COPD
preventable and treatable disease

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Historical opinion

- COPD is disease with slow, relentless progress in older people which prognosis is invariably poor
- not too much preventable because the people smoked, smoke and will smoke…..
- not too much treatable, most patients are satisfied with theophyllins and beta agonist…
- no interest from patients: “ I smoke, so my cough is normal“ …“ I am over 50´ therefore I suffer from breathlessness during exercise“
- no special interest from physicians- COPD can be managed by every physicians - GP´s, internists, pneumologists…..

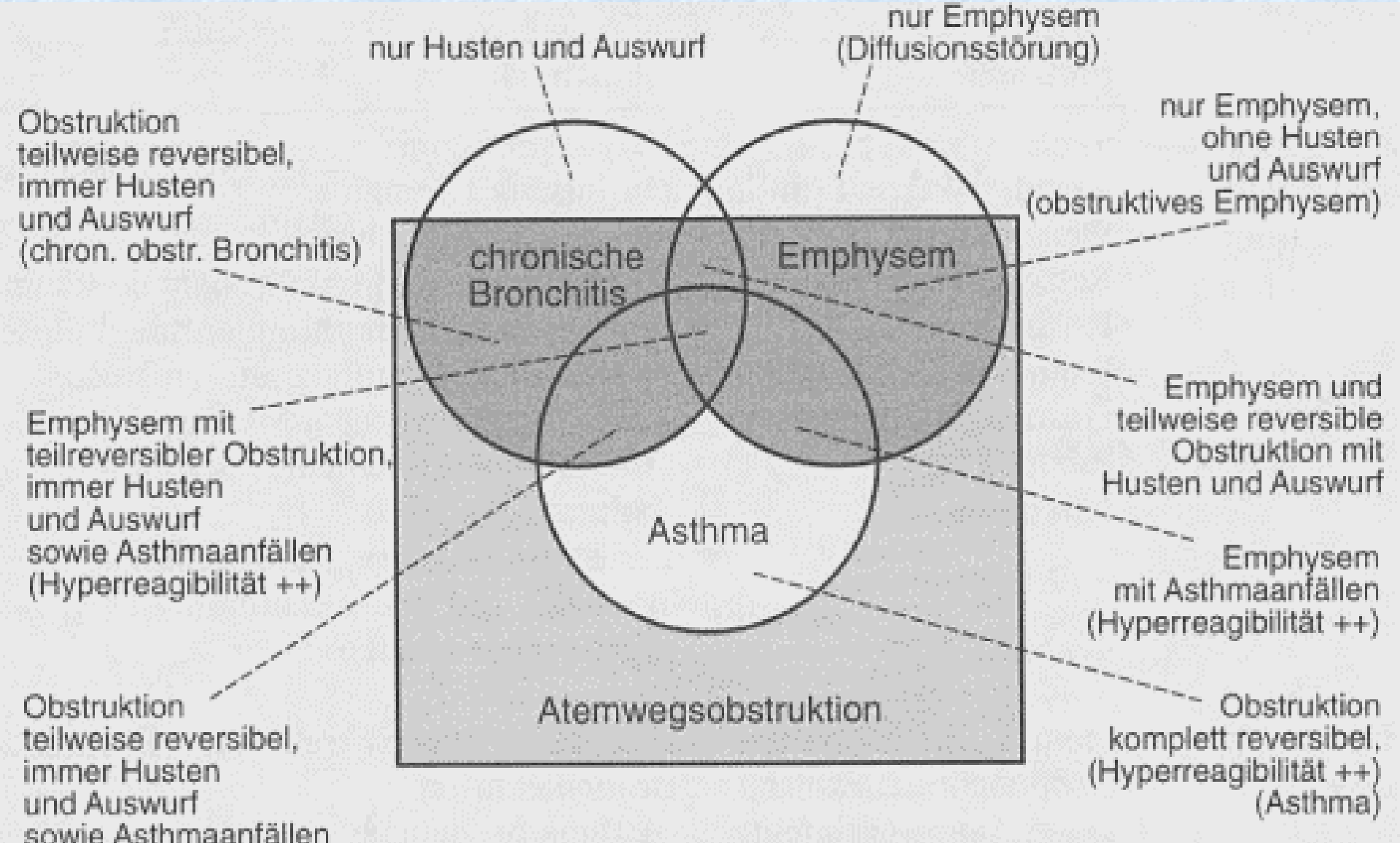
Definition of COPD *(GOLD 2006)*

COPD is a *preventable* and *treatable* disease with some significant *extrapulmonary effects* and important comorbidities that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases. Thus, COPD should be regarded as a pulmonary disease, but these significant comorbidities must be taken into account in a comprehensive diagnostic assessment of severity and in determining appropriate treatment.

Components of COPD

- **Chronic bronchitis** – cough and expectoration of most of the days in 3 month in two consecutive years, without known other reason (bronchiectasie, asthma, cystic fibrosis)
- **emphyzema** – pat. - anatom. definition – dilatation of airways beyond the terminal bronchiolus with destruction of interalveolar septa
- **asthma bronchiale** – chronic inflammatory illness with chronic air flow limitation may leds to COPD

Venn diagram



Prevention of COPD

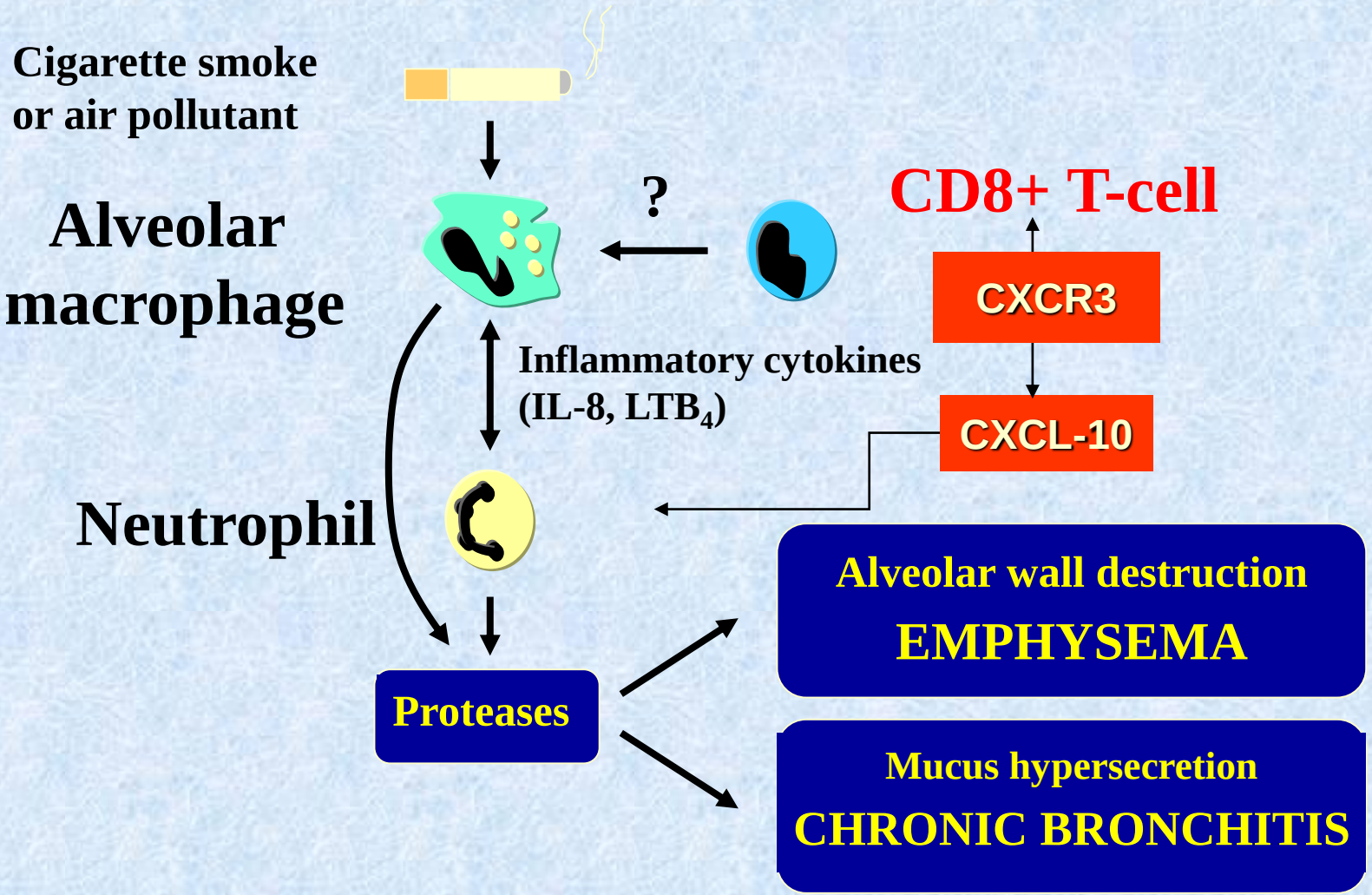
- **primary prevention – does n´t exist with exception of A_1 AT defficience and no smoking advice during pregnancy**

- **Secondary prevention – elimination of all risks factors – no start to smoke, elimination of passive smoking , to stop smoking**

  elimination of general, professional and home air polution

- **terciar prevention – elimination of triggers of exacerbaction, good therapy of COPD , vaccination against influenzae**

Pathogenesis of COPD



Modified from Barnes, 2003

SMOKING INDUCED CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Airway and lung Inflammation in COPD

COPD, an autoimmune disease?

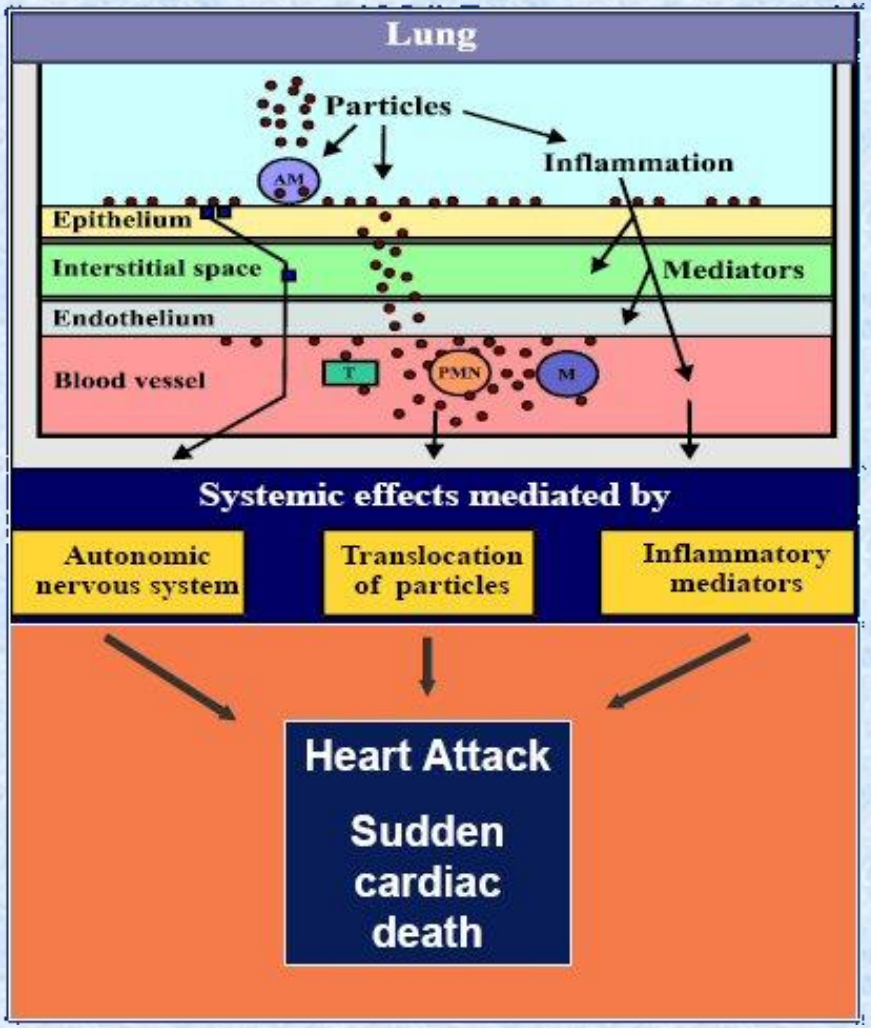
Systemic Inflammation in COPD

Centrilobular emphysema

Panlobular emphysema

Saetta et al. ERJ 1994

Inhaled particles: pulmonary and heart co-morbidity



Lung

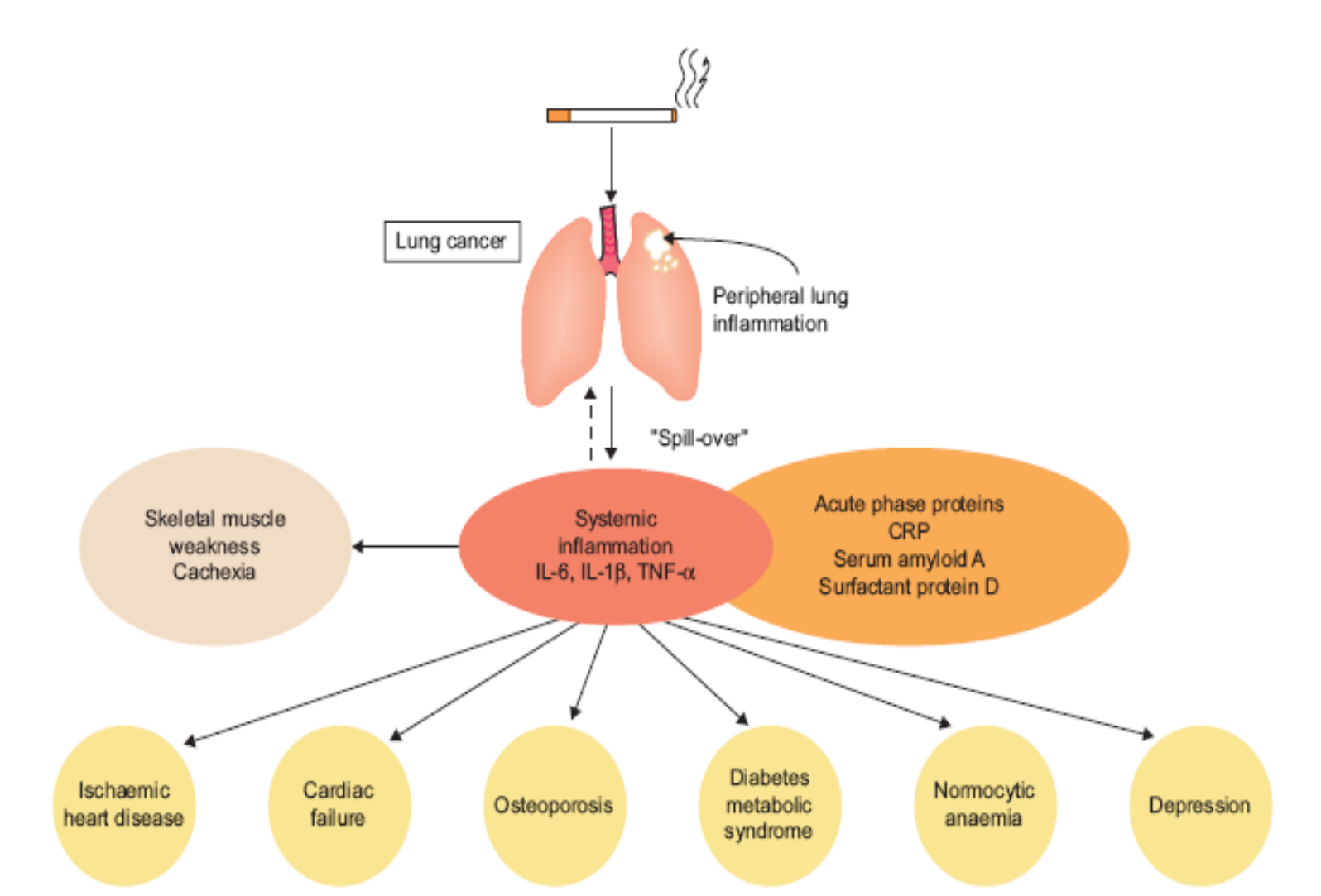
Inflammation

Allergy - Sensitization

Chronic lung diseases

Cardiovascular Effects of Fine and Ultrafine Particles

Systemic effects and comorbidities of chronic obstructive pulmonary disease (COPD)



Barnes PJ et al., Eur Respir J 2009;33:1165–1185

Prevention of Exacerbations of Chronic Obstructive Pulmonary Disease with Tiotropium, a Once-Daily Inhaled Anticholinergic Bronchodilator

COEXISTING ILLNESSES

Vascular (including hypertension) 64%
Cardiac 38%
Gastrointestinal 48%
Musculoskeletal or connective tissue 46%
Metabolic or nutritional 47%
Reproductive or urinary 27%
Neurologic 22%

Niewoehner,et al, Ann Intern Med. 2005;143:317-326

Patogenezis-1

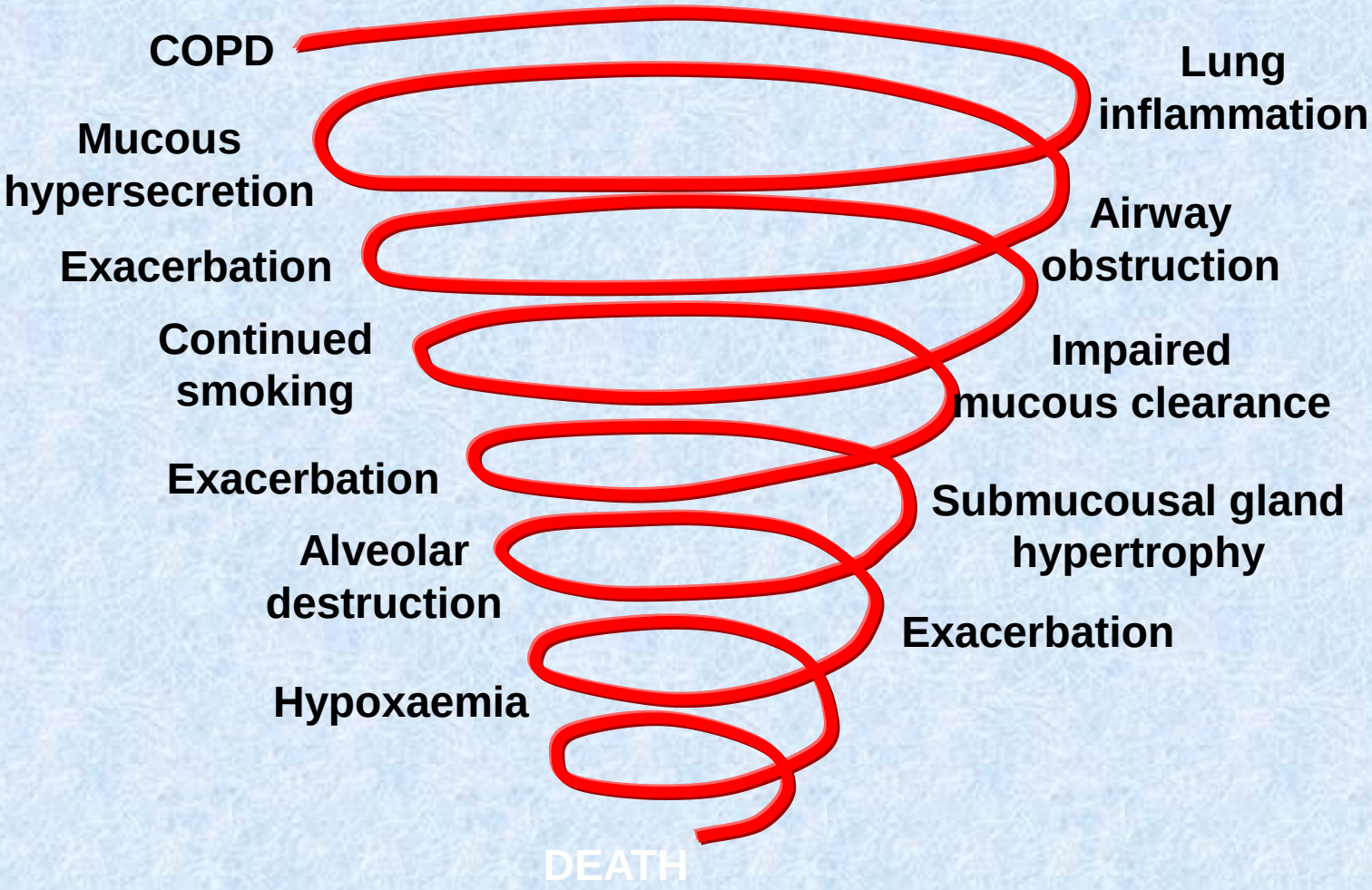
- Perzistant inflammation – smoke, dust particle atracts neutrophils, alveol. makrophages, CD8 T lymphocytes
- enzymes (proteases) of neutrophils and macrophages destruct the lung structure - elastazes, catepsin, colagenases, gelatinases- destruct extracellular matrix – antiproteases
- Inflammatory mediators: LTB4, IL8 TNFα
- oxidative stress – free radicals and oxidant in smoke, inhibition of growth factors - EGF
- Hyperproduction of secretion
- Damage of antiprotease (alfa 1 antitrypsin)

Patogenezis-2

- dysbalance between proteases and antiproteases- AAT, secretory inhibitor of leucocytes proteases
- structural changes in airways and in lungs - remodelation
- mucociliar dysfunction – squamous metaplasie
- Systemic damage - musculature, malnutrition, osteoporozis
- All contribute to chronic air flow limitation, hyperreactivity and hyperinflation

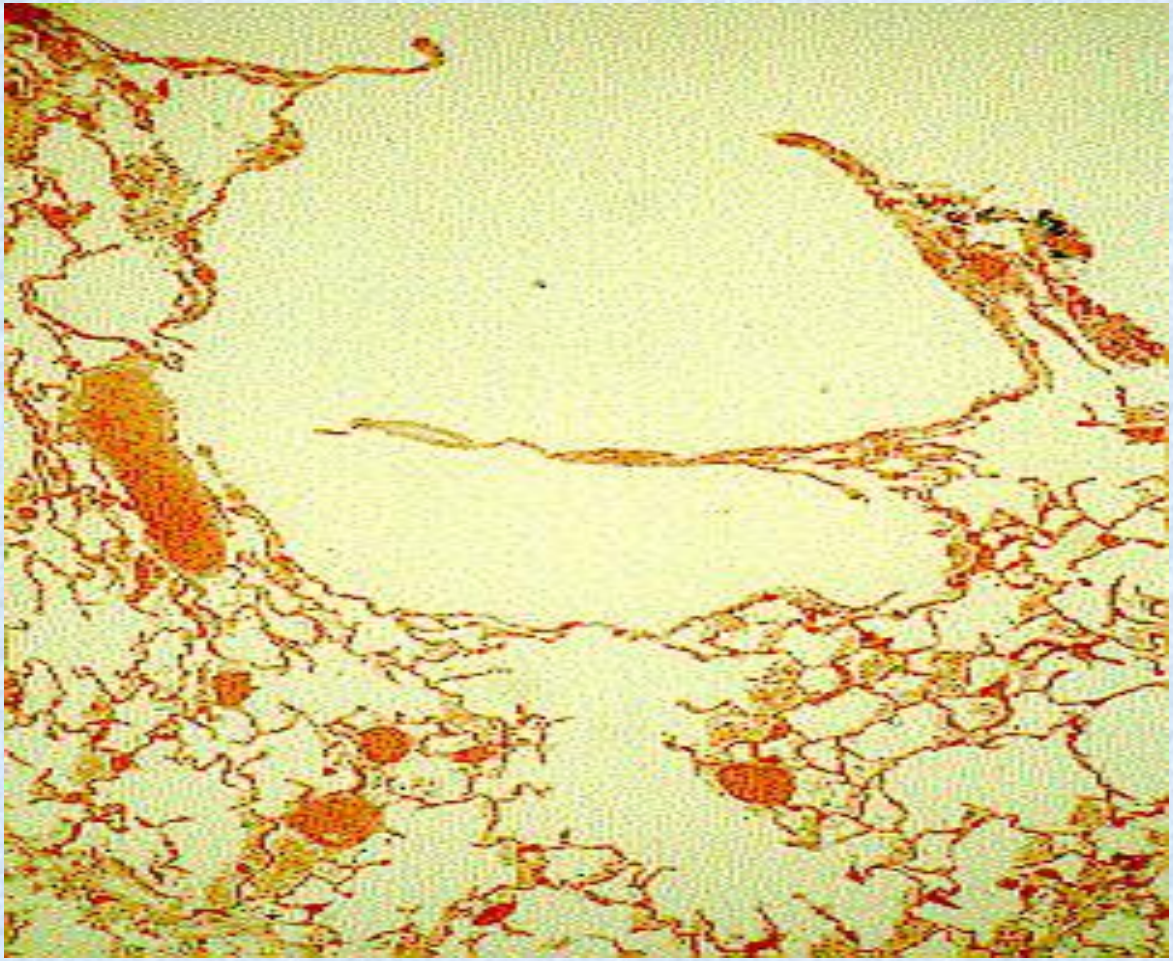
and finaly also to respiratory insufficience

The Downward Spiral in COPD



From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.

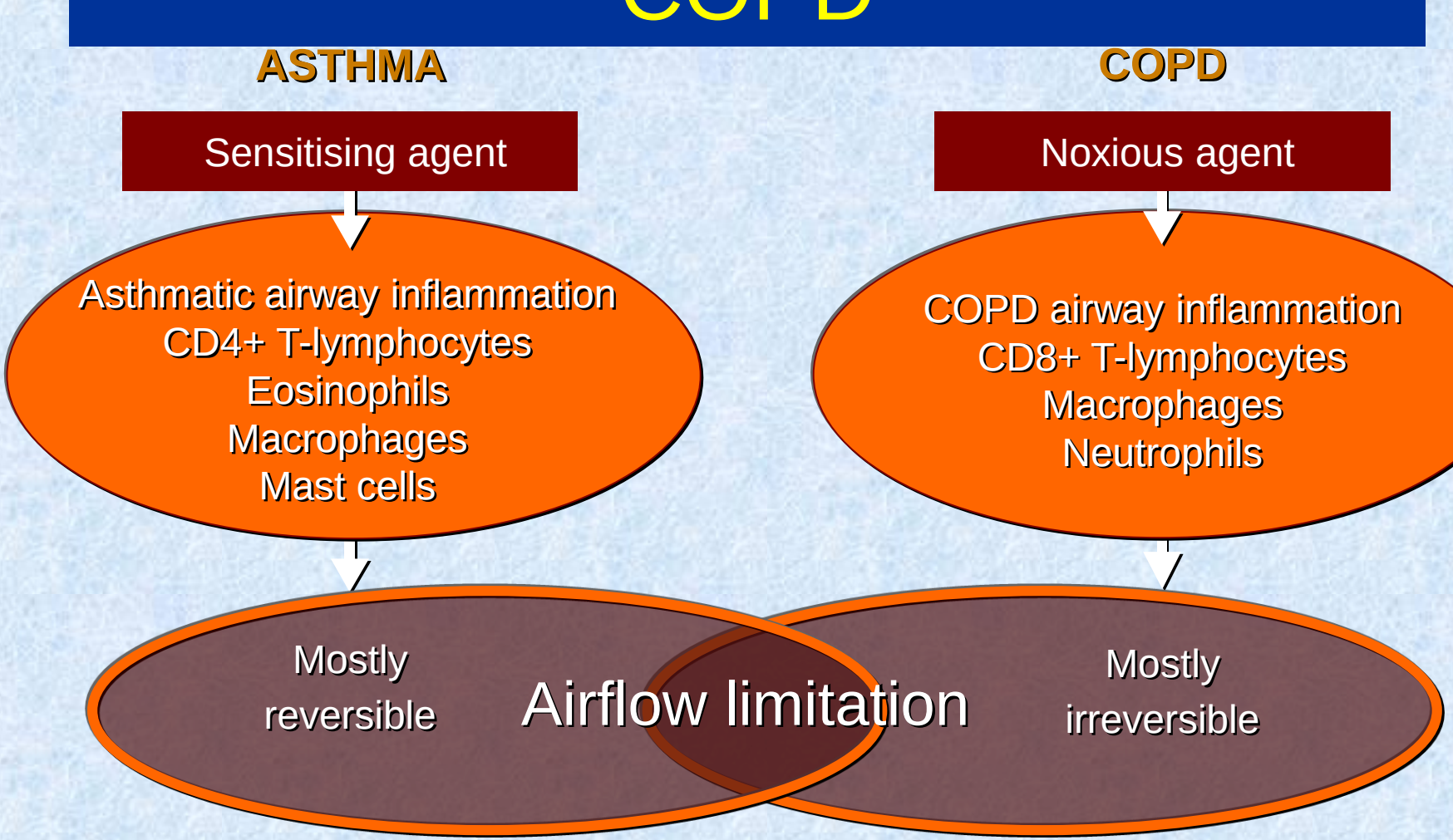
Emphyzema



Patho- phyziology

- **chronic obstructive** ventilation disturbation, reversibility under 12%
  - reversibile component – contraction of the smoth muscles, edema, hypersecretion
  - irreversibile component - emphyzema
- Prolongation of expiratory flow, dynamic compresion of airways at expiration
- **Hyperinflation** , shift of ventilation to the higher volumes
- Efficiency of breath musculature is diminuished
- Ratio V/Q may be „ normal“ - (emphyzema), or smaller
- Increase the phyziological death space, diminuished alveolar ventilation
- Increase of breath work is caused by lost of lung elasticity
- MMV se going down
- Disturbation of exchange of gases – **chronic hypoxemie** – increase of blood pressure in a. pulmonalis

Inflammation in Asthma and COPD



From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.
Sutherland ER, et al. *J Clin Allergy Immunol.* 2003;112:819-827.

COPD- is really so frequent??

- WHO- 2,74 million deaths worldwide *(ACCP, 2003)*
- in 2020 it will be the third most frequent killer disease (*Murray & Lopez. Cambridge: Harvard University Press 1996.)*
- US- 14 million chronic bronchitis, 2 million emphysema – **7 % of population** *(Nat. center for health statistic, CDC, 1996)*
- fourth leading cause of death in US behind heart disease, cancer and stroke (1998)

COPD- is really so frequent??

- increase number of woman with COPD

  - in Canada doubled it from 8 to 17/100 000 between 1980 and 1995 *(Lacasse,CHEST, 116)*

- increase number of younger people

  - in 1987 was in US. under the age of 64 years 26 % of pts with COPD, but in 2001 it was already 50 % !!! *(ACCP, 2003)*

- in Europe prevalence ranged from 3 % in Finnish women to 57 % in Italian men 45 years and older. *(Nowak,Treat Resp Med, 2005)*

- Czech Republic prevalence 8 % *(Kašák,2006)*

Prevalence COPD in the Czech Republic

	2000	2001	2002	2003	2004	2005	2013
COPD at Pneumol. depth.	207 195	213 507	217 759	225 619	245 405	235 895	268 578

2005 - men to women ratio

men 138 144 (58 %) women 97 751 (42 %)

stage III and IV 34 266 (25 %) 22 660 (23 %)

2005 number of hospitalisations 17 101

days in hospital 394 439

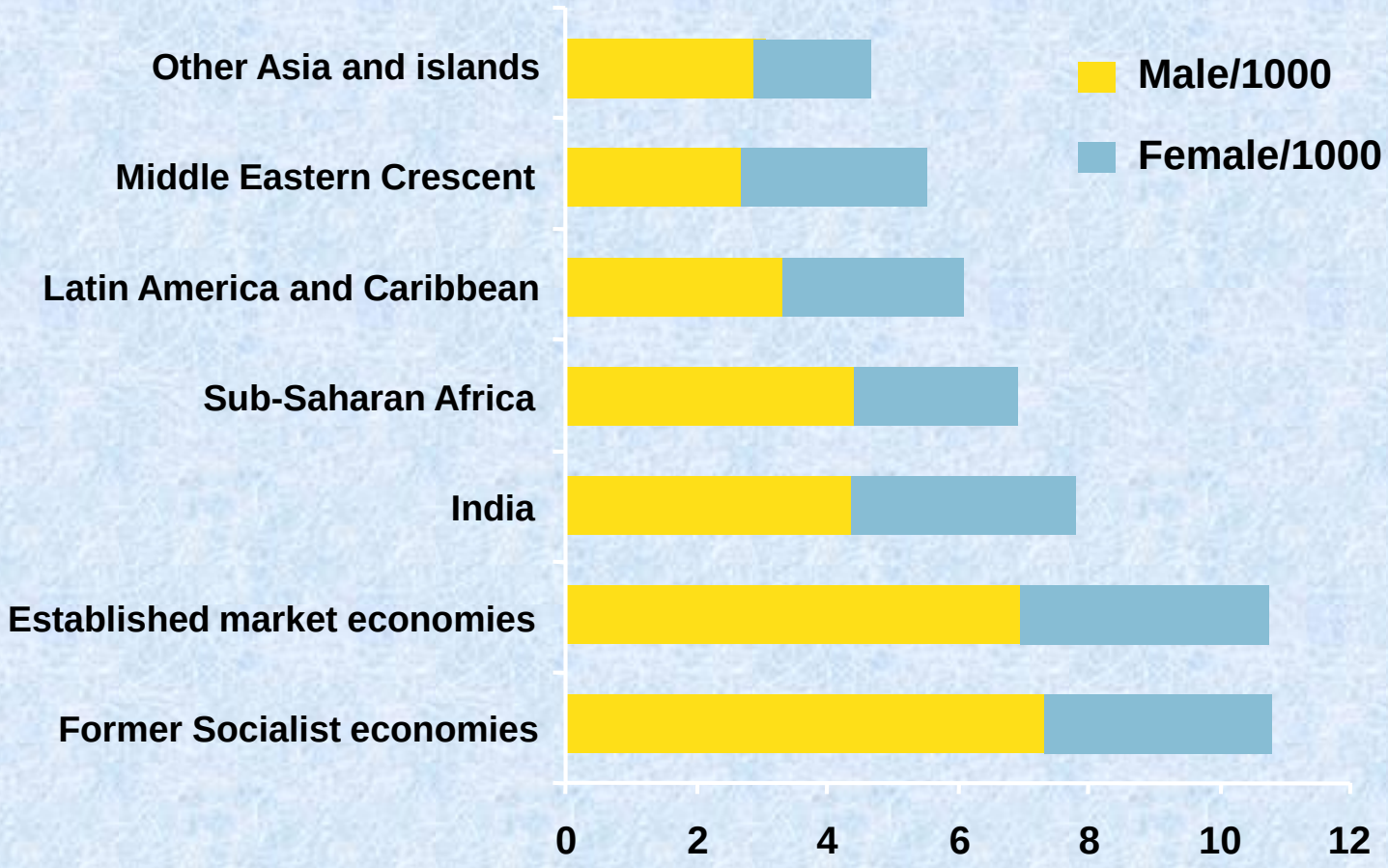
on average days in hospital 16,3 days *UZIS 2005*

Mortality on COPD in Czech Republic

	absolute number	x/100 000
• 1996	1062	10,3/ 100 000
• 2013	3190	21,4/100 000
	men	27,1/100 000
	women	16,0 /100 000

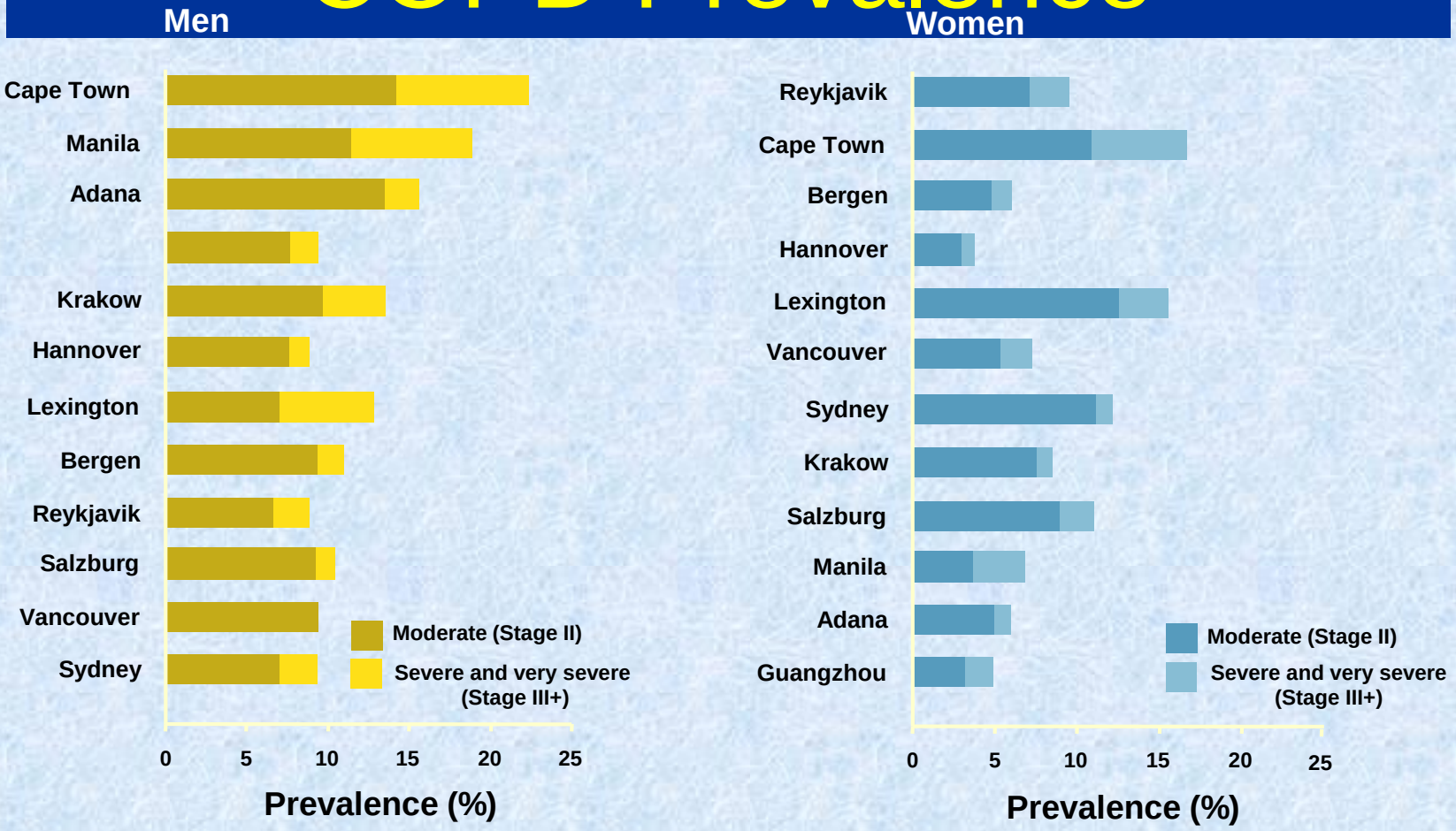
Vondra, Med po promoci,8, Suppl. 1/2007

Worldwide Prevalence of COPD



From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2005.

International Variation in COPD Prevalence



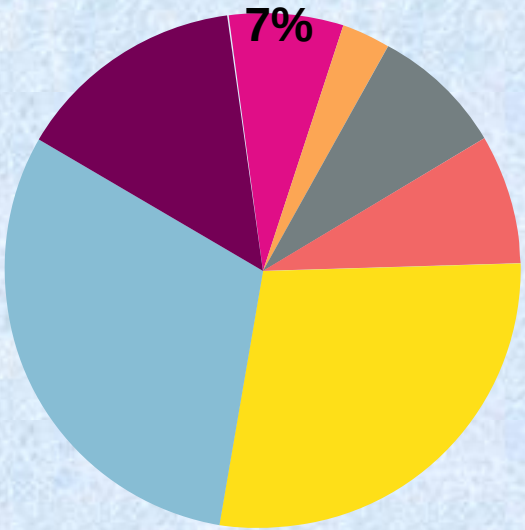
COPD in the European Union

- Fourth-leading cause of death and expected to be third-leading killer within the next 15 years
- Approximately 200,000–300,000 people in Europe die of COPD each year
- Productivity losses due to COPD = €28.5 billion each year

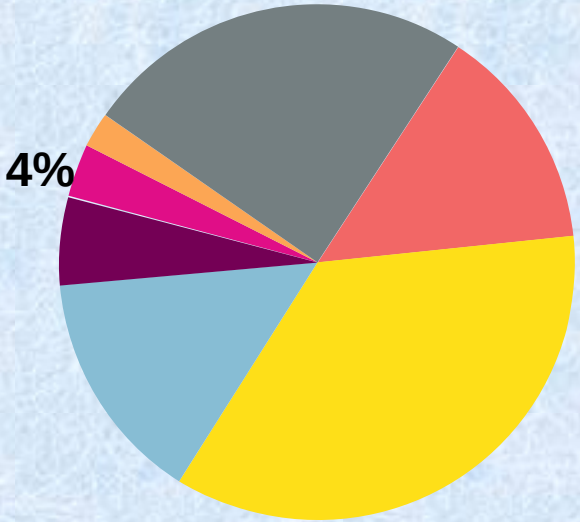
European Lung Foundation. Raise awareness about COPD in the EU. 2006.

Death and Disability Due to Respiratory Disease Worldwide

Main Causes of Death



Main Causes of Global Burden of Diseases In Disability Adjusted Life Years (DALYS)



- Communicable diseases, maternal and perinatal conditions, nutritional deficiencies
- Cardiovascular disease
- Cancer
- Chronic respiratory diseases
- Diabetes
- Other chronic diseases
- Injuries

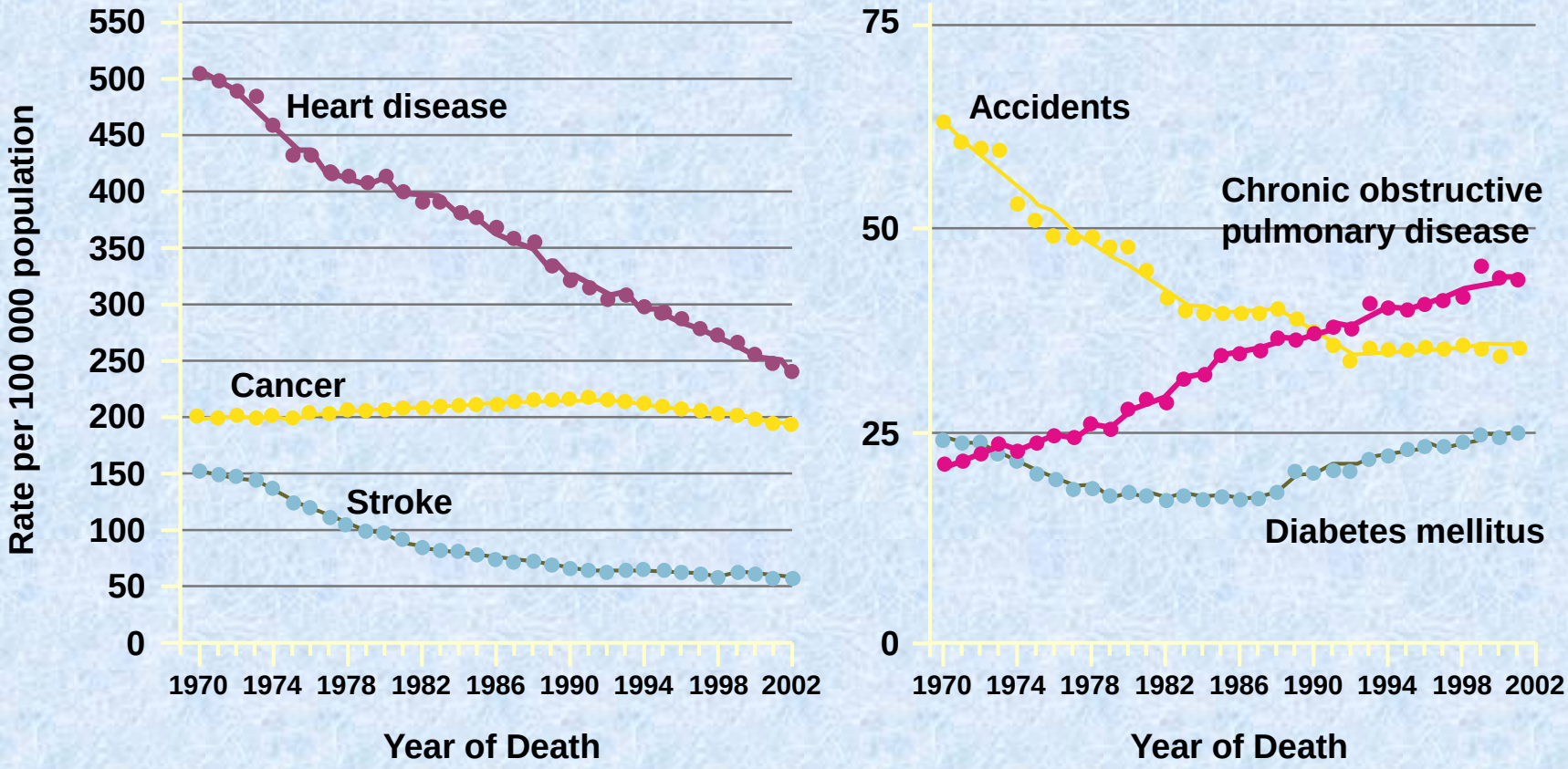
Global Alliance Against Chronic Respiratory Diseases (GARD). Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach. 2007. Available at: http://www.who.int/gard/publications/GARD%20Book%202007.pdf

COPD Is an Increasingly Common Cause of Death Worldwide

Cause of Death	Rank in 2002	Rank in 2030
Ischaemic heart disease	1	1
Cerebrovascular disease	2	2
Lower respiratory infections	3	5
HIV/AIDS	4	3
COPD	5	4
Perinatal conditions	6	9
Diarrhoeal diseases	7	16
Tuberculosis	8	23
Trachea, bronchus, lung cancers	9	6
Road traffic accidents	10	8

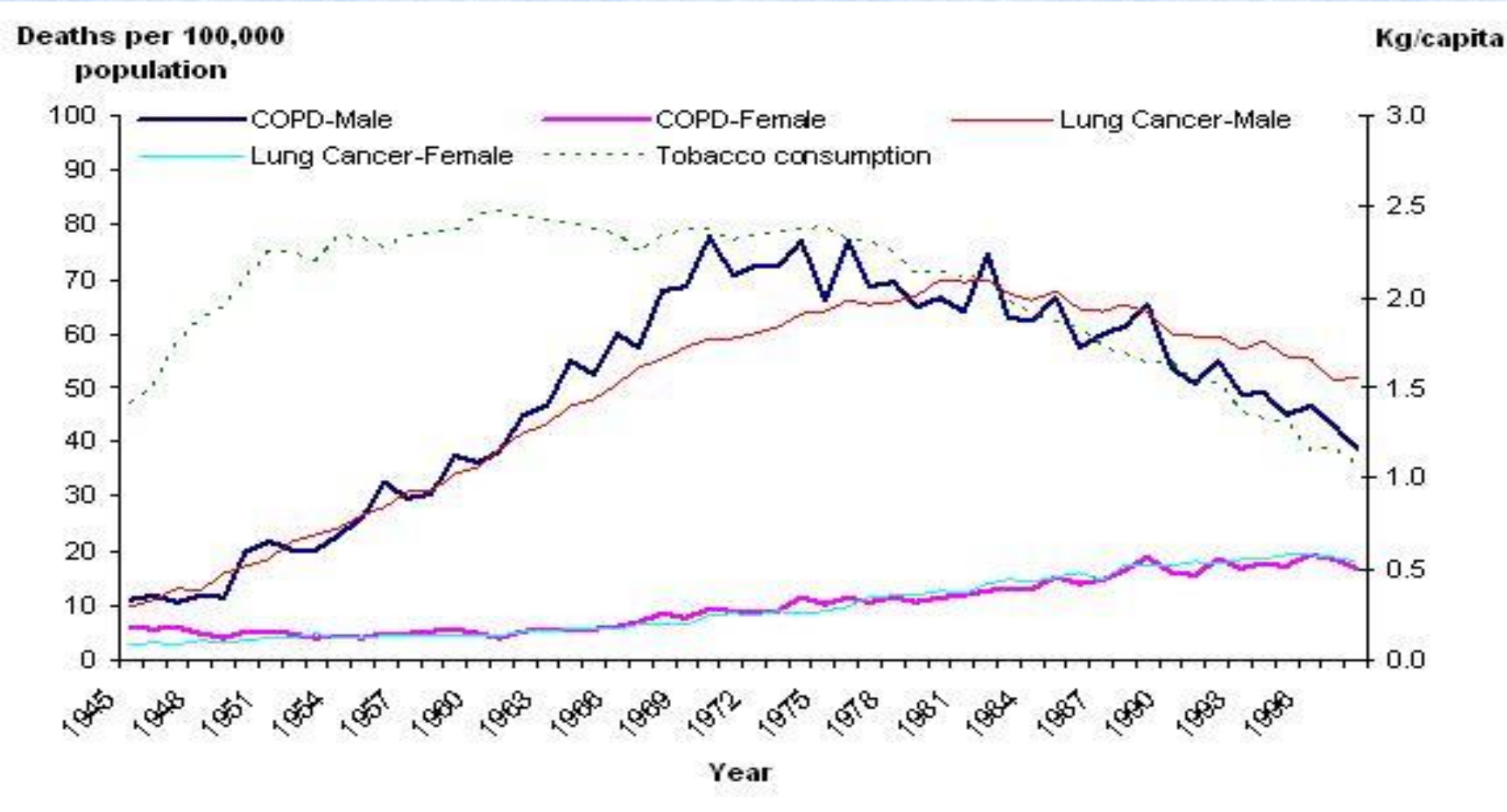
Mathers CD, et al. *PLoS Med*. 2006;3:2011-2030.

COPD Mortality Is Increasing Versus Other Chronic Diseases: United States Data



Global Alliance Against Chronic Respiratory Diseases (GARD). Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach. 2007. Available at: http://www.who.int/gard/publications/GARD%20Book%202007.pdf

Australian experience



Smoking and other risk factors

- **CR: 40 % men and 25 % of women in age 30 -60 years smoke *(UZIS ČR 2004)* cca 29% of adults**

- **in USA smoked about 75 milions persons - cca 30%**

Risk factors -1

- **Individual factors : genetic disposition , bronchial hyperreactivity - dutch hypothesis COPD – one genetic disposition but two phenotypes of illness asthma/COPD. More favorite is today british hypothesis – two different diseases but some characteristic common**
- **Lung growth disturbances – finished in 3 years frequent infection, spastic bronchitis and smoking of mother in the time of gravidity are risky for development of COPD**

Risk factors -2

- **Enviromental factors:**
- **Inhalation of particles 5-10μm deposits in large airways, under 5 μm in lower airways**
- **Tabbaco smoke - 4000 gaseous (92%) and solid materials (8%), 64 cancerogenes**
- **Professional dust and chemicals - cadmium, rock-coal dust**
- **General air pollution and home air pollution (cooking, coal…)**
- **Infection – severe, repeated respiratory infection, HIV poz.,**
- **Nutrition without vegetables, fishes, vitamines ..**

Risk factors of exacerbation

- bacterie- *H. influenzae, S.pneumoniae,M.catarhalis, CH.pneumoniae, M. pneumoniae* –worsening of dyspnoe, purulent sputum, more sputum, fever, leucocytosis, FW, changes on X ray, colonization in 40% pts with CHOPN.
- viruses – rhinoviry, coronaviry, influenza…
- Polution of inhaled air – smog, autumn, winter
- Disruption of therapy of stable COPD !!
- infection vs noninfection reasons for exacerbation is 1:1
- Enhancement of inflammation - in sputum more neutrophils, T lymphocytes, macrophages, Eo, inflammatory interleukins IL 6 a IL 8, more ECP a

Risk Factors for COPD

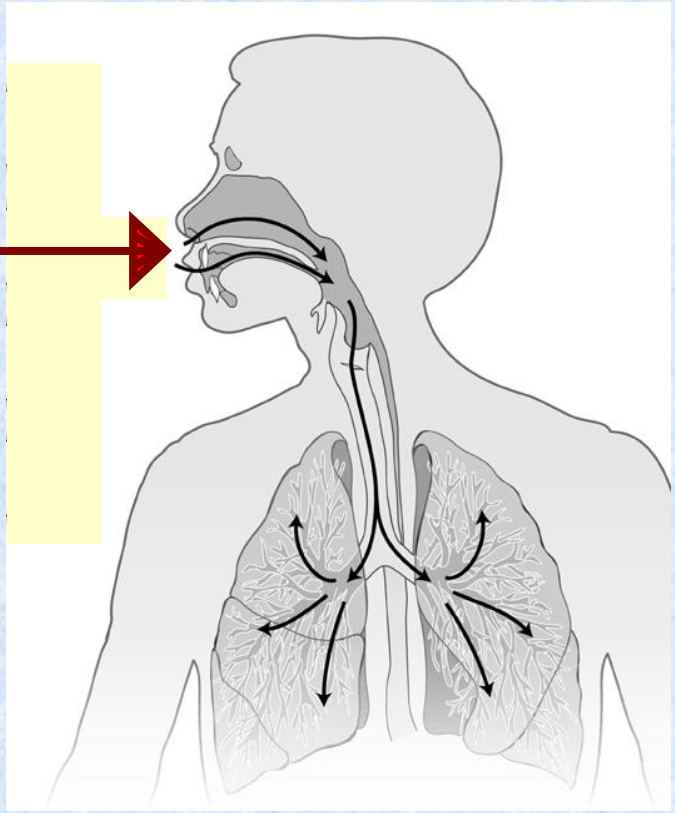
- Susceptibility genes
- Exposure to inhaled particles:
  - Tobacco smoke (active and passive)
  - Occupational dusts, organic and inorganic
  - Indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings
  - Outdoor air pollution

- Poor lung growth and development
- Oxidative stress
- Female gender
- Age
- Respiratory infections
- Low socioeconomic status
- Poor nutrition
- Comorbidities

From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.

Cumulative Exposure to Noxious Particles is the Key Risk Factor for COPD

- Cigarette smoke
- Occupational dust and chemicals
- Environmental tobacco smoke (ETS)
- Indoor and outdoor air pollution



From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.

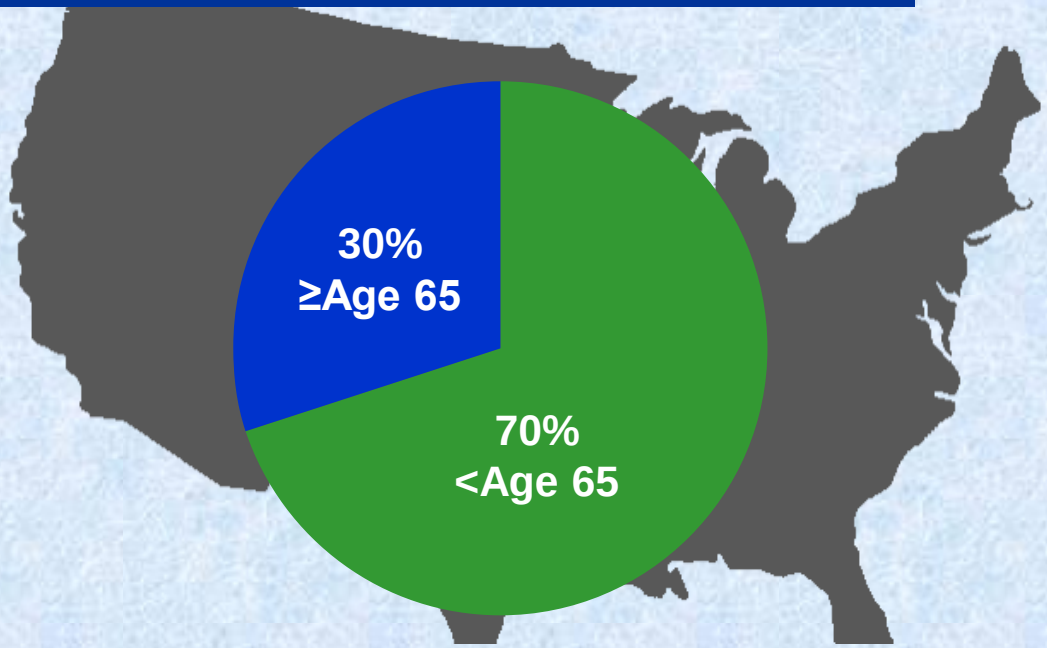
Who Should Be Screened for COPD?

- Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40:
  - Dyspnoea that is progressive, usually worse with exercise, and persistent
  - Chronic cough (may be intermittent and unproductive)
  - Chronic sputum
  - History of tobacco smoke exposure
  - Exposure to occupational dusts and chemicals
  - Risk factors
  - Exposure to smoke from home cooking and heating fuels

From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.

Underdiagnosis of COPD in the United States

- Over 12.7 million people in the United States have been diagnosed with COPD[1]
- Data from NHANES III indicate that approximately 24 million United States adults have evidence of impaired lung function indicative of COPD[2,3]
- Most (70%) of patients with undiagnosed COPD are <65 years of age



Percent with Undiagnosed COPD

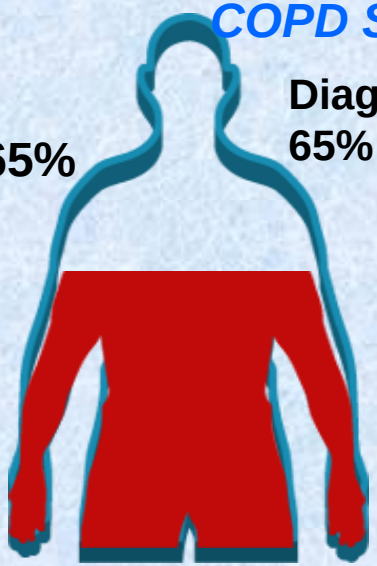
1. Pleis JR, et al. Vital Health Stat. 2006;132: 1-153.
2. ManninoDM, et al. *MMWR Surveill Summ*. 2002;51:1-16.
3. Mannino DM, et al. *Proc Am Thorac Soc.* 2007;4:502-306.

COPD Misdiagnosis Is Common in Women

Hypothetical Male Patient With COPD Symptoms

Diagnosed as COPD by 65% of physicians

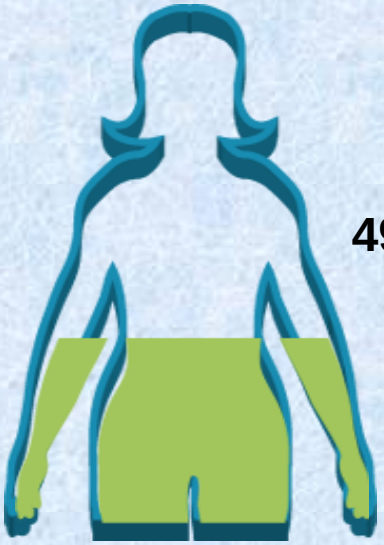
65%



Hypothetical Female Patient With COPD Symptoms

Diagnosed as COPD by 49% of physicians

49%



COPD symptoms in women were most commonly misdiagnosed as asthma

Chapman KR, et al. *Chest.* 2001;119:1691-1695.

Diagnosis of COPD

SYMPTOMS

cough

sputum

shortness of breath

EXPOSURE TO RISK FACTORS

tobacco

occupation

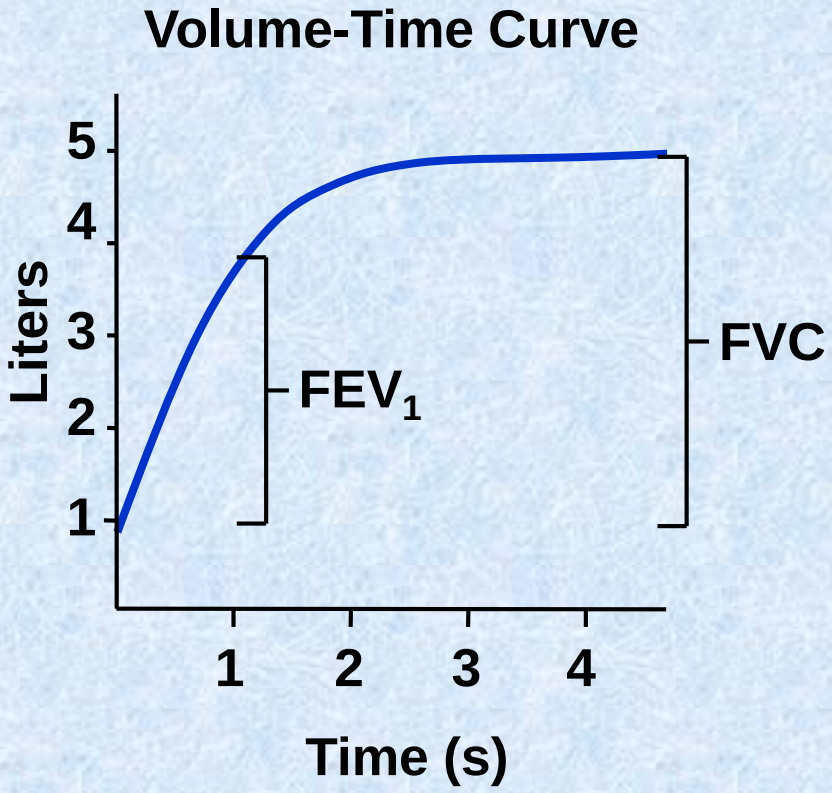
indoor/outdoor pollution

SPIROMETRY

From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.

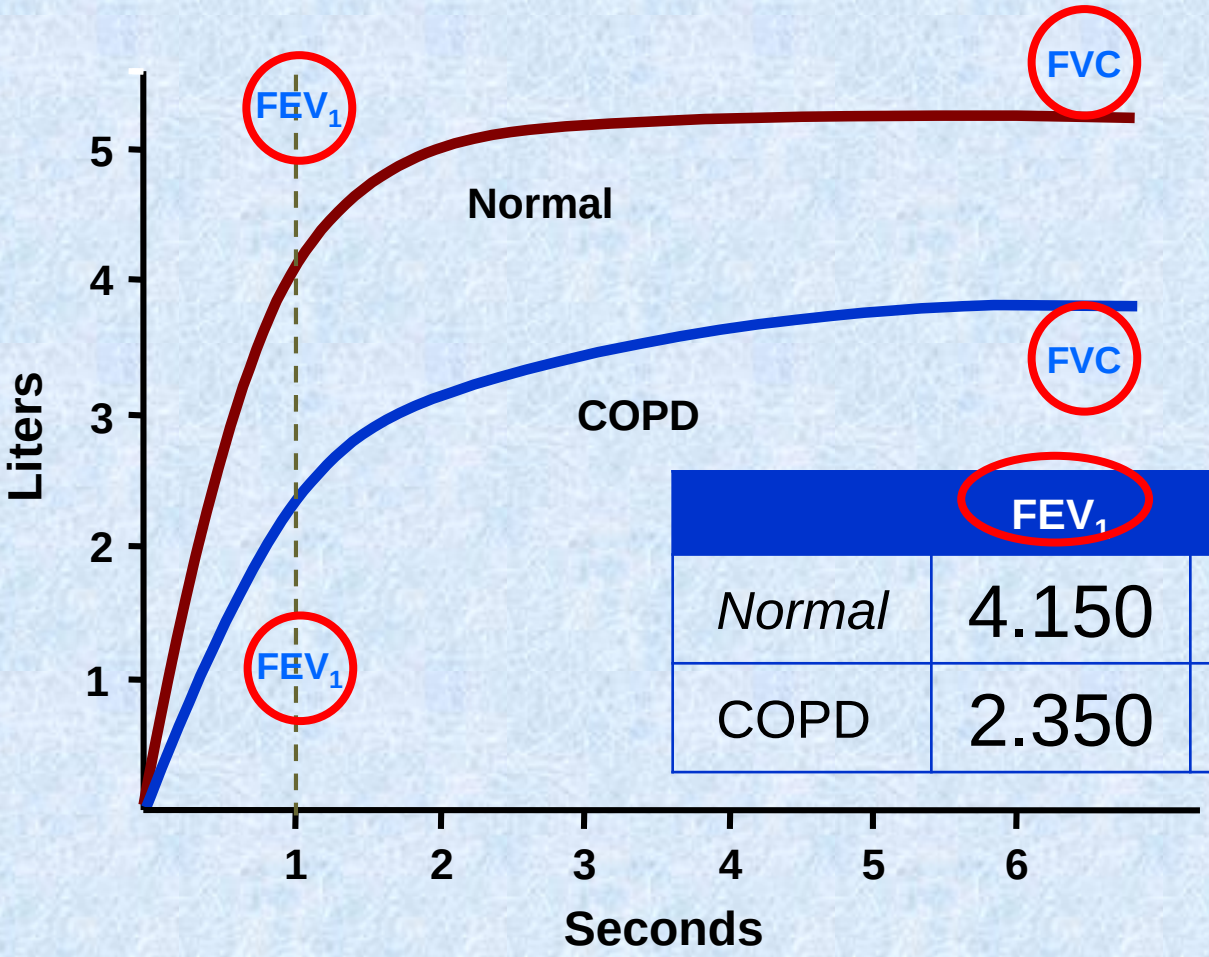
Measures of Pulmonary Function Commonly Used in COPD

- Forced vital capacity (FVC): total volume of air expired after a full inspiration. Patients with obstructive lung disease usually have a normal or only slightly decreased vital capacity
- Forced expiratory volume in 1 second (FEV_1): volume of air expired in the first second during maximal expiratory effort. The FEV_1 is reduced in COPD
- FEV_1/FVC: percentage of the vital capacity which is expired in the first second of maximal expiration. In healthy patients the FEV_1/FVC is usually around 70%. In patients with obstructive lung disease FEV_1/FVC decreases and can be as low as 20-30%



Pulmonary function tests. 2007. Available at: http://meded.ucsd.edu/isp/1998/asthma/html/spirexp.html

Spirometry for COPD Diagnosis and Classification of Severity



	FEV_1	FVC	FEV_1 / FVC
Normal	4.150	5.200	80%
COPD	2.350	3.900	60%

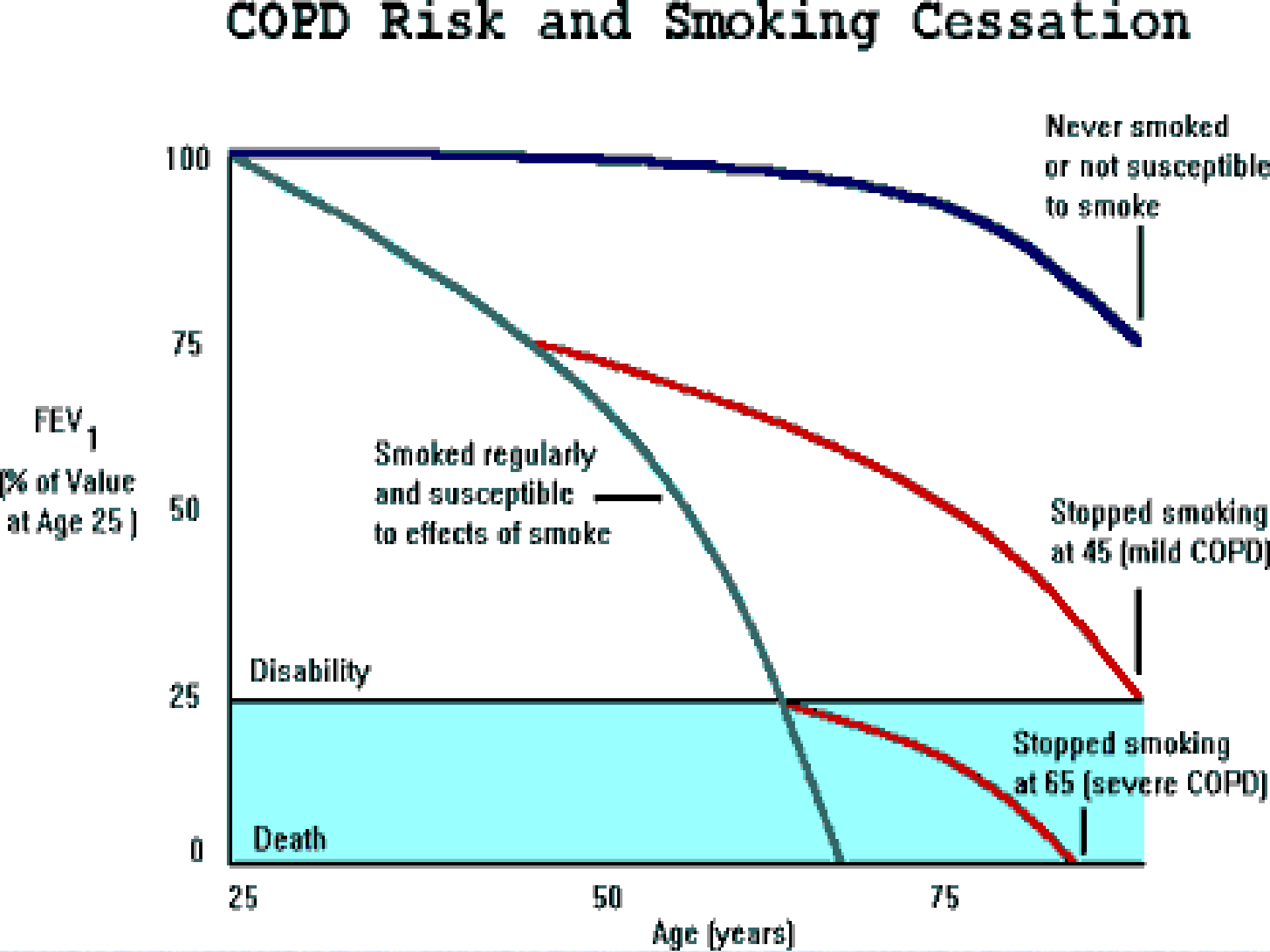
From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.

Spirometry

- Spirometry should be performed after the administration of an adequate dose of a short-acting inhaled bronchodilator to minimise variability (4 puffs of a short-acting bronchodilator such as salbutamol)
- A post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of airflow limitation that is not fully reversible
- Where possible, values should be compared to age-related normal values to avoid over-diagnosis of COPD in the elderly

From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.
Miller MR, et al. *Eur Respir J.* 2005;26:319-338.

COPD Risk and Smoking Cessation



Case finding of COPD

- risk population - 35-70 year
- spirometry - gold standard
- Mild or moderate COPD may be asymptomatic
- From 3158 pts without known dgn „airflow limitation“ were 2430 persons without symptoms, symptoms (cough, dyspnoe) were in 728 . By spirometry in 703 was COPD diagnosed in 18% -126 (I 39%, II 51% , III 9%, IV 1%)
- in persons without symptoms were airflow limitation in 4%
- Spirometry is recommended as screening methods for COPD *Buffels et al. CHEST 2004,125,1394-1399:*

Diagnosis

- *GOLD 2011:*

  Perform spirometry and consider COPD in an individual over age 40 with:

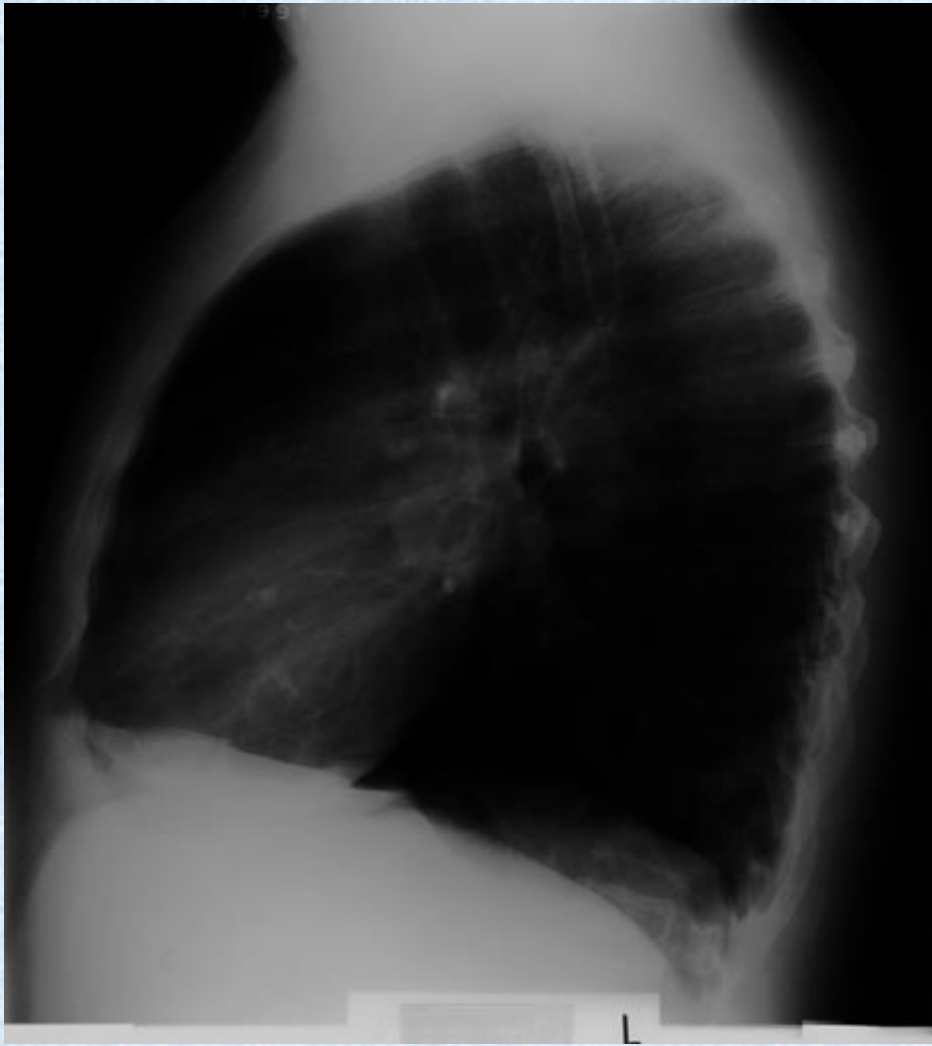
  - dyspnea (progressive, worse with exercise, present every day)
  - chronic cough (may be intermittent and unproductive)
  - chronic sputum production
  - history of exposure to risk factors - tobacco smoke, occupational dusts and chemicals, smoke from home cooking and heating fuel

Differential Diagnosis: COPD and Asthma

COPD	ASTHMA
• Chronic cough • Onset in mid-life • Symptoms slowly progressive • Long smoking history • Dyspnoea during exercise • Largely irreversible airflow limitation	• 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

From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.

Typical X-ray findings



Spirometry

- gold standard for diagnosis and assessment of COPD

- the most reproducible, standardized and objective way of measuring airflow limitation

- a post - bronchodilator $FEV_1/FVC < 70$ % confirms the presence of airflow limitation that is not fully reversible

GOLD 2006

Preventable disease

- reduction of exposure to tobacco smoke including passive smoking
- nicotin replacement therapy, antidepressants bupropion and nortryptiline and varenicline

  (nicotinic acetylcholine receptor agonist) increases long term quit rates
- 3 minutes intervention to quit smoking bring 5-10% cessation rate
- no exposition to occupational dusts and chemicals
- reduction of indoor and outdoor pollutants
- influenza vaccines in all COPD pts, pneumococcal vaccine in pts older than 65 or with FEV1< 40 %

COPD and Comorbidities

- COPD patients are at increased risk for:
  - Myocardial infarction, angina
  - Osteoporosis
  - Respiratory infection
  - Depression
  - Diabetes
  - Lung cancer
- COPD has significant extrapulmonary (systemic) effects including:
  - Weight loss
  - Nutritional abnormalities
  - Skeletal muscle dysfunction

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GOLD Goals for COPD Treatment

- Disease prevention is the ultimate goal of COPD treatment
- Once COPD has been diagnosed, effective management should be aimed at the following goals:
  - Relieve symptoms
  - Prevent disease progression
  - Improve exercise tolerance
  - Improve health status
  - Prevent and treat complications
  - Prevent and treat exacerbations
  - Reduce mortality

From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.

COPD Management: Disease Management should now be focusing on 2 key areas, reducing symptoms and reducing risk

- Relieve Symptoms
- Improve exercise tolerance
- Improve Heath Status

} Reduce symptoms

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

} Reduce risk

In this report the term “Stadium” is now replaced by “Grade” and stated that the FEV1 is an unreliable marker of the severity of breathlessness, exercise limitation, and health status impairment.

COPD is treatable disease

Management of stable COPD

- health education
- pharmacotherapy decreases symptoms and/or complications
- bronchodilator are central – short and long acting $beta_2$ agonists, short and long acting anticholinergics, methylxantines
- long acting BD are more effective than SABA
- add inhaled corticosteroids to BD therapy if $FEV_1 < 50\%$ or if there are frequent exacerbation (3 in 3 years) *(GOLD 2006)*
- exercise training program
- long term oxygen therapy increases survival – 15 hours a day

Figure 2. Spirometric Classification of COPD Severity Based on Post-Bronchodilator FEV_1

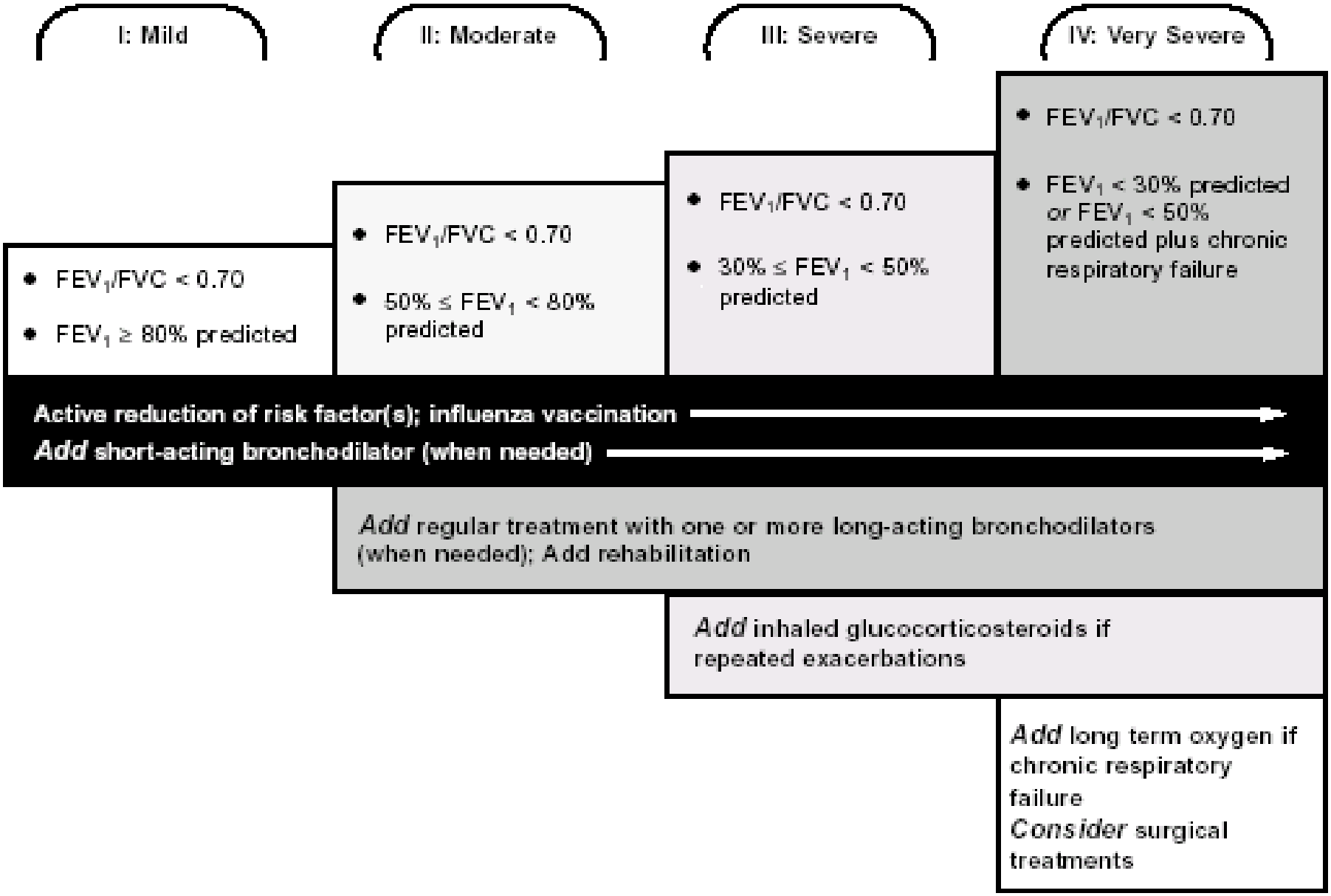
Stage I: Mild	$FEV_1/FVC < 0.70$ $FEV_1 \geq 80\%$ predicted
Stage II: Moderate	$FEV_1/FVC < 0.70$ $50\% \leq FEV_1 < 80\%$ predicted
Stage III: Severe	$FEV_1/FVC < 0.70$ $30\% \leq FEV_1 < 50\%$ predicted
Stage IV: Very Severe	$FEV_1/FVC < 0.70$ $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; respiratory failure: arterial partial pressure of oxygen (PaO_2) less than 8.0 kPa (60 mm Hg) with or without arterial partial pressure of CO_2 ($PaCO_2$) greater than 6.7 kPa (50 mm Hg) while breathing air at sea level.

No more stage 0 - „ at risk“ *(GOLD 2006)*

Figure 7. Therapy at Each Stage of COPD

Postbronchodilator FEV_1 is recommended for the diagnosis and assessment of severity of COPD.



News from GOLD
Grade A, B = I,II, C,D= III, IV

Spirometry stadium

IV III II I

Number of exacerbation

2+ less than 2

C Fix. combination LABA/ ICS or LAMA Alternatives: LABA and LAMA Not ICS alone	D Fix.comb.+ LAMA Alternatives: LABA and LAMA; ICS/LABA and PDE4 inhibitor, LAMA and PDE4 inhibitor Daxas + Fix. comb.
A SABA or SAMA 1 alternative:Saba + SAMA or LABA or LAMA	B LABA or LAMA Alternatives: LABA and LAMA

CAT <10
MRC 0,1

Cat >10
MRC 2+

Terminology

- RABA (R-rapid) :inhaled β_2 agonists with short acting effect but with quick onset of action (SABA+ formoterol)
- SABA, short acting beta agonists:
  fenoterol, salbutamol, terbutalin
- SKS systemic corticosteroids
- IKS inhaled corticosteroids
- LABA inhaled β_2 agonists with long acting effect - salmeterol, formoterol
- U-LABA (ultra LABA or only LABA) –indacaterol (24 hours effect)
- SAMA short acting muscarinc antagonist-ipratropium bromid (Atrovent)
- LAMA long acting muscarinic antagonists-tiotropium bromid (Spiriva), glykopironium bromid
- CysLT1 antileukotrien/antagonists of receptor for cysteinyl leukotriens (LTRA)
- PDE4 inhibitors of phosphodiesterase 4, roflumilast – (DAXAS)
- SAIT specific alergen imunotherapy

Pharmacotherapy of stable disease

- all bronchodilators increase exercise capacity
- long - acting anti-cholinergics reduce the rate of exacerbation and improve the effectiveness of rehabilitation

  tiotropium bromide- SPIRIVA, UPLIFT- improvement of QL, exacerbaction, mortality, but not prevent the decline of FEV1
- combination of SABA, anticholinergics and theophylline – additional improvement in lung function
- regular therapy with ICS not modifies decline of FEV_1 but decreases number of exacerbations and probably reduces all-cause mortality up to 29 % in observ. study
- combination of LABA and ICS is more effective than individual components- Seretide, Symbicort from stage III of COPD

Combination of salmeterol/fluticason proprionat

- double-blind study TORCH
- combination of salmeterol 50 microg plus fluticasone prop. 500 microg vs salmeterol alone, fluticasone alone or placebo.
- 3 years, 6112 pts with COPD moderate-severe
- 12,6% mortality in combination group, 15,2% in placebo, (P= 0,052, reduction of risk of death of 17,5%)
- reduction of exacerbation rate of 25%
- improvement of health status and spirometric values
- *B.Celli: Study brings a message of hope…it shows that pts with this combination live longer and with fewer exacerbation and better quality of life. We can add to oxygen therapy and smoking cessation another type of therapy that impacts mortality.* Salt Lake City, November 2006

COPD 2011

- In the Czech republic is cost for drugs „only“ 20% of the whole health care costs
- The curve of the drug cost is decreasing
- In the Czech republic is 12 visit/ year on averege at the physicians, 160/100 000 of hospitalisation.. decrease, most frequently are hospitalisated people in age 68 year, COPD hospitalisation 9/ 36 day hospital/ sanatorium
- Generic prescription is in EU only in Estonia
- Slowly registration of the new drugs .. More than 1 year (Austria 3 months)

COPD 2012

Clasification according

- 1. control of the present condition
- 2. reduction of the future risk
- Prescrition of Onbrez/indacaterol in the Czech republic is not allowed with Tiotropium
- Daxas not with Fix. Comb.

  not with if the exacerbation increases, but with Tiotropium and LABA

Stadium in the Czech rep: I…. 30%
II….. 40%
III….. 22%
IV…. 8%

CAT: COPD assesment test 8 questions, evaluation between 0 (the best) and 5 (the worst), < 10 – COPD is under control

TCA: asthma control test: 5 questions BUT the 1 is the worst and 5 is the best

25 point full control

COPD Treatment: The treatment recommendations are linked to the 4 new categories A, B, C and D:

A = Pts Characteristic: low risk, less symptoms:
spirometric classification: 1-2 **(previously mild-moderate)**, few symptoms (mMRC 0-1; CAT: <10), exacerbation per year **(≤1)**
FIRST CHOICE of Therapy: SABA or SAMA prn; Alternatives: SABA and SAMA, LABA or LAMA

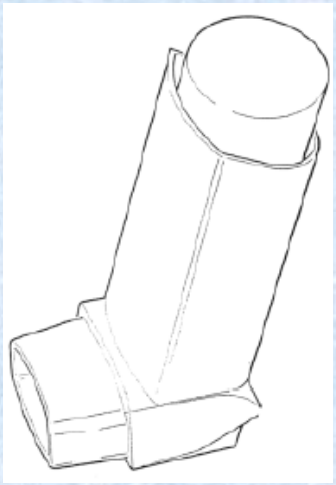
B = Characteristic: low risk, more symptoms:
spirometric classification: 1-2 **(previously mild-moderate),** more symptoms (mMRC >2+; CAT: >10), exacerbation per year **(≤1)**
FIRST CHOICE of Therapy: LABA or LAMA; Alternatives: LABA and LAMA

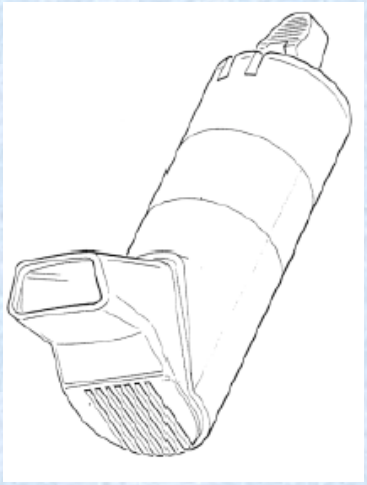
C = Characteristic: high risk, less symptoms
spirometric classification: 3-4 **(previously severe-very severe),** few symptoms (mMRC 0-1; CAT: <10), exacerbation per year **(2+)**
FIRST CHOICE of Therapy: LABA/ICS or LAMA; Alternatives: LABA and LAMA

D = Characteristic: high risk, high symptoms
spirometric classification: 3-4 **(previously severe-very severe),** more symptoms (mMRC >2; CAT: >10), exacerbation per year **(2+)**
FIRST CHOICE of Therapy: LABA/ICS and LAMA; Alternatives: LABA and LAMA; ICS/LABA and PDE4 inhibitor, LAMA and PDE4 inhibitor

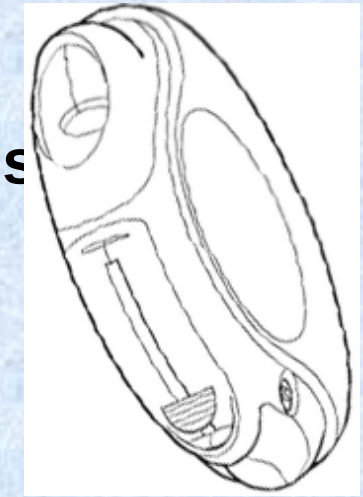
CHOPN- pharmacologic therapy

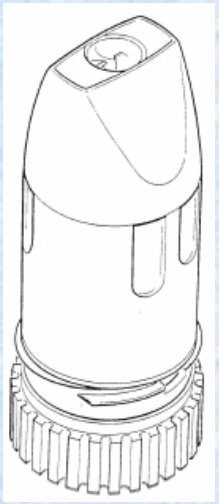
1. Aerosole dosier 2. by breath activated aerosol. dosiers





3. Inhalators of powder forms





4. nebulized aerosols

Tiotropium bromid- Spiriva

Salmeterol/fluticason- Seretide

Formoterol/budesonid-Symbicort

Other therapy of stable disease

- influenza vaccines once each year reduces severe illness and death by 50 %
- pneumococcal vaccine reduces incidence of CAP
- $alfa_1$antitrypsin augmentation therapy – young pts with severe hereditary deficiency of A1AT
- antibiotics - no benefit from winter chemoprophylaxis, are recommended during infectious exacerbation
- mucolytic agent - small benefit in pts with viscous sputum *(GOLD 2006)*
- rehabilitation improves exercise tolerance, diminish dyspnea and hospital admissions (39,8 %) *(B.Celli,2005)*

Surgical treatment

- bullectomy – in carefully selected pts may improve dyspnea and lung function
- LVRS - benefit in survival rate in pts with upper lobe emphysema and low exercise capacity treated by LVRS after 4,3 years in comparison with medical therapy, 54% vs 39%!
- lung transplantation - FEV_1 < 35%, in resp. insuf. or pulmonary hypertension
- *GOLD 2006*

COPD Exacerbation

Exacerbaction of COPD

- are exacerbations preventable ??
- the cause : 2/3 infection, 1/3 unknown,
- smoking cessation, vaccines, imunoregulator, LABA, tiotropium, ICS, combination of LABA + ICS (30%) pulmonary rehabilitation, mucolytic agent – may reduce severity and frequency of exacerbation*(B.Celli, Prim Care Resp J., 2006*
- are exacerbation treatable ??
- home management – increase bronchodilator, ATB, corticosteroids, non-invasive ventilation
- hospital management oxygen + non-invasive/invasive ventilation + other therapy *GOLD 2006*

COPD Exacerbation

Definition Elements

- Worsening dyspnea
- Increased sputum purulence
- Increase in sputum volume

Severity

- Severe - all 3 elements
- Moderate - 2 elements
- Mild - 1 element plus:
  - URI in past 5 days
  - Fever without apparent cause
  - Increased wheezing or cough
  - Increase (+20%) of respiratory rate or heart rate

Modified from Anthonisen et al. Ann Int Med 106:196, 1987

Management of Exacerbations

Home Management

- Bronchodilator therapy
- Glucocorticosteroids
- Antibiotics

Hospital Management

- Bronchodilatory therapy
- Antibiotics
- Oral or intravenous glucocorticosteroids
- Noninvasive mechanical ventilation
- Closely monitor patient's overall condition, including comorbidities

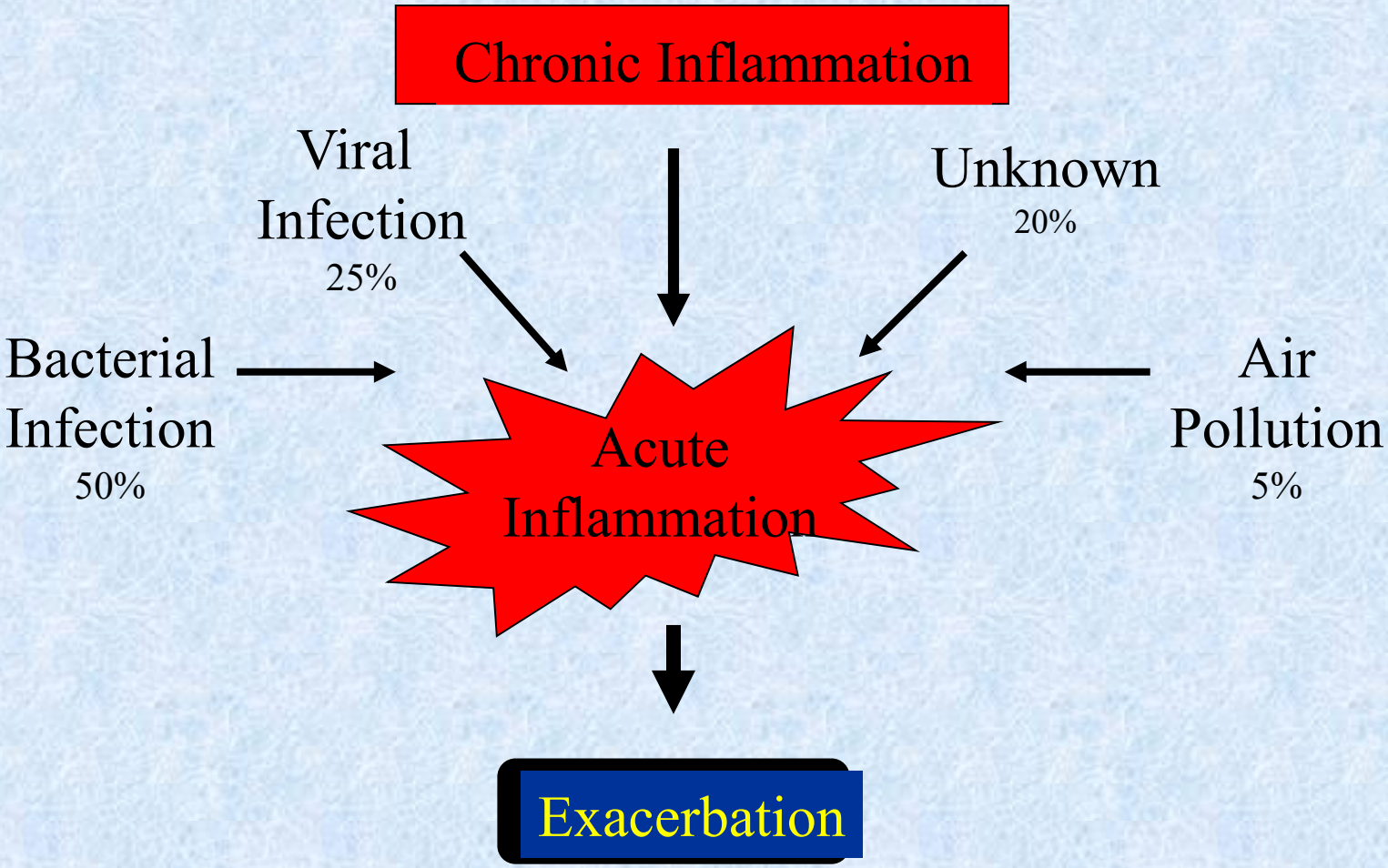
From the *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease*, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2008. Available from: http://www.goldcopd.org.

Assessment of severity of exacerbation

- Peak flow <100 L/min or FEV_1 <1.0 L indicates severe exacerbation
- ABG
- CXR
- EKG
- D-dimer, spiral CT
- Sputum culture

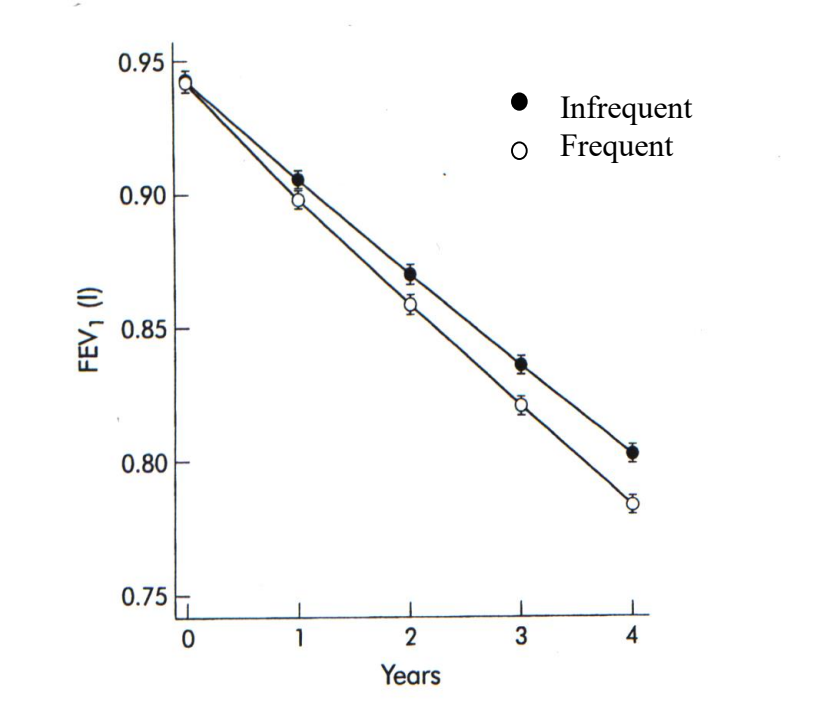
COPD Exacerbation

Pathophysiology - Current Hypothesis



COPD Exacerbation

Effects on Lung Function Decline



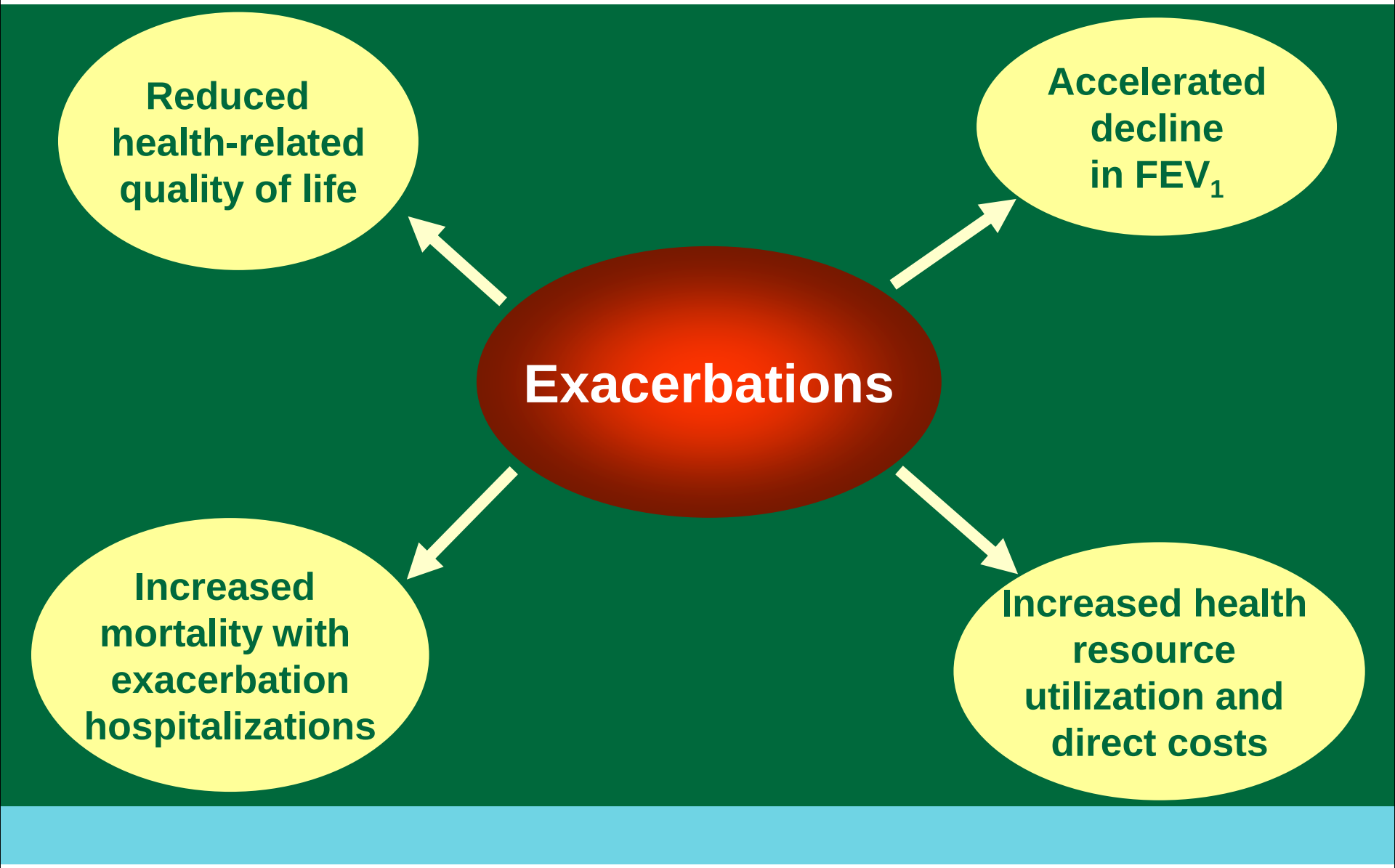
- **109 pts (mean FEV1 = 1.0 L over 4 years**
- **Frequent exacerbators:**
  - faster decline in PEFR and FEV1
  - more chronic symptoms (dyspnea, wheeze)
  - no differences in PaO2 or PaCO2

Conclusion:

Frequent exacerbations accelerate decline in lung function

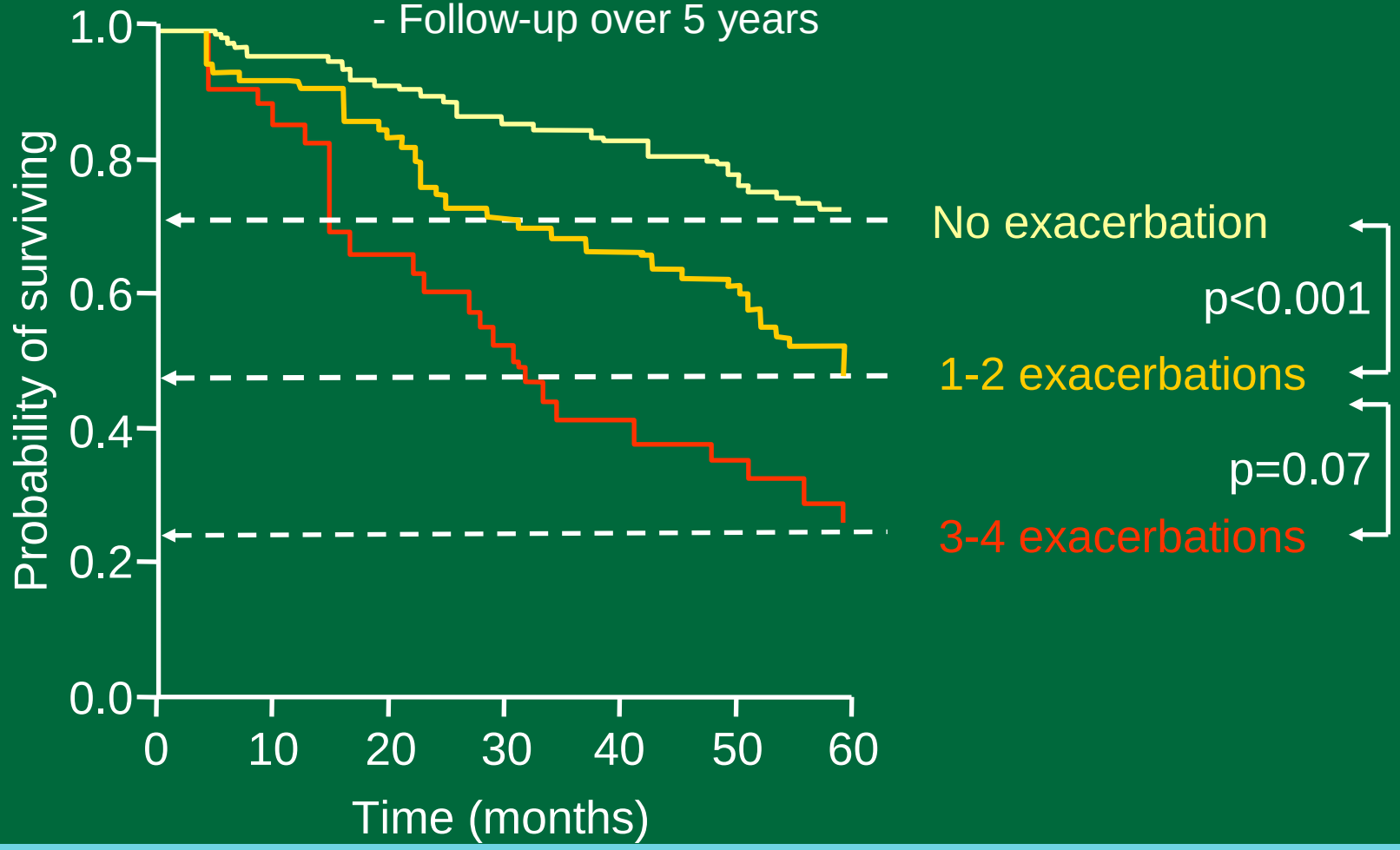
Donaldson et al. Thorax 57:847, 2002

The Clinical Course of COPD: Consequences of Exacerbations



Repeated Exacerbations Reduce the Probability of Survival

- Prospective study, Cohort of 304 males
- Exacerbations requiring hospital treatment during the year
- Follow-up over 5 years



Soler-Cataluña JJ et al. Thorax 2005;64:925-31

Therapy of COPD Exacerbation

Guidelines

Variable	***ACCP-ACP***	***GOLD***
Steroids	Yes, for up to two weeks	Yes, oral or IV for 10-14 days
Oxygen	Yes	Yes - target PaO2 60 torr or Sat of 90% with ABG check
Chest PT	No	Maybe - for atelectasis or sputum control
Mucokinetics	No	Not discussed

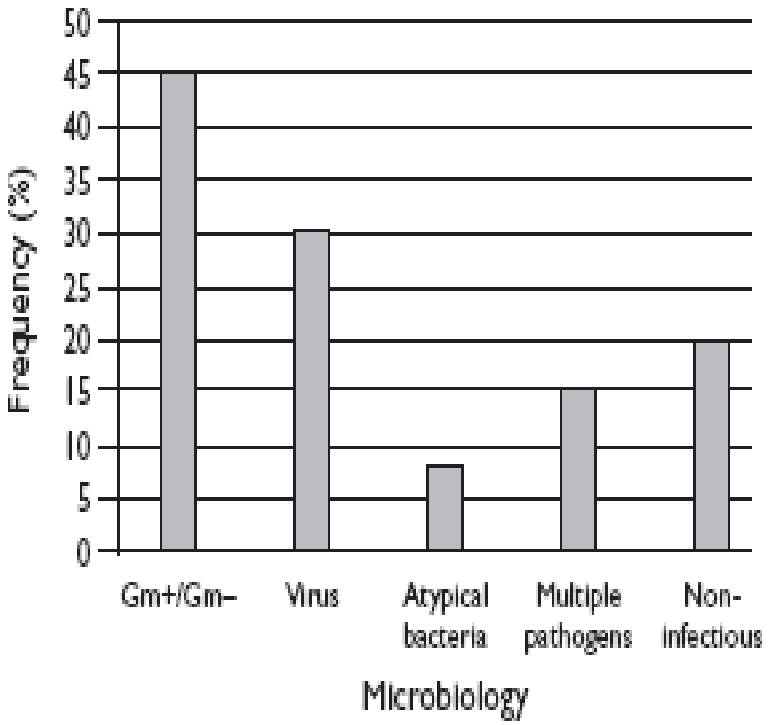
Ann Int Med 134:595, 2001

http:/www.goldcopd.com

Manage Exacerbations: Key Points

- Inhaled bronchodilators ($Beta_2$-agonists and/or anticholinergics), and systemic, preferably oral, glucocortico-steroids are effective for the treatment of COPD exacerbations (Evidence A).
- 80% of AECB are infectious. Environmental factors and medication nonadherence are 20%.

Figure 3. Etiology of Acute Exacerbation of Chronic Bronchitis



Role of Infection in COPD Exacerbation

- Up to 60% of exacerbations are due to respiratory infections.
- Bacterial Infections: H. infleunza, M. catarrhalis, S. pneumoniae.

Acquisition of new strains vs. colonization

- Viral Infections: Influenza, Parainfluenza, Coronavirus, Rhinovirus.

Coinfection is common

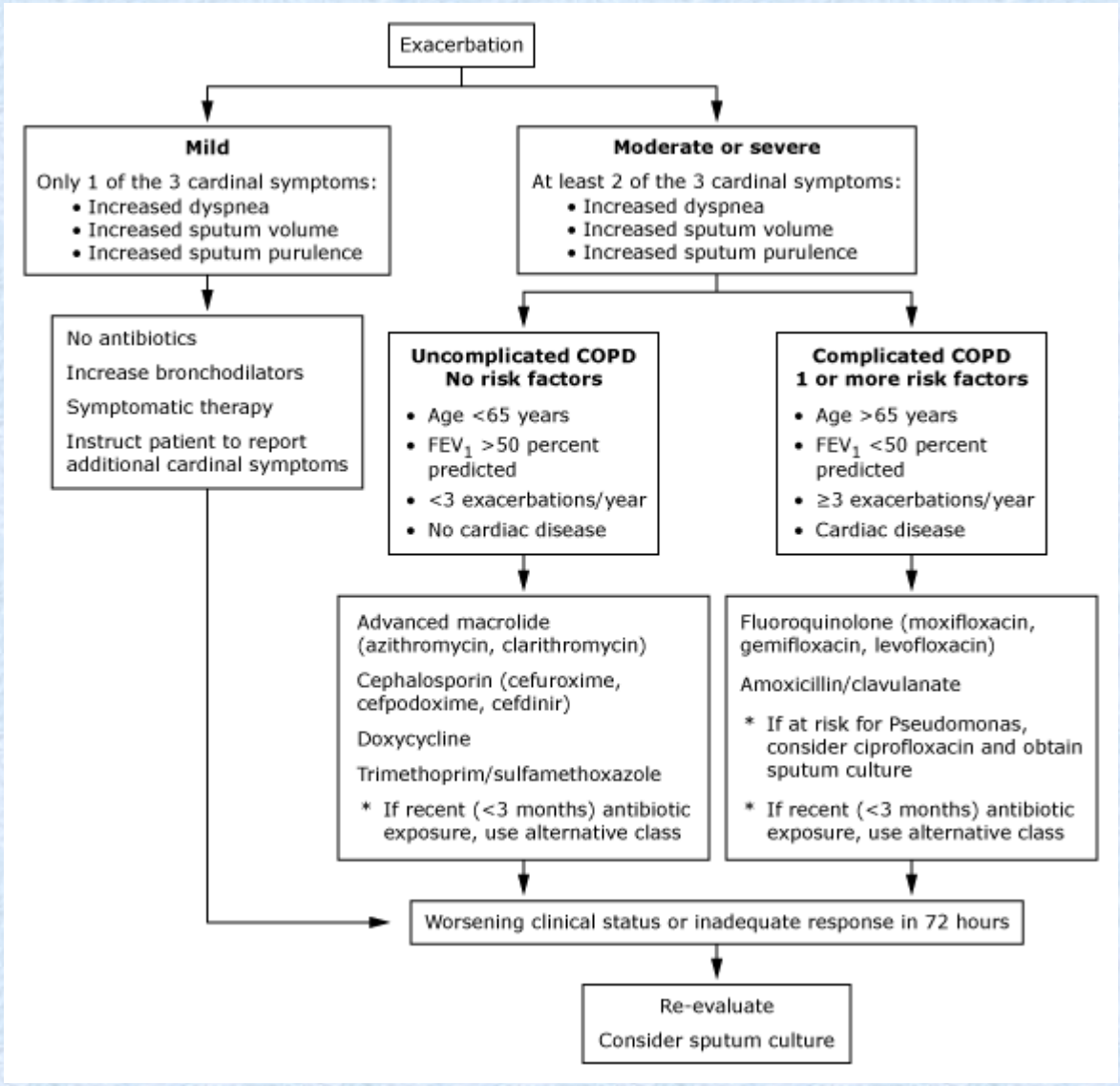
Antibiotic Therapy for COPD Exacerbation

- Placebo-controlled studies demonstrated that antibiotics **improve clinical outcome** in many patients with COPD exacerbation.
- A recent meta-analysis demonstrated **improved Survival** in moderate -to-severe COPD treated with antibiotics compared to placebo (Puhan *et al.* 2007)

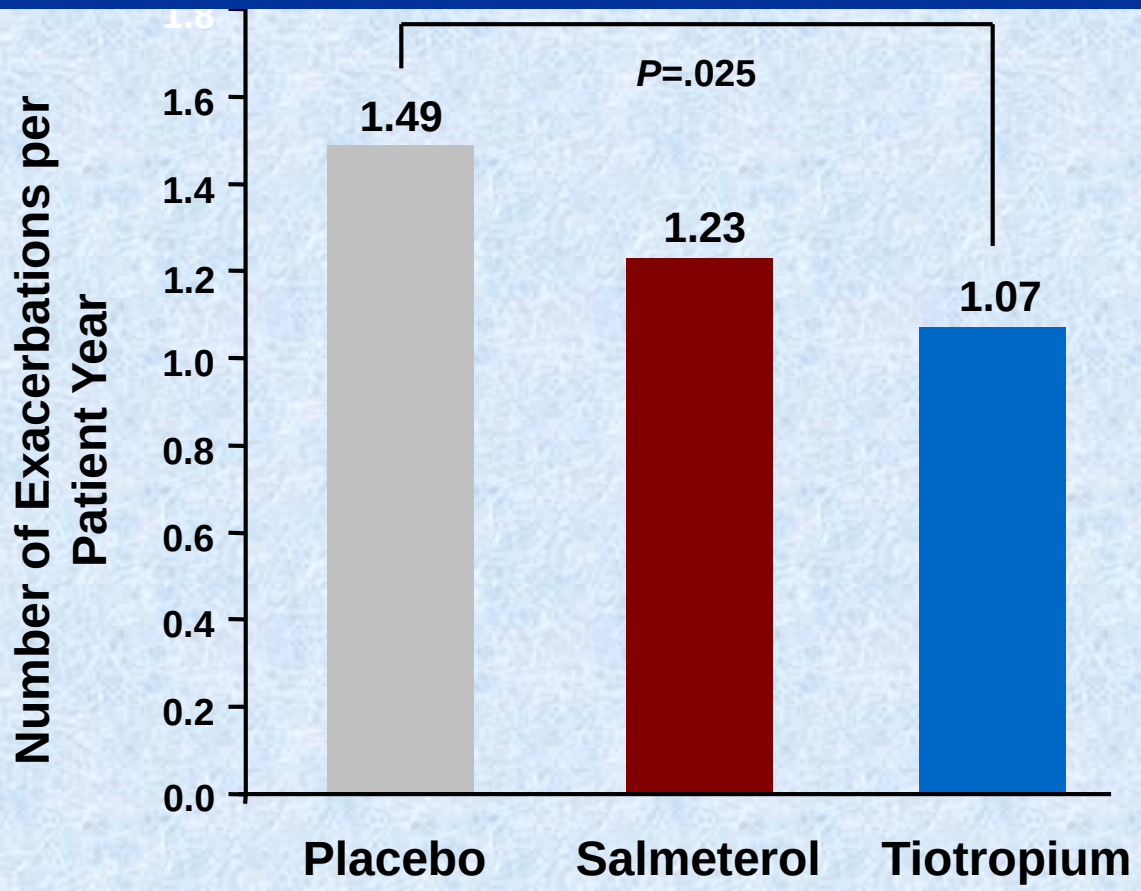
Indications for Antibiotics in COPD Exacerbation

- Increased sputum purulence with increased SOB of sputum volume.
- Need for hospitalization.
- Need for mechanical ventilation.
- Risk factors for poor outcome:
  - Comorbidities
  - Severe underlying COPD (FEV-1<50%)
  - Frequent exacerbations (> 3/year)
  - Recent antibiotic use (within the past 3 months)

Antibiotic Treatment for Exacerbation of COPD



Long-acting Bronchodilators Reduce Exacerbations



Brusasco V, et al. *Thorax*, 2003, 58, 399-404; reproduced with permission from the BMJ Publishing Group.

NIPPV

Manage Exacerbations:NIV

- Noninvasive intermittent positive pressure ventilation (NIPPV) in acute exacerbations improves blood gases and pH, reduces in-hospital mortality, decreases the need for invasive mechanical ventilation and intubation, and decreases the length of hospital stay (Evidence A).

NIPPV

- Selection criteria:
  - Moderate to severe dyspnea with use of accessory muscles and paradoxical abdominal motion
  - Moderate to severe acidosis and hypercapnia
  - Respiratory frequency >25/min

Aims of NPPV

- Improve gas exchange (decrease CO_2 and increase O_2)
- Rest or improve respiratory muscles
- Stabilize the upper airway
- Improve quality of life/exercise tolerance
- Prevent cardiovascular consequences of nocturnal hypercapnia and hypoxia

Assisted ventilation

1. Noninvasive positive pressure ventilation (NPPV) should be offered to patients with exacerbations when, after optimal medical therapy and oxygenation, respiratory acidosis (pH <7.36) and or excessive breathlessness persist. All patients considered for mechanical ventilation should have arterial blood gases measured.

2. If pH <7.30, NPPV should be delivered under controlled environments such as intermediate intensive care units (ICUs) and/or high-dependency units.

3. If pH <7.25, NPPV should be administered in the ICU and intubation should be readily available.

4. The combination of some continuous positive airway pressure (CPAP) (e.g. 4–8 cmH_2O) and pressure support ventilation (PSV) (*e.g.* 10–15 cmH_2O) provides the most effective mode of NPPV.

NIPPV

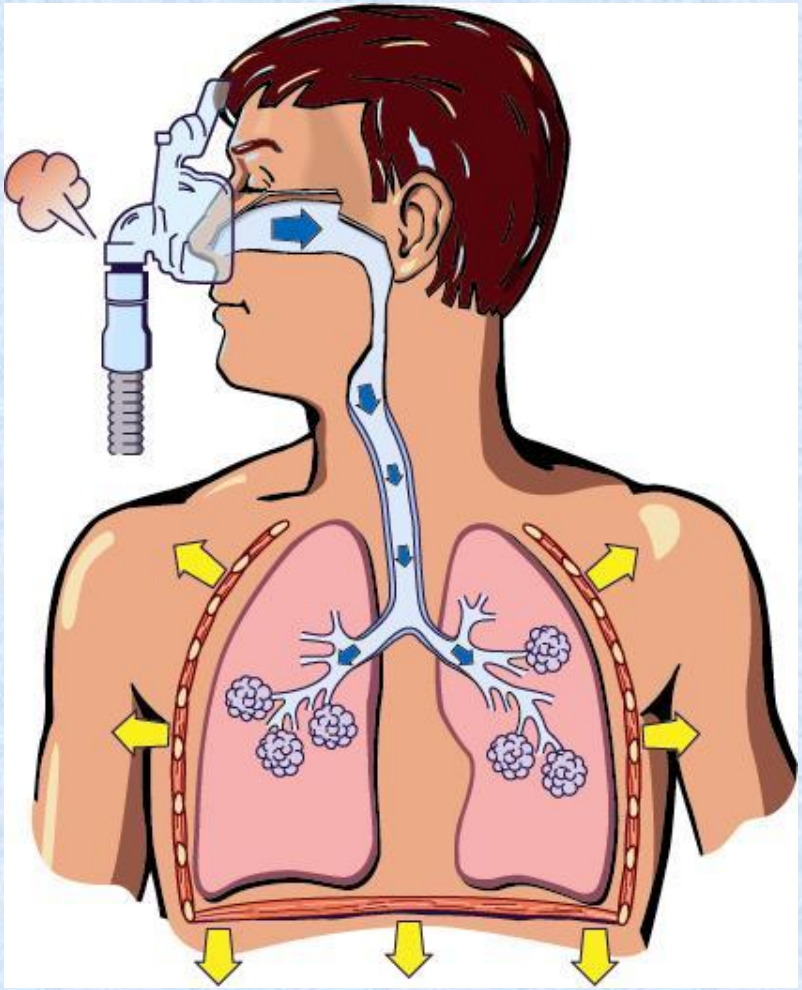
- Exclusion criteria:
  - Respiratory arrest
  - Cardiovascular instability
  - Somnolence, impaired mental status, uncooperative patient
  - High aspiration risk
  - Viscous or copious secretions
  - Recent facial or gastroesophageal surgery
  - Craniofacial trauma
  - Extreme obesity

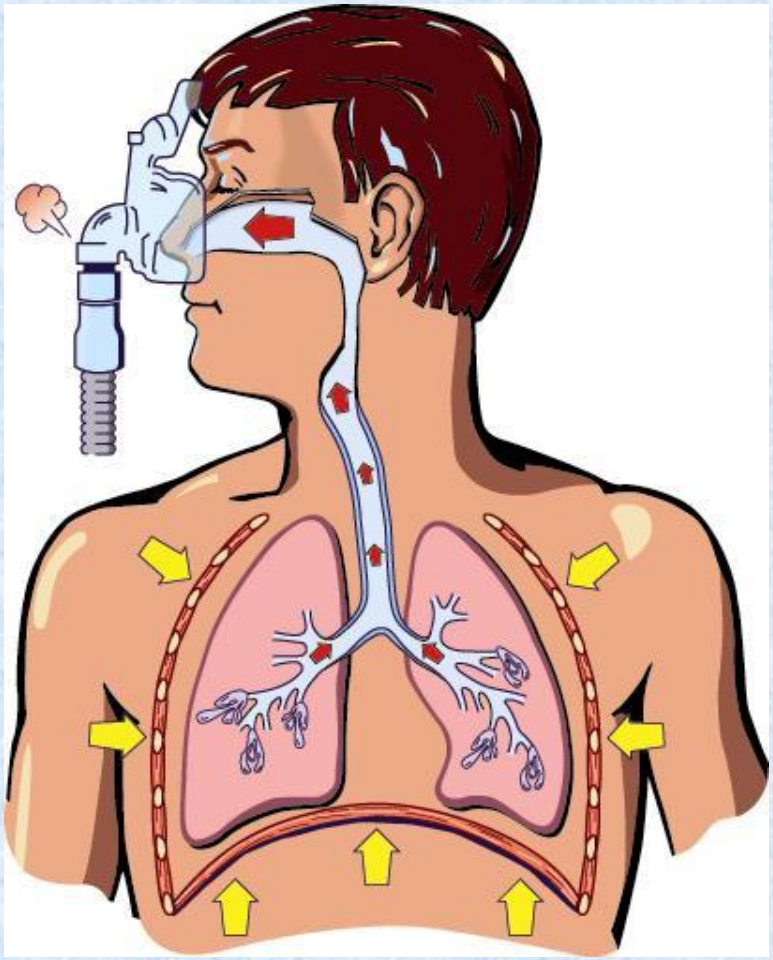
Assisted ventilation

- Patients meeting exclusion criteria should be considered for immediate intubation and ICU admission.

.

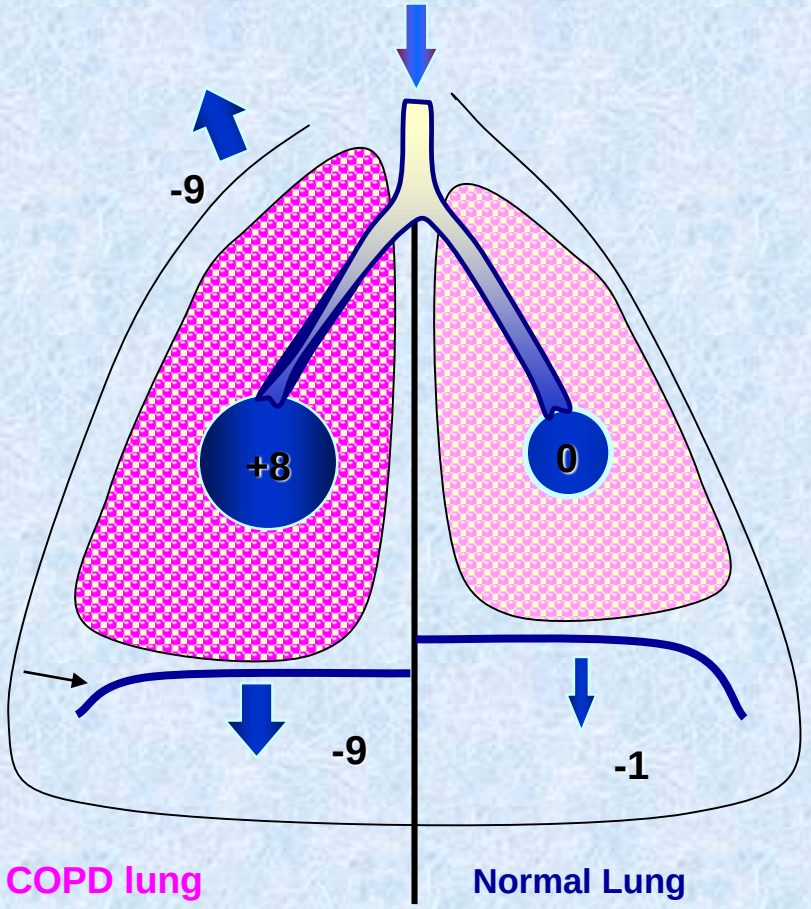
NIPPV





Auto-PEEP (Intrinsic PEEP)

- In patients with COPD
  - Rate of lung emptying becomes impaired because of increased expiratory resistance and expiratory airflow limitation
  - Therefore, a ***positive pressure*** is present at end expiration (PEEP)
- Patient must overcome a positive pressure before inspiration can begin
  - Inspiration requires negative pressure



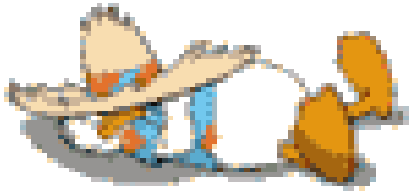
Example : if PEEPi = +8, the patient effort must be > -8 to create air flow

Indications for ICU Admission in COPD Exacerbation

1. Severe dyspnea that responds inadequately to initial emergency therapy
2. Confusion, lethargy, or respiratory muscle fatigue (the last characterized by paradoxical diaphragmatic motion)
3. Persistent or worsening hypoxemia despite supplemental oxygen or severe/worsening respiratory acidosis (pH < 7.30)
4. Assisted mechanical ventilation is required, whether by means of endotracheal tube or noninvasive technique

Conclusions

- COPD is preventable
- COPD is treatable
- good message for physicians, for patients, for general public and health authorities – to tell them !!
- thanks new knowledge we have more effective tools for management of COPD: vaccines, rehabilitation programmes, combination of LABA and ICS, LAMA, oxygen therapy, smoking cessation, non-invasive ventilation, LVRS, lung transplantation
- more spirometry in people with suspected COPD
- we are still waiting for medication preventing the decline of FEV_1
- the nihilistic attitude to COPD is unjustified (*B.Celli 2005*)



Thank You for Attention!!!!