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Joint session EFIM-ERS

The Role of Comorbidities in COPD

Sergio Harari

Dept. of Medical Sciences San Giuseppe Hospital MultiMedica Milan
Dept. of Clinical Sciences and Community Health, University of Milan, Italy

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COPD and comorbidities

- **COPD as the pulmonary component of multimorbidity**
- **Complexity of COPD exacerbations**
- **Treat the patient with COPD or any chronic disease not just COPD or the index chronic disease**

COPD and comorbidities

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Diagnosis of COPD

SYMPTOMS

shortness of breath
chronic cough
sputum

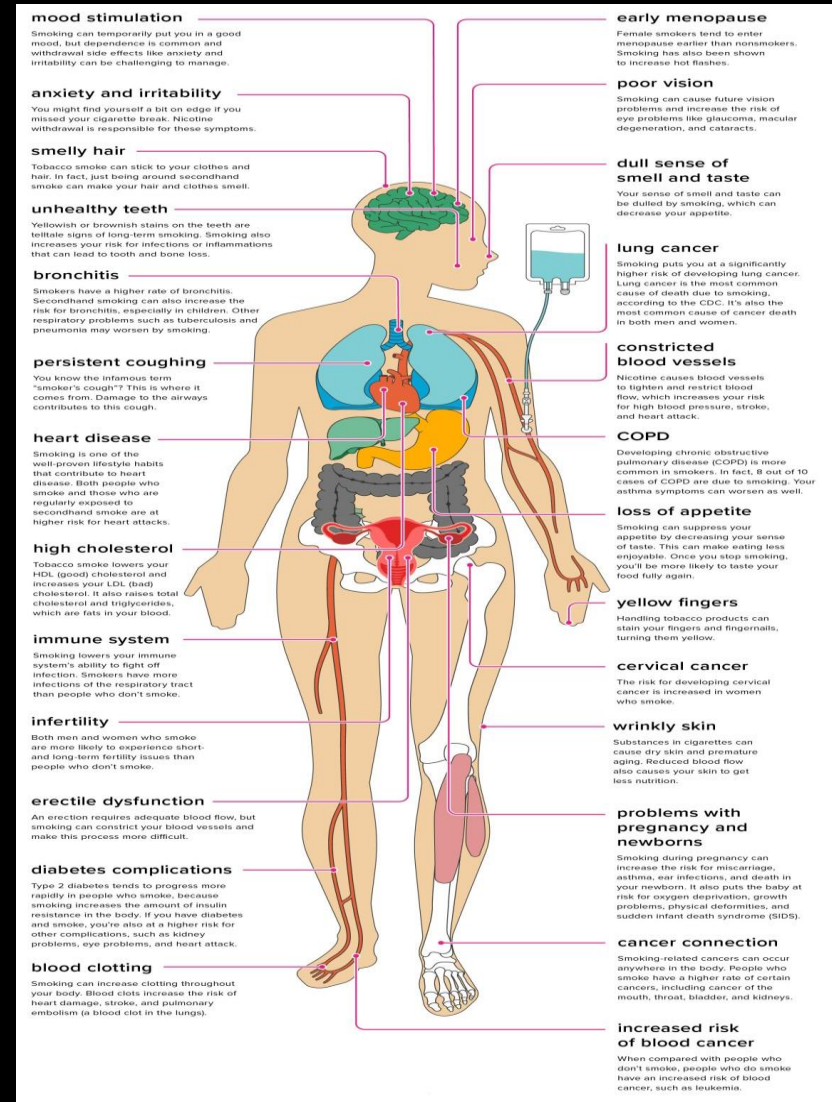
EXPOSURE TO RISK FACTORS

tobacco
occupation
indoor/outdoor pollution

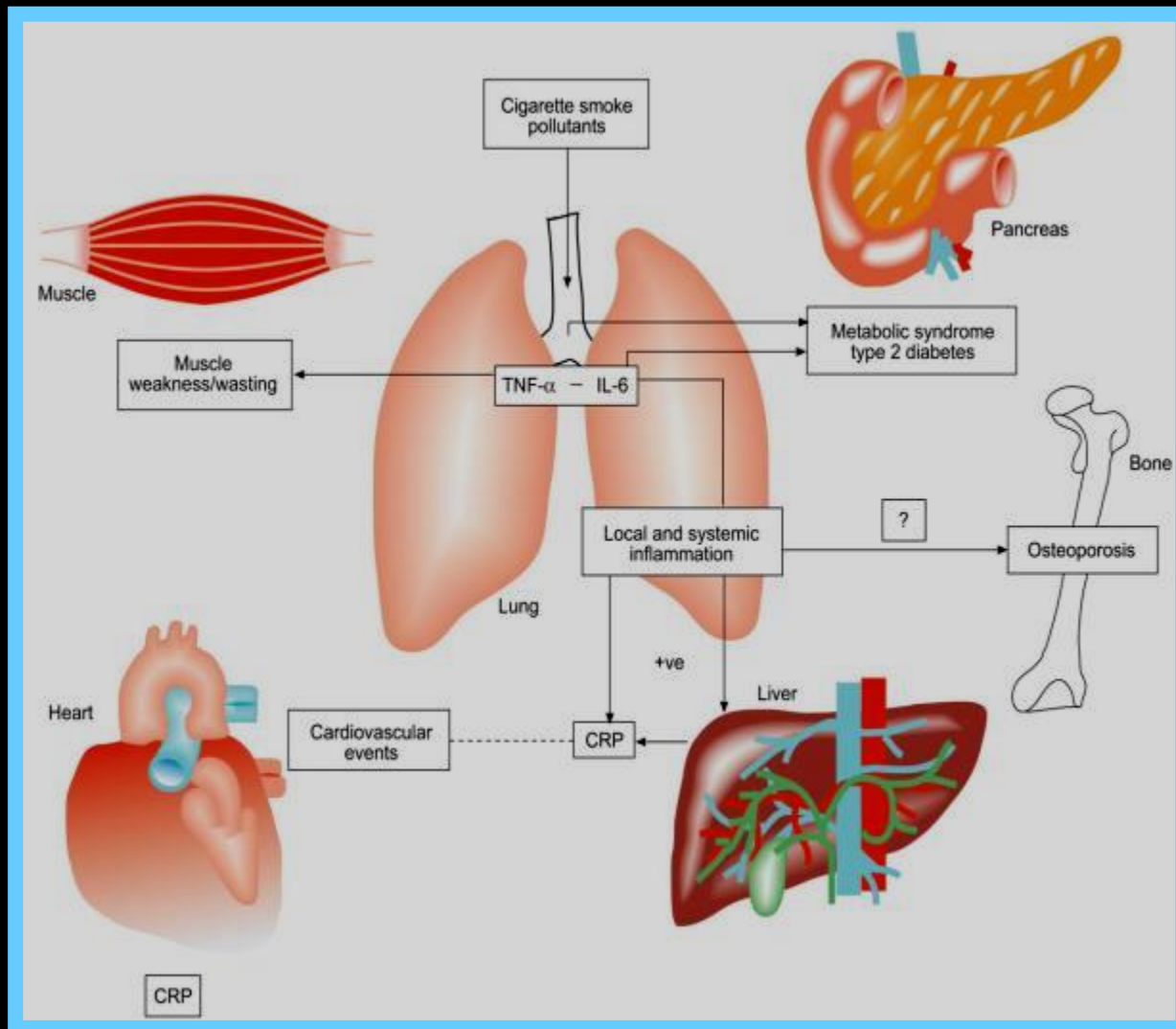
SPIROMETRY: Required to establish diagnosis

THE 10 MOST FREQUENT CHRONIC DISEASES INDUCED BY SMOKING

- Cardiovascular diseases
- Cerebrovascular Diseases
- Lung Cancer
- Chronic Respiratory Diseases (COPD)
- Metabolic diseases (diabetes)
- Rheumatic diseases
- Reproductive Effects in Women
- Premature, Low Birth-Weight Babies
- Blindness, age related macular degeneration
- Other types of cancer (eg Colon, Cervix, Liver, Stomach and Pancreatic Cancer)



COMPLEX CHRONIC CO-MORBIDITIES OF COPD



FROM SYSTEMIC EFFECTS OF COPD TO COPD AS PULMONARY COMPONENT OF MULTIMORBIDITY

BRN Reviews

REVIEW

From systemic effects of COPD to COPD as pulmonary component of multimorbidity

Lowie EGW Vanfleteren, MD, PhD^{1,2}, Sigrid AA Vikjord, MD³, Martin Ingvar, MD, PhD⁴ and Leonardo M Fabbri, MD, PhD⁵

¹COPD Center, Department of Respiratory Medicine and Allergology, Sahlgrenska University Hospital, Gothenburg, Sweden; ²Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; ³HUNT Research Centre, Norwegian University of Technology and Science, NTNU, Levanger, Norway; ⁴Osler Center for Integrative Medicine, Karolinska Institutet Stockholm, Stockholm, Sweden; ⁵Section of Cardiorespiratory and Internal Medicine, Department of Medical Sciences, University of Ferrara, Ferrara, Italy

ABSTRACT

Chronic obstructive pulmonary disease (COPD) was originally defined as a chronic disease of the airways due to an abnormal inflammatory response to tobacco smoking. However, although primarily a pulmonary disease, the systemic consequences of COPD have been subject of intensive research for more than two decades. Extrapulmonary manifestations and/or comorbidities are invariably present in COPD and contribute significantly to morbidity and mortality. These observations warrant a strategy in which COPD should be seen as the pulmonary component of chronic multimorbidity that develops in a patient in response to a spectrum of risk factors. Specific multimorbidity combinations are associated with specific COPD phenotypes, suggesting that lung and other organ disease trajectories are entangled from an early disease state onwards. The management of the patient with multimorbid COPD should include an active search for the most impactful comorbidities and a patient-tailored multidisciplinary shared-decision treatment plan embedded in clinical pathways with supportive informatics. (BRN Rev. 2020;6(2):161-78)

Corresponding author: Lowie EGW Vanfleteren, lowie.vanflecteren@gu.se

Key words: Ageing. Chronic bronchitis. Chronic diseases. Emphysema. Senescence.

FROM SYSTEMIC EFFECTS OF COPD TO COPD AS PULMONARY COMPONENT OF MULTIMORBIDITY



ATHEROSCLEROSIS

CONGESTIVE HEART FAILURE
ISCHEMIC HEART DISEASES:
Angina Pectoris
Myocardial Infarction

CEREBROVASCULAR DISEASES:
Stroke
Transient Cerebral Ischemia

ANAEMIA

CHRONIC PULMONARY DISEASES:
Chronic Bronchitis
Asthma
Emphysema

THROMBOEMBOLIC
MANIFESTATIONS

SARCOPENIA
DISABILITY

OSTEOPOROSIS
ARTHROSIS

AUTOIMMUNE DISEASES:
Rheumatoid Arthritis

ANOREXIA

INSULINE RESISTANCE
TYPE 2 DIABETES

ALZHEIMER'S DISEASE
DEMENTIA

INFLAMM-AGEING

TNF- α RANTES MCP-1 IL-8 ICAM

IL-1 beta LTA TNF- α

IL-1 beta IL-6 IL-18 TNF- α

IL-1 IL-6 TNF- α

TNF- α IL-1 beta IL-6
IL-8 MCP-1

IL-6

IL-6 TNF- α

IL-6 TNF- α IL-1 beta

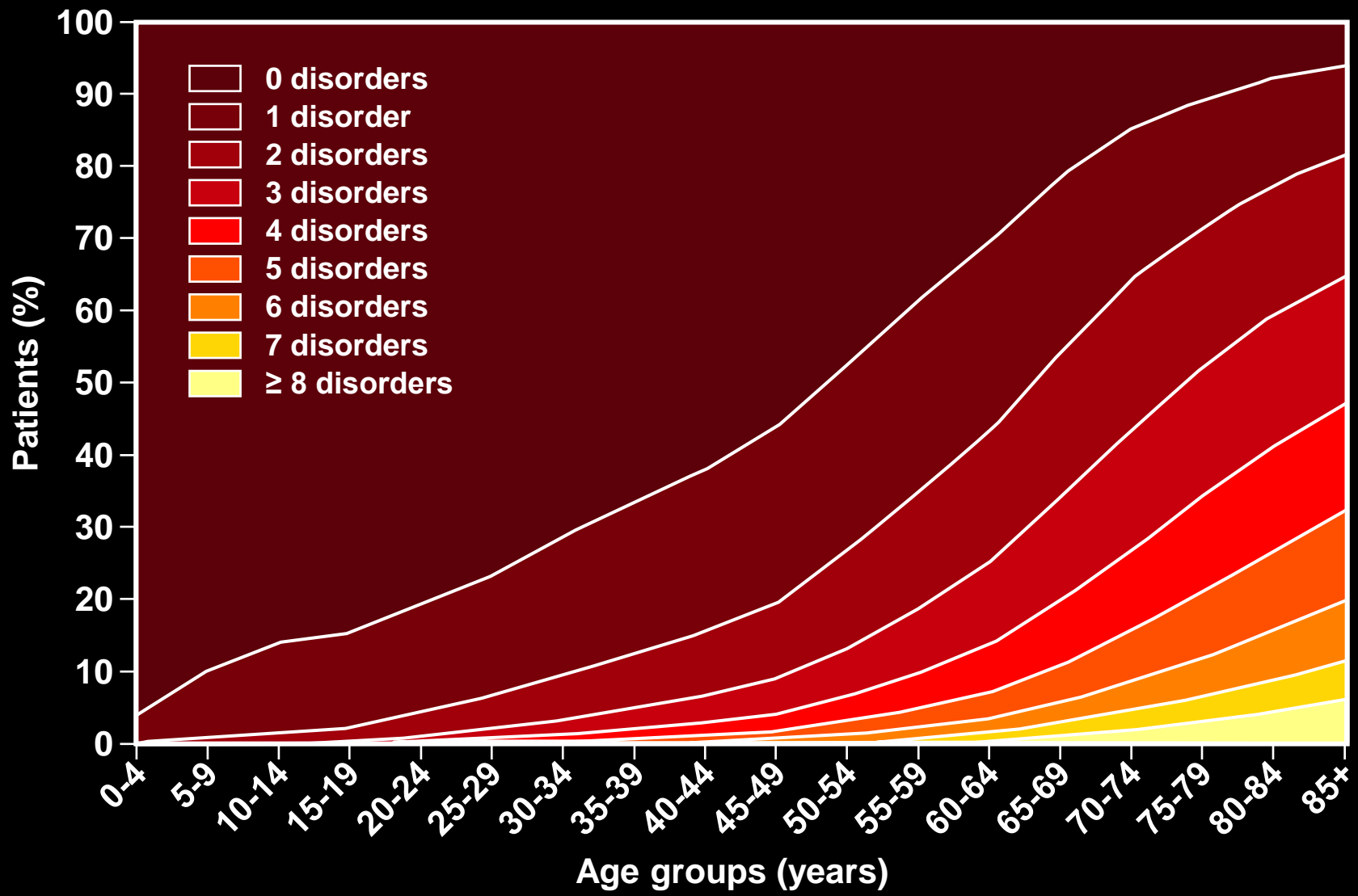
IL-1 IL-6 IL-18 TNF- α IFN- γ

TNF- α

IL-1Ra IL-6 TNF- α IGF1

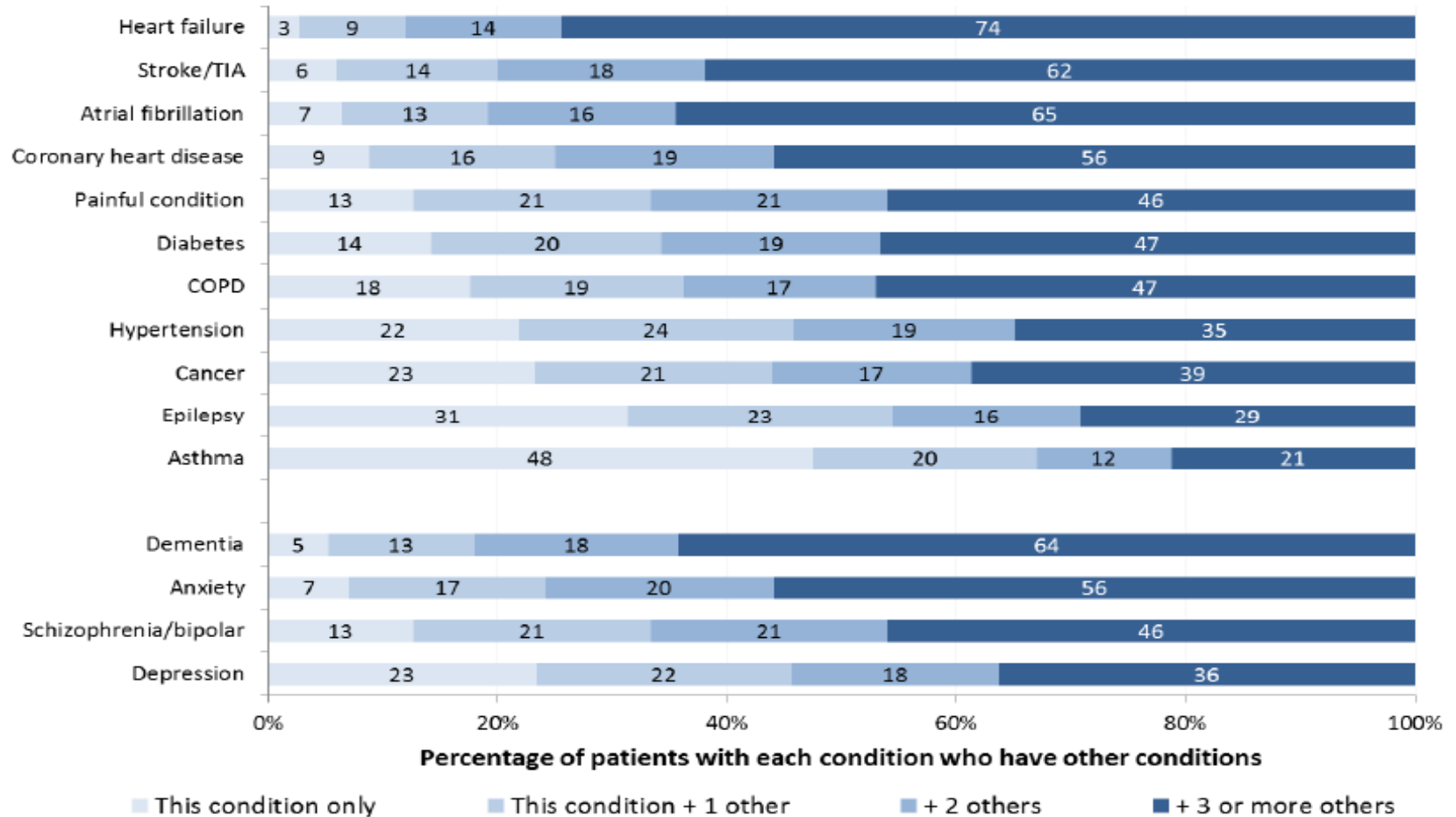
IL-6 TNF- α IL-1 beta

NUMBER OF CHRONIC DISORDERS BY AGE-GROUP

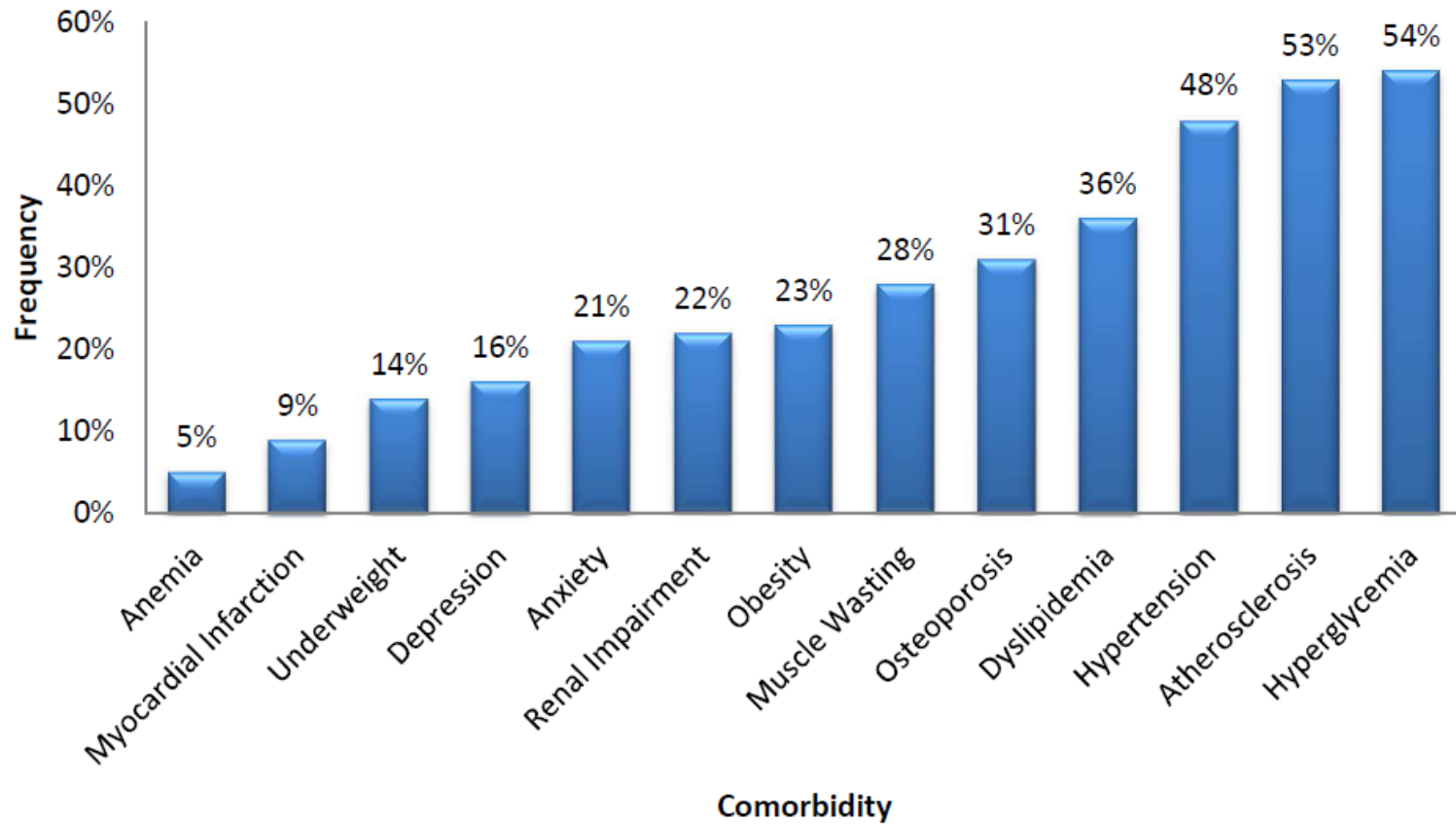


PERCENTAGE OF PATIENTS WITH EACH CONDITION THAT HAVE OTHER CONDITIONS

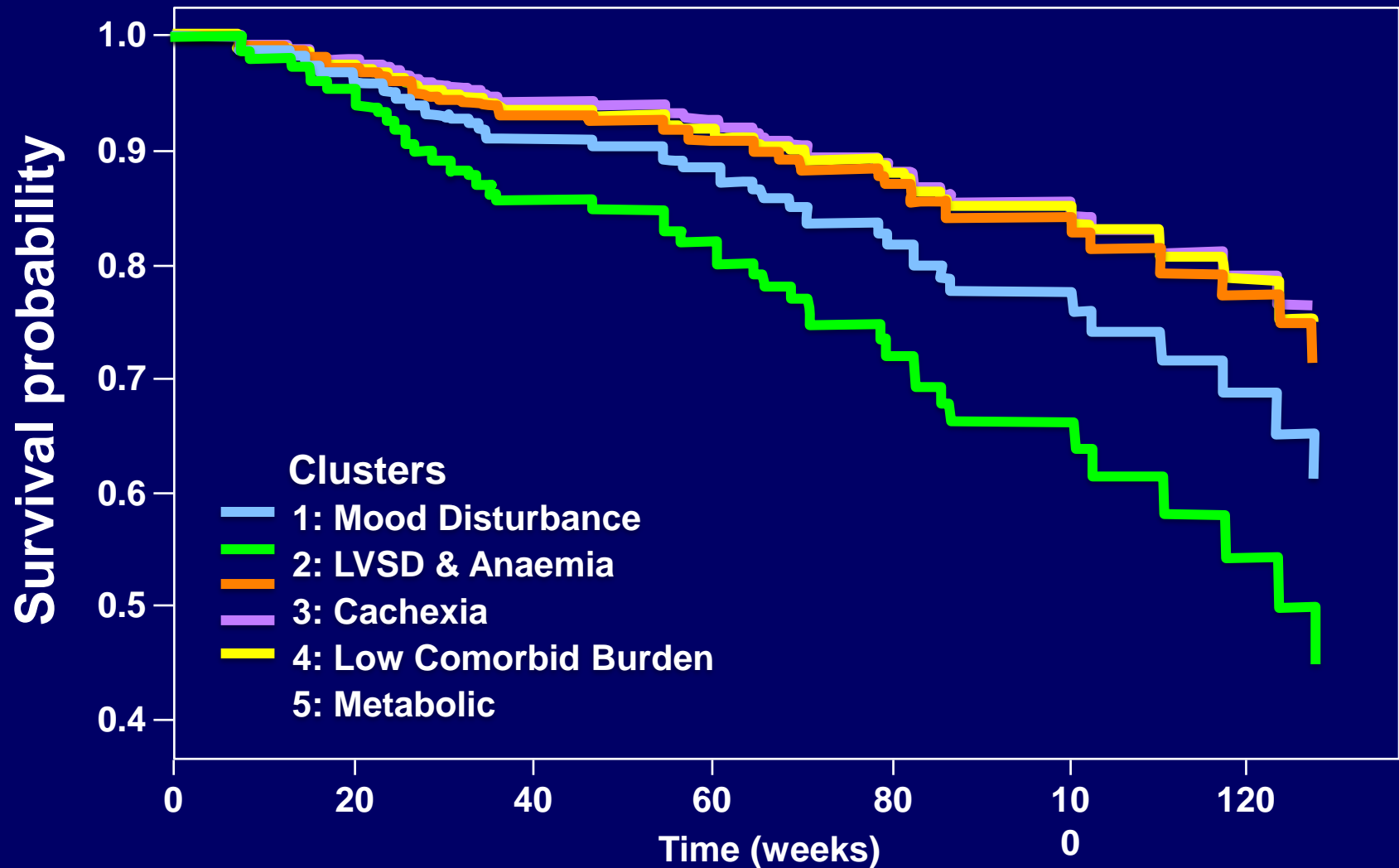
Supplementary figure S1: Number of conditions experienced by patients with common, important diseases



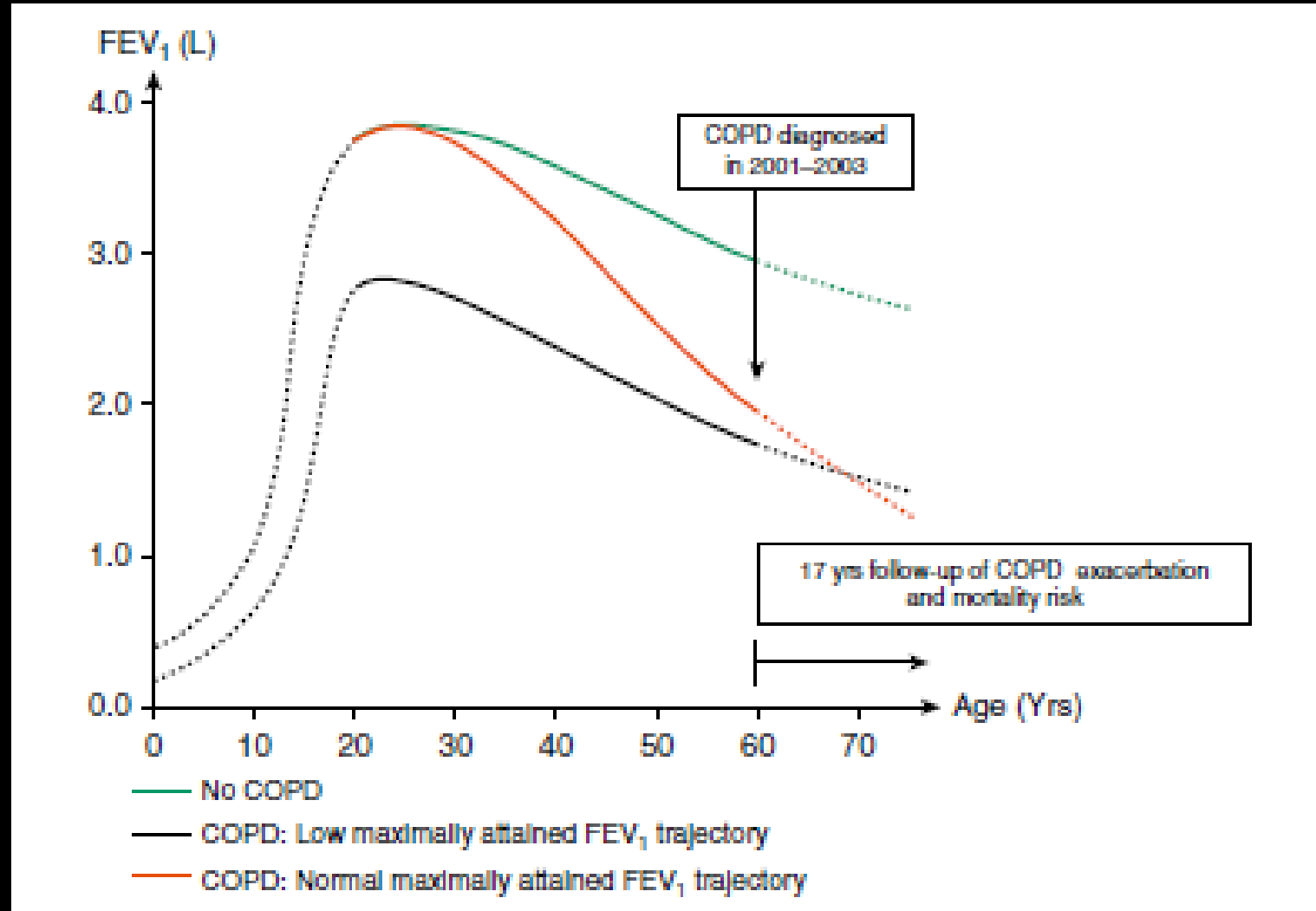
FREQUENCIES OF OBJECTIFIED COMORBIDITIES



SURVIVAL IN ADVANCED COPD ACCORDING TO COMORBIDITY PHENOTYPE



LUNG FUNCTION TRAJECTORIES LEADING TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS PREDICTORS OF EXACERBATIONS AND MORTALITY

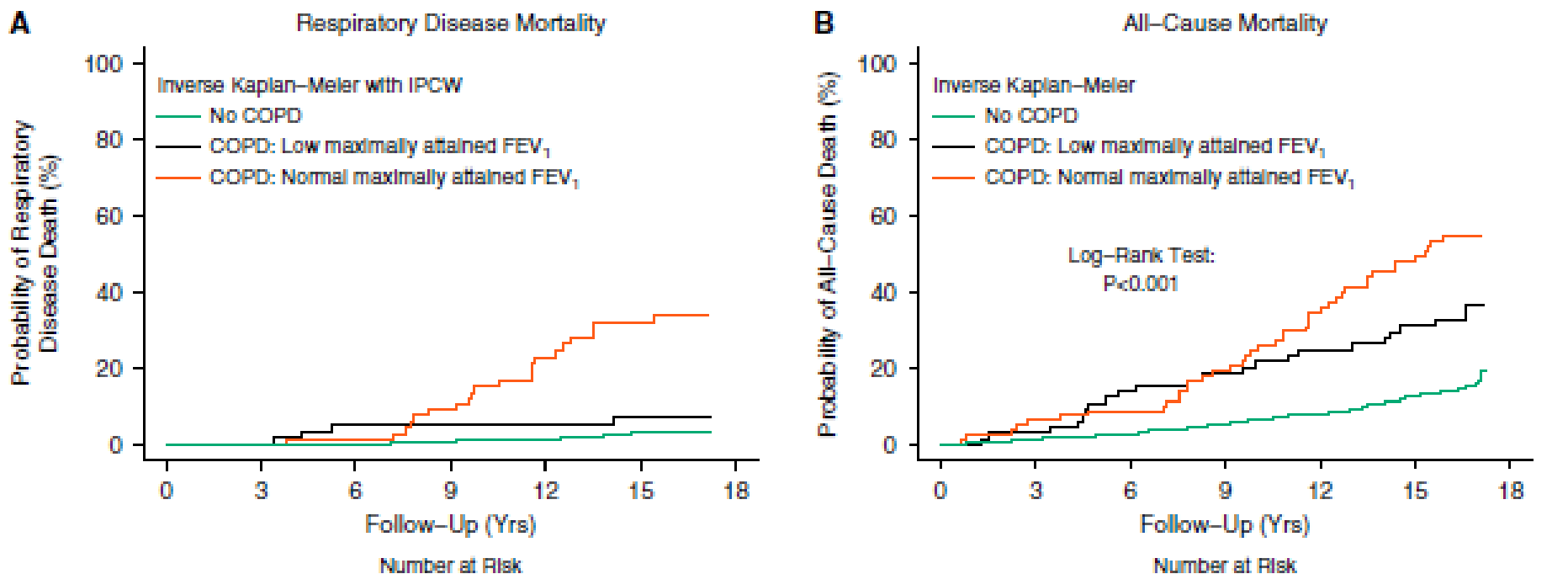


LUNG FUNCTION TRAJECTORIES LEADING TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS PREDICTORS OF EXACERBATIONS AND MORTALITY

Table 1. General Characteristics and Lung Function of 1,170 Participants according to the Three Trajectories Defined by Level of FEV₁ in Percent Predicted Value at Study Enrollment in 1976–1978 or in 1981–1983 and Presence of COPD at Baseline Examination in 2001–2003

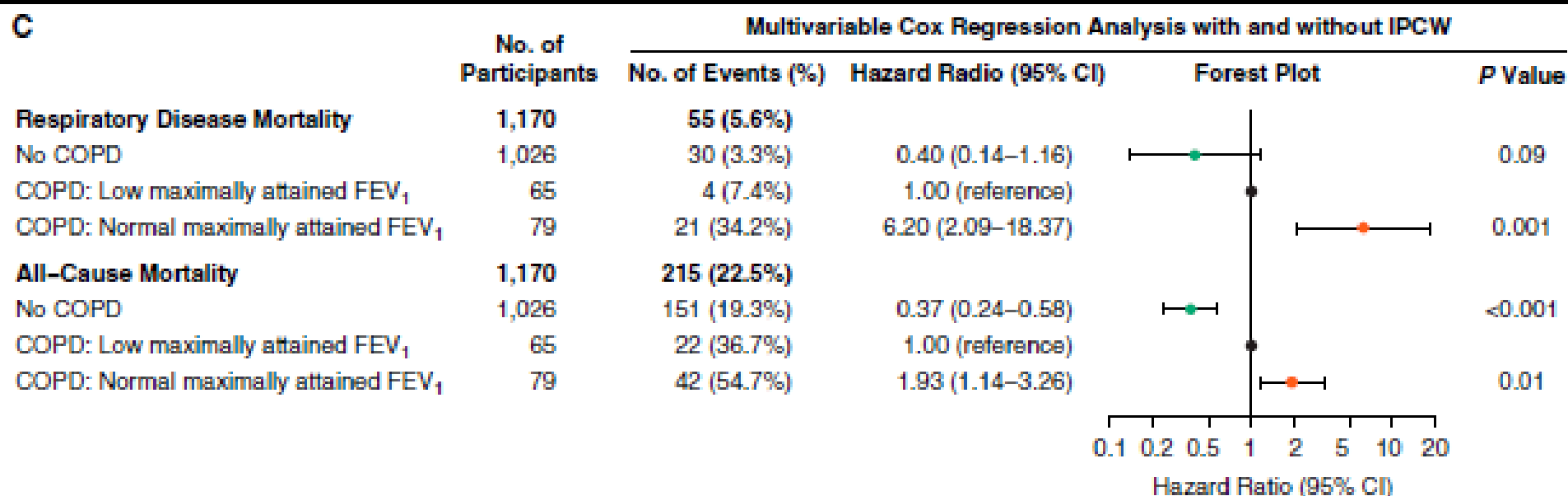
Characteristics	No COPD at Baseline Examination (n = 1,026)	COPD at Baseline Examination		P Value*
		Low Maximally Attained FEV ₁ Trajectory (n = 65)	Normal Maximally Attained FEV ₁ Trajectory (n = 79)	
At study enrollment in 1976–1978 or in 1981–1983				
Sex, M	511 (50%)	29 (45%)	49 (62%)	0.04
Age, yr				
Mean ± SD	33 ± 6	33 ± 5	34 ± 5	0.32
Range	21–40	22–40	21–40	
FEV ₁				
Mean ± SD, L	3.7 ± 0.8	2.7 ± 0.5	3.6 ± 0.8	<0.001
Percent predicted value	95 ± 10	69 ± 7	90 ± 8	<0.001
FEV ₁ /FVC, %	86 ± 7	75 ± 9	84 ± 8	<0.001
Smoking status				0.46
Never smoker	327/1,023 (32%)	8/64 (13%)	5/79 (6%)	
Former smoker	157/1,023 (15%)	2/64 (3%)	3/79 (4%)	
Current smoker	539/1,023 (53%)	54/64 (84%)	71/79 (90%)	
Smoking onset before age 14 yr	46/682 (7%)	11/57 (19%)	10/74 (14%)	0.47
Asthma	11/1,003 (1%)	2/64 (3%)	3/77 (4%)	>0.99
Height, cm	172 ± 9	171 ± 9	173 ± 10	0.38
Body mass index, kg/m ²	23 ± 3	23 ± 3	24 ± 4	0.28
At baseline examination in 2001–2003				
Age, yr				
Mean ± SD	57 ± 7	58 ± 6	59 ± 6	0.24
Range	41–66	44–65	43–66	
FEV ₁				
Mean ± SD, L	3.1 ± 0.7	1.9 ± 0.6	2.1 ± 0.6	0.10
Percent predicted value	98 ± 13	63 ± 12	66 ± 13	0.13
Decline in FEV ₁				
Mean ± SD, ml/yr	27 ± 19	29 ± 17	61 ± 22	<0.001
Median (IQR), ml/yr	26 (22)	27 (21)	61 (28)	<0.001
Percentage of baseline value per year	0.7 ± 0.4	1.1 ± 0.7	1.7 ± 0.5	<0.001
≥40 ml/yr	218 (21%)	15 (23%)	67 (85%)	<0.001

LUNG FUNCTION TRAJECTORIES LEADING TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS PREDICTORS OF EXACERBATIONS AND MORTALITY



LUNG FUNCTION TRAJECTORIES LEADING TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS PREDICTORS OF EXACERBATIONS AND MORTALITY

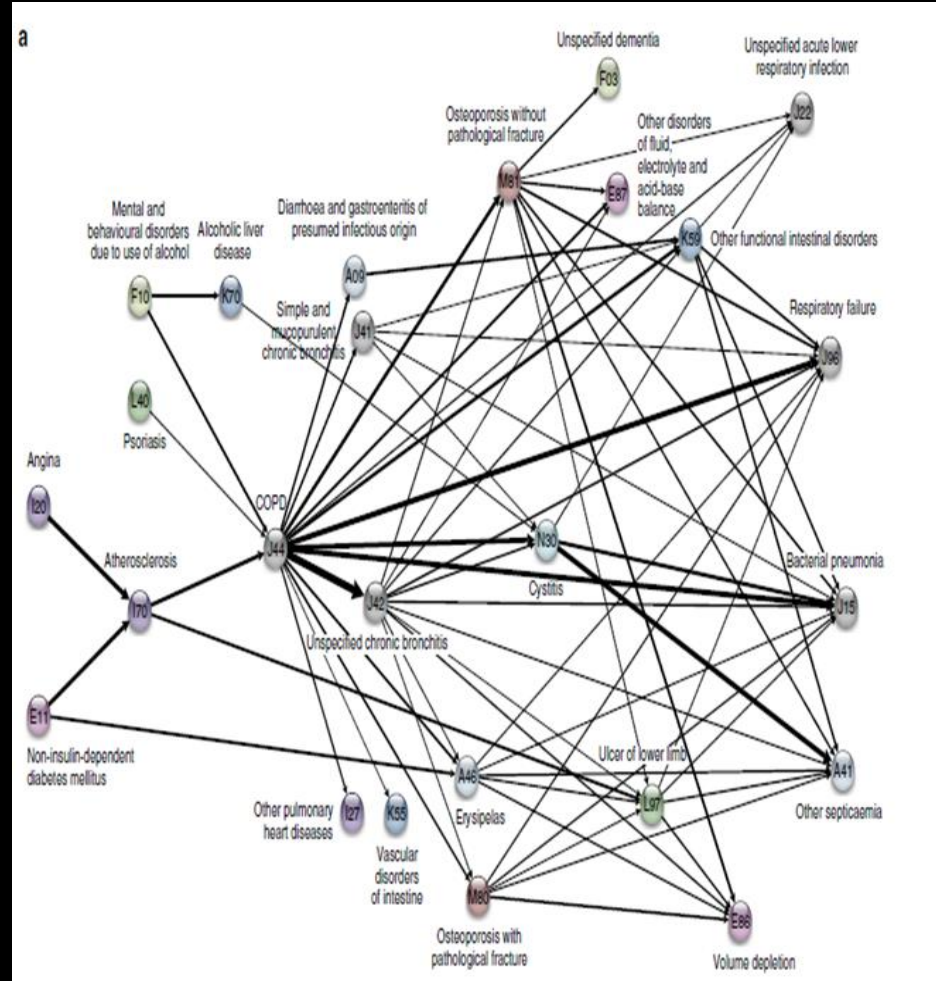
C



TEMPORAL DISEASE TRAJECTORIES CONDENSED FROM POPULATION-WIDE REGISTRY DATA COVERING 6.2 (ALL) DANISH

Chronic obstructive pulmonary disease (COPD) is central to disease progression and hence important to diagnose early to reduce future risk

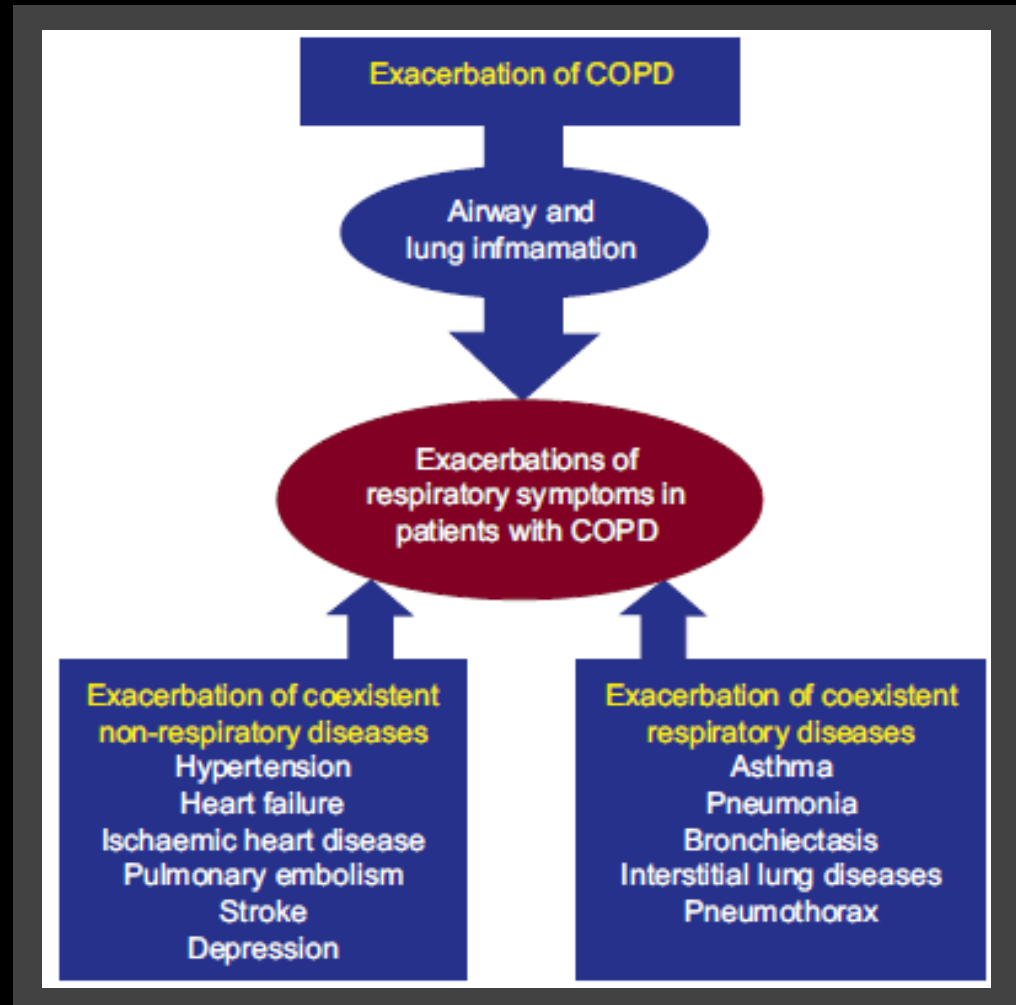
Trajectory analyses may be useful for predicting and preventing future diseases of individual patients



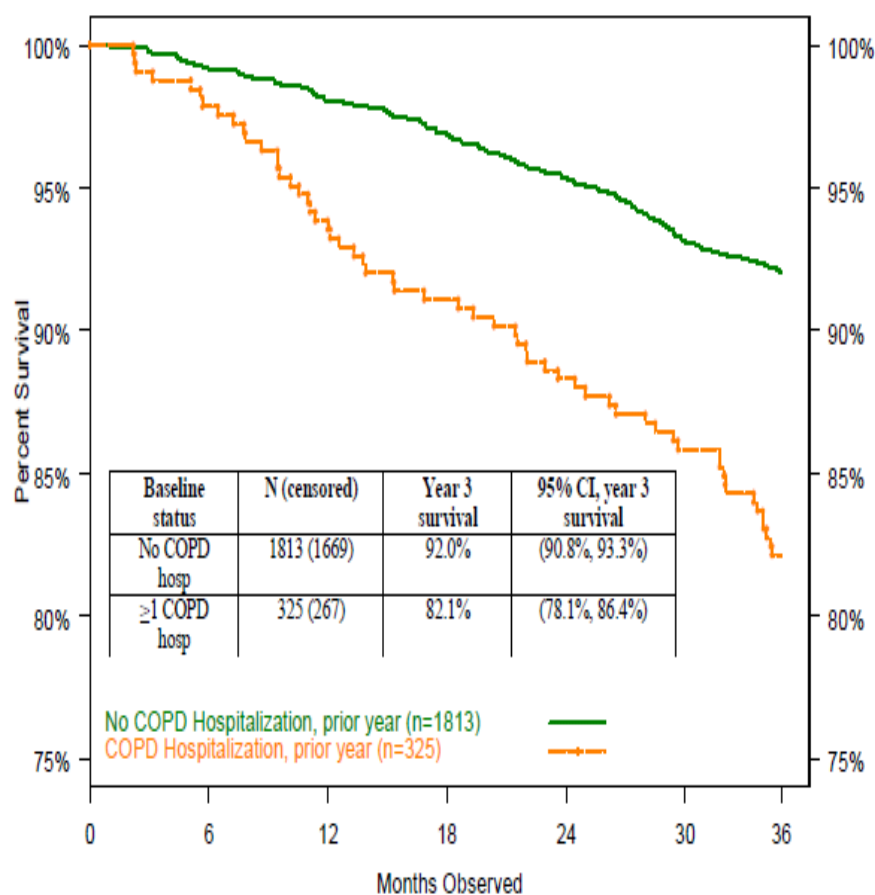
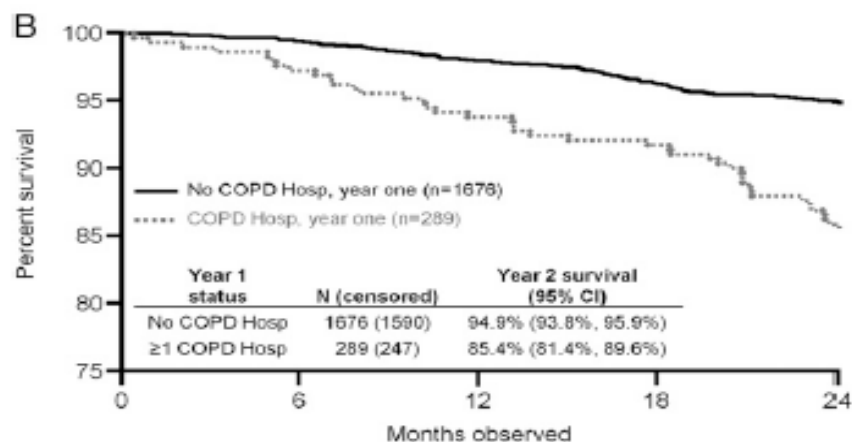
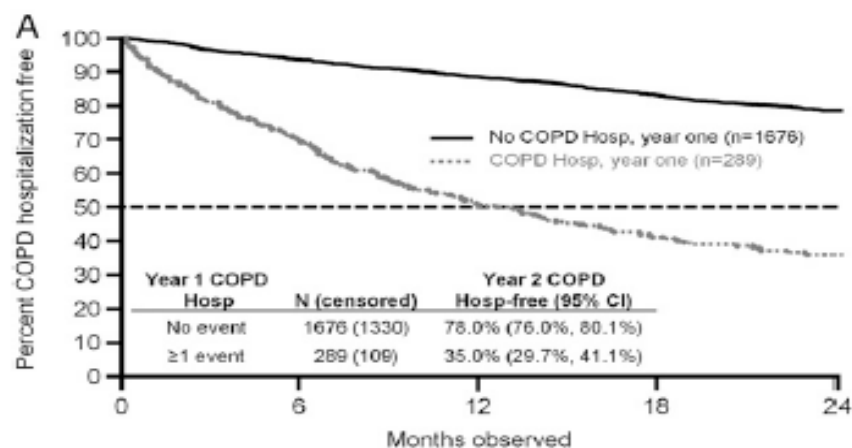
COPD and comorbidities

- COPD as the pulmonary component of multimorbidity
- *Complexity of COPD exacerbations*
- Treat the patient with COPD or any chronic disease not just COPD or the index chronic disease

EXACERBATIONS OF RESPIRATORY SYMPTOMS IN PATIENTS WITH COPD MAY NOT BE EXACERBATIONS OF COPD



RISK OF MORTALITY IN PATIENTS WITH OR WITHOUT HISTORY OF HOSPITALIZATIONS DUE TO COPD EXACERBATIONS IN THE ECLIPSE STUDY



ONE-YEAR AND LONG-TERM MORTALITY IN PATIENTS HOSPITALIZED FOR COPD

University Hospital, Compostela, Spain

757 patients assessed

Age 74.8, males 77%

Hospital stay 12.2 days, 3.6% ICU

1-year mortality 26.2%

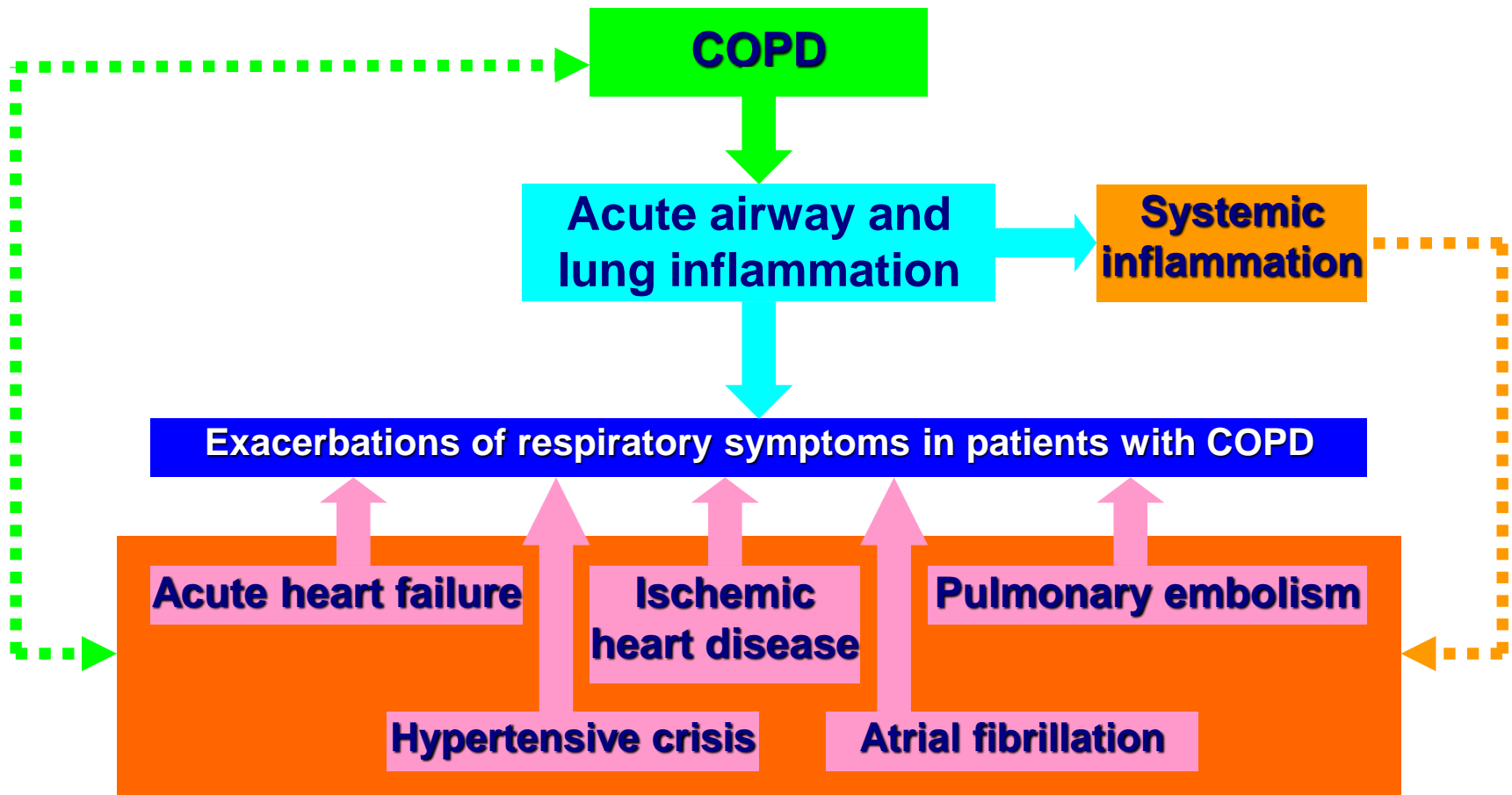
5-year mortality 64.3%

Causes of death were respiratory and cardiovascular disorders

COMORBIDITIES AND SUBGROUPS OF PATIENTS SURVIVING SEVERE ACUTE HYPERCAPNIC RESPIRATORY FAILURE IN THE ICU

- **Multimorbidity was associated with longer time to hospital discharge**
- **Hospital readmission or death occurred in 46% of patients over 3.5 months post-discharge**
- **Multi-morbidity is common, most often unrecognized, and may be associated with poor outcome**

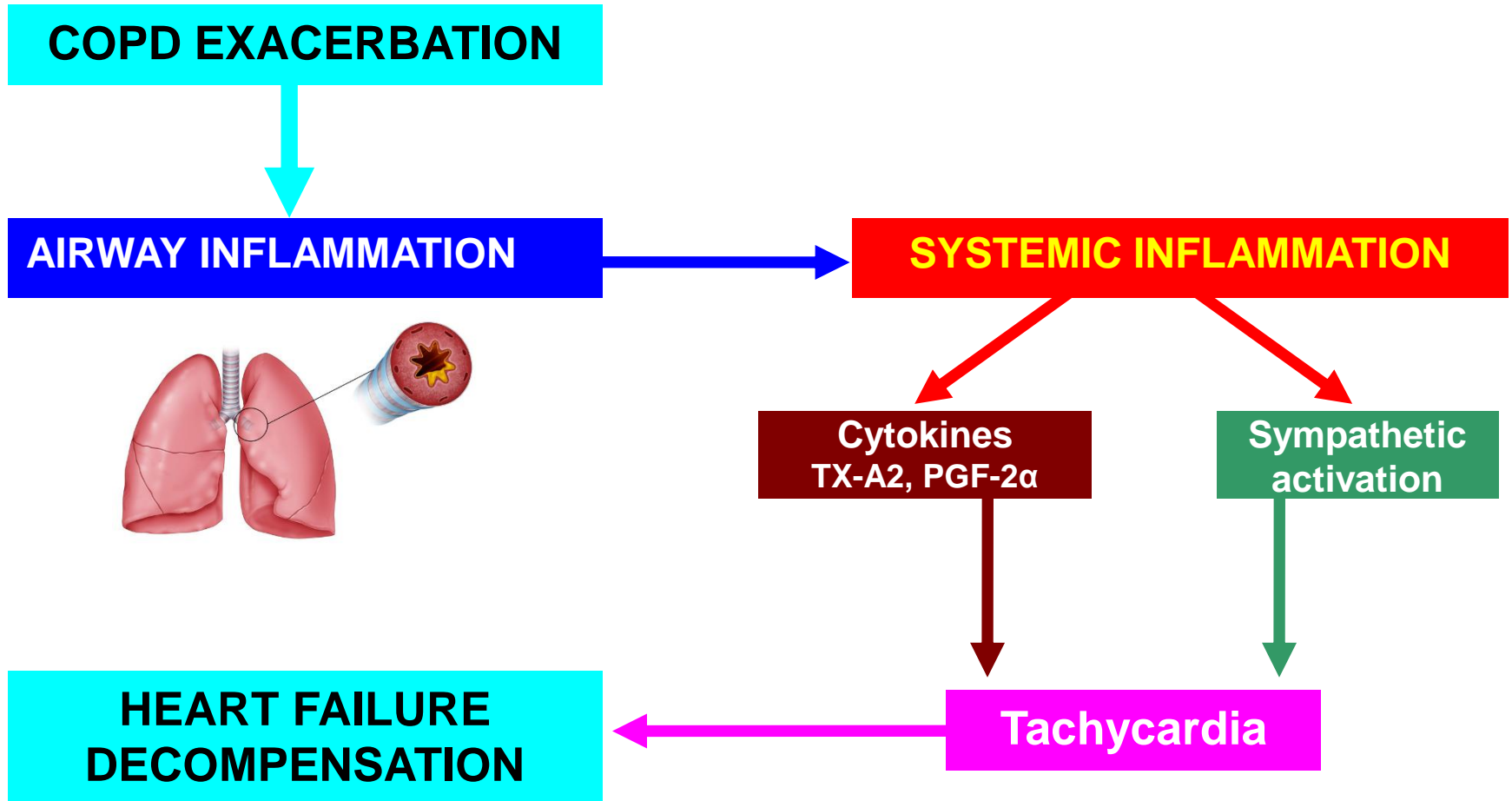
Origin of dyspnea exacerbations in patients with COPD



Agustí A, Faner R. *Proc Am Thorac Soc.* 2012;9:43-6.

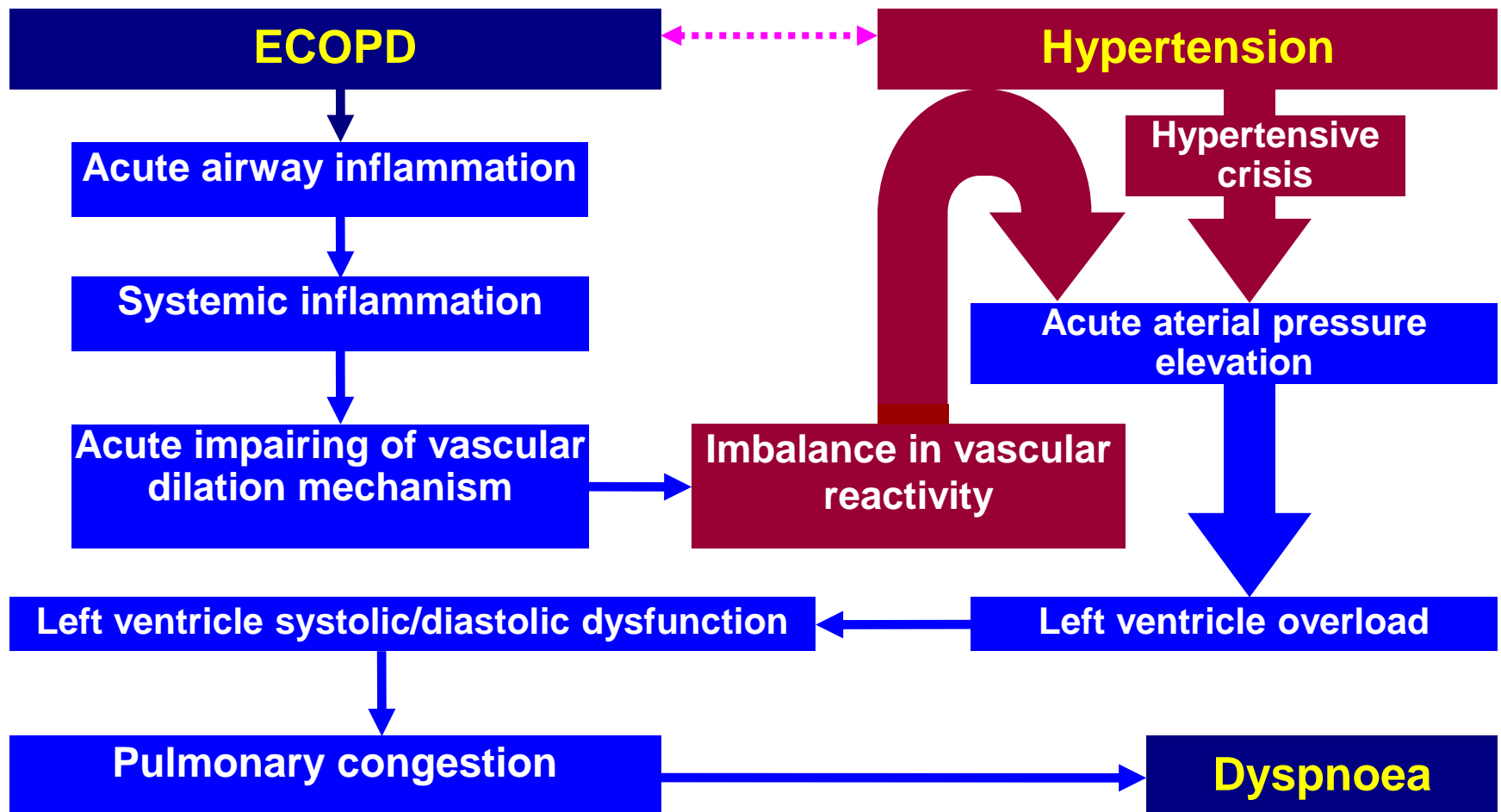
Beghé B, et al. *Eur Respir J.* 2013;41:993-5.

Exacerbations of airway inflammation and cardiovascular effects

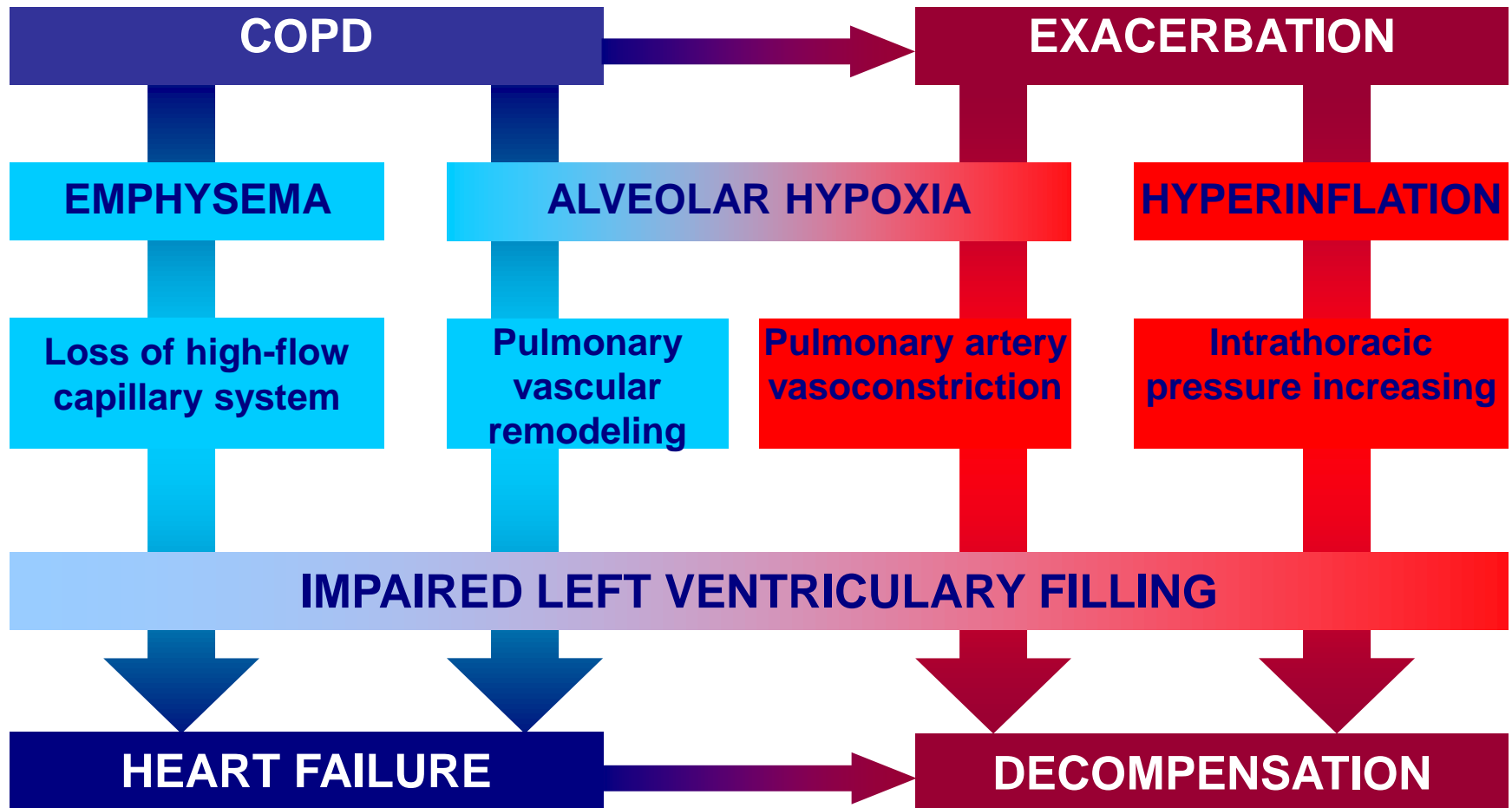


Takayama K, et al. *Nat Med.* 2005;11:562–566.

Hypertension – cause of respiratory symptoms exacerbations in COPD



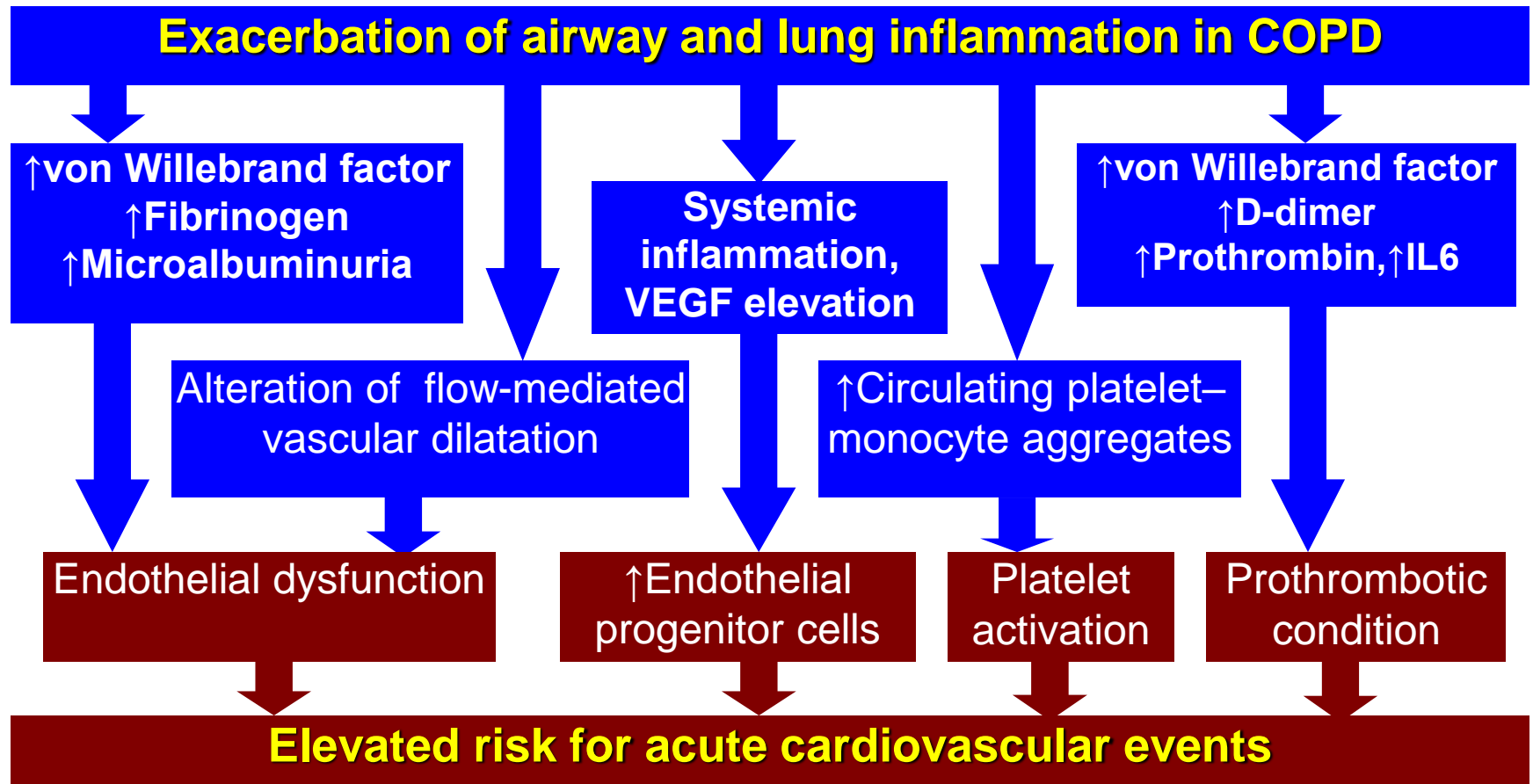
Haemodynamic mechanisms of heart dysfunction in COPD



Barr RG, et al. *N Engl J Med*. 2010;362:217–227.

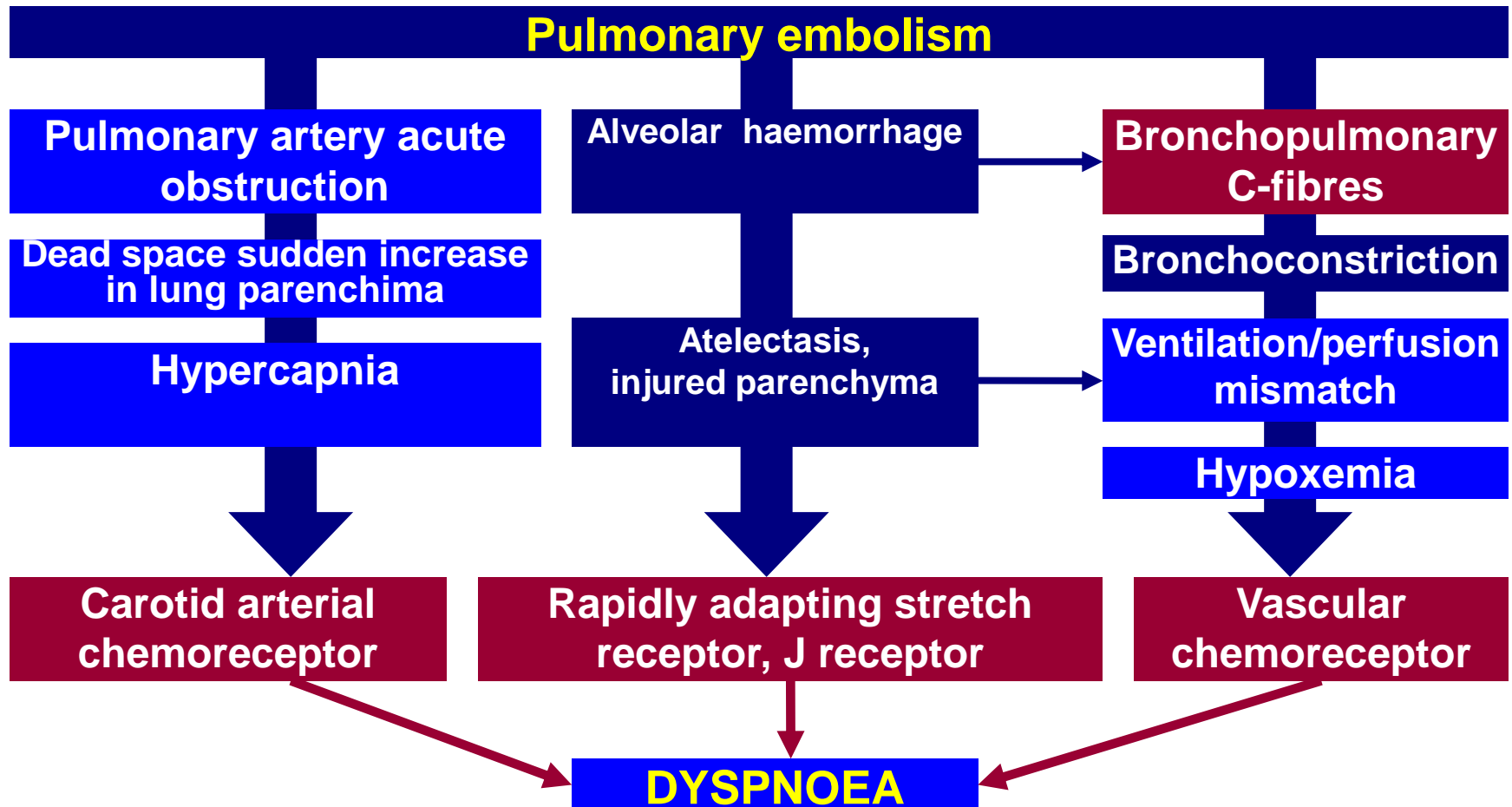
Watz H, et al. *Chest*. 2010;138:32-8.

Mechanisms of risk for cardiovascular events in ECOPD



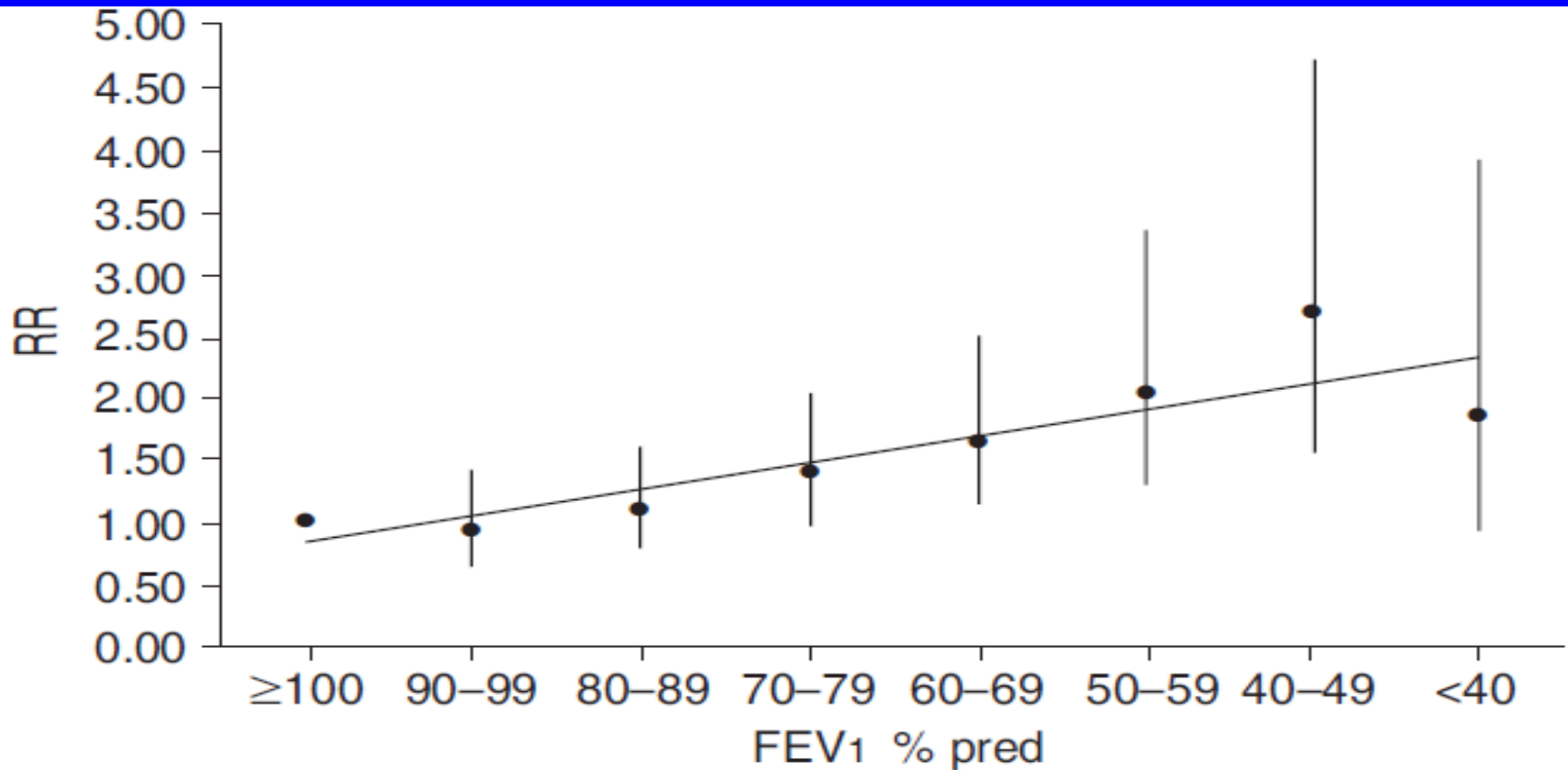
Roca M, et al. *Eur J Clin Invest*. 2013;43:510-21

Pulmonary embolism – cause of respiratory symptoms exacerbations in COPD



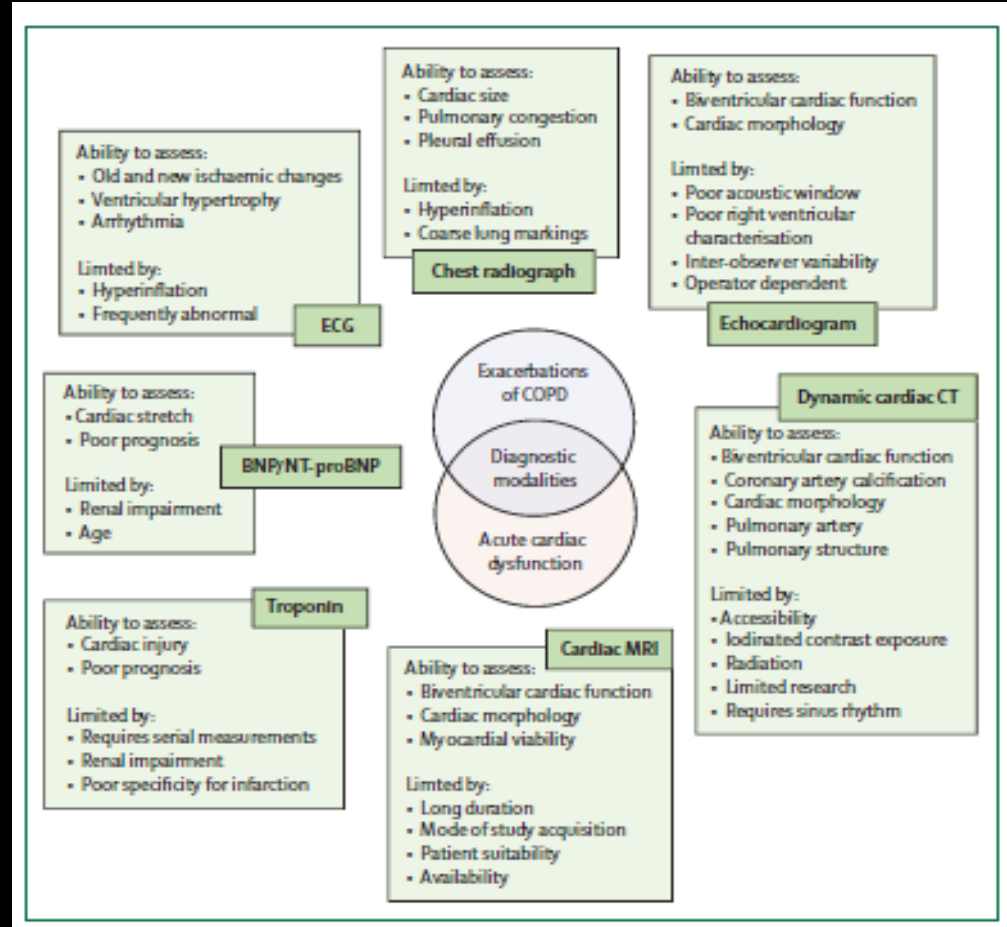
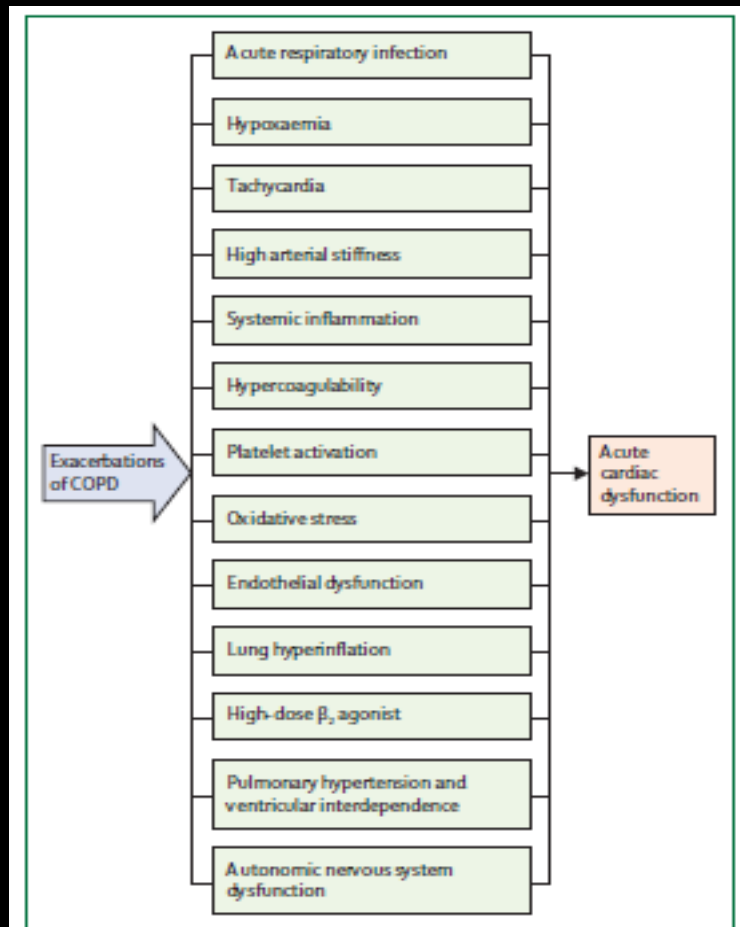
Atrial fibrillation – cause of respiratory symptoms exacerbations in COPD

Lung function and risk of atrial fibrillation hospitalization in COPD

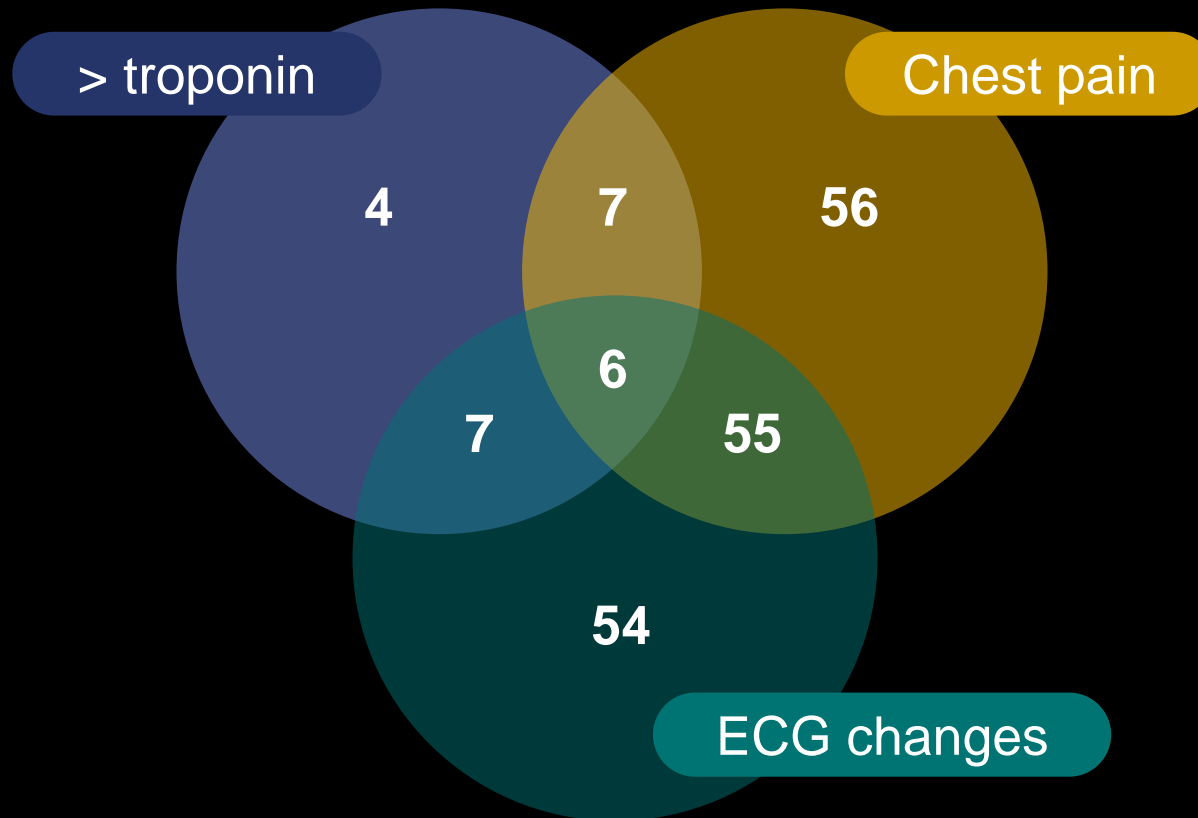


Buch P, et al. *Eur Respir J*. 2003;21:1012-6.

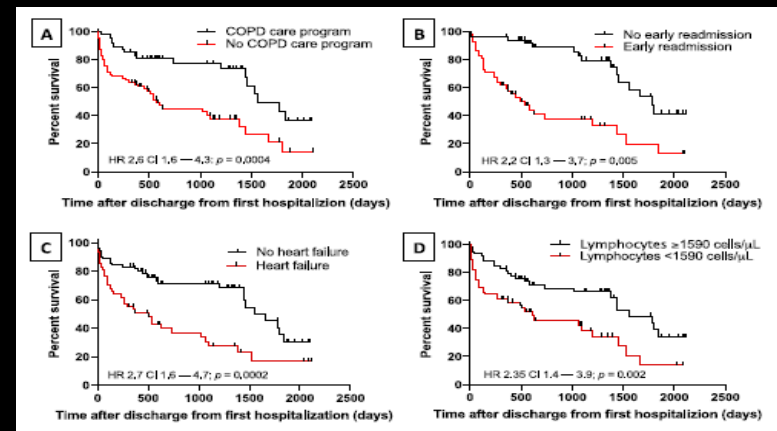
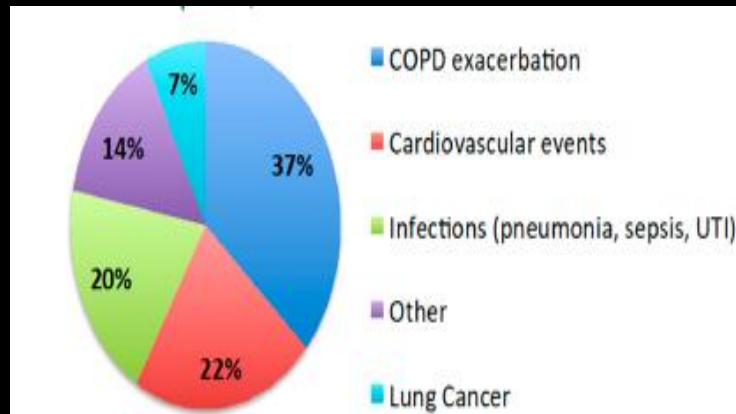
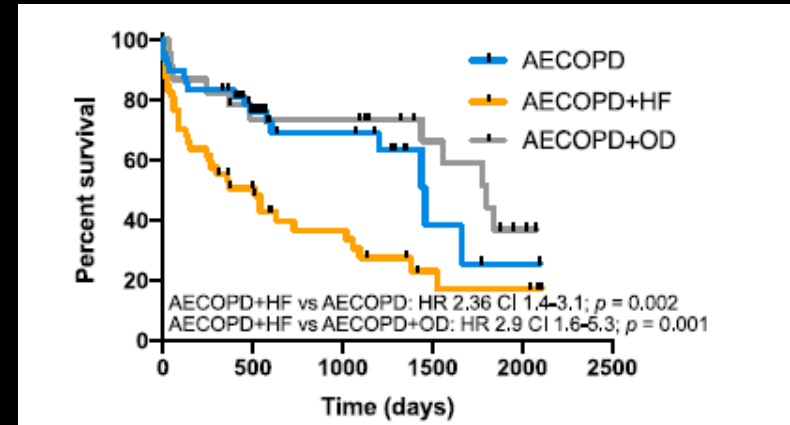
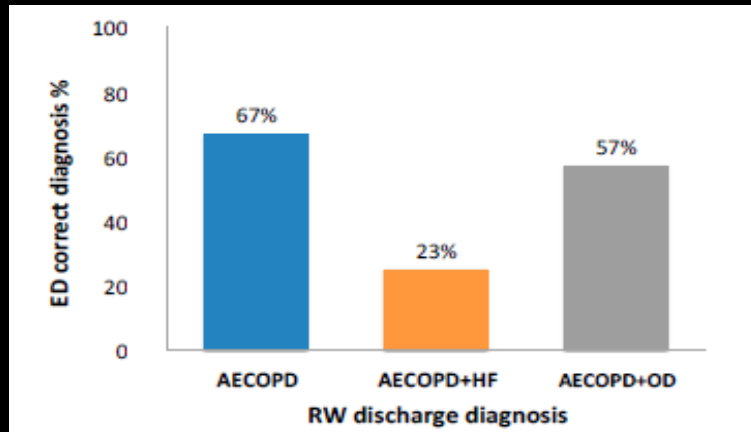
CARDIAC DYSFUNCTION DURING EXACERBATIONS OF COPD



BIOCHEMICAL MARKERS OF CARDIAC DYSFUNCTION PREDICT MORTALITY IN ACUTE EXACERBATIONS OF COPD



HEART FAILURE IS HIGHLY PREVALENT AND DIFFICULT TO DIAGNOSE IN SEVERE EXACERBATIONS OF COPD PRESENTING TO THE EMERGENCY DEPARTMENT



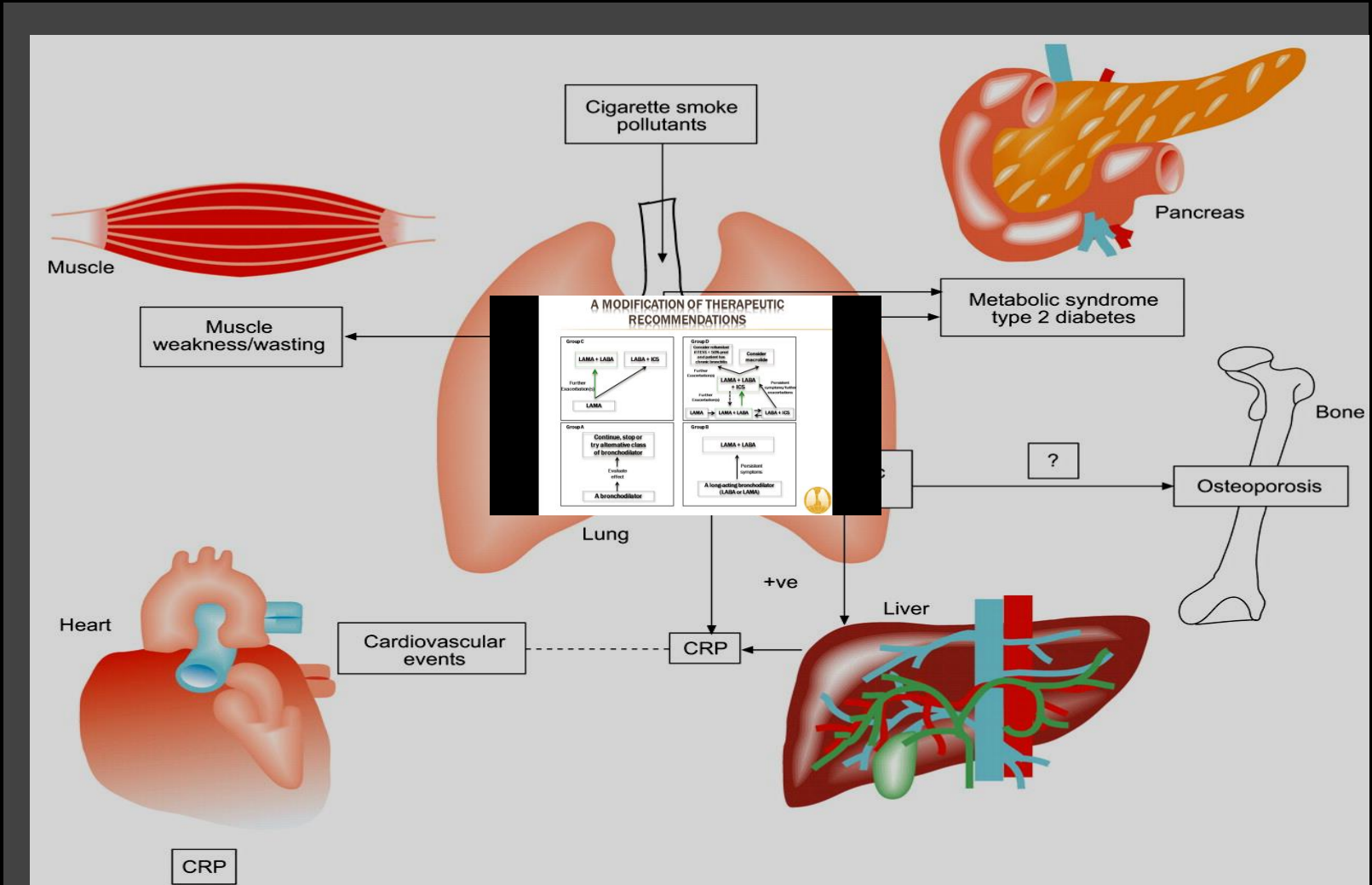
NATRIURETIC PEPTIDE TESTING FOR PREDICTING ADVERSE EVENTS FOLLOWING HEART FAILURE HOSPITALIZATION

Changes in BNP or NT-proBNP following treatment should be considered an important part of the pre-discharge decision making for patients hospitalized with AHF

COPD and comorbidities

- COPD as the pulmonary component of multimorbidity
- Complexity of COPD exacerbations
- *Treat the patient with COPD or any chronic disease not just COPD or the index chronic disease*

COPD AS THE PULMONARY COMPONENT OF MULTIMORBIDITY

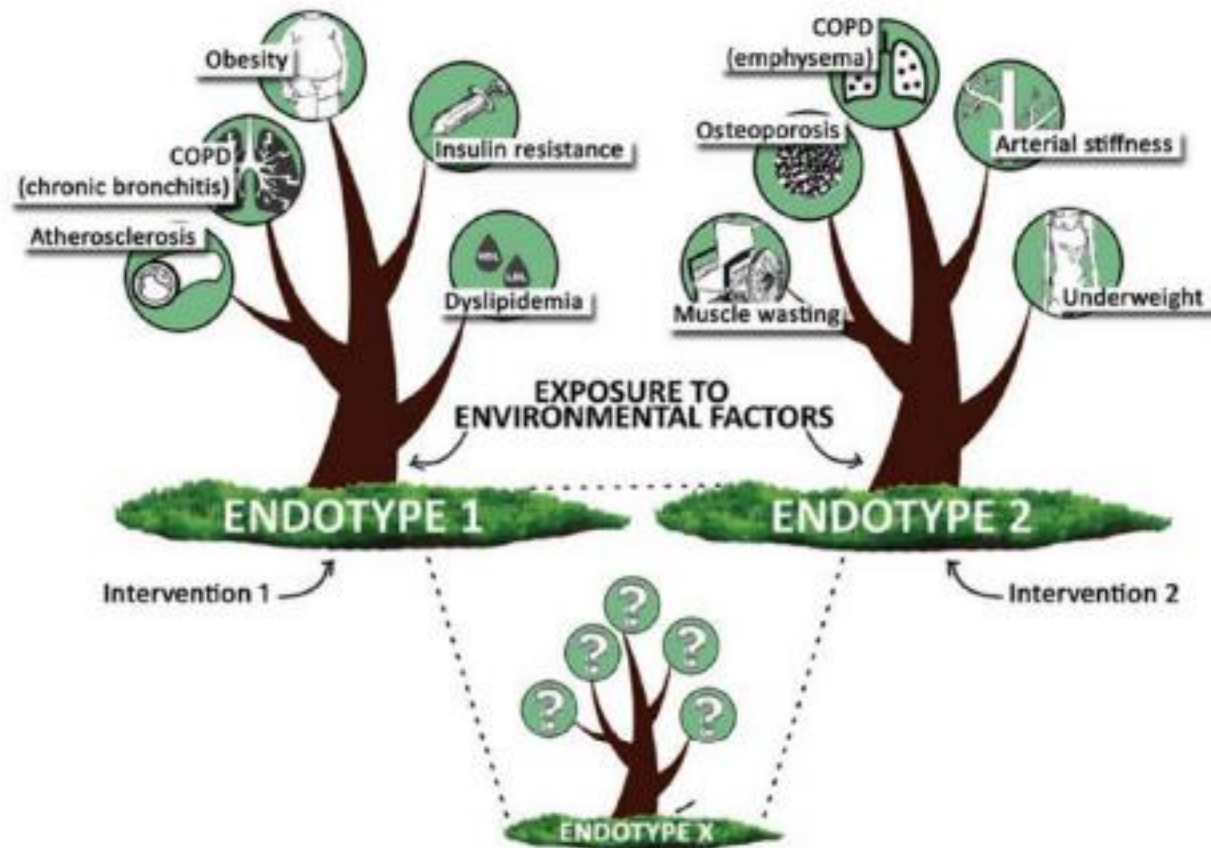


FROM SYSTEMIC EFFECTS OF COPD TO COPD AS PULMONARY COMPONENT OF MULTIMORBIDITY

TABLE 1. Chronic diseases that have been reported to be more prevalent in patients with COPD, and that have an impact on severity and prognosis.

Cardiovascular diseases	Chronic respiratory diseases
Hypertension	Asthma
Chronic heart failure	Bronchiectasis
Ischaemic heart diseases	Obstructive sleep disorders
Arrhythmias	Lung cancer
Peripheral artery disease	Interstitial lung diseases
Stroke and transient cerebrovascular ischaemia	Pulmonary hypertension
Thromboembolism	Tuberculosis
Metabolic diseases	Endocrine diseases
Metabolic syndrome	Diabetes
Obesity	Osteoporosis
Nutritional disorders	Hypothyroidism
Central nervous system disorders	Gastrointestinal diseases
Respiratory disorders during sleep	Gastroesophageal reflux
Anxiety and depression	Inflammatory bowel diseases
Psychiatric diseases	Chronic liver diseases
Cognitive impairment	
Degenerative disorders	
Kidney/genitourinary	Haematological disorders
Chronic kidney failure	Anaemia
Benign prostatic hypertrophy	
Erectile dysfunction	

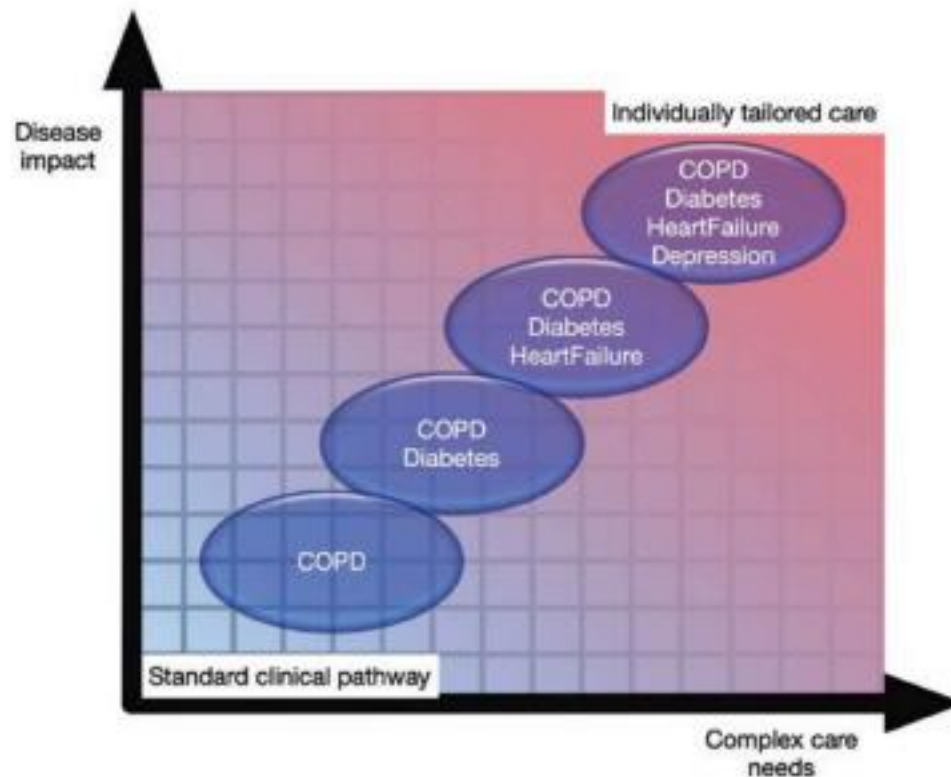
FROM SYSTEMIC EFFECTS OF COPD TO COPD AS PULMONARY COMPONENT OF MULTIMORBIDITY



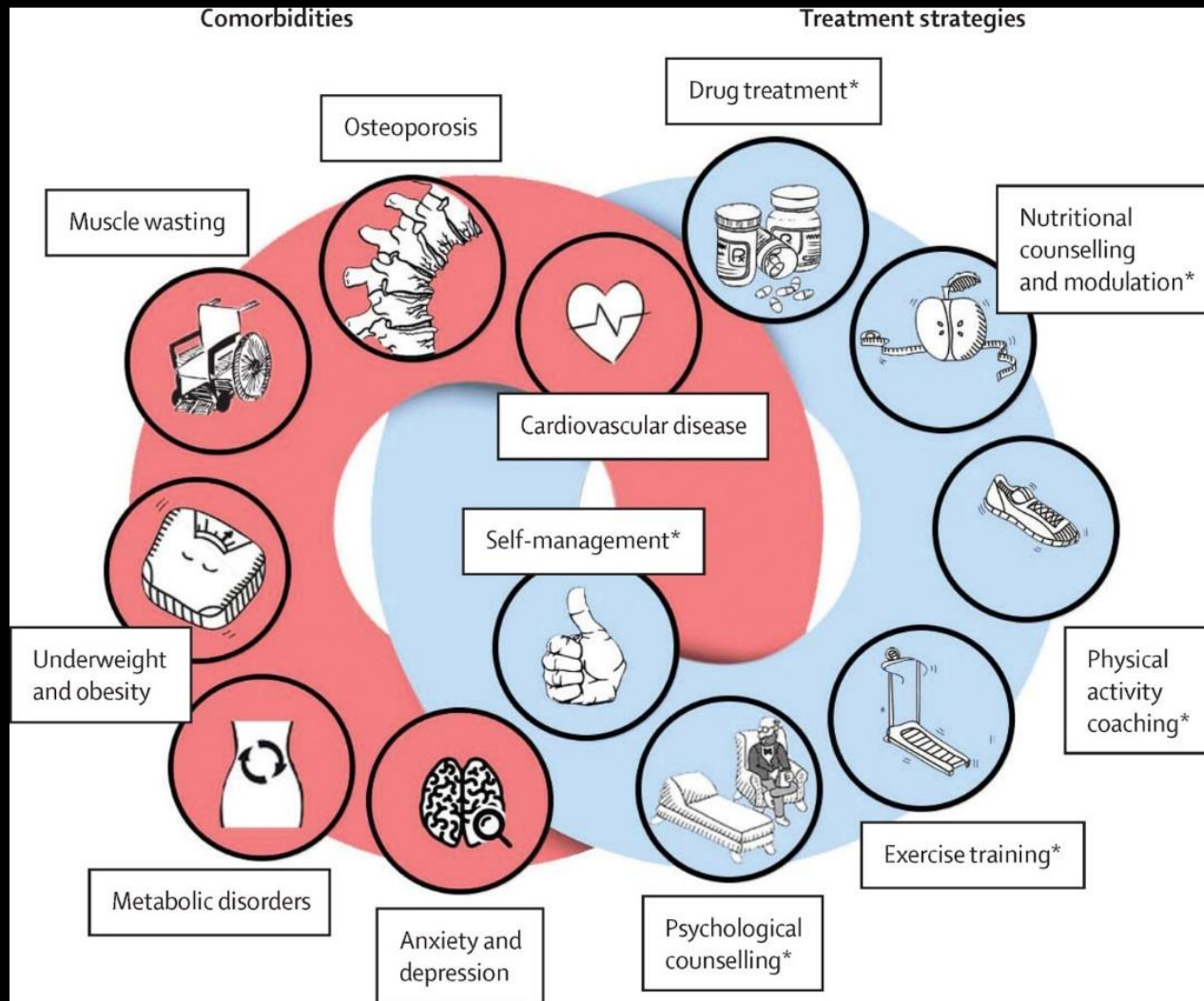
NON-CARDIAC COMORBIDITIES AND MORTALITY IN PATIENTS WITH HEART FAILURE WITH REDUCED VS. PRESERVED EJECTION FRACTION: a study using the Swedish Heart Failure Registry

- **Non-cardiac comorbidities contribute significantly but differently to mortality, both in HFrEF and HFpEF**
- **No significant variation was found in the impact over the 12-year study period**
 - **These results emphasize the importance of including the management of comorbidities as a part of a standardized heart failure care in both HF phenotypes**

FROM SYSTEMIC EFFECTS OF COPD TO COPD AS PULMONARY COMPONENT OF MULTIMORBIDITY



MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE BEYOND THE LUNGS



CONCLUSIONS

Patient with COPD have invariably concomitant chronic diseases that should be searched and treated according to current disease guidelines for COPD and concomitant chronic diseases

Treatment of stable COPD and of exacerbations should always consider the complexity of the mechanism underlying symptoms and their worsening