

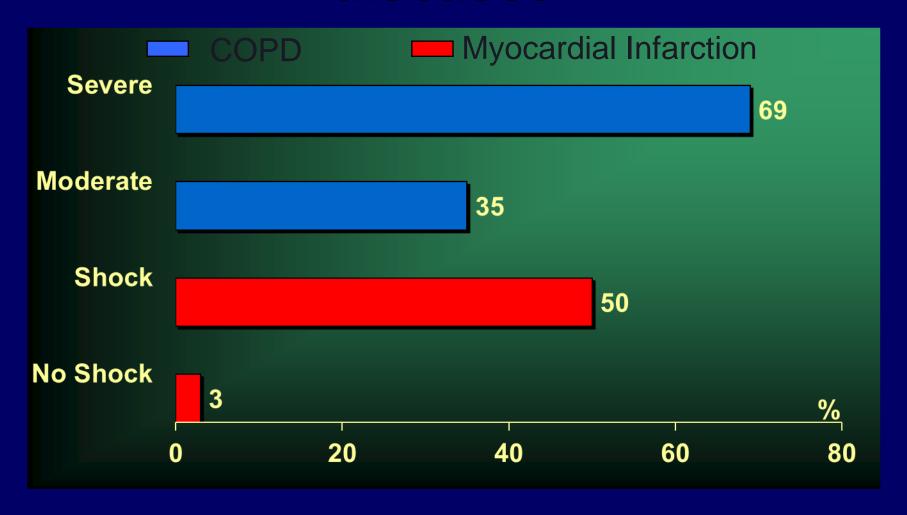
ΕΙΣΑΓΩΓΗ ΣΤΗ ΧΡΟΝΙΑ ΑΠΟΦΡΑΚΤΙΚΗ ΠΝΕΥΜΟΝΟΠΑΘΕΙΑ

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ΥΠΟΘΕΤΙΚΗ ΕΡΩΤΗΣΗ

Τι θα θελατε να παθετε ΠΑΡΟΞΥΝΣΗ ΧΑΠ η' εμφραγμα του μυοκαρδιου?????

Mortality comparisons across diseases

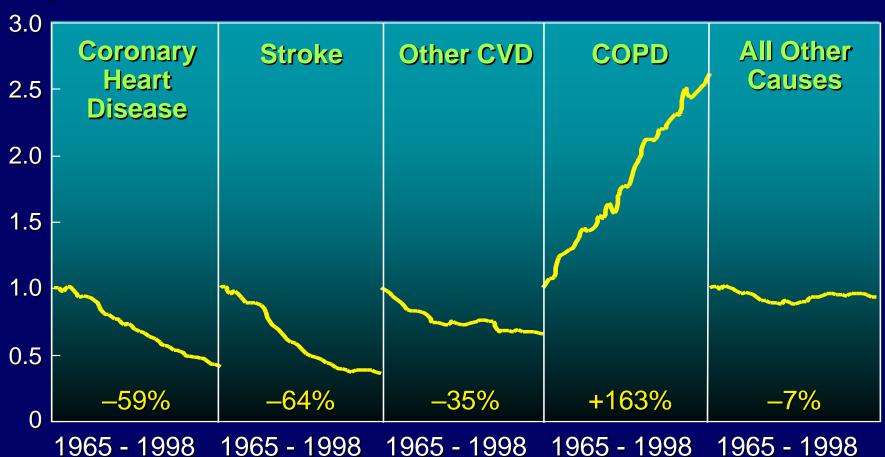


COPD

- √ "COPD is a preventable and treatable disease state characterised by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. It also produces significant systemic consequences."
- √ 5th leading cause of death
- ✓ Pathogenesis remains unclear

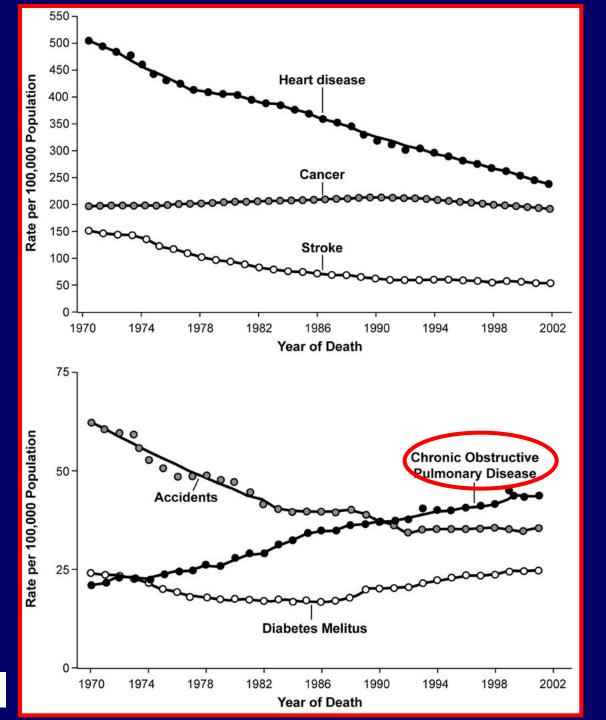
Percent Change in Age-Adjusted Death Rates, U.S., 1965-1998

Proportion of 1965 Rate



Source: NHLBI/NIH/DHHS

Of the six leading causes of death in the United States, only COPD has been increasing steadily since 1970





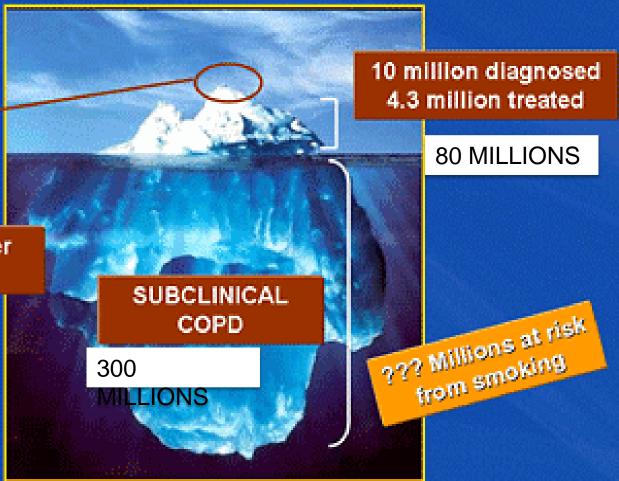
Clinical COPD Is Just the Tip of the Iceberg

45 MILLIONS

2 million, severe disease*

450 MILLIONS

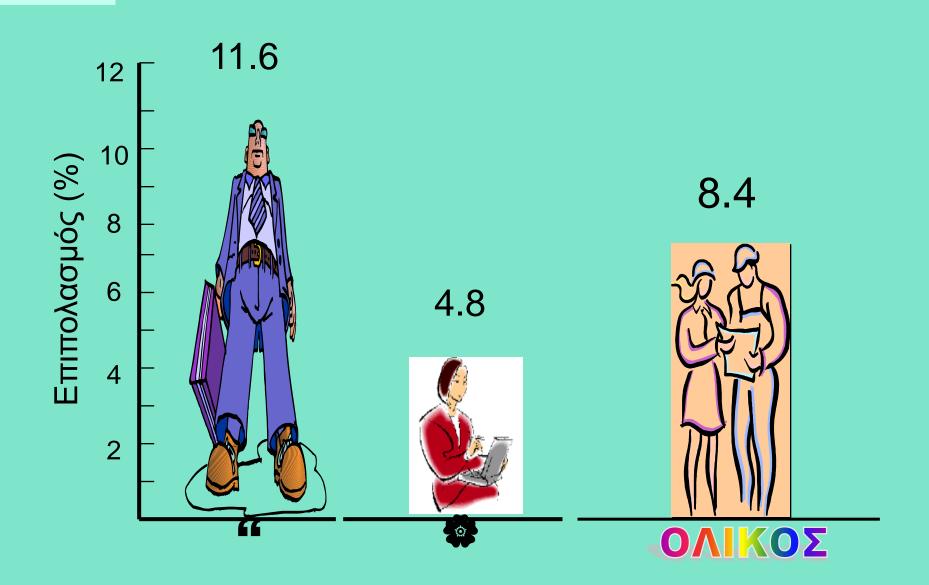
21.7 million suffer from COPD

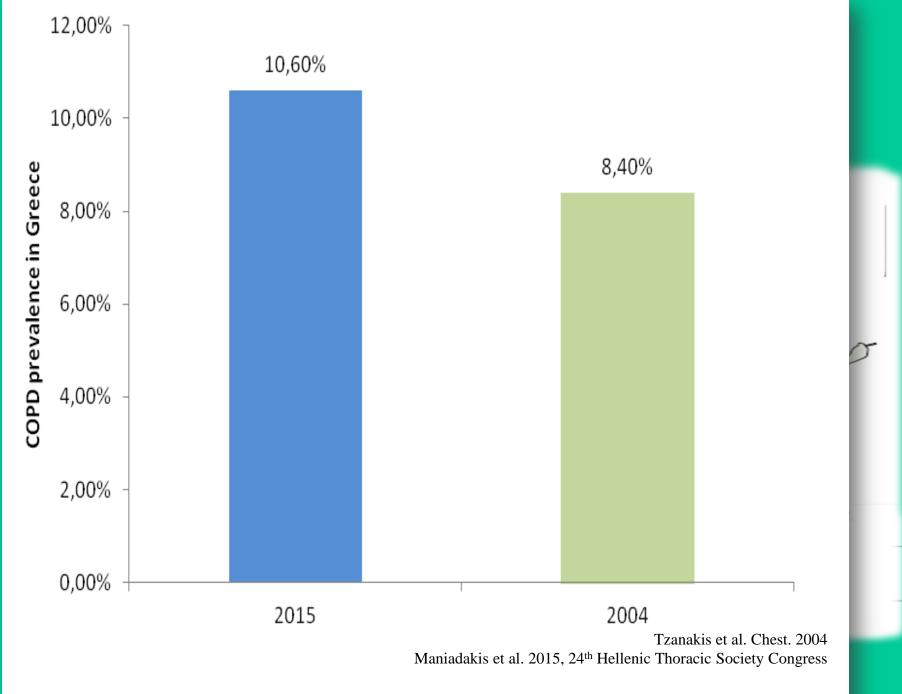


*Repeated exacerbations and hospitalizations.

Mannino et al. MMWR Surveill Summ. 2002;51:1-16.

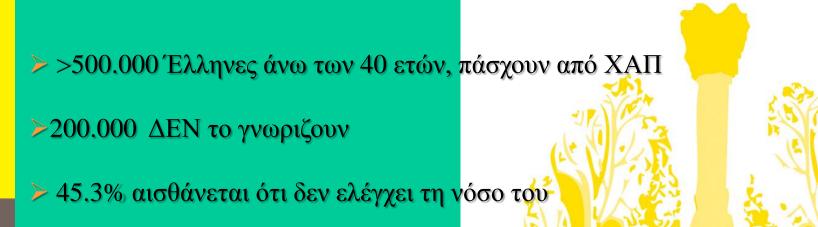
Επιπολασμός (Crude)





Η ΧΑΠ στην Ελλάδα





Μελέτη της Εθνικής Σχολής Δημόσιας Υγείας (Ε.Σ.Δ.Υ) για λογαριασμό της Ελληνικής Πνευμονολογικής Εταιρείας (Ε.Π.Ε). Δεκέμβριος 2015

Risk Factors for COPD

Genes

Exposure to particles

- Tobacco smoke
- Occupational dusts, organic and inorganic
- Indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings
- Outdoor air pollution

Lung growth and development

Oxidative stress

Gender

Age

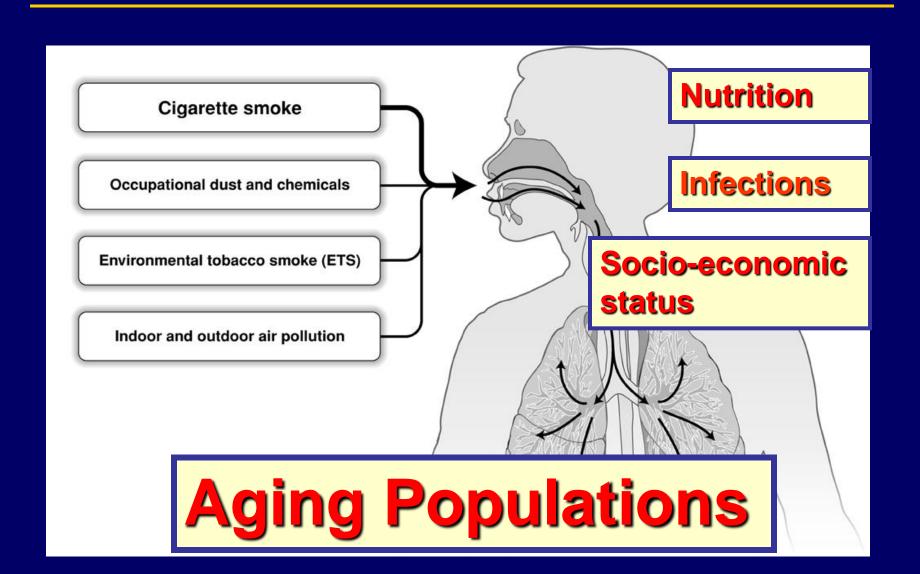
Respiratory infections

Socioeconomic status

Nutrition

Comorbidities

Risk Factors for COPD



INFLAMMATION IN COPD

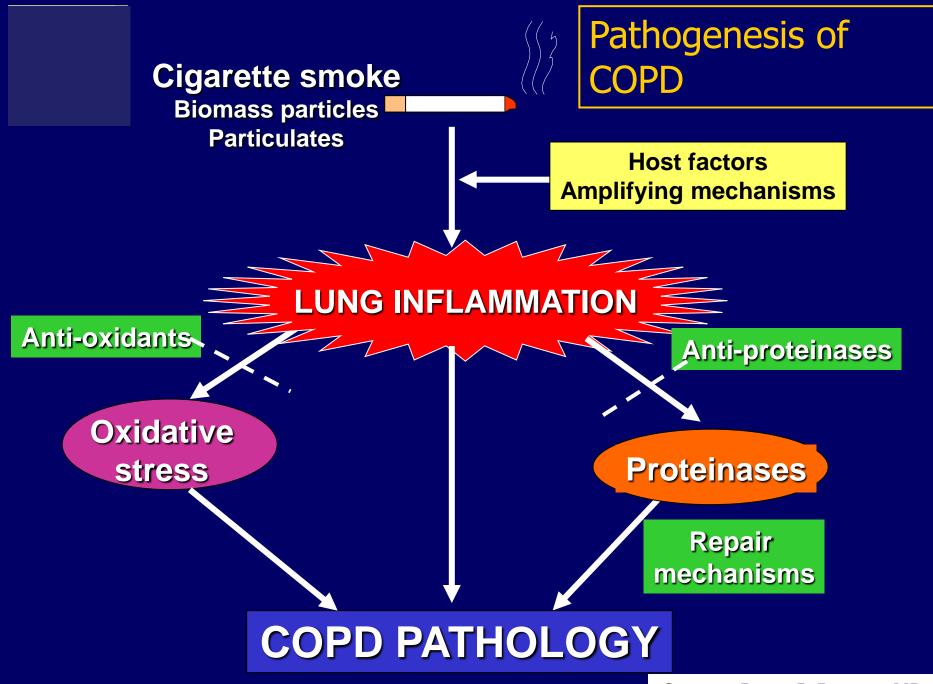
Small airway disease

Airway inflammation Airway remodeling

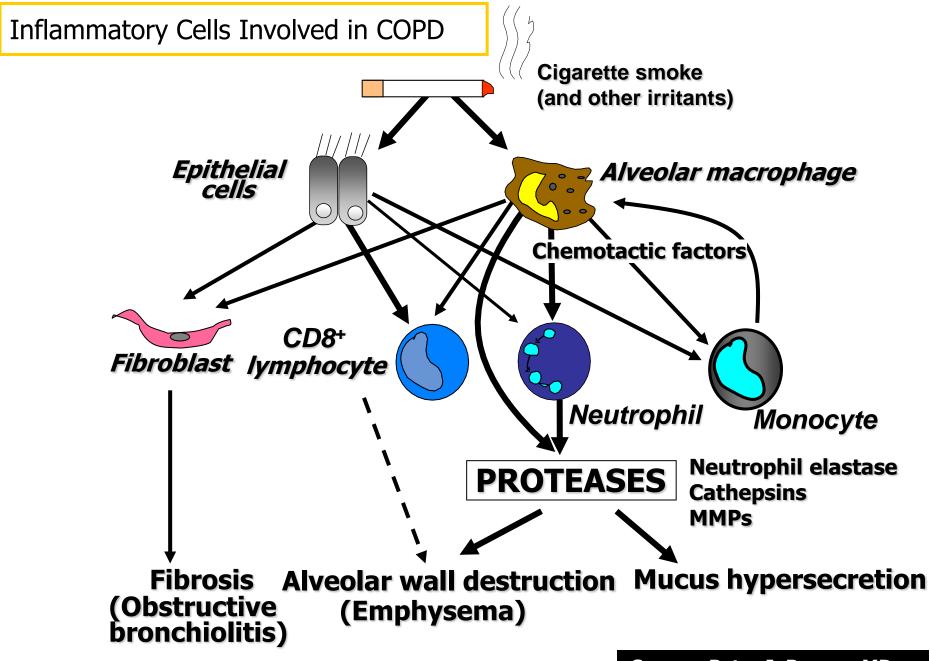
Parenchymal destruction

Loss of alveolar attachments
Decrease of elastic recoil

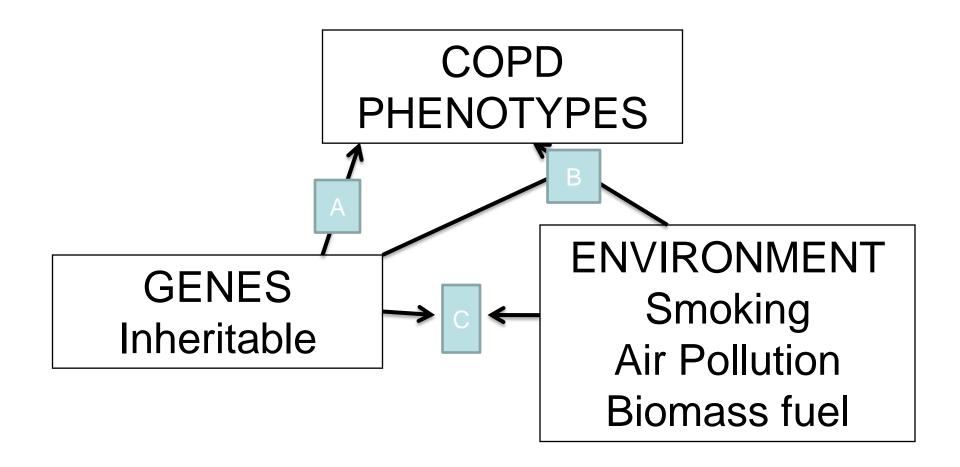
AIRFLOW LIMITATION



Source: Peter J. Barnes, MD



Source: Peter J. Barnes, MD



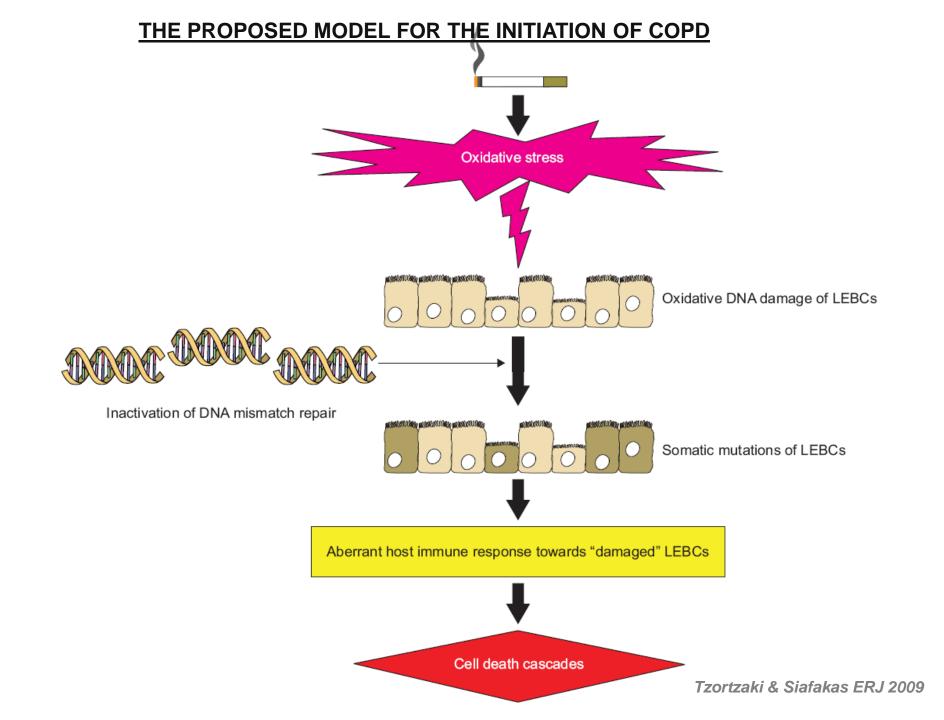
 $A = \alpha 1$ -antitrypsin

GENETICS

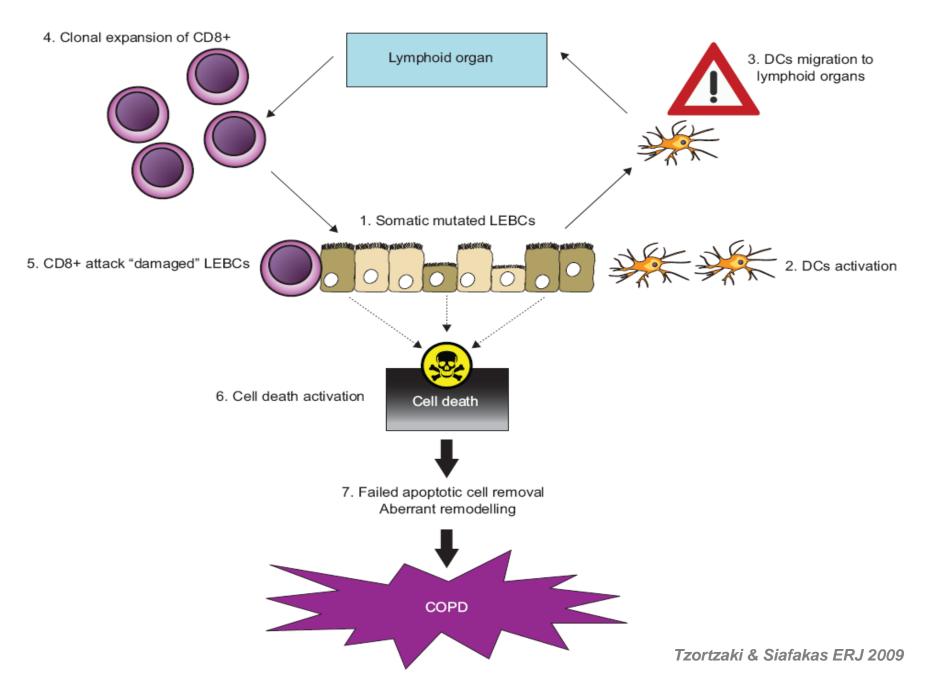
B = Smoking

EPIGENETICS

C= Nutrition



ACQUIRED SOMATIC MUTATIONS OF LUNG EPITHELIAL BARRIER CELLS IN COPD



Diagnosis of COPD

SYMPTOMS
cough
sputum
shortness of breath

EXPOSURE TO RISK FACTORS

tobacco occupation indoor/outdoor pollution

D'

SPIROMETRY

Differential Diagnosis: COPD and Asthma

COPD

- Onset in mid-life
- Symptoms slowly progressive
- Long smoking history
- Dyspnea during exercise
- Largely irreversible airflow limitation

ASTHMA

- Onset early in life (often childhood)
- Symptoms vary from day to day
- Symptoms at night/early morning
- Allergy, rhinitis, and/or eczema also present
- Family history of asthma
- Largely reversible airflow limitation

COPD Phenotypes

- Chronic Bronchitis (Blue bloater)
- n Emphysema (Pink puffer)
- **A1-antitrypsin deficiency**
- n Frequent exacerbators
- Patients with or without systemic involvement
- n COPD with or without comorbidities
- Significant hyperinflation
- Fast decliner (FEV1)
- n ACOS
- n Current smoker



Pink Puffer

Individuals in this category tend to have the following features:

Intense dyspnoea often with purse-lip breathing

Thin and often elderly

Small sputum volume

Rarely develop oedema or overt heart failure

Investigations may show:

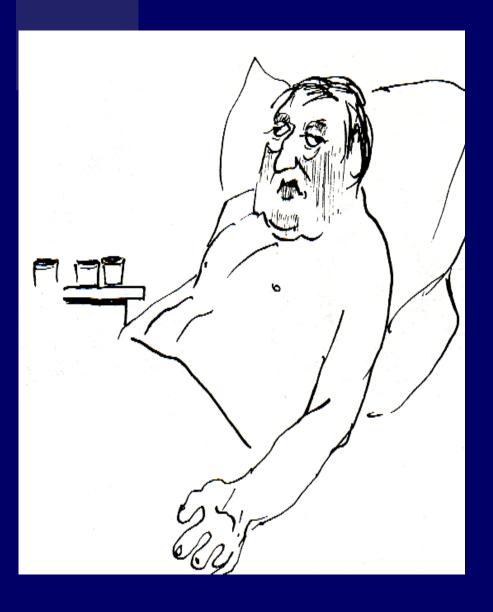
Near-normal blood gas values (until terminally)

Very severe airways obstruction

Increased total lung capacity

Radiological evidence of emphysema

Impairment of transfer factor.



Blue Bloater

Individuals in this category tend to have the following features:

Relatively mild dyspnoea

Often obese

Large sputum volume and frequent infective exacerbations

Often oedematous and easily lapse into congestive heart failure.

Investigation may show:

Abnormal blood gases—hypercapnia, hypoxaemia with elevated plasma bicarbonate and polycythaemia, severe nocturnal hypoxaemia during REM sleep

Sometimes only moderately severe airways obstruction

Fairly normal total lung capacity

No radiological evidence of emphysema

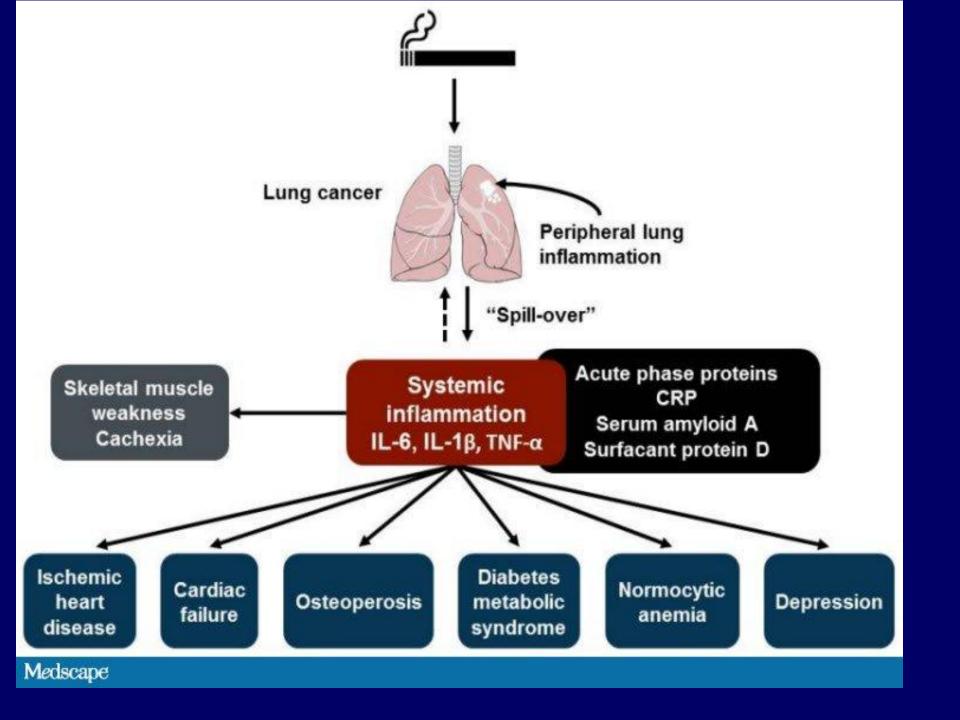
Little or no reduction in transfer factor.

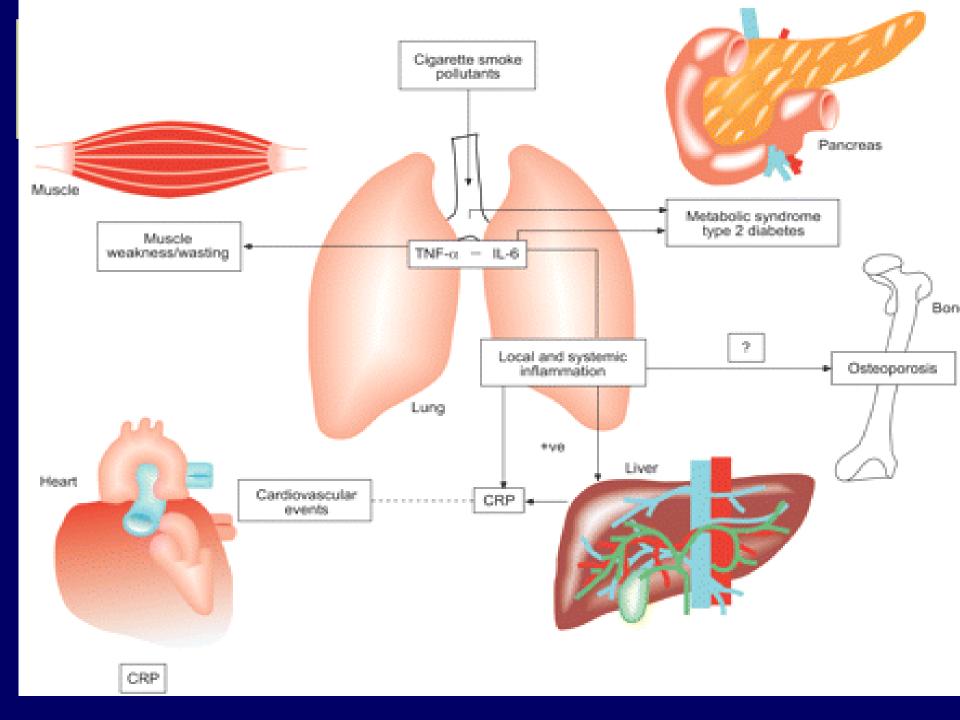
Phenotype: Emphysema and Hyperinflation

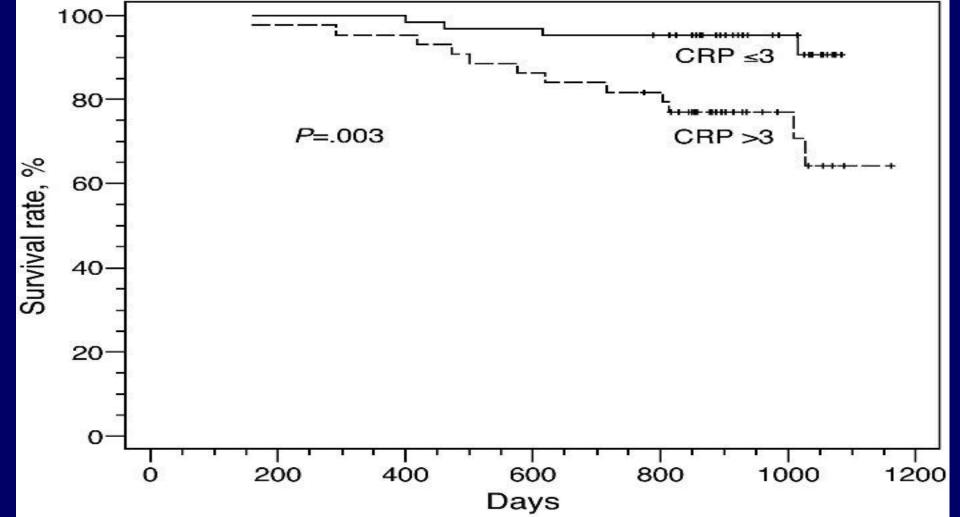
- limitations in functional capacity
- decreased diffusion capacity
- homogeneous distribution of emphysema → high risk for death
- IC/TLC ratio predicts respiratory and all-cause mortality better than FEV_1 (Casanova et al. AJRCCM 2005;171:591-97)
- different therapeutic options depending on emphysema distribution (National Emphysema Treatment Trial Research Group. NEJM 2003; 348:1059-73)

Phenotype: COPD with Systemic Involvement

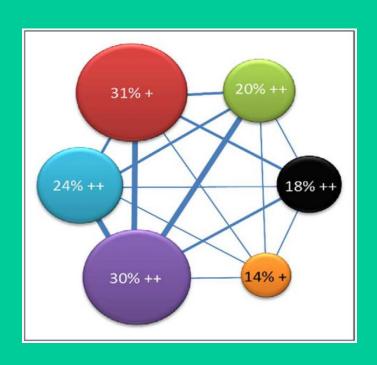
- hypoxemia → poor prognosis, but correction associated with improved survival
- BMI $< 0.21 \rightarrow$ independent predictor of death
- peripheral muscle dysfunction → poor exercise capacity, independent predictor of survival
- anemia in 10-20% of patients → correlation with mortality
- overflow of inflammatory cytokines and activated cells in peripheral circulation?











16% of COPD patients have persistent systemic inflammation

Phenotype: COPD with comorbidities

- diabetes → patients with COPD have a 1.8 RR of developing type II diabetes
- atherosclerosis → increased risk of vascular events in patients with COPD, perhaps through elevated CRP
- osteoporosis → increased risk in patients with COPD, even in the absence of steroid use
- peptic ulceration → more frequent in patients with COPD, helicobacter seropositivity increased in COPD
- *Anaemia* = 10-20%

Sevenoaks et al. Resp Research 2006; 7:70-9

COPD and Co-Morbidities

COPD patients are at increased risk for:

- Myocardial infarction, angina
- Osteoporosis
- Respiratory infection
- Depression
- Diabetes
- Lung cancer

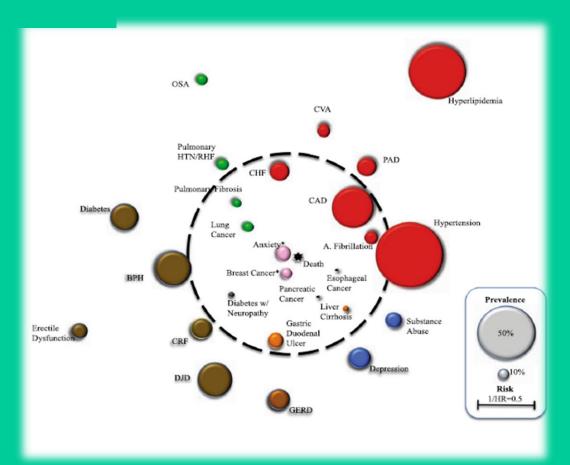
COPD and Co-Morbidities

COPD has significant extrapulmonary

(systemic) effects including:

- Weight loss
- Nutritional abnormalities
- Skeletal muscle dysfunction

Αυξημένος επιπολασμός της υπέρτασης & της καρδιαγγειακής νόσου στη ΧΑΠ



52% υπέρταση

44% υπερλιπιδαιμία

30% στεφανιαία νόσος

22% διαβήτης

16% καρδιακή ανεπάρκεια

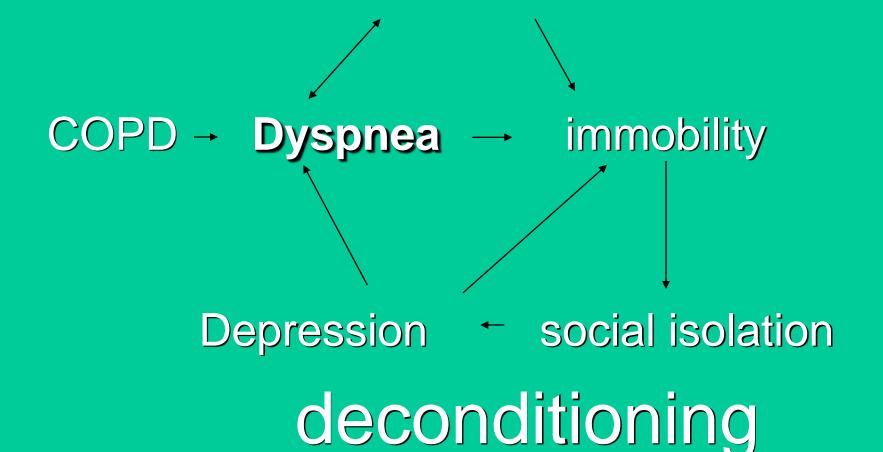
Το άγχος και η κατάθλιψη είναι συχνα νοσήματα συνοσηρότητας στη ΧΑΠ (Anxiety and depression are major comorbidities in COPD)

- π Σε μια συστηματική ανασκόπηση που επικεντρώθηκε σε ασθενείς με ΧΑΠ, η επίπτωση της κατάθλιψης κυμαινόταν από 37 έως 71%, και του άγχους από 50 σε 75%, στοιχεία που είναι συγκρίσιμα ή και μεγαλύτερα από τα ποσοστά επικράτησης σε άλλες σοβαρές ασθένειες όπως καρκίνος, AIDS, καρδιακές παθήσεις και νεφρική νόσο.
- Σε εξωτερικούς ασθενείς με ΧΑΠ μελέτες δείχνουν ποσοστά κατάθλιψης που κυμαίνονται από 7% έως 80% και άγχους που κυμαίνονται από 2% έως 80%. Η επικράτηση της γενικευμένης αγχώδους διαταραχής κυμαίνεται από 10% έως 33% και της διαταραχής πανικού από 8% έως 67%.

Prevalence in Advanced Disease: Systematic Review (64 studies)		
	Depression (%)	Anxiety (%)
COPD	37-71	51-75
Cancer	3-77	13-79
AIDS	10-82	8-34
Heart Disease	9-36	49
Renal Disease	5-60	39-70
(Solano, J Pain sympt Manage 2006 31:58)		

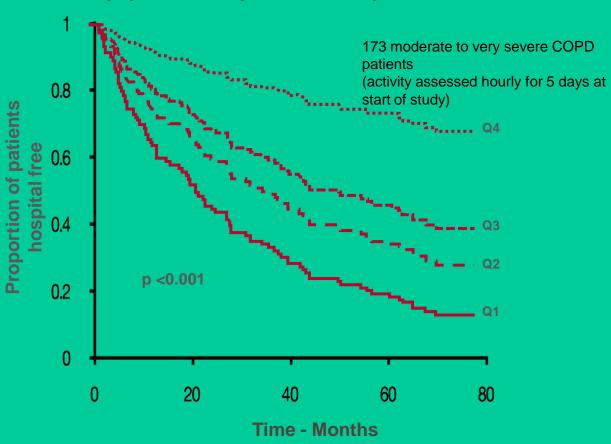
Vicious circle of COPD

lack of exercise



Reduced physical activity in COPD is associated with increased hospitalization rates

Time to first COPD hospitalization by quartile of daily physical activity * measured by accelerometer



^{*} Q1= least active to Q4 = most active quartile

^{*} Q1 = Lowest physical activity by quartile

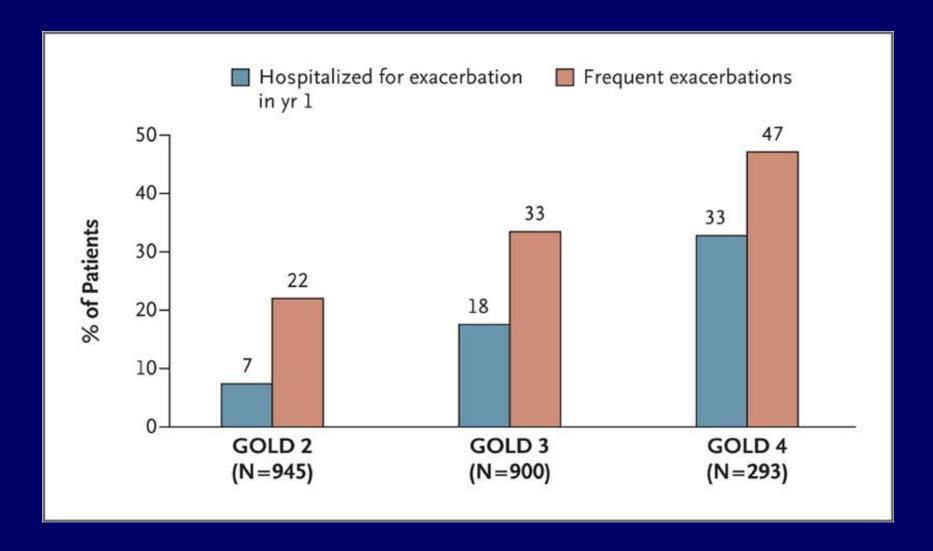
Management COPD Exacerbations

Key Points

An exacerbation of COPD is defined as:

"An event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD."

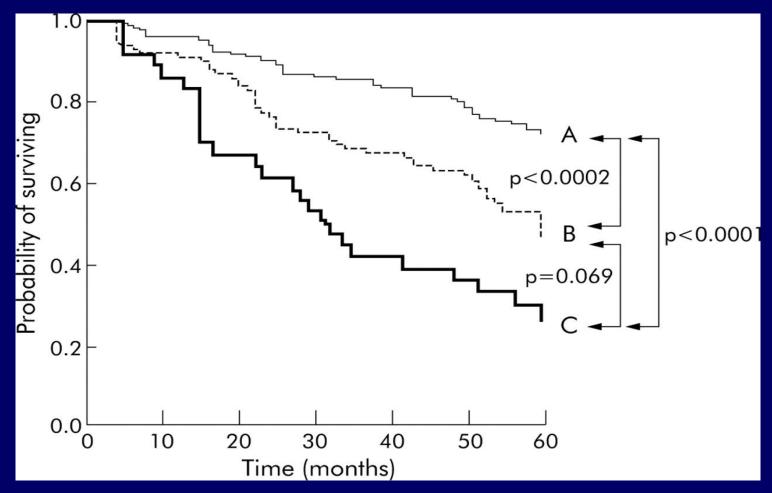
Association of Disease Severity with the Frequency and Severity of Exacerbations during the First Year of Follow-up in Patients with Chronic Obstructive Pulmonary Disease.







Kaplan-Meier survival curves by frequency of exacerbations in patients with COPD: group A, patients with no acute exacerbations of COPD; group B, patients with 1–2 acute exacerbations of COPD requiring hospital management; group C, patients with ≥3 acute exacerbations of COPD.



Soler-Cataluña J J et al. Thorax 2005;60:925-931



Management COPD Exacerbations

Key Points

- The most common causes of an exacerbation are infection of the tracheobronchial tree and air pollution, but the cause of about one-third of severe exacerbations cannot be identified (Evidence B).
- Patients experiencing COPD exacerbations with clinical signs of airway infection (e.g., increased sputum purulence) may benefit from antibiotic treatment (Evidence B).

Management of Stable COPD All Stages of Disease Severity

- Avoidance of risk factors
 - smoking cessation
 - reduction of indoor pollution
 - reduction of occupational exposure
- Influenza vaccination

Therapy at Each Stage of COPD

I: Mild

II: Moderate

III: Severe

IV: Very Severe

- FEV₁/FVC < 70%
- FEV₁ ≥ 80%

- FEV₁/FVC < 70%
 - 50% < FEV₁ < 80% predicted
- FEV₁/FVC < 70%
- 30% ≤ FEV₁ <
 50% predicted

- FEV₁/FVC < 70%
- FEV₁ < 30%
 predicted
 or FEV₁ < 50%
 predicted plus
 chronic respiratory

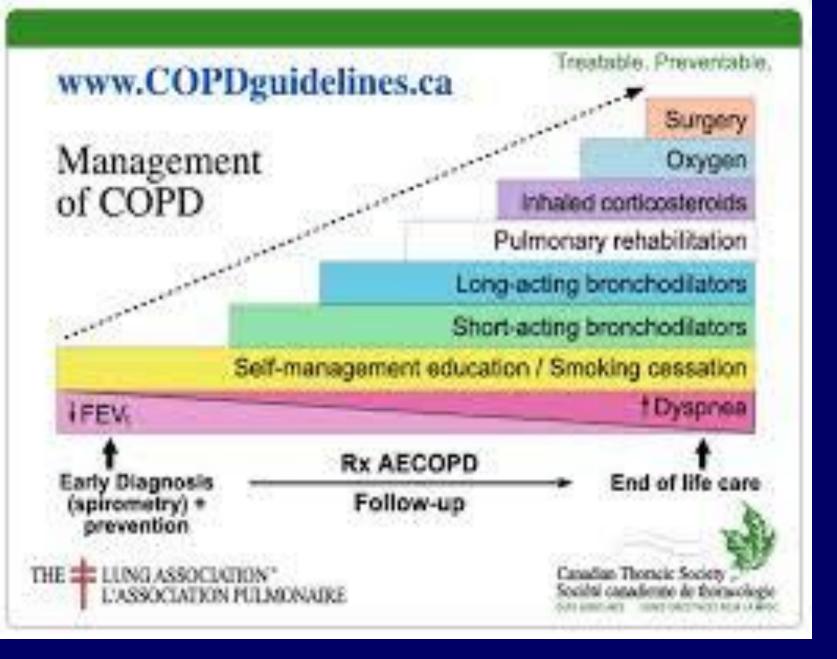
Active reduction of risk factor(s); influenza vaccination

Add short-acting bronchodilator (when needed)

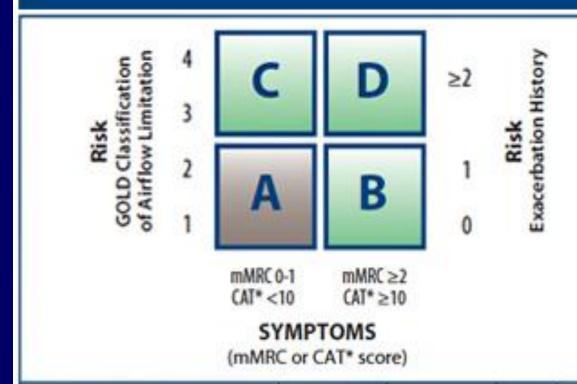
Add regular treatment with one or more long-acting bronchodilators (when needed); **Add** rehabilitation

Add inhaled glucocorticosteroids if repeated exacerbations

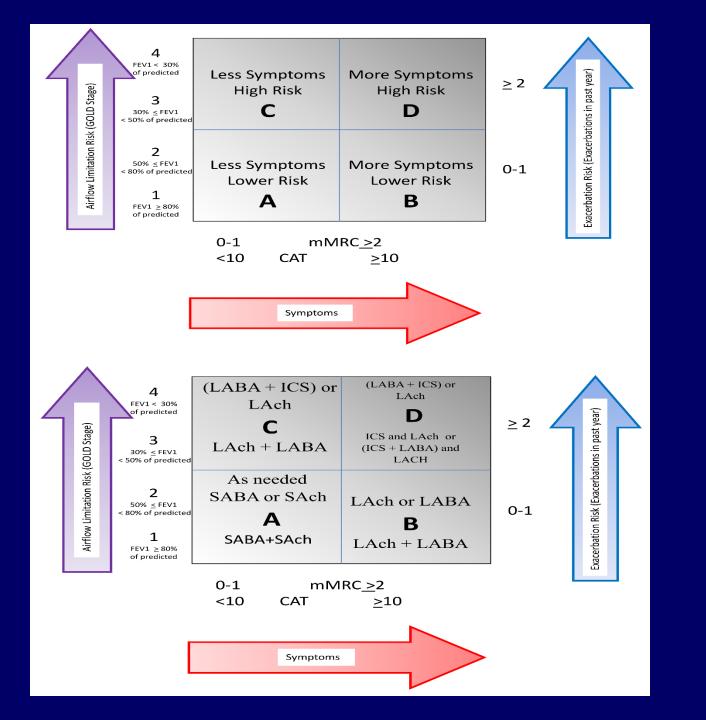
Add long term oxygen if chronic respiratory failure.
Consider surgical treatments



Patient classification¹



	Spirometric classification	Exacerbations per year	mMRC	CAT*
GROUP A: low risk, less symptoms	GOLD 1-2	s 1	0-1	<10
GROUP B: low risk, more symptoms	GOLD 1-2	≤1	≥2	≥10
GROUP C: high risk, less symptoms	GOLD 3-4	≥2	0-1	<10
GROUP D: high risk, more symptoms	GOLD 3-4	≥2	≥2	≥10



Manage Stable COPD: PharmacologicTherapy

Patient	First choice	Second choice	AlternativeChoices
Α	SAMA prn <i>or</i> SABA prn	LAMA or LABA or SABA and SAMA	Theophylline
В	LAMA <i>or</i> LABA	LAMA and LABA	SABA <i>and/or</i> SAMA Theophylline
С	ICS +LABA or LAMA	LAMA and LABA	PDE4-inh. SABA and/ <i>or</i> SAMA Theophylline
D	ICS + LABA or LAMA	ICS andLAMA or ICS + LABA and LAMA or ICS+LABA and PDE4-inh.or LAMA and LABA or LAMA and PDE4-inh.	Carbocysteine SABA and/ <i>or</i> SAMA Theophylline

Βασικοι συνδιασμοι φαινοτυπων της ΧΑΠ

ΒΑΣΙΚΟΙ ΣΥΝΔΙΑΣΜΟΙ ΦΑΙΝΟΤΥΠΩΝ ΤΗΣ ΧΑΠ

ΟΜΑΔΑ Α= ΧΡΟΝΙΑ ΒΡΟΓΧΙΤΙΔΑ, ΦΛΕΓΜΟΝΩΔΗΣ ΣΥΧΝΕΣ ΠΑΡΟΞΥΝΣΕΙΣ ΣΥΣΤΗΜΑΤΙΚΕΣ ΕΚΔΗΛΩΔΕΙΣ/ ΣΥΝ ΝΟΣΗΡΟΤΗΤΕΣ

ΟΜΑΔΑ Β= ΕΜΦΥΣΗΜΑ,
ΤΑΧΕΙΑ ΜΕΙΩΣΗ FEV1
ΣΗΜΑΝΤΙΚΗ ΥΠΕΡΔΙΑΤΑΣΗ
+/- ΠΑΡΟΞΥΝΣΕΙΣ

ΘΕΡΑΠΕΙΑ ΒΑΣΗ ΤΩΝ ΦΑΙΝΟΤΥΠΩΝ

OMAΔA A= ICS, LAMA, LABA, PDF4 INHIBITORS

 $OMA\Delta A B = LABA + LAMA$

Management of Stable COPD

Other Pharmacologic Treatments

- Antibiotics: Only used to treat infectious exacerbations of COPD
- Antioxidant agents: No effect of nacetylcysteine on frequency of exacerbations, except in patients *not* treated with inhaled glucocorticosteroids
- Mucolytic agents, Antitussives, Vasodilators: Not recommended in stable COPD

Translating COPD Guidelines into Primary Care KEY POINTS

- Spirometric confirmation is a key component of the diagnosis of COPD and primary care practitioners should have access to high quality spirometry.
- □ Σπιρομερτηση απαραίτητη για τη διάγνωση
- Θα πρέπει να επαναλαμβάνεται τουλάχιστον μια φορά το χρόνο

Η ΧΑΠ ΔΕΝ ΕΊΝΑΙ ΠΟΤΕ ΜΟΝΗ

ΣΕ ΑΡΡΩΣΤΟΥΣ

ΜΕ ΥΠΕΡΤΑΣΗ, ΔΙΑΒΗΤΗ, ΣΤΗΘΑΓΧΗ

ΟΣΤΕΟΠΟΡΩΣΗ,ΚΑΤΑΘΛΙΨΗ,

ΑΝΩ ΤΩΝ 40 ΕΤΩΝ ΚΑΠΝΙΣΤΕΣ

ΠΡΕΠΕΙ ΝΑ ΥΠΟΨΙΑΣΤΟΥΜΕ Κ ΧΑΠ Κ

ΝΑ ΤΟΥΣ

ΣΤΕΙΛΟΥΜΕ ΓΙΑ ΣΠΙΡΟΜΕΤΡΗΣΗ

ΣΥΜΠΕΡΑΣΜΑΤΑ

- Η ΧΑΠ είναι μια πολύ συχνή ΧΡΟΝΙΑ νόσος με μεγάλη θνητότητα κ μεγάλο οικονομικό κόστος
- □ Μπορεί να προληφθεί κ να θεραπευτεί
- Παρουσιάζει σημαντικές συν νοσηρότητες
- Οι παροξύνσεις βάζουν σε κίνδυνο τη ζωή των ασθενών
- Η θεραπεία της είναι μακροχρόνια

GOLD Website Address

http://www.goldcopd.org



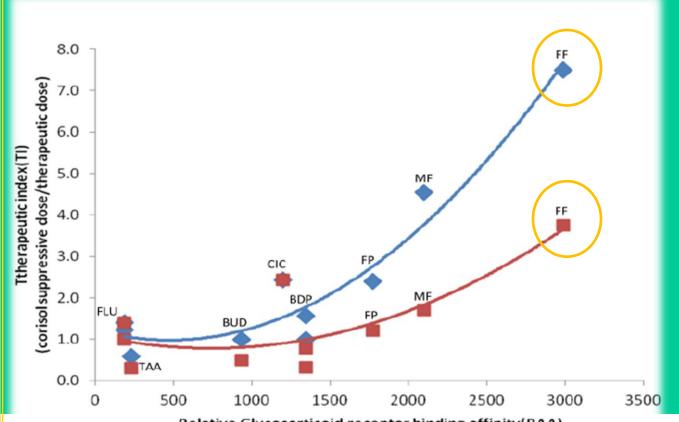


Ο ρόλος του παθολόγου στην ανίχνευση της ΧΑΠ

ΣΕ ΑΡΡΩςΤΟΥς ΜΕ ΥΠΕΡΤΑςΗ, ςΑΚ.ΔΙΑΒΗΤΗ,ΟςΤΕΟΠΩΡΩςΗ ,ςΤΗΘΑΓΧΗ ,ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ,ΑΡΡΥΘΜΙΕς Κ. ΙςΤΟΡΙΚΟ ΚΑΠΝΙςΜΑΤΟς ςΚΕΨΟΥ ΤΗΝ ΧΑΠ Κ ΖΗΤΗςΕ ΜΙΑ ςΠΙΡΟΜΕΤΡΗςΗ.



Φούροϊκή Φλουτικαζόνη: Υψηλός θεραπευτικός δείκτης



FF: fluticasone furoate

MF: mometasone furoate

FP: fluticasone propionate

CIC: ciclesonide

BUD: budesonide

BDP: beclomethasone dipropionate

TAA: triamcinolone acetonide

FLU: flunisolide

πεύγκριση του Relvar με το Τιοτρόπιο για την ασφάλεια και αποτέλεσματικότητα σε ασθενείς με μέτρια και σοβαρή ΧΑΠ και υψηλό καρδιαγγειακό κίνδυνο*

Table 4 Adverse events ^a		
	FF/VI	TIO
	(n=310)	(n=313)
AEs during treatment, n (%)		
Any AE during treatment	113 (36)	99 (32)
Drug-related AE	21 (7)	12 (4)
AE leading to withdrawalb	CEENIO	14 (4)
Serious AEs	ate Of FI	10 (3)
Drug-related AE AE leading to withdrawalb Serious AEs Fatal AEs Most frequent apparent effermasop Nasop Back part TIO treatment Of the position of the positio	CLE CV Salety	2 (<1)
Most frequence parent	a the CV	
Heads no apparant o	.0 (6)	23 (7)
Nasop	16 (5)	13 (4)
Back p. TIO TIECO	9 (3)	9 (3)
	9 (3)	5 (2)
AEs of species (10 lest, d n (%)		
Cardiovas ular effects	13 (4)	15 (5)
Local steroid effects/candidiasis	17 (5)	11 (4)
Hypersensitivity	5 (2)	4 (1)
LRTI excluding pneumonia	3 (<1)	4 (1)
Bone disorders/fractures	3 (<1)	1 (<1)
Pneumonia	3 (<1)	0
Ocular effects/glaucoma	0	1 (<1)

Notes: ^aNumber of subjects reporting an event (not number of events); ^bany AE leading to permanent withdrawal from the study or withdrawal of study drug; ^cAEs reported in ≥3% of subjects in either treatment group; ^dprespecified AEs of special interest with corticosteroid and LABA treatment.

Abbreviations: AE, adverse event; FF/VI, fluticasone furoate/vilanterol (100/25 mcg); LRTI, lower respiratory tract infection; TIO, tiotropium (18 mcg).

...safety measures were similar between groups, and cardiovascular monitoring did not reveal increased CVD risk.

...More TIO-treated than FF/VI-treated subjects were withdrawn from the study due to AEs. Two TIO-treated subjects died (one due to cardiopulmonary arrest and the other due to cardiorespiratory arrest and cardiac failure).

A randomized, blinded, double-dummy, parallel-group study compared a once-daily morning dose of FF/VI 100/25 mcg delivered via ELLIPTATM with TIO 18 mcg via HandiHaler® for 12 weeks in subjects with diagnosed COPD, forced expiratory volume in 1 second (FEV1) 30%–70% predicted, and CVD or CVD risk. The primary endpoint was change from baseline in 24-hour weighted mean FEV1 on Day 84.

Εξατομικευμένη διαχείρηση των ασθενών με ΧΑΠ

COPD patients who could benefit most from ICS Risk of exacerbations exacerbation risk: high breathlessness: low **A*** **B**** exacerbation risk: low exacerbation risk: low breathlessness: low breathlessness: high This group also includes C patients This group also includes D patients with lower risk of exacerbations who with lower risk of exacerbations who may not require ICS¹ may not require ICS¹ LABA or LAMA LABA + LAMA

Breathlessness

Adapted from Agusti A & Fabbri L. Lancet Resp Med. 2014 based on GOLD patient categories.

*Consider adding roflumilast, azithromycin, theophylline, or antioxidants if COPD is uncontrolled with ICS1.

1. Agusti A & Fabbri L. Lancet Resp Med. 2014;2:869-871. 2. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (Updated 2015). http://www.goldcopd.org/uploads/users/files/GOLD_Report_2015_Sept2.pdf (Accessed 03/12/2015).



Phenotype: Males/Females

FEMALES → younger

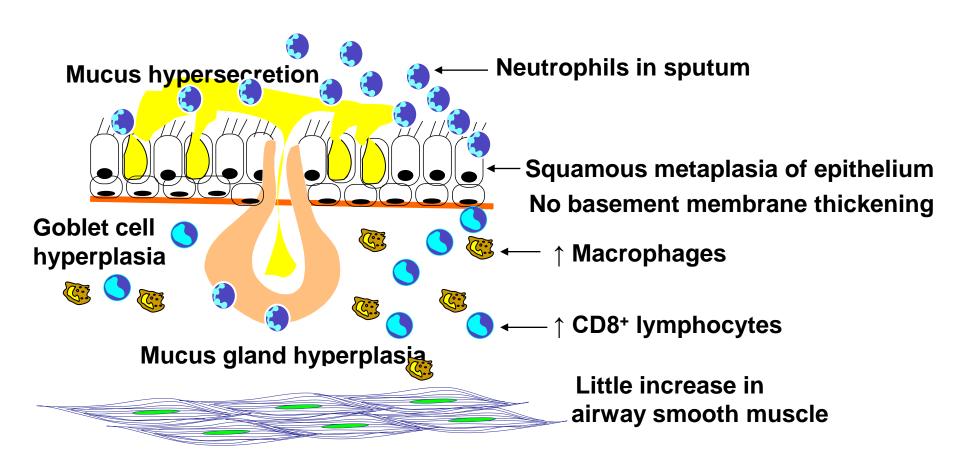
less smoking history

less comorbidity scores

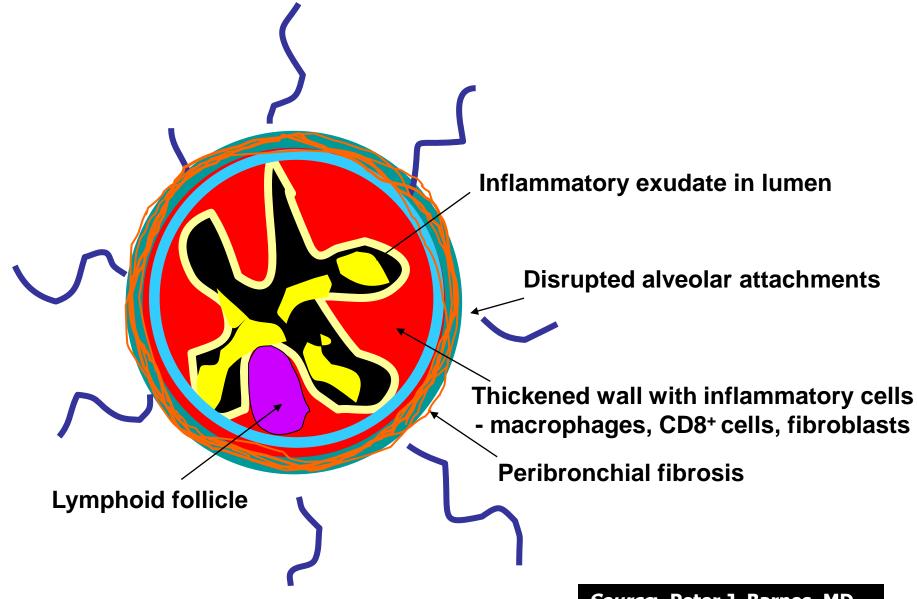
less responsive to long-term exercise therapy lower scores in quality of life questionnaires more reactive airways, more exacerbations more dyspnea for the same degree of airflow limitation

de Torres et al. Chest 2005; 128:20012-6

Changes in Large Airways of COPD Patients

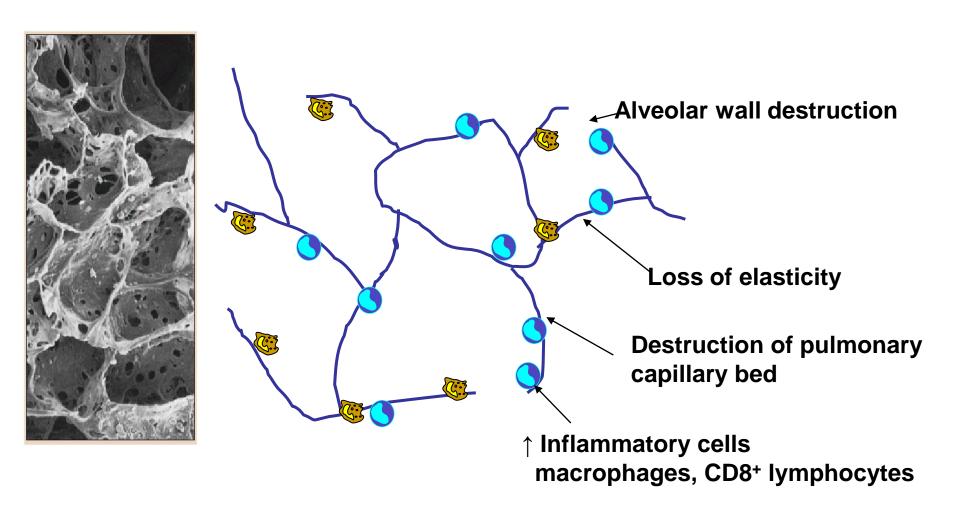


Changes in Small Airways in COPD Patients



Source: Peter J. Barnes, MD

Changes in the Lung Parenchyma in COPD Patients



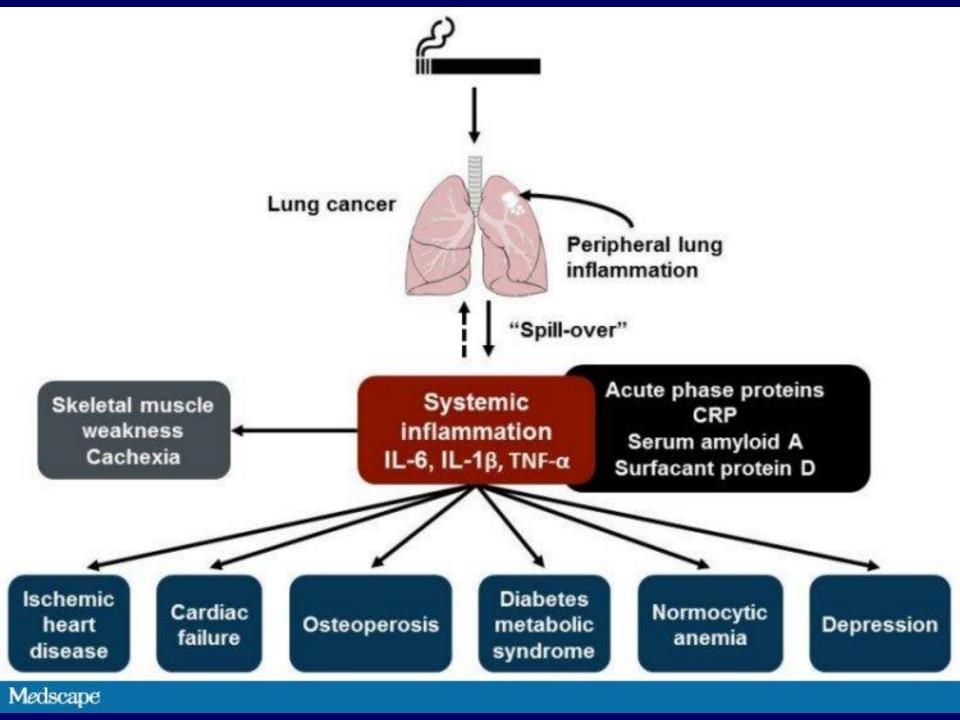
Source: Peter J. Barnes, MD

Increased Oxidative stress in COPD

• Cigarette smoke contains an estimated 1017 oxidants/free radicals and 4,700 chemical compounds, including that can generate hydroxyl radicals (-OH) and hydrogen peroxide (H2O2).

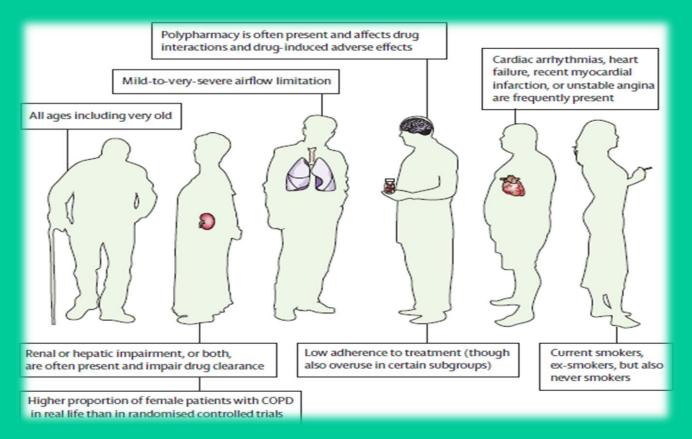


 Cigarette smoke also recruits immune and inflammatory cells to the lungs, which on activation release more oxidants causing an oxidant/antioxidant imbalance.





Οι θέσεις ομοφωνίας (GOLD) για τη σημασία των συνοδών νοσημάτων στη ΧΑΠ



"COPD occurs together with concomitant chronic diseases (including cardiovascular diseases), which contribute to the severity and prognosis of COPD."





Classification of COPD Severity by Spirometry

Stage I: Mild $FEV_1/FVC < 0.70$

 $FEV_1 \ge 80\%$ predicted

Stage II: Moderate FEV₁/FVC < 0.70

 $50\% \leq \text{FEV}_1 < 80\%$ predicted

Stage III: Severe FEV₁/FVC < 0.70

 $30\% \le FEV_1 < 50\%$ predicted

Stage IV: Very Severe FEV₁/FVC < 0.70

FEV₁ < 30% predicted *or*

 $FEV_1 < 50\%$ predicted *plus*

chronic respiratory failure

EDITORIALS



Preventing Exacerbations of COPD — Advice from Hippocrates

Nikolaos M. Siafakas, M.D., Ph.D.

Severe acute exacerbations of chronic obstructive pulmonary disease (COPD) are devastating, lifethreatening events; the 30-day mortality is greater than that with acute myocardial infarction (26% vs. 7.8%).^{1,2} Acute exacerbations of COPD dramatically change the course of the disease, since they are associated with a rapid decline in lung function and worsening quality of life.³ They also represent a substantial economic burden to society.³ Prevention of exacerbations remains a primary goal of management³ but is difficult because the cause of acute exacerbations of COPD remains largely unknown.⁴

Recent studies have shown that, when used

proximately 5% in the patients receiving azithromycin. More important, there was an increased prevalence of macrolide-resistant bacteria colonizing the airway, although this was not associated with an increased incidence of pneumonia, a finding that is in agreement with previous reports involving fewer patients.^{7,8}

However, the risk of microbial resistance associated with the long-term use of azithromycin in patients with COPD must be considered as part of the risk-benefit ratio of this treatment. Although the effect on microbial resistance in the community is still unknown, the study by Albert et al. showed that among patients who



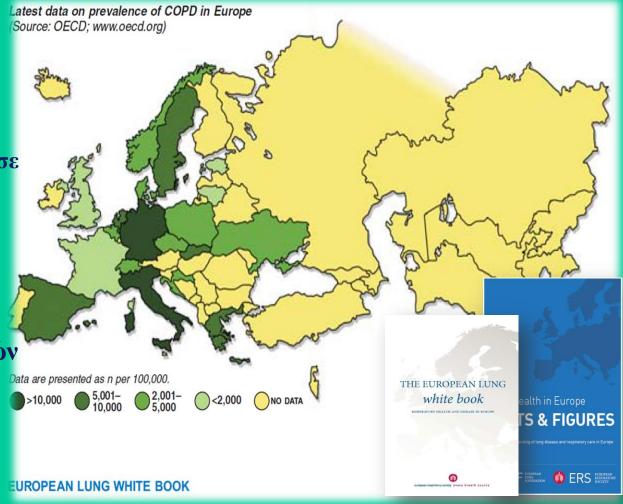
Ο επιπολασμός στη ΧΑΠ

√ 5–10%των ενηλίκων 40 ετώνπαρουσίαζειΧΑΠ.

Υψηλότερο επιπολασμό παρουσιάζουν οι άνδρες σε σχέση με τις γυναίκες.

39

Το 40-50%
των δια βίου καπνιστών
θα παρουσιάσουν
ΧΑΠ
στη ζωή τους.





COPD Phenotypes

- □ Chronic Bronchitis (Blue bloater)
- Emphysema (Pink puffer)
- A1-antitrypsin deficiency
- Frequent exacerbators
- Patients with or without systemic involvement
- **COPD** with or without comorbidities
- Significant hyperinflation
- **Fast decliner (FEV1)**
- ACOS
- Current smoker

