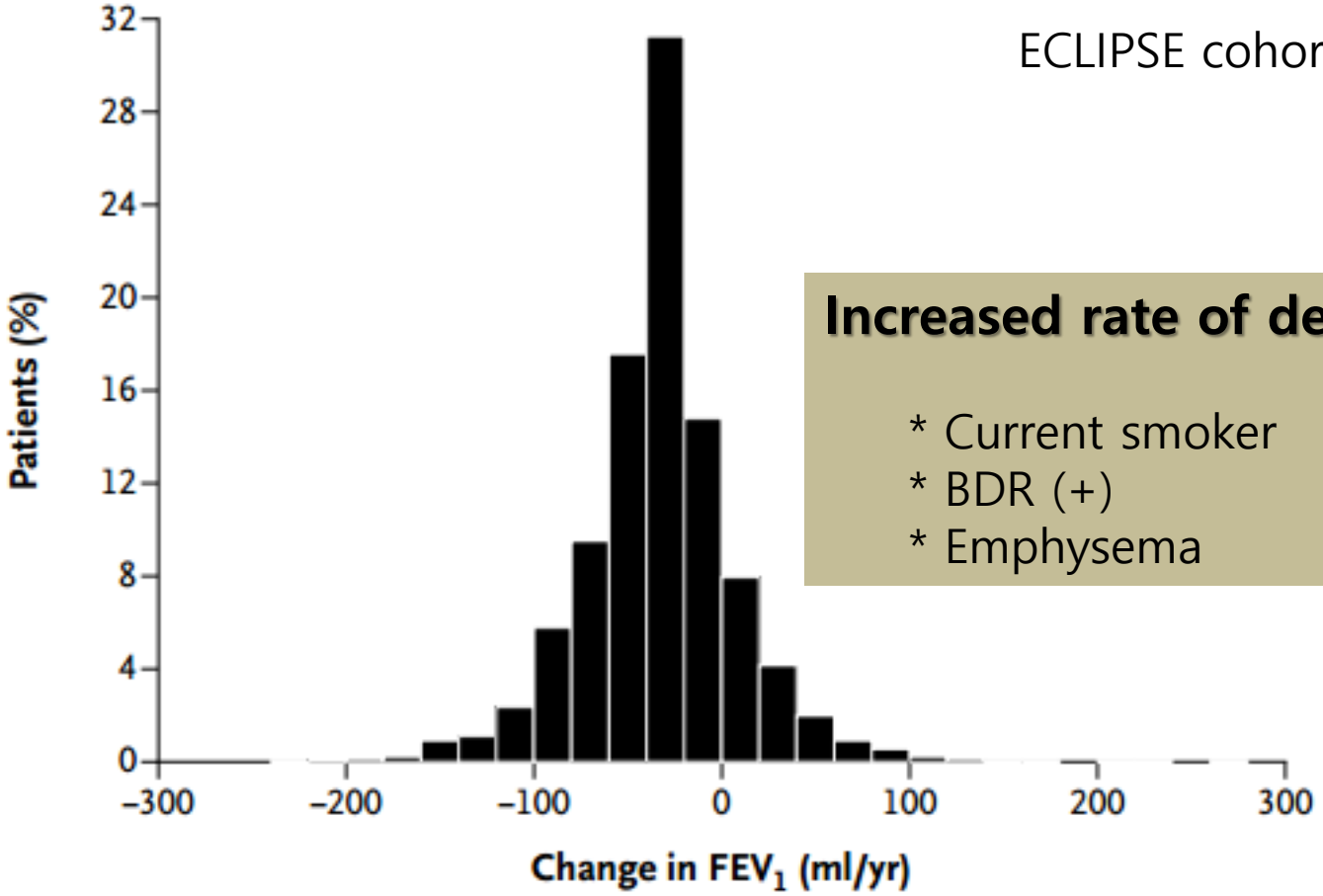
We cannot consider both of <u>FEV1 & EXACERBATION</u> yet…

Lange P et al. Am J Resp Crit Care Med 2012;186:975~81

Lung Function Trajectory



Changes in FEV_1 over time



ECLIPSE cohort

Increased rate of decline

* Current smoker
* BDR (+)
* Emphysema

Vestbo J, et al. N Engl J Med. 2011;365(13):1184–92.

Longitudinal assessment in COPD patients: multidimensional variability and outcomes

Ciro Casanova[1,2], Armando Aguirre-Jaíme[2], Juan P. de Torres[3], Victor Pinto-Plata[4], Rebeca Baz[2], Jose M. Marin[5], Miguel Divo[4], Elizabeth Cordoba[2], Santiago Basaldua[2], Claudia Cote[6†] and Bartolomé R. Celli[4]

- 1151 outpatients (1058 males) with COPD in the USA & Spain
- 2 Yrs longitudinal assessmemt
- F/U yearly from 1997 until 2009 or until death

Eur Respir J 2014; 43: 745–753

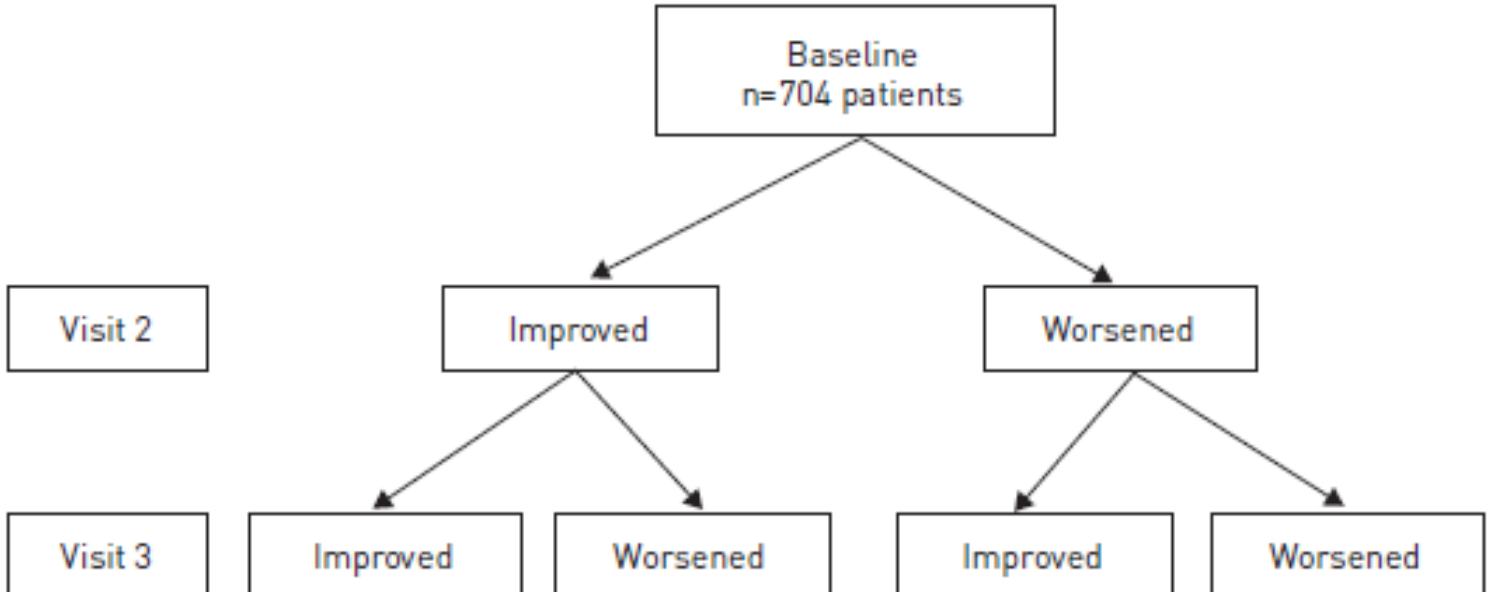


TABLE 2 Distribution of annual individual longitudinal pattern of forced expiratory volume in 1 s (FEV_1) estimated over at least five measures and according to different thresholds

	FEV_1				BODE index
	⩾40 mL·year^{-1}	⩾100 mL·year^{-1}	3%	6%	1 point
Stable progressive	85 (21)	48 (12)	24 (6)	4 (1)	34 (9)
Stable nonprogressive	104 (26)	194 (48)	133 (33)	294 (73)	199 (53)
Unstable	214 (53)	161 (40)	246 (61)	105 (26)	142 (38)

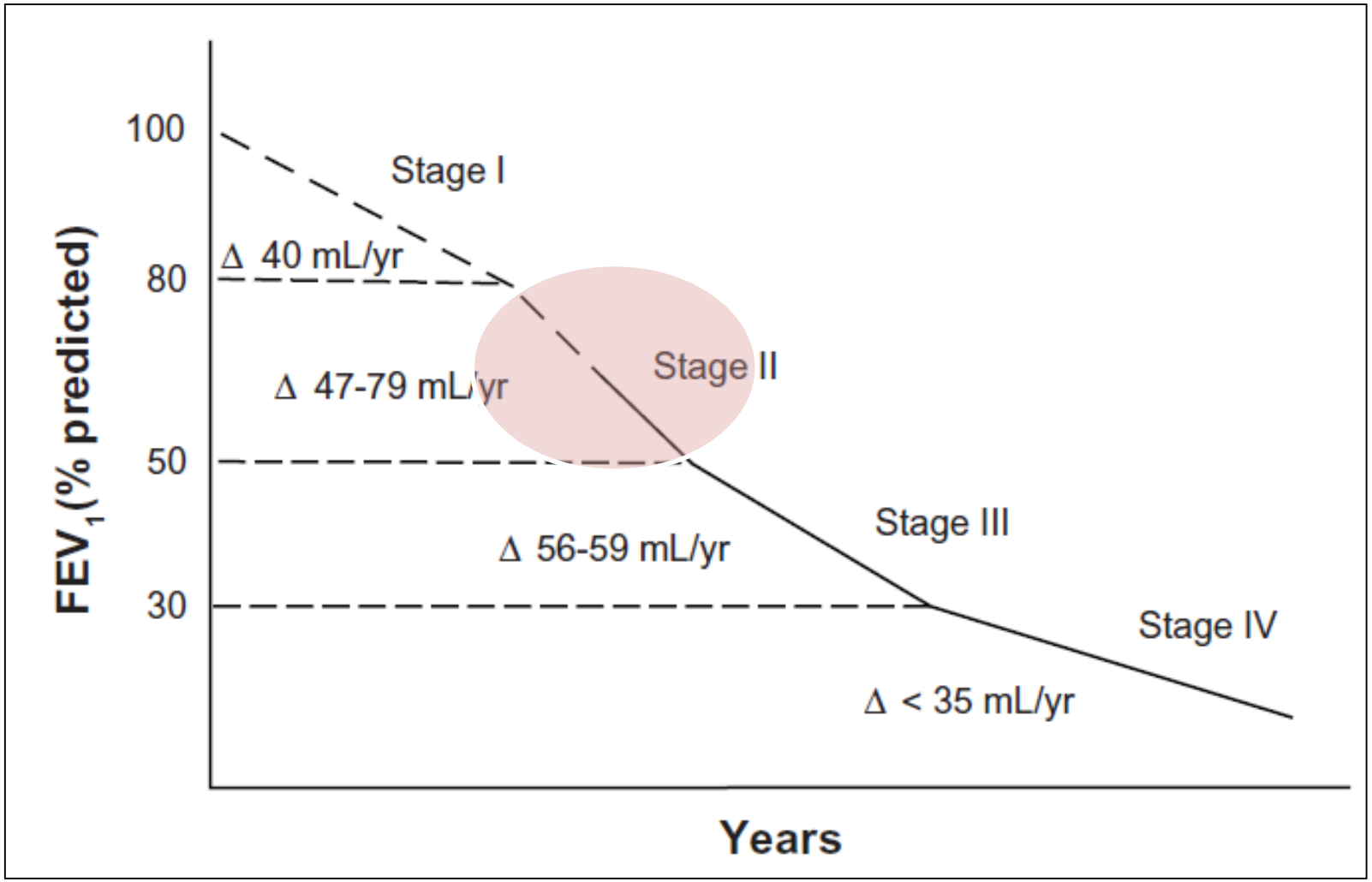
Data are presented as n (%). BODE: body mass index, airflow obstruction, dyspnoea, exercise capacity.

Longitudinal 2-year pattern and mortality after 12 and 24 months

Variable and cut-off point	Patients	Mortality			
		12 months	p-value	24 months	p-value
BMI					
⩾0	368 (54)	7.4		16.2	
⩽ -1	42 (6)	7.1		11.9	
Unstable	273 (40)	7.8		18.9	
			0.478		0.284
FEV_1 mL					
⩾40	144 (20)	8.6		20.1	
<40	128 (18)	5.6		14.6	
Unstable	430 (62)	7.3		16.1	
			0.636		0.434
FEV_1 %					
⩾3	77 (11)	9.1		20.8	
<3	202 (30)	4.5		13.8	
			0.145#		0.373#
mMRC dyspnoea score					
⩾1	28 (4)	3.6		7.4	
<1	402 (58)	5.3		14	
Unstable	261 (38)	10.8		21	
			0.023#		0.028#
6MWD m					
⩾50	32 (5)	15.6		34.4	
<50	346 (51)	4.1		13.4	
Unstable	293 (44)	11		19.5	
			0.001		0.004
BODE index					
⩾1	66 (10)	21.2		35.4	
<1	244 (36)	2.9		10.1	
Unstable	378 (54)	7		17.3	
			<0.001		<0.001

FEV_1 % change over time did not relate directly to mortality

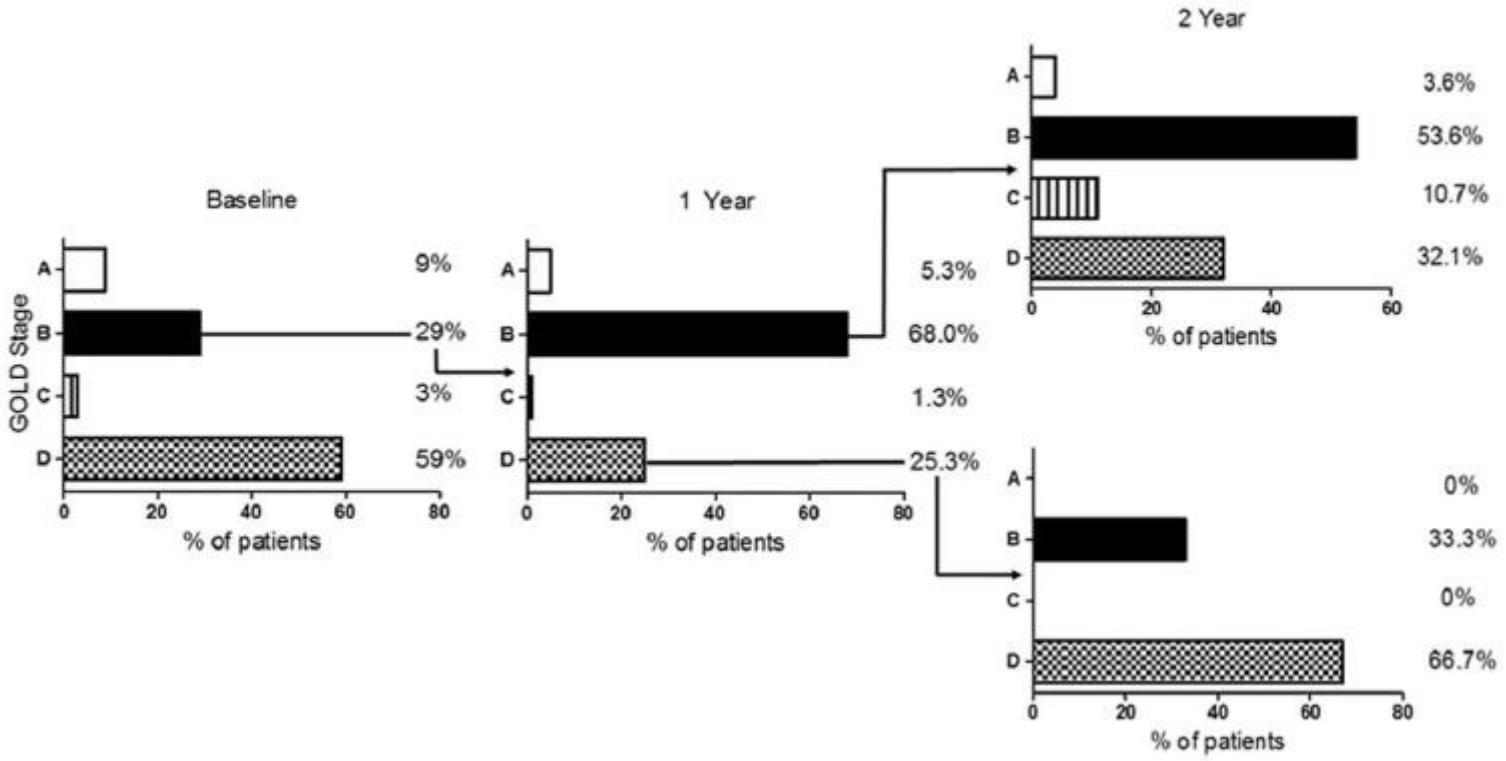
FEV_1 Impact on Lung Function Decline



Tantucci et al IJCOPD 2012

GOLD B progression across 2 yrs

COPDMAP cohort, N=370



Lawrence et al. BMC Pulmonary Medicine (2017) 17:42

GOLD B progression across 2 yrs

COPDMAP cohort, N=370

B → D VS **B → B**

Baseline

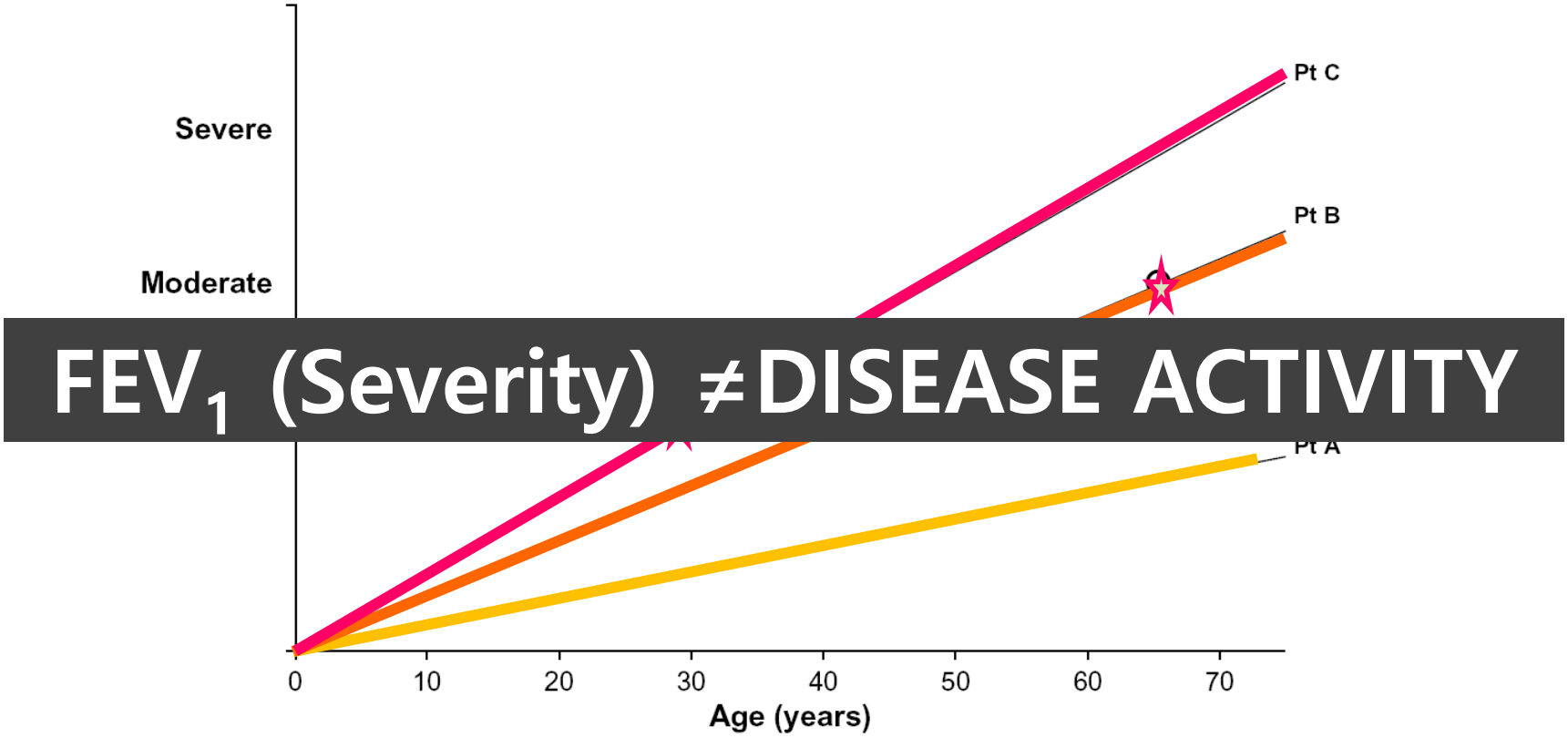
↓ FEV1 % predicted (69.7% vs 62.4%; p = 0.016)
↑ SGRQ score (40.1 vs 50.0; p = 0.019)
↑ CAT score (14.0 vs 21.0; p =0.006)
↑ CRP levels (3.0 vs 4.5; p = 0.06)

At 1 yr

↑ exacerbations (1.5 v 0.2, p =0.0001)
↑ CAT scores (20.0 v 15.5, p = 0.018)
↑ SGRQ total scores (50.0 v 41.1, p = 0.001),
↑ CRP (5.0 v 3.0, p = 0.017),
↓ 6MWD (347.3 v 440.5, p= 0.023).

Lawrence et al. BMC Pulmonary Medicine (2017) 17:42

Severity and Activity



FEV_1 (Severity) ≠ DISEASE ACTIVITY

Contents

75/Male (a)

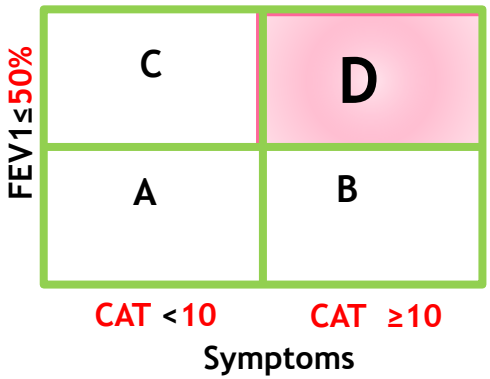
75/Male (b)

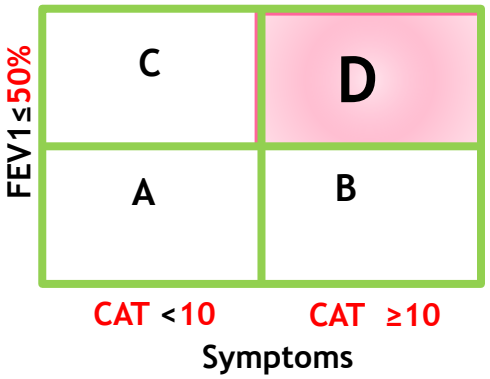
- Progressive dyspnea for 3 months
- Current smoker, 100 PY
- Spirometry FEV_1<30%
- CAT =18

No Exacerbation

GOLD 2011

3 Exacerbations





Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Pharmacologic Therapy FIRST CHOICE

ICS/LABA = Inhaled corticosteroid/Long acting beta 2 agonist
LAMA = Long-Acting Muscarinic Antagonists
SABA = Short acting beta 2 agonist

75/Male (a)

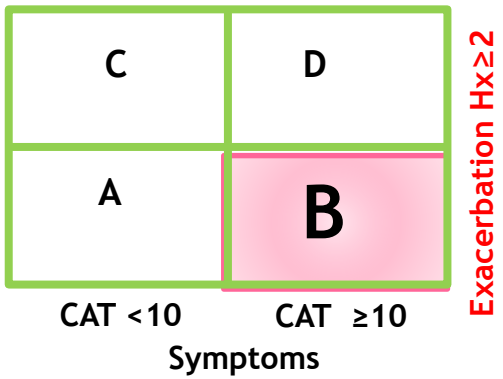
75/Male (b)

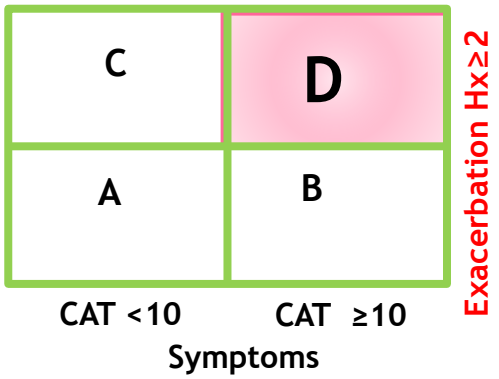
- Progressive dyspnea for 3 months
- Current smoker, 100 PY
- Spirometry FEV_1<30%
- CAT =18

No Exacerbation

3 Exacerbations

GOLD 2017





GOLD 2017

C

LAMA

D

A

Bronchodilator

B

mMRC 0-1
CAT < 10

mMRC ≥ 2
CAT ≥ 10

Exacerbation history

≥ 2

1

0

75/Male (a)

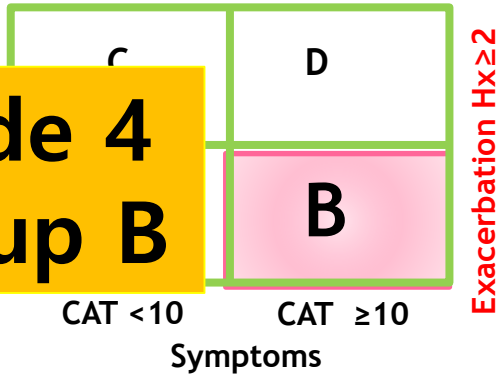
75/Male (b)

- Progressive dyspnea for 3 months
- Current smoker, 100 PY
- Spirometry FEV_1<30%
- CAT =18

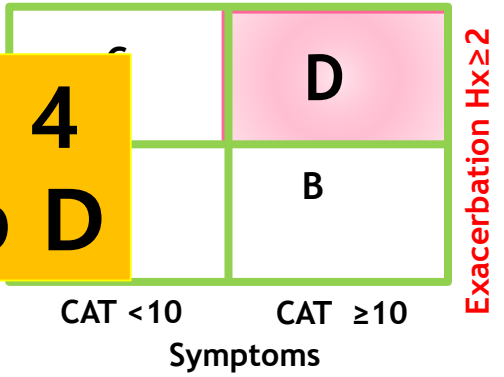
More Personalized Treatment

GOLD 2017

Grade 4 Group B



Grade 4 Group D

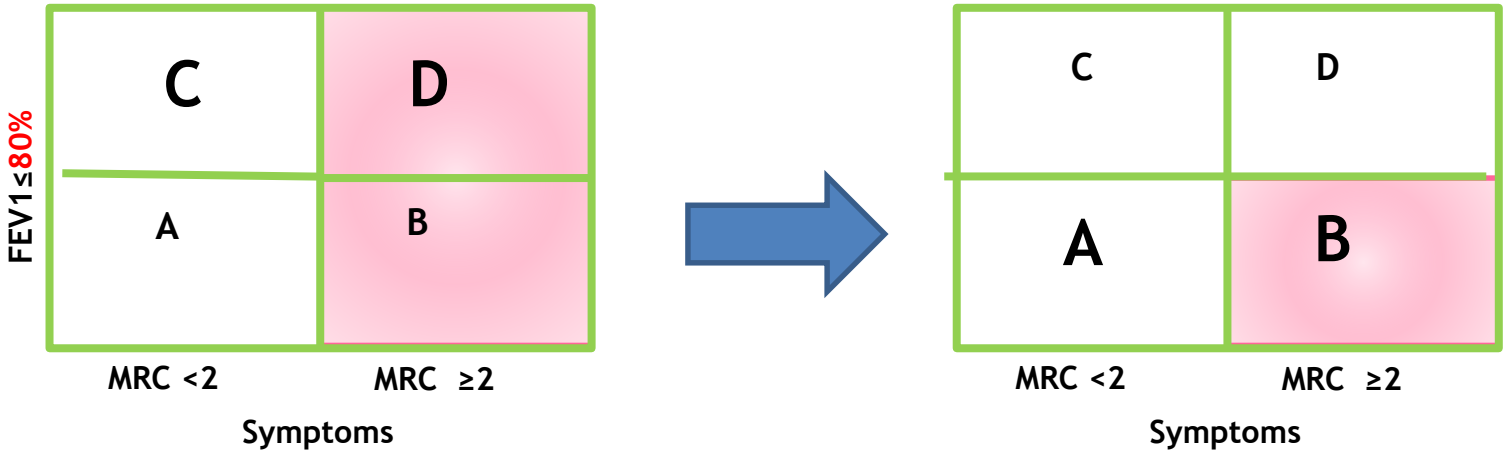


Interpretation of clinical trial

LANTERN

26-week, multicentre, randomised, double-blind, parallel-group, double-dummy study

QVA149 vs ICS/LABA



Exacerbation ≤ 1

GOLD 2011

Exacerbation ≤ 1

GOLD 2017

Vogelmeier CF, et al. Lancet Resp Med. 2012

Real World Treatment of COPD in Primary care Setting

Retrospective chart review

N=200, USA

Prevalence of stage appropriate Tx

	Number with Pulmonary function testing Confirmed Diagnosis	Proportion with stage appropriate treatment n (%)
Stage I		4 (57%)
Stage II		11 (31%)
Stage III		23 (50%)
Stage IV	9	2 (22%)
Total with COPD	97	39 (40%)

Spirometry ; 58.5%

Chavez PC, et al. COPD. 2009;6:446–451.

2015 COPD 적정성 평가 결과

대상기관 및 대상자 : 6,691개소, 141,782명

- 상급종합: 36,259명(25.5%)
- 종합병원: 55,189명(38.93%)
- 의원: 42,595명(30.0%)

< 평가등급별 현황 >

(단위: 기관, %)

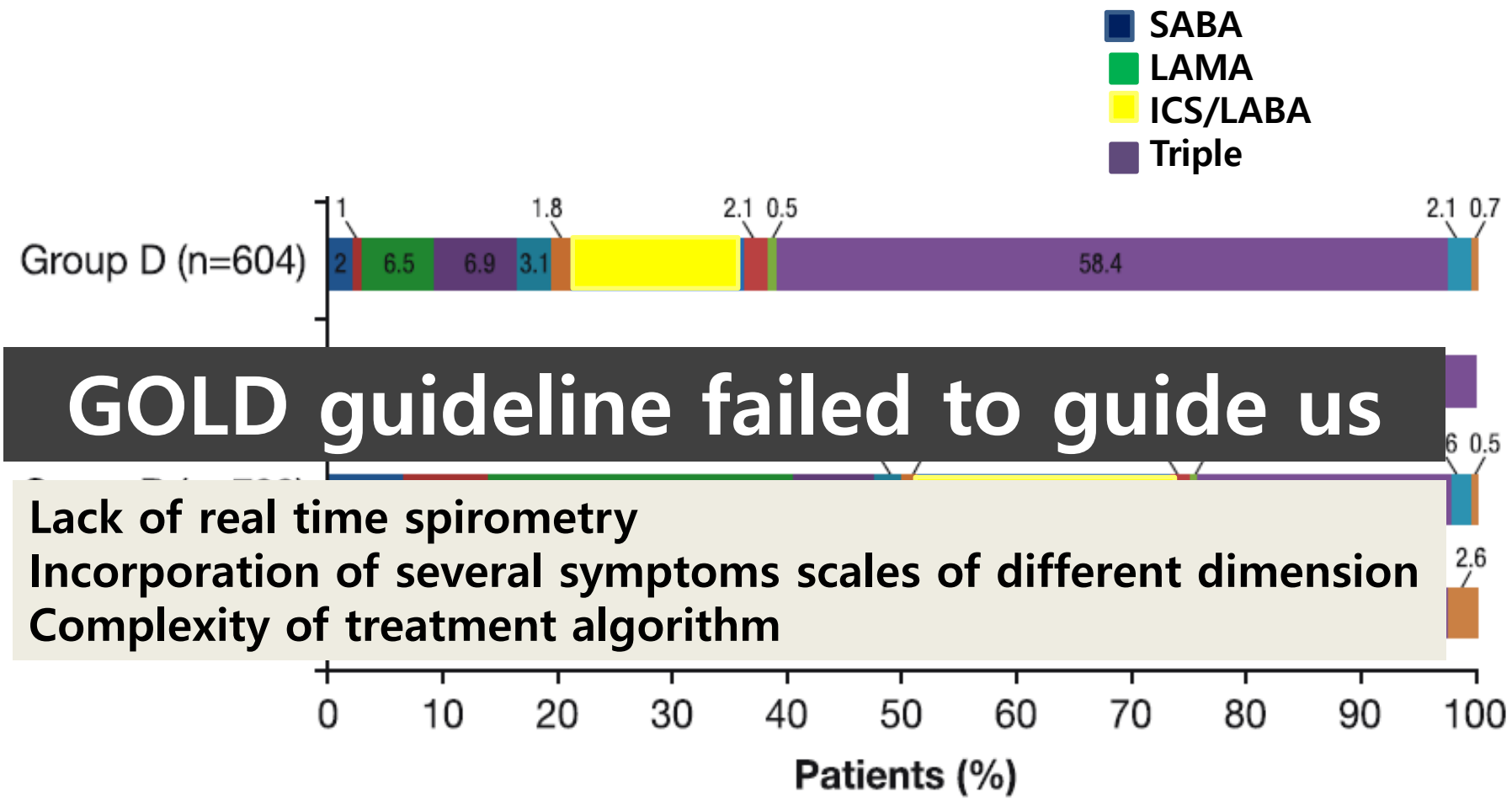
구분	종합점수 산출	1등급		2등급		3등급		4등급		5등급	
		기관	비율	기관	비율	기관	비율	기관	비율	기관	비율
전체	1,499	296	19.75	342	22.82	349	23.28	250	16.68	262	17.48
상급종합병원	43	40	93.02	3	6.98	-	-	-	-	-	-
종합병원	266	90	33.83	104	39.10	68	25.56	3	1.13	1	0.38
병원	243	34	13.99	81	33.33	84	34.57	36	14.81	8	3.29
의원	927	131	14.13	151	16.29	193	20.82	205	22.11	247	26.65
요양병원	7	-	-	-	-	1	14.29	2	28.57	4	57.14
보건의료원	9	1	11.11	3	33.33	3	33.33	2	22.22	-	-
보건소	4	-	-	-	-	-	-	2	50.00	2	50.00

▲ 만성폐쇄성폐질환 2차 적정성평가 평가등급별 현황

(단위: %, %p)

평가영역		지표명	구분	전체	상급종합	종합병원	병원	의원
평가지표	검사	1. 폐기능검사 시행률	1차	58.70	78.91	66.80	50.09	37.77
			2차	62.53	82.30	68.43	52.35	42.36
			(증감)	(3.83↑)	(3.39↑)	(1.63↑)	(2.26↑)	(4.59↑)
	치료지속성	2. 지속방문 환자비율	1차	85.46	83.77	88.52	85.25	82.12
			2차	92.12	91.45	94.17	93.47	88.40
			(증감)	(6.66↑)	(7.68↑)	(5.65↑)	(8.22↑)	(6.28↑)
	처방	3. 흡입기관지확장제 처방 환자비율	1차	67.93	91.40	78.84	58.70	35.30
			2차	71.19	92.61	80.04	60.41	40.46
			(증감)	(3.26↑)	(1.21↑)	(1.20↑)	(1.71↑)	(5.16↑)

Real World Treatment according to GOLD 2011



GOLD guideline failed to guide us

Lack of real time spirometry
Incorporation of several symptoms scales of different dimension
Complexity of treatment algorithm

Resp Med 2014;108:729~736

International Journal of COPD

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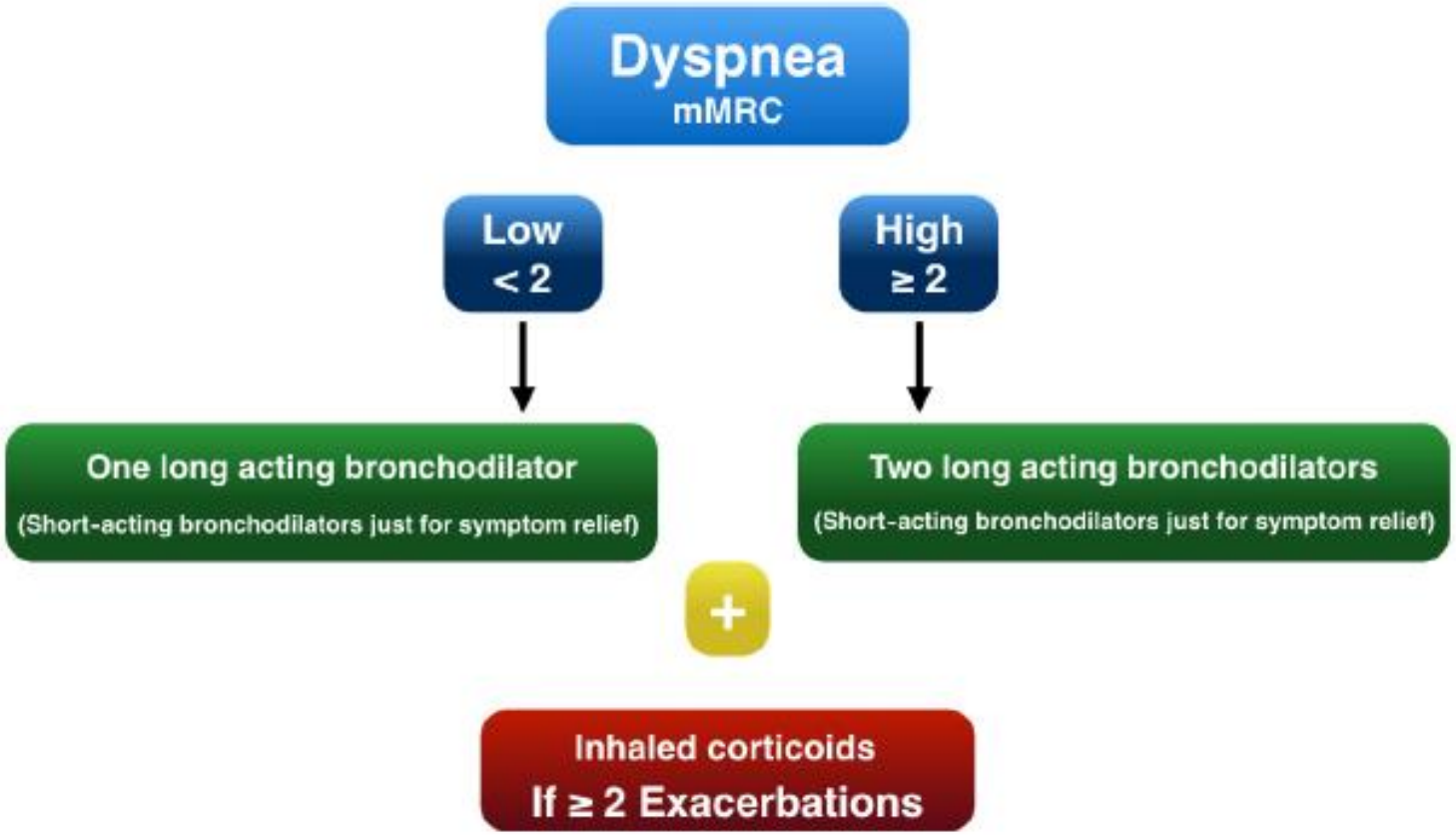
ORIGINAL RESEARCH

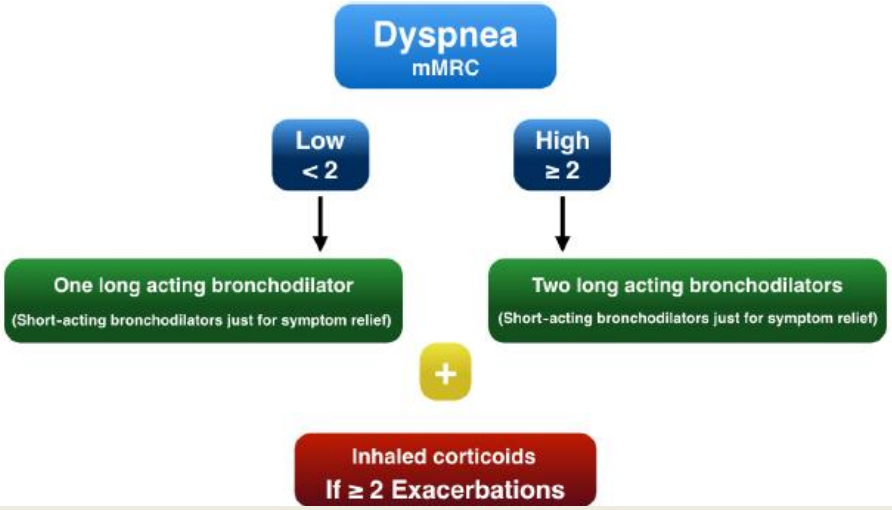
Agreement between a simple dyspnea-guided treatment algorithm for stable COPD and the GOLD guidelines: a pilot study

100 patients in primary care
150 attending specialized care in a respiratory clinic.
Cross sectional study

Proposed treatment algorithm

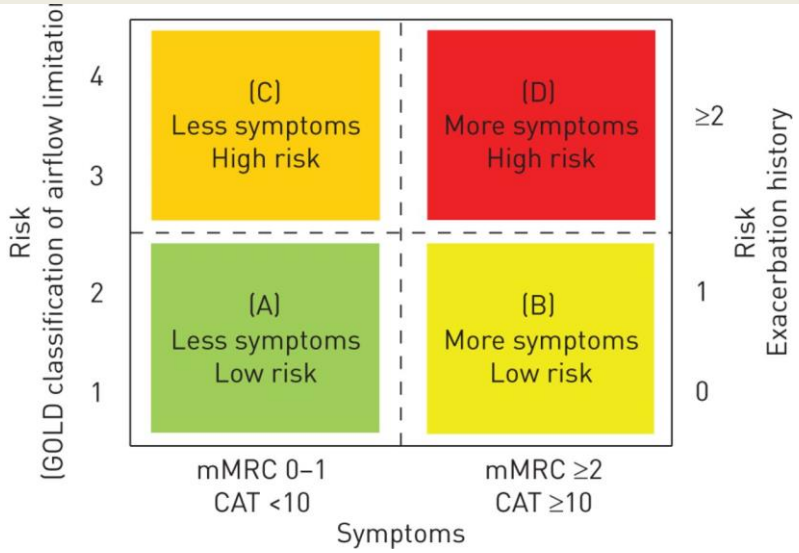


Cabera et al. Int J COPD 2016:11;1217



VS

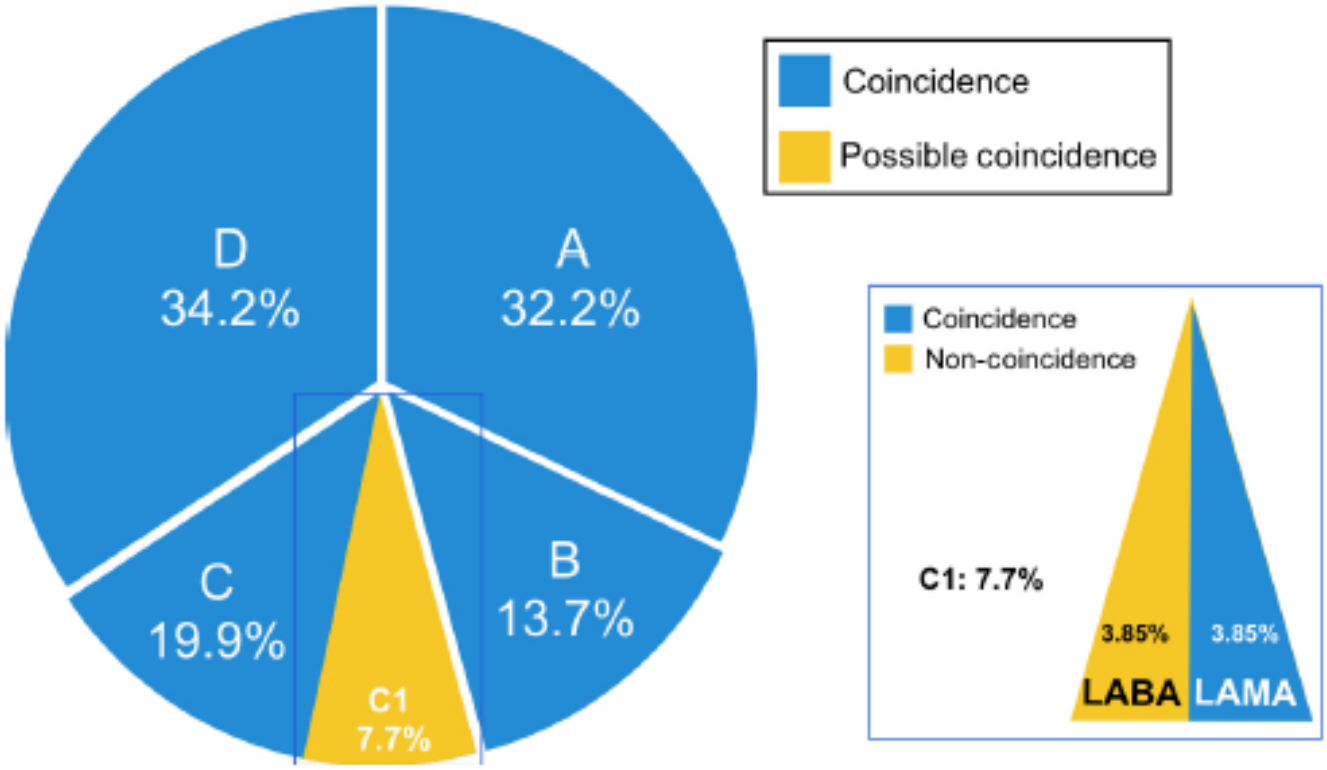
Result : Coincidence of pharmacologic treatment



Patient Group	First Choice	Alternative Choice
A	SAMA or SABA prn	LAMA LABA SABA and SAMA
B	LAMA or LABA	LAMA and LABA
C	ICS+LABA or LAMA	LAMA and LABA LAMA and PDE4 (-) LABA and PDE4 (-)
D	ICS+LABA and/or LAMA	ICS+LABA and LAMA ICS+LABA and PDE4 (-) LAMA and LABA LAMA and PDE4 (-)

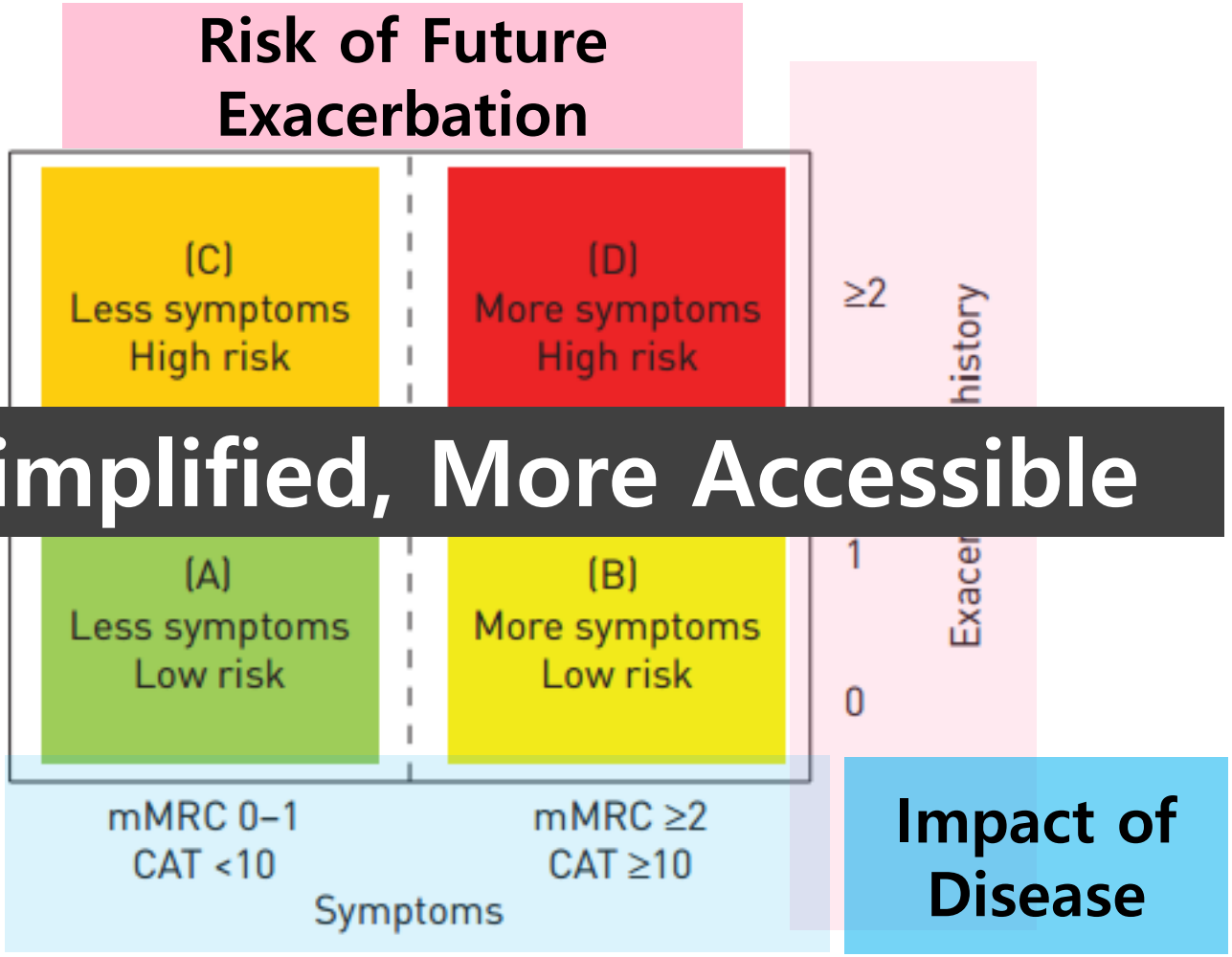
Cabera et al. Int J COPD 2016:11;1217

Agreement between a simple Sx guided treatment algorithm and the GOLD guidelines



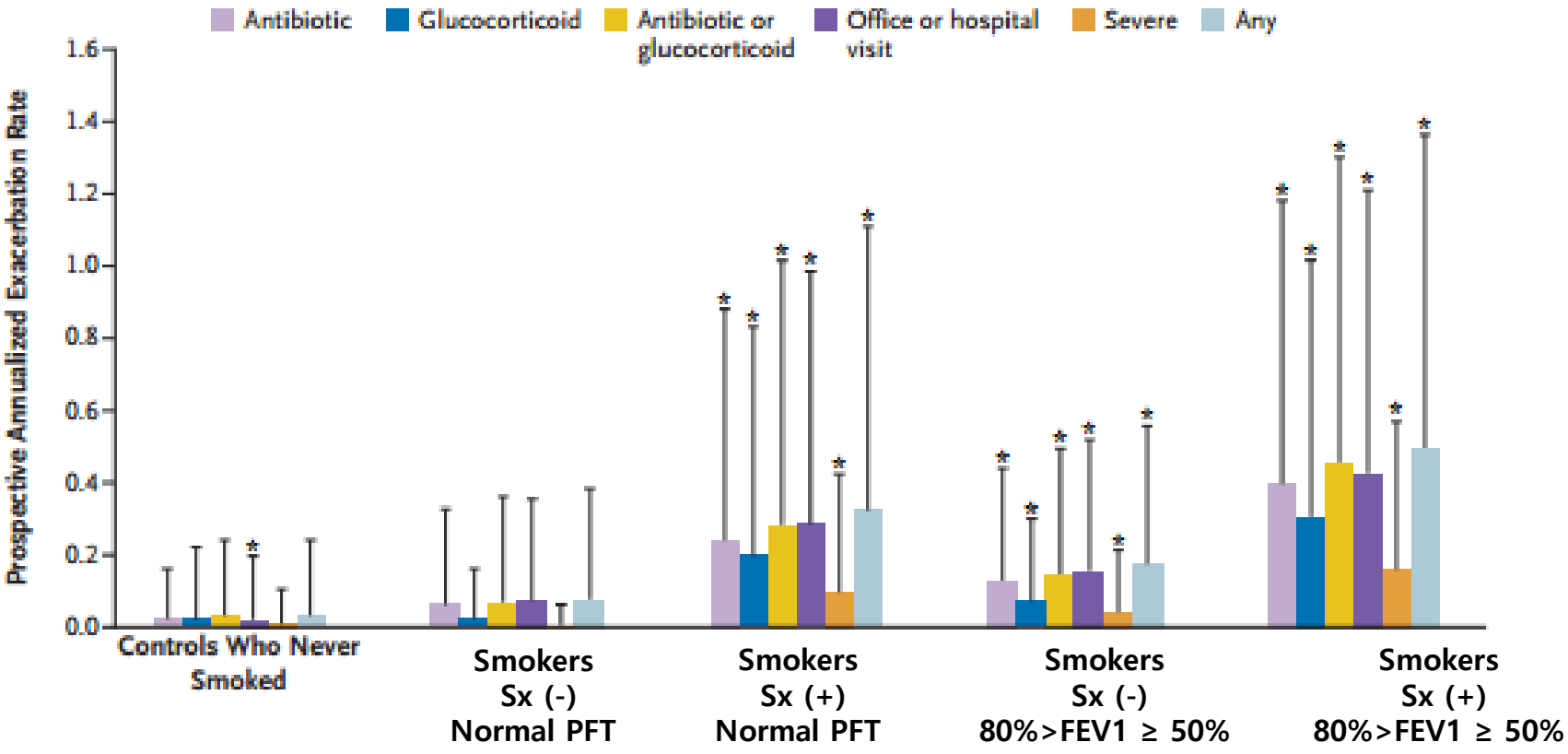
Cabera et al. Int J COPD 2016:11;1217

GOLD 2017



More Simplified, More Accessible

Clinical significance of Symptoms with preserved spirometry: SPIROMICS



Woodruff et al. N Engl J Med 2016;374:1811-21

FEV_1 removal is right because..

1. Pharmacologic Tx failed to modify disease progression (ie.FEV_1)
2. FEV_1 does not always deteriorate
   1) Severity and Activity
   2) Trajectory of lung function decline
   3) FEV_1 decline rate is greater in early COPD
3. Benefit of Revised Assessment system
   1) More personalized approach
   2) More simplified and more accessible
   3) Symptom is more important even in non obstructive lung disease

Contents

Summary

- FEV1은 COPD질환을 정의하고 예후를 예측하는 강력한 인자이나 개인의 예후를 예측하는 데에는 한계가 있다.
- 2017 GOLD update에서는 약물 치료를 위한 환자 평가시 FEV1은 고려하지 않도록 하였다.
- 개정된 환자 평가도구는 폐기능 검사를 할 수 없는 상황, 즉 악화 혹은 설비가 없는 경우에도 치료를 늦추지 않고 바로 시작할 수 있다.
- 개정된 평가도구는 기존 평가법에 비해서 개인 맞춤형 치료를 제공할 수 있다.

감사합니다

TABLE 2 Cox proportional hazards regression analyses for all-cause mortality and hospitalisati

Independent variable	Estimate
Mortality	
Forced expiratory volume in 1 s % predicted	0.982 (0.969–0.996
Age years	1.052 (1.021–1.085
Body mass index kg·m^{-2}	0.931 (0.882–0.983
Fat-free mass index kg·m^{-2}	1.146 (1.036–1.267
Number of comorbidities	1.100 (1.001–1.210
6-min walking distance m	0.997 (0.996–0.999
Hospitalisations	
Modified Medical Research Council dyspnoea score	1.246 (1.119–1.387
Forced expiratory volume in 1 s % predicted	0.974 (0.966–0.982
Exacerbations in previous 12 months	1.195 (1.123–1.270
Age years	1.021 (1.005–1.038
Body mass index kg·m^{-2}	0.979 (0.960–0.999
Hypertension	0.669 (0.526–0.851
Angina	0.565 (0.371–0.858
Osteoarthritis	0.695 (0.489–0.987
Diabetes	0.604 (0.392–0.932
Depression requiring treatment	0.657 (0.473–0.912
Number of comorbidities	1.209 (1.113–1.314
Arterial oxygen saturation %	0.929 (0.902–0.956

Data are presented as hazard ratio (95% confidence interval), unless otherwise stated.

Agusti et al. Eur Respir J 2013; 42: 636–646