

Pulmonary Symposium

Novotel, Poznan 8 April 2017



BETWEEN GOLD GUIDELINES AND EVERYDAY REALITY IN COPD

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WHO IS MS/MR COPD?



MALE, SMOKERS OR EX-SMOKER

40 years old, mainly > 65

Dyspnea on exercise \pm cough&sputum

Wheezing at night or after exercise

In-expiratory ronchi and/or wheezing

Acute exacerbations of symptoms (30%)

Invariably (> 80%) associated with other chronic diseases (chronic multimorbidity)

COPD AS PULMONARY COMPONENT OF MULTIMORBIDITY

Leonardo M. Fabbri, MD, FERS

Definition and assessment of severity of COPD

Management of of COPD

COPD as pulmonary component of multimorbidity

Treatment of concomitant chronic diseases in COPD

Conclusions

GLOBAL STRATEGY FOR DIAGNOSIS, MANAGEMENT AND PREVENTION OF COPD DEFINITION OF COPD 2011



2011

COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation **that is usually progressive and associated with an enhanced chronic inflammatory** response in the airways and the lung to noxious particles or gases. **Exacerbations and comorbidities contribute to the overall severity in individual patients**

2017

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by **persistent respiratory symptoms** and airflow limitation that is **due to airway and/or alveolar abnormalities usually** caused by significant exposure to noxious particles or gases

Diagnosis of COPD

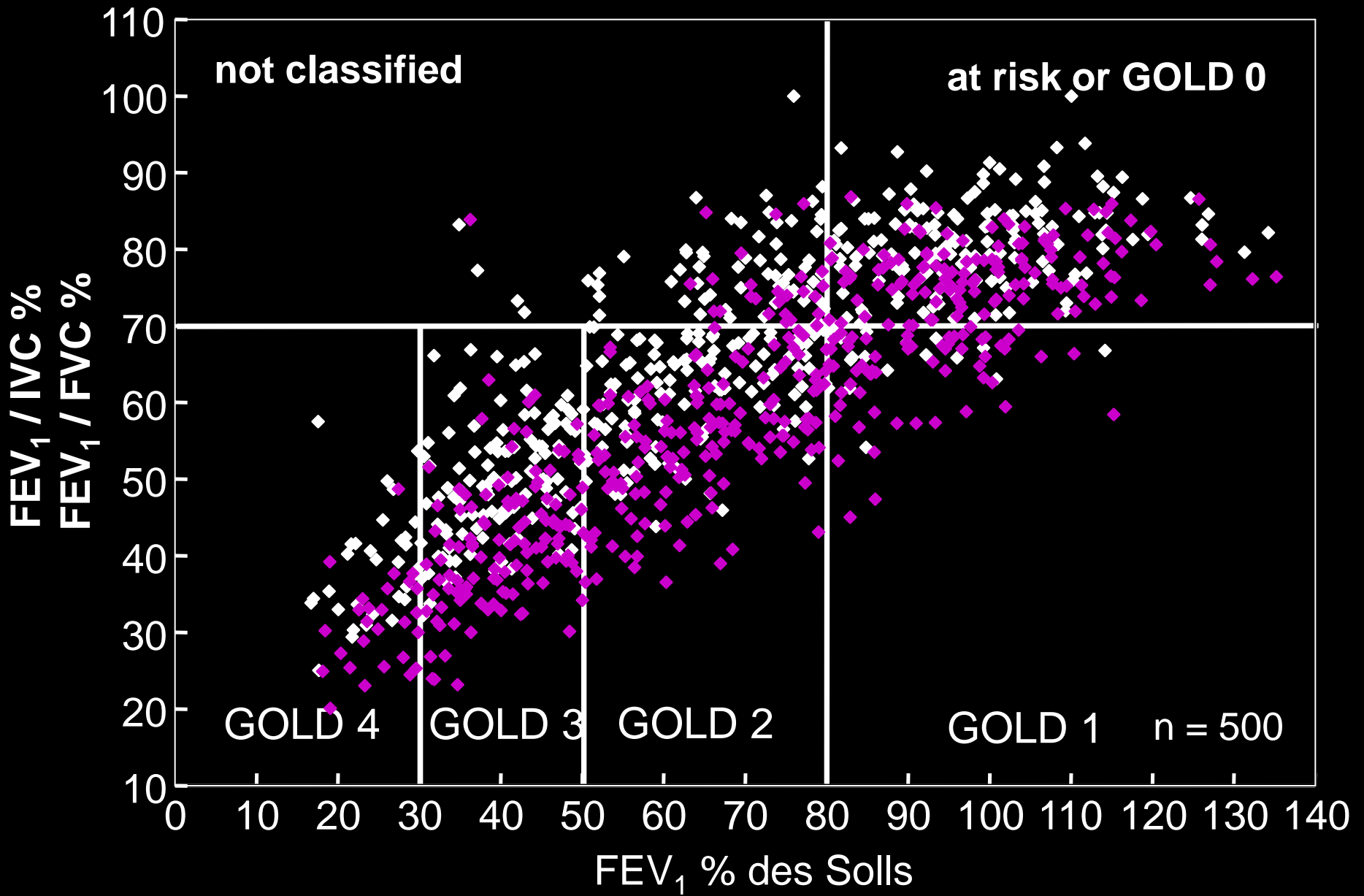
SYMPTOMS

shortness of breath
chronic cough
sputum

EXPOSURE TO RISK FACTORS

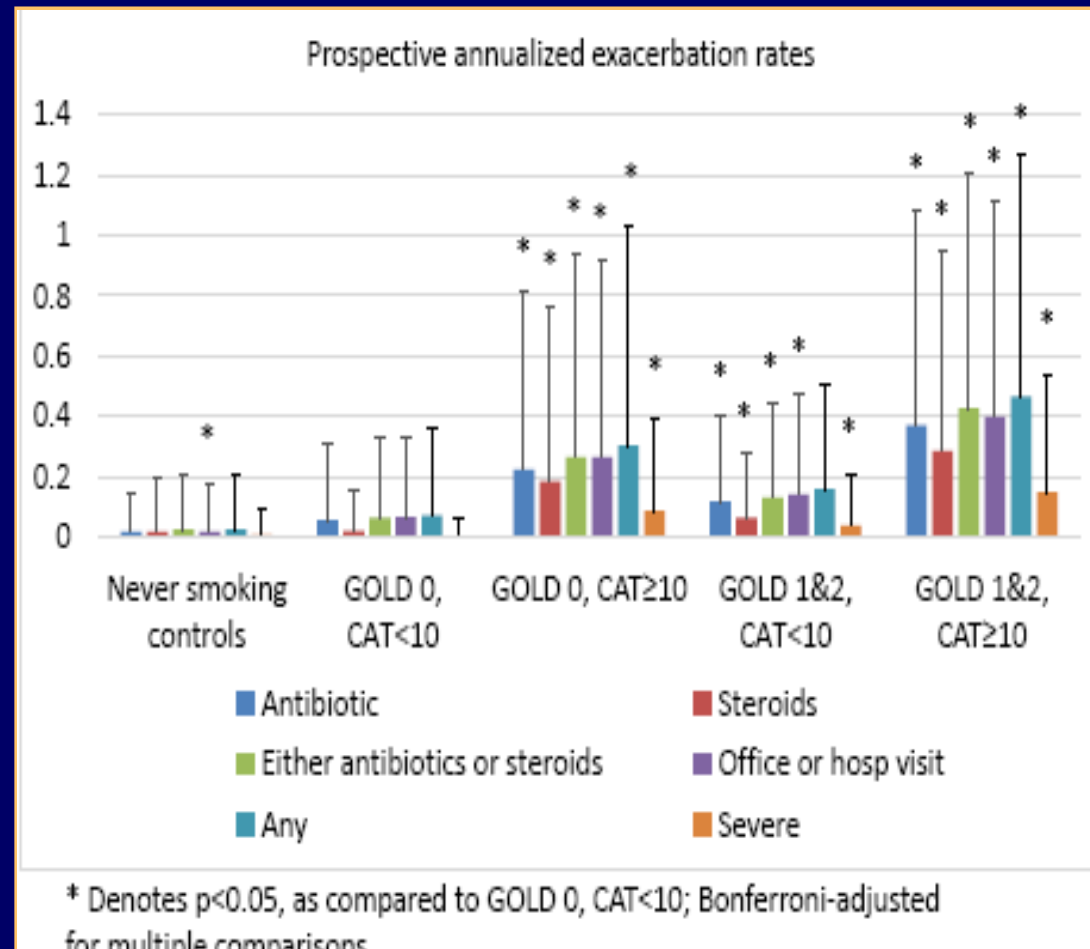
tobacco
occupation
indoor/outdoor pollution

SPIROMETRY: Required to establish diagnosis



CLINICAL SIGNIFICANCE OF SYMPTOMS IN SMOKERS WITH PRESERVED SPIROMETRY

Smokers with symptoms despite preserved FEV1/FVC have more frequent respiratory exacerbations, activity limitations and evidence of airway disease and are currently using a range of respiratory medications without any evidence base

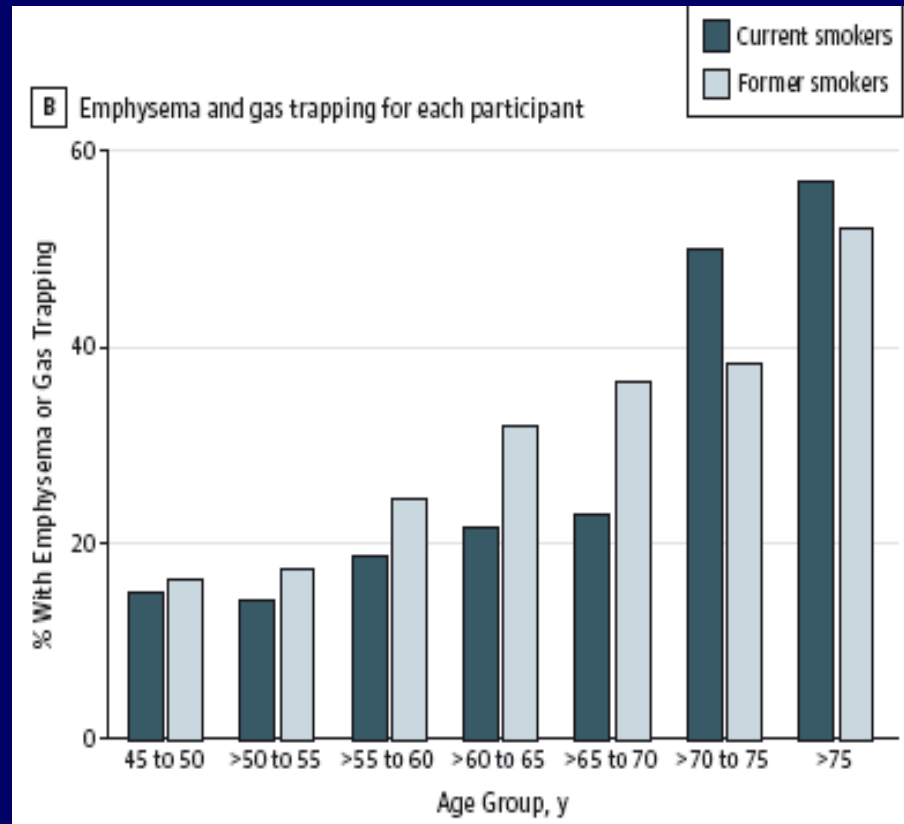


CLINICAL AND RADIOLOGIC DISEASE IN SMOKERS WITH NORMAL SPIROMETRY

Lung disease and impairments were common in smokers without spirometric COPD

Based on these results, we project that there are 35 million smokers > 55 years in the USA who may have unrecognized disease

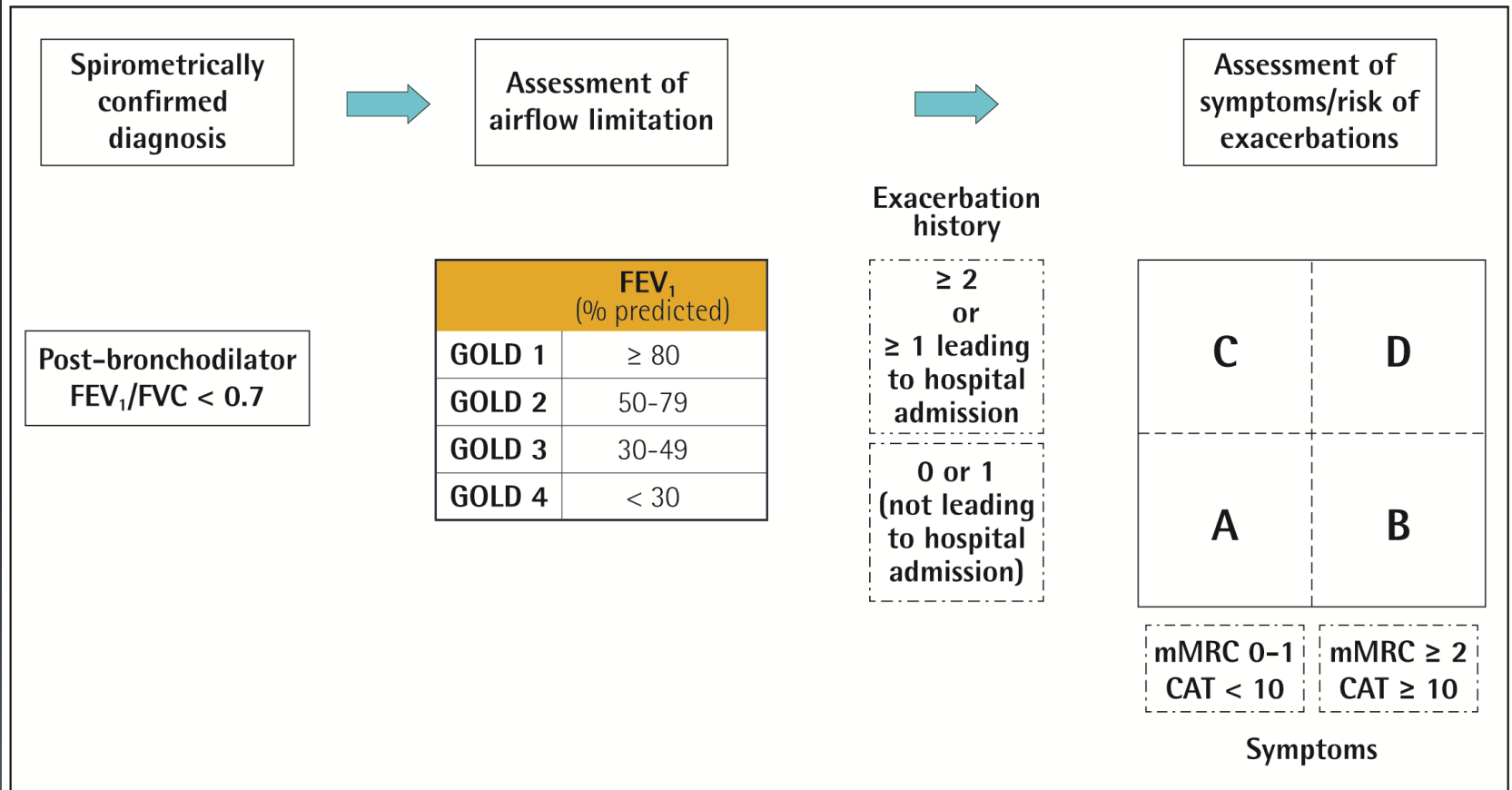
The effect of chronic smoking on the lungs and the individual is substantially underestimated when using spirometry alone.





ABCD Assessment Tool

Figure 2.4. The refined ABCD assessment tool



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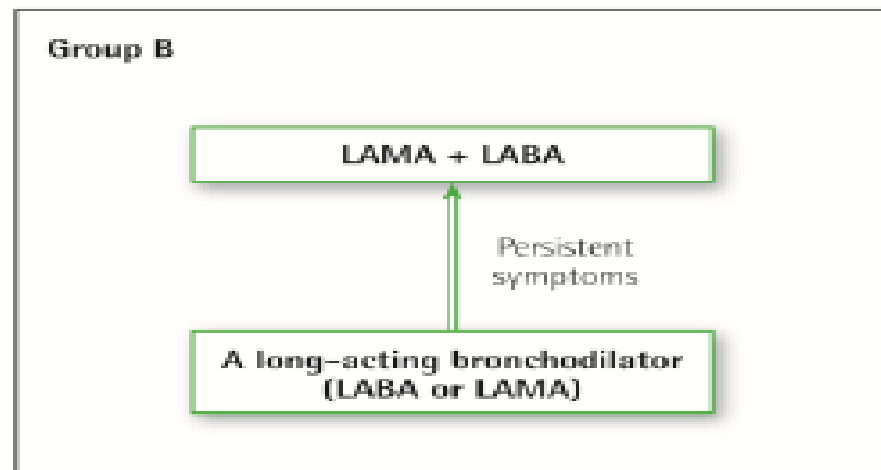
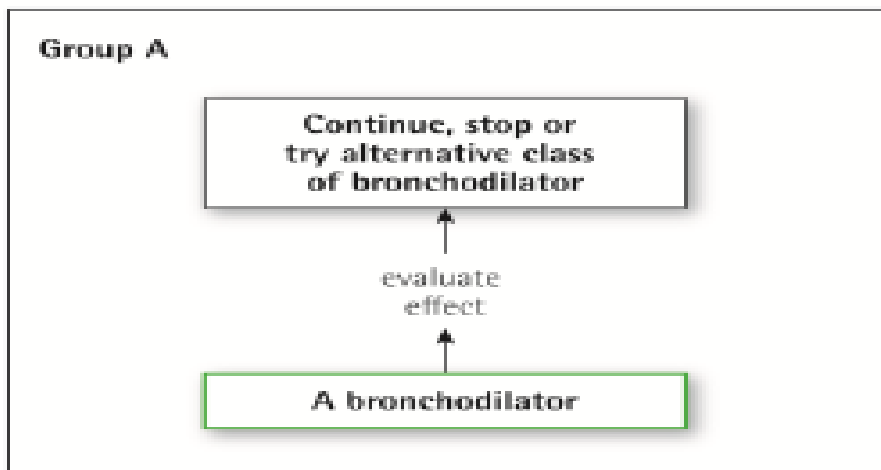
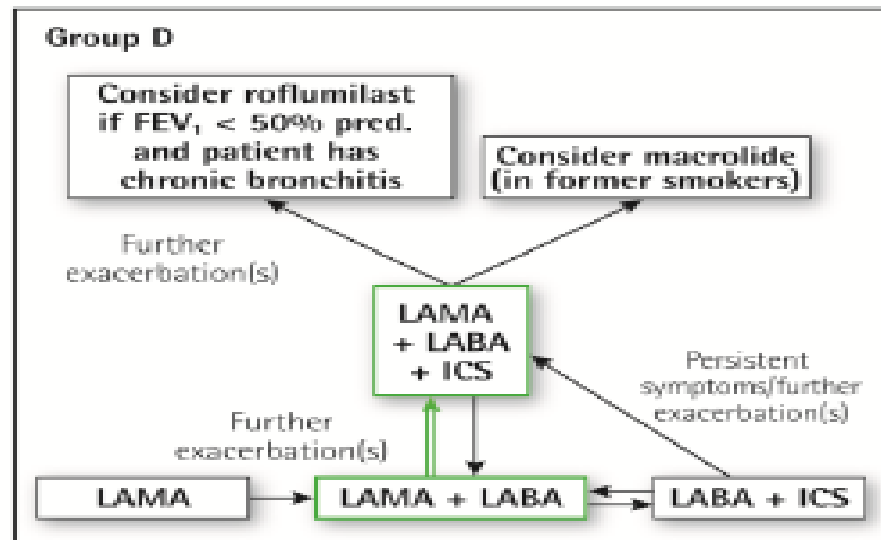
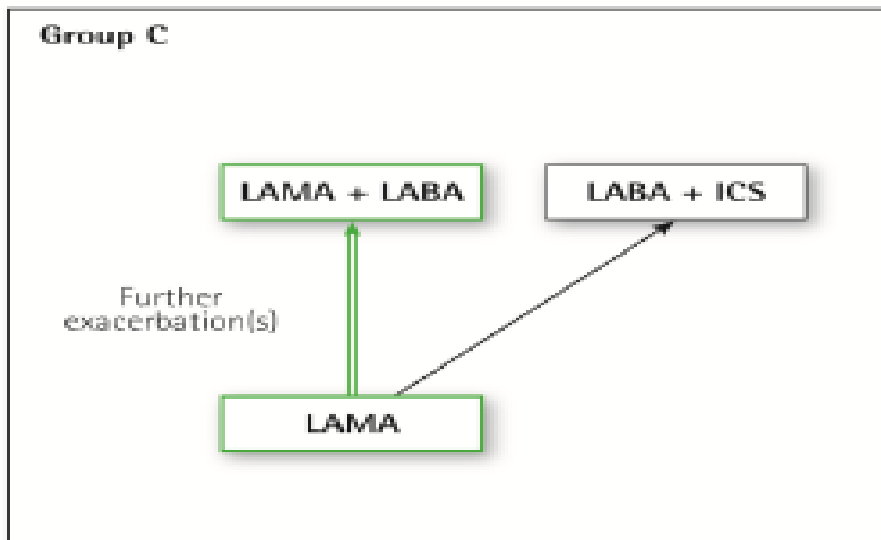
Management of of COPD

COPD as pulmonary component of multimorbidity

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GOLD 2017 THERAPEUTIC RECOMMENDATIONS



*Roflumilast not available in Australia

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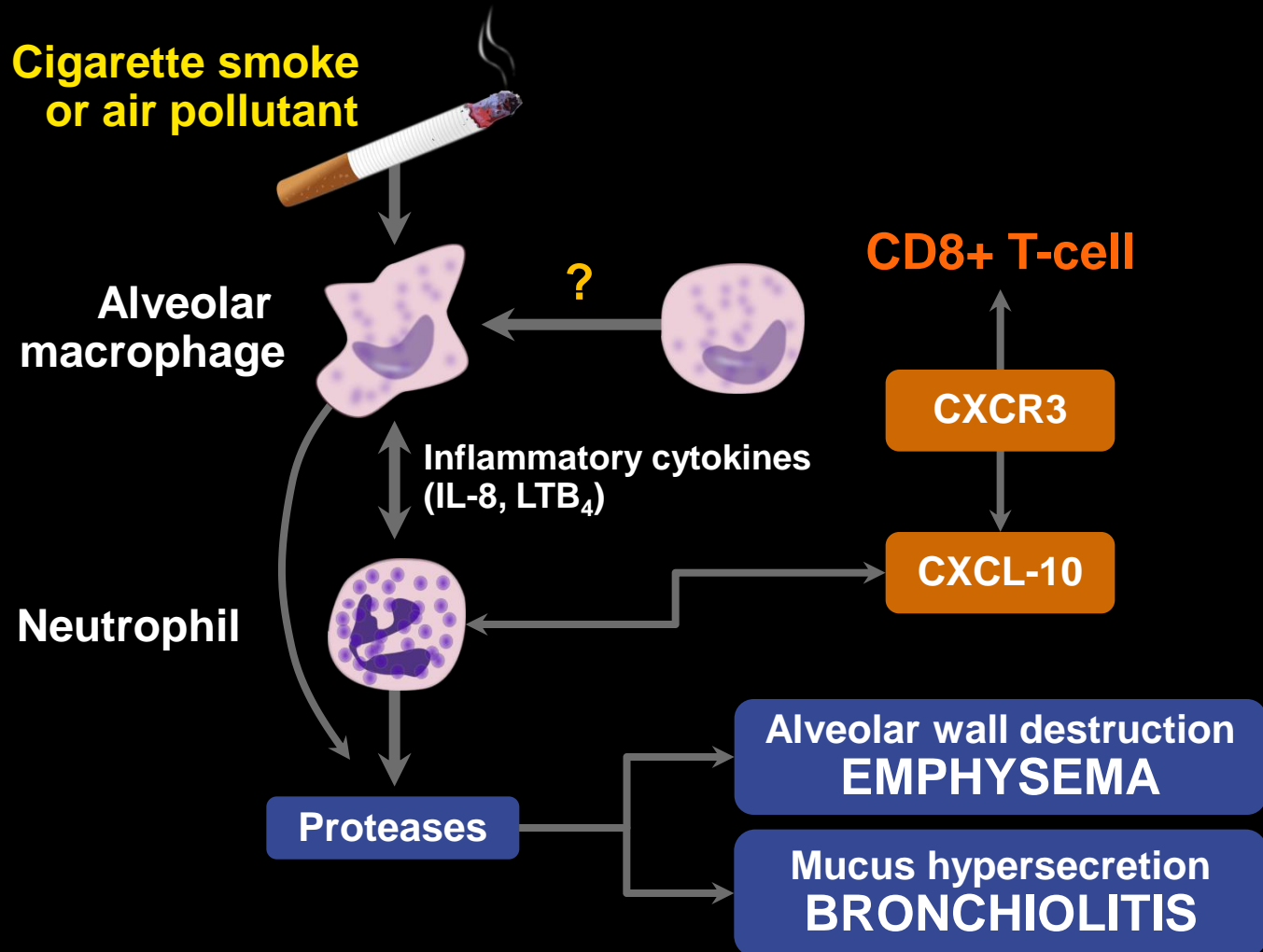
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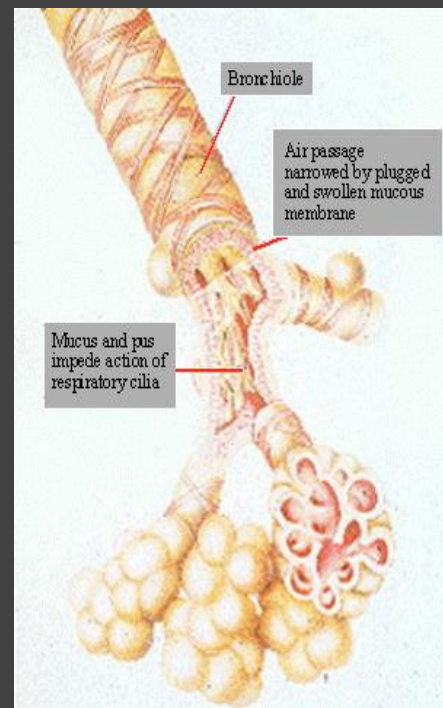
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PATHOGENESIS OF COPD

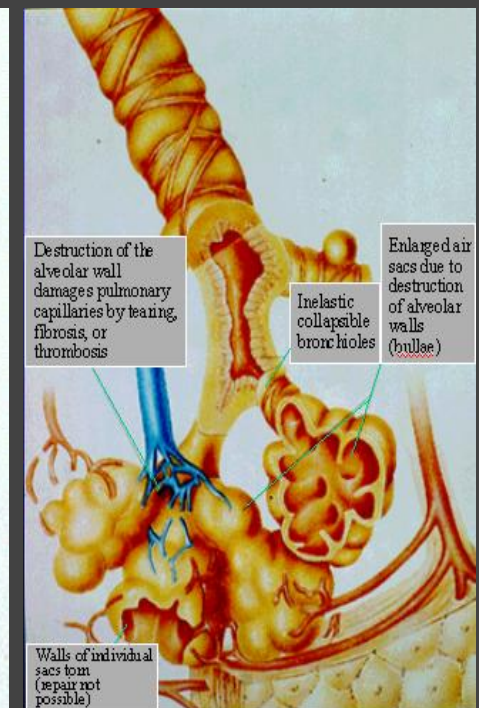


COPD

- **GOLD Definition:** the presence of airflow limitation that is not fully reversible and a history of exposure to a noxious agent / risk factor (cigarette smoke)
- **Airflow limitation**
 - Small airways
 - Remodeling, fibrosis
 - Alveoli: Emphysema
 - Destruction and enlargement of mature Airspace distal to terminal bronchioles

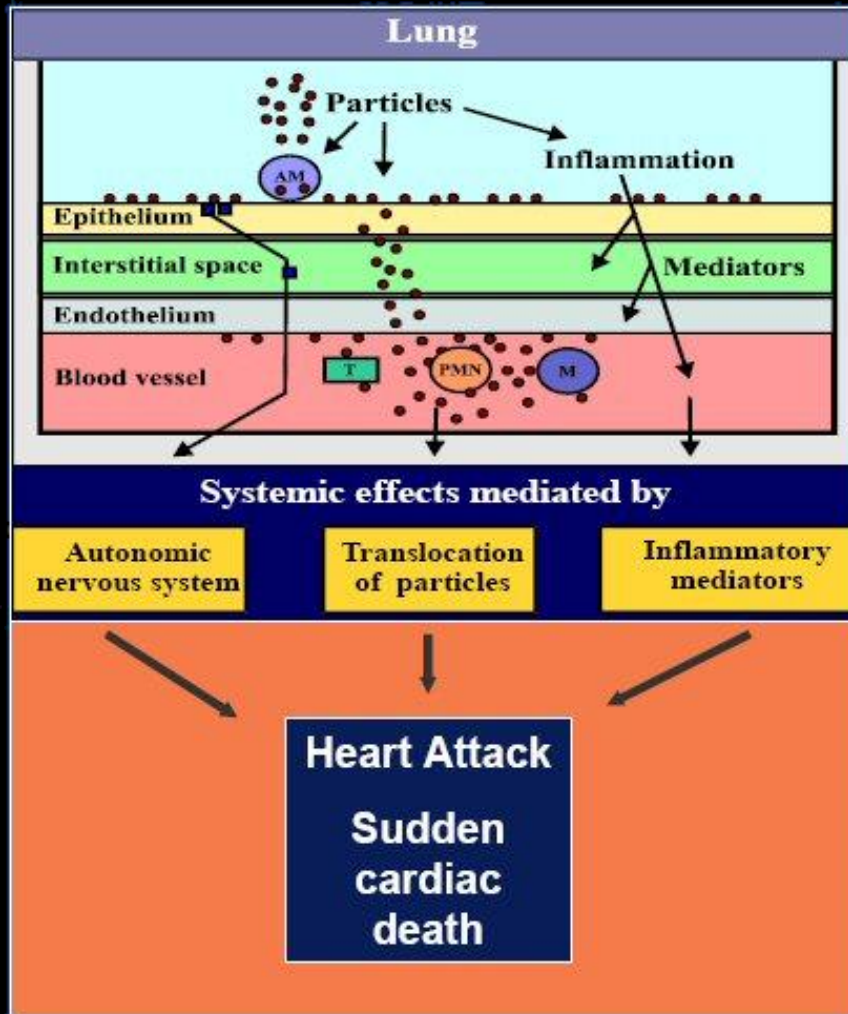


**Small Airway
Obstruction**



Emphysema

Inhaled particles: pulmonary and heart co-morbidity



Lung
Inflammation
Allergy - Sensitization
Chronic lung diseases

**Cardiovascular Effects of
Fine and Ultrafine Particles**

Courtesy of W MacNee

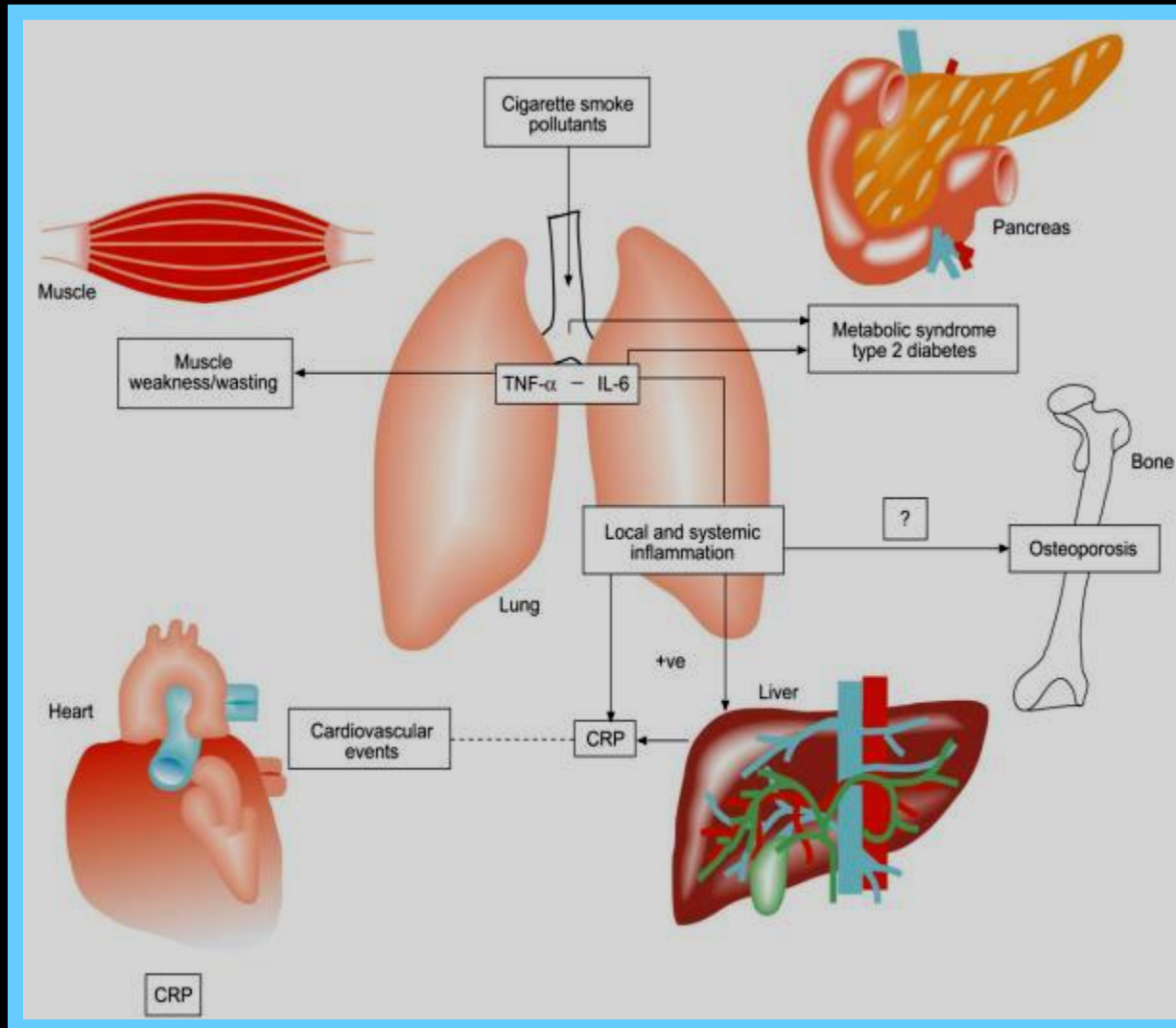
LEADING CAUSES OF DEATH IN U.S.

1. Myocardial Infarction
2. Cancer
3. Cerebrovascular Diseases
4. COPD



Cigarette Related
Diseases
Leading Causes of
Death Worldwide 2010

COMPLEX CHRONIC CO-MORBIDITIES OF COPD



ATHEROSCLEROSIS

ALZHEIMER'S DISEASE
DEMENTIA

CONGESTIVE HEART FAILURE
ISCHEMIC HEART DISEASES:
Angina Pectoris
Myocardial Infarction

INSULINE RESISTANCE
TYPE 2 DIABETES

CEREBROVASCULAR DISEASES:
Stroke
Transient Cerebral Ischemia

TNF-alfa RANTES MCP-1 IL-8 ICAM

IL-1 beta LTA TNF-alfa

IL-1 beta IL-6 IL-18 TNF-alfa

IL-1Ra IL-6 TNF-alfa IGF1

INFLAMM-AGEING

IL-1 IL-6 TNF-alfa

ANOREXIA

ANAEMIA

TNF-alfa

TNF-alfa IL-1 beta IL-6
IL-8 MCP-1

IL-1 IL-6 IL-18 TNF-alfa IFN-gamma

CHRONIC PULMONARY DISEASES:
Chronic Bronchitis
Asthma
Emphysema

AUTOIMMUNE DISEASES:
Rheumatoid Arthritis

IL-6 TNF-alfa IL-1 beta

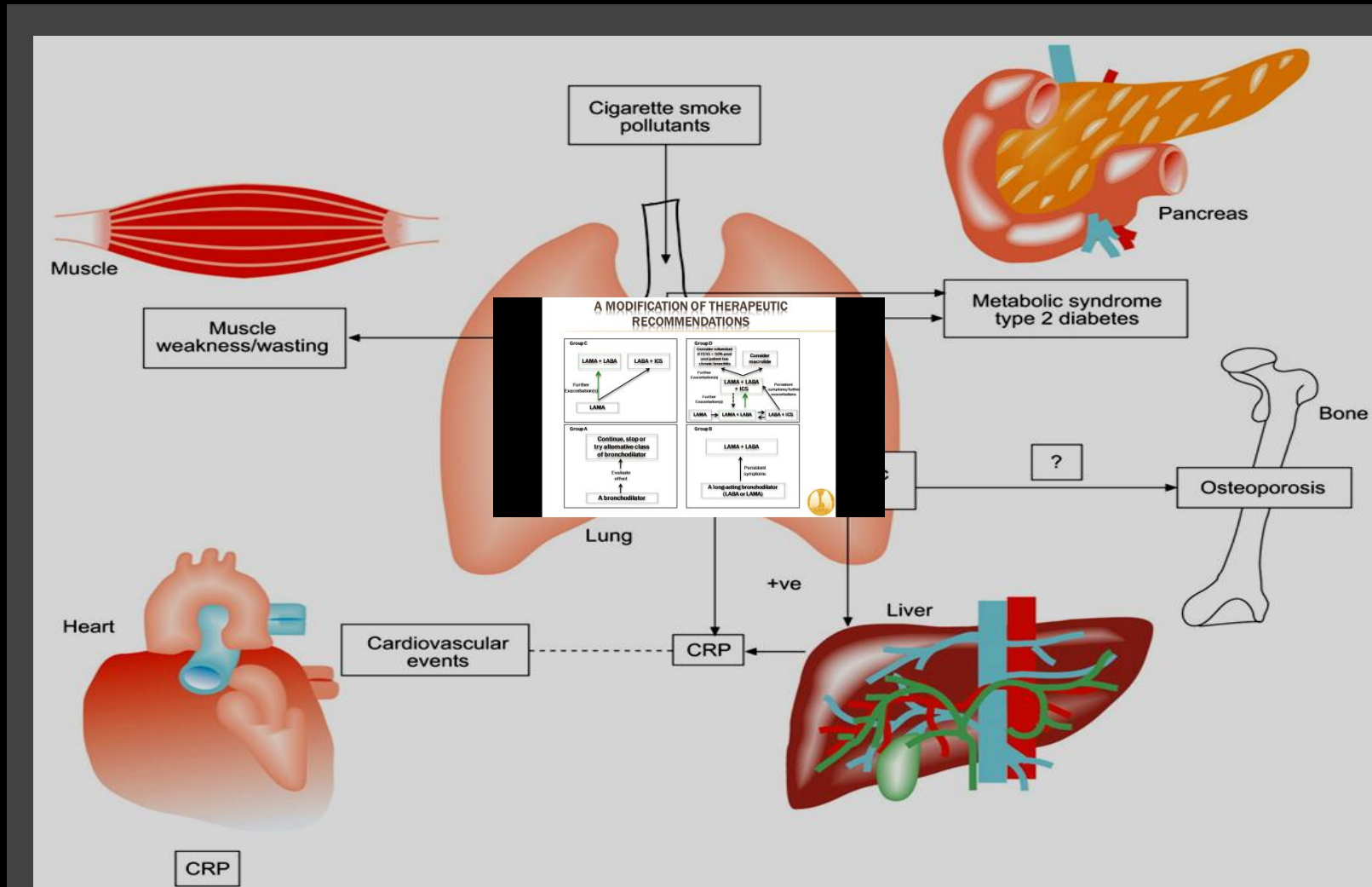
IL-6 TNF-alfa

THROMBOEMBOLIC
MANIFESTATIONS

OSTEOPOROSIS
ARTHROSIS

SARCOPENIA
DISABILITY

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C.R. 20 October 2015

- Male, 88 year
- Moderate dyspnea on exercise
 - No chronic bronchitis
 - No occupational exposure
 - Ex-smoker (20 p/y).
- Diagnosis of COPD 6 months ago in conjunction with an AECOP requiring hospitalization
- Recommended regular inhalation treatment with aerosolized bronchodilator/steroids (not taken)

HOSPITALIZED AND TREATED FOR EXCERBATION OF COPD

- **Three days admission 6 months ago, after few days of cough, sputum, dyspnea, fever**
 - **Normal chest X-Ray**
- **No fever, cyanosis, nor edema at admission**

HOSPITALIZED AND TREATED FOR EXCERBATION OF COPD

- SaO₂ 87% (no arterial blood gases available)
- CRP 8.8 mg/dL (0-0.5) - < 0.6 at discharge
- proBNP ECLIA 2515 pico gr/ml (0-194)**
- Troponin T hs 13 ng/L (50 ng/L)
- No spirometry before, during or after admission

COMORBIDITIES

- **Obese (BMI=36)**
 - **Diabetes**
- **Arterial hypertension**
 - **Dyslipidemia**
 - **Atrial fibrillation**
- **Ischaemic heart disease**
- **Heart failure with increased PaP (55mmHg)**
 - **Benign Prostatic Hypertrophy**

TREATMENT

- **Metformin**
- **Olmesartan**
- **Medoximil**
- **Larcanedipin**
- **Carvedilol**
- **Finasteride**
- **Silodosin**
- **Warfain**

C.R. 20 October 2015

Since 1 year:

- Moderate progressive dyspnoea on exercise (mMRC2)
 - Dyspnea in the early morning
 - Occasional cough, no purulent sputum

Reduced fremitus, in/inspiratory ronchi, bilateral basal in/inspiratory crackles

C.R. 20 October 2015

SPIROMETRY

(not diagnostic for COPD)

- **FEV₁: 1.37 L (50% predicted)**
 - Post-BD FEV₁=1.40 L (+2%)
 - FVC: 2.05 L 54% predicted)
 - **FEV₁/FVC: 68 %**
- RV: 2.95 L (104 % predicted)
 - **RV/TLC: 59 %**
- 6MWT: 280 m, SaO₂ 95%-88%

SIX MINUTE WALKING TEST (6MWT)

SaO₂ pre: 95%

SaO₂ post: 88%

PA pre 140/85 mm Hg

PA post 160/80 mm Hg

FC pre 70/min

FC post 85/min

Meters: 280

Meters: ≥ 350	Good
250–349	Mild impairment
150–249	Moderate
≤ 149	Severe

CONCLUSIONS AND RECOMMENDATIONS AT FIRST VISIT

- Tiotropium 2.5 ug 2 inhalation in the evening
- Recommended rehabilitation, including weight reduction
 - Confirmed ongoing treatment of comorbidities
 - Weekly telephone contact
 - Hematochemical exams + chest X ray
 - Clinical control at 1 month

CONCLUSIONS AND RECOMMENDATIONS AT FOLLOW UP

- Tiotropium 2 inhalation in the evening+
- Formoterol/budesonide combination bid
- Rehabilitation, weight reduction, exercise
- Confirmed ongoing treatment of comorbidities
 - Montly telephone contacts
 - Clinical control at 3 months

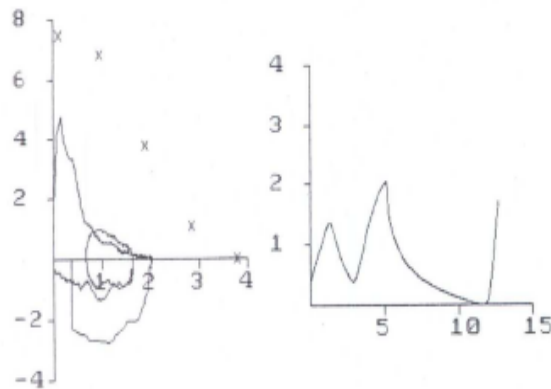
GLOBAL STRATEGY FOR DIAGNOSIS, MANAGEMENT AND PREVENTION OF COPD DEFINITION OF COPD 2016



COPD, a disease, is characterized by persistent airflow limitation, ie $FEV_1/FVC < 70\%$

		oss.	teorici	%	lim.
VC	l	2.45	3.93	62	3.01-4.85
FVC	l	2.22	3.79	59	2.79-4.79
FEV1	l	1.21	2.74	44	1.90-3.58
FEV1/VC	%	49.39	71.46	69	59.7-83.3
FEV1/FVC	%	54.50			
FIV1	l	2.02			
FEF25-75	l/s	0.55	2.43	22	0.72-4.14
PEF	l/s	4.83	7.49	64	5.50-9.48
MEF75	l/s	2.35	6.86	34	4.05-9.67
MEF50	l/s	0.59	3.79	16	1.62-5.96
MEF25	l/s	0.22	1.09	20	-0.19-2.37
IVC	l	2.45	3.93	62	3.01-4.85

Teorici di Riferimento: Polgar 71 (6<eta'<18) ERS93 (18<=eta')



REALITY

patient was being treated with

Tiotropium 2 inhalations in the morning

Formoterol/budesonide combination bid

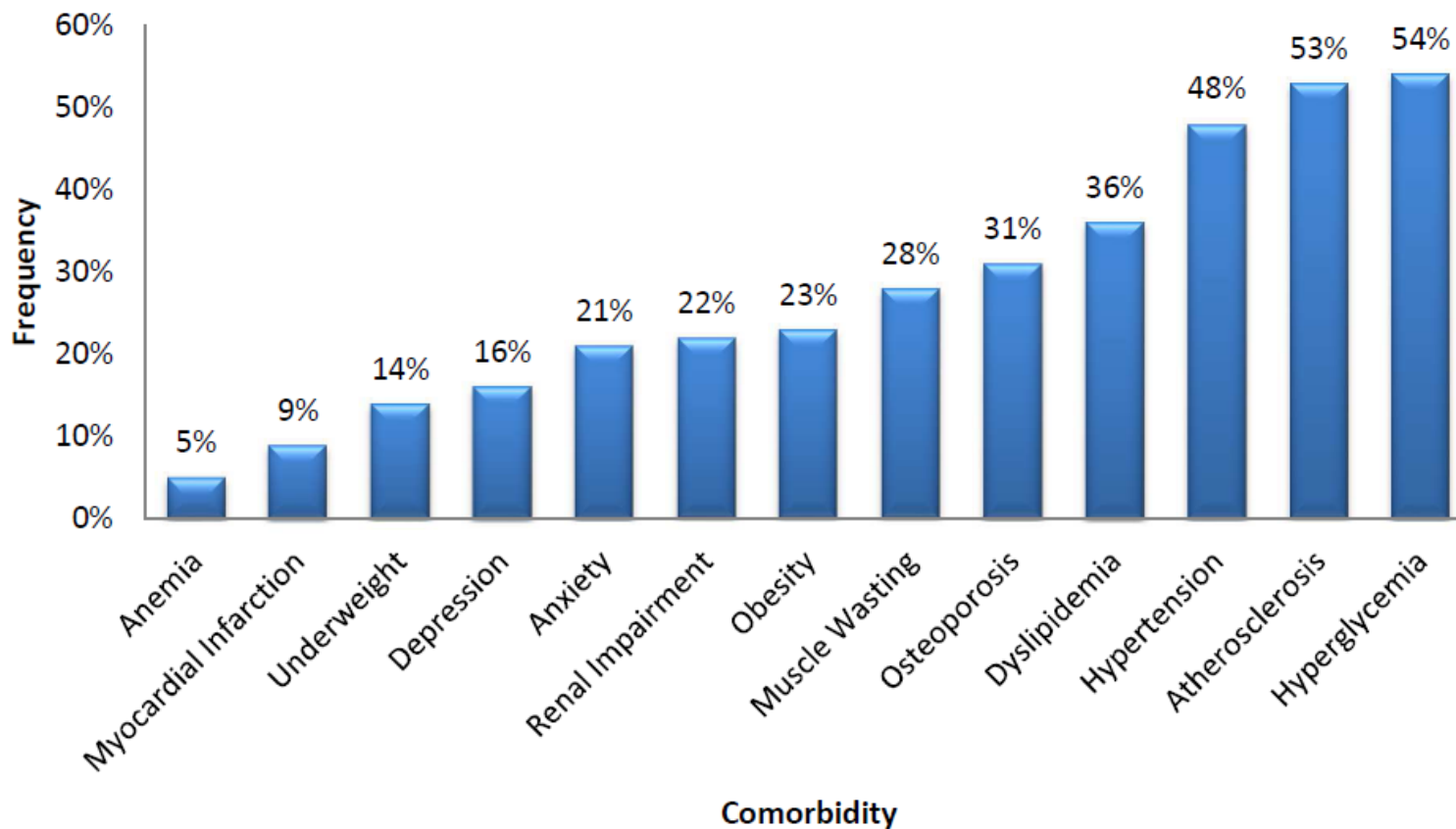
Aspirin 75 mg 1 tablet OD

Valsartan 160 mg 1 cp al mattino

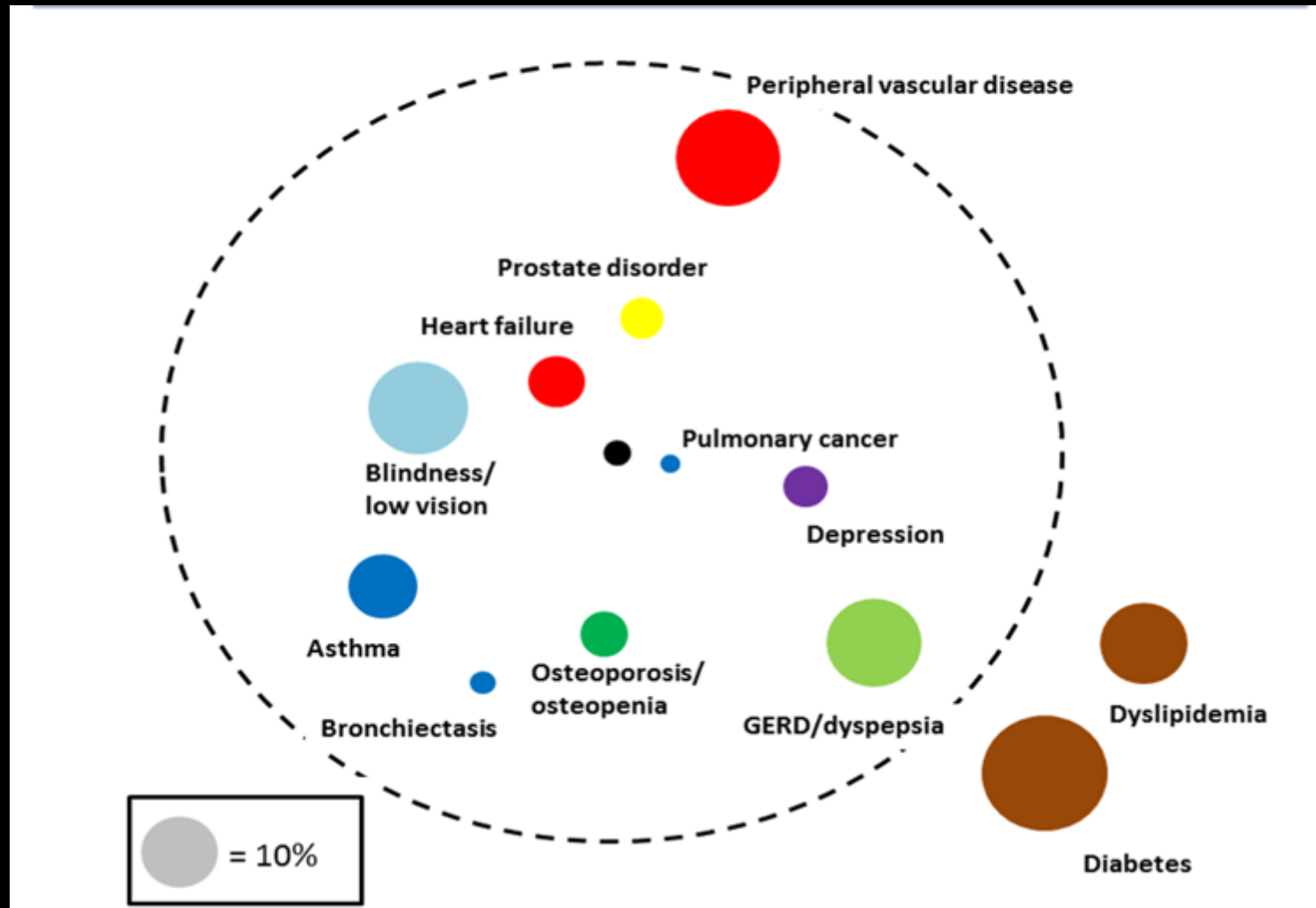
O₂ 1 L/min during exercise

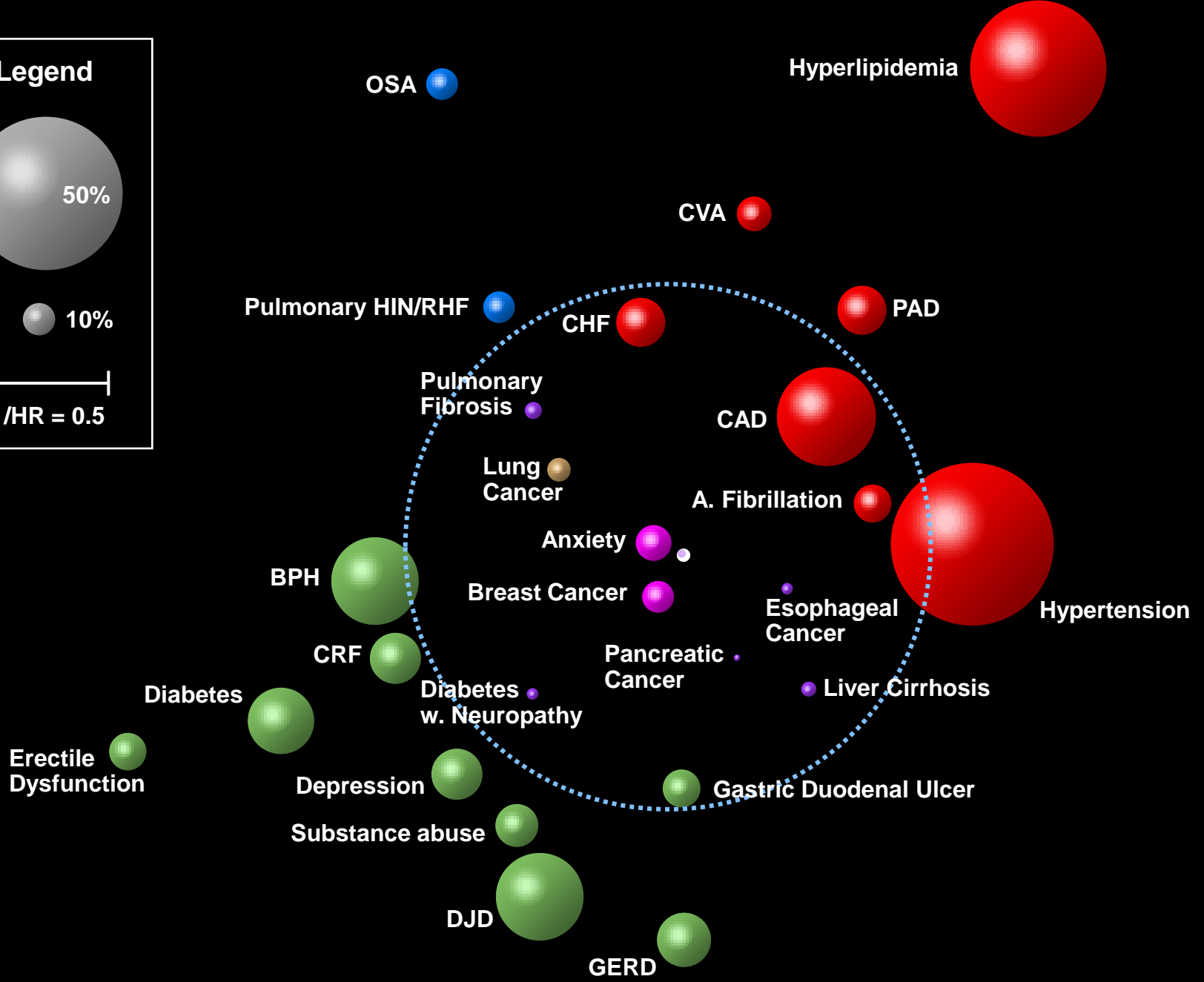
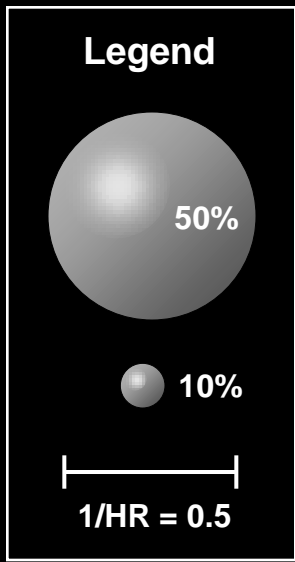
No rehabilitation

FREQUENCIES OF OBJECTIFIED COMORBIDITIES



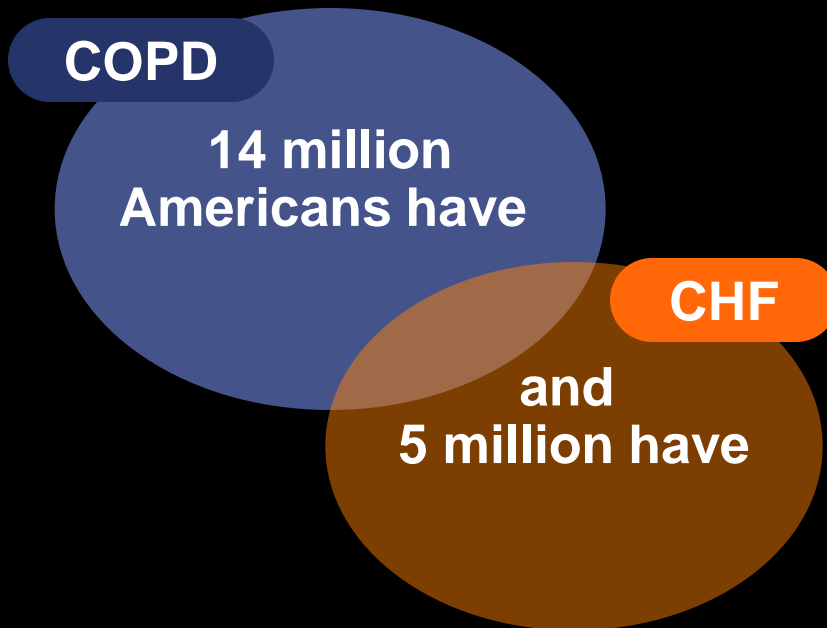
ASSOCIATION BETWEEN COMORBIDITIES OF COPD AND RISK OF > 2 EXACERBATIONS/YEAR





COPD vs CHF

- Up to 1\5 of elderly pts. with COPD have CHF
- Up to 1\3 of elderly pts. with CHF have COPD



The risk ratio of developing HF in COPD pts is 4.5

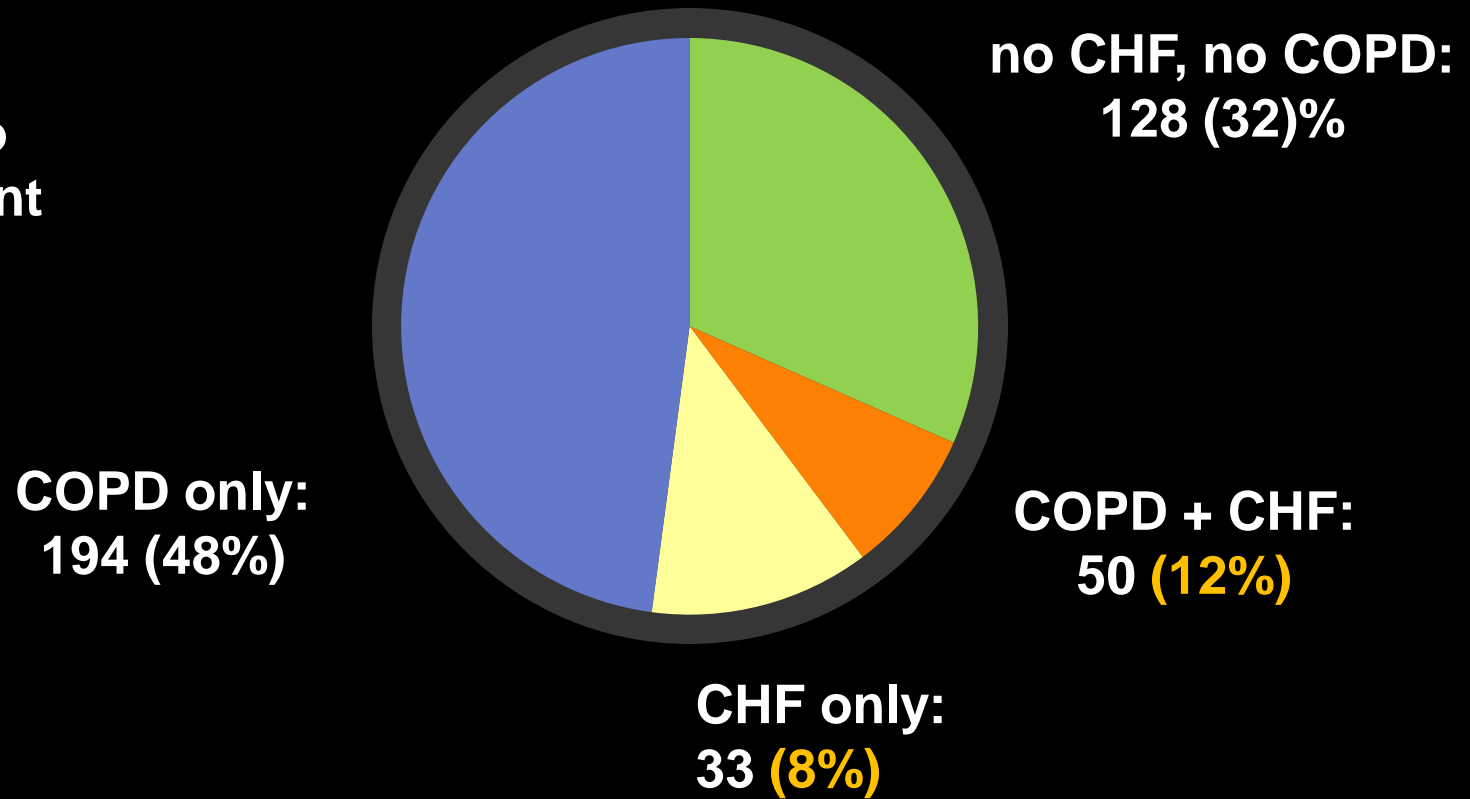
The rate-adjusted hospital prevalence of CHF is 3 times greater among pts. discharged with a diagnosis of COPD compared with patients discharged without mention of COPD

UNRECOGNIZED HEART FAILURE IN ELDERLY PATIENTS WITH STABLE COPD

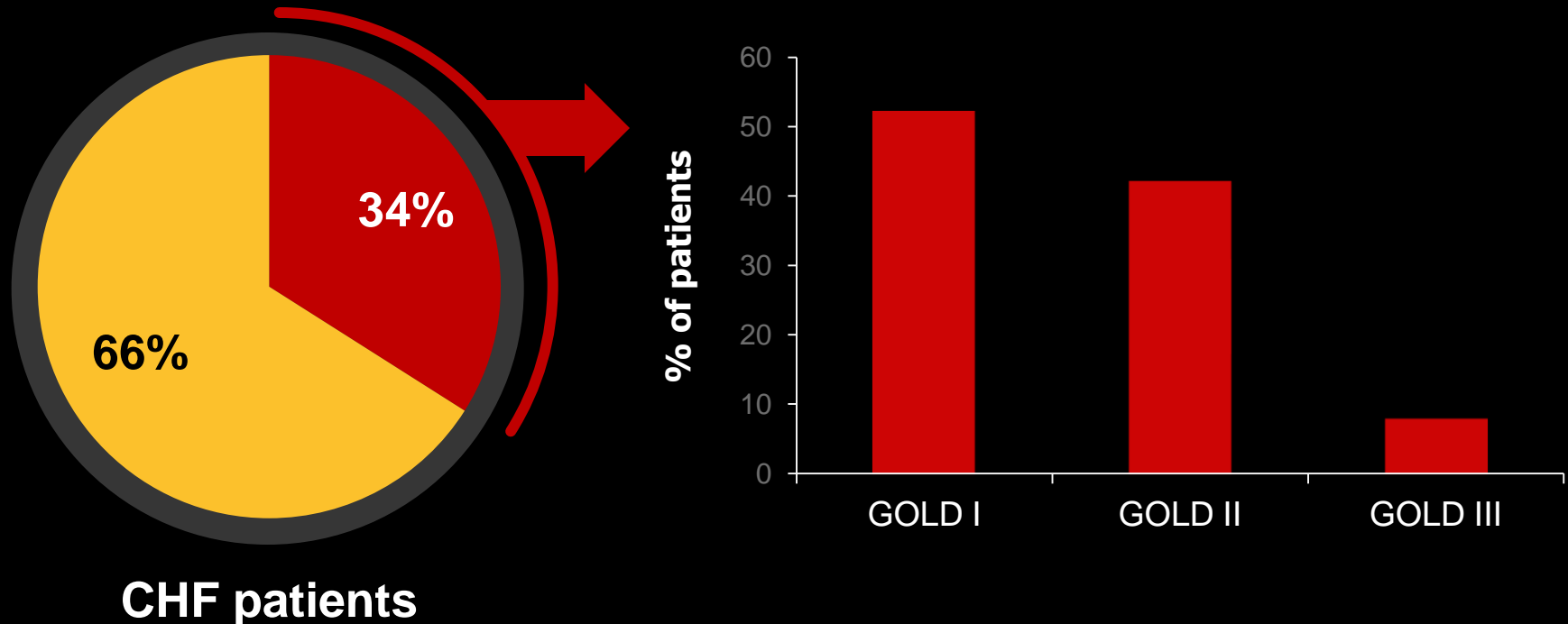
405 elderly with a diagnosis of COPD, but no CHF by GPs



Echo + spiro reassessment

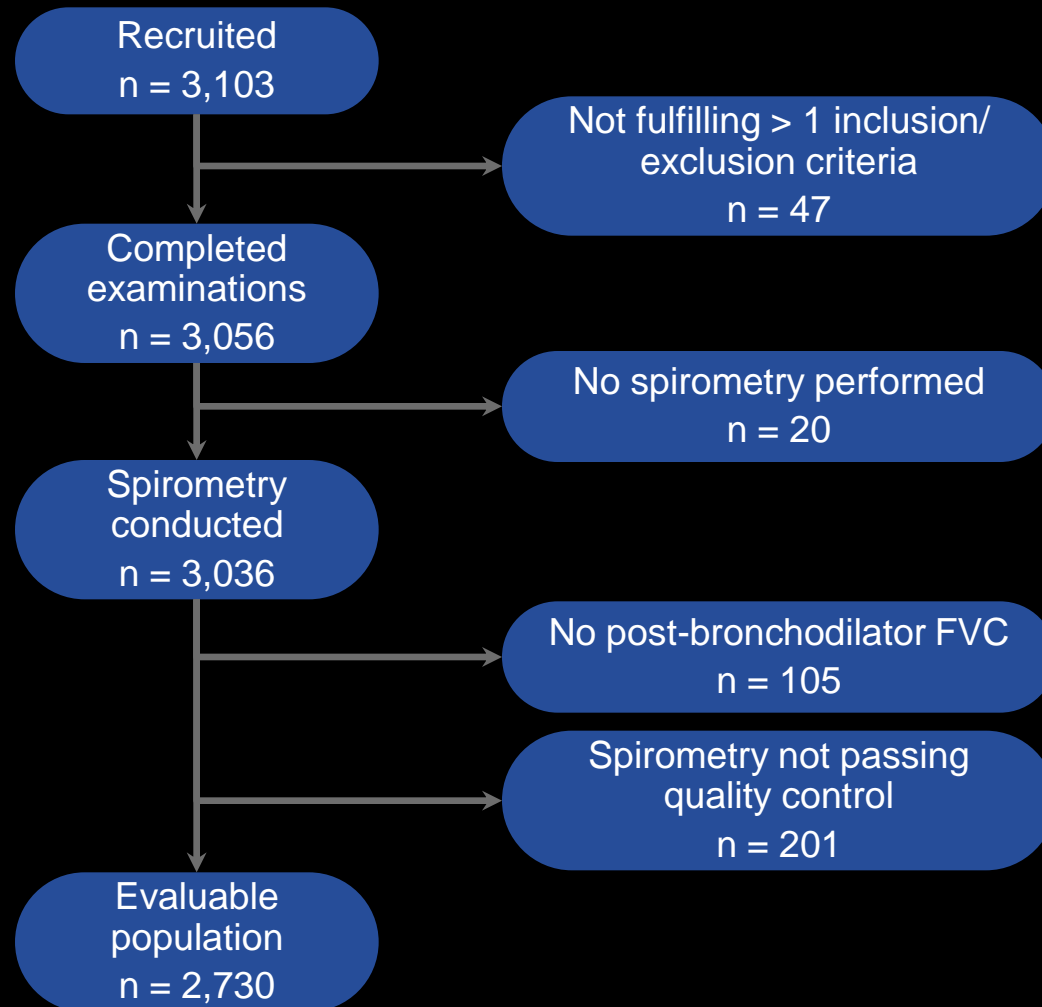


ECHOCARDIOGRAPHY, SPIROMETRY, AND SYSTEMIC ACUTE-PHASE INFLAMMATORY PROTEINS IN SMOKERS WITH COPD OR CHF: AN OBSERVATIONAL STUDY

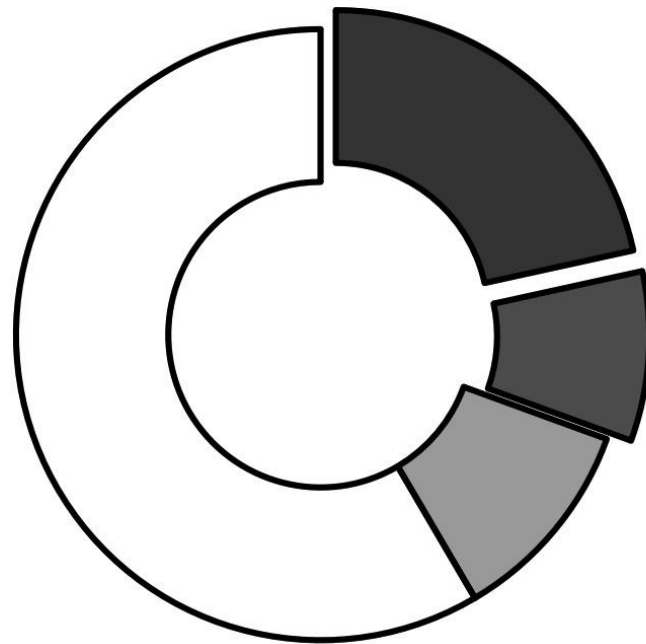


Only 10 of 42 (<25%) pts. with both CHF and COPD were aware of airflow limitation and properly treated

LUNG FUNCTION ABNORMALITIES IN PATIENTS WITH ISCHEMIC HEART DISEASES

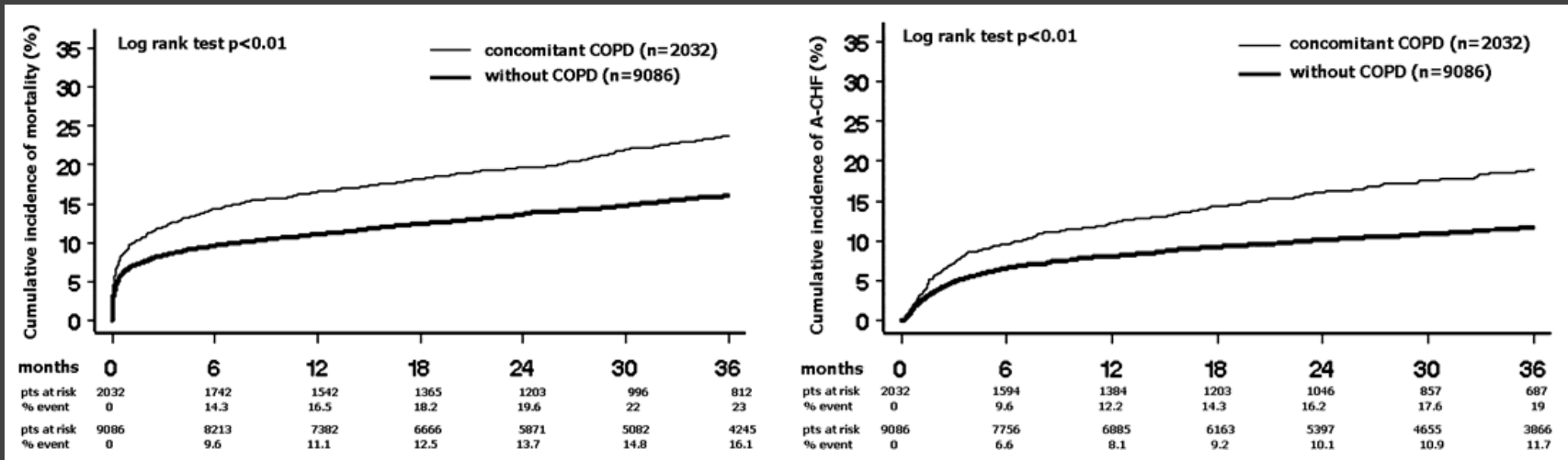


LUNG FUNCTION ABNORMALITIES IN PATIENTS WITH ISCHEMIC HEART DISEASES



- Normal lung function (58.5%)
- Undiagnosed airflow limitation (21.5%)
- Previously diagnosed airflow limitation (9.0%)
- Restrictive lung function (11.0%)

IMPACT OF COPD ON LONG-TERM OUTCOME AFTER STEMI RECEIVING PRIMARY PCI



As compared to patients without COPD, **patients with STEMI and concomitant COPD** are at **greater risk for**

- death (25% vs 16.5%)
- hospital readmissions due to cardiovascular causes (recurrent MI, HF and bleedings)

Campo G. et al. Chest 2013;144:750-7

FROM COMORBIDITIES TO MULTIMORBIDITY

	% RENAL IMPAIRMENT	% ANEMIA	% HYPERTENSION	% OBESITY	% UNDERWEIGHT	% MUSCLE WASTING	% HYPERGLYCEMIA	% DYSLIPIDEMIA	% OSTEOPOROSIS	% ANXIETY	% DEPRESSION	% ATHEROSCLEROSIS	% MYOCARDIAL INFARCTION
RENAL IMPAIRMENT (n= 47)		6	49	9	32	45	43	36	38	13	11	47	11
ANEMIA (n= 11)	27		45	36	9	18	64	18	36	18	18	73	0
HYPERTENSION (n= 103)	22	5		27	12	23	58	35	26	20	16	62	12
OBESITY (n= 50)	8	8	56		0	0	72	42	18	12	18	72	4
UNDERWEIGHT (n= 30)	50	3	40	0		93	37	27	57	21	4	17	3
MUSCLE WASTING (n= 60)	35	3	40	0	47		42	22	55	33	14	29	9
HYPERGLYCEMIA (n= 116)	17	6	52	31	10	22		41	29	22	20	55	12
DYSLIPIDEMIA (n= 77)	22	3	47	27	10	17	62		20	14	18	63	11
OSTEOPOROSIS (n= 66)	27	6	41	14	26	50	52	23		29	23	49	13
ANXIETY (n= 43)	14	5	47	14	14	44	58	26	42		40	46	12
DEPRESSION (n= 33)	15	6	49	27	3	24	67	42	42	52		70	19
ATHEROSCLEROSIS (n= 106)	20	8	57	31	5	15	57	43	28	17	21		14
MYOCARDIAL INFARCTION (n= 19)	26	0	63	11	5	26	68	42	42	29	35	75	

CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND CARDIAC DISEASES: AN URGENT NEED FOR INTEGRATED CARE

The aim of this review was to summarize the evidence on the relationship between COPD and the three most frequent and important cardiac comorbidities in COPD patients – i.e.,

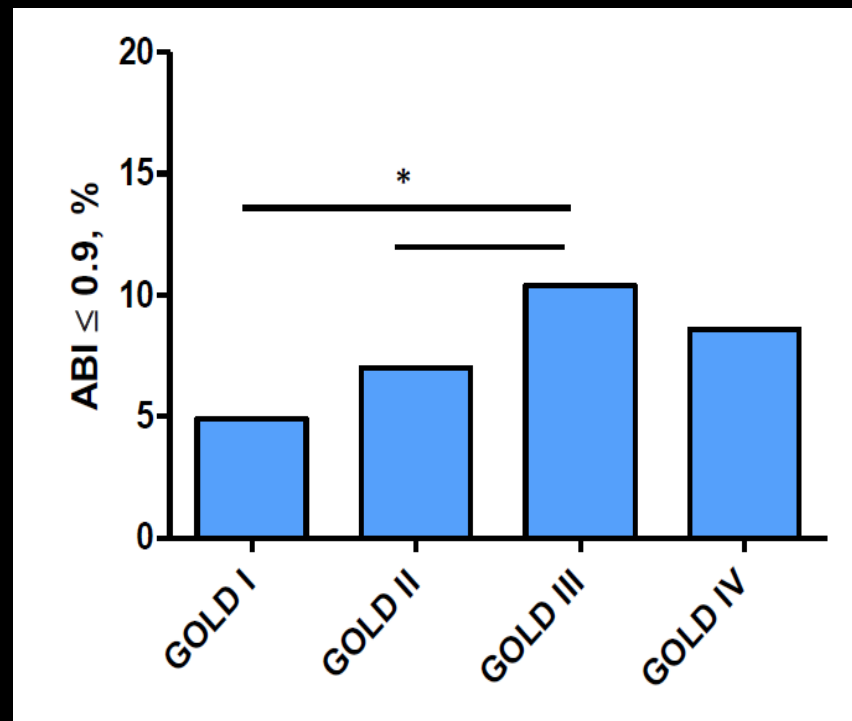
ISCHAEMIC HEART DISEASE, HEART FAILURE, AND ATRIAL FIBRILLATION

We believe that these cardiac disorders should always be searched for in COPD patients, and we provide up-to-date practical indications for treatment and management of patients with COPD and heart diseases

PERIPHERAL ARTERY DISEASE AND ITS CLINICAL RELEVANCE IN PATIENTS WITH COPD IN THE COSYCONET STUDY

In a large cohort of patients with COPD, 8.8% were diagnosed with PAD which is higher than the prevalence in non-COPD controls

PAD was associated with a clinically relevant reduction in functional capacity and health status



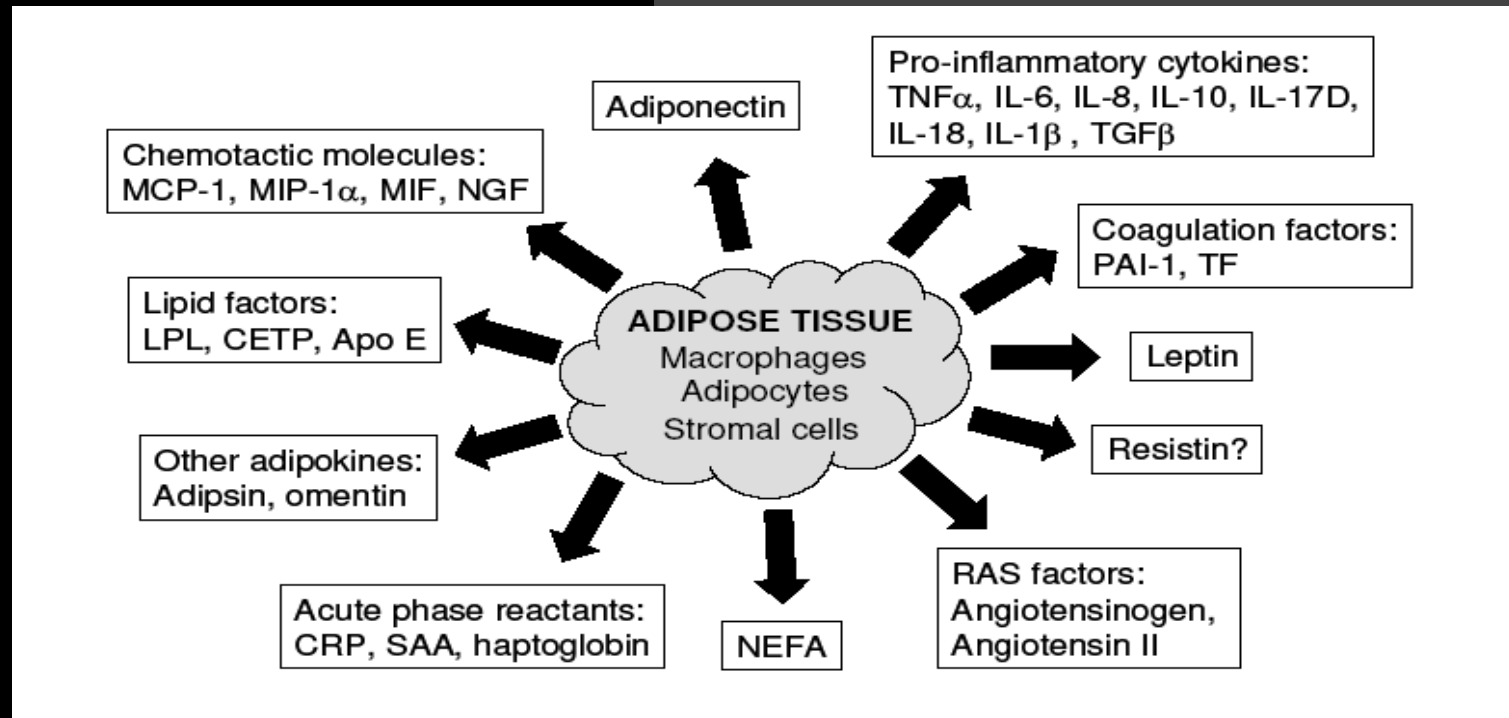
OBESITY IS ASSOCIATED WITH INCREASED MORBIDITY IN MODERATE TO SEVERE COPD

Obesity is prevalent (> 35%) among individuals with COPD and is associated with worse COPD-related outcomes, ranging from QOL and dyspnea to 6MWD and severe AECOPD

These associations were strengthened when obesity was analyzed as a dose dependent response

Obesity in patients with COPD may contribute to a worse COPD-related course

METABOLIC SYNDROME IS FREQUENT IN PATIENTS WITH COPD



OSA AND RISK OF CARDIOVASCULAR DISEASES

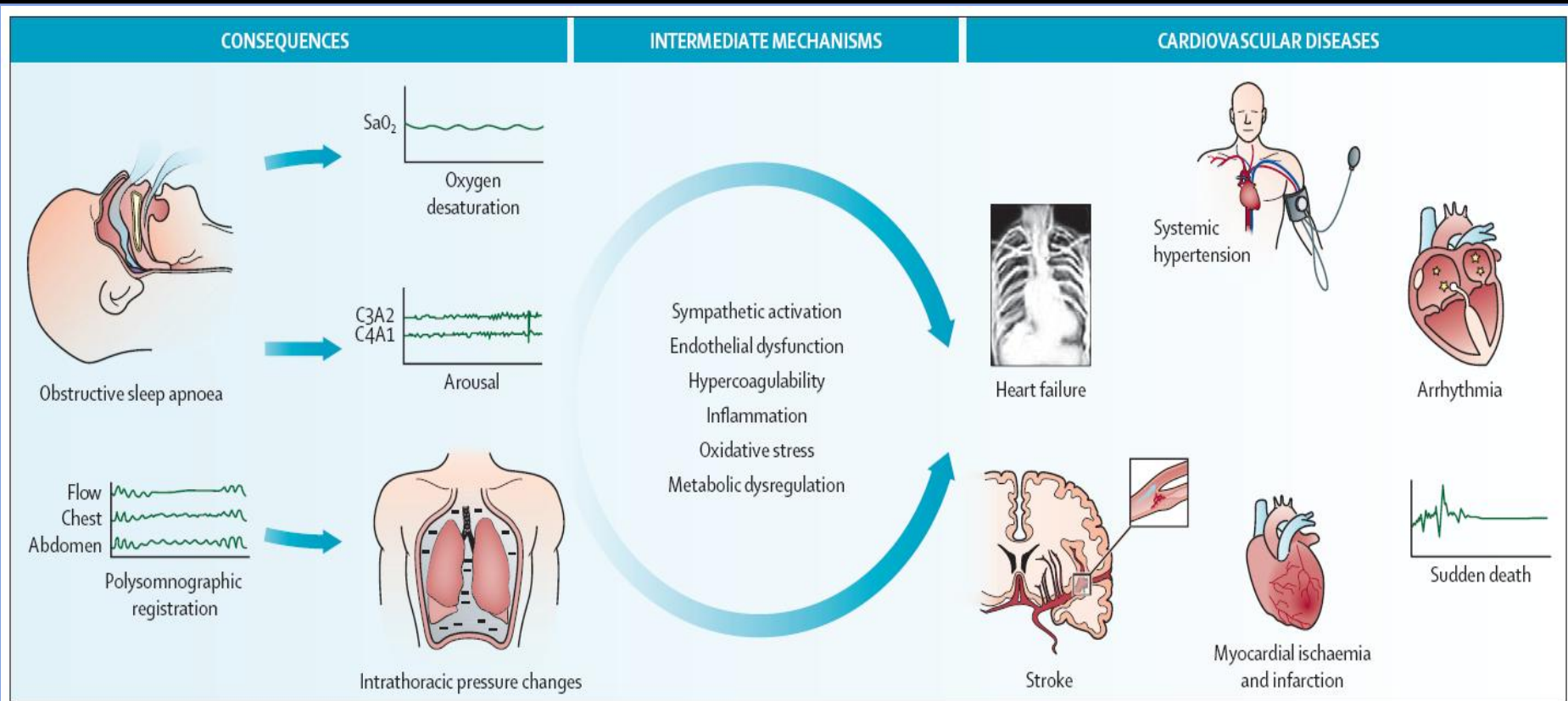
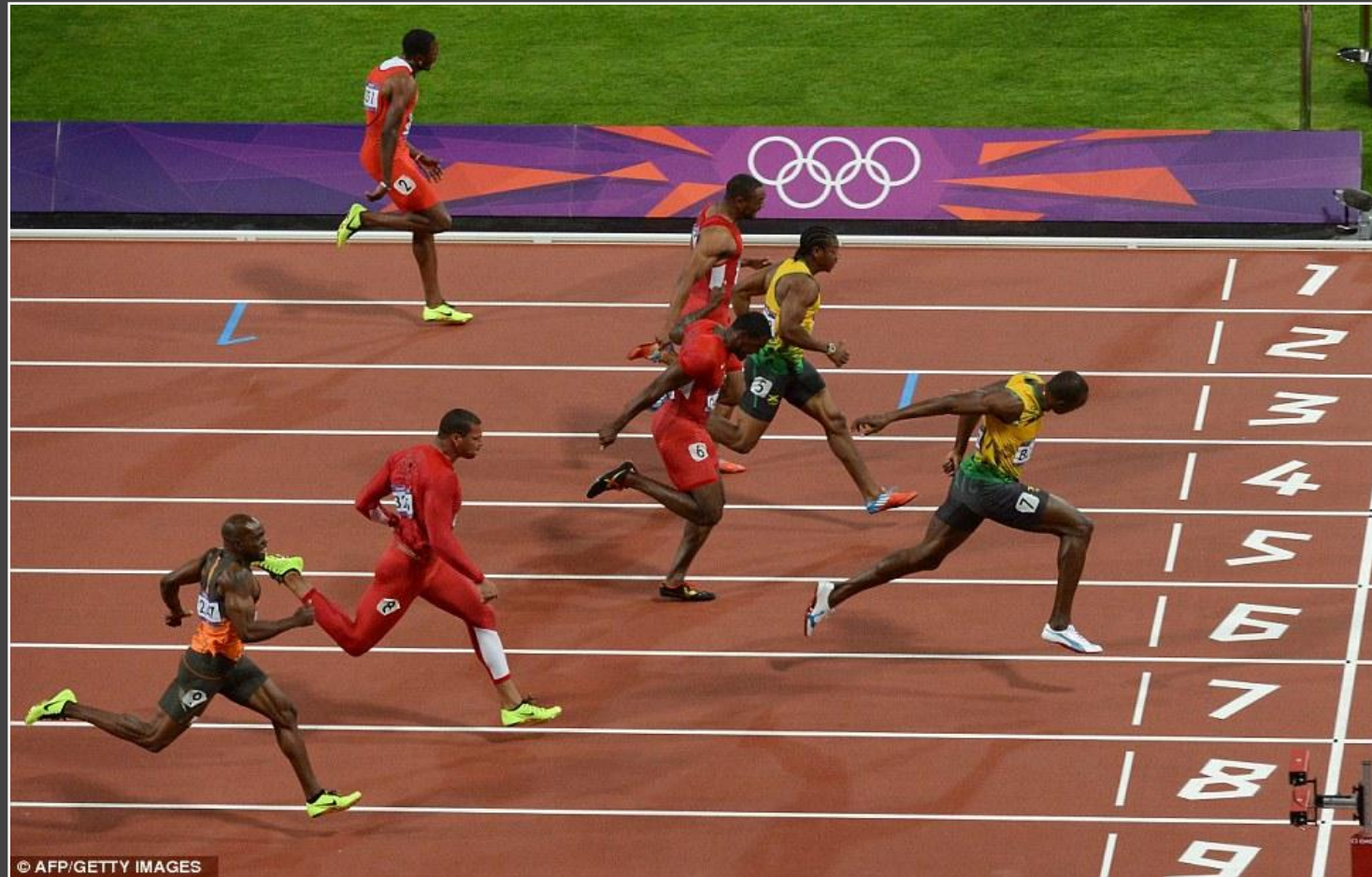


Figure: Obstructive sleep apnoea consequences and intermediate mechanisms that potentially contribute to risk of cardiovascular disease

The events associated with collapse of the upper airway lead to brain arousal, intrathoracic pressure changes, and hypoxaemia and reoxygenation. Several intermediate mechanisms link obstructive sleep apnoea with the initiation and progression of cardiovascular diseases. SaO₂=oxygen saturation. C3A2 and C4A1=electroencephalographic channels.

SIMULTANEOUS DEVELOPMENT OF CHRONIC DISEASES



Courtesy of K.F. Rabe, 2014

Multimorbidity: clinical assessment and management

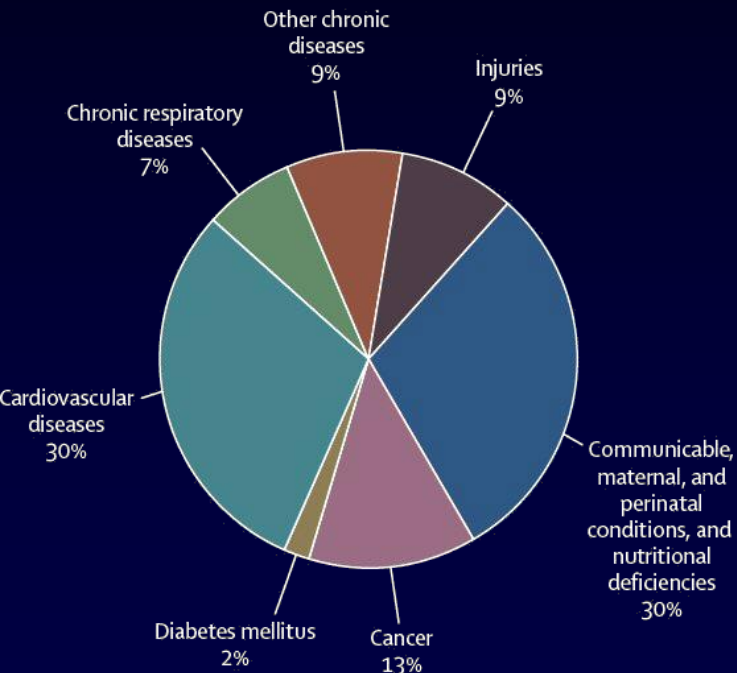
**Multimorbidity: assessment, prioritisation and
management of care for people with commonly
occurring multimorbidity**

NICE guideline

Methods, evidence and recommendations

31 March – 12 May 2016

Chronic diseases represent a huge proportion of human illness



58 million deaths in 2005:

- **Cardiovascular disease** 30%
- **Cancer** 13%
- **Chronic respiratory diseases** 7%
- **Diabetes** 2%

NONCOMMUNICABLE DISEASES

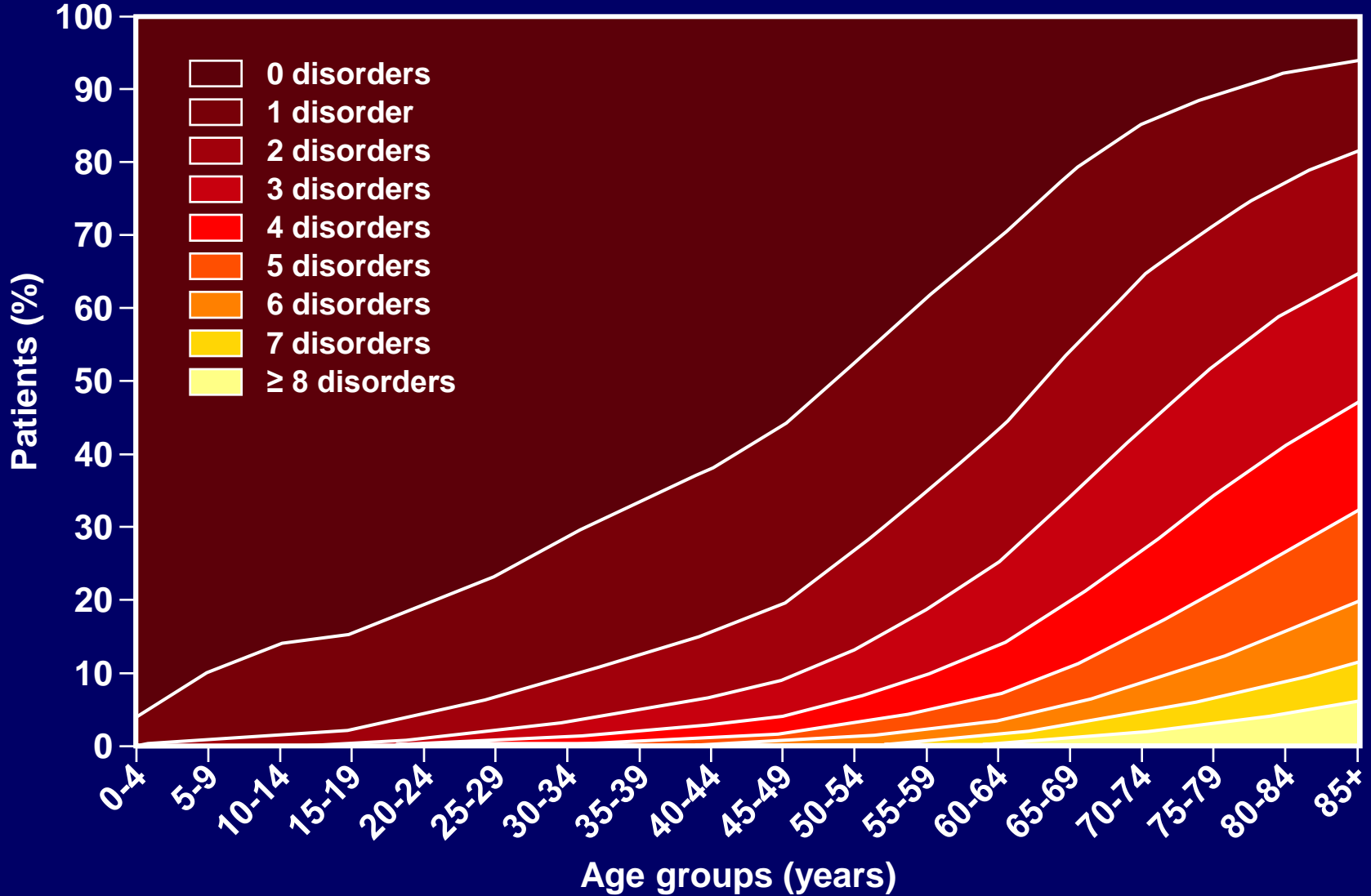
Noncommunicable diseases will be the predominant global public health challenge of the 21st century

Prevention of premature deaths due to noncommunicable diseases and reduction of related health care costs will be the main goals of health policy.

Improving the detection and treatment of noncommunicable diseases and preventing complications and catastrophic events will be the major goals of clinical medicine.

Hunter DJ and Reddy KS. N Engl J Med 2013; 369:1336-1343

NUMBER OF CHRONIC DISORDERS BY AGE-GROUP



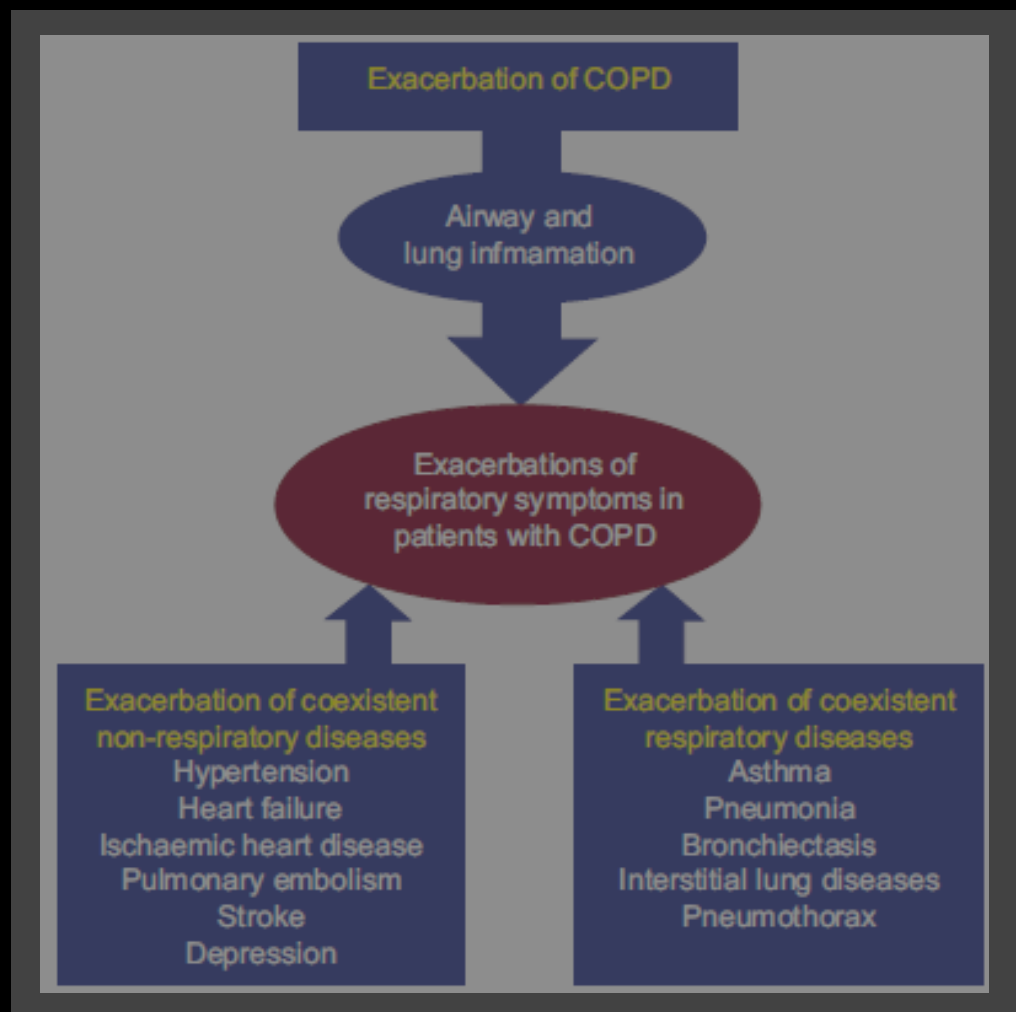
Barnett, K et al, 2012 Jul 7;380(9836):37-43

EPIDEMIOLOGY OF MULTIMORBIDITY AND IMPLICATIONS FOR HEALTH CARE, RESEARCH, AND MEDICAL EDUCATION: A CROSS-SECTIONAL STUDY

Our findings challenge the single-disease framework by which most health care, medical research, and medical education is configured. A complementary strategy is needed, supporting generalist clinicians to provide personalised, comprehensive continuity of care, especially in socioeconomically deprived areas.

Barnett, K et al, 2012 Jul 7;380(9836):37-43

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



*Beghé B, Verduri A, Roca M and Fabbri LM. Eur Respir J 2013; 41: 993-5
Roca M, Verduri A, Clini EM, Fabbri LM and Beghé B. Eur J Clin Invest, 2013;43:510*

G.Z.L.

- **Male, 72 year/old**
- **Lawyer**
- **Very heavy smoker (165 p/y).**
- **Very severe airflow limitation, GOLD D**
- **Arterial hypertension**
- **Treatment: lisinopril, frusemide, beclometasone/formoterol, tiotropium**

CLINICAL HISTORY-1

Since 5-6 days:

- Increasing dyspnoea
- cough and purulent sputum without chest pain
- fever (temp 37.8 ° C)

CLINICAL HISTORY-2

BP:180/80mmHg

HR 90/min

SpO2 89%

RR 25/min

BT 37.5° C

- **Dyspnoea, fatigue, use of accessory muscles**
- **Chest auscultation: reduced breath sounds, diffuse expiratory wheezing**
- **Sinus tachycardia (110 bpm)**

CLINICAL HISTORY-3

BLOOD TESTS

- WBC= 12.130 ↑
- HB =15,9 gr/dl
- Creatinine: 0,8 mg/dl
- Troponin: 0,01 mg/dl
- CRP= 12,50 mg/dl ↑
- D-Dimer 580 ng/ml

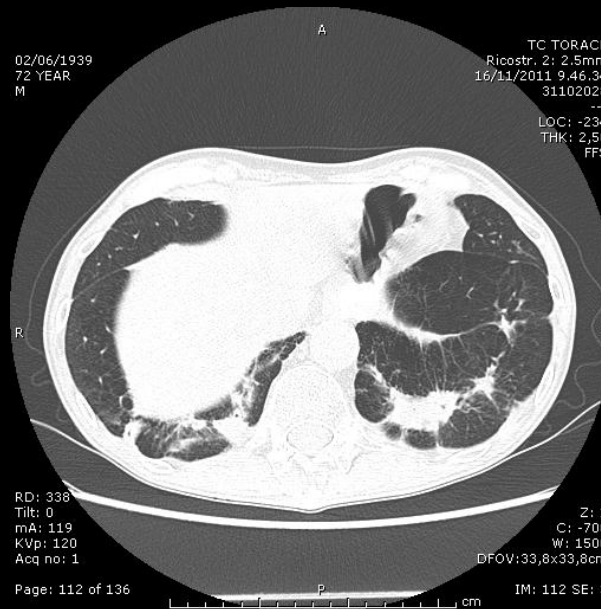
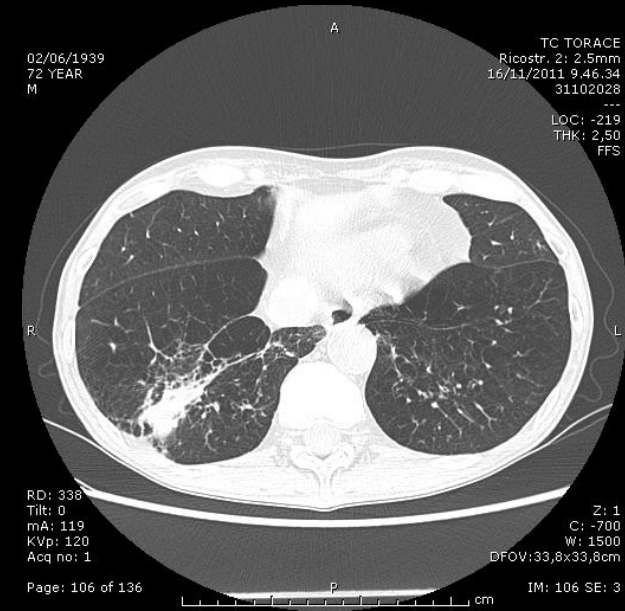
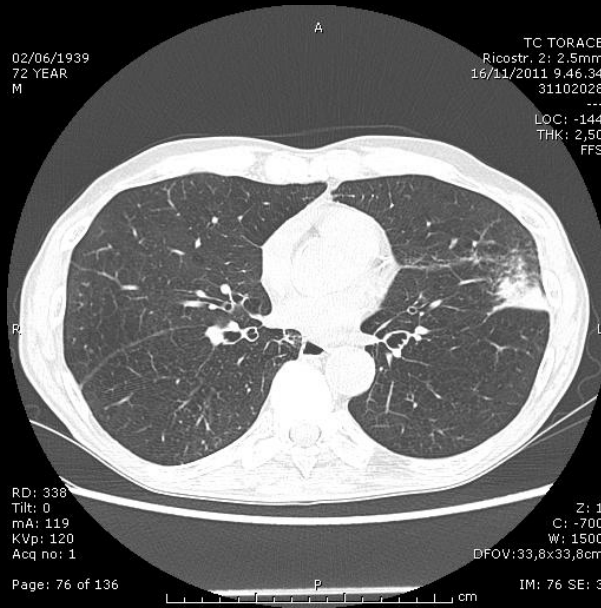
ARTERIAL BLOOD GASES

- PH= 7.40
- PO₂= 57 mmHg ↓
- PCO₂= 50 mmHg ↑
- HCO₃ = 30 mmol/L ↑
- Sat O₂ 88%

CHEST X-RAY



CT-SCAN before treatment

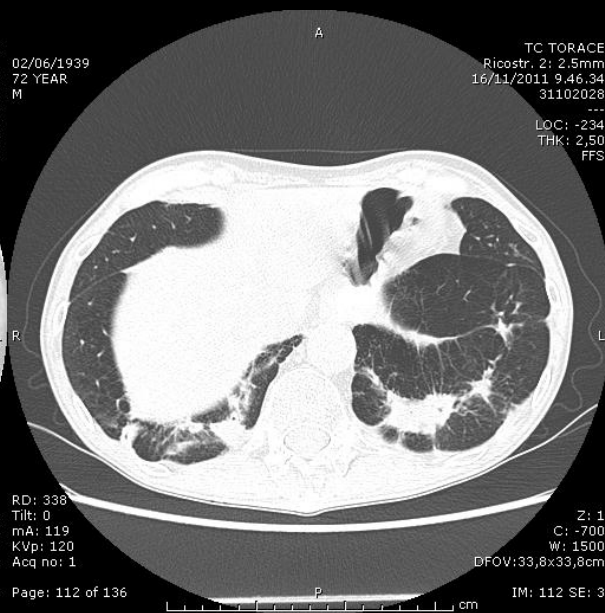
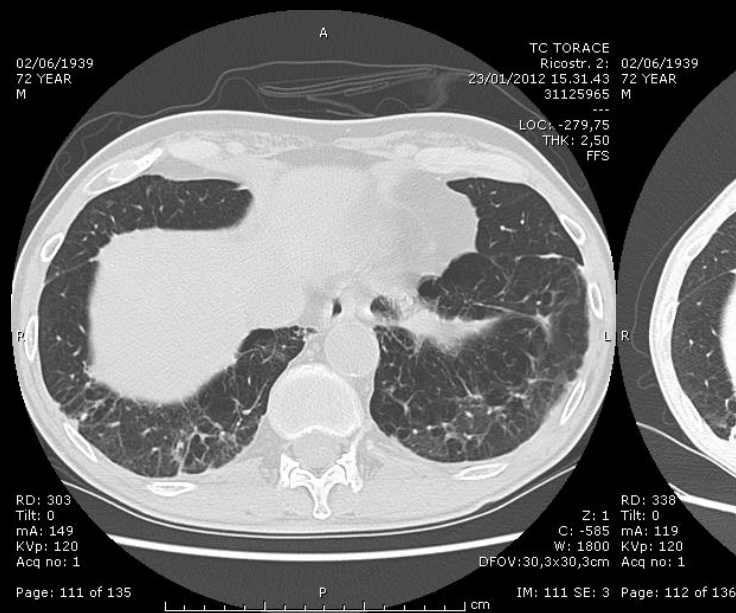


TREATMENT

- O2 therapy at 1 L/min, continuous
- Metylprednisolone 40 mg/die ev od
- Ampicillin/Sulbactam 1,5 g/die ev tid
- Nebulized beclomethasone 1 fl, ipratropium ½ fl, salbutamol 8 gtt qid

CT SCAN at follow up

CT SCAN at admission



Which treatment was effective?

- **Bronchodilators and steroids**

- **Antibiotics**

- **Diuretics**

- **All of the above**

- **We don't know!**

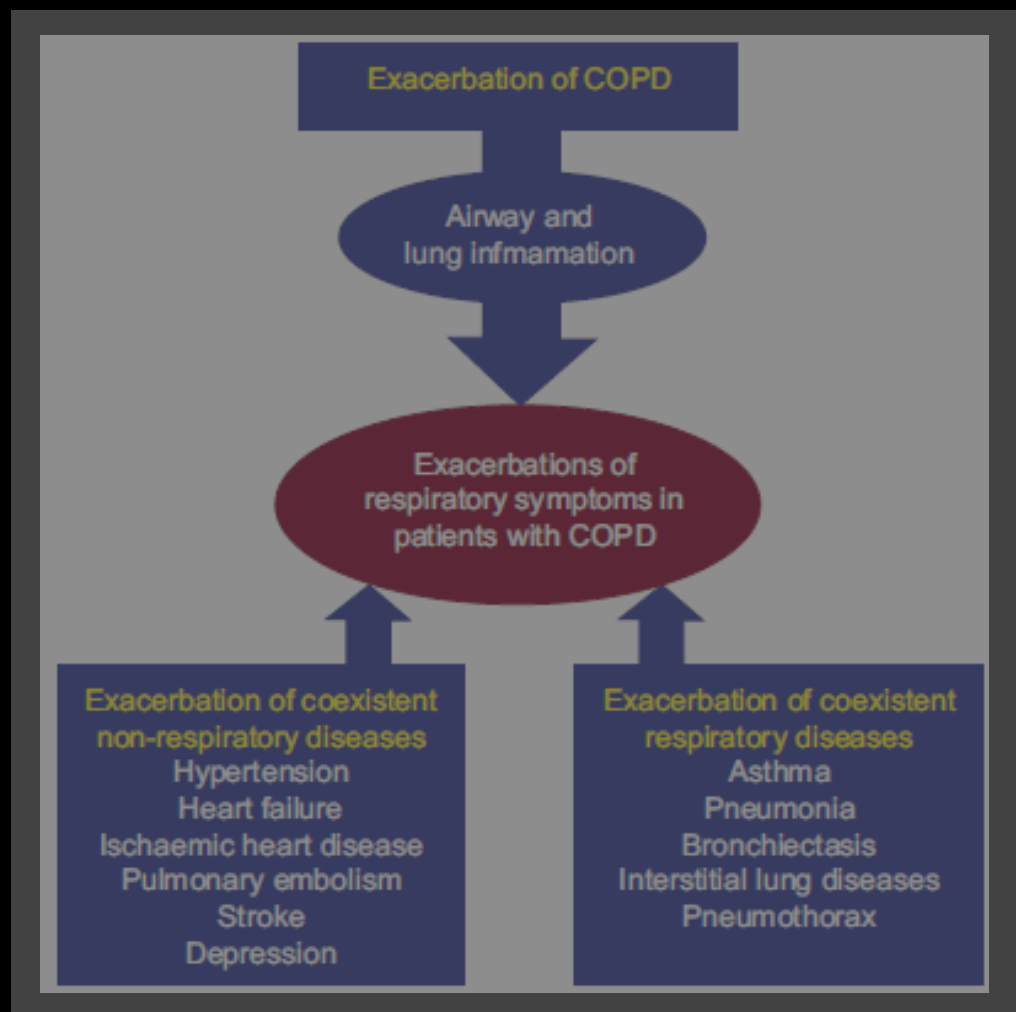
COMORBIDITIES AND SUBGROUPS OF PATIENTS SURVIVING SEVERE ACUTE HYPERCAPNIC RESPIRATORY FAILURE IN THE ICU

- 67% had COPD), only 19 previously diagnosed
 - Non-COPD patients were primarily obese
- Obstructive sleep apnea was 51% in COPD and 81% in non-COPD patients
- Previously undiagnosed cardiac dysfunction with preserved ejection fraction was highly prevalent (44%), as well as hypertension (67%)

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

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

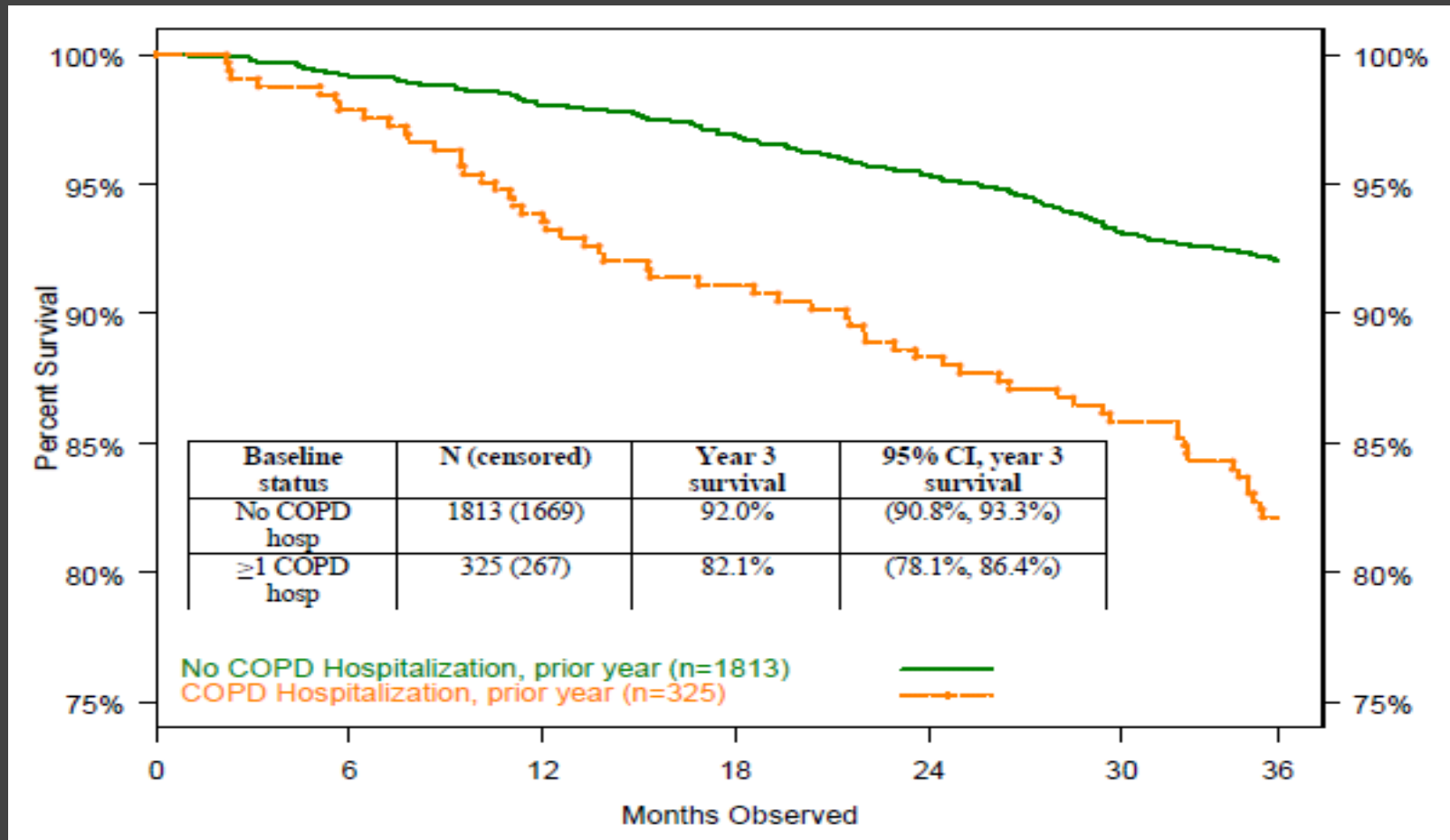


*Beghé B, Verduri A, Roca M and Fabbri LM. Eur Respir J 2013; 41: 993-5
Roca M, Verduri A, Clini EM, Fabbri LM and Beghé B. Eur J Clin Invest, 2013;43:510*

DIFFERENTIAL DIAGNOSIS OF ACUTE EXACERBATIONS OF COPD

- AECOPD is a clinical diagnosis, defined as worsening of respiratory symptoms and change in medication and/or hospital admission
- However, there is no defined etiology (usually, airway inflammation and bronchitis)
- Role of cardiac comorbidities as putative triggers of AECOPD is currently under investigation

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

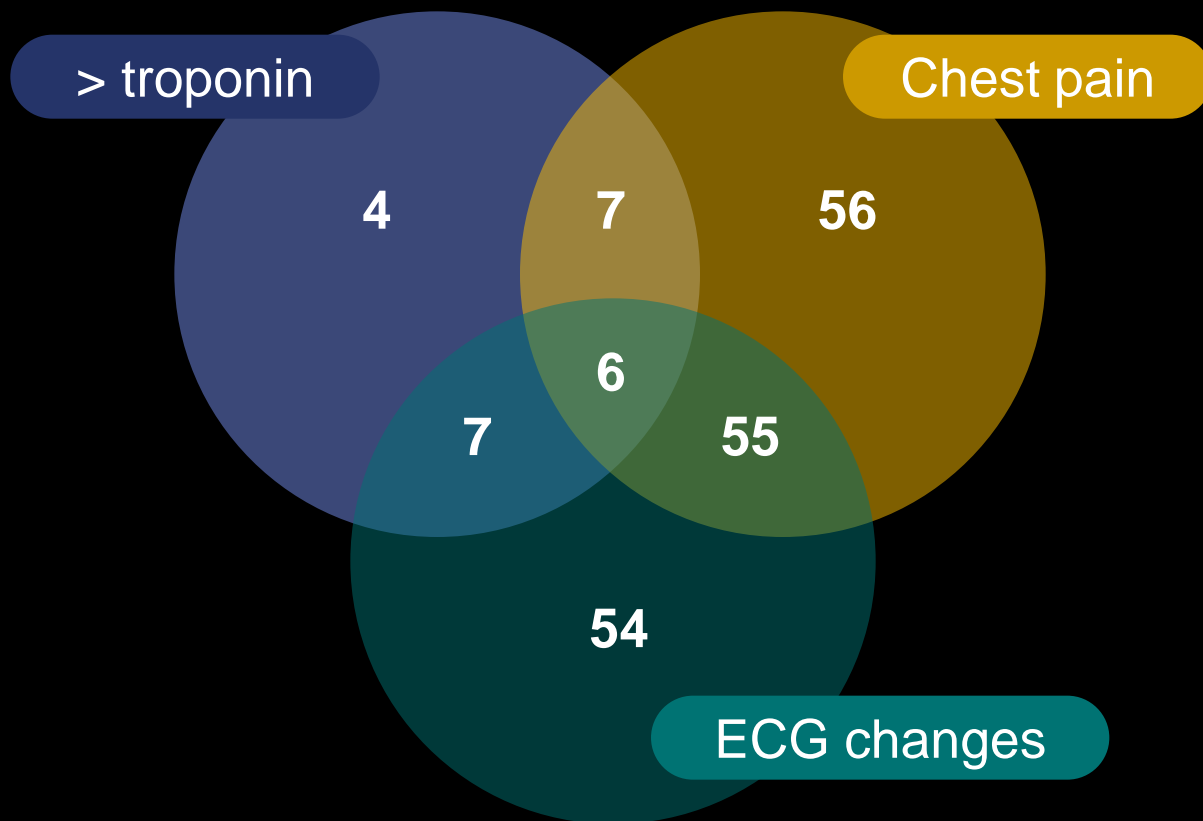


BIOCHEMICAL MARKERS OF CARDIAC DYSFUNCTION PREDICT MORTALITY IN ACUTE EXACERBATIONS OF COPD

Elevated levels of NT-proBNP and troponin T are strong predictors of early mortality among patients admitted to hospital with acute exacerbations of COPD independently of other known prognostic indicators

The pathophysiological basis for this is unknown, but indicates that cardiac involvement in exacerbations of COPD may be an important determinant of prognosis

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



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

Raised troponin, chest pain and serial ECG changes are common in patients admitted to hospital with exacerbation of COPD

Overall, 20/242, ie 1/12 patients with ECOPD met the criteria for myocardial infarction

Whether these patients would benefit from further cardiac investigation is unknown

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

Raised troponin, chest pain and serial ECG changes are common in patients admitted to hospital with exacerbation of COPD

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Whether these patients would benefit from further cardiac investigation is unknown

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



Manage COPD Exacerbations

BRONCHODILATORS

STEROIDS

ANTIBIOTICS

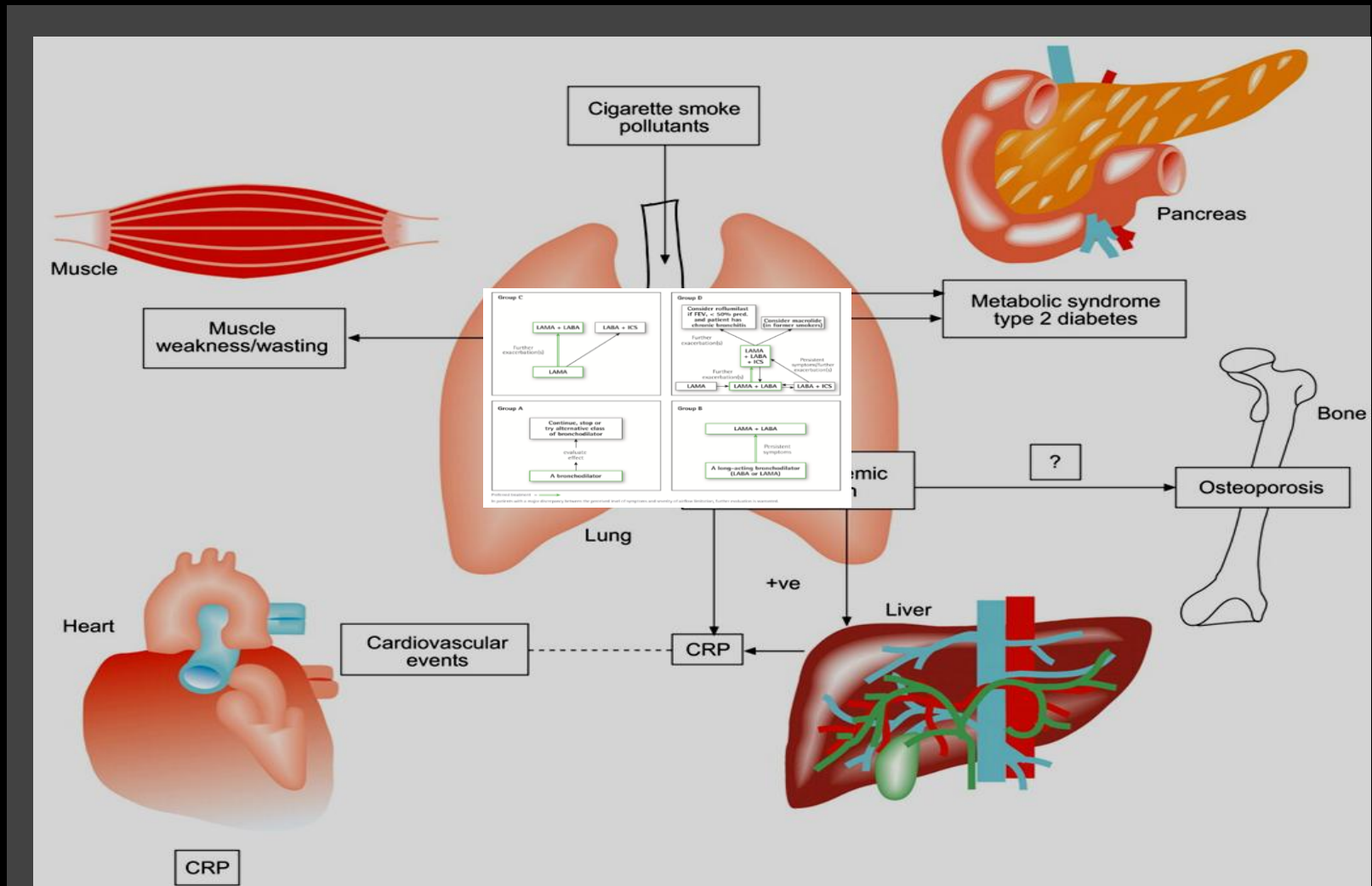
OXYGEN/NON INVASIVE VENTILATION

MECHANICAL VENTILATION

COPD EXACERBATIONS: home versus hospital Leonardo M. Fabbri

- ✓ **COPD, COPD PHENOTYPES AND
MULTIMORBIDITY**
- ✓ **COMPLEXITY OF ACUTE EXACERBATIONS**
- ✓ **PREVENTION AND MANAGEMENT OF ACUTE
EXACERBATIONS**

COPD AS THE PULMONARY COMPONENT OF MULTIMORBIDITY



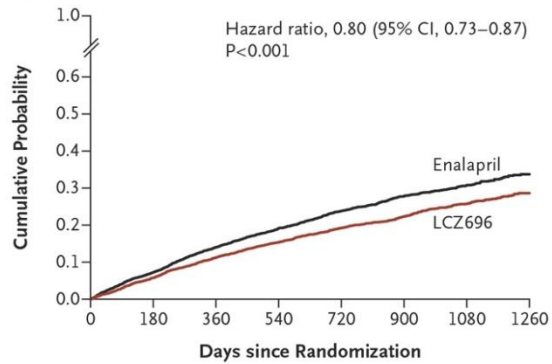
ANGIOTENSIN–NEPRILYSIN INHIBITION VERSUS ENALAPRIL IN HEART FAILURE

We compared the angiotensin receptor–neprilysin inhibitor LCZ696 with enalapril in patients who had heart failure with a reduced ejection fraction.

LCZ696 was superior to enalapril in reducing the risks of death and of hospitalization for heart failure

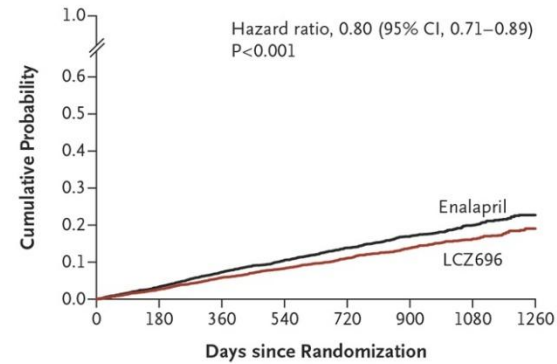
ANGIOTENSIN-NEPRILYSIN INHIBITION VERSUS ENALAPRIL IN HEART FAILURE

A Primary End Point



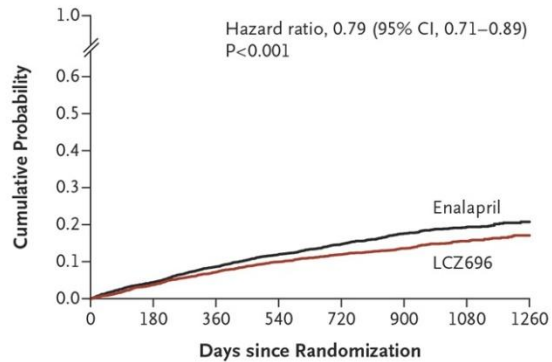
No. at Risk		0	180	360	540	720	900	1080	1260
LCZ696	Enalapril	4187	3922	3663	3018	2257	1544	896	249
		4212	3883	3579	2922	2123	1488	853	236

B Death from Cardiovascular Causes



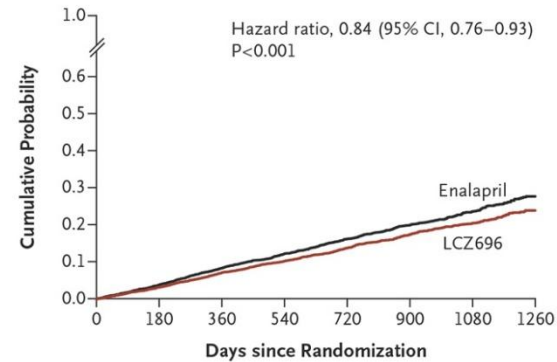
No. at Risk		0	180	360	540	720	900	1080	1260
LCZ696	Enalapril	4187	4056	3891	3282	2478	1716	1005	280
		4212	4051	3860	3231	2410	1726	994	279

C Hospitalization for Heart Failure



No. at Risk		0	180	360	540	720	900	1080	1260
LCZ696	Enalapril	4187	3922	3663	3018	2257	1544	896	249
		4212	3883	3579	2922	2123	1488	853	236

D Death from Any Cause



No. at Risk		0	180	360	540	720	900	1080	1260
LCZ696	Enalapril	4187	4056	3891	3282	2478	1716	1005	280
		4212	4051	3860	3231	2410	1726	994	279

SACUBRITIL-VALSARTAN:THE NEWEST ADDITION TO THE TOOLBOX FOR GUIDELINES DIRECTED MEDICAL THERAPY FOR HEART FAILURE

Sacubitril/valsartan combines a neprilysin inhibitor with an angiotensin receptor blocker.

As an inhibitor of neprilysin, an enzyme that degrade biologically active natriuretic peptides, this first-in-class therapy increases levels of circulating natriuretic peptides resulting in natriuretic, diuretic, and vasodilatory effects

American College of Cardiology/American Heart Association/Heart Failure Society of America recently updated guideline recommendations for Stage C patients with heart failure with reduced ejection fraction to recommend angiotensin converting enzyme inhibitors, angiotensin receptor blockers or sacubitril/valsartan in conjunction with other evidence-based therapies to reduce morbidity and mortality.

Rodgers et al, Am J Medicine , 2017, in press

COPD AS PULMONARY COMPONENT OF MULTIMORBIDITY

Leonardo M. Fabbri, MD, FERS

Definition and assessment of severity of COPD

Management of of COPD

COPD as pulmonary component of multimorbidity

Treatment of concomitant chronic diseases in COPD

Conclusions

GLOBAL STRATEGY FOR DIAGNOSIS, MANAGEMENT AND PREVENTION OF COPD DEFINITION OF COPD 2011



2011

COPD, a common preventable and treatable disease, is characterized by persistent airflow limitation **that is usually progressive and associated with an enhanced chronic inflammatory** response in the airways and the lung to noxious particles or gases. **Exacerbations and comorbidities contribute to the overall severity in individual patients**

2017

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by **persistent respiratory symptoms** and airflow limitation that is **due to airway and/or alveolar abnormalities usually** caused by significant exposure to noxious particles or gases

Diagnosis of COPD

SYMPTOMS

shortness of breath
chronic cough
sputum

EXPOSURE TO RISK FACTORS

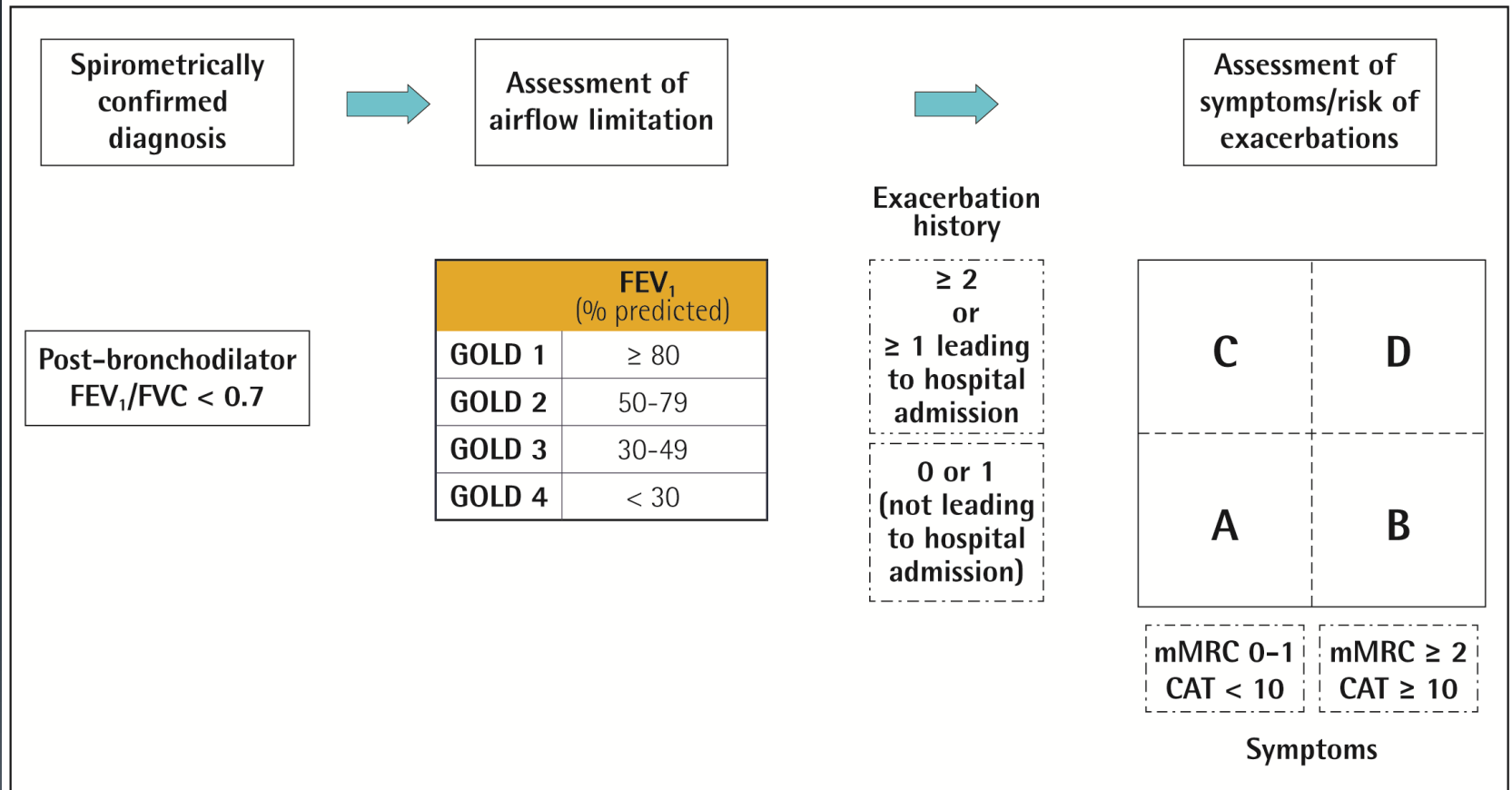
tobacco
occupation
indoor/outdoor pollution

SPIROMETRY: Required to establish diagnosis

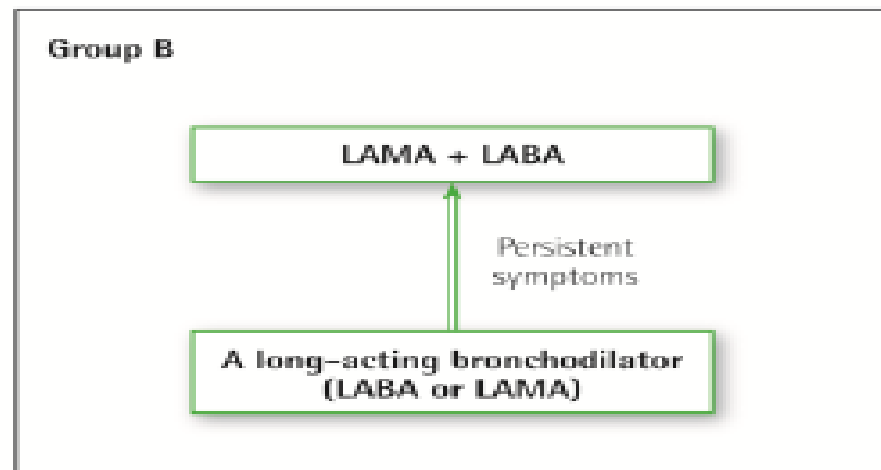
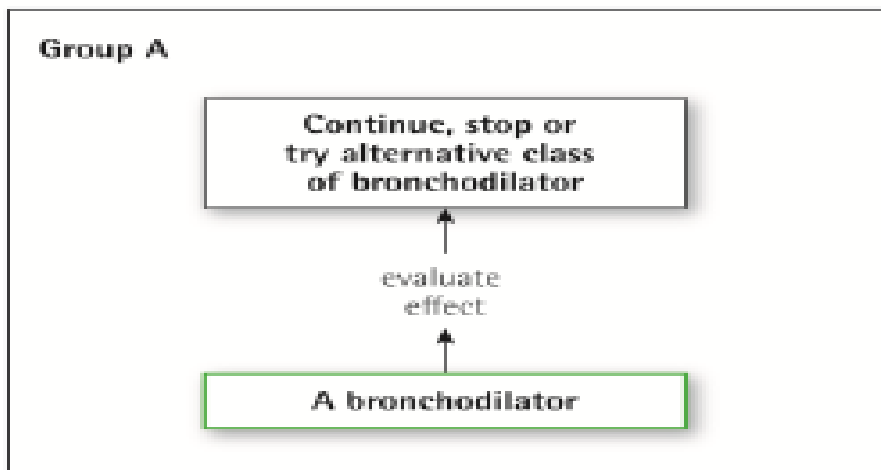
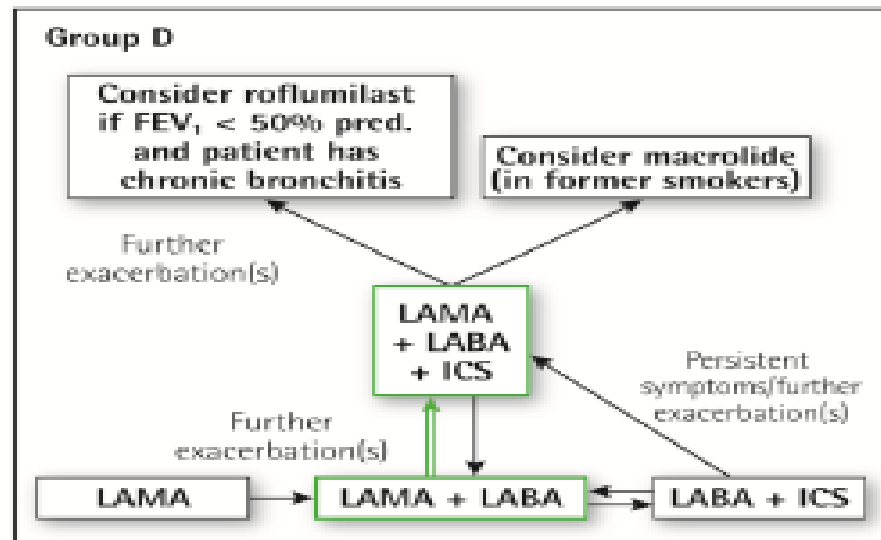
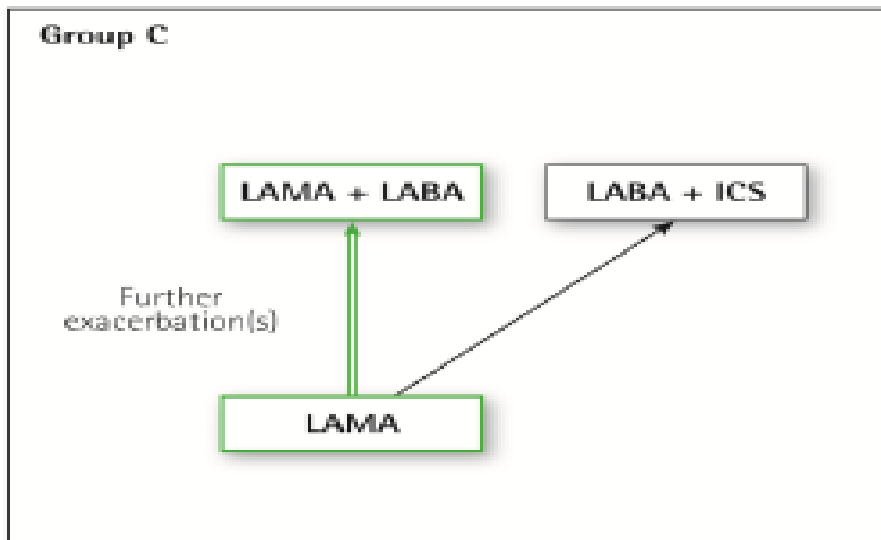


ABCD Assessment Tool

Figure 2.4. The refined ABCD assessment tool

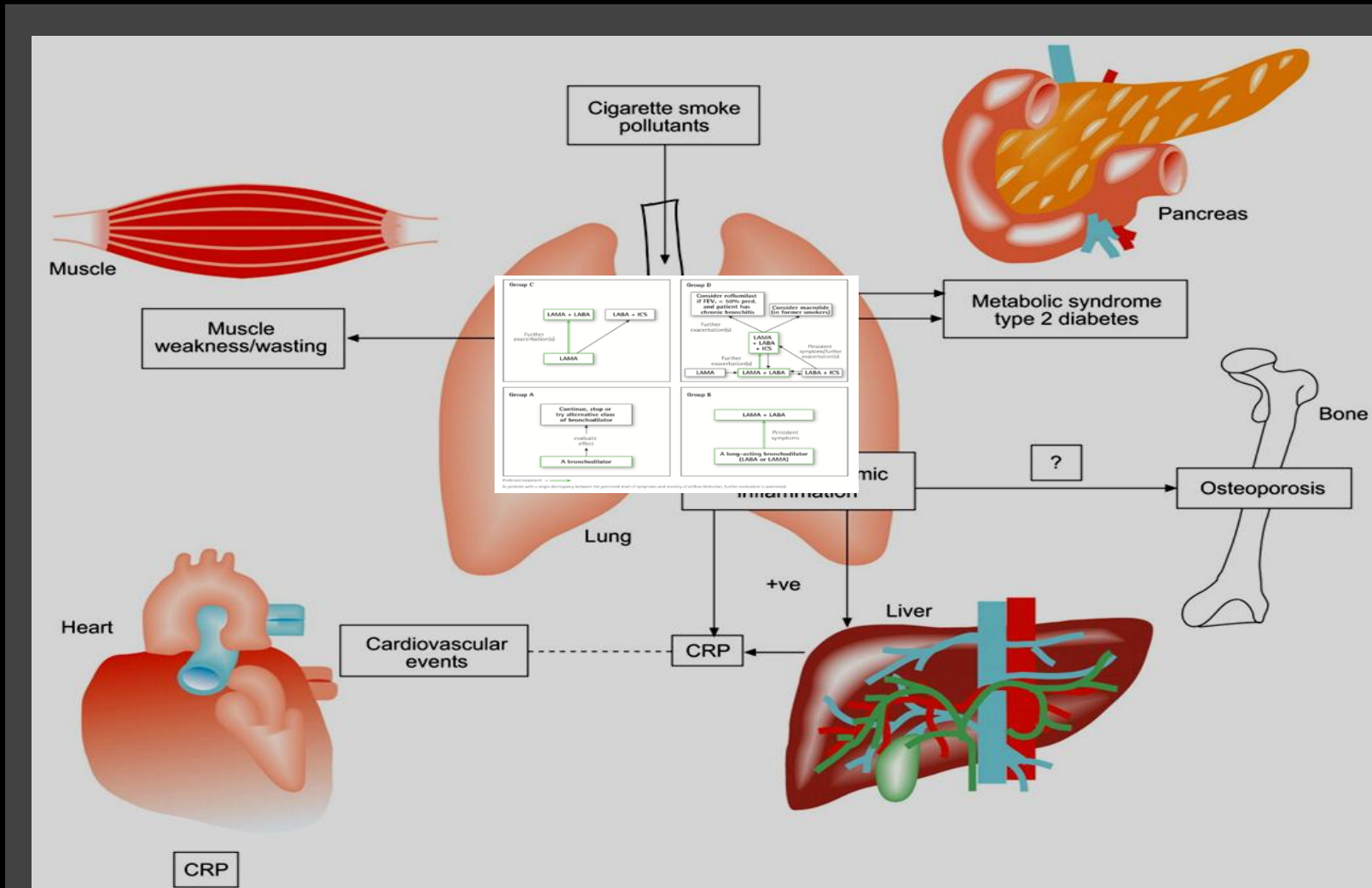


GOLD 2017 THERAPEUTIC RECOMMENDATIONS

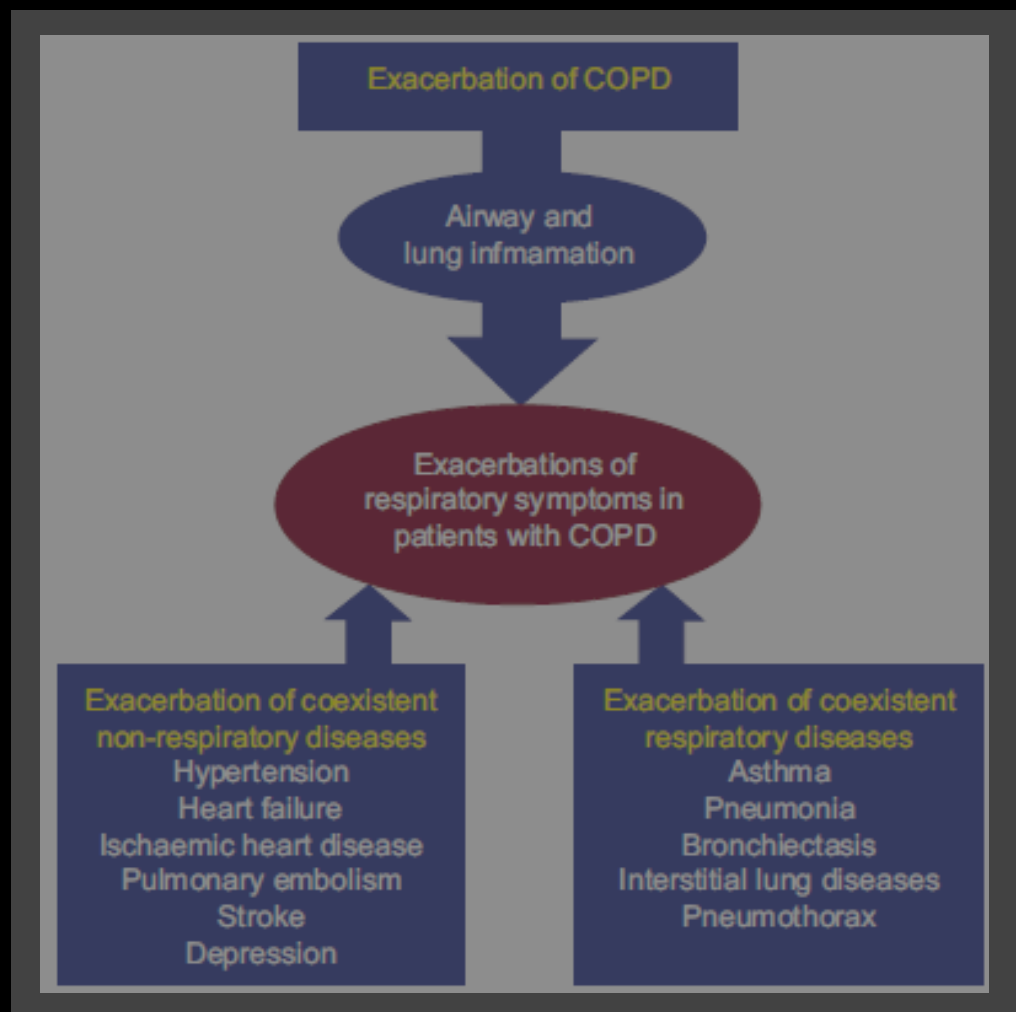


*Roflumilast not available in Australia

COPD AS THE PULMONARY COMPONENT OF MULTIMORBIDITY



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Roca M, Verduri A, Clini EM, Fabbri LM and Beghé B. Eur J Clin Invest, 2013;43:510*

Pulmonary Symposium

Novotel, Poznan 8 April 2017



BETWEEN GOLD GUIDELINES AND EVERYDAY REALITY IN COPD

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Professor of Respiratory and Internal Medicine (-2016)

University of Modena and Reggio Emilia