



## **FEV<sub>1</sub>: η θετική άποψη**

**Στέλιος Θ. Λουκίδης MD FCCP**

**ERS secretary group 5.2**

**Ιατρική σχολή ΕΚΠΑ**




REVIEW

## Global assessment of the COPD patient: Time to look beyond FEV<sub>1</sub>?

Andriana I. Papaioannou<sup>a</sup>, Stelios Loukides<sup>b</sup>, Konstantinos I. Gourgoulianis<sup>a</sup>, Konstantinos Kostikas<sup>a,\*</sup>

Journal of Respiratory Medicine (2008) 102 (Supplement 1), S27–S35



respiratoryMEDICINE 

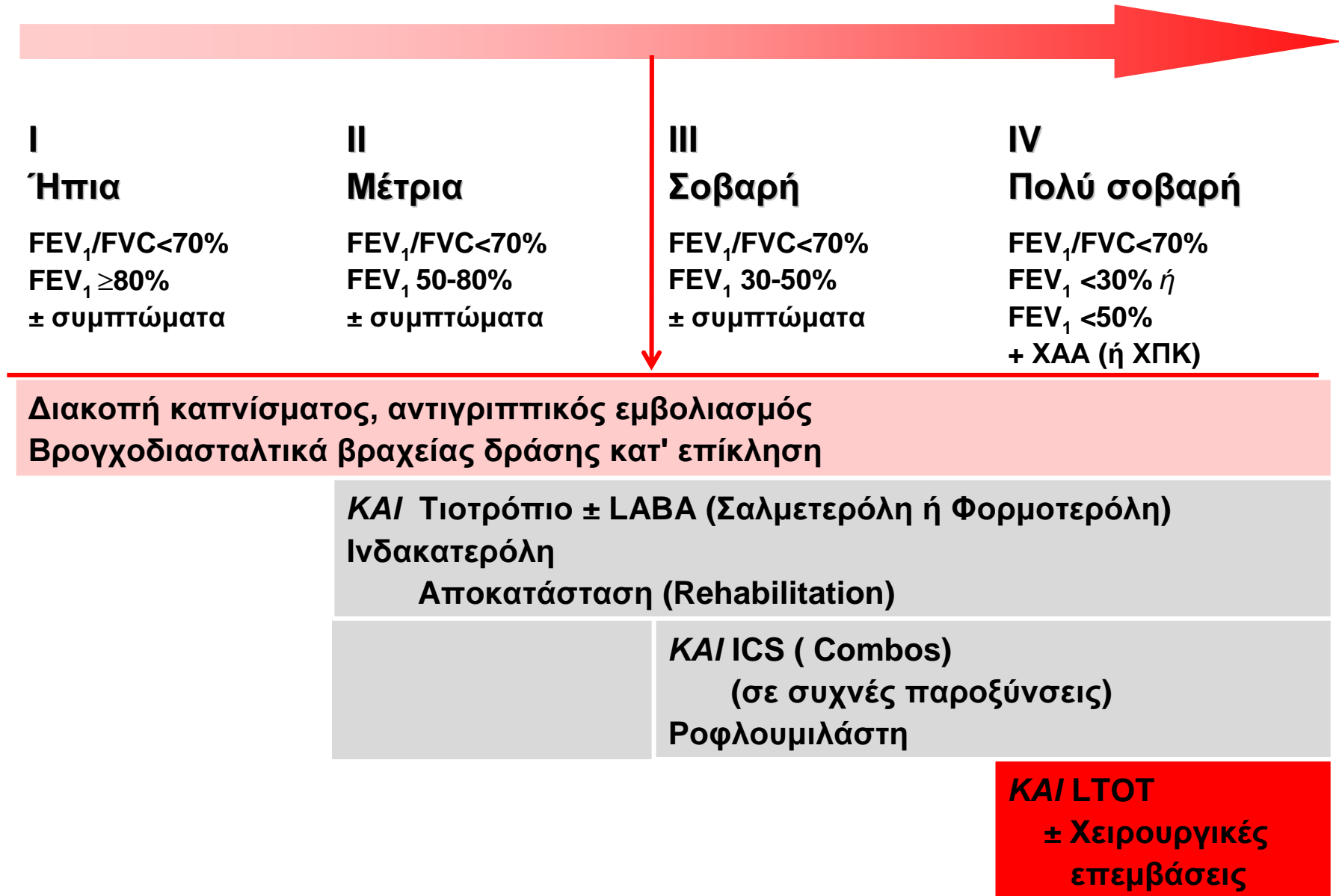
## Predictors of Survival in COPD: More than Just the FEV<sub>1</sub>

Bartolome R. Celli<sup>1</sup>, Claudia G. Cote<sup>2</sup>, Suzanne C. Lareau<sup>3,\*</sup> and Paula M. Meek<sup>4</sup>

## Σχεδιασμός

- Διάγνωση-Ανακάλυψη περιπτώσεων

# Διάγνωση-Θεραπεία σταθερής ΧΑΠ



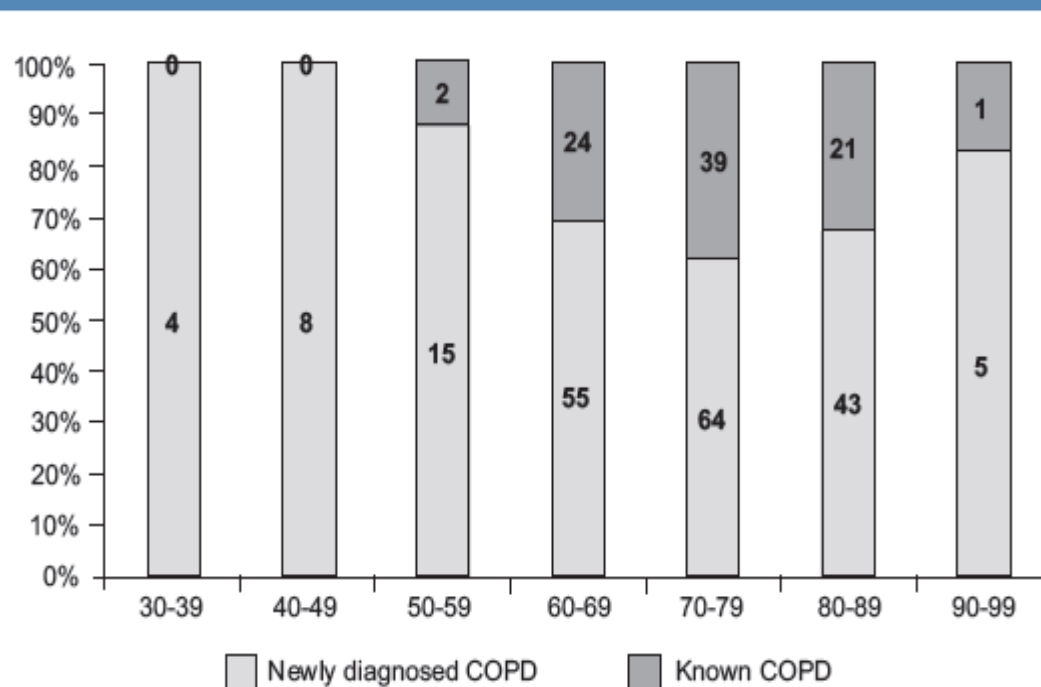
# FEV<sub>1</sub>: Ανακάλυψη νέων περιπτώσεων

Table 2. Distribution of COPD patients according to GOLD COPD stages and by sex.

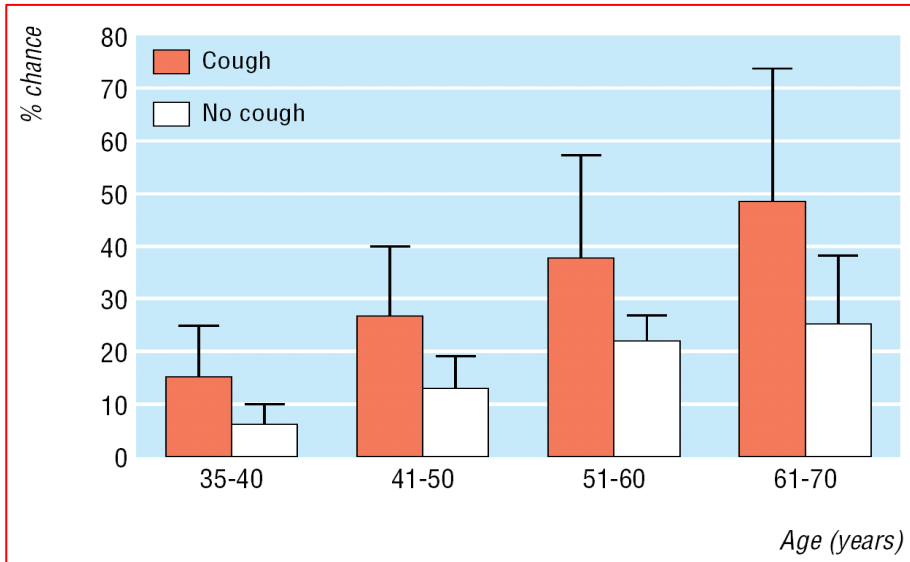
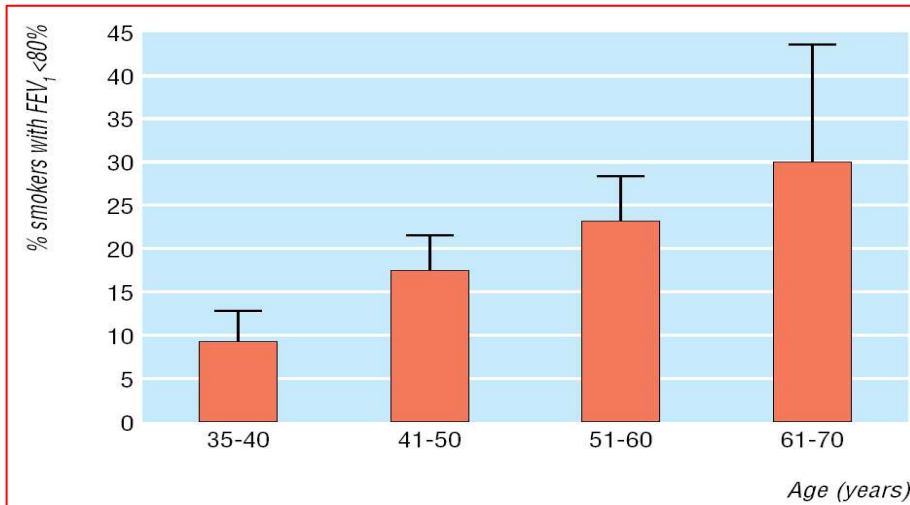
	COPD (n=281)	COPD old (n=87)	COPD new (n=194)
Stage I	74 (26.3%)	16 (18.4%)	58 (29.9%)
Men/Women	60/14	14/2	46/12
Stage II	152 (54.1%)	39 (44.8%)	113 (58.3%)
Men/Women	136/16	34/5	102/11
Stage III	53 (18.9%)	30 (34.5%)	23 (11.8%)
Men/Women	48/5	27/3	21/2
Stage IV	2 (0.7%)	2 (2.3%)	0 (0%)
Men/Women	2/0	2/0	0/0

Data are presented as actual numbers with percentages in every subgroup in parenthesis.

Figure 2. 100% stacked columned chart representing known versus newly diagnosed COPD patients distributed by patients' ages and by sex. Numbers in columns represent the absolute numbers of patients with COPD.



# Ερωτηματολόγια: Απλά ενδείξεις...



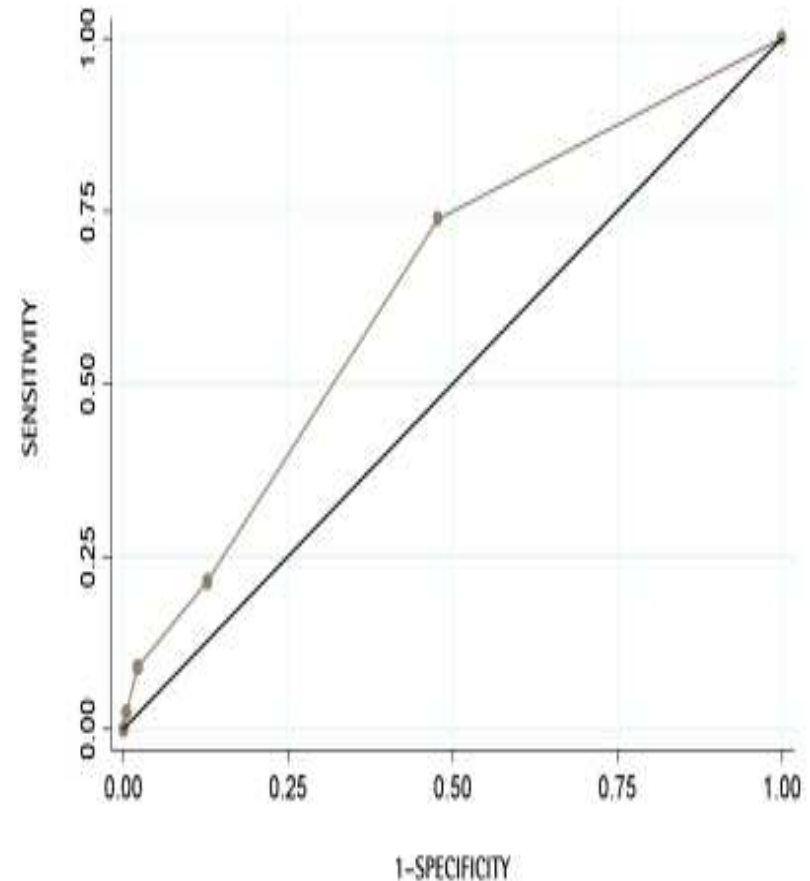
Symptom	No of patients reporting symptom	No (% , 95% CI) of patients with FEV <sub>1</sub> <80%	Odds ratio* (95% CI)	Negative predictive value (%)
Family history:				
Asthma	33	6 (18, 7 to 35)	1.03 (0.38 to 2.77)	82
Allergy	28	6 (21, 8 to 41)	1.35 (0.49 to 3.70)	83
Symptom:				
Tiredness	90	19 (21, 13 to 31)	1.77 (0.77 to 4.06)	87
Chronic wheeze	44	12 (27, 15 to 43)	2.15 (0.94 to 4.88)	85
Chronic dyspnoea	79	19 (24, 15 to 35)	2.19 (0.98 to 4.90)	87
Chronic cough	64	17 (27, 16 to 39)	2.50 (1.14 to 5.52)	87
No of symptoms:				
1	105	23 (22, 14 to 31)	2.28 (0.93 to 5.60)	89
2	59	17 (29, 18 to 42)	3.02 (1.37 to 6.64)	88
3	23	8 (35, 16 to 57)	3.01 (1.17 to 7.70)	85

# Ερωτηματολόγια-MRC: Μπορούν?

Table 4. Results of the CFQ and associated likelihood ratios for each score

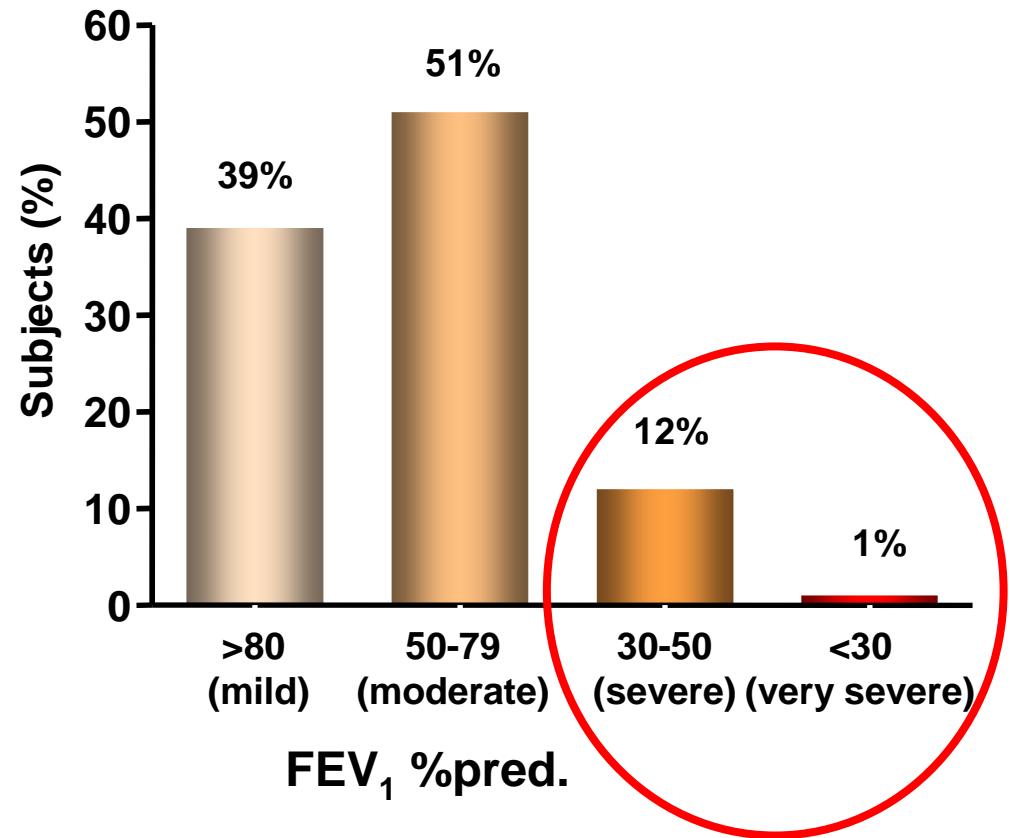
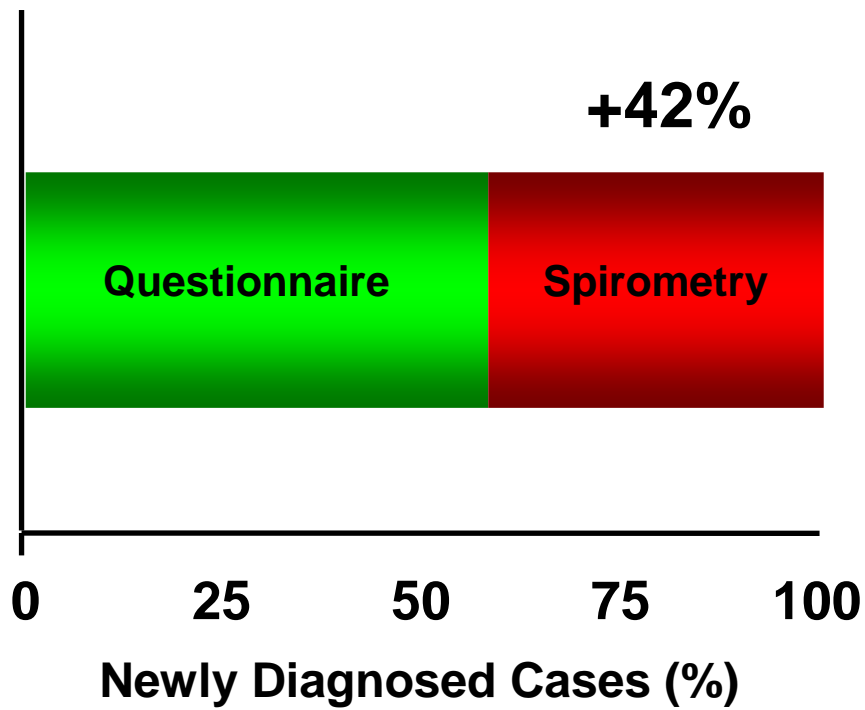
CFQ SCORE	TOTAL (N=996*), N (%)	PATIENTS WITH COPD <sup>†</sup> N=205 N (%)	PATIENTS WITHOUT COPD <sup>†</sup> (N=791), N (%)	LIKELIHOOD RATIO (95% CI)
0	317 (31.8)	45 (22.0)	272 (34.4)	0.64 (0.48-0.84)
1	224 (22.5)	34 (16.6)	190 (24.0)	0.69 (0.50-0.96)
2	180 (18.1)	38 (18.5)	142 (18.0)	1.03 (0.75-1.43)
3	155 (15.6)	45 (22.0)	110 (13.9)	1.58 (1.16-2.15)
4	85 (8.5)	27 (13.2)	58 (7.3)	1.80 (1.17-2.76)
5	35 (3.5)	16 (7.8)	19 (2.4)	3.25 (1.70-6.21)

Figure 2. Receiver operating characteristic curve for Medical Research Council dyspnea scale scores



ROC—receiver operating characteristic.

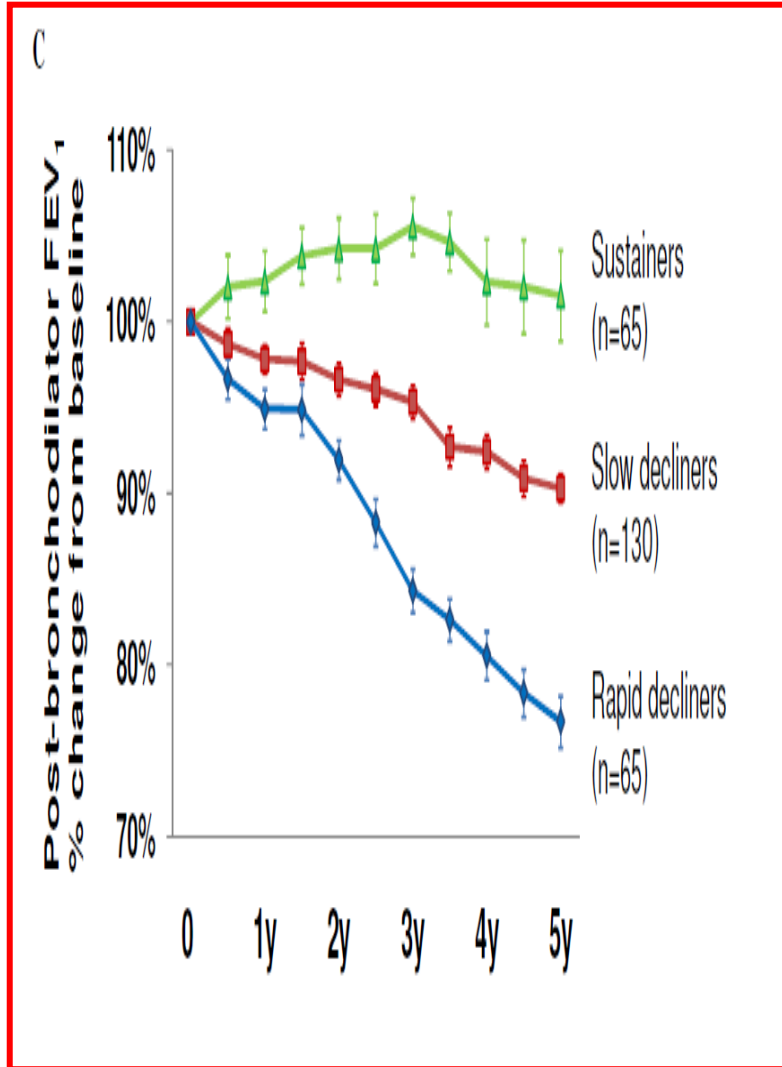
# Η προσθήκη της FEV<sub>1</sub>



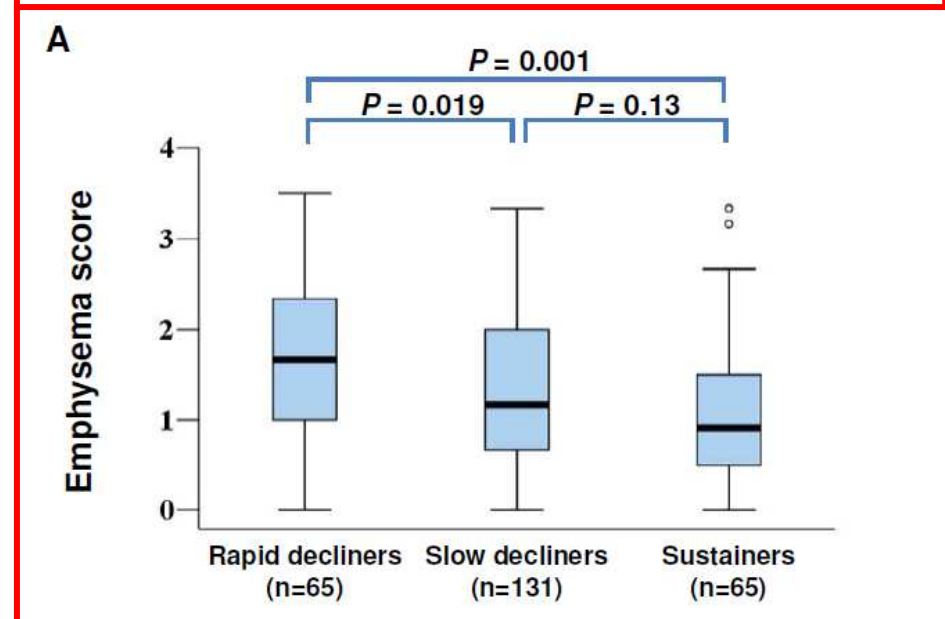
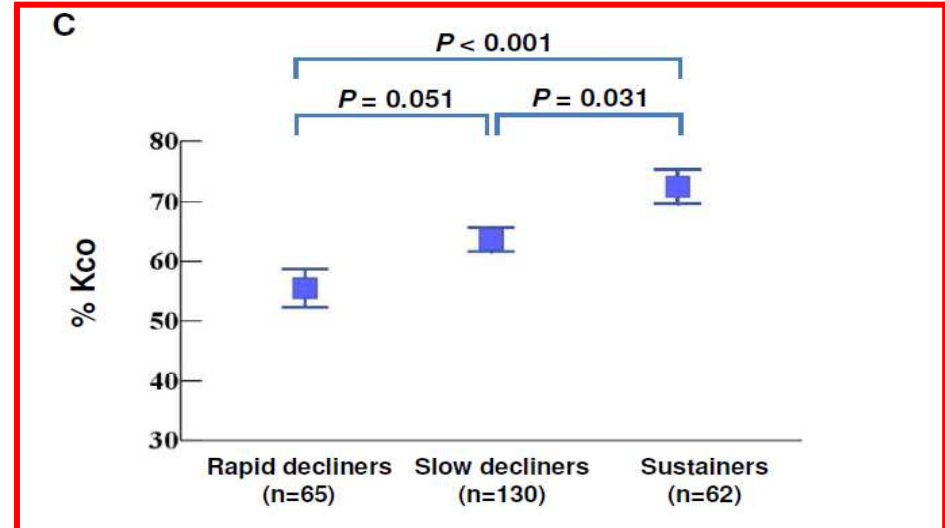
## Σχεδιασμός

- Διάγνωση-Ανακάλυψη περιπτώσεων
- Απώλεια –ρυθμός  $FEV_1$ : Τελικά σημαίνει πολλά

# Decline FEV<sub>1</sub> & εμφύσημα



Nishimura M et al AJRCCM 2011



## Σχεδιασμός

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- Συσχέτιση με επιβίωση

# Επιβίωση Lung health study

**Table 2 Characteristics of Analyzed Population at Year 5 (n = 5,320) with 500 deaths at up to 10 years of follow-up**

	N	%	Person-Years of Follow-up	Deaths per 1,000 Person Years
<b>Sex</b>				
Female	1,992	37.4	17,221	9.4
Male	3,328	62.6	28,587	11.8
<b>Age Group, years</b>				
35-39	25	0.5	214	9.3
40-49	1,708	32.1	14,995	4.7
50-59	2,436	45.8	20,954	11.4
60+	1,151	21.6	9,644	19.7
<b>Body Mass Index, kg/m<sup>2</sup></b>				
< 25	2,536	47.7	21,849	10.7
25- 30	2,098	39.4	18,075	10.6
> = 30	686	12.9	5,884	12.7
<b>Education (years)</b>				
< 12	639	12.0	5,496	14.0
12	1,595	30.0	13,735	11.5
> 12	3,086	58.0	26,577	10.0
<b>Race</b>				
White	5,136	96.5	44,226	10.6
Non-White	184	3.5	1,582	19.6
<b>Smoking Status</b>				
Former	1,386	26.1	12,063	7.5
Intermittent	627	11.8	5,403	10.2
Current	3,307	62.2	28,342	12.5
<b>Randomization Group</b>				
Intervention, Ipratropium	1,791	33.7	15,470	9.6
Intervention, Placebo	1,770	33.3	15,271	10.5
Control	1,759	33.1	15,067	12.7
<b>Stage (pre-bronchodilator)*</b>				
Stage 3 or 4	341	6.4	2,831	21.5
Stage 2	3,587	67.4	30,875	11.3
Stage 1	995	18.7	8,674	7.3
Restricted	92	1.7	768	15.6
Normal	305	5.7	2,659	5.6
<b>Stage (post-bronchodilator)*</b>				
Stage 3 or 4	183	3.4	1,475	29.8
Stage 2	3,048	57.3	26,237	12.0
Stage 1	1,242	23.3	10,775	7.2
Restricted	126	2.4	1,059	13.2
Normal	721	13.6	6,262	7.8

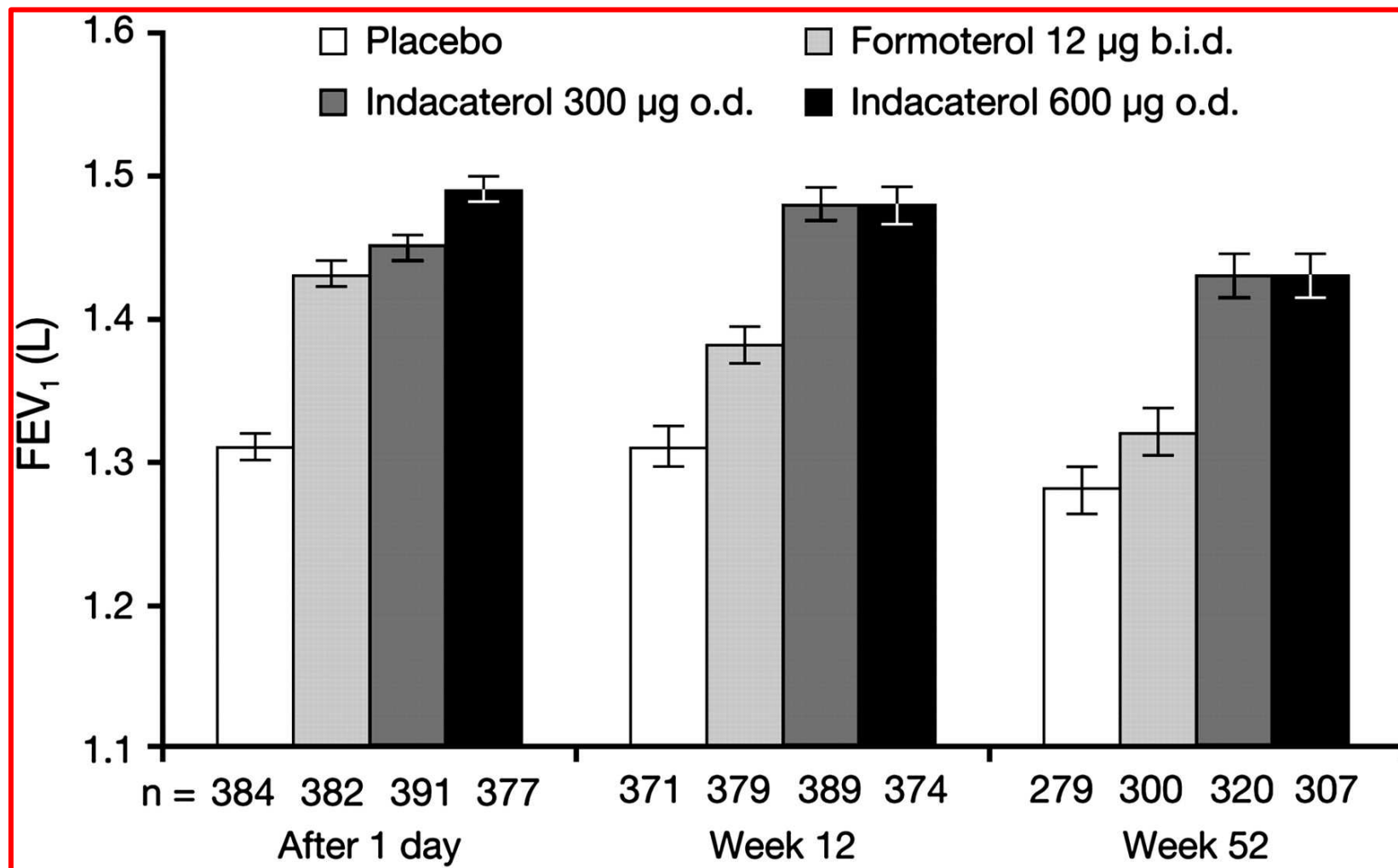
**Table 5 Results from Year 5 sample, mortality follow-up of up to 10 years**

	Hazards Ratio	95% Confidence Interval
<b>Sex</b>		
Male	1.36	(1.12, 1.64)
Female	1.00	
<b>Age</b>		
	1.09	(1.07, 1.10)
<b>Body Mass Index</b>		
	1.01	(0.98, 1.03)
<b>Education</b>		
< 12 Years	1.24	(0.96, 1.59)
12 Years	1.10	(0.90, 1.34)
> 12 Years	1.00	
<b>Race</b>		
White	1.00	
Black	1.77	(1.22, 2.56)
<b>Smoking Status</b>		
Former Smoker	0.63	(0.50, 0.80)
Intermittent Smoker	0.85	(0.64, 1.13)
Current Smoker	1.00	
<b>Randomization Group</b>		
Intervention, Ipratropium	0.86	(0.69, 1.07)
Intervention, Placebo	0.91	(0.74, 1.13)
Control	1.00	
<b>Stage (Pre-bronchodilator)*</b>		
Stage 3 or 4	2.68	(1.51, 4.75)
Stage 2	1.60	(0.94, 2.69)
Stage 1	1.12	(0.63, 1.98)
Restricted	2.25	(1.04, 4.86)
Normal	1.00	
<b>Stage (Post-bronchodilator)*</b>		
Stage 3 or 4	2.46	(1.63, 3.73)
Stage 2	1.11	(0.82, 1.51)
Stage 1	0.74	(0.52, 1.06)
Restricted	1.36	(0.74, 2.47)
Normal	1.00	

## Σχεδιασμός

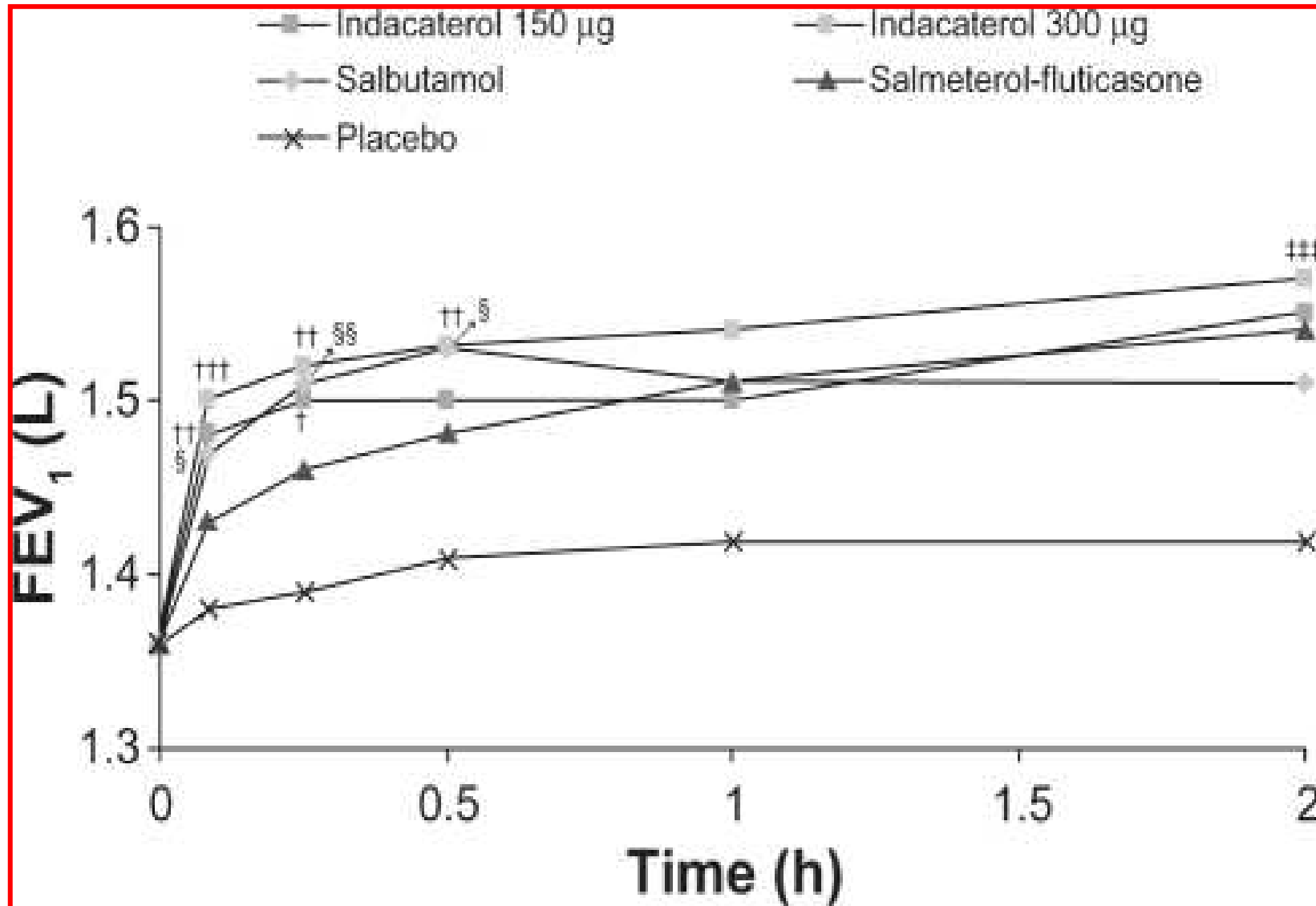
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- Απώλεια –ρυθμός  $FEV_1$ : Τελικά σημαίνει πολλά
- Συσχέτιση με επιβίωση
- Φαρμακευτική αξιολόγηση και όχι μόνο...

## Trough FEV<sub>1</sub> : Υπάρχει άλλος τρόπος?

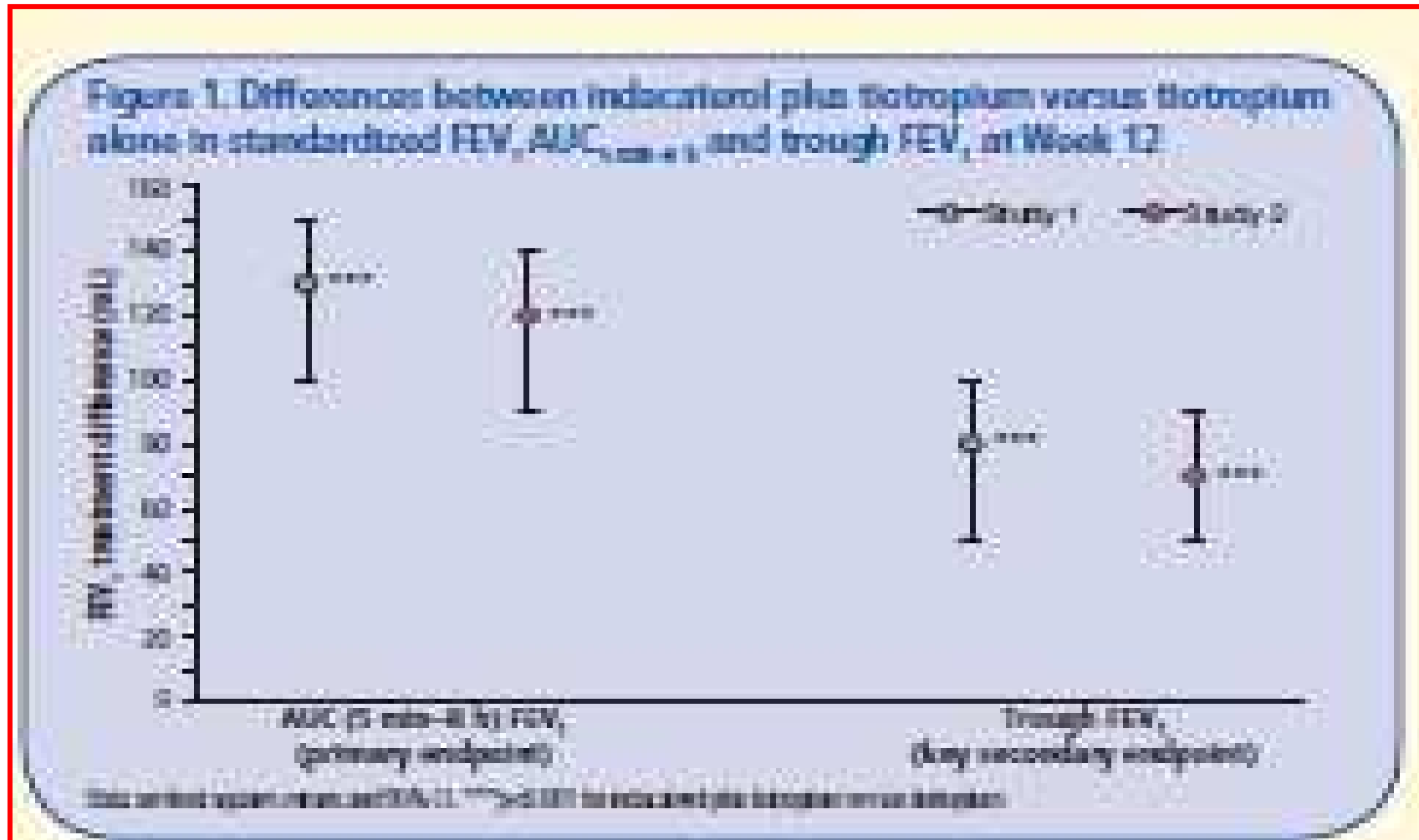


Dahl R et al. Thorax 2010;65:473-479

# Έλεγχος άμεσης έναρξης



# Αξιολόγηση συνεργικής δράσης





# Μετα-ανάλυση COCHRANE

- 11 μελέτες
- ↓ θεραπευτικές αποτυχίες OR 0.48; 95% CI 0.34 - 0.68
- ↑ **FEV<sub>1</sub> για 72 ώρες +140 ml (95% CI 80-200 ml)**
- Βελτίωση δύσπνοιας και αερίων αίματος στις 6-72 h

ΑΛΛΑ...

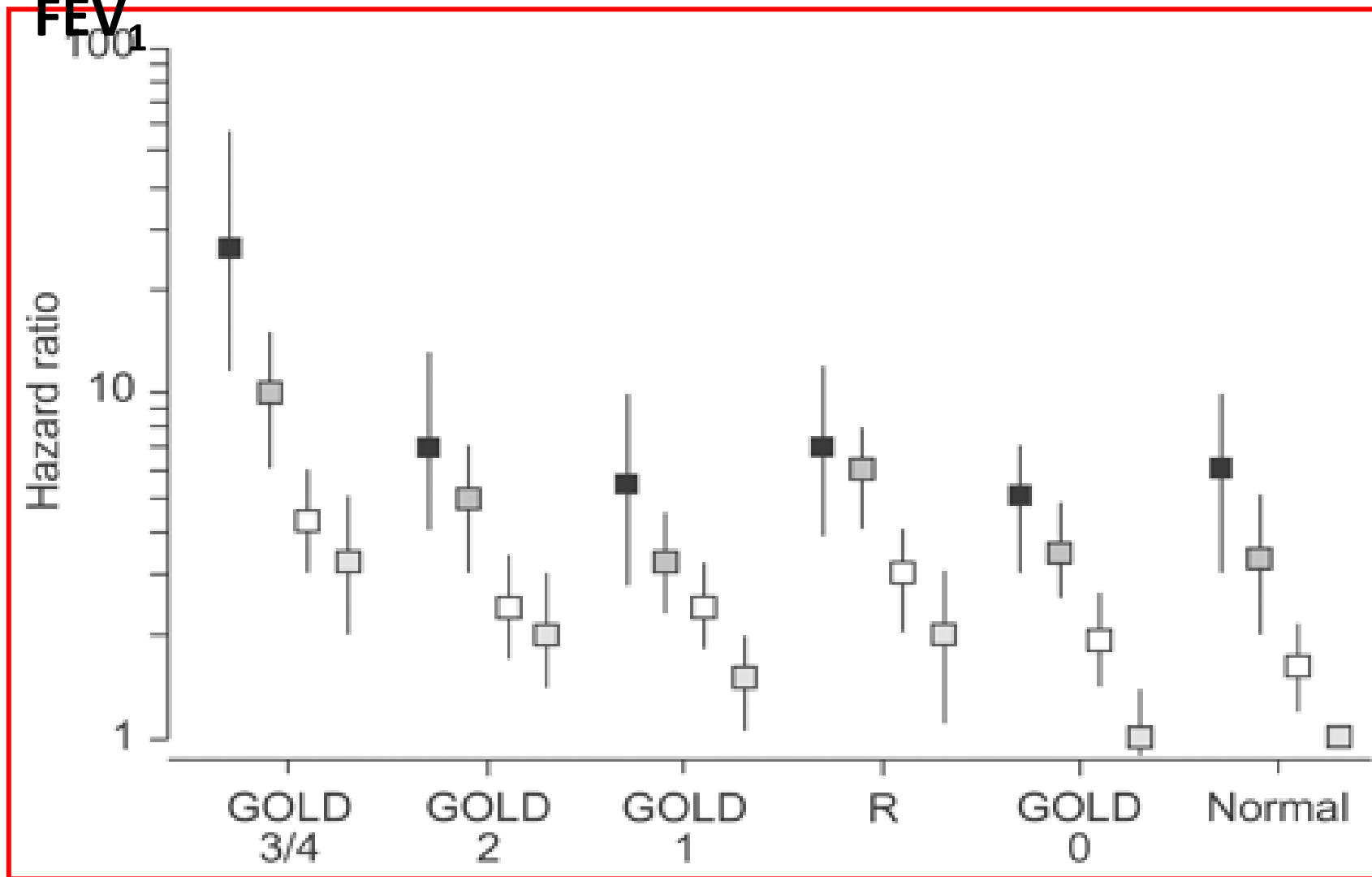
- Καμία διαφορά στη θνησιμότητα
- ↑ ανεπιθύμητες ενέργειες OR 2.33
- ↑ κίνδυνος υπεργλυκαιμίας OR 4.95

## Σχεδιασμός

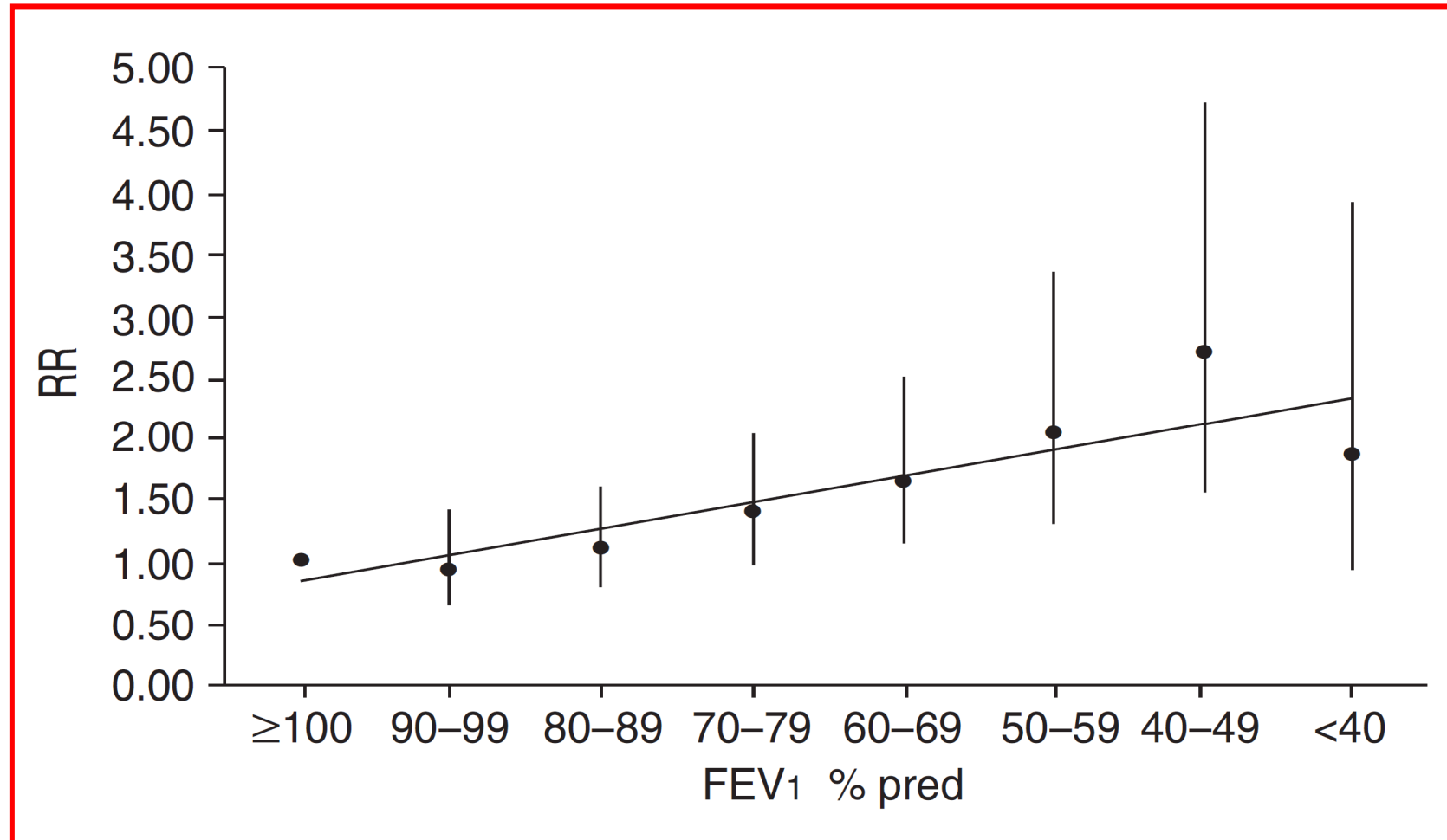
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- Φαρμακευτική αξιολόγηση και όχι μόνο...
- Συν-νοσηρότητες

# ΧΑΠ & Συν-νοσηρότητες: Στενή σχέση με την

FEV<sub>1</sub>



# ΧΑΠ & Αρρυθμίες

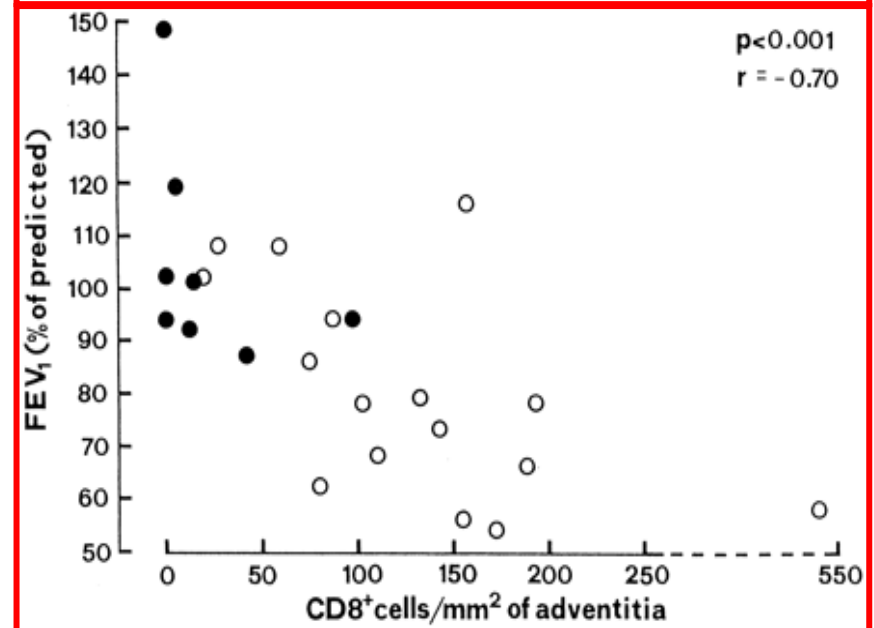
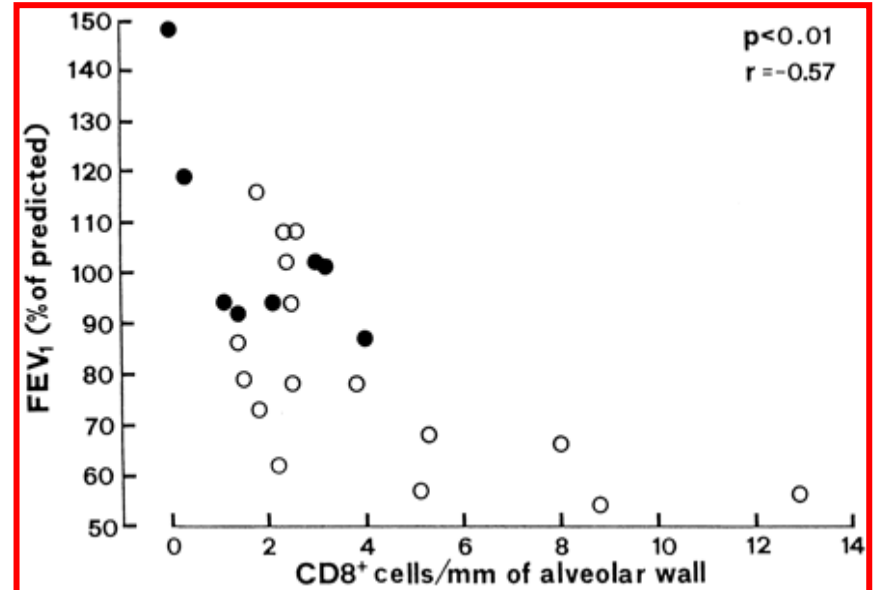
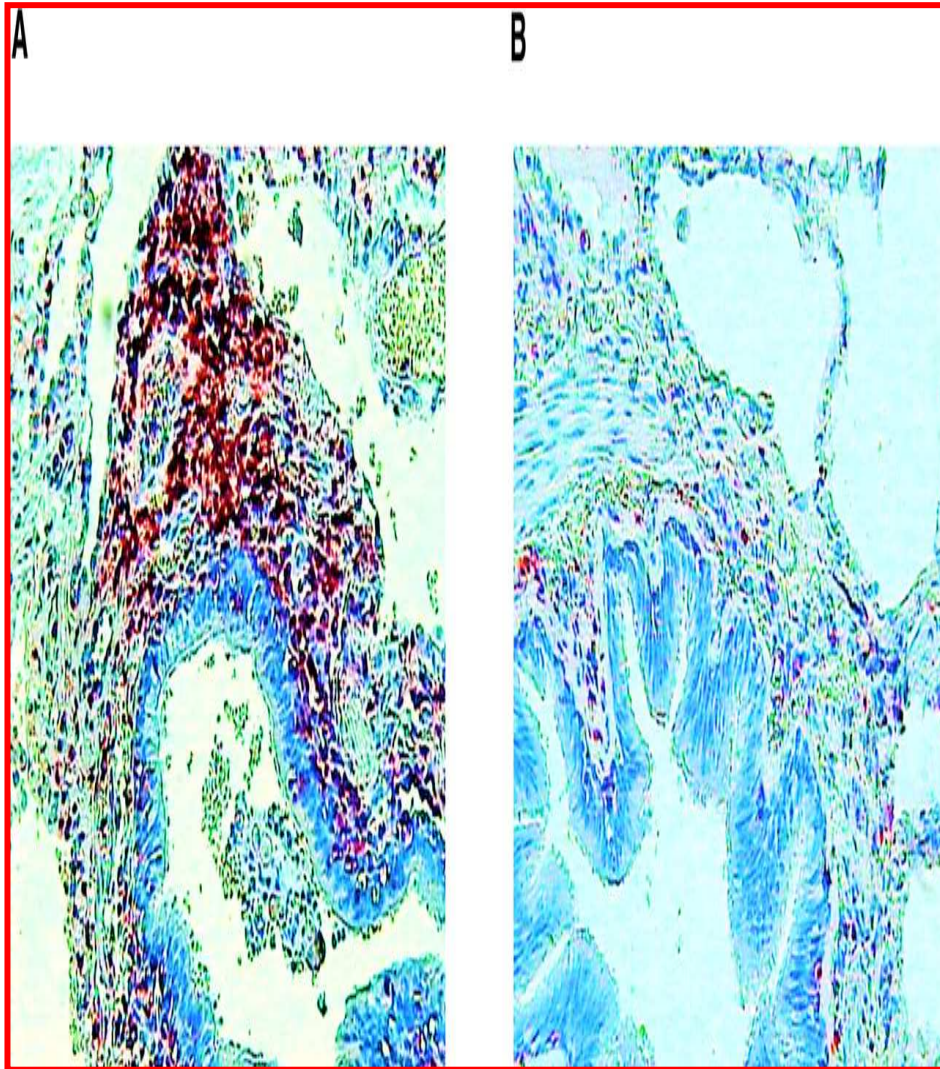


13,430 males and females without previous myocardial infarction  
Copenhagen City Heart Study, 5-year follow-up  
Relative Risk for Atrial Fibrillation

## Σχεδιασμός

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- Συν-νοσηρότητες
- Φλεγμονή και  $FEV_1$

# Παλιές ιστορίες...



Turato G et al, Saetta M et al Blue 2002,1999

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- Φλεγμονή και  $FEV_1$
- Σύγκριση με τους άλλους δείκτες

# Δείκτες

## BODE

**Table 2** Variables and point values used for the computation of the multidimensional BODE Index.<sup>40</sup>

Variable	Points on BODE index			
	0	1	2	3
FEV <sub>1</sub> (% of predicted)	≥65	50–64	36–49	<35
Distance walked in 6 min (m)	≥350	250–349	150–249	<149
MMRC dyspnea scale	0–1	2	3	4
Body mass index (kg/m <sup>2</sup> )	>21	≤21		

FEV<sub>1</sub>: Forced expiratory volume in 1 s; MMRC: modified Medical Research Council.

## ADO

	0 points	1 point	2 points	3 points	4 points	5 points
FEV <sub>1</sub> (% predicted)	≥65%	≥36–64%	≥35%	..	..	..
Dyspnoea (MRC scale)	0–1	2	3	4	..	..
Age (years)	40–49	50–59	60–69	70–79	80–89	≥90

FEV<sub>1</sub>: forced expiratory volume in 1 s. MRC=Medical Research Council.

**Table 6:** Assignment of points for the ADO index

## HADO

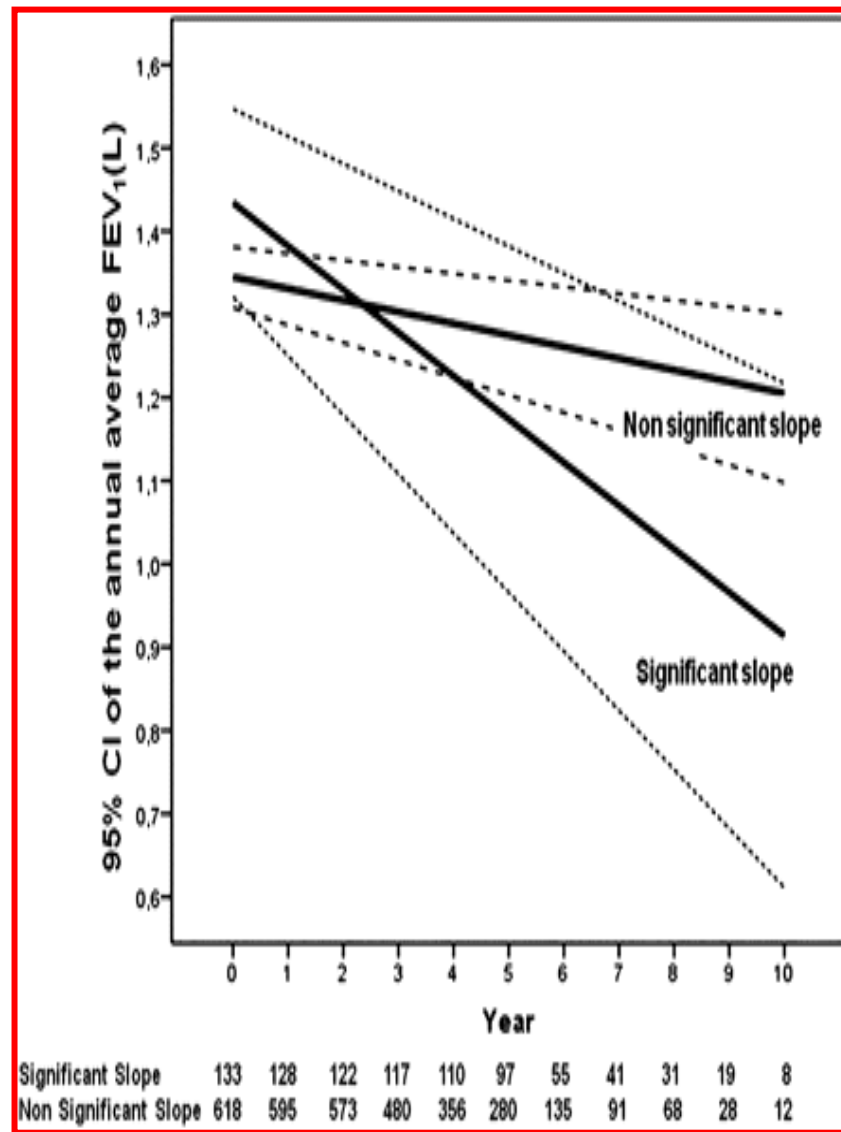
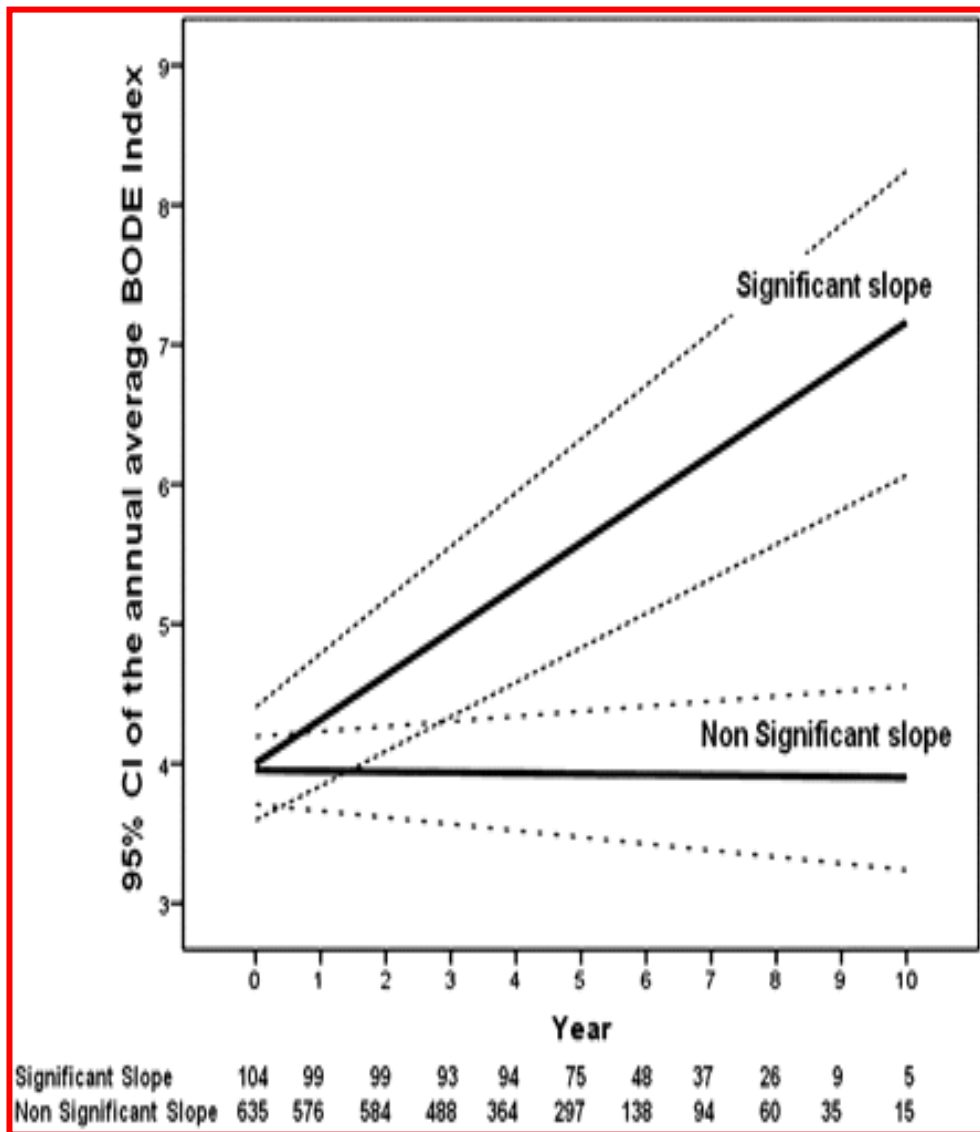
HADO-score	value
<b>FEV1%</b>	
≤65	3
50 to 64	2
36 to 49	1
≤35	0
<b>Dyspnea scale</b>	
1	3
2	2
3	1
4 to 5	0
<b>Physical Activity</b>	
3	3
2	2
1	1
0	0
<b>Health status</b>	
very good/excellent	3
good	2
fair	1
bad	0

## DOSE

**TABLE 4. DOSE INDEX SCORING SYSTEM**

	DOSE Index Points			
	0	1	2	3
MRC Dyspnea Scale score	0–1	2	3	4
Obstruction FEV <sub>1</sub> % predicted	>50	30–49	<30	
Smoking status	Nonsmoker	Smoker		
Exacerbations per year	0–1	2–3	>3	

# BODE vs FEV<sub>1</sub>?



## DOSE vs FEV<sub>1</sub> : Διαφορετικοί παράμετροι

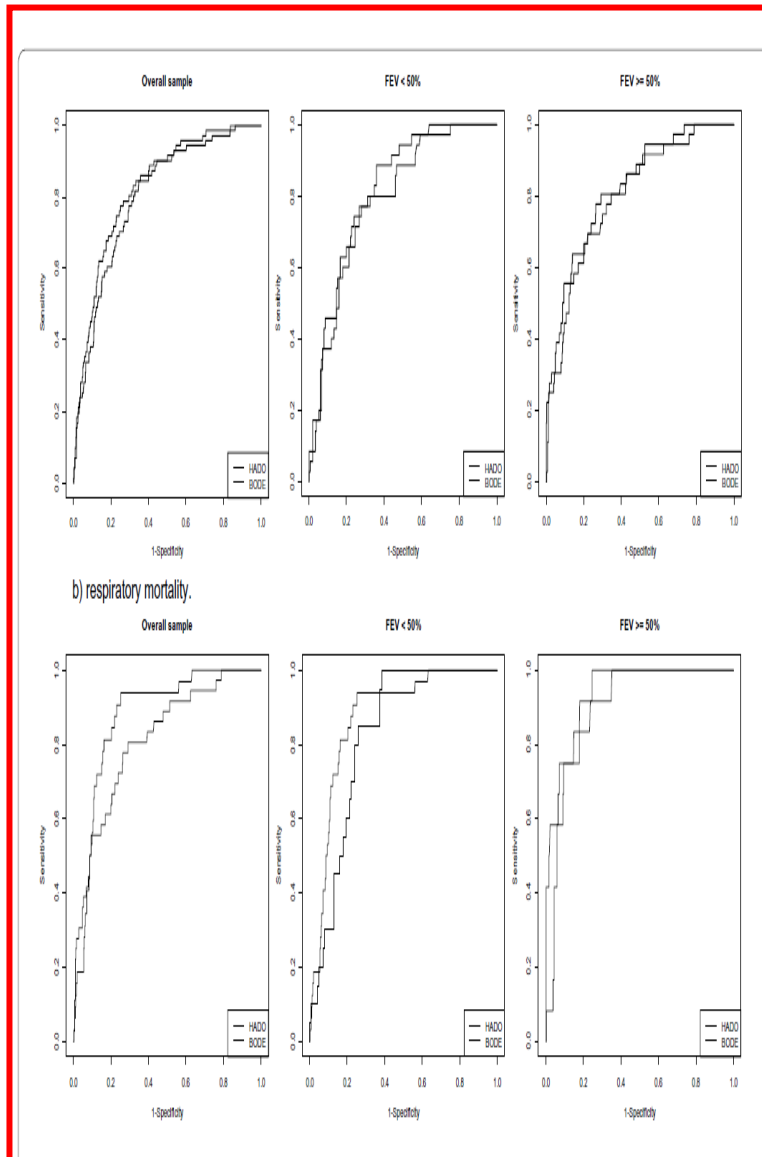
TABLE 7. CORRELATIONS BETWEEN TOTAL DOSE INDEX SCORE, ITS COMPONENT ITEMS, AND MARKERS OF DISEASE SEVERITY

	SGRQ (Tokyo)	CCQ (Devon Derivation)	Emergency Visits (Devon Derivation)	Bed Days (Devon Derivation)	6MWT (Holland)
DOSE	0.49*	0.64*	0.19*	0.17*	0.43*
MRC Dyspnea Scale	0.48*	0.67*	0.18*	0.18*	0.39*
Obstruction FEV <sub>1</sub> % predicted	0.45*	0.34*	0.09	0.06	0.30*
Smoking status	0.10	0.18*	0.01	0.02	0.10
Exacerbations per year	0.02	0.26*	0.21*	0.21*	0.17

*Definition of abbreviation: 6MWT = 6-minute walk test.*

\*  $P < 0.01$ .

# BODE & HADO vs FEV<sub>1</sub>: επιβίωση



	All Patients (n = 543)	Alive (n = 472)	Dead (n = 71)	P-Value
BODE index	2.8 ± 1.8	2.6 ± 1.6	4.2 ± 1.9	<.001
HADO score	6.8 ± 2.1	7 ± 2	5.6 ± 2.1	<.001
FEV <sub>1</sub> , L	1.46 ± 0.44 L	1.50 ± 0.44	1.20 ± 0.36	<.001
FEV <sub>1%</sub>	55.0 ± 13.3	55.9 ± 13	49 ± 14	<.001

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- Φαρμακευτική αξιολόγηση και όχι μόνο...
- Συν-νοσηρότητες
- Φλεγμονή και  $FEV_1$
- Σύγκριση με τους άλλους δείκτες
- Μύθοι και πραγματικότητες...

# Μύθοι & Πραγματικότητες

## Μύθοι

Η αξιολόγηση της σπυρομέτρησης χρειάζεται πολλούς παραμέτρους

Δεν προσφέρει πολλά στη διαχείριση ασθενών με ΧΑΠ

Όχι τόσο χρήσιμη στην έγκαιρη διάγνωση

Ακριβή

Χάνει καθαρά από τους άλλους δείκτες

Δεν αντιπροσωπεύει τίποτα πέρα από μια τιμή

## Πραγματικότητα

Χρειάζεται FEV<sub>1</sub>, FVC, και το λόγο

Χρήσιμη: Διάγνωση-σταδιοποίηση-φαρμακευτική ανταπόκριση

Ίσως η μόνη χρήσιμη

Φθηνότερη από το μελλοντικό κόστος της ΧΑΠ

Δεν υστερεί σε τίποτα –κάθε δείκτης την περιέχει

Σχετίζεται με την επιβίωση, συννοσηρότητες, φαινότυπους, γενετικό κίνδυνο, φλεγμονή



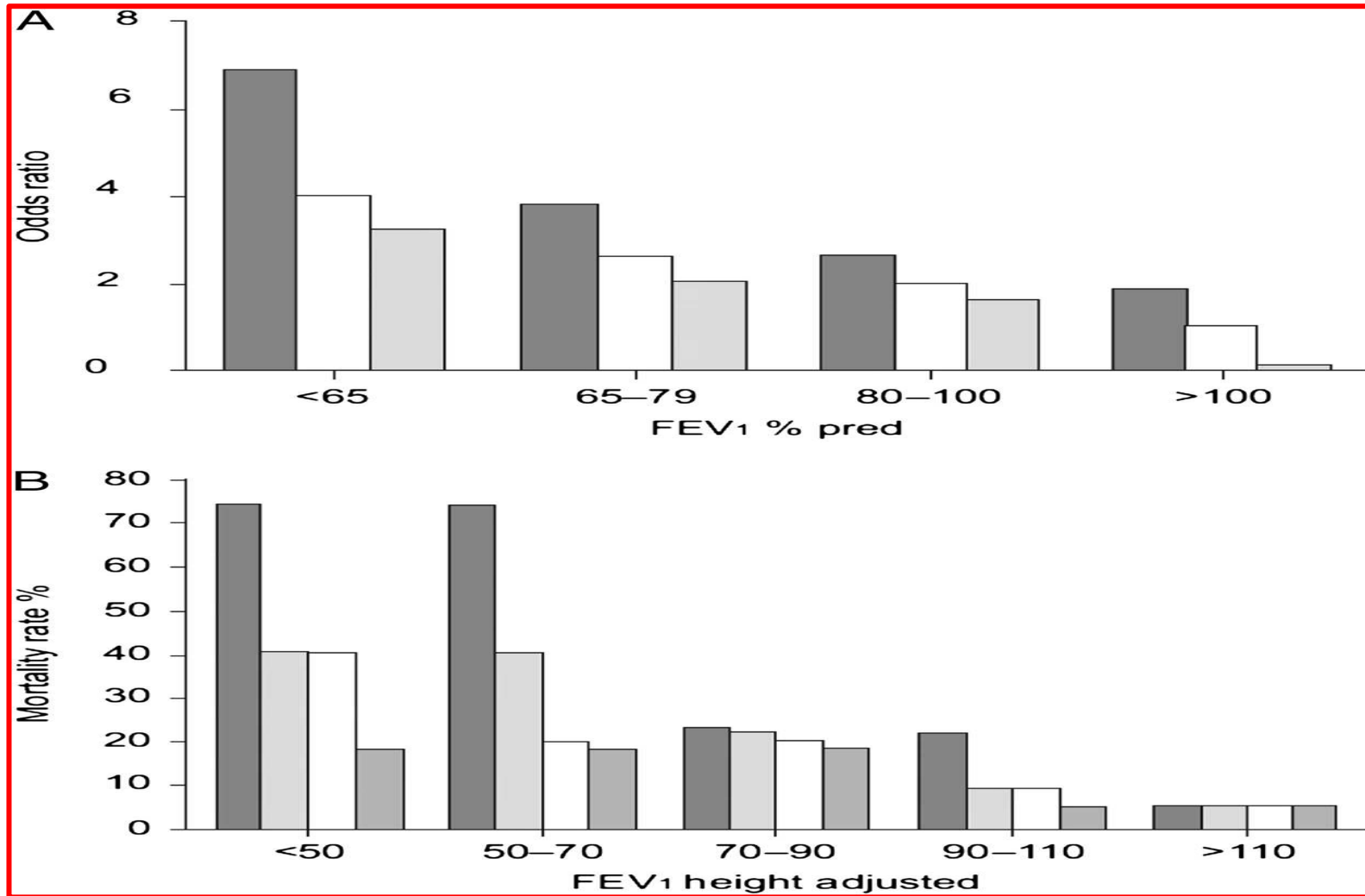
## **FEV<sub>1</sub>: η θετική άποψη -Δευτερολογία**

**Στέλιος Θ. Λουκίδης MD FCCP**

**ERS secretary group 5.2**

**Ιατρική σχολή ΕΚΠΑ**

# FEV1, κάπνισμα και OR για CDV



Nussbaumer-Ochsner Y , Rabe K F Chest 2011;139:165-173

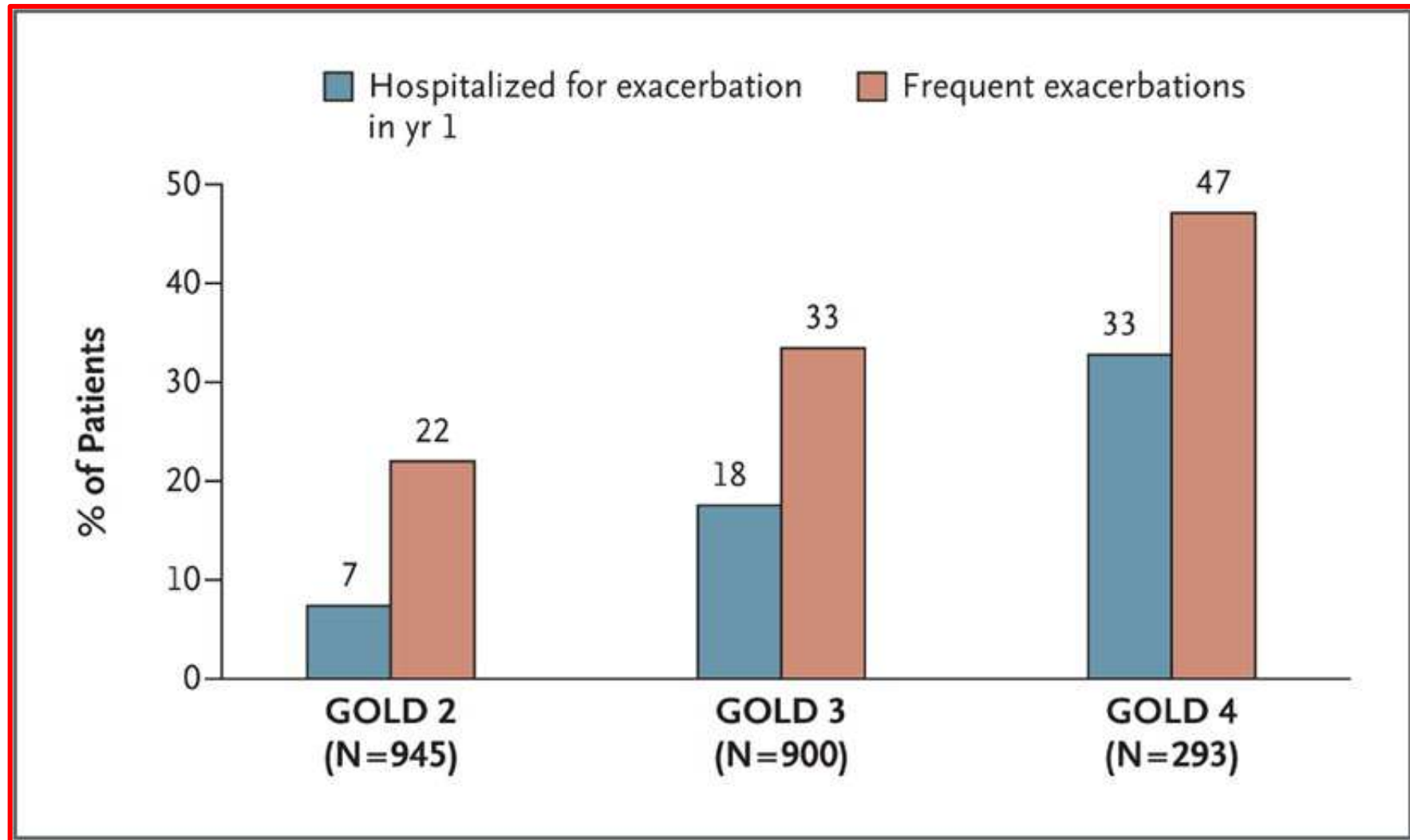
## Μειωμένη FEV<sub>1</sub> και CDV θνησιμότητα

Variables	p Value for Trend‡	p Value for Trend§	FEV <sub>1</sub> Quintile†				
			1	2	3	4	5
Mean FEV <sub>1</sub> , % predicted			63	80	88	96	109
Cardiovascular mortality	< 0.001	< 0.001	3.36 (1.54–7.34)	2.00 (1.03–3.89)	2.22 (1.23–4.01)	0.93 (0.39–2.25)	1.0
Cardiovascular hospitalization	0.024	0.049	1.69 (0.84–3.40)	1.44 (0.78–2.65)	1.60 (0.88–2.90)	0.99 (0.52–1.88)	1.0
Cardiovascular death or hospitalization	< 0.001	< 0.001	2.44 (1.37–4.33)	1.70 (1.08–2.67)	1.78 (1.18–2.70)	1.06 (0.62–1.82)	1.0
Mortality from ischemic heart disease	< 0.001	< 0.001	5.65 (2.26–14.13)	3.11 (1.38–7.03)	3.69 (1.50–9.06)	1.50 (0.54–4.20)	1.0
Hospitalization from ischemic heart disease	0.103	0.182	1.52 (0.67–3.42)	1.39 (0.66–2.91)	1.25 (0.61–2.59)	0.95 (0.45–2.02)	1.0

Data are presented as RR (95% CI) and have been adjusted for various factors including modified Framingham risk score for coronary heart disease, age, smoking status, gender, diabetes, systolic and diastolic BP, cholesterol, BMI, race, and treated hypertension

Data from NHANES I (patients 40-60 years at baseline, n=1,861)

# Παροξύνσεις ΧΑΠ: Υπάρχουν σε όλα τα στάδια



## Δύσπνοια-σύγκριση με IC/TLC

**Table 2 Correlations of the BDI score with airflow limitation and static hyperinflation**

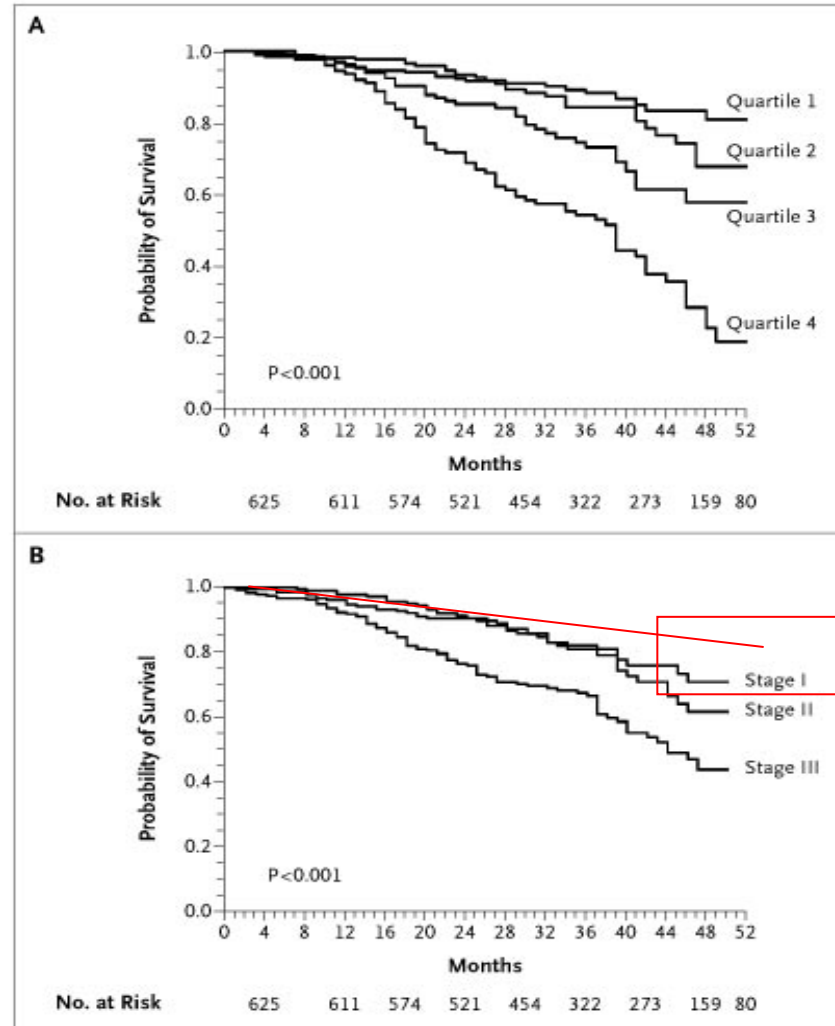
	Spearman's rank correlation coefficients		Pearson's correlation coefficient	
	Rs	p value	R	p value
Dyspnea vs. Airflow limitation				
BDI score vs. FEV <sub>1</sub> (L)	0.60	< 0.0001	0.60	< 0.0001
BDI score vs. FEV <sub>1</sub> (%pred)	0.56	< 0.0001	0.57	< 0.0001
BDI score vs. FEV <sub>1</sub> /FVC	0.56	< 0.0001	0.57	< 0.0001
Dyspnea vs. Static Hyperinflation				
BDI score vs. IC (L)	0.45	< 0.0001	0.48	< 0.0001
BDI score vs. IC/predicted TLC	0.46	< 0.0001	0.51	< 0.0001
BDI score vs. IC/TLC	0.47	< 0.0001	0.48	< 0.0001

# BODE vs FEV<sub>1</sub> : Από μία άλλη σκοπιά

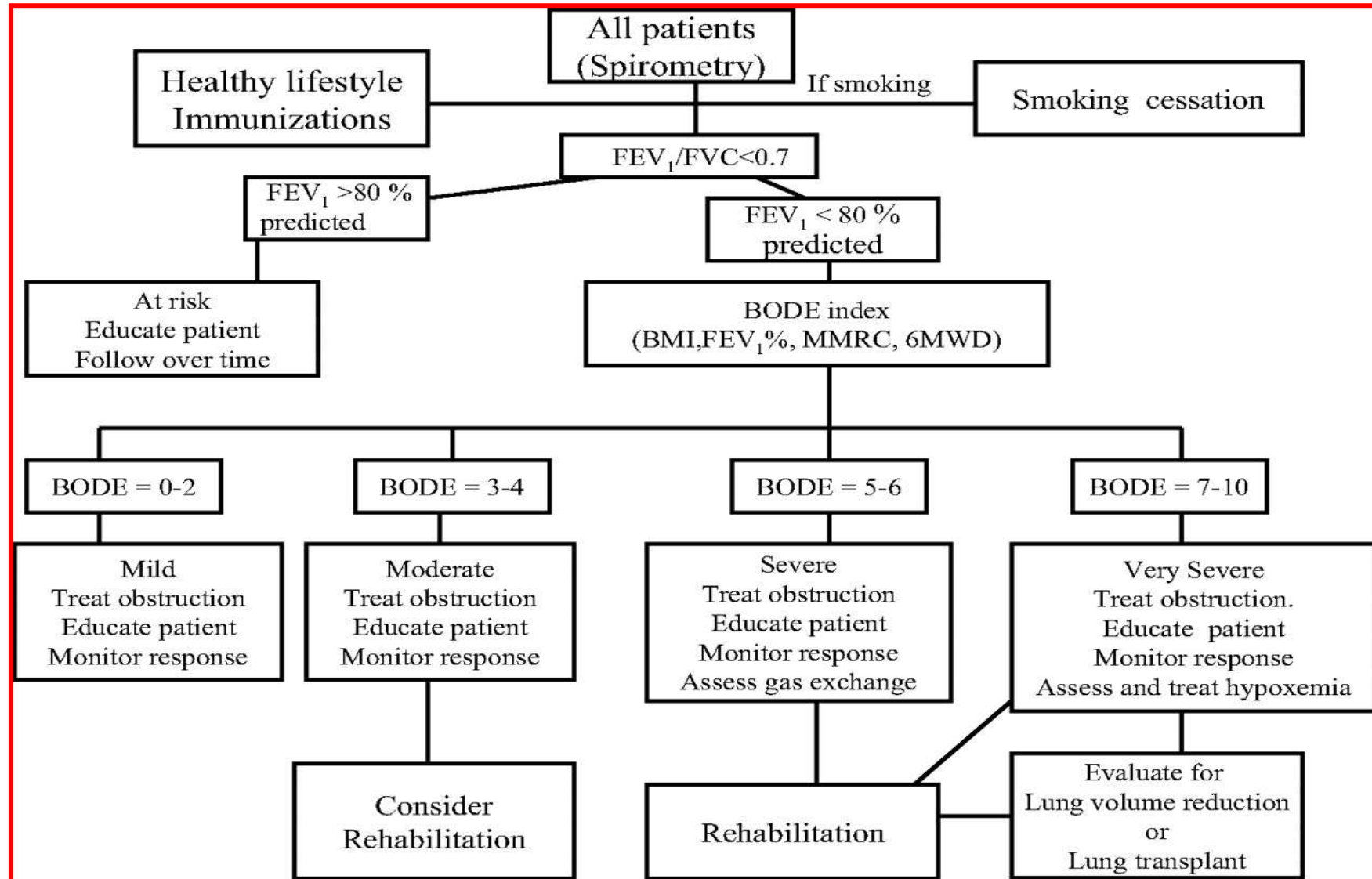
**Table 1.** Characteristics of the First 207 Patients, According to Whether They Survived.\*

Characteristic	Survived (N=182)	Died (N=25)	P Value
	mean ±SD		
Age (yr)	66±9	70±7	0.03
FVC (liters)	2.78±0.89	2.27±0.57	0.04
FEV <sub>1</sub>			
	Liters	1.31±0.63	0.84±0.33
Percent of predicted	43±19	28±12	0.001
FRC (%)	150±43	170±52	0.12
Inspiratory capacity (liters)	2.0±0.7	1.6±0.5	0.007
MMRC dyspnea scale†	2.7±0.89	3.3±0.87	0.001
Distance walked in 6 min (m)	264±113	175±86	0.001
Body-mass index‡	26±5	23±5	0.002
Hematocrit (%)	42±5	39±5	0.01
Albumin (g/ml)	4.0±0.3	3.8±0.4	0.08
Smoking history (pack-yr)	88±48	77±48	0.36
Charlson index§	2.9±1.3	5.9±1.9	0.02

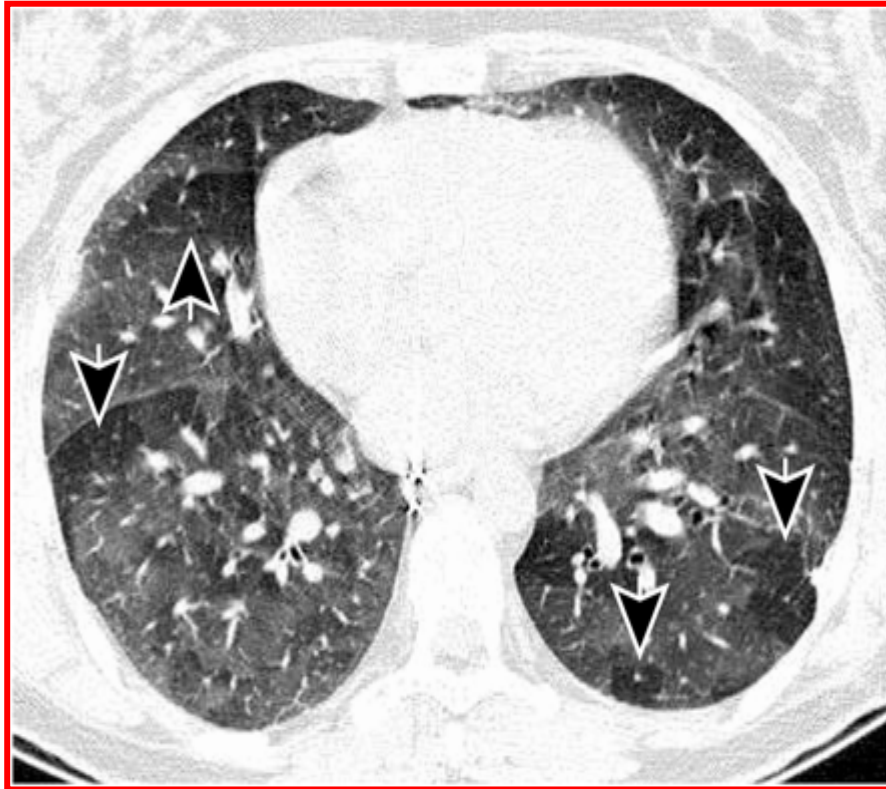
- \* FVC denotes forced vital capacity, FEV<sub>1</sub> forced expiratory volume in one second, and FRC functional residual capacity.  
 † Scores on the modified Medical Research Council (MMRC) dyspnea scale can range from 0 to 4, with a score of 4 indicating that the patient is too breathless to leave the house or becomes breathless when dressing or undressing.  
 ‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.  
 § Scores on the Charlson index can range from 0 to 33, with higher scores indicating more coexisting conditions.



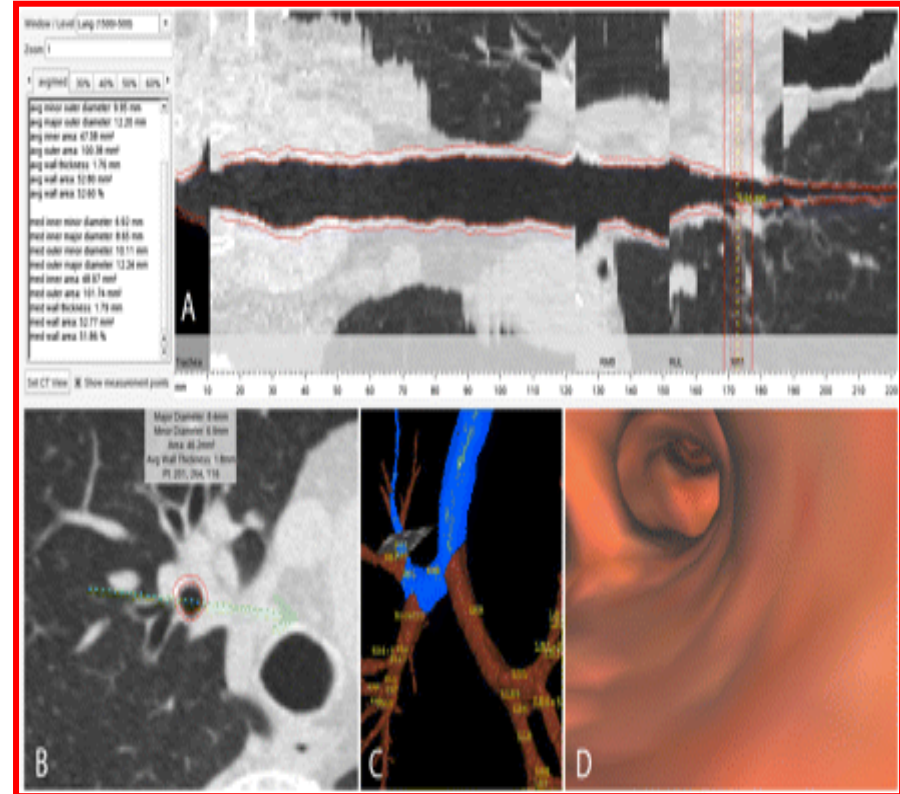
## Ένας διαφορετικός αλγόριθμος



# HRCT: Αραίωση, πάχυνση τοιχώματος, παγίδευση



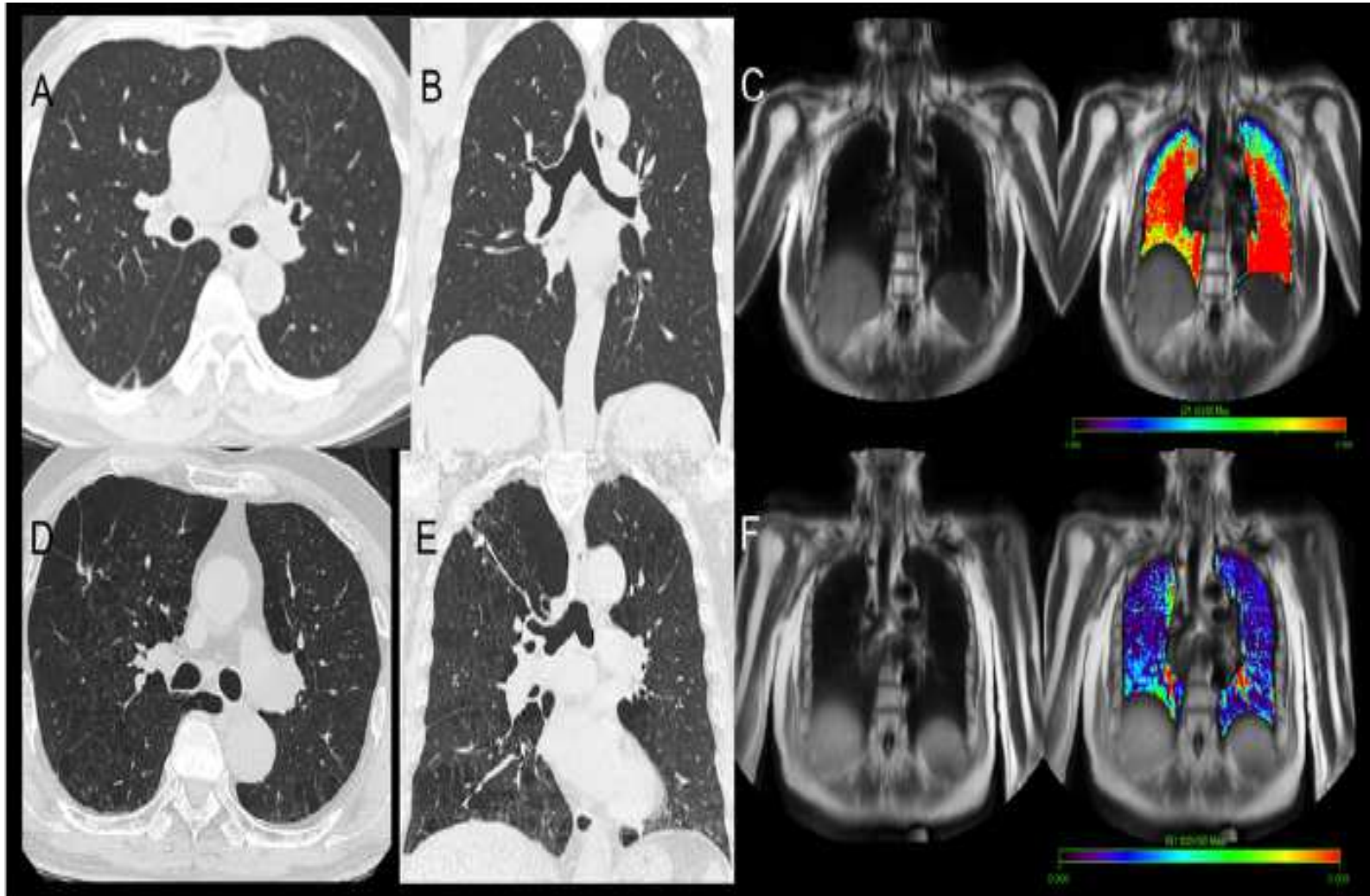
Σοβαρή ΧΑΠ όχι σε  
ήπια  
BODE  
IC/TLC



FEV<sub>1</sub>

Coxson H et al Proc ATS 2009

# O<sub>2</sub> MRI & ΧΑΠ



DLCO-FEV1

Ohno Y et al AJR2008



The ideal approach is not to measure any single biomarker in order to detect elevated or decreased levels, but to try to identify the particular phenotype that is related to the specific biomarker –parameter and the underlying mechanism. Most likely a single parameter is not sufficient and the combination of more than one parameters may approach more effectively the characterization of a specific phenotype. We believe that we are not close but we are definitely not that far from this achievement. We still have a lot to learn and improve .....