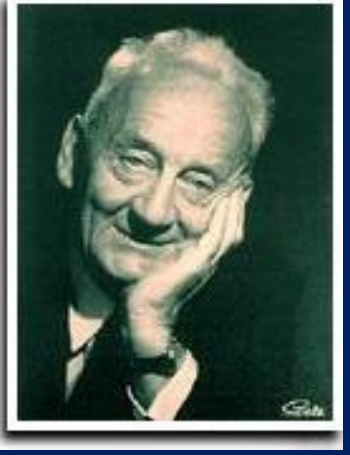


Újabb ismeretek COPD-ben

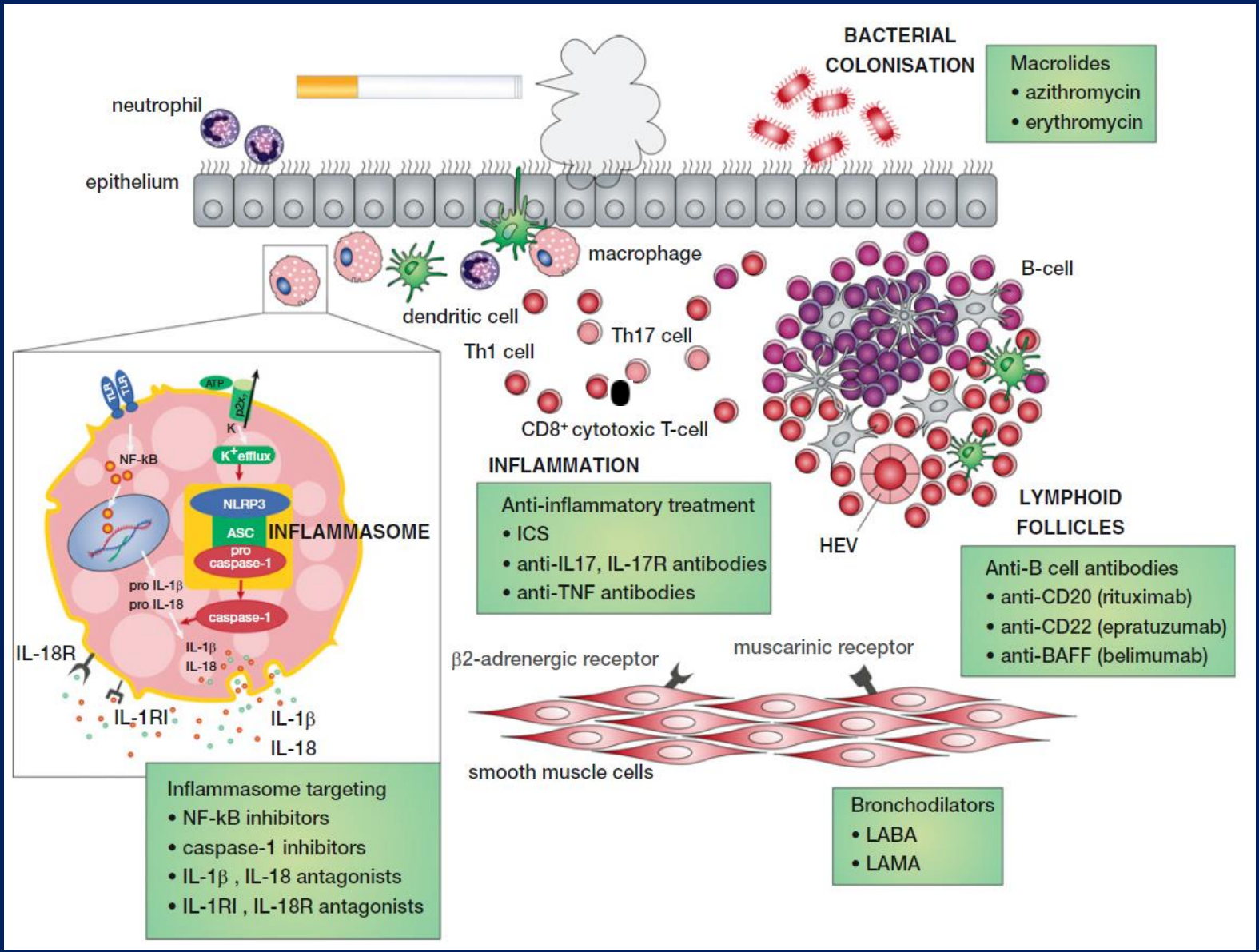
Somfay Attila

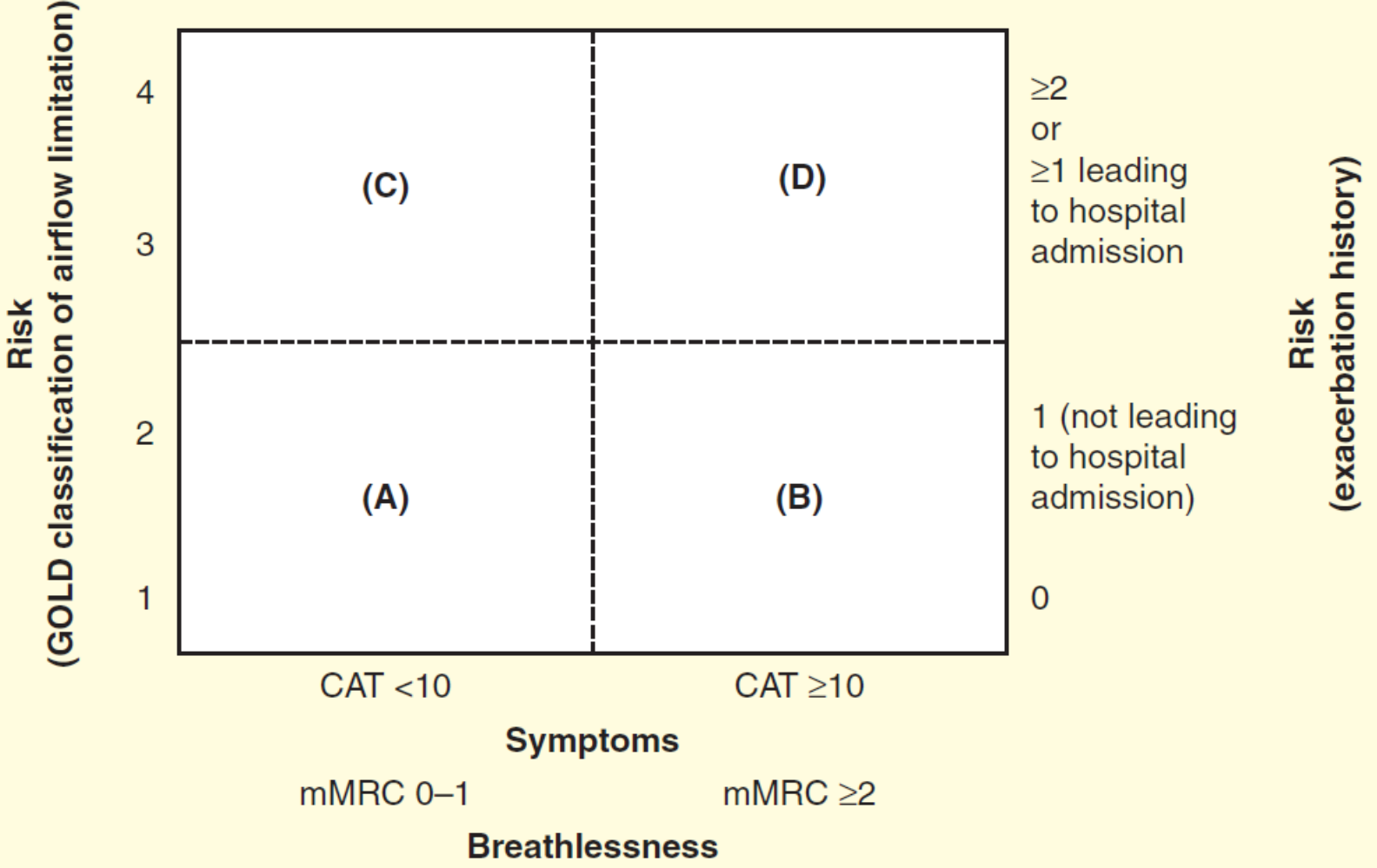
SZTE Tüdőgyógyászati Tanszék

MTT Továbbképzés
2015. január 23.

Patogenezis és terápiás célpontok

Brusselle, Ann ATS 2014



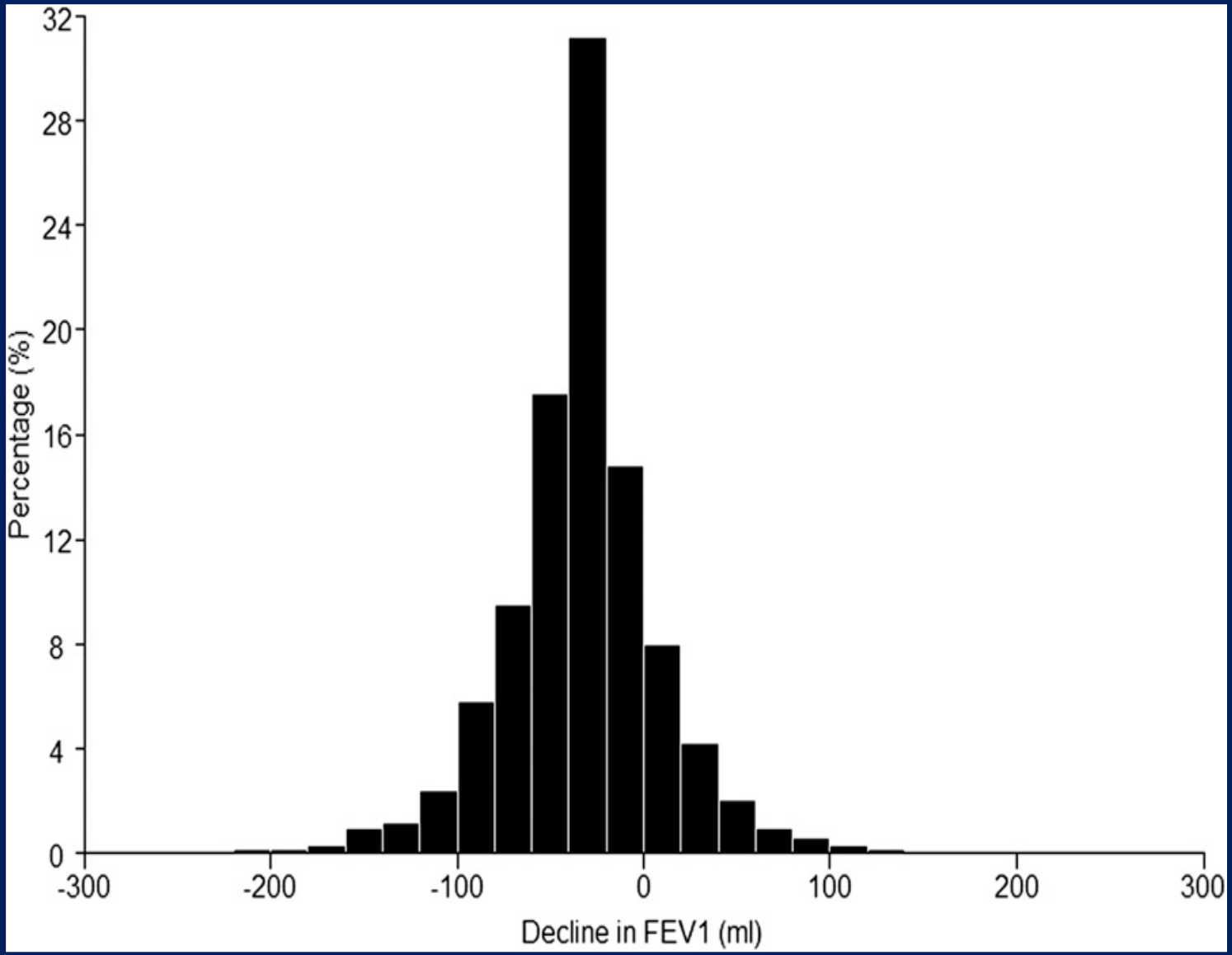


Patient category	Characteristics	Spirometric classification	Exacerbations per year	CAT	mMRC
A	Low risk, less symptoms	GOLD 1–2	≤1	<10	0–1
B	Low risk, more symptoms	GOLD 1–2	≤1	≥10	≥2
C	High risk, less symptoms	GOLD 3–4	≥2	<10	0–1
D	High risk, more symptoms	GOLD 3–4	≥2	≥10	≥2

GOLD 2014

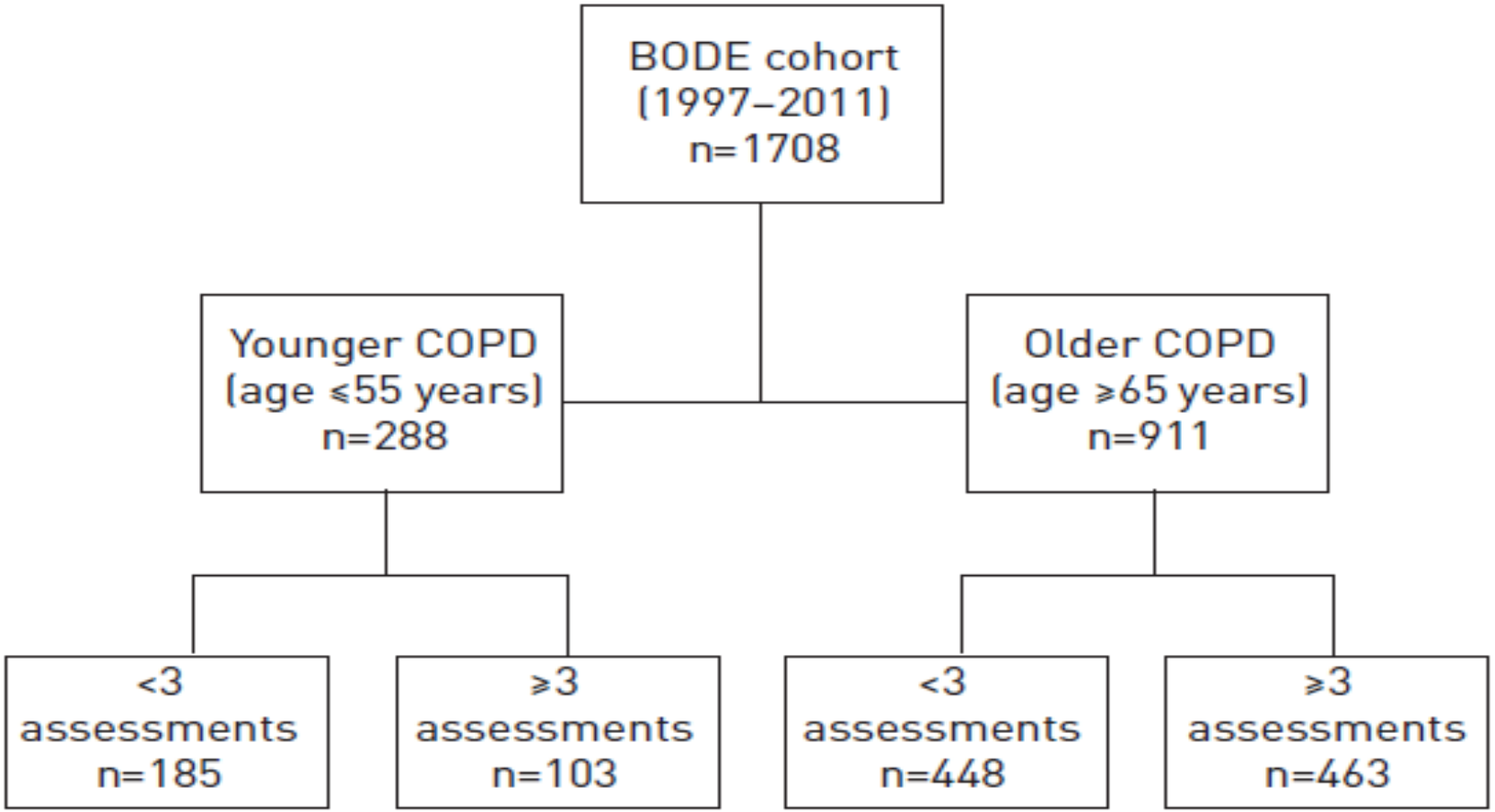
ECLIPSE: A COPD nem feltétlenül progresszív

Vestbo, AJRCCM 2014



Disease progression in young patients with COPD: rethinking the Fletcher and Peto model

Eur Respir J 2014; 44: 324–331



Sanchez-Salcedo, ERJ 2014

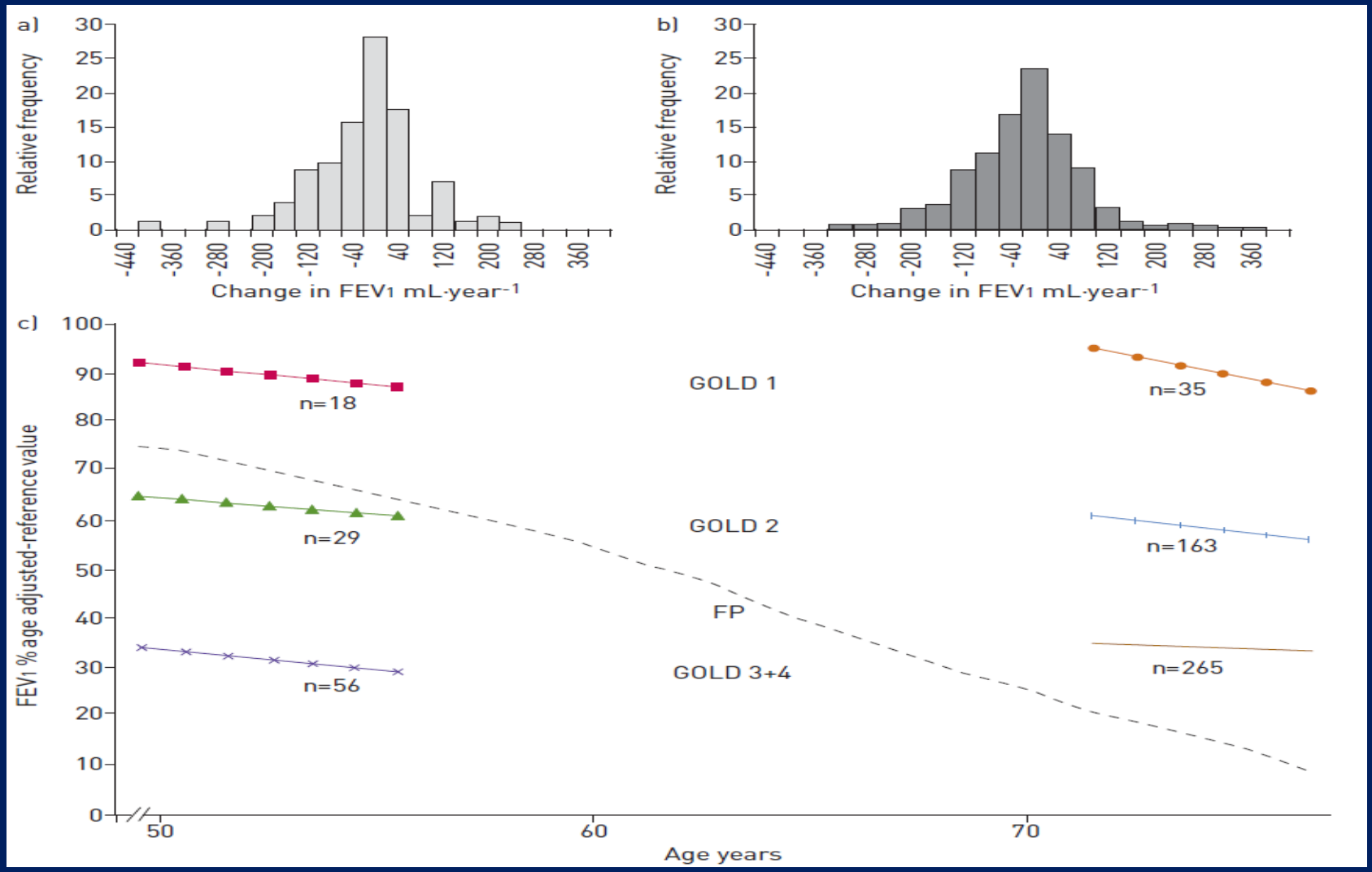
Variable	Younger COPD	Older COPD	p-value
Subjects n	103	463	
Baseline characteristics			
Age years	50±4	72±5	
Males	85	92	0.02
Follow up months	62 (43–98)	50 (36–69)	<0.001
Survival	90	65	<0.001
Active smoker	59	20	<0.001
FEV_1 % predicted	53±24	48±20	0.06
GOLD 1	17.4	7.6	0.002
GOLD 2	28.2	35.2	0.17
GOLD 3	37.9	41.0	0.55
GOLD 4	16.5	16.2	0.94
Assessments	4 (3–6)	4 (3–5)	0.01
Charlson index	2.3±1.5	5.0±2.5	<0.001
BODE index	3.4±2	4.1±2	0.049
Quartile 1	31	28	0.55
Quartile 2	39	30	0.13
Quartile 3	20	25	0.32
Quartile 4	10	17	0.14
Annual change			
FEV_1 mL·year^{-1}	-38.8±93	-40.6±96	0.86
FEV_1 % predicted	-0.75±3	-0.66±3.8	0.80
BODE index	0.19±0.5	0.23±0.6	0.42
Rapid decliners# >40 ml/év	42	46	0.41

A FEV1 vesztés üteme a kiindulási stádium függvényében

Sanchez-Salcedo, ERJ 2014

Fiatal: -38.8ml/év

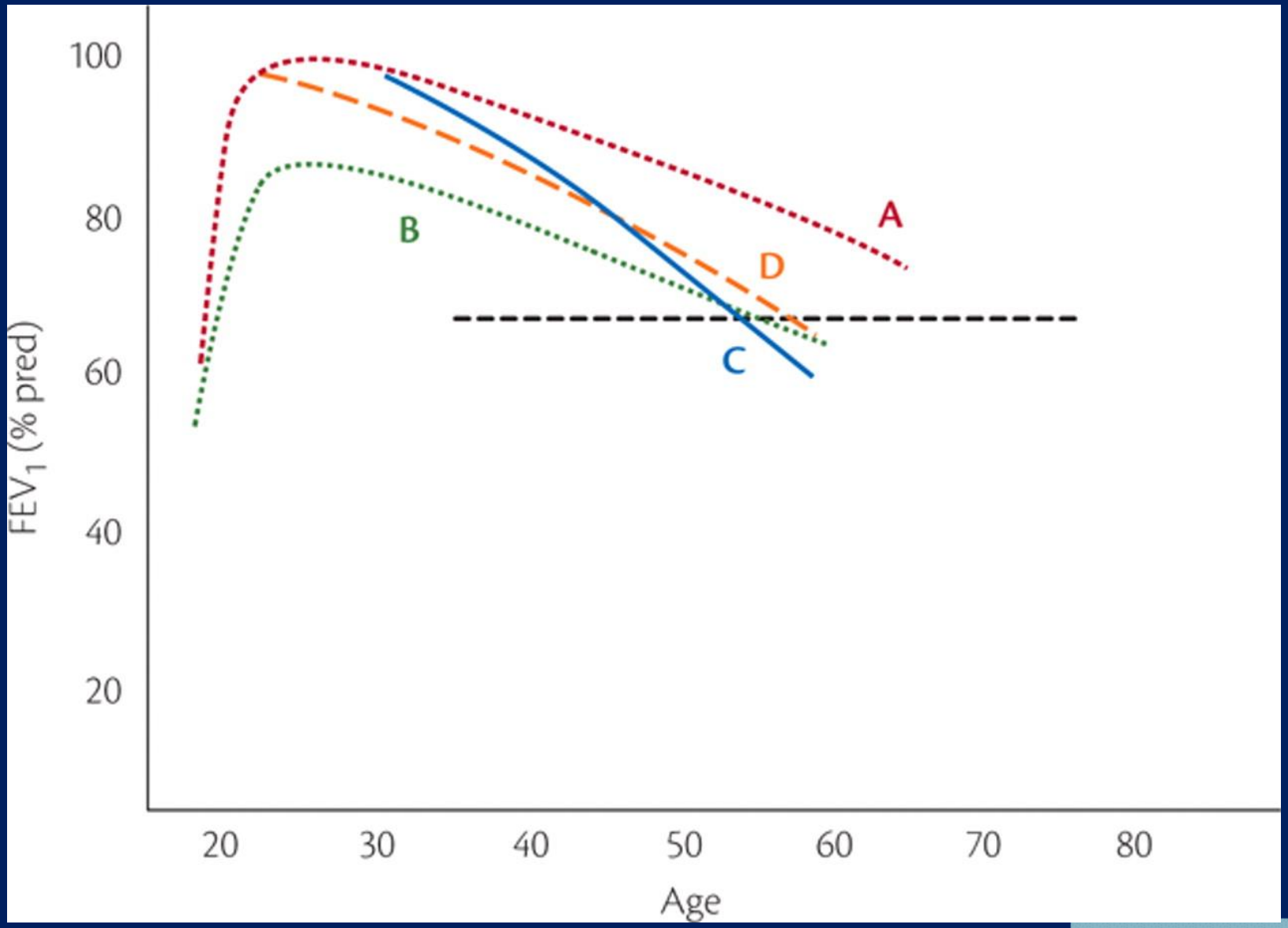
Idős: -40.6ml/év



Sanchez-Salcedo, ERJ 2014

A betegség súlyosbodása a fiatal is az idős csoportban azonos volt, ami arra utal, hogy funkcióvesztésre történő „érzékenyítés” már korábban megtörtént (tracking).

Funkcióvesztés különböző „genetika-környezet” kölcsönhatásban



MacNee, 2011

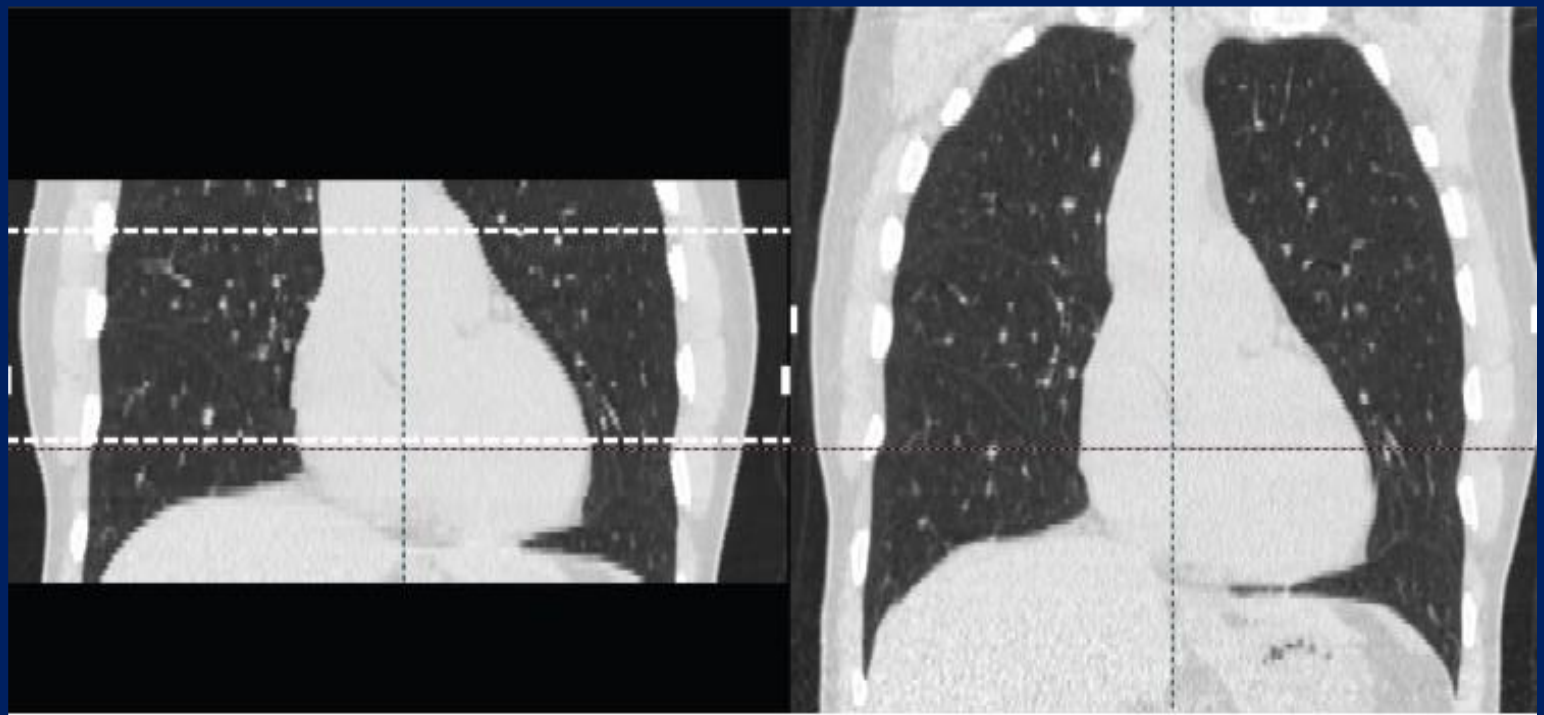
Annals of Internal Medicine 2014;161:863-873. | ORIGINAL RESEARCH

Association Between Emphysema-like Lung on Cardiac Computed Tomography and Mortality in Persons Without Airflow Obstruction

A Cohort Study

Elizabeth C. Oelsner, MD, MPH; Eric A. Hoffman, PhD; Aaron R. Folsom, MD, MPH; J. Jeffrey Carr, MD; Paul L. Enright, MD; Steven M. Kawut, MD, MS; Richard Kronmal, PhD; David Lederer, MD, MS; Joao A.C. Lima, MD; Gina S. Lovasi, PhD; Steven Shea, MD, MS; and R. Graham Barr, MD, DrPH

MESA study **n=2695**

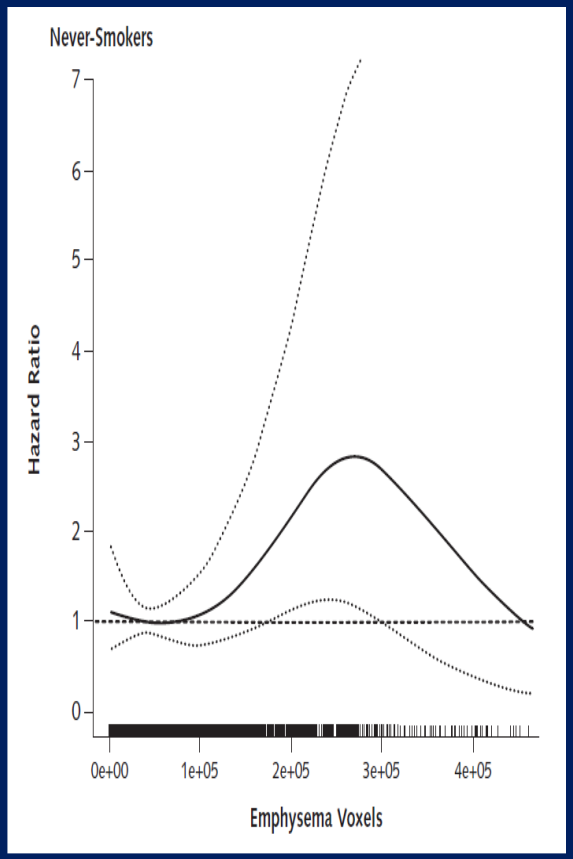


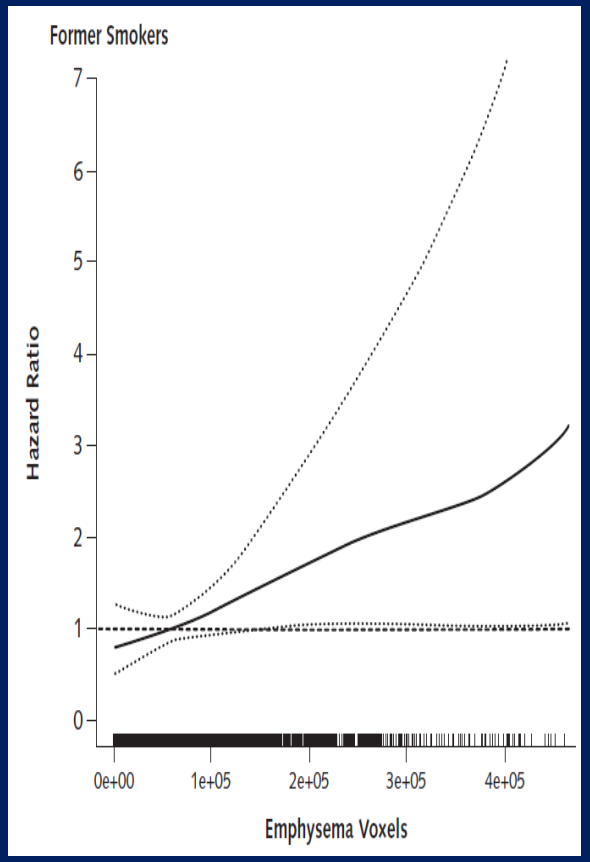
A mortalitás rizikója és az emphysema mértéke

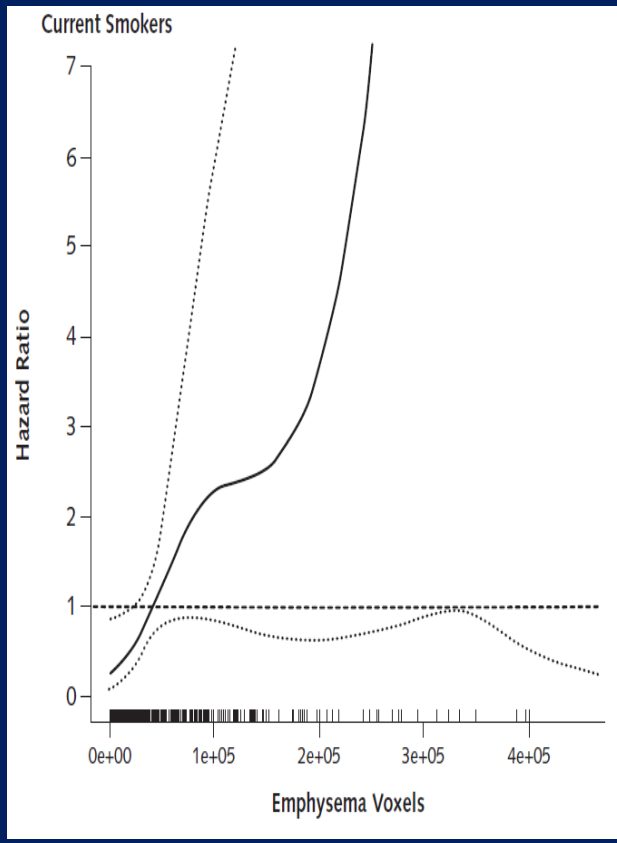
Oelsner, Ann Intern Med 2014

Mortalitás (1/1000 betegév)

9.26 **10.06** **13.18**

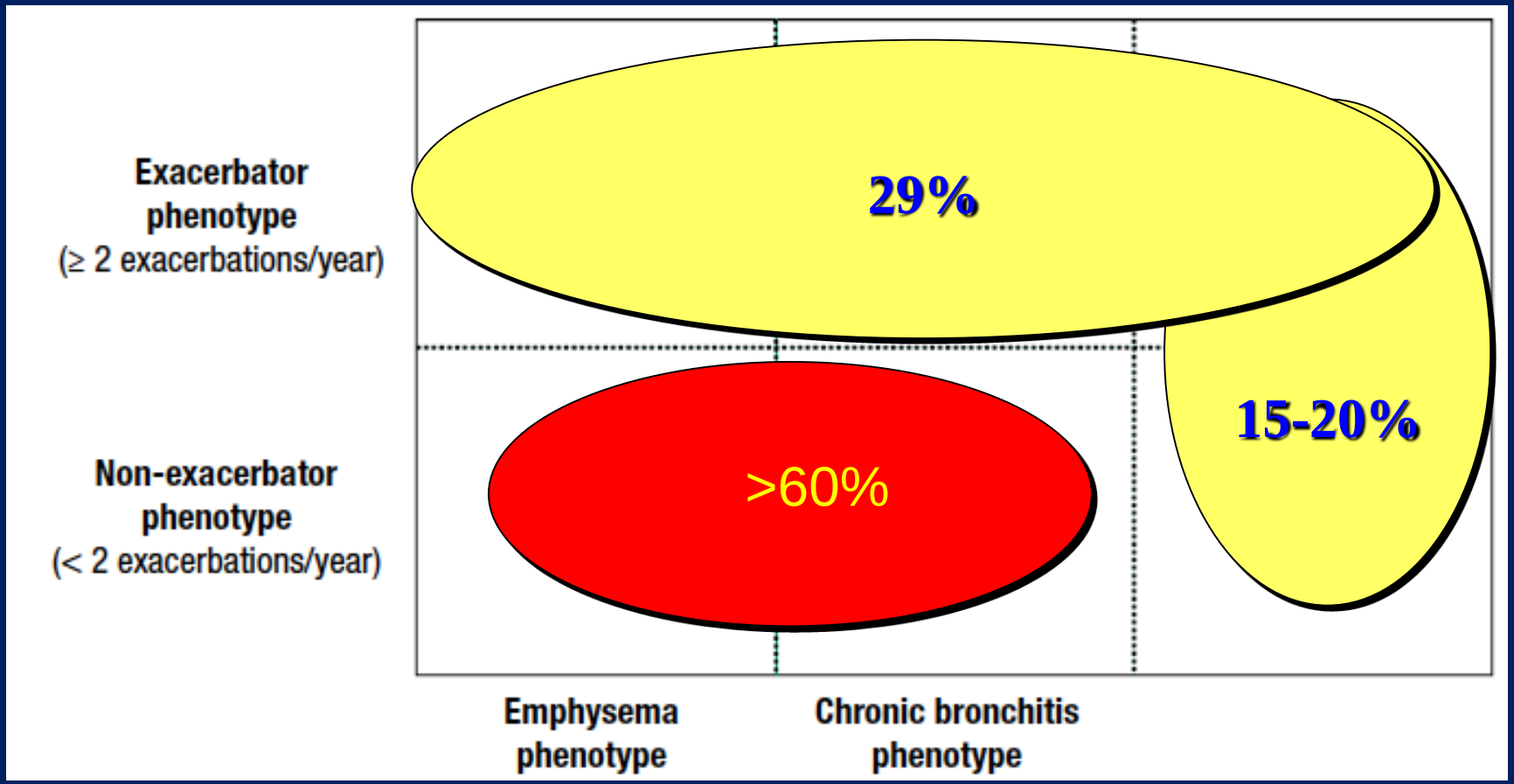






Spanyol COPD irányelv

Miravitlles, Arch Bronconeumol 2014



Prevalence and characteristics of three clinical phenotypes of chronic obstructive pulmonary disease (COPD)

Izquierdo-Alonso, Respir Med 2013

40 pulm. szakrendelés, random első 5 COPD-s beteg, 2 hónap alatt, n=344

Phenotype 1: EMPHYSEMA (at least one of the criteria) **43 %**

1. Pulmonary emphysema proved by CT.
2. Diffusion test with TLCO/VA values inferior to 80% and thorax radiography suggesting emphysema, according to the criteria described by Miniati et al.[36–38]

Phenotype 2: Chronic bronchitis.

1. Habitual coughing and expectoration (chronic bronchitis criteria).[4] **45 %**
2. Diffusion test with TLCO/VA values superior to 80%.
3. Absence of pulmonary emphysema demonstrated through imaging techniques, CT, or thorax radiography, according to the previous criteria.
4. Absence of asthma antecedents.

Phenotype 3: "COPD-asthma" **12 %**

1. Diffusion test with TLCO/VA values superior to 80%.
2. Absence of pulmonary emphysema demonstrated through imaging techniques, CT, or thorax radiography, according to the previous criteria.
3. Personal history of asthma before the age of 40.[6]

Klinikai jellemzők

Izquierdo-Alonso, Respir Med 2013

	Group 1	Group 2	Group 3	*p*
Age (years)	66 (9)	69 (9)	64 (10)	<0.05 (*, ***)
Sex (male %)	82.5	92.6	76.9	<0.05 (*, ***)
Packs/year	49 (23)	51 (25)	54 (32)	0.53
Active smoker (%)	29.8	24.8	28.9	0.63
Height (cm)	165 (7.7)	165 (8.2)	165 (7.4)	0.84
BMI (kg/m^2)	25 (4)	30 (5)	28 (4)	<0.001 (&)
FEV_1 (% predicted)	46.6 (21)	55.2 (21)	54.4 (21.8)	<0.05 (*)
FVC (% predicted)	72.8 (24)	71.3 (20)	73.2 (21)	0.85
FEV_1/FVC	48 (14)	58 (11)	58 (10)	<0.001 (*, **)
TLCO (%)	53 (24)	71 (21)	70 (20)	<0.001 (*, **)
TLCO/VA (%)	60 (25)	84 (20)	85 (24)	<0.001 (*, **)
PaO_2 (mmHg)	66 (11)	64 (9)	69 (11)	0.27
$PaCO_2$ (mmHg)	41 (6)	42 (7)	44 (5)	0.48
PH	7.42 (0.03)	7.42 (0.03)	7.42 (0.02)	0.95
Dyspnea (MRC)				
I	7.0%	14.2%	22.5%	<0.05 (*, **)
II	37.8%	48%	47.5%	
III	32.1%	27.7%	27.5%	
IV	18.9%	9.5%	2.5%	
V	4.2%	0.7%	0	

Exacerbáció és társbetegségek

Izquierdo-Alonso, Respir Med 2013

	Group 1	Group 2	Group 3	*p*
Exacerbations in the last year.	2.08 (1.38)	2.16 (1.30)	1.86 (1.21)	0.56
Patients with any exacerbation in the last year (%).	68.8%	63.9%	64.9%	0.25
Only one	44.8%	39.1%	50%	0.57
Two or more	55.2%	60.9%	50%	
No. of visits to the emergency room in the last year due to COPD.	1.73 (1.12)	1.76 (1.25)	1.69 (0.79)	0.43
Hospital admittances in the last year due to COPD exacerbation.	1.32 (0.67)	1.32 (0.78)	1.33 (0.71)	0.82
ICU admittances in the last year due to COPD exacerbation (% patients).	1.4%	4.8%	2.6%	0.26

	Group 1	Group 2	Group 3
Arterial hypertension (%)	32.6	60.8	33.3
Dyslipidemia (%)	28.6	41.4	25.6
Diabetes (%)	12	23.4	10.3
Cardiovascular disease (%)	6.3	13.5	15
Arrhythmia (%)	9.1	8.1	10
Cerebrovascular disease (%)	4.9	6.8	5.0
Peripheral vascular disease (%)	7.7	14.2	10
Cardiac insufficiency (%)	9.8	13.5	10
SAS (%)	4.9	23.6	12.5

Terápia

Izquierdo-Alonso, Respir Med 2013

	Group 1	Group 2	Group 3
Ipratropium	6.3	6.1	7.5
LABA	36.4	33.1	17.5
Inhaled corticoid (IC)	28	26.4	15
Tiotropium	85,3	83.8	77.5
LABA/IC	69.9	64.2	85
Theophylline	18.2	12.8	5
OCD	23.8	16.9	10
HMV	0.7	6.1	5
CPAP	2.1	13.5	7.5
ACE inhibitors	16.8	35.1	22.5
ARB II	14.4	25	7.5
Antiaggregants	18.2	25	17.5
Statins	27.3	34.5	25
Treatment against smoking	18.9	10.1	12.5

ACOS – klinikai jellegzetességek (COPDGene)

Hardin, ERJ 2014

Fenotipizálás CT-vel + genetika

	COPD	COPD and asthma	p-value
Subjects n	3120	450	
Age years	64.0±8.4	60.0±8.7	<0.001
Females	1335 (42.8)	252 (56)	<0.001
African-American	627 (20.1)	167 (37.1)	<0.001
Pack-years	54.2±27.8	45.7±25.1	<0.001
BMI $kg \cdot m^{-2}$	27.9±6.1	28.8±6.9	0.006
FEV_1 L	1.45±0.63	1.40±0.62	0.16
FEV_1 % predicted	50.3±18.0	50.3±17.9	0.95
FEV_1/FVC	0.49±0.13	0.51±0.13	0.02
Emphysema	13.54±12.95	9.93±11.5	<0.001
Bronchodilator responsiveness	1120 (36.13)	177 (39.42)	0.19
Absolute BDR L	0.09±0.16	0.11±0.16	0.11

ACOS – klinikum és CT (COPDGene)

Normálás: kor, nem, rassz, csomagév

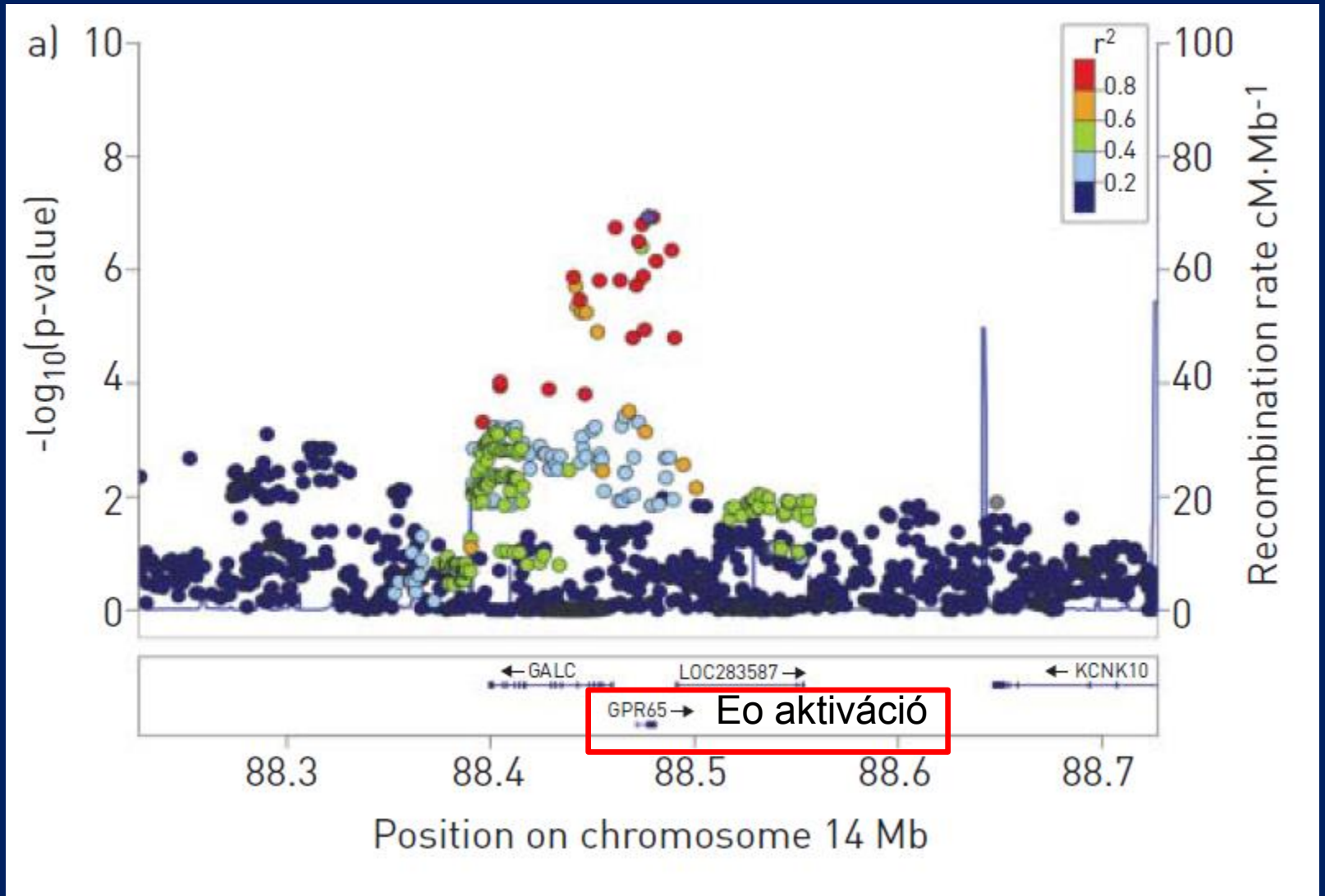
Hardin, ERJ 2014

	COPD	COPD and asthma	Effect size	p-value
Females	1335 (42.8)	252 (56.0)	1.59 (1.29–1.95)	<0.001
African-American	627 (20.1)	167 (37.1)	1.74 (1.39–2.18)	<0.001
Bronchodilator responsiveness	1120 (36.1)	177 (39.4)	1.19 (0.97–1.47)	0.10
Absolute BDR L	0.09 ± 0.16	0.11 ± 0.16	0.02 ± 0.008	0.03
BODE score	2.9 ± 2.1	3.1 ± 2.0	0.25 ± 0.1	0.02
SGRQ score	39.7 ± 21.5	47.4 ± 22.7	6.81 ± 1.1	<0.001
Exacerbations per year	0.7 ± 1.2	1.2 ± 1.6	0.56 ± 0.06	<0.001
Severe exacerbations	646 (20.7)	153 (34.0)	1.70 (1.36–2.12)	<0.001
Hay fever	442 (17.8)	186 (50.3)	4.66 (3.68–5.90)	<0.001
High school graduates	1828 (58.6)	261 (58.0)	1.10 (-0.19–0.39)	0.54
Maternal asthma	162 (7.0)	57 (19.0)	2.22 (1.59–3.12)	<0.001
Paternal asthma	123 (5.9)	47 (17.5)	2.64 (1.82–3.83)	<0.001
Log emphysema[#] %	1.91 ± 1.4	1.44 ± 1.6	-0.23 ± 0.07	<0.001
Pi10 mm	3.71 ± 0.14	3.78 ± 0.16	0.06 ± 0.01	<0.001
Segmental airway wall area %	62.8 ± 3.0	63.6 ± 3.3	0.61 ± 0.16	<0.001
Subsegmental airway wall area %	65.6 ± 2.3	66.4 ± 2.7	0.66 ± 0.20	0.001
Gas trapping[¶] %	39.7 ± 20.7	35.6 ± 21.5	0.88 ± 1.5	0.55

ACOS – genetika (COPDGene)

GWAS és SNP: 14-es és 8-as kromoszóma kaukázusiban, 1,4,7,8,10,13 afro-amerikaiban

Hardin, ERJ 2014



ACOS jellemzők (COPDGene)

Hardin, ERJ 2014

-nagyobb exacerbációs rizikó

- emiatt nagyobb mortalitás

-De ezt a spanyolok nem tapasztalták
(kisebb esetszám, kevesebb nő, csak kaukázusi rassz,
Izquierdo-Alonso et al. Prevalence and characteristics of three clinical phenotypes of COPD. Respir Med 2013; 107: 724–731)

-több a nő

- CT: kevesebb E, vastagabb légutak

ECLIPSE: Se eosinophilek

Singh, ERJ 2014

	Perzisztensen >2%	intermittáló	Perzisztensen <2%	ANOVA p
n	554	728	201	
Post BD FEV1 L	1.45	1.37	1.33	0.003
Post BD FVC L	3.20	3.05	3.01	0.005
FEV1 %	51	49	48	0.009
mMRC	1.4	1.6	1.7	0.006
SGRQ	44	47	49	0.002
d E (LAA%)	1.3	1.8	2.7	0.01

A dyspnoe kérdőív (mMRC)

Fokozat	A nehézlégzést kiváltó fizikai terhelés foka
0	Csak megerőltető terhelésre fullad
1	Légszomj, ha siet vagy enyhe emelkedőn megy fel
2	Vízszintes talajon a vele egykorúaknál lassabban megy nehézlégzés miatt, vagy saját ütemű séta során is meg kell állni légszomj miatt
3	vízszintesen haladva 100 m vagy néhány perc után meg kell állnia légszomj miatt
4	Az öltözködés nehézlégzést vált ki, vagy a lakását sem tudja elhagyni a légszomj miatt

A COPD állapotfelmérő teszt

Az Ön neve:_____

Mai dátum:_____

Milyen az Ön COPD betegséggel kapcsolatos közérzete? Kérjük, végezze el a COPD Állapotfelmérő Teszt™-et (COPD Assessment Test, CAT)
Az alábbi kérdőív alapján Ön és az Önt ellátó egészségügyi szakember jobban fel tudja majd mérni, hogy a COPD (krónikus obstruktív tüdőbetegség) milyen hatást gyakorol az Ön közérzetére és mindennapi életére. A válaszok és a tesztpontszám segítségével Ön és az Ön orvosa a kezelés minél nagyobb sikere érdekében jobban tudja majd kezelni az Ön COPD betegségét.

Minden alábbi megállapításnál ahhoz a számhoz tegyen (X) jelet, amelyik legjobban jellemzi az Ön aktuális állapotát. Fontos, hogy minden megállapításnál csak egy számot jelöljön be.

Példa: Nagyon boldog vagyok | 0 | X | 2 | 3 | 4 | 5 | Nagyon szomorú vagyok

			PONTSZÁM
Soha nem köhögök	0 1 2 3 4 5	Állandóan köhögök	☐
Egyáltalán nincs váladék (nyák) a légutaimban	0 1 2 3 4 5	A légutaim teljesen tele vannak váladékkal (nyákkal)	☐
Egyáltalán nem érzek mellkasi feszülést	0 1 2 3 4 5	Nagyon erős mellkasi feszülést érzek	☐
Emelkedőn felfelé vagy egy lépcsőfordulót megtéve nem fulladok	0 1 2 3 4 5	Emelkedőn felfelé vagy egy lépcsőfordulót megtéve nagyon fulladok	☐
A betegségem egyáltalán nem korlátoz az otthoni tevékenységeimben	0 1 2 3 4 5	Otthoni tevékenységem nagy mértékben korlátozott	☐
Tüdőbetegségem ellenére nyugodtan el merekmenni otthonról	0 1 2 3 4 5	Tüdőbetegségem miatt nem merek teljesen nyugodtan elmenni otthonról	☐
Mélyen alszom	0 1 2 3 4 5	Tüdőbetegségem miatt nem alszom mélyen	☐
Rengeteg az energiám	0 1 2 3 4 5	Teljesen erőtlen vagyok	☐
		ÖSSZESÍTETT PONTSZÁM	☐☐

Az ellenőrzés során a stabil, nem exacerbálódott betegekben kitöltendő minden megjelenés során és össze kell hasonlítani a korábbi értékekkel.

Az mMRC-vel hasonlóan kell eljárni.

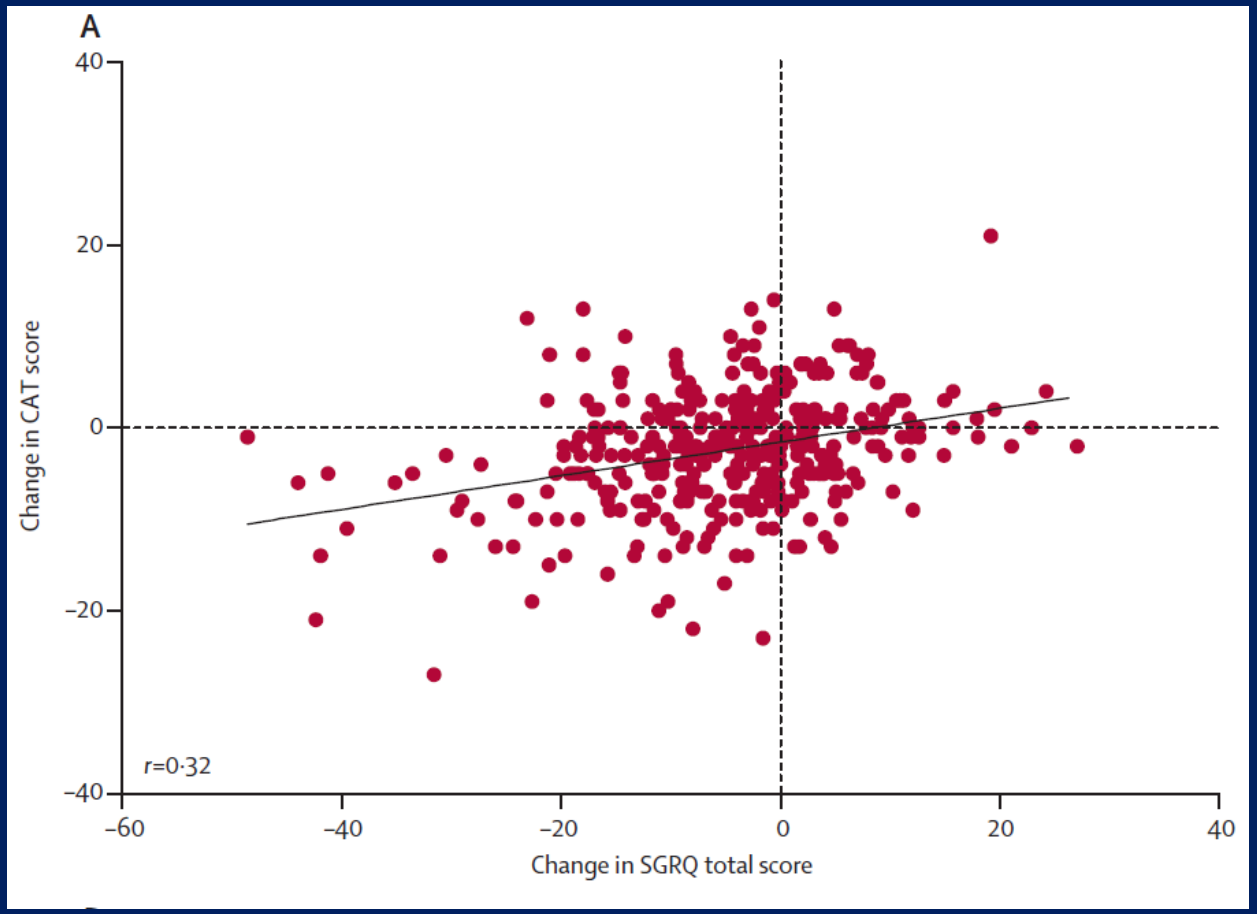
Így lehet megítélni az intervenció hatását a tünetekre, ami a beteg számára a legfontosabb végpont.

Minimum clinically important difference for the COPD Assessment Test: a prospective analysis

Lancet Respir Med 2014; 2: 195–203

Samantha S C Kon, Jane L Canavan, Sarah E Jones, Claire M Nolan, Amy L Clark, Mandy J Dickson, Brigitte M Haselden, Michael I Polkey, William D-C Man

1. 8 hetes ambuláns rehabilitáció előtt és után

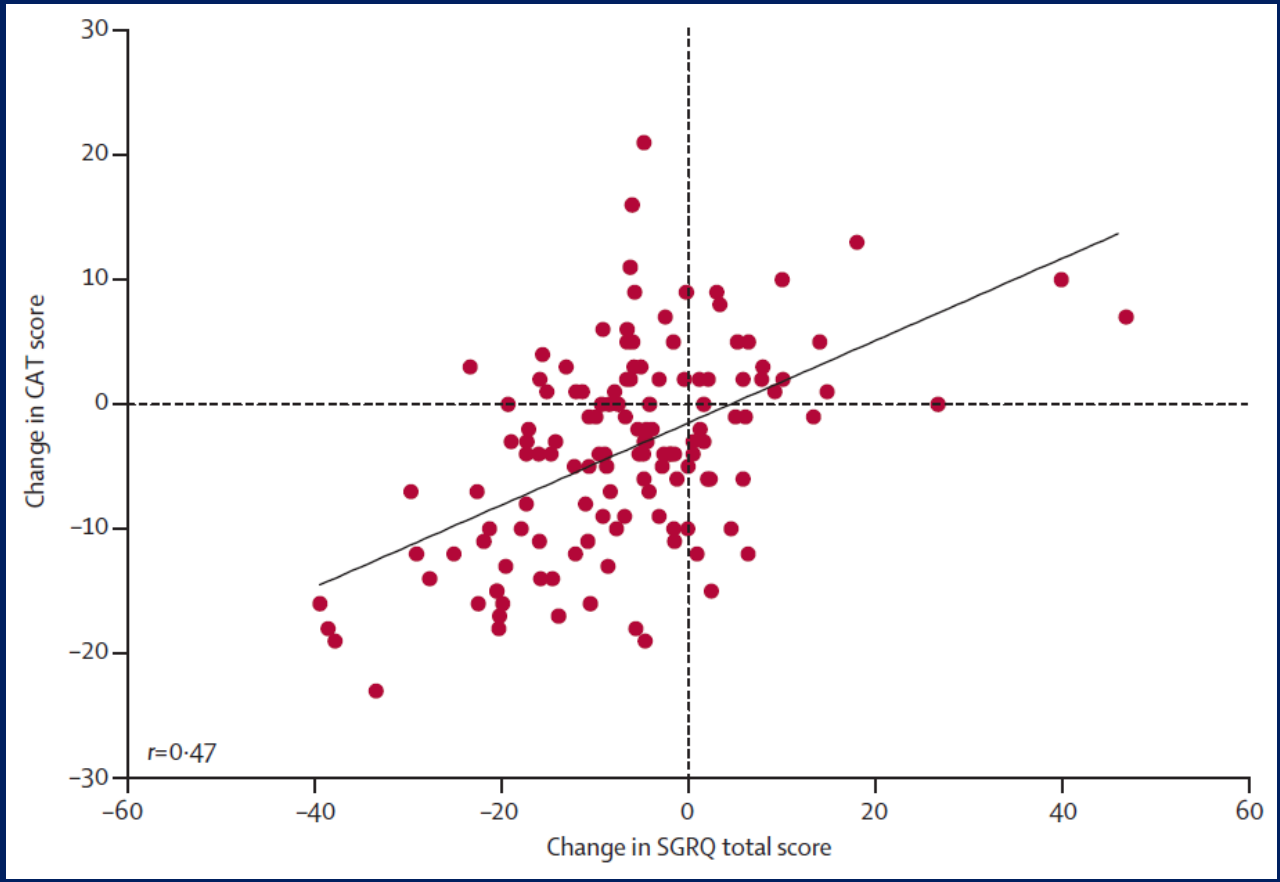


N=565
FEV_1%: 47.6 (45.9…49.3)
Kor: 70(9) év
CAT: 21.4 (20.8…22.0)
SGRQ: 51.0 (49.3…52.6)

Delta CAT:
-2.5 (-3…..-1.9)

Delta SGRQ:
-5.0 (-6.1…-3.8)

2. Súlyos excerbáció után elbocsájtáskor, majd 3 hónap múlva

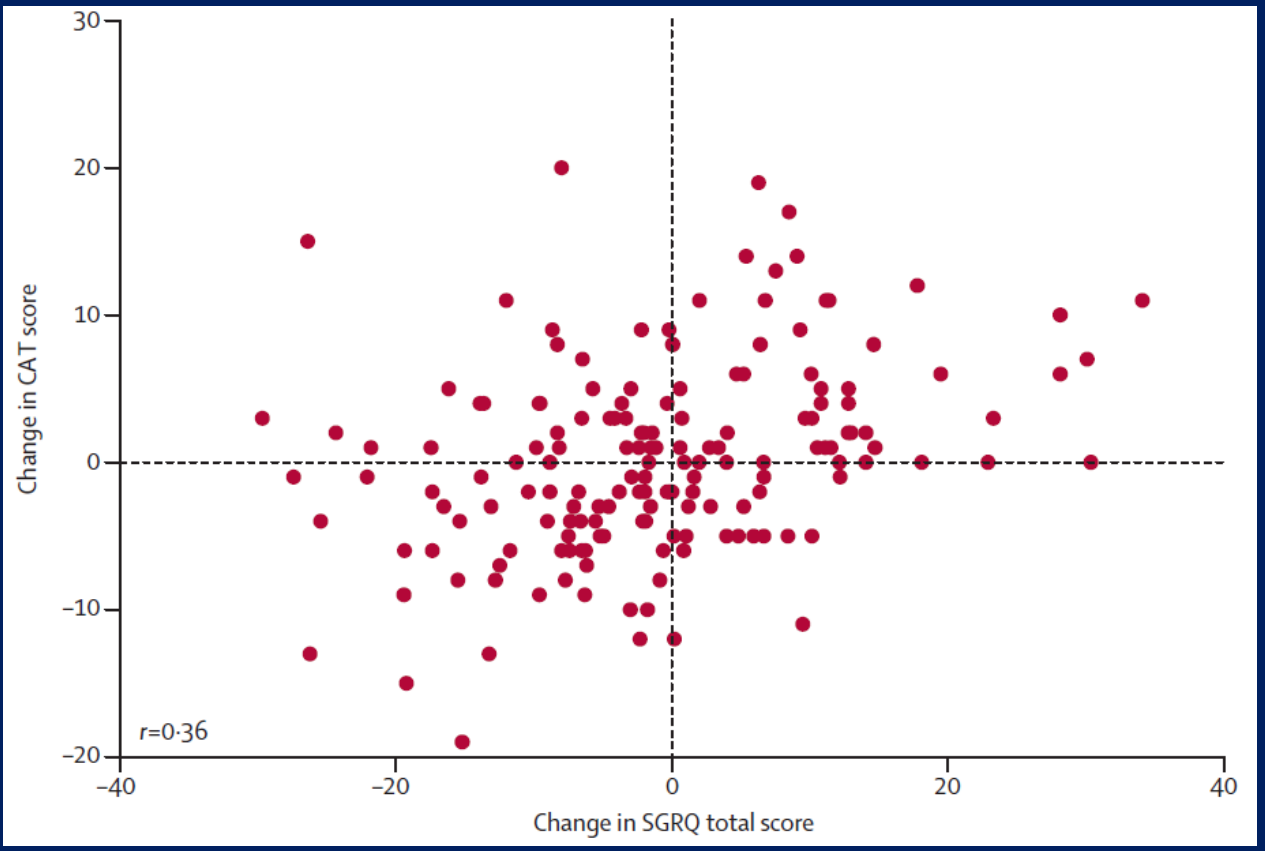


N=147
FEV_1%: 42 (39…46)
Kor: 71(11) év
CAT: 23.5 (22.3…24.8)
SGRQ: 57.1 (54.6…59.6)

Delta CAT:
-3 (-4.4…..-1.6)

Delta SGRQ:
-6.8 (-8.8…-4.9)

3. Stabil állapotban, majd 1 év múlva



N=164
FEV_1%: 47.6 (44.4…50.8)
Kor: 70(8) év
CAT: 20.1 (19.1…20.2)
SGRQ: 50.6 (40.8…53.1)

Delta CAT:
0.6 (-0.4...1.5)
Delta SGRQ:
-0.3 (-4.4…3.9)

Konklúzió

MCID CAT esetén: 2

A változás (delta CAT) a terápia hatékonyságának megítélésére alkalmas

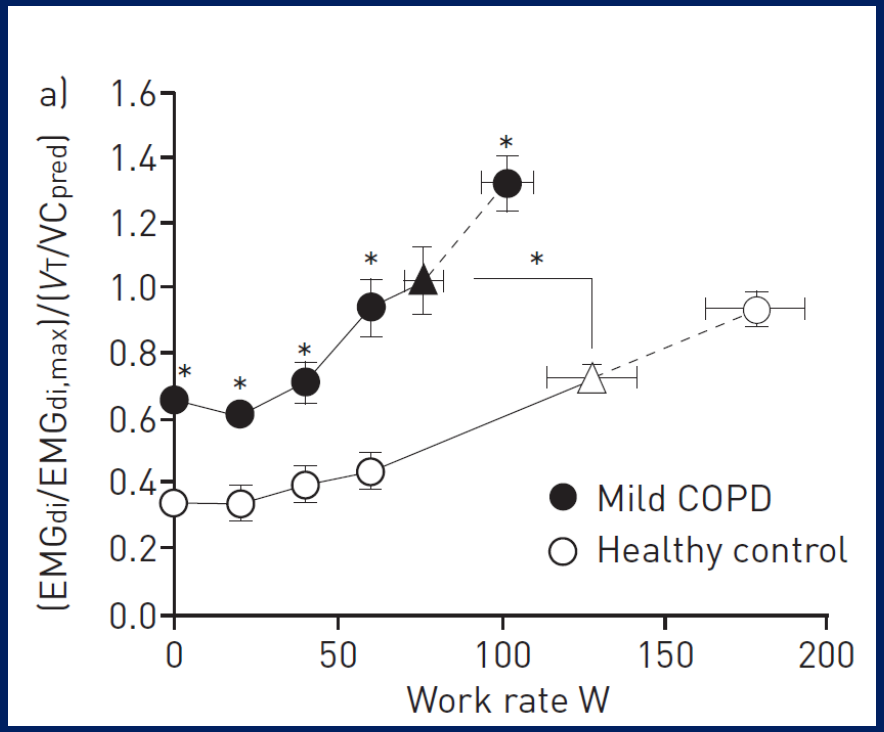
Terhelési intolerancia GOLD 1-ben

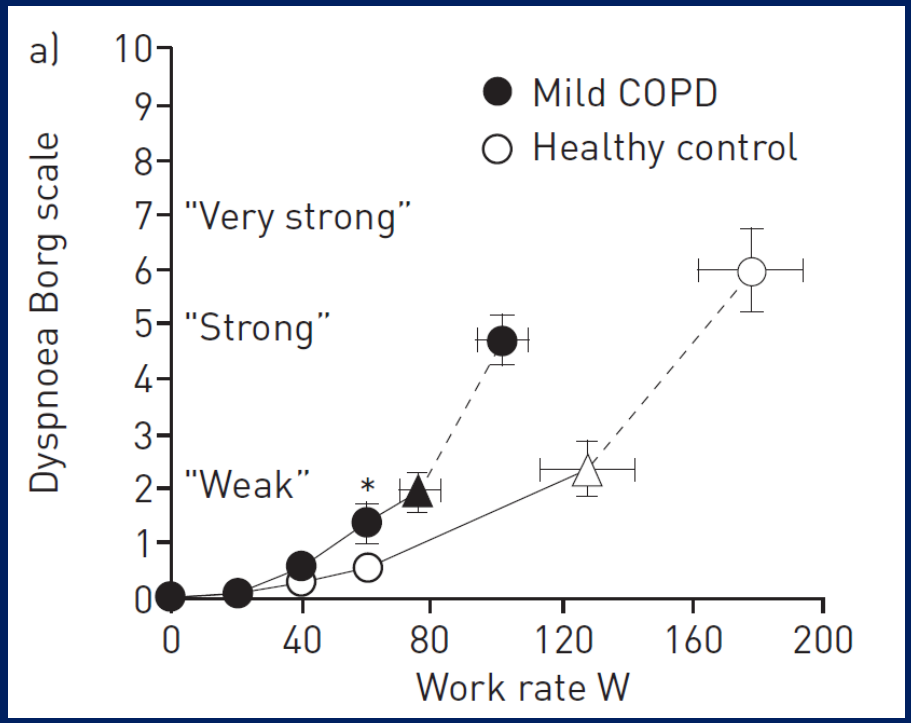
Guenette, ERJ 2014

	Controls	Mild COPD
Subjects, n	16	16
Males/females, n	8/8	8/8
Age years	63±9	67±7
Body mass index kg·m^{-2}	27.5±2.5	26.8±6.1
Smoking history pack-years	0.3±0.8	46.9±28.8***
Baseline Dyspnoea Index focal score	11.3±0.9	9.1±2.2**
Oxygen cost diagram mm	89±11	74±14**
COPD Assessment Test	4±4	13±8***
Peak incremental $V'O_2$ L·min^{-1}	2.55±0.88	1.61±0.48***
Peak incremental $V'O_2$ % predicted	114±27	80±14***
Peak incremental work rate W	178±62	102±30***
Peak incremental work rate % pred	116±21	76±20***
Pulmonary function		
Post-bronchodilatior		
FEV1 % pred	120±12	93±9***
FEV1/FVC %	77±5	63±4***

Neuromechanikai disszociáció GOLD 1-ben

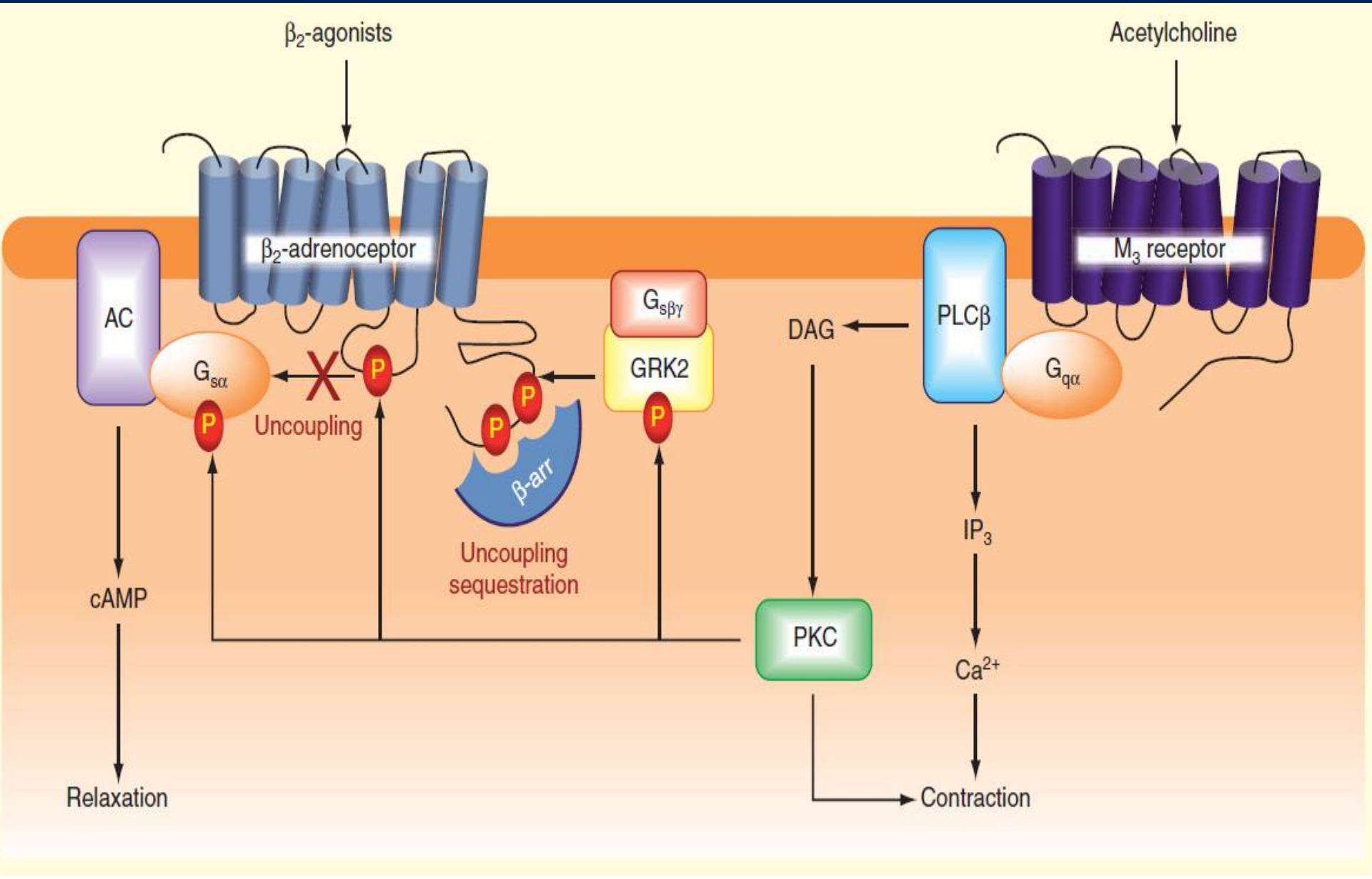
Guenette, ERJ 2014





Interakció az M3 és β2 adrenerg receptorok között

Bateman, Expert Rev Respir Med 2014



Paradox BD válasz- releváns fenotípus?

Bhatt, Lancet Resp Med 2014

-COPDGene;

-poszt BD ≥12% és 200mL FEV_1 vagy FVC csökkenés

- pozitív korreláció: afro-amerikai (7 vs 3%); CT-n légúti vastagabb légutak - kevesebb emphysema, rosszabb dyspnoe és terhelhetőség, gyakoribb exacerbáció

-ECLIPSE: reverzibilitás = rosszabb prognózis, de: E is rosszabb prognózis

- légúti instabilitás szerepe? – regionális VE javulás gázinhalációs MRI-vel, ami nem vezetett FEV_1 emelkedéshez !

(Kirby M, Mathew L, Heydarian M, Etemad-Rezai R, McCormack DG, Parraga G. Chronic obstructive pulmonary disease: quantification of bronchodilator effects by using hyperpolarized (3)He MR imaging. *Radiology 2011;* **261: 283–92).**

- ezen betegekben a BD kerülendő

Recommended first choice
Alternative choice

(C)	(D)
ICS + LABA, or LAMA LABA + LAMA or LABA + PDE-4i or LAMA + PDE-4i	**ICS + LABA +/or LAMA** ICS + LABA + PDE-4i or LABA + LAMA or LAMA + PDE-4i
SABA or SAMA p.r.n. LABA or LAMA or SABA + SAMA (A)	**LABA or LAMA** LABA + LAMA (B)

GOLD 2014

GOLD 2011 besorolás validálása

COPD Gene n = 4484 (2008 jan – 2011 ápr)

Han, Lancet Resp 2012

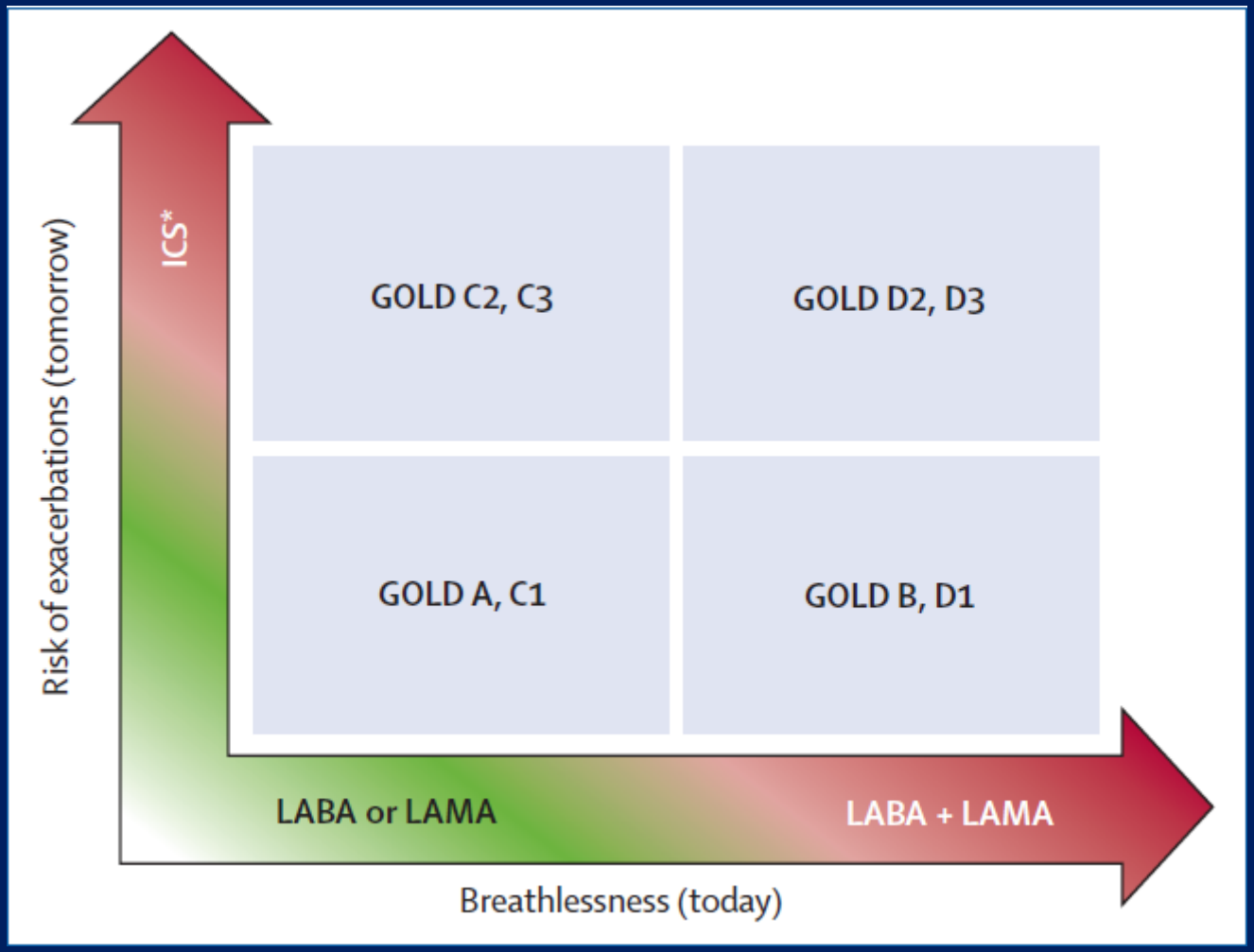
21 USA központ, 45-80 év, ≥ 10 csomagév

	mMRC classification system		CAT (SGRQ) classification method	
	mMRC 0–1	mMRC ≥2	SGRQ <25	SGRQ >25
Symptom category				
A	A (33·6% [1507])	..	A (29·4% [1317])	..
B	..	B (20·5% [919])	..	B (24·7% [1109])
C	C (7·9% [355])	..	C (4·9% [221])	..
D	..	D (38·0% [1703])	..	D (41·0% [1837])
Symptom subcategories				
C1*	C1 (5·8% [259])	..	C1 (3·9% [173])	..
C2†	C2 (1·5% [68])	..	C2 (0·8% [38])	..
C3‡	C3 (0·6% [28])	..	C3 (0·2% [10])	..
D1*	..	D1 (24·4% [1096])	..	D1 (26·4% [1182])
D2†	..	D2 (5·0% [222])	..	D2 (5·6% [252])
D3‡	..	D3 (8·6% [385])	..	D3 (9·0% [403])

BD – ICS terápia helye

(2 dimenziós állapotfelmérés)

Agusti, Lancet Resp Med 2014



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Withdrawal of Inhaled Glucocorticoids and Exacerbations of COPD

Helgo Magnussen, M.D., Bernd Disse, M.D., Ph.D., Roberto Rodriguez-Roisin, M.D., Anne Kirsten, M.D., Henrik Watz, M.D., Kay Tetzlaff, M.D., Lesley Towse, B.Sc., Helen Finnigan, M.Sc., Ronald Dahl, M.D., Marc Decramer, M.D., Ph.D., Pascal Chanez, M.D., Ph.D., Emiel F.M. Wouters, M.D., Ph.D., and Peter M.A. Calverley, M.D., for the WISDOM Investigators*

2014. szeptember 8.

GOLD 3 - 4 + legalább 1 dokumentált exacerbáció a megelőző évben

CÉL: Megmaradó LABA-LAMA kezelés mellett fokozatosan ICS elvonás hatásának elemzése

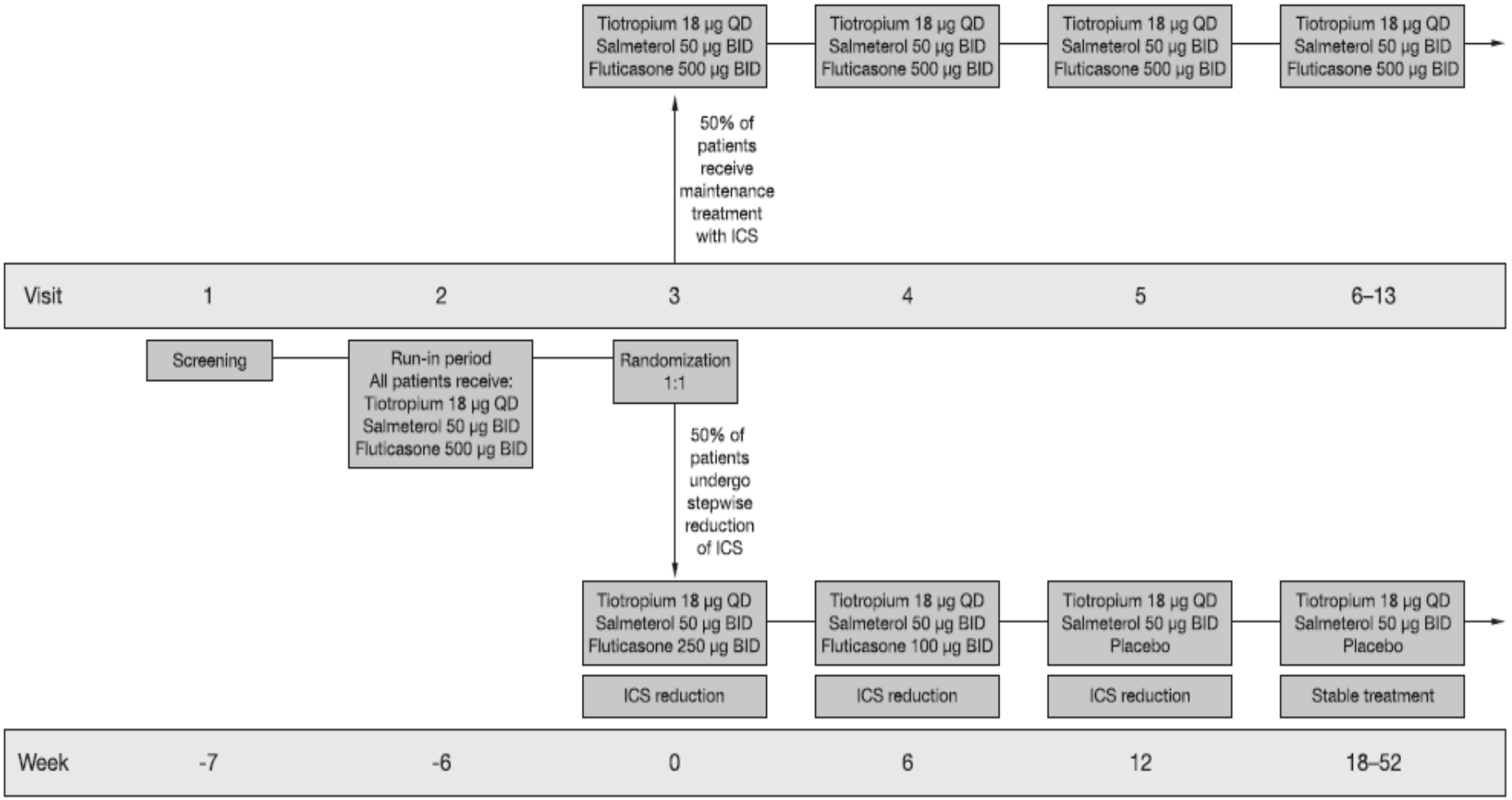
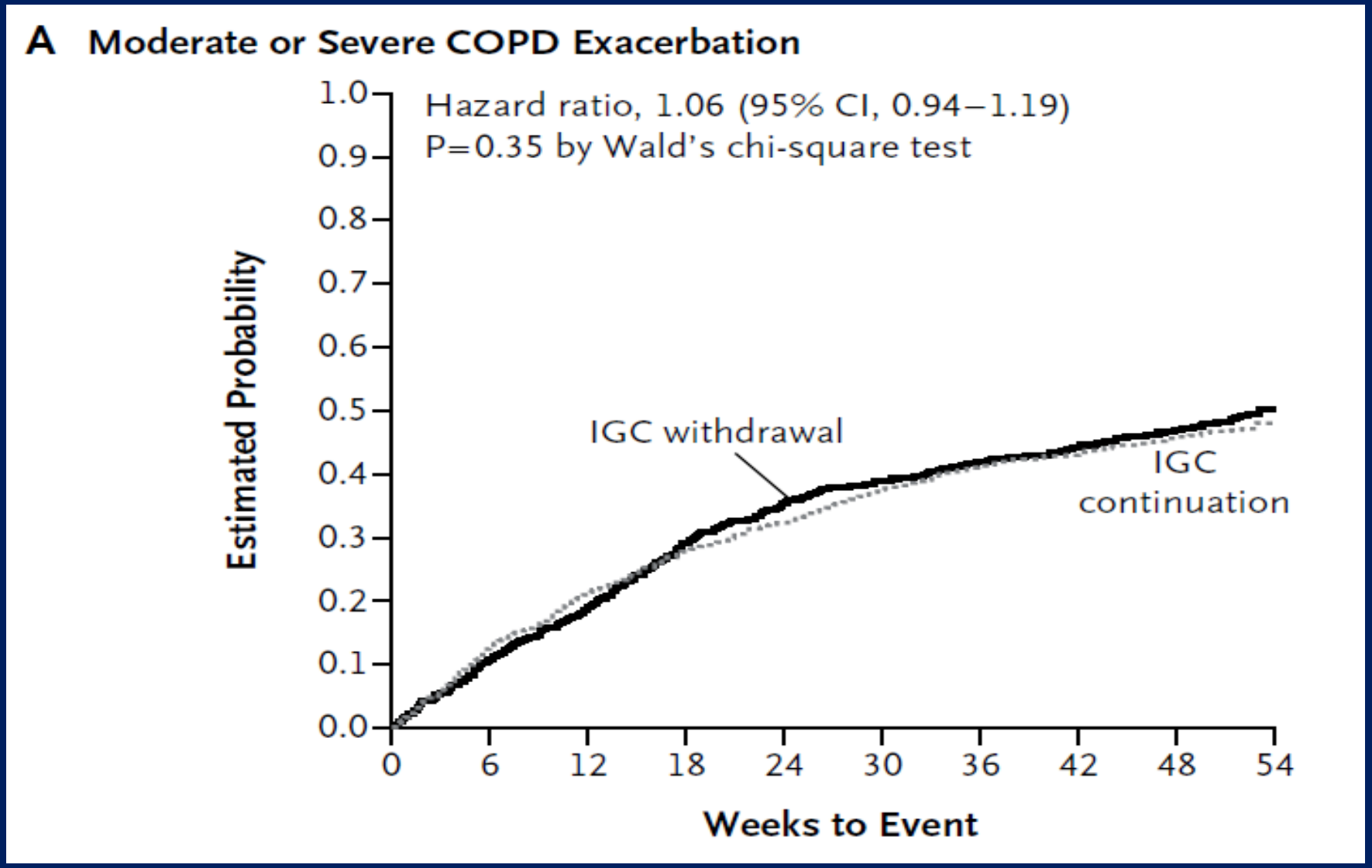
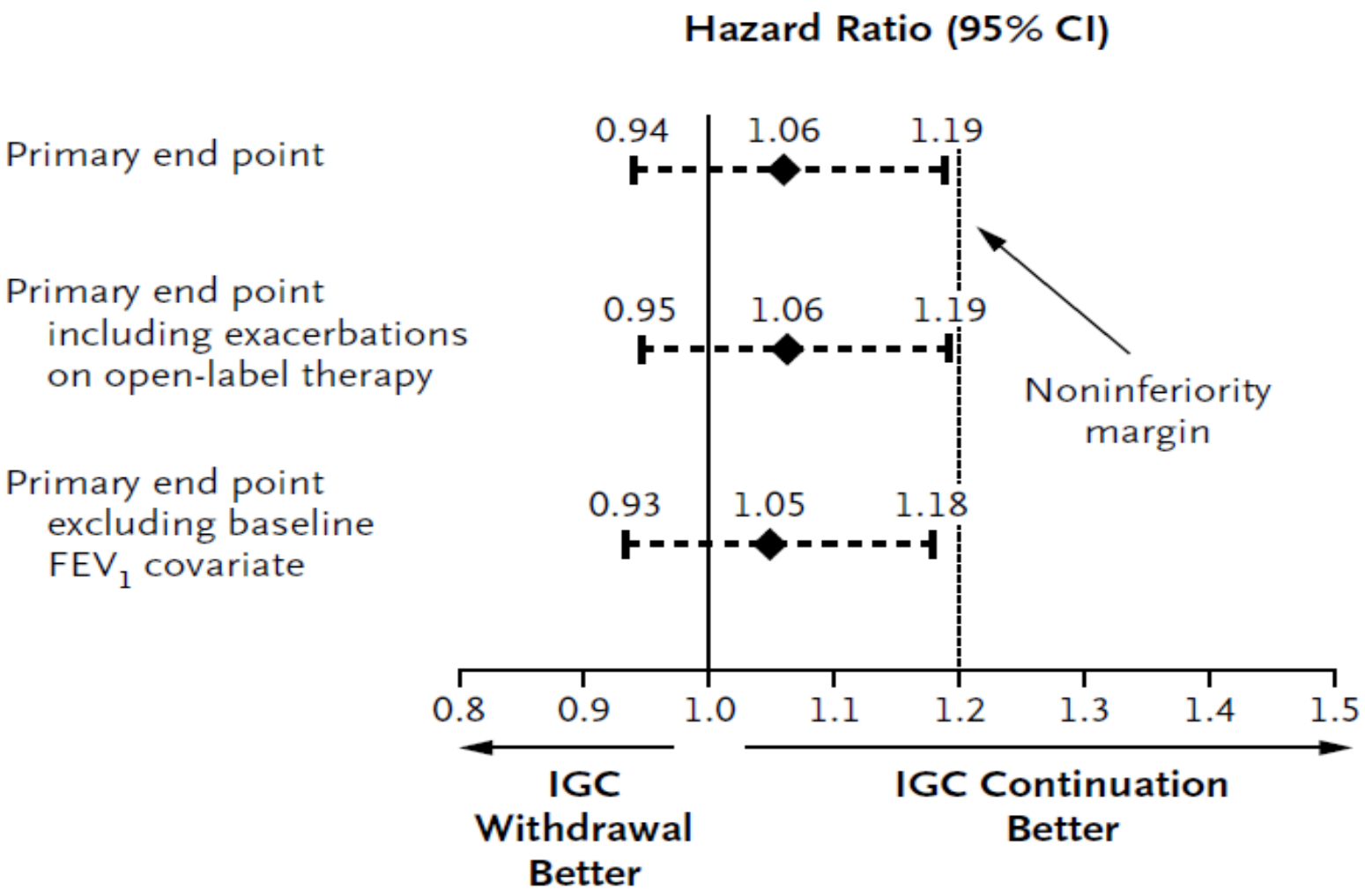


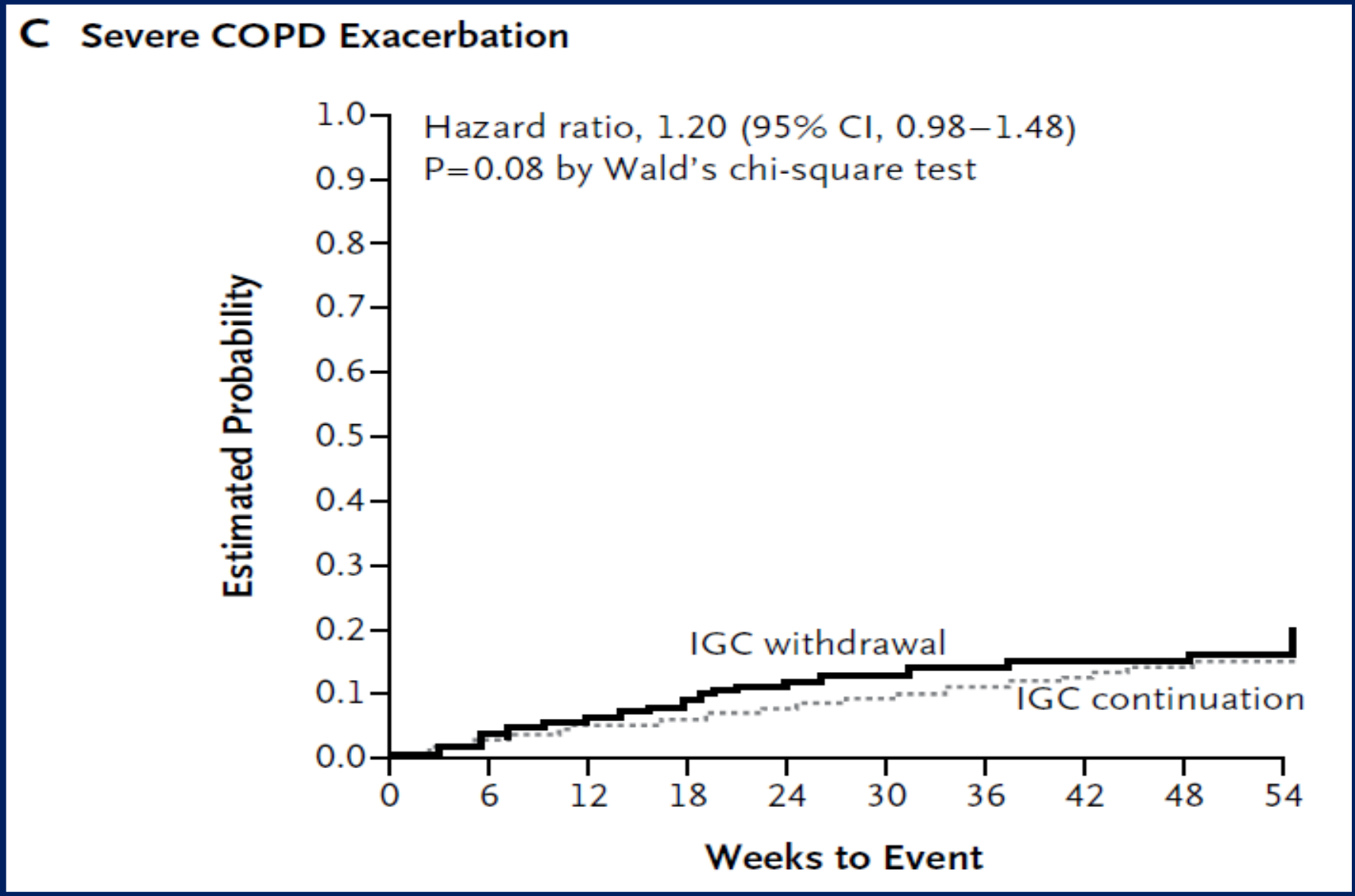
Table 1. Characteristics of the Patients at Baseline.*

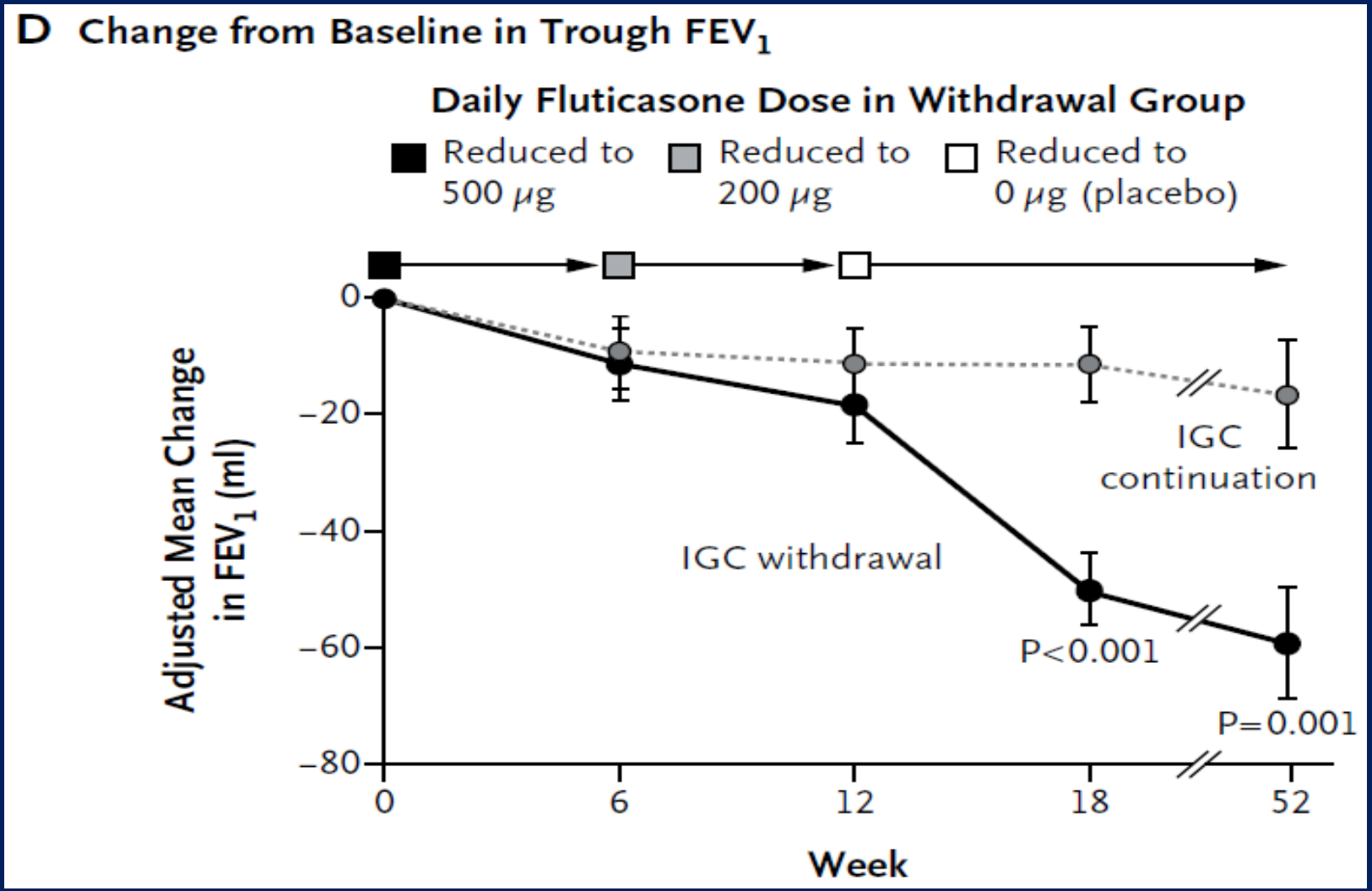
Characteristic	Glucocorticoid Continuation (N=1243)	Glucocorticoid Withdrawal (N=1242)	All Patients (N=2485)
Male sex — no. (%)	1013 (81.5)	1036 (83.4)	2049 (82.5)
Age — yr	63.6±8.6	64.0±8.4	63.8±8.5
Former smoker — no. (%)†	811 (65.2)	843 (67.9)	1654 (66.6)
Duration of COPD — yr	7.75±5.99	8.00±6.47	7.87±6.23
Percentage of predicted FEV_1 after bronchodilation — no. (%)			
30–49%: GOLD 3	760 (61.1)	761 (61.3)	1521 (61.2)
<30%: GOLD 4	473 (38.1)	474 (38.2)	947 (38.1)
Other category‡	10 (0.8)	7 (0.6)	17 (0.7)
Baseline lung function§			
Patients with available data — no.	1223	1218	2441
FEV_1			
Value — liters	0.97±0.36	0.98±0.36	0.98±0.36
Percentage of predicted value	34.2±11.2	34.3±10.8	34.2±11.0
Score on mMRC scale¶			
Patients with available data — no.	1238	1237	2475
Mean score	1.8±0.9	1.9±0.9	1.8±0.9
SGRQ score‖			
Patients with available data — no.	1136	1126	2262
Mean score	46.35±17.89	45.91±18.19	46.13±18.04
Medication use — no. (%)			
LAMA	588 (47.3)	578 (46.5)	1166 (46.9)
LABA	807 (64.9)	798 (64.3)	1605 (64.6)
Inhaled glucocorticoid	876 (70.5)	862 (69.4)	1738 (69.9)
Triple therapy with LAMA, LABA, and inhaled glucocorticoid, with or without other pulmonary medication — no. (%)**	479 (38.5)	491 (39.5)	970 (39.0)

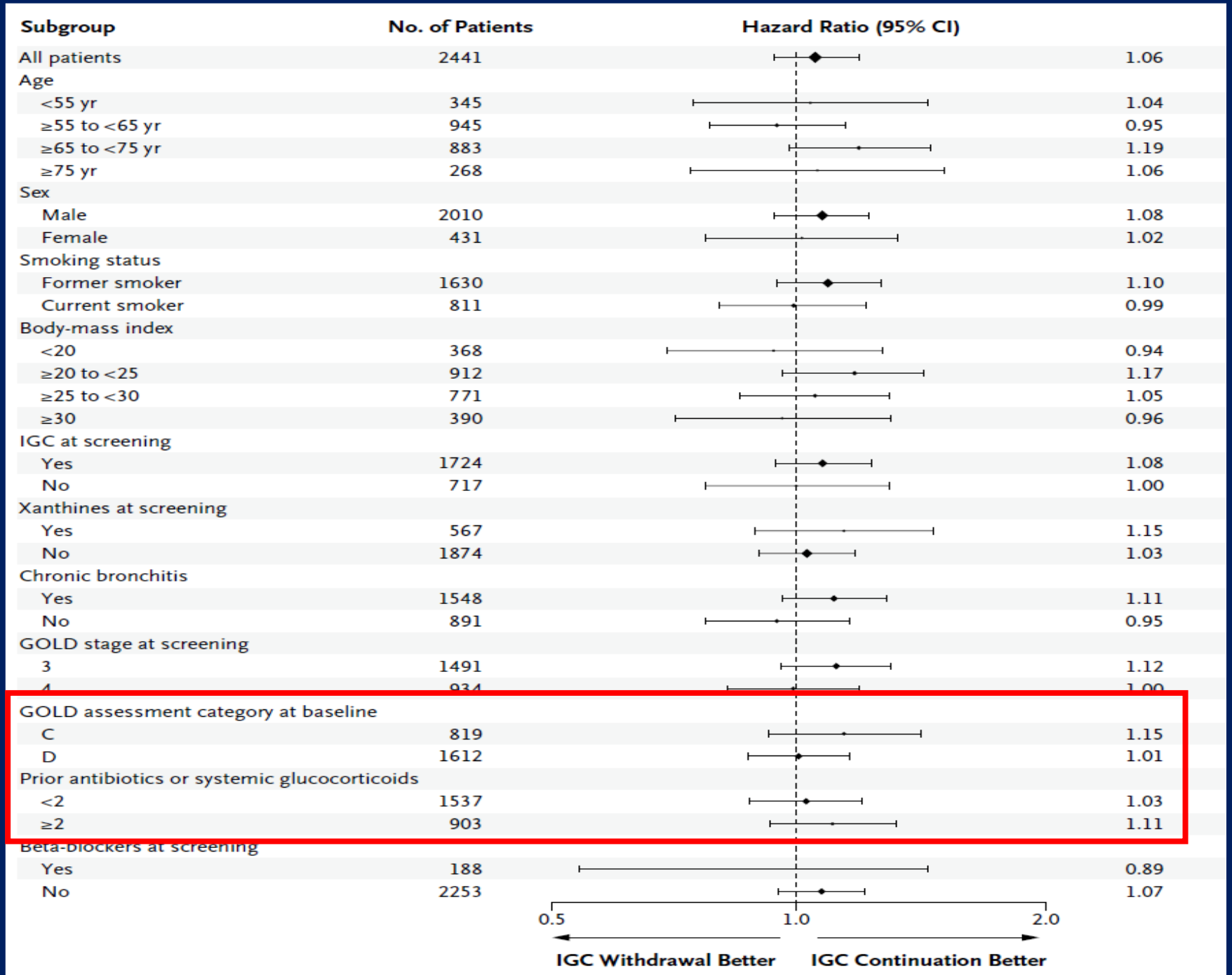

A Moderate or Severe COPD Exacerbation
Hazard ratio, 1.06 (95% CI, 0.94–1.19)
P=0.35 by Wald's chi-square test
Estimated Probability
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
IGC withdrawal
IGC continuation
0
6
12
18
24
30
36
42
48
54
Weeks to Event

B **Primary End Point and Sensitivity Analyses**




C Severe COPD Exacerbation
Hazard ratio, 1.20 (95% CI, 0.98–1.48)
P=0.08 by Wald's chi-square test
Estimated Probability
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
IGC withdrawal
IGC continuation
0
6
12
18
24
30
36
42
48
54
Weeks to Event


D Change from Baseline in Trough FEV1
Daily Fluticasone Dose in Withdrawal Group
Reduced to 500 μg
Reduced to 200 μg
Reduced to 0 μg (placebo)
Adjusted Mean Change in FEV1 (ml)
0
−20
−40
−60
−80
IGC continuation
IGC withdrawal
P<0.001
P=0.001
0
6
12
18
52
Week


Subgroup
No. of Patients
Hazard Ratio (95% CI)
All patients 2441 1.06
Age
<55 yr 345 1.04
≥55 to <65 yr 945 0.95
≥65 to <75 yr 883 1.19
≥75 yr 268 1.06
Sex
Male 2010 1.08
Female 431 1.02
Smoking status
Former smoker 1630 1.10
Current smoker 811 0.99
Body-mass index
<20 368 0.94
≥20 to <25 912 1.17
≥25 to <30 771 1.05
≥30 390 0.96
IGC at screening
Yes 1724 1.08
No 717 1.00
Xanthines at screening
Yes 567 1.15
No 1874 1.03
Chronic bronchitis
Yes 1548 1.11
No 891 0.95
GOLD stage at screening
3 1491 1.12
4 934 1.00
GOLD assessment category at baseline
C 819 1.15
D 1612 1.01
Prior antibiotics or systemic glucocorticoids
<2 1537 1.03
≥2 903 1.11
Beta-blockers at screening
Yes 188 0.89
No 2253 1.07
0.5
1.0
2.0
IGC Withdrawal Better
IGC Continuation Better

Kétségek

- Rövid ICS nélküli időszak (kevesebb, mint 1 év), mi történik utána?
- A non-inferioritás HR=1.20 határa megfelelő-e? (Általában 20% körüli AE csökkenés a korábbi ICS vizsgálatokban)
- Súlyos AE átmeneti fokozódása
- Stabil, AE nélküli betegek kizárva: mi lesz az elvonás hatása ezekben (logikusan elvégezhető lenne)…INSTEAD válasz
- Stabil állapotban Se v. köpet Eo (20-30%) hatása?

INSTEAD: a randomised switch trial of indacaterol *versus* salmeterol/fluticasone in moderate COPD

Andrea Rossi[1], Thys van der Molen[2], Ricardo del Olmo[3], Alberto Papi[4], Luis Wehbe[5], Matthew Quinn[6], Chengxing Lu[6], David Young[7], Ray Cameron[7], Enrica Bucchioni[8] and Pablo Altman[6]

ERJ, 2014. december

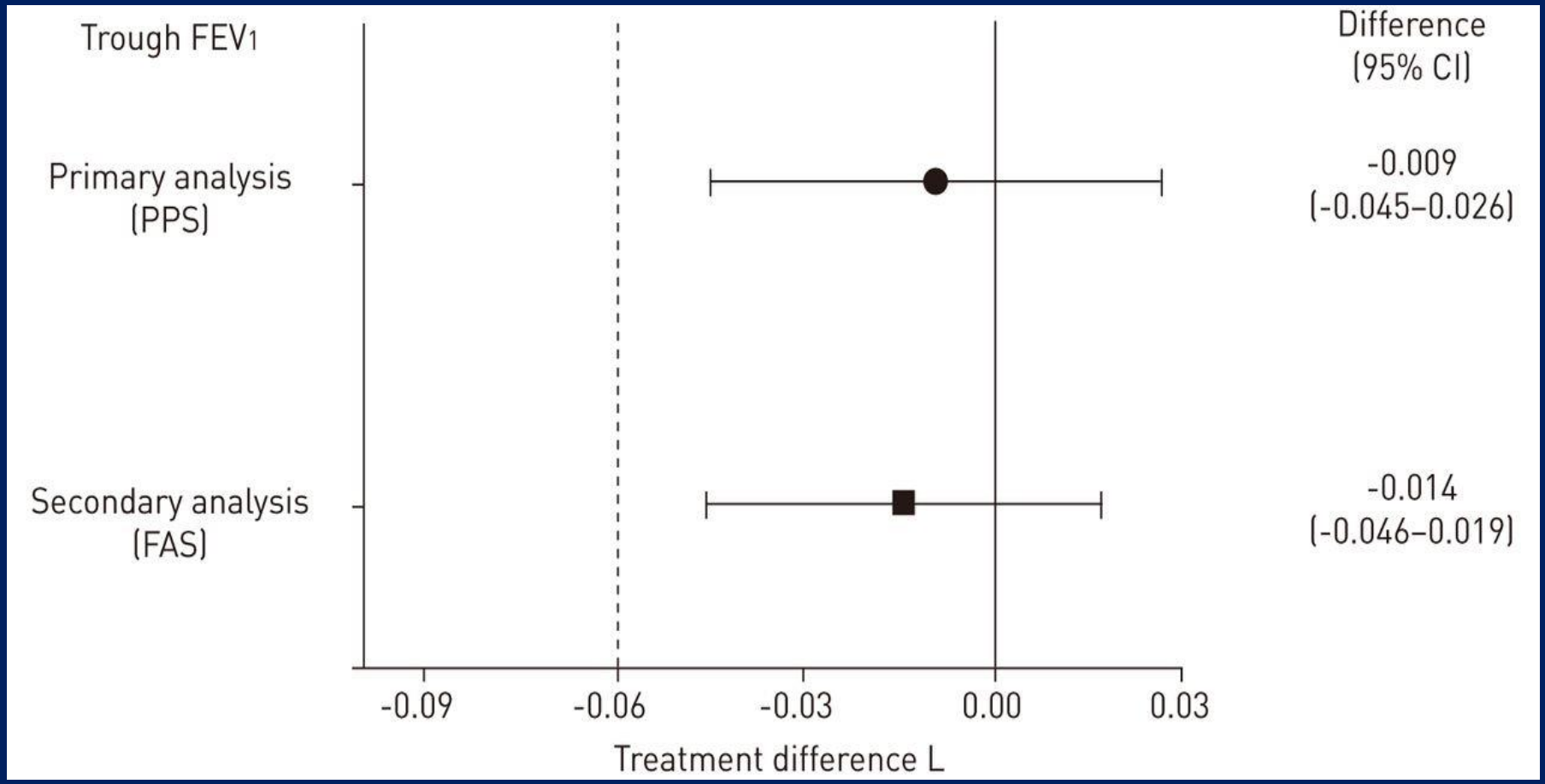
- **GOLD 2, n= 581**
- **legalább 3 hónapja SFC 50/500**
- **legalább 1 éve nem volt exacerbáció**

TABLE 1 Baseline demographics and clinical characteristics

	Indacaterol 150 µg n=293	SFC 50/500 µg n=288
Age years	65.3±8.39	66.8±8.53
Male sex	204 (69.6)	197 (68.4)
Ethnicity		
Caucasian	252 (86.0)	252 (87.5)
Native American	22 (7.5)	21 (7.3)
Asian	2 (0.7)	1 (0.3)
Other	17 (5.8)	14 (4.9)
Duration of COPD years	5.8±5.4	6.7±5.8
Severity of COPD#		
Moderate	291 (99.3)	287 (99.7)
Missing	2 (0.7)	1 (0.3)
Smoking history		
Ex-smokers	214 (73.0)	216 (75.0)
Pack-years¶	41.4±26.3	42.0±26.1
Pre-bronchodilator FEV_1 L	1.55±0.39	1.53±0.41
Post-bronchodilator FEV_1+ L	1.68±0.40	1.67±0.42
Post-bronchodilator FEV_1 % predicted+	64.0±8.11	64.2±8.28
FEV_1 reversibility %	9.2±7.0	10.2±10.2
Post-bronchodilator FEV_1/FVC+ %	53.7±8.9	53.6±9.1

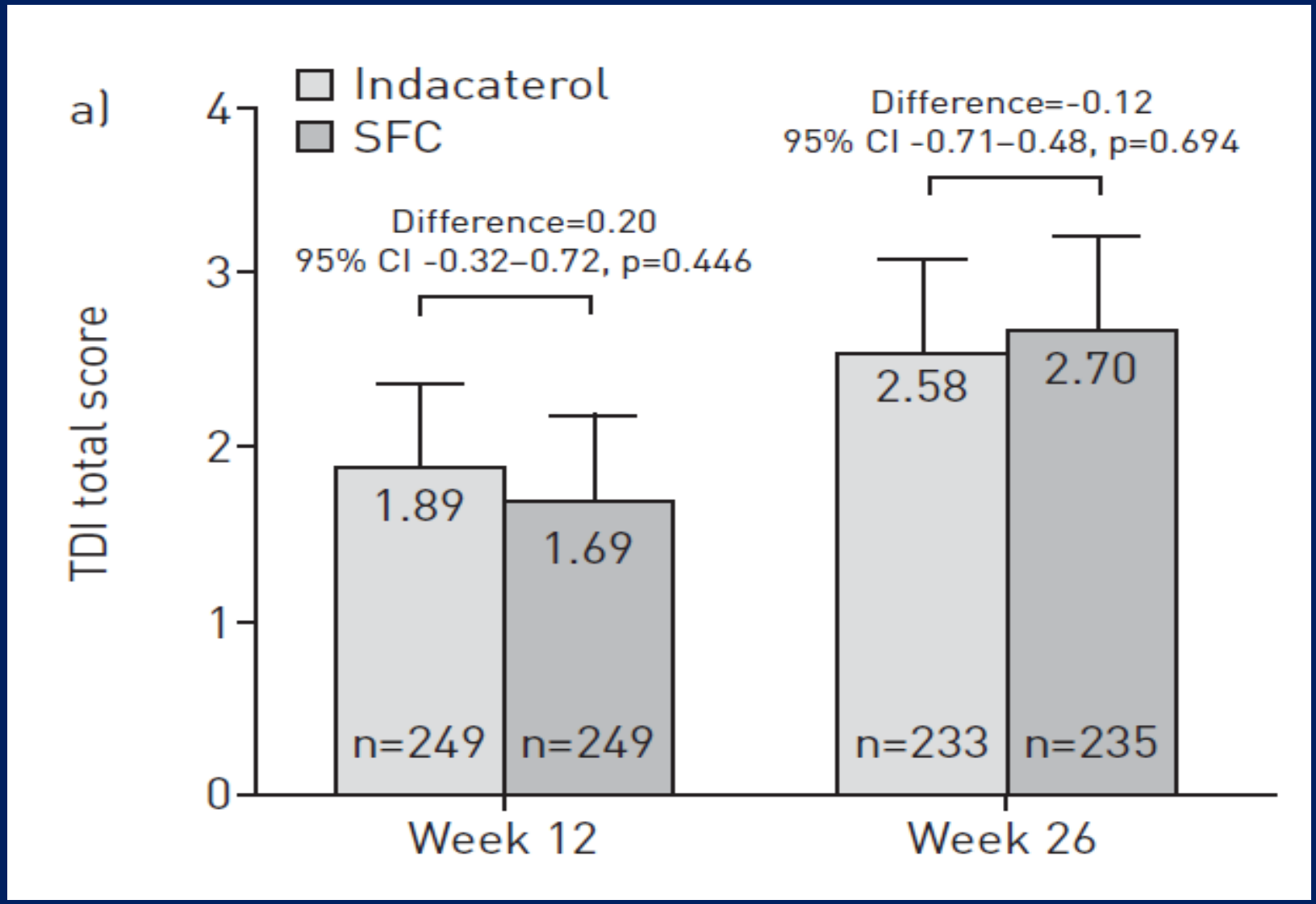
Elsődleges végpont : mélyponti FEV_1 12 hét után

Rossi, ERJ 2014



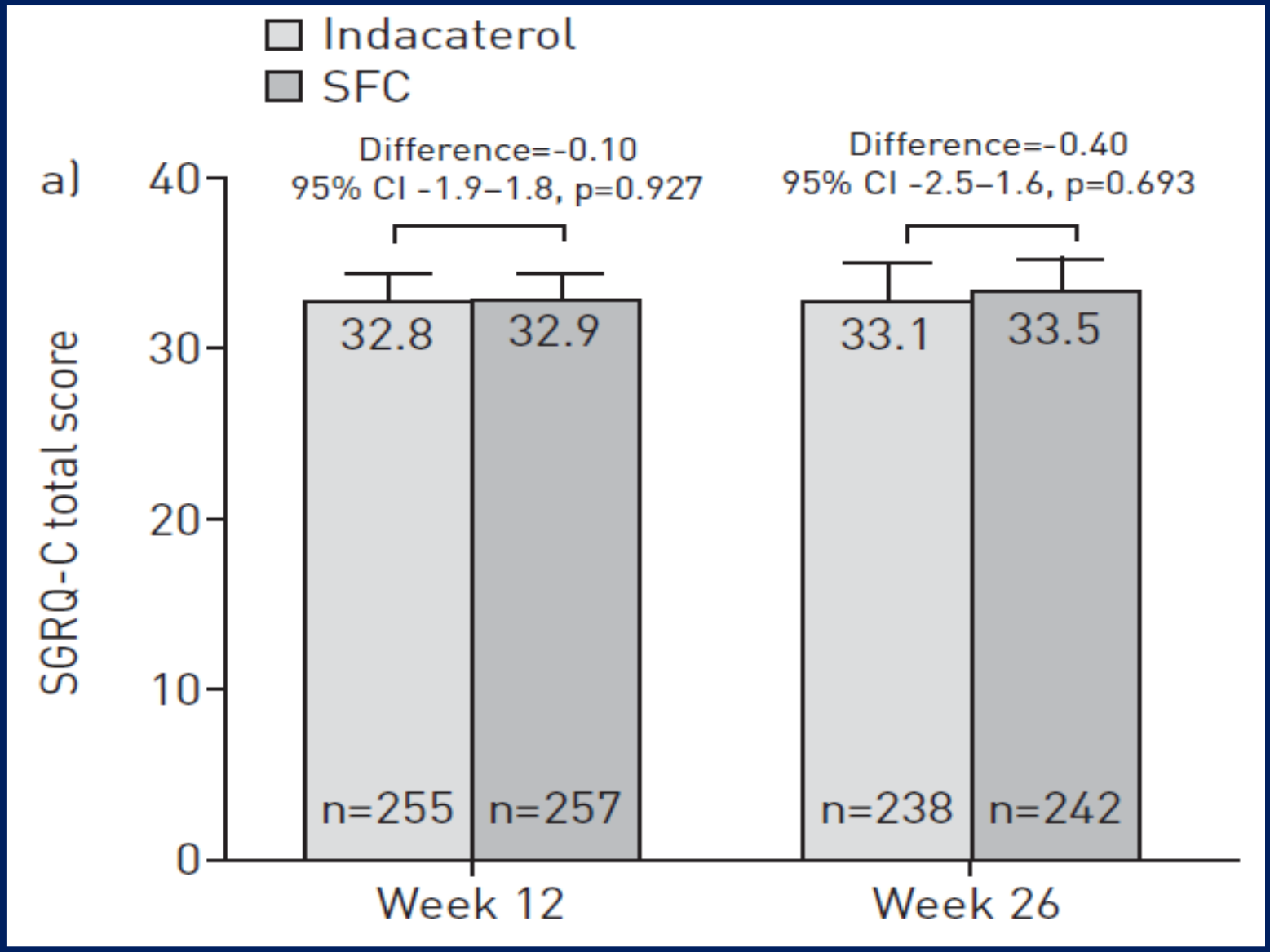
Dyspnoe

Rossi, ERJ 2014



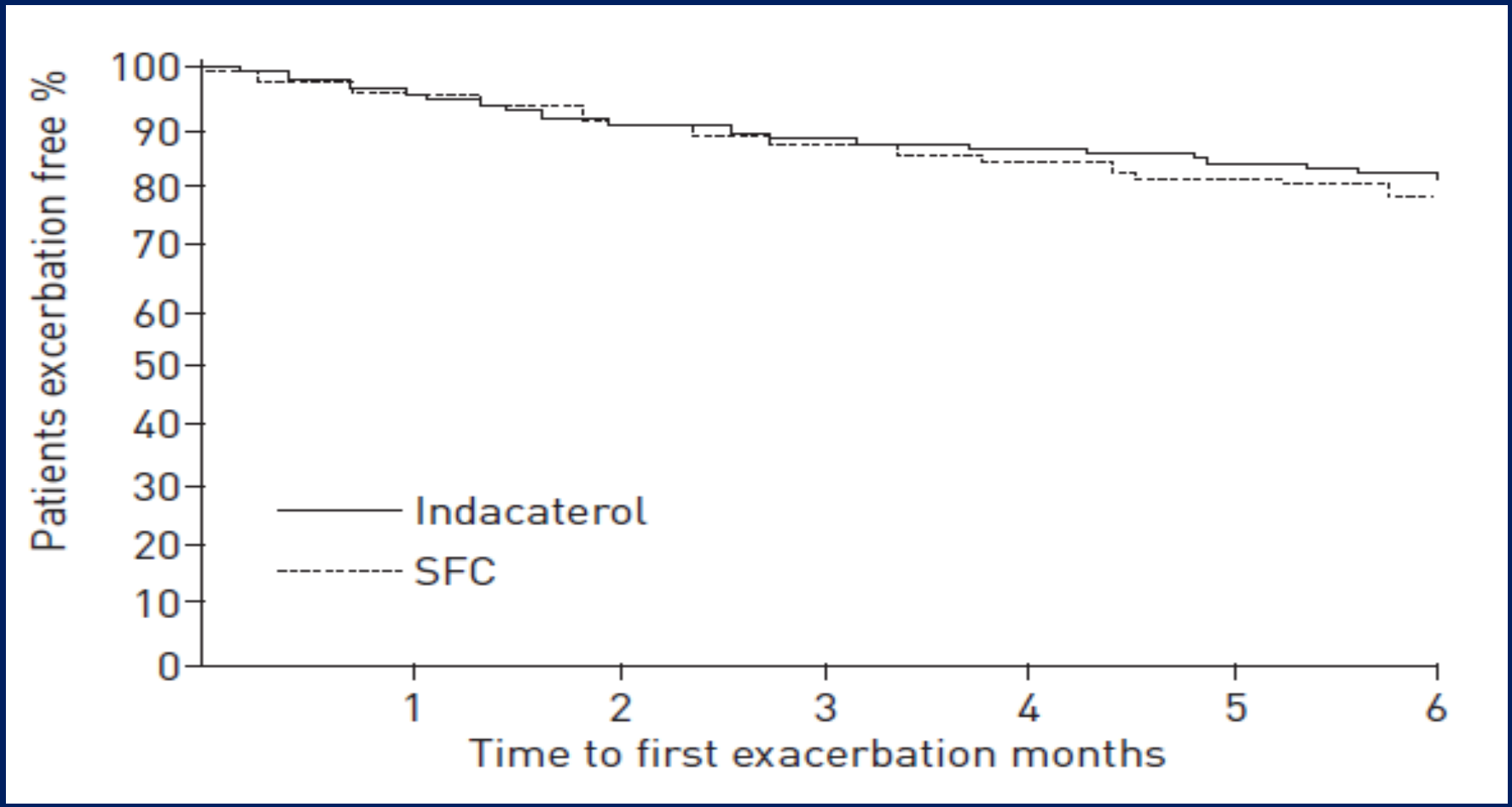
Életminőség

Rossi, ERJ 2014



Exacerbáció

Rossi, ERJ 2014



Rohamoldó használatban sem volt különbség

ICS/LABA vs LABA idős COPD-ben

Gershon, JAMA 2014

DESIGN, SETTING, AND PATIENTS Population-based, longitudinal cohort study conducted in Ontario, Canada, from 2003 to 2011. All individuals aged 66 years or older who met a validated case definition of COPD on the basis of health administrative data were included. After propensity score matching, there were 8712 new users of LABA–inhaled corticosteroid combination therapy and 3160 new users of LABAs alone who were followed up for median times of 2.7 years and 2.5 years, respectively.

CONCLUSIONS AND RELEVANCE Among older adults with COPD, particularly those with asthma and those not receiving a long-acting anticholinergic medication, newly prescribed LABA and inhaled corticosteroid combination therapy, compared with newly prescribed LABAs alone, was associated with a significantly lower risk of the composite outcome of death or COPD hospitalization.

Pneumonia előfordulásában nem volt különbség

What to use INSTEAD of inhaled corticosteroids in COPD?

Peter M.A. Calverley

ERJ, 2014. december

„What is now clear is that the way we use ICS in COPD should change if we are to offer the safest and most effective treatment to our patients.”

- eosinophilia
- asztma (40 éves kor előtt diagnosztizált)
- klinikai instabilitás

Comparing the effectiveness of small-particle versus large-particle inhaled corticosteroid in COPD

Postma, Int J COPD 2014

Patients and methods: Smokers and ex-smokers with COPD ≥40 years old initiating or stepping-up their dose of extrafine beclomethasone or fluticasone were matched 1:1 for demographic characteristics, index prescription year, concomitant therapies, and disease severity during 1 baseline year. During 2 subsequent years, we evaluated treatment change and COPD exacerbations, defined as emergency care/hospitalization for COPD, acute oral corticosteroids, or antibiotics for lower respiratory tract infection.

Results: Mean patient age was 67 years, 57%–60% being male. For both initiation (n=334:334) and step-up (n=189:189) patients, exacerbation rates were comparable between extrafine beclomethasone and fluticasone cohorts during the 2 year outcome period. Odds of treatment stability (no exacerbation or treatment change) were significantly greater for patients initiating extrafine beclomethasone compared with fluticasone (adjusted odds ratio 2.50; 95% confidence interval, 1.32–4.73). Median ICS dose exposure during 2 outcome years was significantly lower ($P<0.001$) for extrafine beclomethasone than fluticasone cohorts (315 µg/day versus 436 µg/day for initiation, 438 µg/day versus 534 µg/day for step-up patients).

Conclusion: We observed that small-particle ICS at significantly lower doses had comparable effects on exacerbation rates as larger-particle ICS at higher doses, whereas initiation of small-particle ICS was associated with better odds of treatment stability during 2-years' follow-up.

POPE - Phenotypes of COPD in Central and Eastern Europe Study

Cél

Az ambuláns praxisban gondozott betegek csoportjában…

Primary aims

- To determine the proportion of patients within the GOLD 2011 strategy disease severity (Stage 1,2,3,4) and risk classification category (A,B,C,D) in an unselected group of consecutively examined patients with COPD in the CEE region

Secondary aims

- To evaluate the prevalence of disease phenotypes according to predefined criteria
- To evaluate the diagnostic approach to COPD in CEE countries
- To assess the differences in treatment habits in CEE countries

” lack of evidence of the effectiveness of a particular treatment

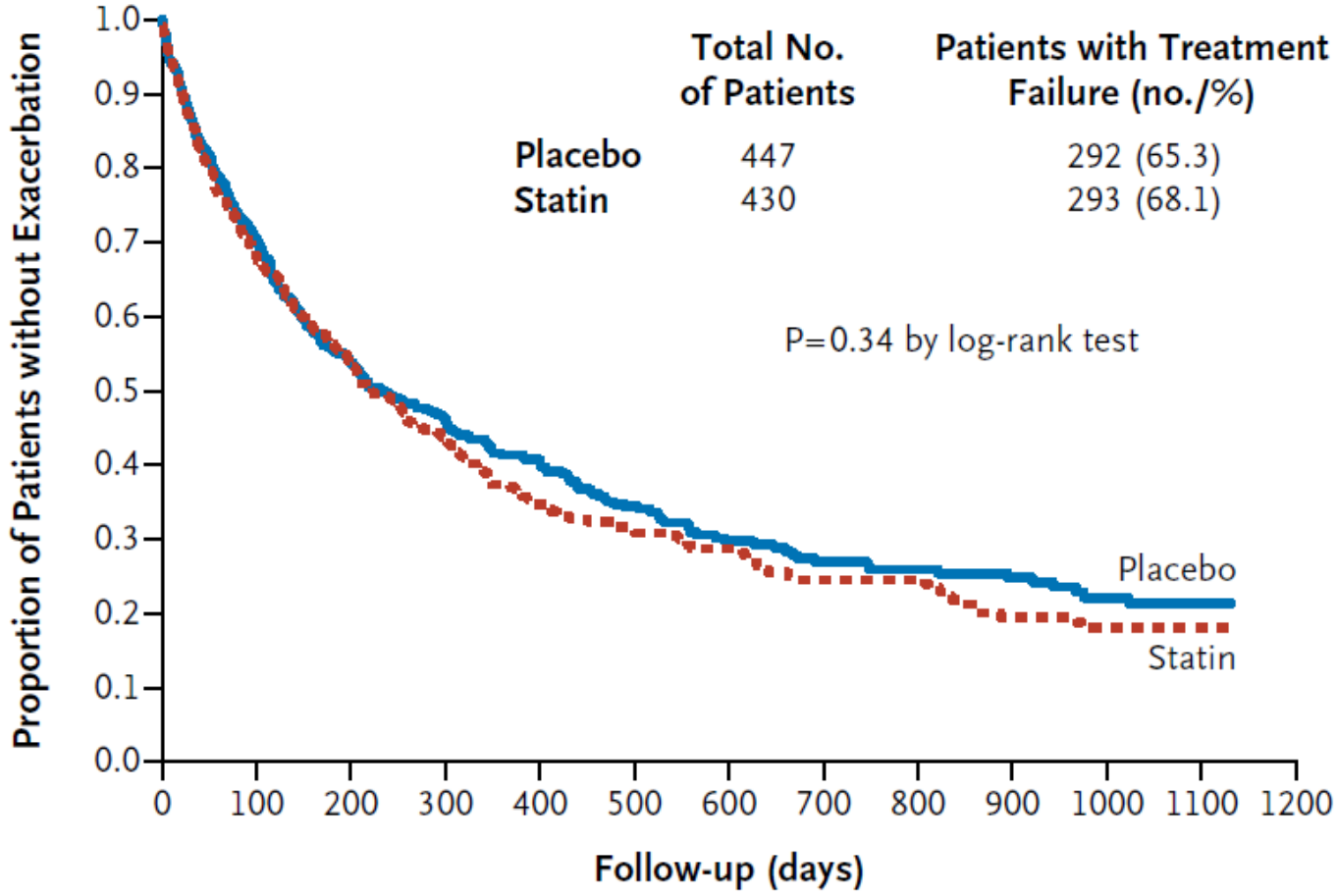
is not the same as evidence that is not effective ”

www.goldcopd.org 2012.március 13.

Statins as adjunct therapy in COPD: how do we cope after STATCOPE?

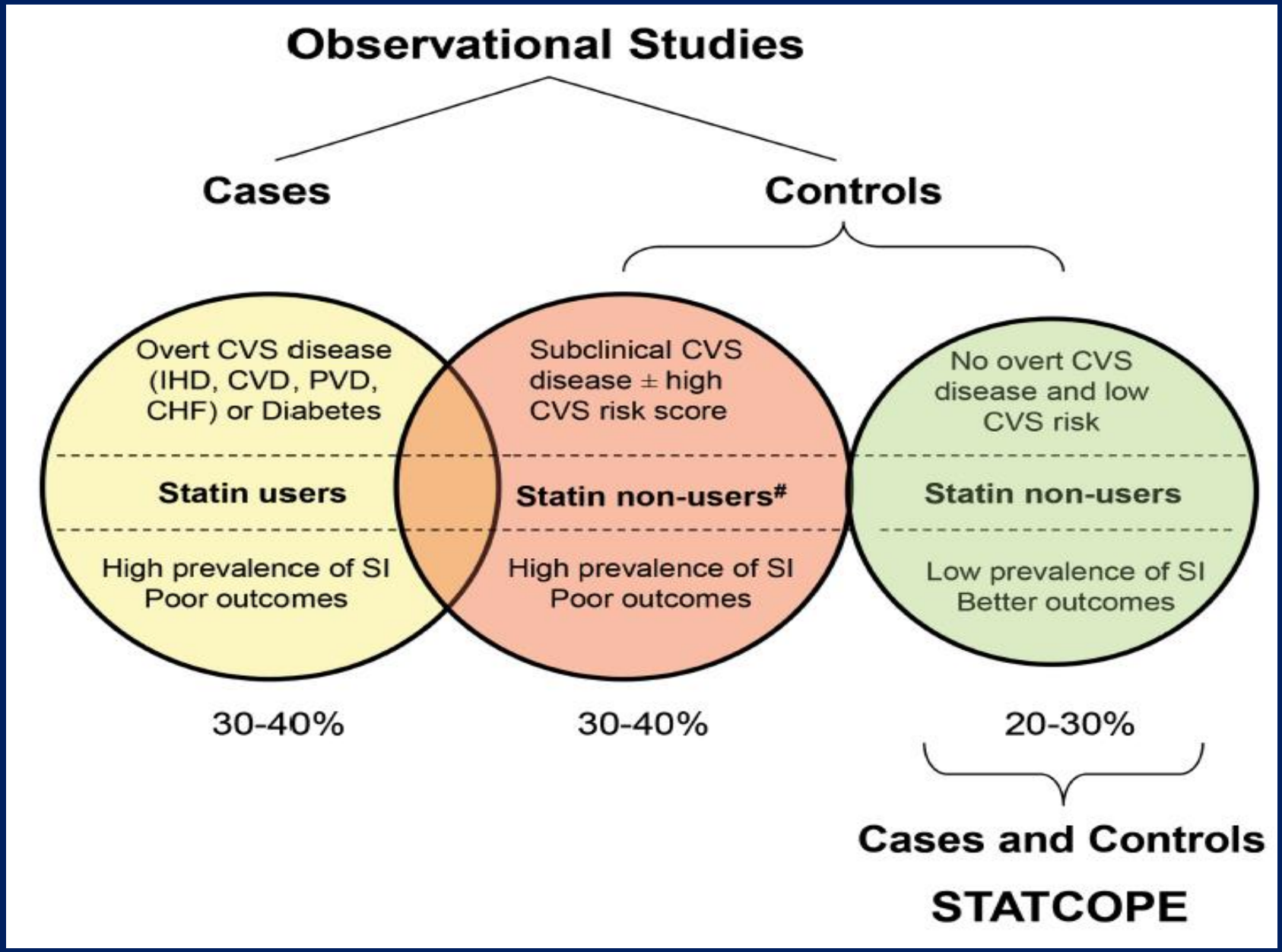
Robert P Young,[1] Raewyn J Hopkins,[1] Alvar Agusti[2]

Thorax, 2014



Criner, NEJM 2014

Young, Thorax 2014

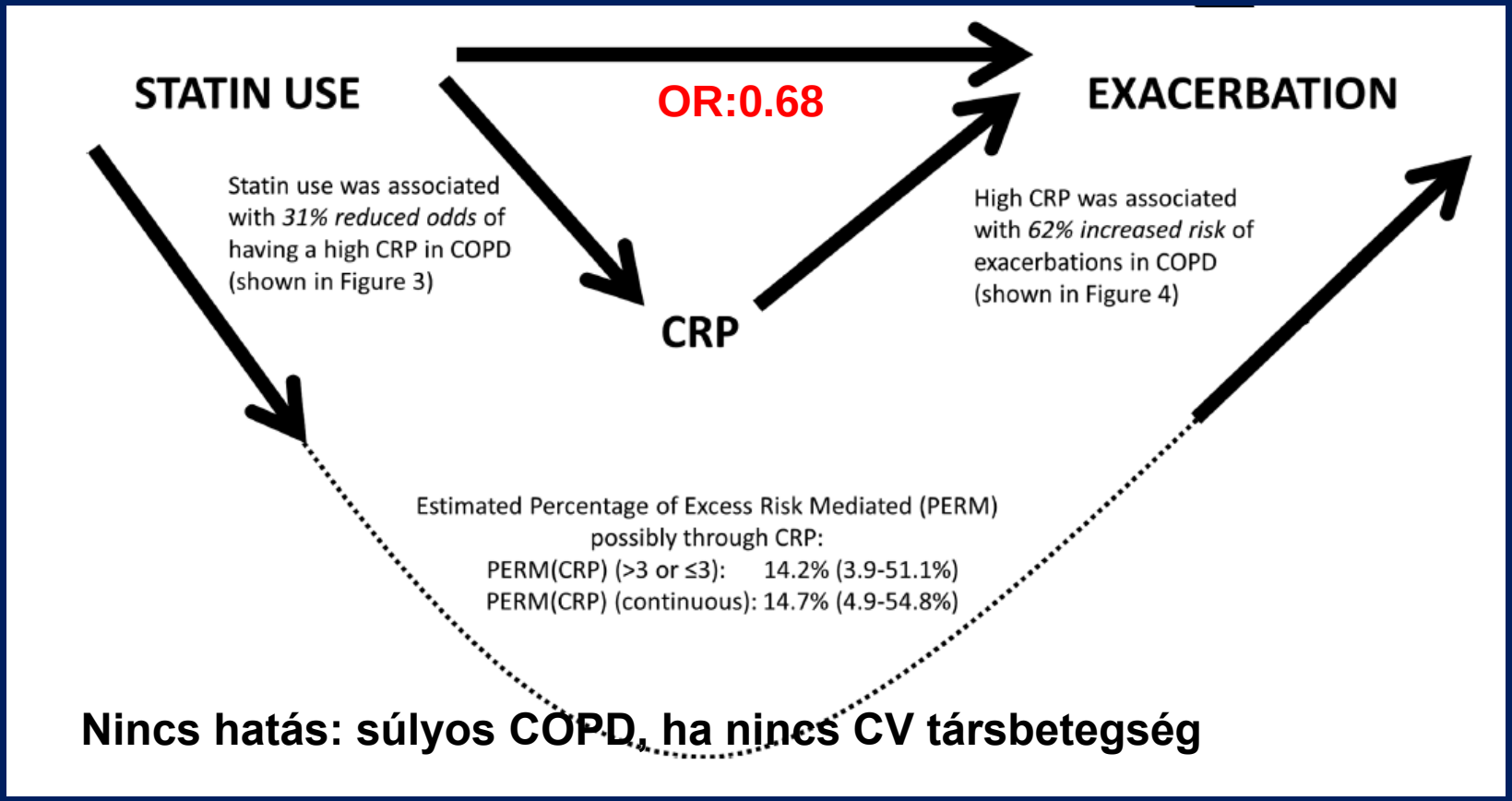


Statin use and exacerbations in individuals with chronic obstructive pulmonary disease

Truls S Ingebrigtsen,[1,2,3] Jacob L Marott,[2] Børge G Nordestgaard,[2,3,4] Peter Lange,[2,3,5,6] Jesper Hallas,[7] Jørgen Vestbo[8,9]

Thorax, 2015

Copenhagen General Population Study (2003-2008), n=5794

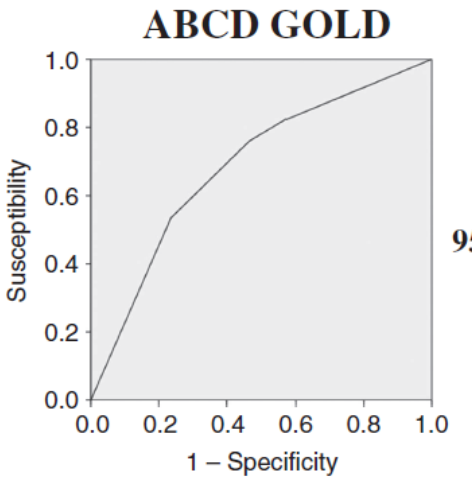


Nincs hatás: súlyos COPD, ha nincs CV társbetegség

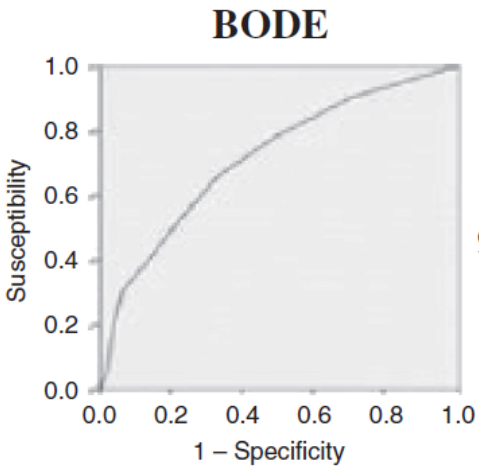
Mortalitás előjelzése

De Torres, Thorax 2014

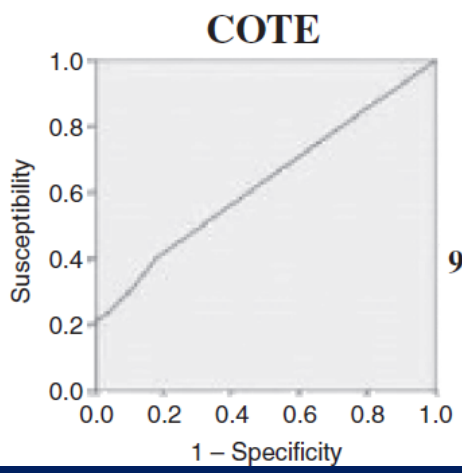
N = 707 GOLD 1-4, követés: 50 (23-85) hónap



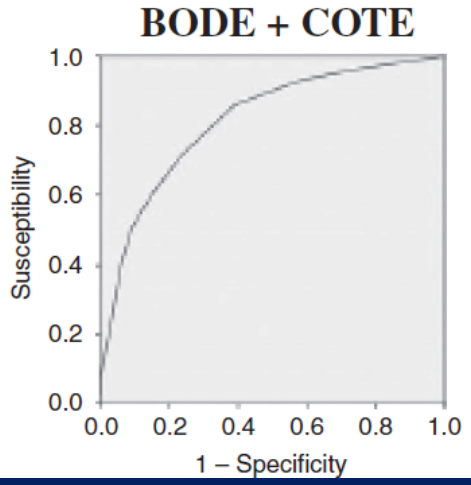
0.68
95% CI: 0.64 to 0.73



0.71
95% CI: 0.67 to 0.76



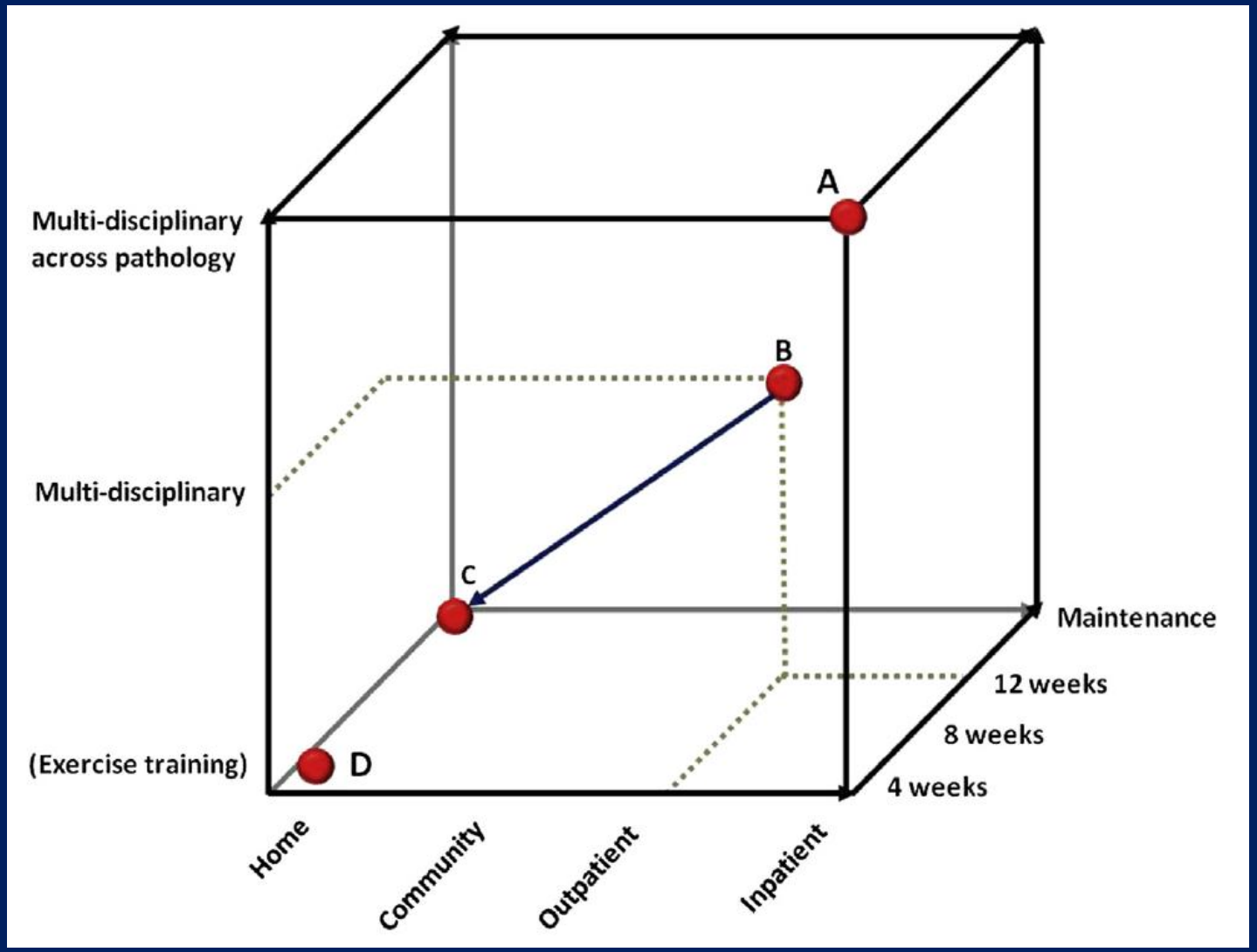
0.62
95% CI: 0.57 to 0.68



0.81
95% CI: 0.77 to 0.85

A rehabilitáció helyszínei

Troosters, Clin Chest Med 2014



COPD JOURNAL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

informa healthcare

COPD, 00:1–10, 2014
ISSN: 1541-2555 print / 1541-2563 online

DOI: 10.3109/15412555.2014.922066

ORIGINAL RESEARCH

An International Comparison of Pulmonary Rehabilitation: A Systematic Review

Laura Desveaux,[1,2] Tania Janaudis-Ferreira,[2,3] Roger Goldstein,[1,2,4,5] and Dina Brooks[1,2,4,5]

- Elektronikus adatbázisok 2013 szeptemberig
- 7 review: USA, UK, Kanada, Irország, Ausztrália, Új-Zéland, Svédország
- ambuláns (55-99%), terheléses tréning (77-100%), oktatás (74-100%)

„The current availability of PR services ≤1.2% of individuals with COPD”