Διακοπή καπνίσματος σε *Ασθενείς* *με* ***Αποφρακτικού τύπου Πνευμονοπάθειες***

Ι. Μητρούσκα

Πνευμονολογική Κλινική

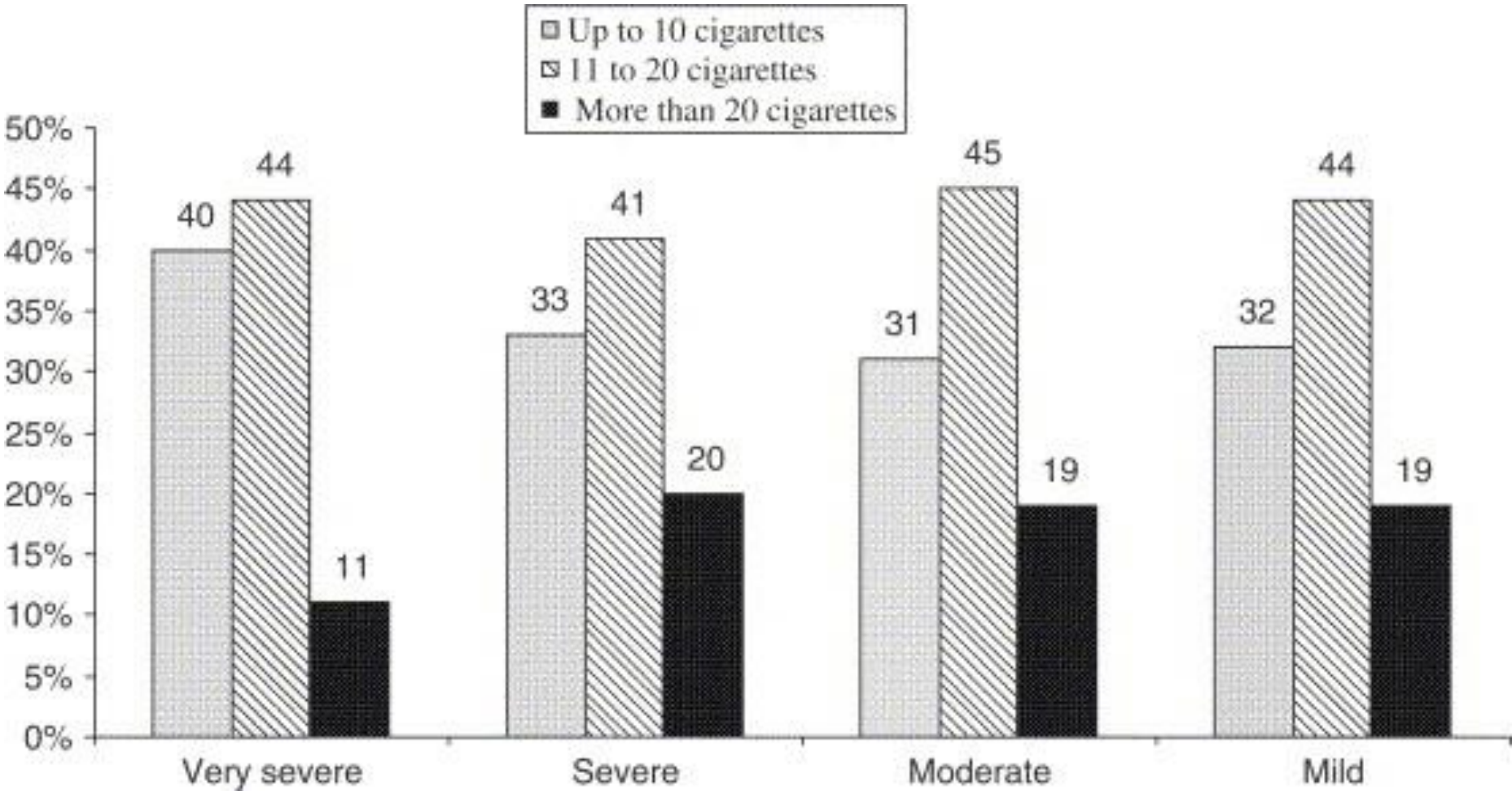
ΠΑΓΝΗ Κρήτης

Καπνίζουν οι ασθενείς με πνευμονοπάθεια;

- **Αποφρακτική νόσος πνεύμονα**
  - **Άσθμα**
  - **Χρόνια Αποφρακτική Πνευμονοπάθεια**

Κάπνισμα μεταξύ ασθενών με ΧΑΠ

(11.973 pts Spanish study)

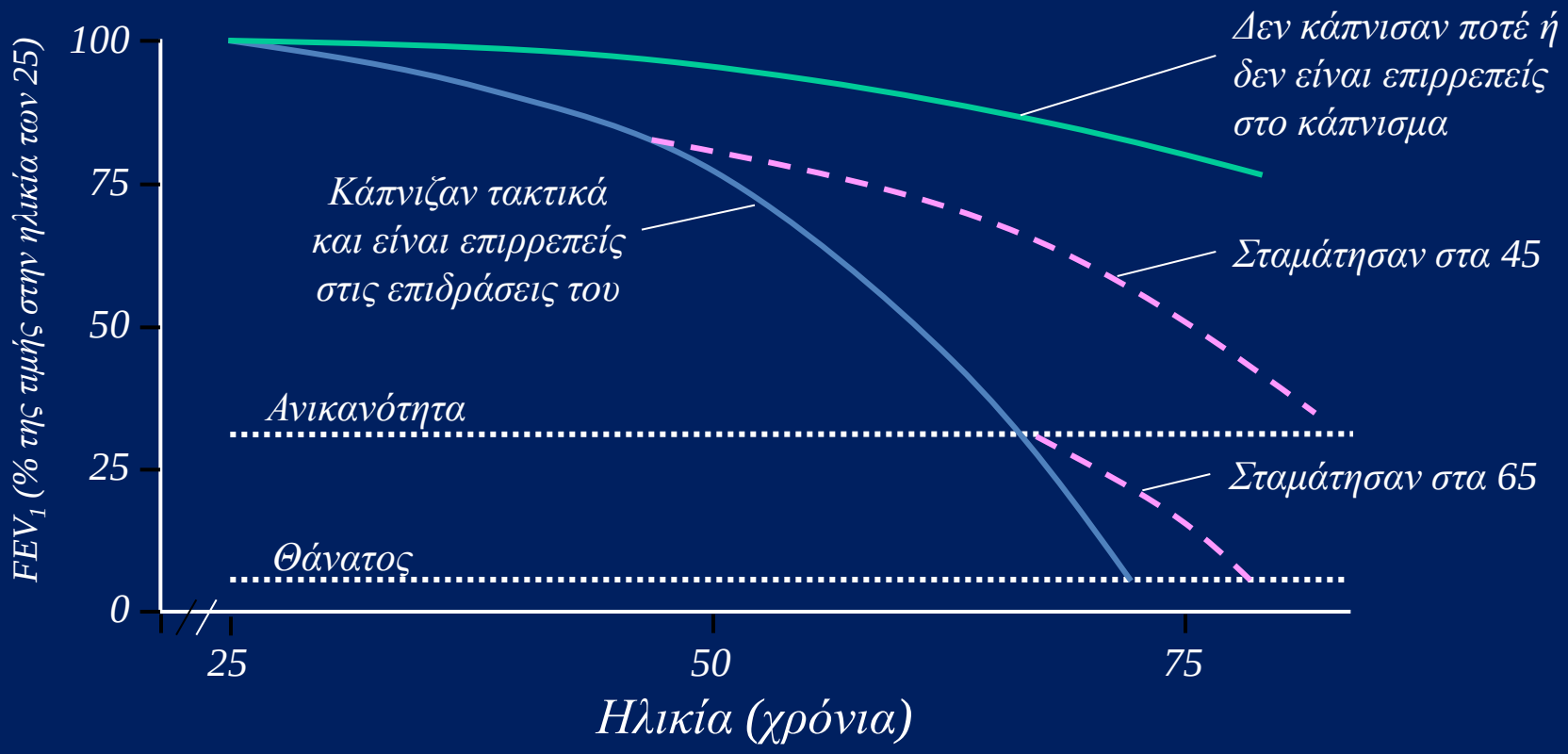


Viejo-Banuelos J. Resp Med 2006 (100): 2137-43

Smoking prevalence among chronic obstructive pulmonary disease patients in large randomised, placebo-controlled trials with inhaled corticosteroids and/or long-acting β_2-agonists and/or long-acting anti-muscarinic drugs

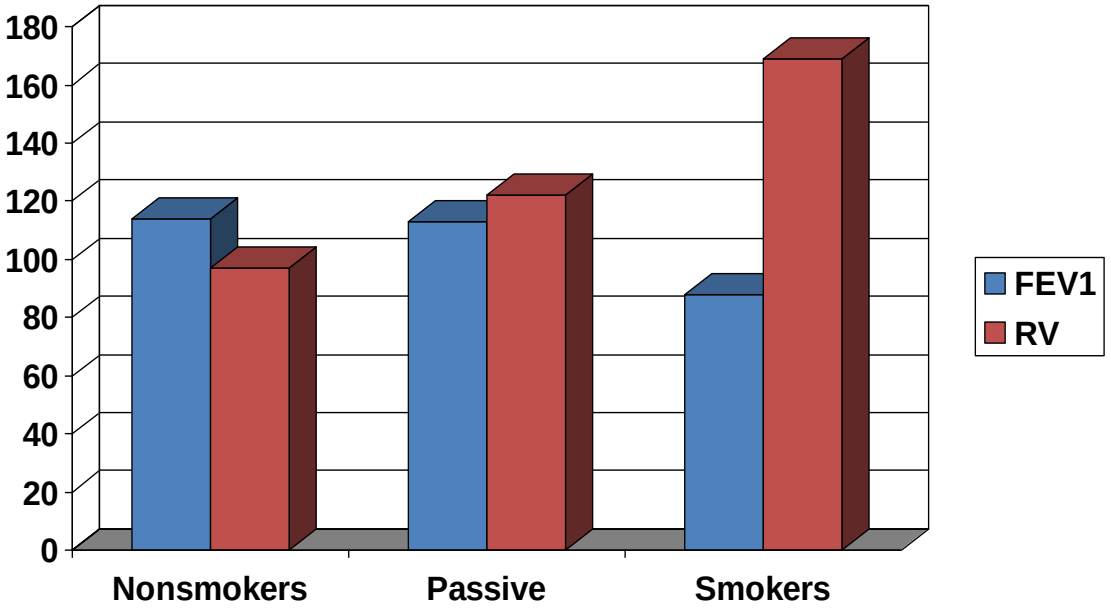
Study	Subjects n	Age yrs	FEV_1	Smokers %
VESTBO	290	59	2.4 (86)	77
EUROSCOP	647	53	2.5 (80)	54
TRISTAN	1465	63	1.4 (45)	51
TORCH	5343	65	1.2 (45)	45
ISOLDE	751	64	1.4 (50)	38
INSPIRE	1323	65	1.3 (39)	38

Η διακοπή του καπνίσματος εεπιβραδύνει την εξασθένηση της λειτουργίας των πνευμόνων

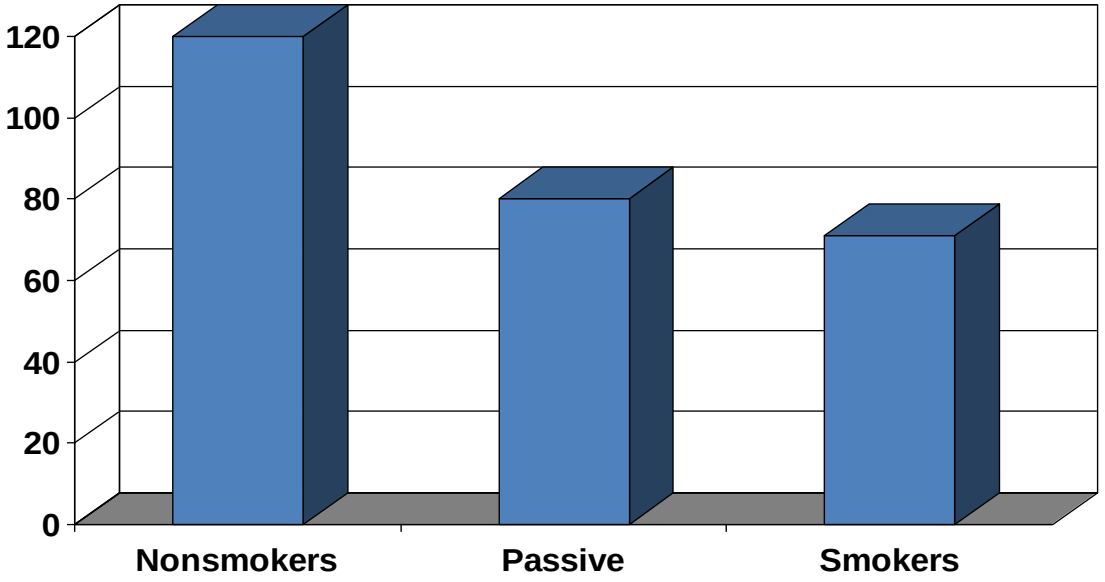


Fletcher et al, Br Med J 1977.

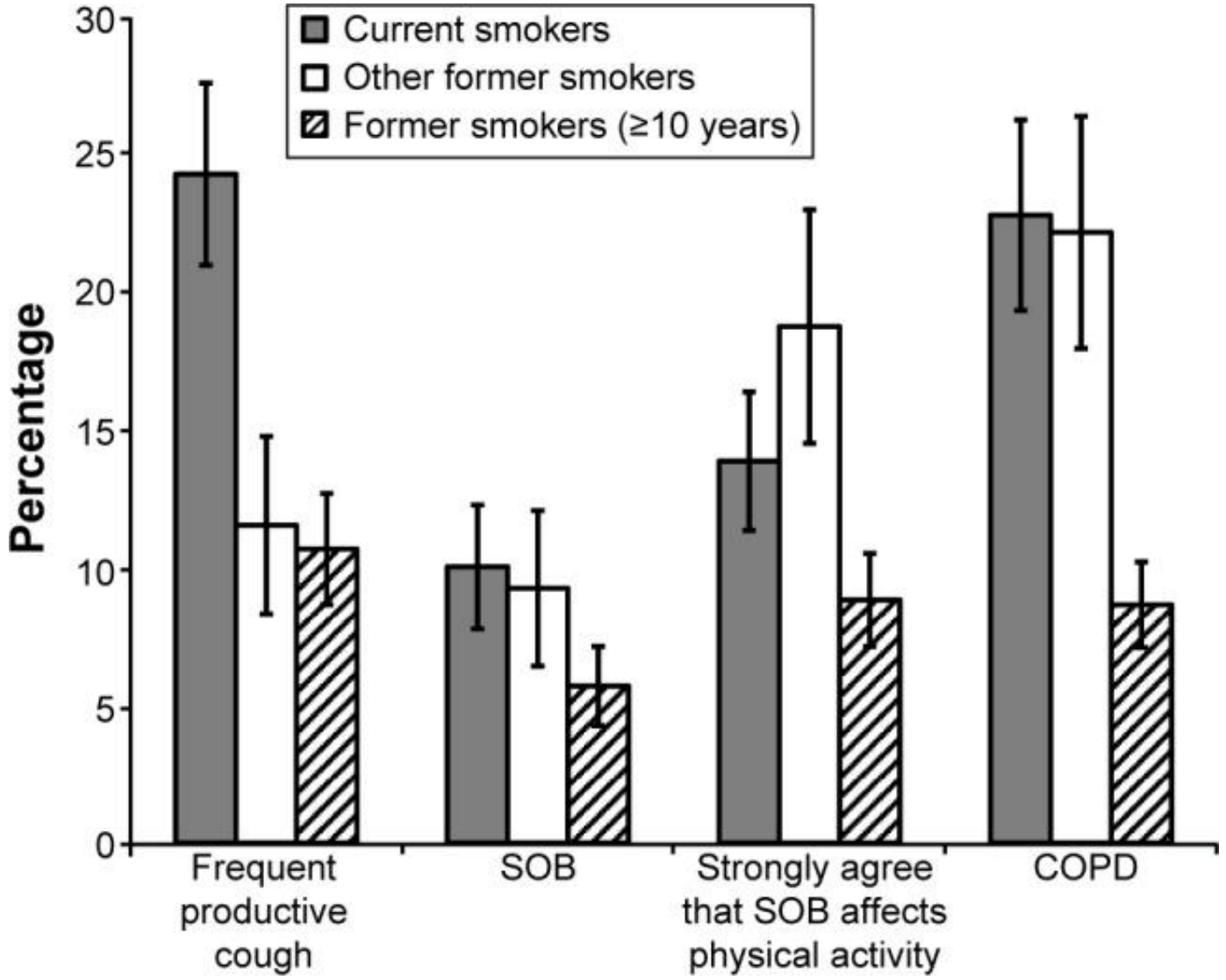
FEV1 and RV, % predicted



DLCO, % predicted



Smoking duration, respiratory symptoms (asthma;)and COPD in adults aged ≥45 years with a smoking history

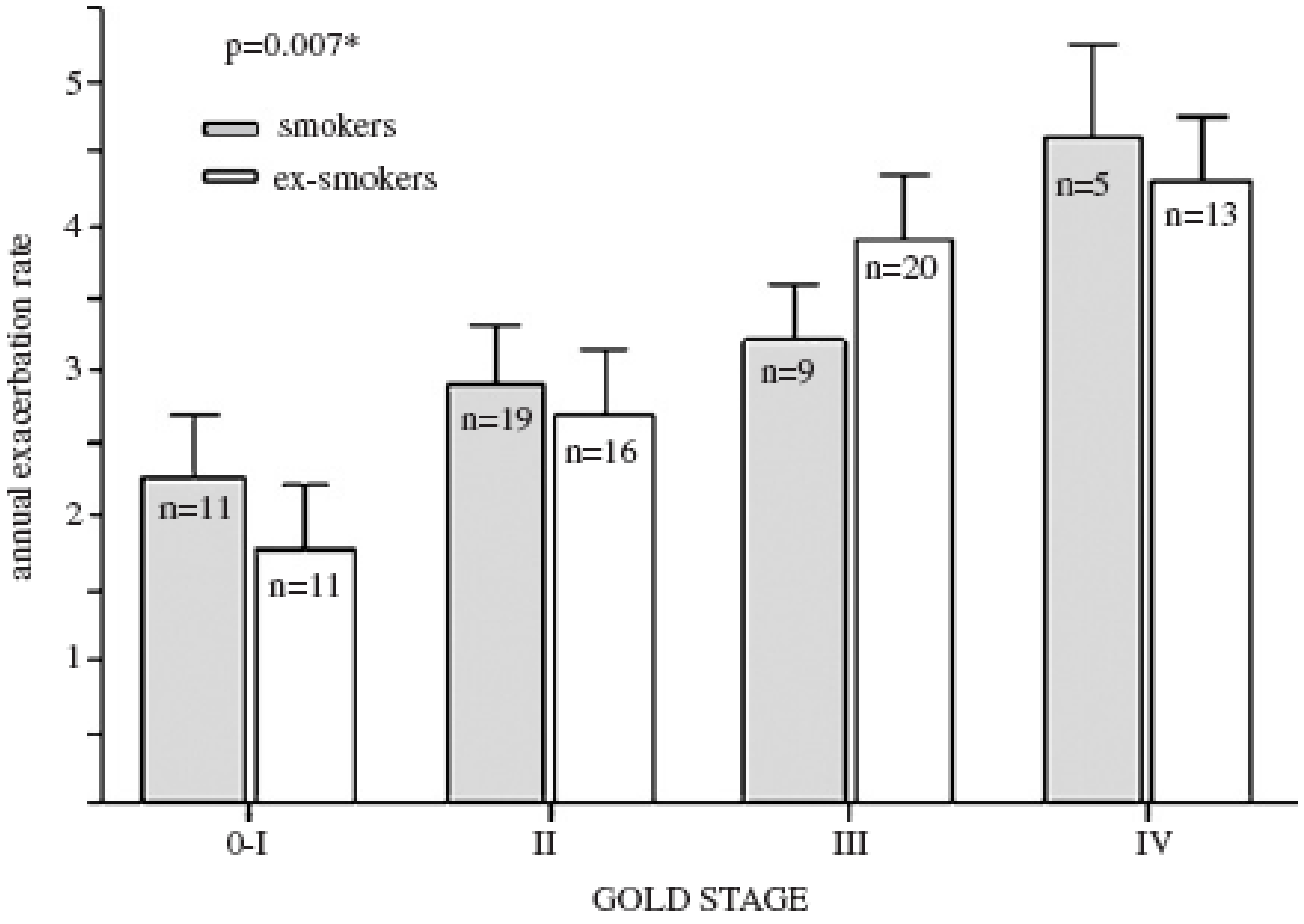


Yong Liu: Int J Chron Obstruct Pulmon Dis. 2015; 10: 1409–1416

Κάπνισμα και παροξυσμός

- **Είναι οι παροξυσμοί συχνότεροι;**
- **Διαφέρει η έκβαση του παροξυσμού της αποφρακτικής νόσου σε νυν καπνιστές**

Παροξυσμοί σε σχέση με το στάδιο της ΧΑΠ *(κατά GOLD)*



D. Makris Respir Med. Dec 2006

- **Το κάπνισμα επηρεάζει τους *αμυντικούς μηχανισμούς του πνεύμονα:***

  - ***Καταστέλλει την αντιμικροβιακή δραστηριότητα των μακροφάγων***
    - ***Green GM. N Engl J Med 1967;276(8)***

  - ***Επιβραδύνει την κάθαρση μικροβιακών προϊόντων από τους πνεύμονες***
    - **Jakab GJ. Am Rev Resp Dis 1977;115 (1)**

- **Οι λοιμώξεις του αναπνευστικού θεωρούνται η κύρια αιτία του παροξυσμού της ΧΑΠ**
  - ***Επηρεάζει το κάπνισμα την ευαισθησία στις λοιμώξεις;***

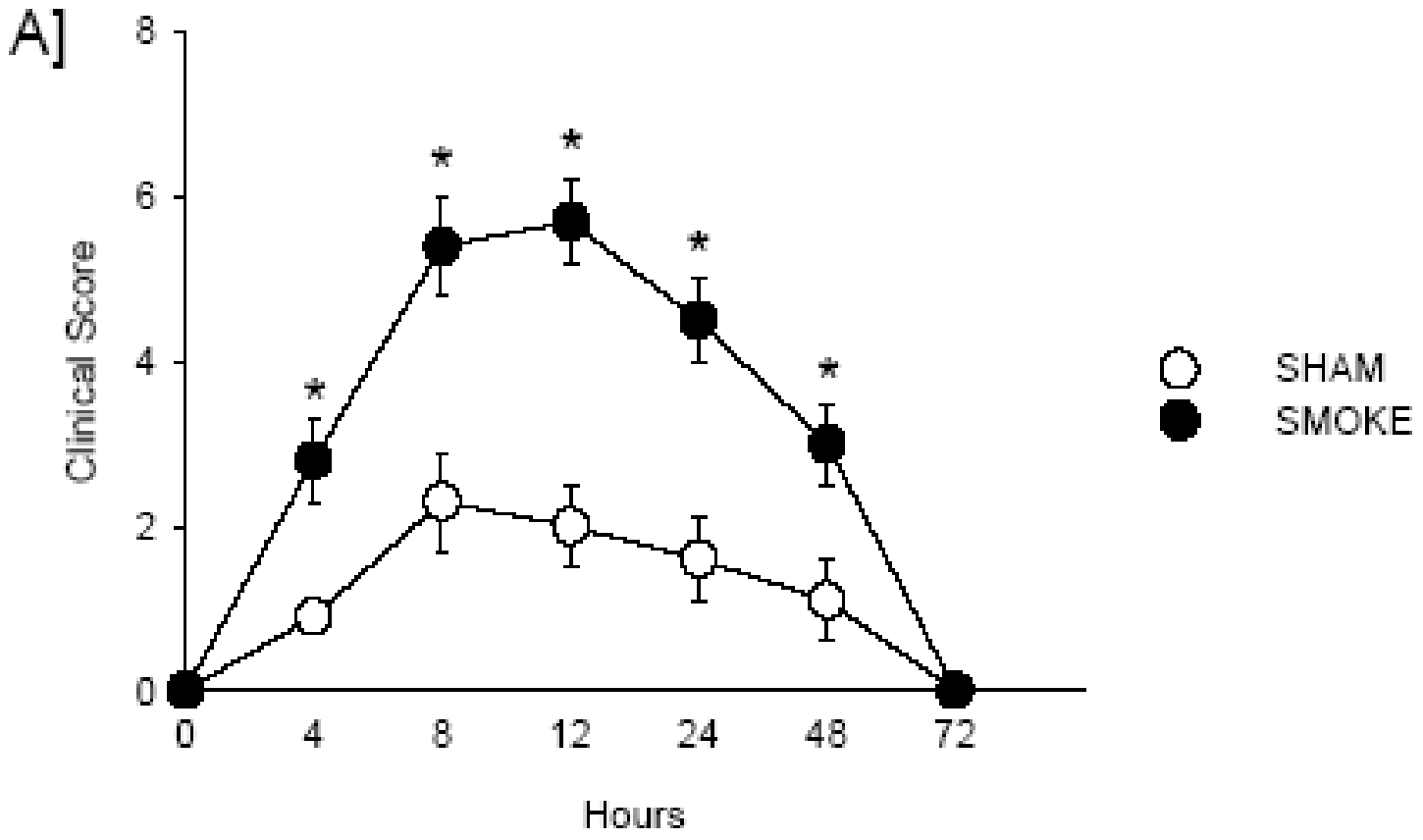
Garcia-Aymerich J. Am J Resp Crit Care Med 2001;164: 1002

Επηρεάζει το κάπνισμα την *Ψευδομονάδα;*

- **Η P-aeruginosa δεν προκαλεί λοίμωξη σε υγιείς ιστούς**
  - ***Plotkowski MC. Am J Resp Cell Mol Biol 1999;20(5)***

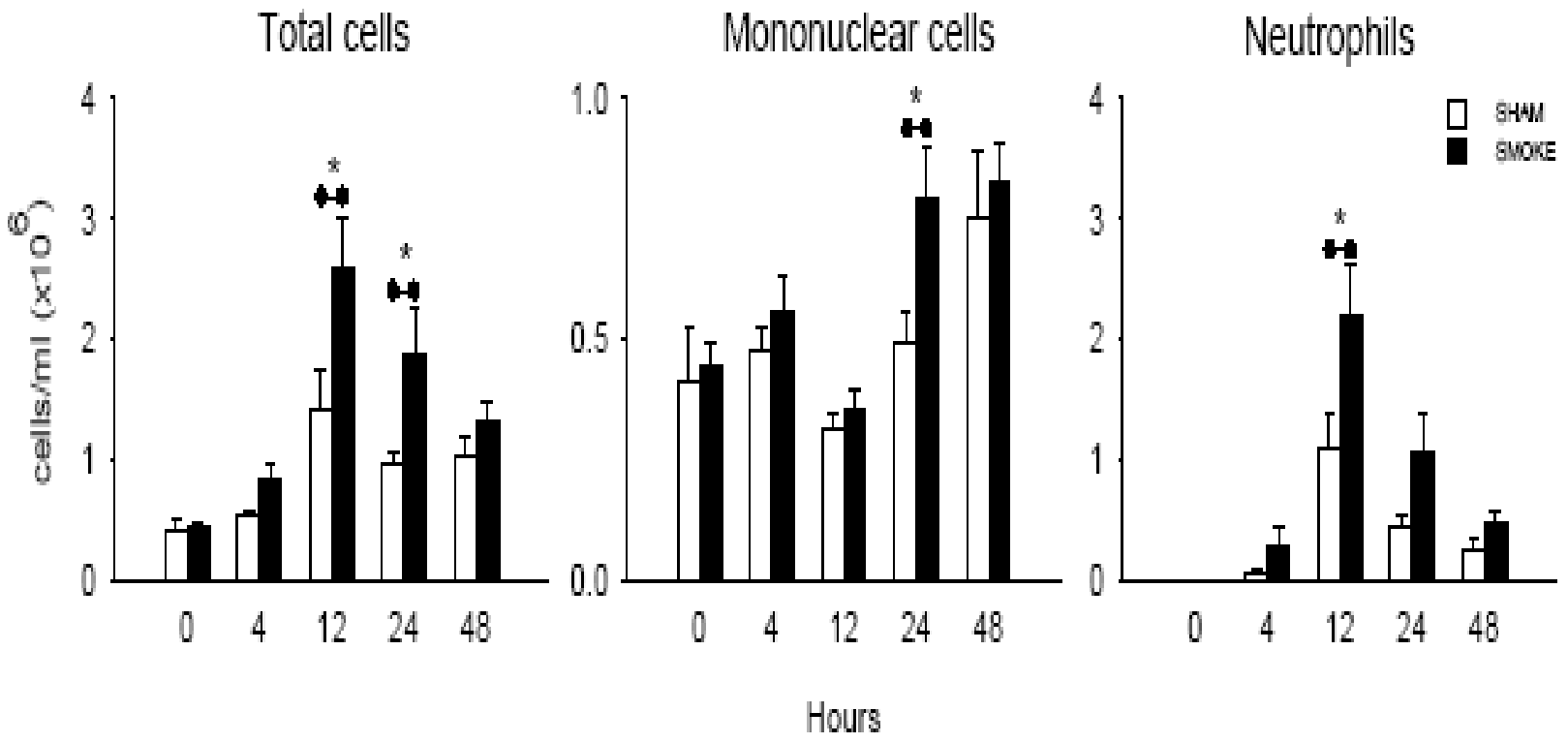
- **Το κάπνισμα προδιαθέτει σε αποικισμό και λοίμωξη από P. aeruginosa;**

Επίδραση του καπνίσματος στην λοίμωξη από ψευδομονάδα



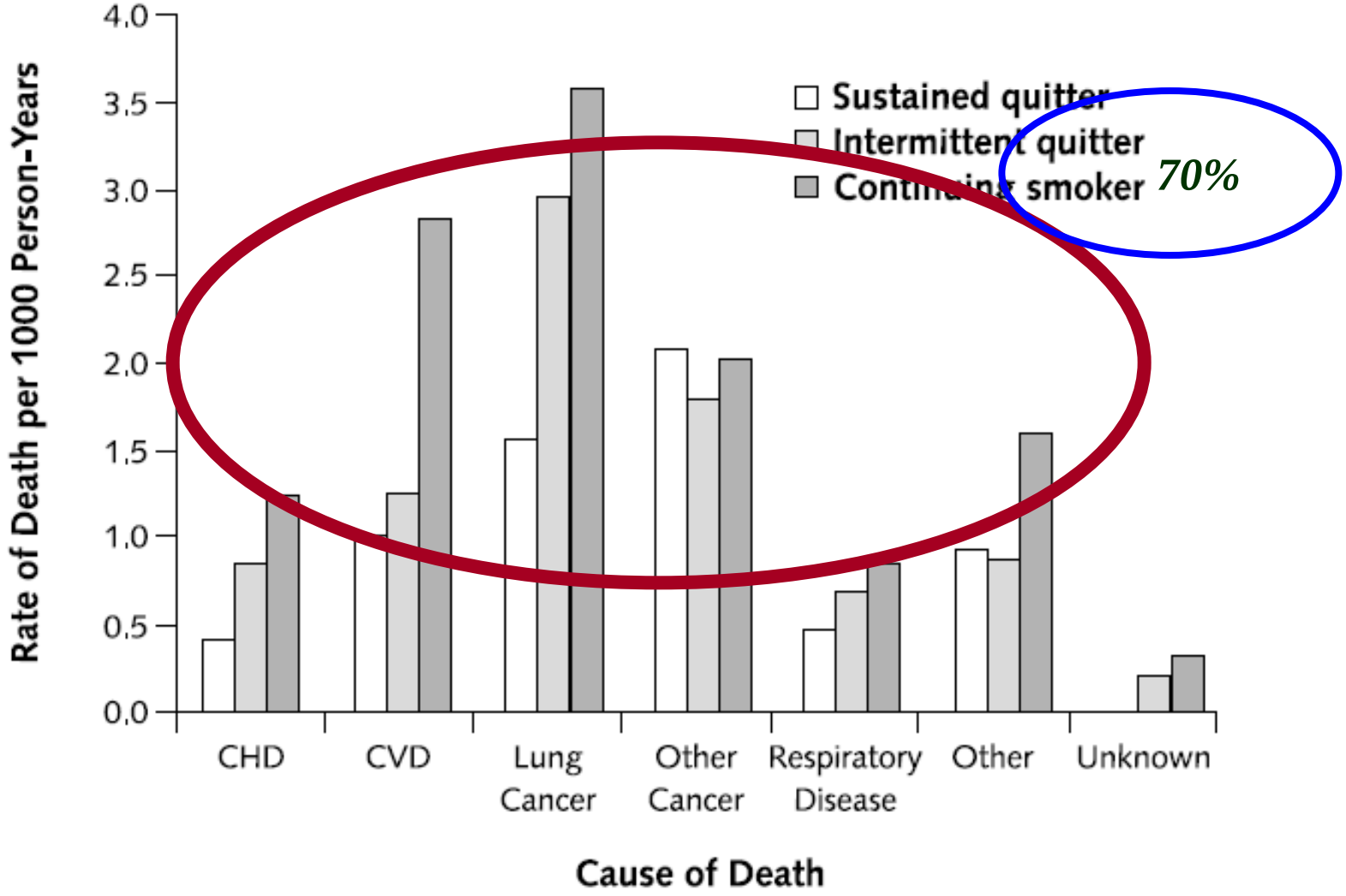
Drannik A. AJRCCM 164 Aug 2004

Επίδραση του καπνίσματος στην λοίμωξη από ψευδομονάδα



Drannik A. AJRCCM 164 Aug 2004

Το κάπνισμα ↑↑ τον κίνδυνο θανάτου από κάθε αιτία στους ασθενείς με ΧΑΠ



Anthonisen NR Annals of Internal Med 2005;142:233-239

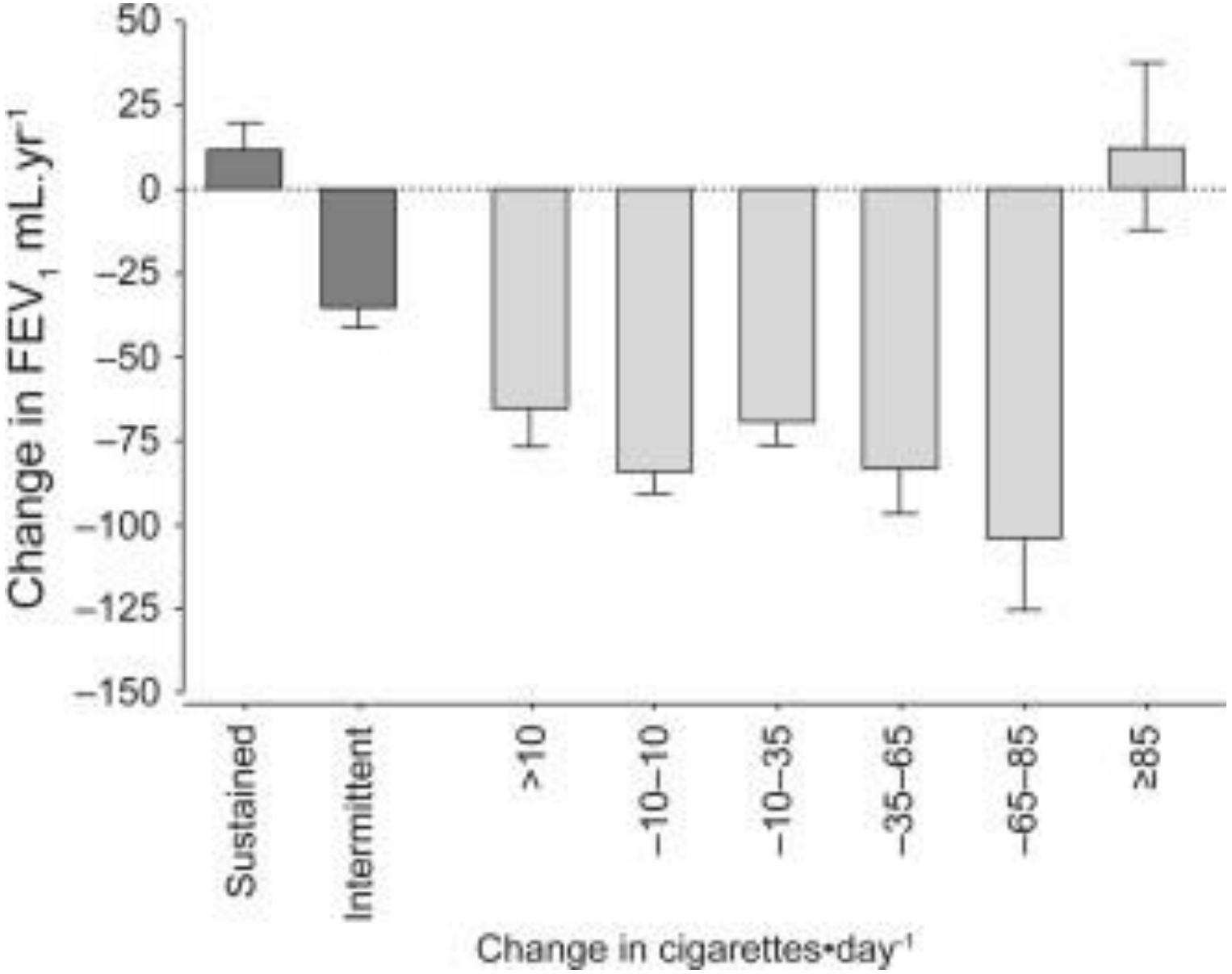
Διακοπή καπνίσματος
σε ασθενείς με ΧΑΠ

Η διακοπή του καπνίσματος αλλάζει το στάδιο κατά GOLD

Lung Health Study
5.600 pts 14.5 years

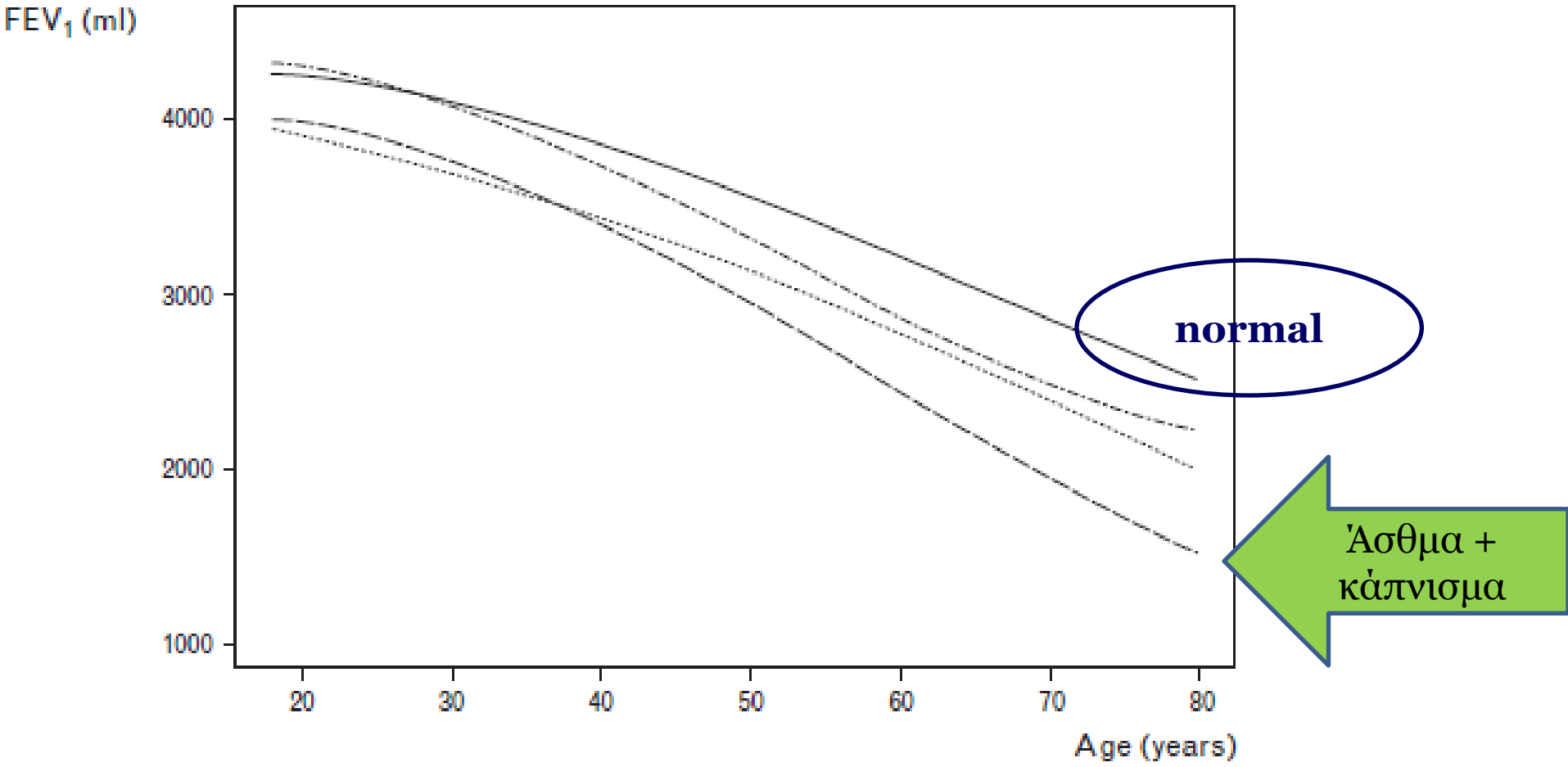
Quitters :
Higher lung function
Higher survival rate

Hogg J. Lancet 364 (21) 2004



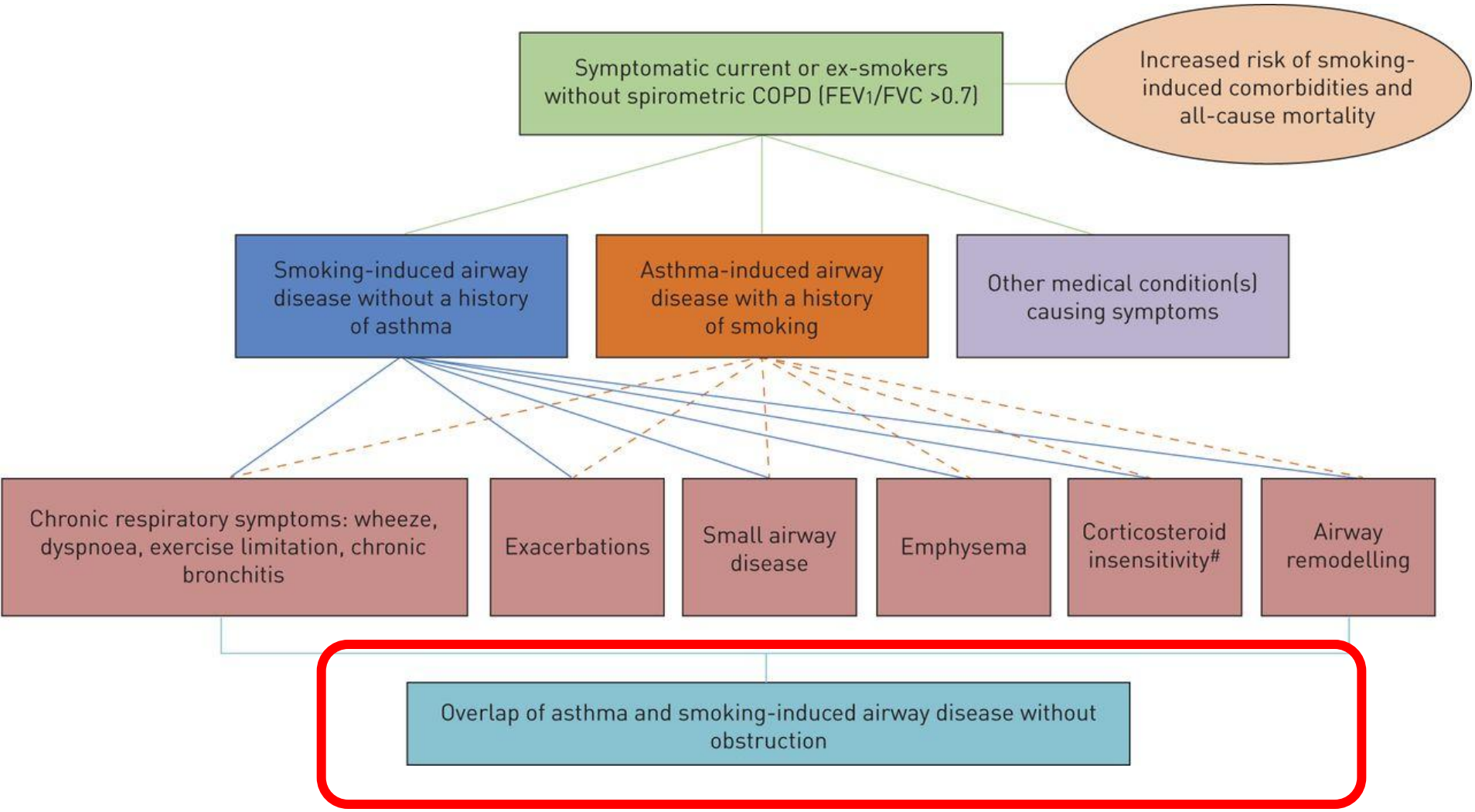
Lung Health Study

Ελάττωση της FEV1 σε σχέση με την ηλικία



Thomson N Cur Opin in Pulm Med 2009; 15:39-45

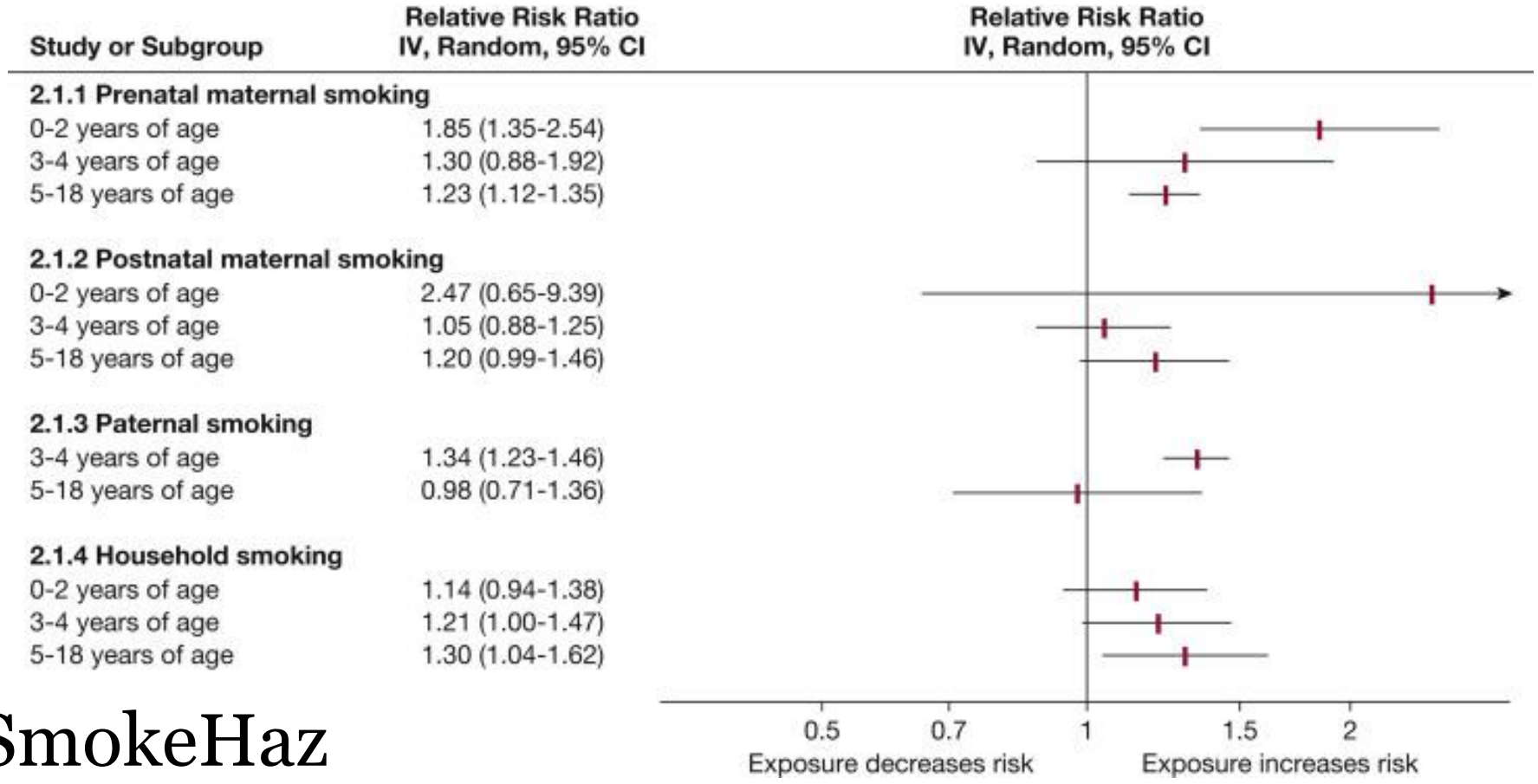
Asthma and smoking-induced airway disease without spirometric COPD



Neil C. Thomson:Eur Respir J 2017; 49

Meta analyses assessing the effect of exposure to passive smoking on the risk of

developing asthma in children.

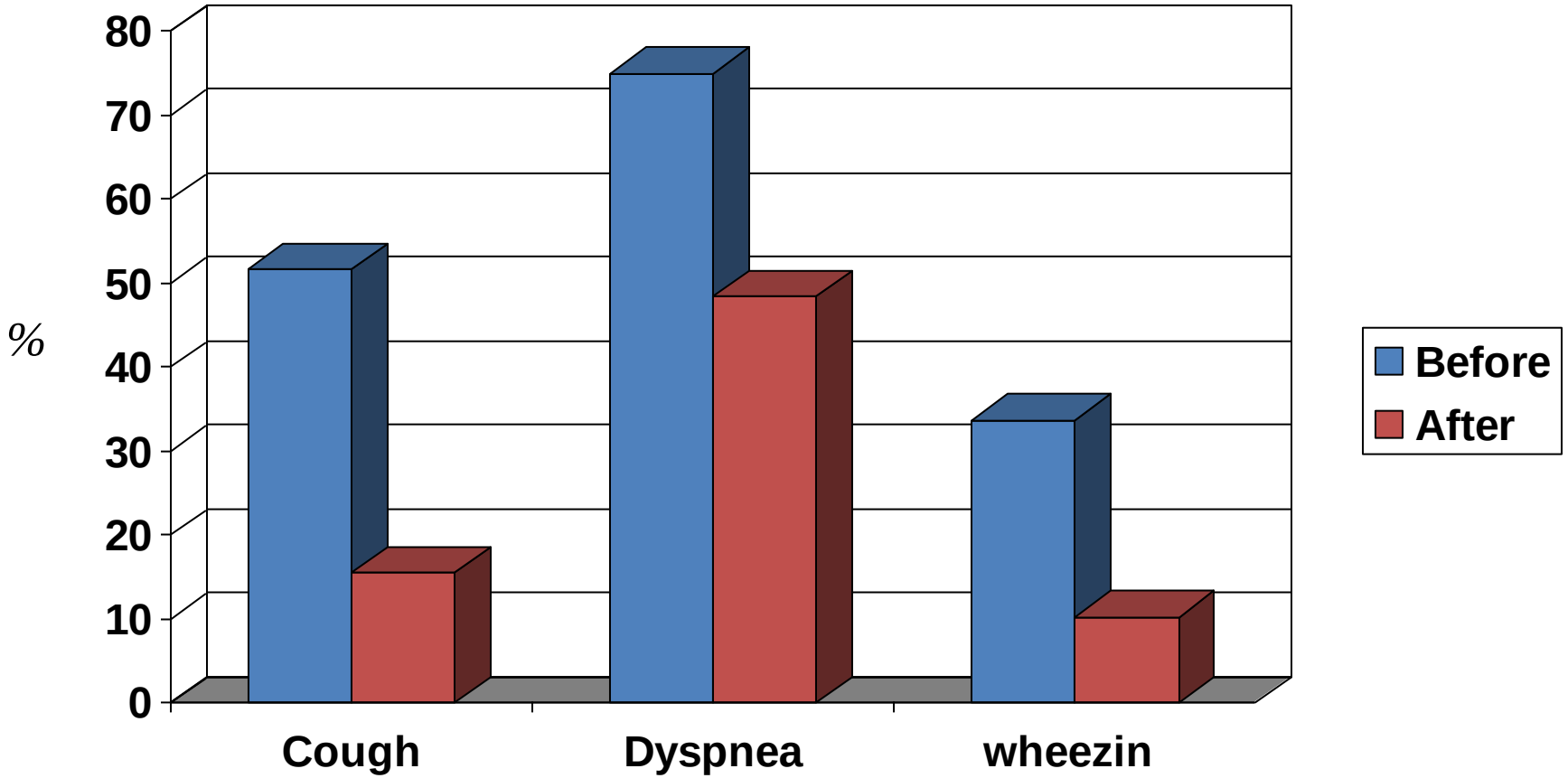


SmokeHaz

Leah Jayes CHEST 2016; 150(1):164-179

30 μέρες χωρίς κάπνισμα

COPD/Asthma



Etter JF Eur Resp J 2010, 35: 1249-1255

Key studies that examined personal smoking and adverse asthma outcomes

References	N	Participants	Findings
Thomson et al[29]	760	BTS Severe Asthma Registry with severe refractory asthma: 69 (9%) current smokers 210 (28%) ex-smokers 461 (62%) never smokers	Compared with never smokers, current smokers had poorer asthma control (ACQ 4.1 vs 2.9, $P<0.001$), more unscheduled health care visits (6 vs 4, $P=0.008$), more rescue oral steroids (6 vs 4 courses, $P=0.04$), higher anxiety (13 vs 8, $P<0.001$), and depression (10 vs 6, $P<0.001$), but no differences in spirometry
To et al[28]	519	From eight Canadian primary care practices, 137 of 519 with physician-diagnosed, mild-to-moderate asthma were smokers at baseline; after 12 months, 11% (n=15/137) quit, and 4% (n=16/382) of those not smoking at baseline commenced	Compared with continuous smokers (within a 12 month period), individuals who quit had less chest tightness (OR, 0.21; 95% CI, 0.06, 0.82) and fewer nocturnal symptoms (OR, 0.24; 95% CI, 0.07, 0.85), but no difference in acute health care utilization. Those who became smokers had increased chest tightness, nighttime symptoms, and ≥1 asthma attack within 6 months
Cerveri et al[7]	9092	ECRHS I (n=17,840 from 28 centers) and II (n=10,296), where 1,045 of 9,092 participants in the current analysis had asthma at baseline	26% of current smokers with asthma (n=949) continued to smoke despite significantly more having chronic cough and sputum production than never and ex-smokers (52% vs 42% and 43%). There was no difference in FEV_1% of predicted or FEV_1/FVC between smoking subgroups with asthma
Boulet et al[27]	893	Telephone survey of Canadian adults: 108 (12%) current smokers 268 (30%) past smokers 514 (58%) nonsmokers	Current smokers were more likely to have daytime asthma symptoms (30% vs 17% nonsmokers and 18% ex-smokers), and report asthma symptoms as a reason for absenteeism ($P<0.01$)
Zheng et al[32]	4070	Meta-analysis of ten controlled studies in smokers vs nonsmokers with asthma using inhaled corticosteroids	Compared with nonsmokers with asthma, smoking was associated with an attenuated inhaled corticosteroid response, reduced mean change in FEV_1, reduced posttreatment FEV_1, and increased use of concomitant medication

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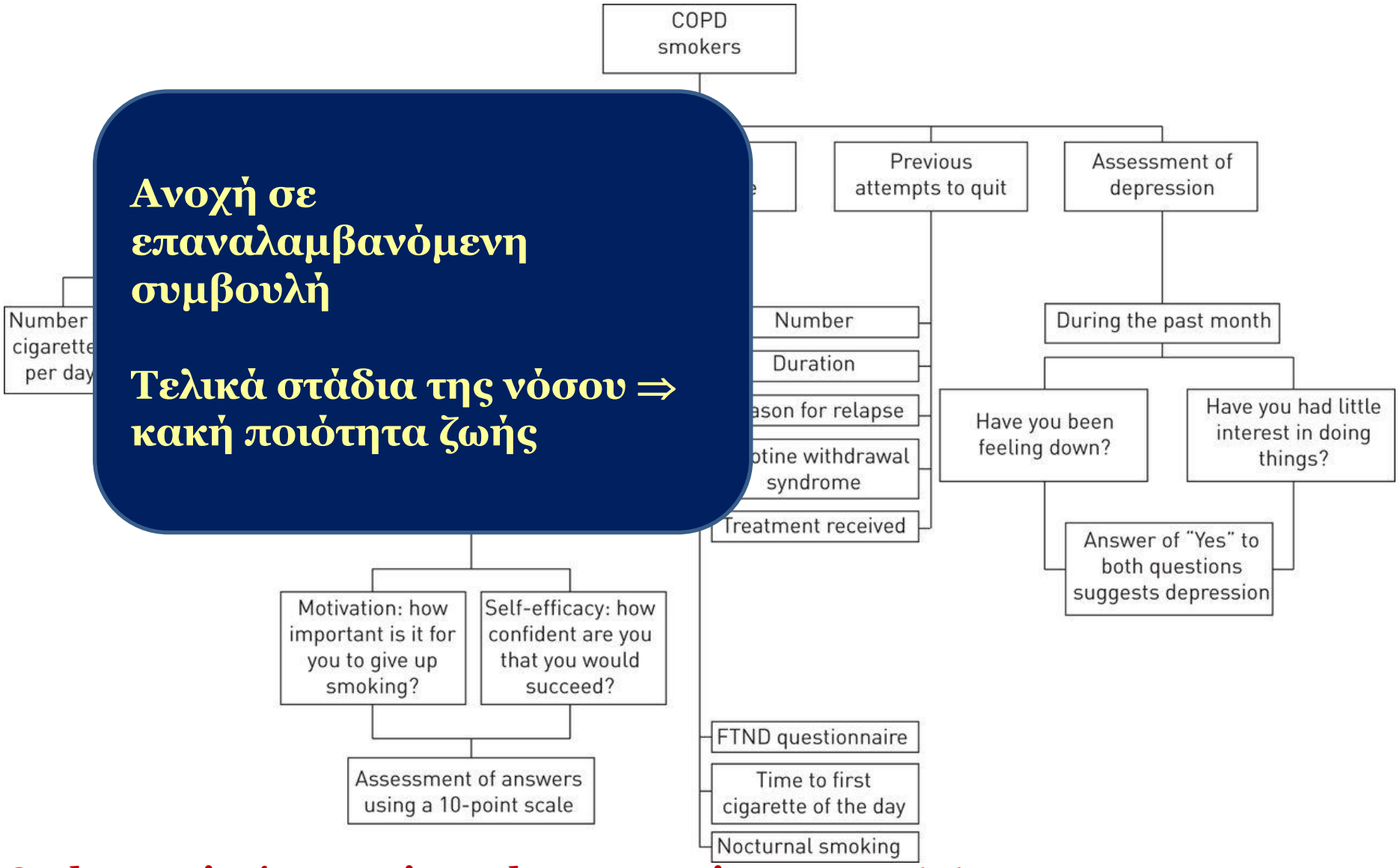
Assessment and recording of smoking status in patients with COPD.



Ανοχή σε επαναλαμβανόμενη συμβουλή

Τελικά στάδια της νόσου ⇒ κακή ποιότητα ζωής

Carlos A. Jiménez-Ruiz et al. Eur Respir J 2015;46:61-79

A CO monitor may be used to tailor disease specific advice to COPD patients:

- "CO is one of the gases that you inhale when you smoke cigarettes.
- It displaces oxygen from your red blood cells worsening breathlessness.
-
- Cigarettes also damage your lungs over time.
- ***If you quit smoking, your CO levels will drop to normal within 24 h."***

Assessment of motivation and self-efficacy in smokers with COPD

- "How important is it for you to give up smoking?"

- "You responded that your motivation was at a two. What would need to happen for you to get from your current two to an eight?"
- **"If you were to stop smoking how confident are you that you would succeed?"**

Assessment of depression in smokers with COPD

- In smokers with COPD, healthcare professionals proactively ask about depression and assess the level of depression. For example, using two simple questions:
  - *During the past month, have you been bothered by feeling down, depressed, or hopeless?*
  - *During the past month, have you often been bothered by having little interest or pleasure in doing things?*
- An answer of "yes" to either of the questions is a strong sign of depression

Characteristics of counselling for smoking cessation in smokers with chronic obstructive pulmonary diseases

- Clear explanation of the relationship between smoking and COPD, and the relationship between smoking cessation and improvement of COPD
-
- Use of spirometric results, CO monitors and “lung age” to increase motivation to quit
- Setting a quit date, identifying high-risk situations and developing coping skills
- Arranging follow-up visits in order to specifically address smoking cessation
- Explanation of the withdrawal syndrome
- Providing self-help materials
- Sending personal letters, e-mails and SMS

Benefits of smoking cessation in chronic obst… COPD)

During the first consultation, smokers with COPD receive firm advice that **tobacco smoking is the main or only cause of their illness and current symptoms**

- …
- … for…
- Smoking cessation improves responses to bronchodilator drugs and inhaled corticosteroids
- Smoking cessation reduces the incidence of acute exacerbations Smoking cessation reduces bronchial infections

Carlos A. Jiménez-Ruiz et al. Eur Respir J 2015;46:61-79

Συμβουλευτική σε ασθενείς με ΧΑΠ

- Dose-response effect from face to face counseling
- Group therapy : as effective as individual counseling

- Very intensive support (hospitalization + NRT)
  - 247 COPD pts (11 days hospitalization)
  - 3rd day : target quit day with NRT + daily exercise
  - 1h/day meeting for smoking cessation
  - After 1 year quit rate = 52% vs 7%
    - Sundblad Nic Tog Res 2008 Sweden

Tonnesen P ERJ 2013 22:127; 38-43

Ασθενείς με ΧΑΠ

Υποκατάστατα νικοτίνης

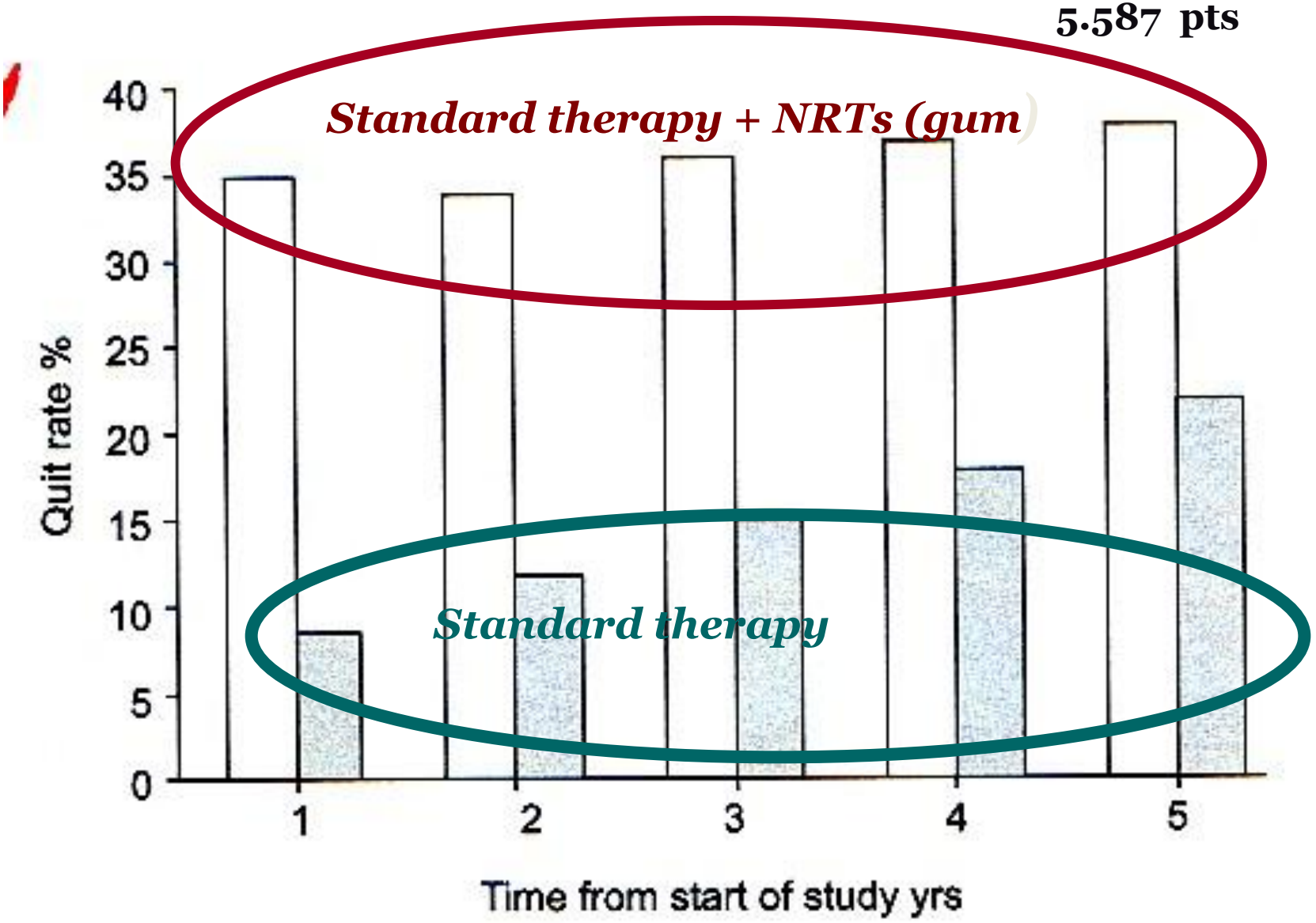
Προτιμούνται:
Patches
inhalers

- 105 μελέτες
  - OR = 1.8 NRTs vs placebo
    - 7% αποχή στους 6-12 μήνες ματά από χρήση NRTs για 3 μήνες
    - Η ενίσχυση της συμπεριφοράς ⇒ + 7-8%

Cochrane μέτα ανάλυση:
17% NRTs group
10% controls

Tonnesen P ERJ 2007;29:390-417

5.587 pts



Anthonisen N: Lung Health Study
Tonnesen P ERJ 2007;29:390-417

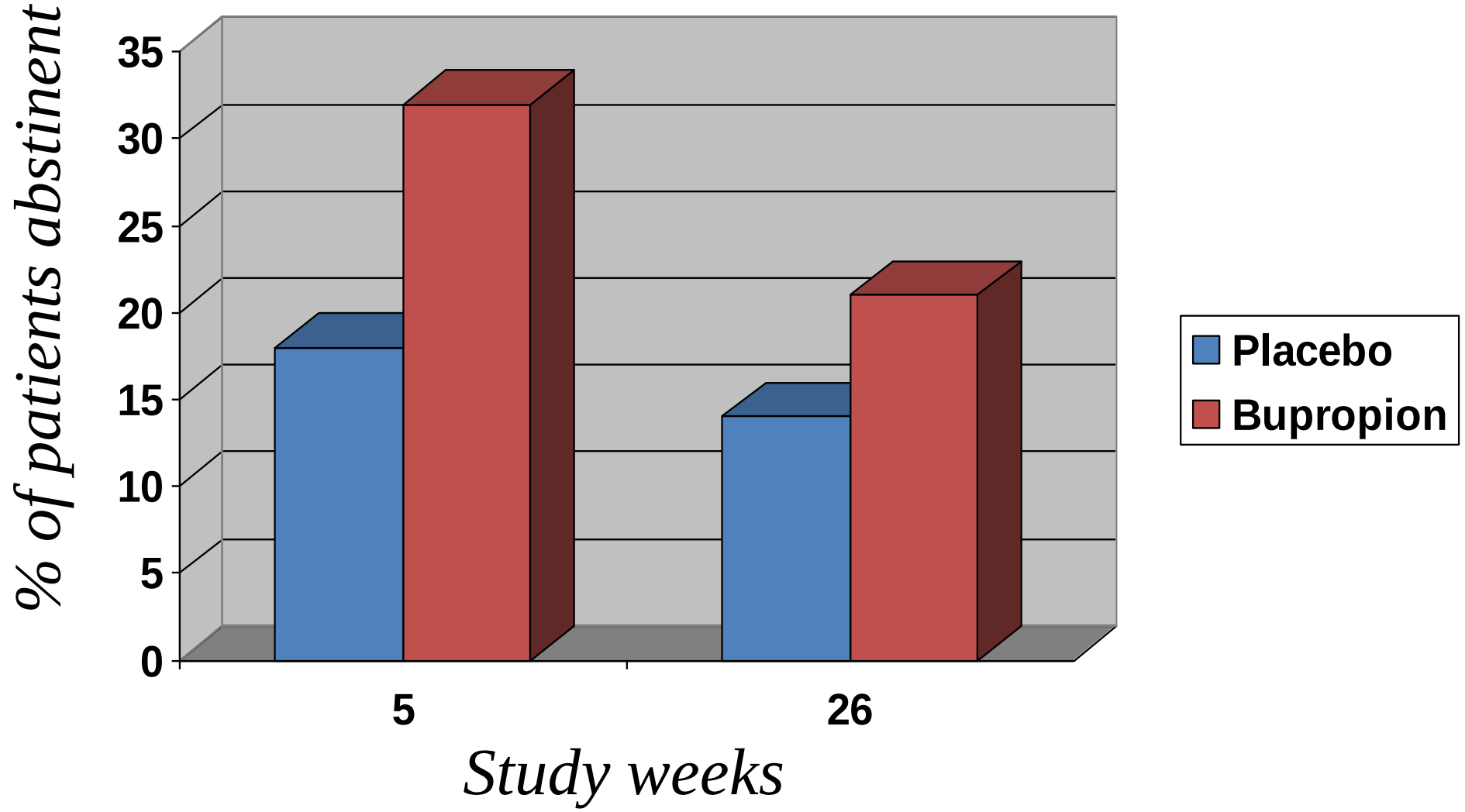
Double-blind, PCR smoking cessation studies in COPD

Medication	Subjects n	FEV_1 % pred	12-month sustained quit rates	
			Active	Placebo
Varenicline	505	70	18.6	5.6
Bupropion SR	404	72	10	8
NRT	370	56	14	5

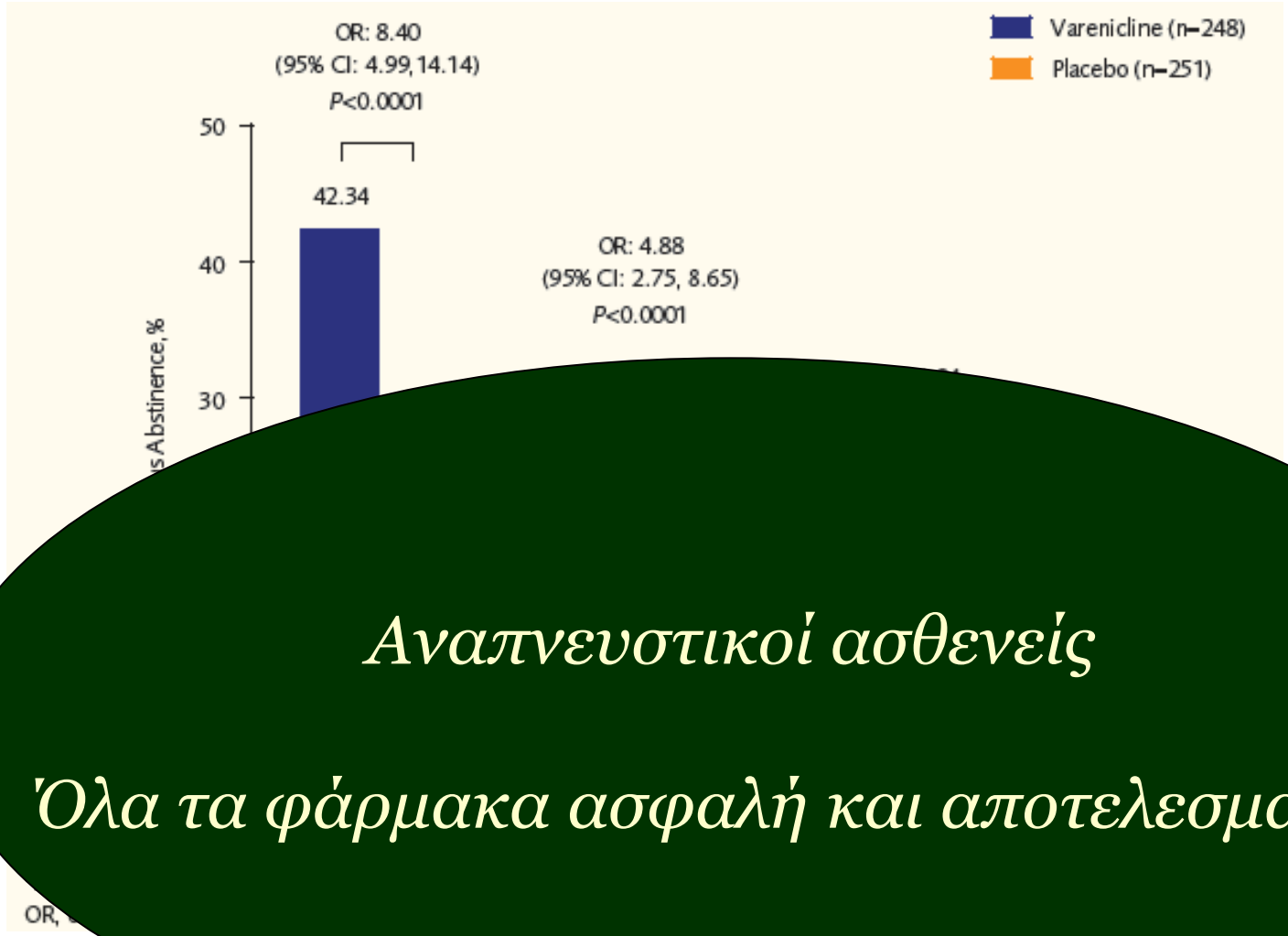
Tonnesen P ERJ 2013 22:127; 38-43

Double-blind, placebo-controlled randomised smoking cessation studies in chronic obstructive pulmonary disease patients

Συνεχής αποχή σε ασθενείς με ΧΑΠ



Tanhkin DP. Lancet 357; May 2001



Αναπνευστικοί ασθενείς

Όλα τα φάρμακα ασφαλή και αποτελεσματικά

Tashkin DP (27 centers) Chest 2010 Sep 23

Meta-analysis of smoking cessation trials in chronic obstructive pulmonary disease patients

Study	Subjects n	Prolonged abstinence rate
Lung Health Study [36]	5887	12 months: 34% *versus* 9% (NRT)
Hilberink [37]	392	6 months: 16% *versus* 9% (NRT)
Tønnesen [20]	370	12 months: 14% *versus* 5% (NRT)
Tashkin [21]	404	6 months: 16% *versus* 9% (BUP)
Wagena [38]	255	6 months: 30% *versus* 19% (BUP)
Pederson [39]	64	6 months 27% *versus* 16%
Crowley [40]	49	6 months: 14% *versus* 14%
Brandt [41]	56	12 months: 32% *versus* 16%
Tashkin [22]	499	12 months: 19% *versus* 6% (VAR)

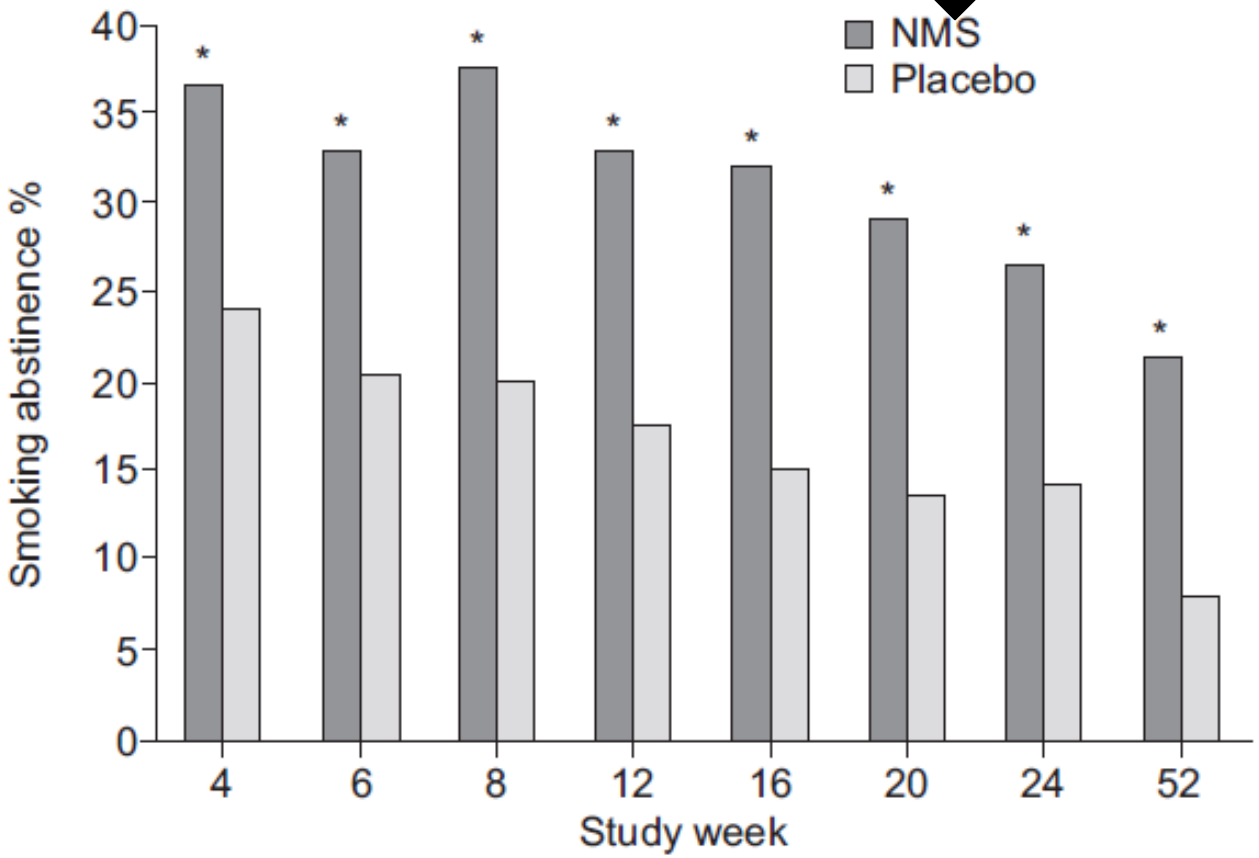
Tonnesen P ERJ 2013 22:127; 38-43

Pharmacological treatments for smokers with chronic obstructive pulmonary disease (COPD)

Intervention	First author [ref.]	Subjects	Design	Duration	Outcome quit rate %	Statistical significance?
Nicotine replacement therapy	Tønnesen [47]	370 smokers with COPD	NST/ placebo, low CBT/ high CBT	12 weeks	At 12 months: NST 17%; placebo 10% No difference between high or low CBT	Yes OR 2.88 (1.34–6.16)
Bupropion (BP) and nortriptyline (NT)	Tashkin [48]	404 smokers with COPD	BP/ placebo	12 weeks	At 6 months: BP 16%; placebo 9%	Yes p<0.005
	Wagena [49]	255 smokers at risk of or with COPD	BP/NT/ placebo	12 weeks	At 6 months: BP 28%; NT 25%; placebo 15%	Yes for BP *versus* placebo No for NT *versus* placebo
	Van Schayck [50]	255 smokers at risk of or with COPD	BP/NT/ placebo	12 weeks	At 12 months: BP 20.9%; NT 20%; placebo 13.5%	No
Varenicline (VRN)	Tashkin [51]	504 smokers with COPD	VRN/ placebo	12 weeks	At 12 months: VRN 18.6%; placebo 5.6%	Yes OR 4.04 (2.13–7.67)

Carlos A. Jiménez-Ruiz et al. Eur Respir J 2015;46:61-79

Nicotine mouth spray



Tønnesen P, Lauri H, Perfekt R, *et al.* Efficacy of a nicotine mouth spray in smoking cessation: a randomised, double-blind trial. *Eur Respir J* 2012; 40: 548–554.

Summary of the relevant issues for smoking cessation in patients with asthma

- **Smoking rate among asthma patients is similar to the general population**
- **Smoking has detrimental effects on asthma**
  - *Greater decline in forced expiratory volume in 1 s*
  - *Lack of response to medications (bronchodilator drugs and inhaled corticosteroids)*
  - *Increased need for use of concomitant medications*
- **Asthma patients who smoke can suffer from higher nicotine dependence and are less likely to attend education programs**

- **Counselling and use of pharmacological treatments is a good approach for smoking cessation in asthma patients; nevertheless, there is a lack of smoking cessation trials in these patients**

The “five As” strategic model for treating tobacco use and dependence, for the patient willing to quit

Ask	Systematically identify all tobacco users at every visit
	Current | former| never
Advise	Strongly urge all tobacco users to quit
	“Continuing to smoke makes your asthma worse, and quitting may dramatically improve your health”
	“Quitting smoking may reduce the number of ear infections (and asthma attacks) your child has”
Assess	Determine willingness to make a quit attempt
	Determine stage of change[a]
	“How do you feel about your smoking at the moment?”
	“Are you ready to stop smoking now?”
Assist	Aid the patient in quitting (provide medication and counseling)
	Help the patient with a quit plan
	Recommend the use of approved medication except when contraindicated or the evidence is insufficient
	Provide practical counseling (total abstinence, make the home smoke free, build positively on past quit experiences, avoid alcohol, and other triggers)
	Provide supplementary materials (National Quitline network)
Arrange	Ensure follow-up contact, within a week of the quit date

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Therapeutic interventions in patients with asthma

- There are few studies of smoking cessation in patients with asthma.
  - In an observational study of ever-smokers with asthma, the median time until quitting was 17 years
    - *Eisner MD, Am J Public Health 2000; 90: 1307–1311*
  - A small interventional study of 32 smokers with asthma found 66% quit at 6 weeks but the longer term success was not reported
    - *Chaudhuri RAm J Respir Crit Care Med 2006; 174: 127–133*
  - A study of 57 smokers with asthma treated with NRT, bupropion and counselling found a 12-month quit rate of 28%
    - *Piccillo G, Respir Med 2008; 102: 256–265*

Smoking cessation in smokers with asthma

- The prevalence of smoking among peoplewith asthma is similar to the general population, i.e. ~20–25%

- Adults enrolled in the telephone counseling service, Quitline, were only a small fraction of all smokers attempting to quit, but those with asthma and/or COPD were found to be less likely to have quit smoking after 30 days.

- This contrasts similar abstinence rates at a smoking cessation clinic in Greece, which considered individual asthma, COPD, and overlap subgroups separately
  - Gratziou C, et al. Smoking cessation effectiveness in smokers with COPD and asthma under real life conditions. *Respir Med*. 2014;108(4):577–583

Asthma-specific considerations *when quitting*

Consideration		Asthma-specific action
1	Importance	Recommend to quit smoking at every opportunity Target adolescents and young adults for whom smoking cessation can have the greatest benefit
2	Information	Discuss "lung age" to illustrate the lung function deficit from smoking ± asthma Describe corticosteroid insensitivity as a mechanism of worsening asthma control Highlight that smokers with asthma often have repeated and more frequent attempts to quit and emphasize that the process is cumulative Offer written asthma-specific information that might be web based
3	Management	Optimize asthma management while planning to nominate the quit date, which might necessitate increasing doses of ICS and/or other add-on therapy Use the current standard approach for smoking cessation, until there is an evidence base that differs for smokers with asthma
4	Admission	Regard this opportunity as a "teachable moment" In the absence of contraindications, inpatient NRT and counseling can be given as a priority, and other pharmacotherapies can be commenced as appropriate
5	Follow-up	Close and longer-term follow-up is essential, given those with asthma have a tendency to relapse, have more quit attempts and not complete asthma educational programs. Consider reminder text messages and educational prompts by cellular phone for those interested

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Καπνιστές που νοσηλεύονται;
Νεότερα δεδομένα

- Έναρξη της παρέμβασης για τον κάπνισμα στη διάρκεια της νοσηλείας ⇒ αύξηση του ποσοστού διακοπής του καπνίσματος
  - ***Συμβουλευτική υποκατάστασ παρέχεται σε εισάγονται στο***

Ποσοστών διακοπής με:

1. *Της υποστηρικτικής αγωγής*
2. *Προσθήκη φαρμακοθεραπείας*

Rigotti NA Arch Inter Med 2008,

E-cigarette

Airway irritation, mucus hypersecretion, and inflammatory response, including systemic changes, have been observed after the exposure to e-cigarettes, leading to an increase in respiratory symptoms and changes in respiratory function and the host defense mechanisms.

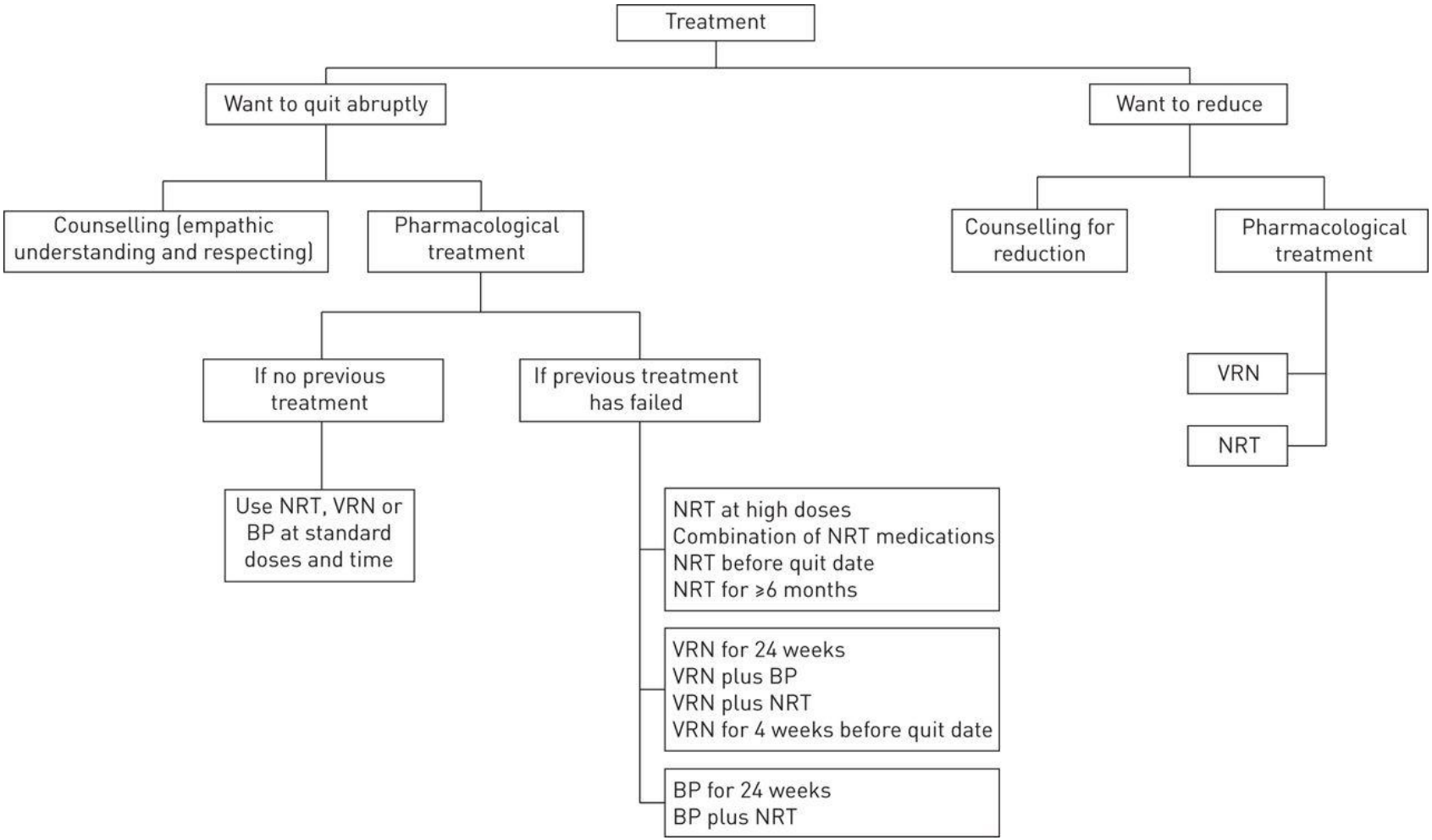
E-cigarette has been linked with an increase of symptoms in individuals with asthma, cystic fibrosis, and chronic obstructive pulmonary disease

As smokers with asthma may be several decades younger than smokers with COPD, **cessation benefits will be larger in terms of quality-adjusted life years gained and so probably more cost-effective.**

Carlos A. Jiménez-Ruiz et al. Eur Respir J 2015;46:61-79

Hoogendoom M Thorax 2010 65:711-718

The therapeutic approach used by most Task Force members for smokers that find it difficult to quit.



Carlos A. Jiménez-Ruiz et al. Eur Respir J 2015;46:61-79

Συμπεράσματα

- **Διακοπή του καπνίσματος** → Μια από τις πιο αποτελεσματικές παρεμβάσεις της ιατρικής περίθαλψης με χαμηλό κόστος

- **Υποστήριξη και φαρμακοθεραπεία** → Η πιο αποτελεσματική προσέγγιση για τους, αποφασισμένους για την διακοπή του καπνίσματος, ασθενείς.

- Ακόμη και οι σύντομες συμβουλές αυξάνουν τα ποσοστά διακοπής του καπνίσματος

Εφαρμογή για 1 χρόνο: minimal counseling intensive counseling pharmacotherapy

Intervention	Type of analysis: base case or sensitivity analysis (SA)	Life-years gained	QALYs gained	Reduction in mortality†	Difference in intervention costs (€ $\times 10^6$)	Savings in COPD-related costs (€ $\times 10^6$)	Cost per life year gained (€)	Cost per QALY gained (€)
Minimal counselling	Base case analysis	210	280	90	6.8	2.0	22400	16900
	SA1: 12-month point prevalence rates	210	300	160	6.8	2.5	20900	14400
	SA2: No discounting	260	340	100	6.8	3.0	14300	11000
	SA3: Network meta-analysis	310	420	150	6.8	3.1	11800	8800
	SA4: Cohort instead of dynamic	200	260	100	6.8	1.9	24600	18200
Intensive counselling	Base case analysis	690	960	340	15.6	7.6	11600	8200
	SA1: 12-month point prevalence rates	600	810	280	15.6	5.9	16200	11900
	SA2: No discounting	850	1160	380	15.6	11.5	4800	3500
	SA3: Network meta-analysis	750	1050	370	15.6	8.3	9600	6900
	SA4: Cohort instead of dynamic	680	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	8600
Pharmacotherapy	Base case analysis	1590	2240	830	23.2	17.9	3300	2400
	SA1: 12-month point prevalence rates	1260	1740	630	23.2	13.0	8000	5800
	SA2: No discounting	1960	2690	[illegible]	[illegible]	[illegible]	Cost saving	Cost saving
	SA3: Network meta-analysis	1710	2400	920	23.3	19.2	2300	1600
	SA4: Cohort instead of dynamic	1550	2170	850	23.2	17.1	3900	2800
	SA5: Excluding studies with nortriptyline	1570	2190	820	30.6	17.3	8500	6100

Hoogendoom M Thorax 2010 65:711-718

Efficacy of smoking cessation after 6–12 months from meta-analysis of eight smoking cessation trials in chronic obstructive pulmonary disease patients

Treatment	OR (95% CI)	p-value
Nothing/usual care	1	
Counselling alone	1.82 (0.96–3.34)	0.07
Counselling + antidepressants	3.32 (1.53–7.21)	0.002
Counselling + NRT	5.08 (4.32–5.97)	<0.001
Counselling + varenicline	4.04 (2.13–7.67)	<0.001

Benefits of smoking cessation in asthma

- Continued [illegible] effects on asth[illegible]

One study found that
After several weeks of quitting persons with asthma
showed improved pulmonary function and
a reduction in neutrophils in their sputum

as[illegible]
benefit[illegible]
medications compar[illegible]okers

  - A Canadian study of 893 persons with asthma found that smokers had poorer asthma control, made greater use of acute care

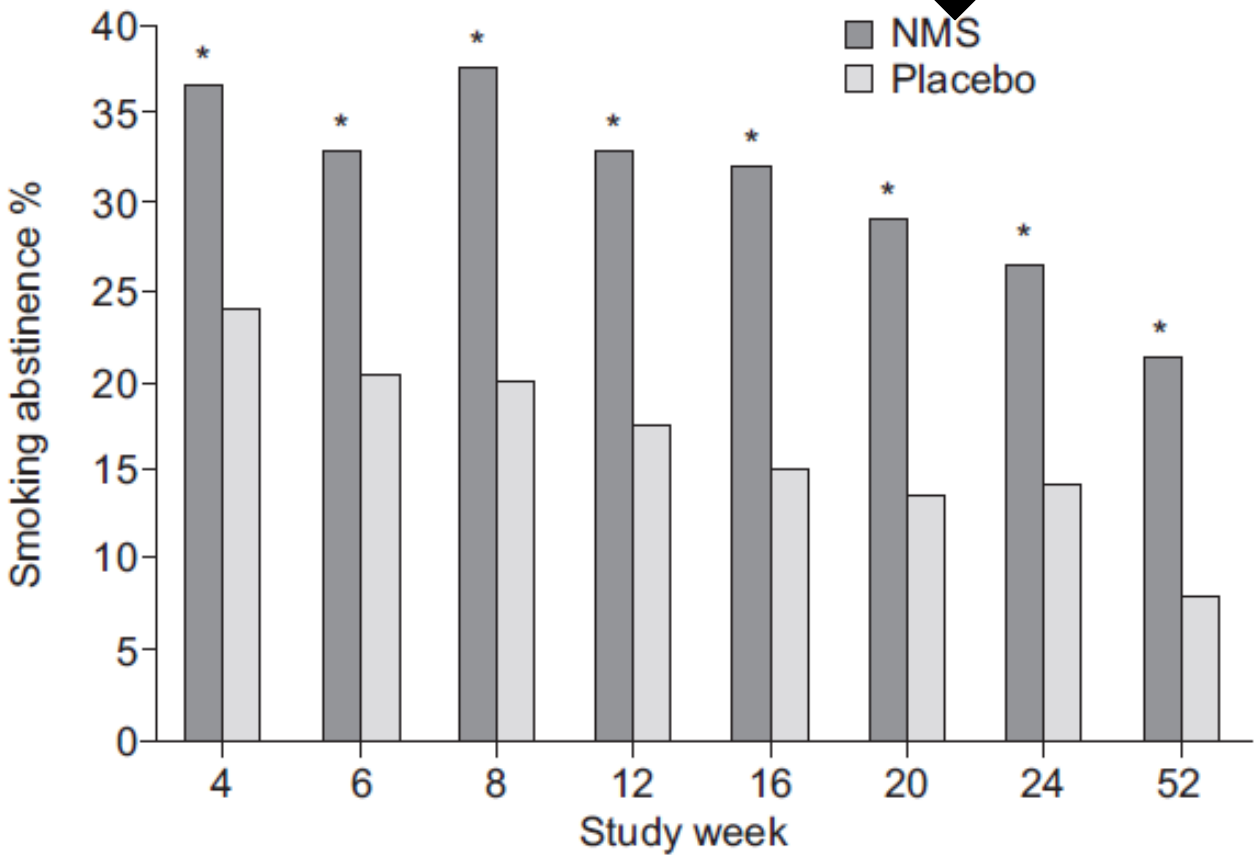
Θεραπεία καπνίσματος σε ασθενείς με ΧΑΠ

- 5 μελέτες
- 6491 ασθενείς με ΧΑΠ
  - Εντατικό πρόγραμμα ενίσχυσης συμπεριφοράς
  - Θεραπεία με υποκατάστατα νικοτίνης
  - Θεραπεία με υδροχλωρική βουπροπιόνη

- **Η ενίσχυση της συμπεριφοράς είναι ιδιαίτερα αποτελεσματική στη μακροχρόνια αποχή των ασθενών με ΧΑΠ από το κάπνισμα**

Wagena EJ. Respir Med 2004; 98 Sep (9):805-15

Nicotine mouth spray



Tønnesen P, Lauri H, Perfekt R, *et al.* Efficacy of a nicotine mouth spray in smoking cessation: a randomised, double-blind trial. *Eur Respir J* 2012; 40: 548–554.