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COPD and obesity

Frits Franssen, MD, PhD
CIRO+ and Maastricht University Medical Center
The Netherlands

Disclosure belangen spreker

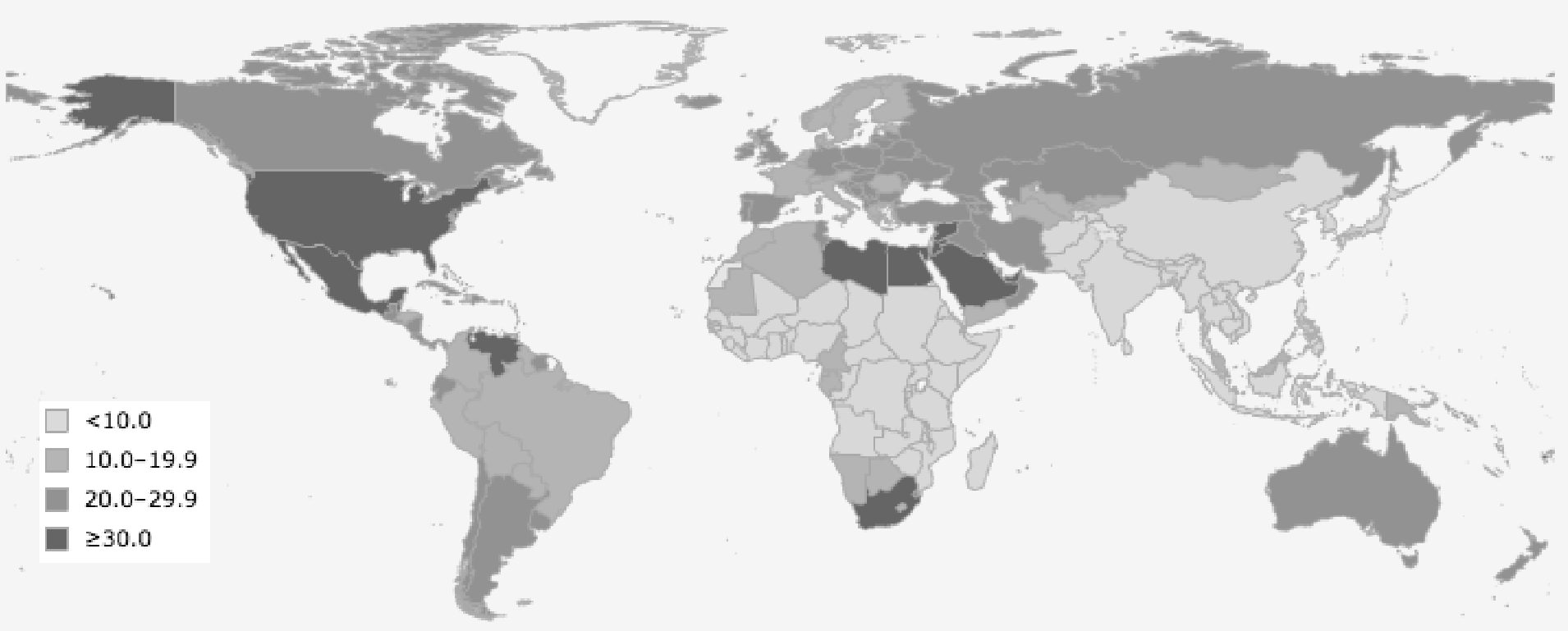
(potentiële) belangenverstrengeling	Frits Franssen
Voor bijeenkomst mogelijk relevante relaties met bedrijven	AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Mundipharma, Novartis, TEVA
• Sponsoring of onderzoeksgeld • Honorarium of andere (financiële) vergoeding • Aandeelhouder • Andere relatie, namelijk …	

COPD and obesity: agenda

1) Epidemiology
2) Impact of obesity on
   * Diagnosis and treatment
   * Symptoms
   * Lung function
   * Exercise capacity
   * Clinical phenotypes
   * Prognosis
3) How to manage the obese COPD patient
4) Summary and discussion

‘Globesity’

Obesity (BMI > 30 $kg \cdot m^{-2}$) is a complex multifactorial chronic condition that develops from an interaction of genotype and the environment

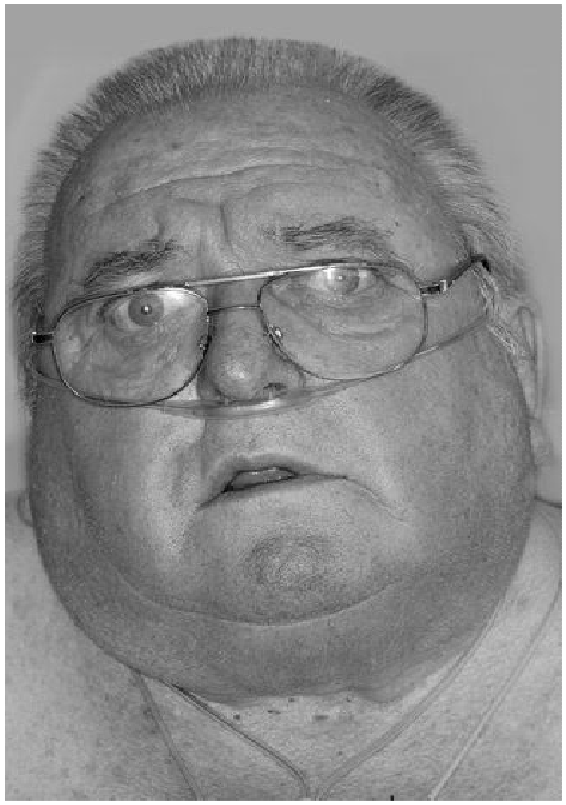


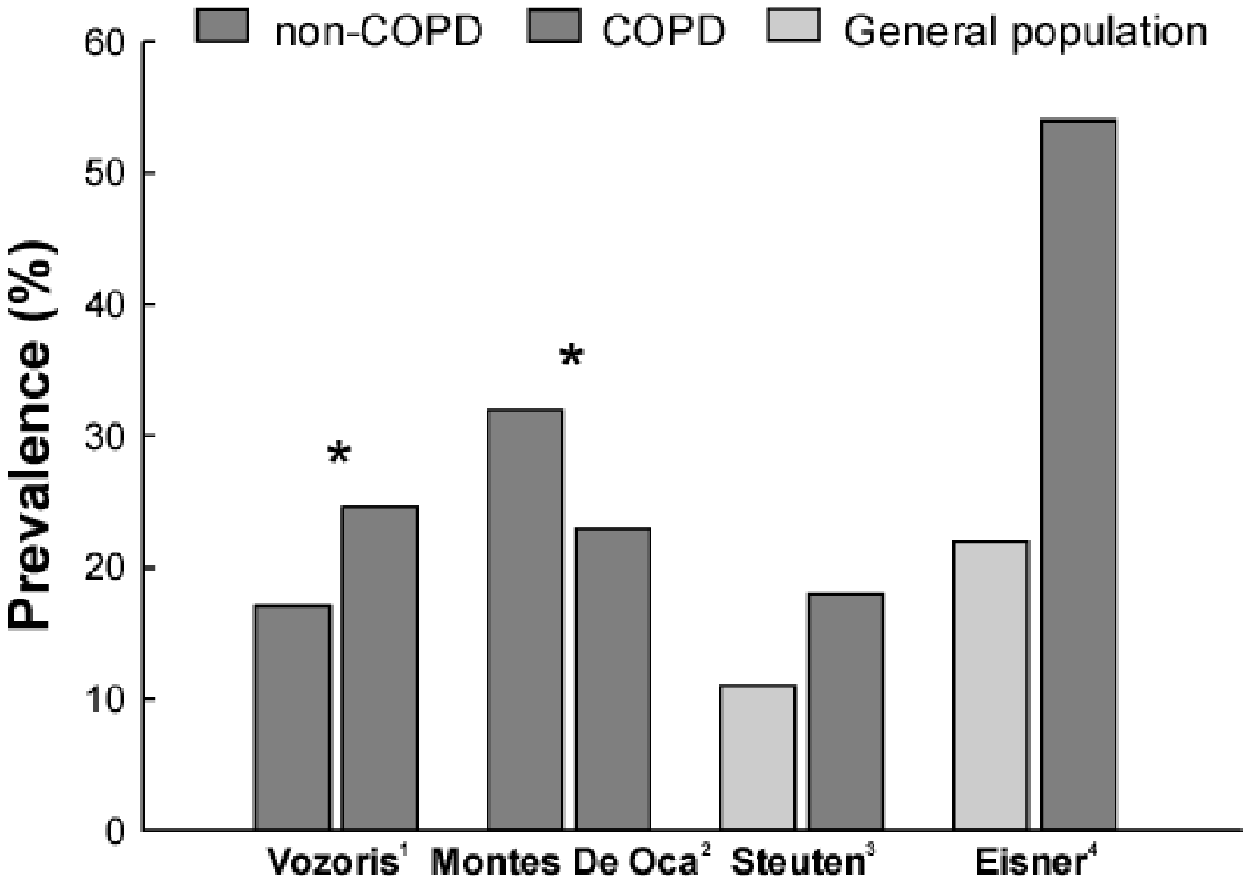
The worldwide prevalence of obesity has doubled since 1980, resulting in an estimated number of 500 million obese adults around the world in 2008

Obesity is a major cause of worldwide morbidity and mortality

WHO, Global Database on BMI, 2014

Prevalence of obesity in COPD

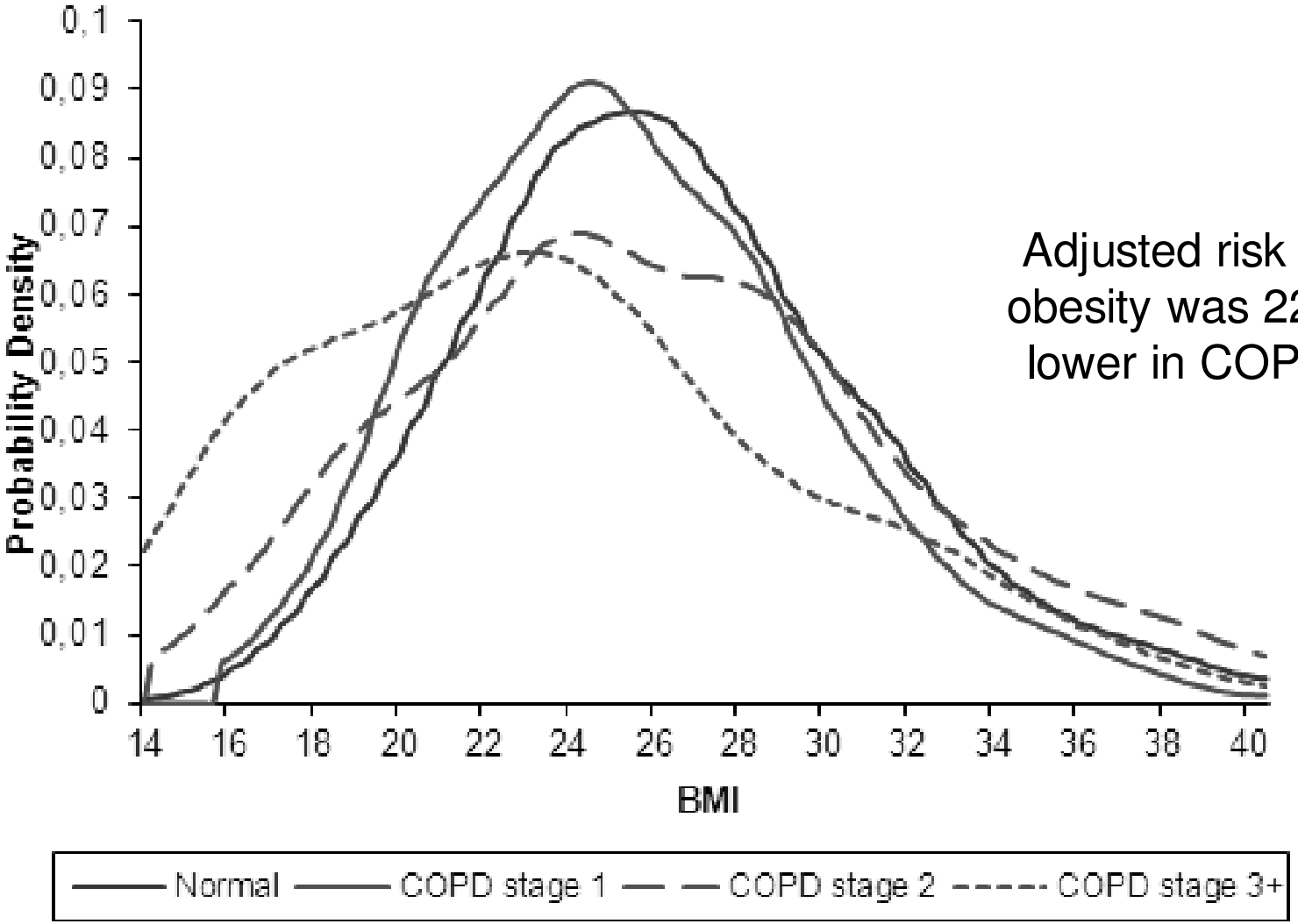




The prevalence of obesity in COPD varies across studies, probably as a result of differences in general and COPD specific risk factors for obesity

[1]Vozoris et al., Can Respir J 2012; [2]Montes De Oca et al., Respir Med 2008; [3]Steuten et al., Prim Care Respir J 2006; [4]Eisner et al., Respir Res 2007

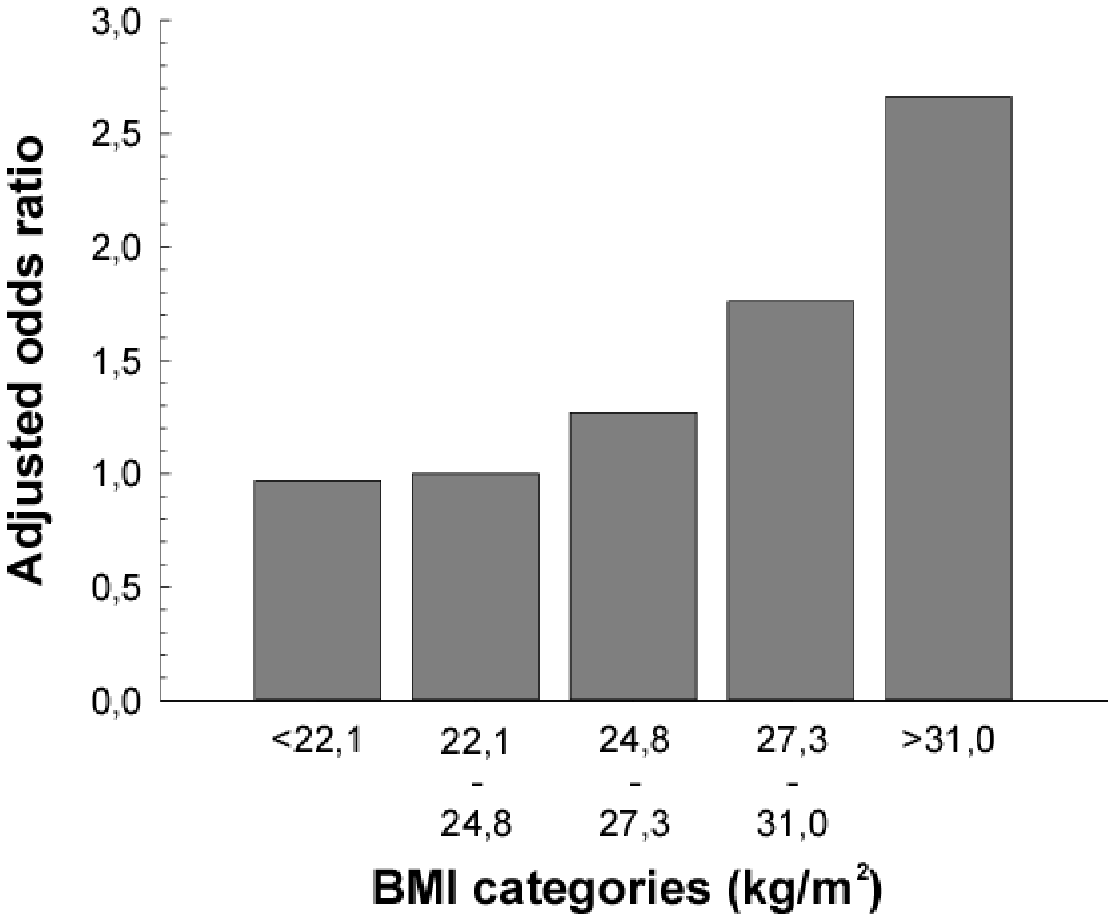
Prevalence of obesity in the Burden of Obstructive Lung Disease (BOLD) initiative (n=18.606)



Adjusted risk of obesity was 22% lower in COPD

Vanfleteren et al., Chron Respir Dis 2016

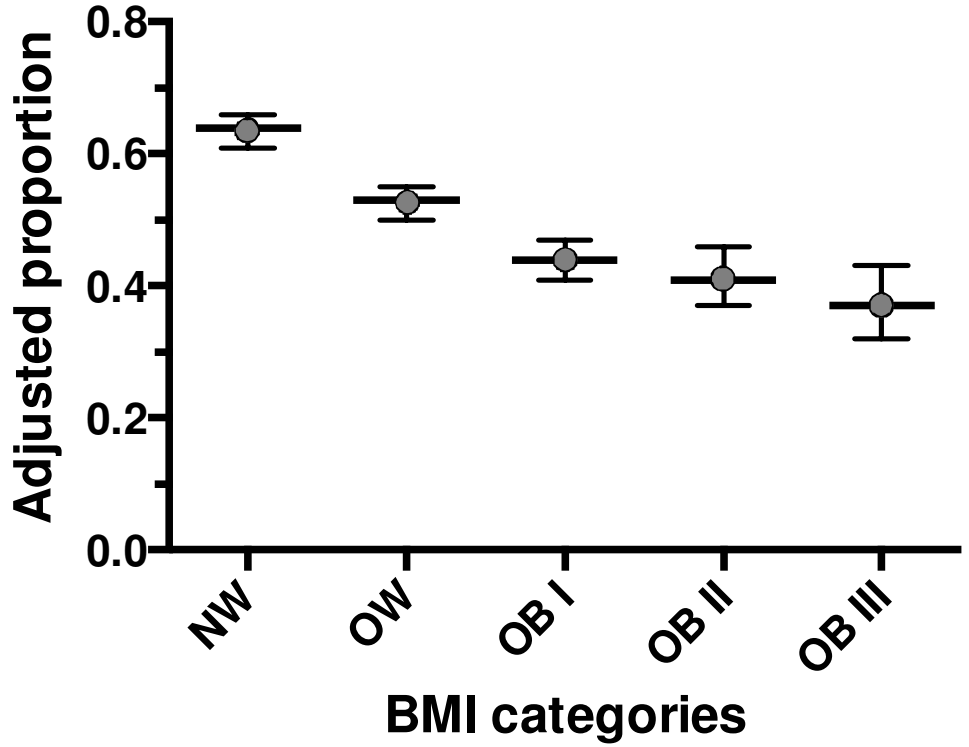
Obesity is a risk factor for dyspnea



Sin et al., NHANES III, Arch Intern Med 2002

Obesity is a risk factor for misdiagnosis of COPD

52% of patients (n=5.493) with a clinical COPD diagnosis had chronic airflow limitation

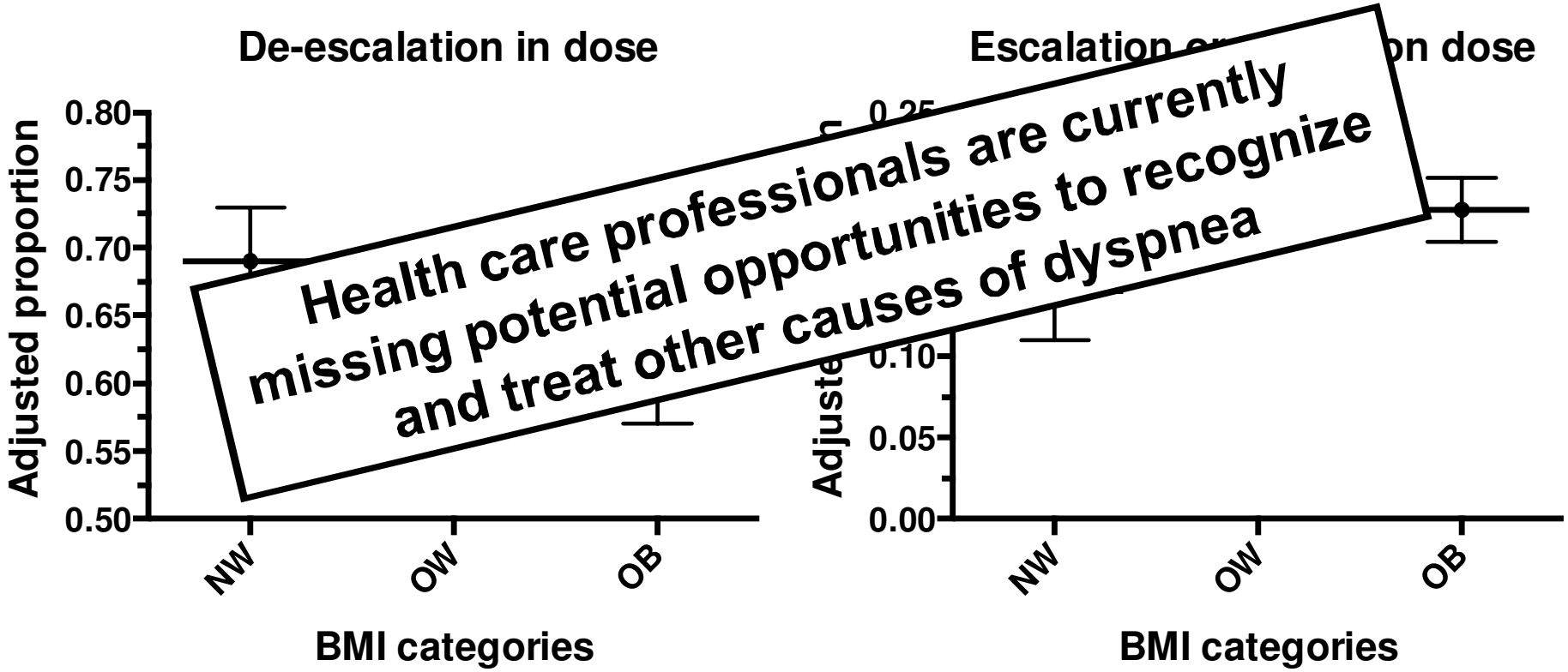


The proportion of patients with chronic aiflow limitation decreased as BMI increased

Collins et al., Chest 2014

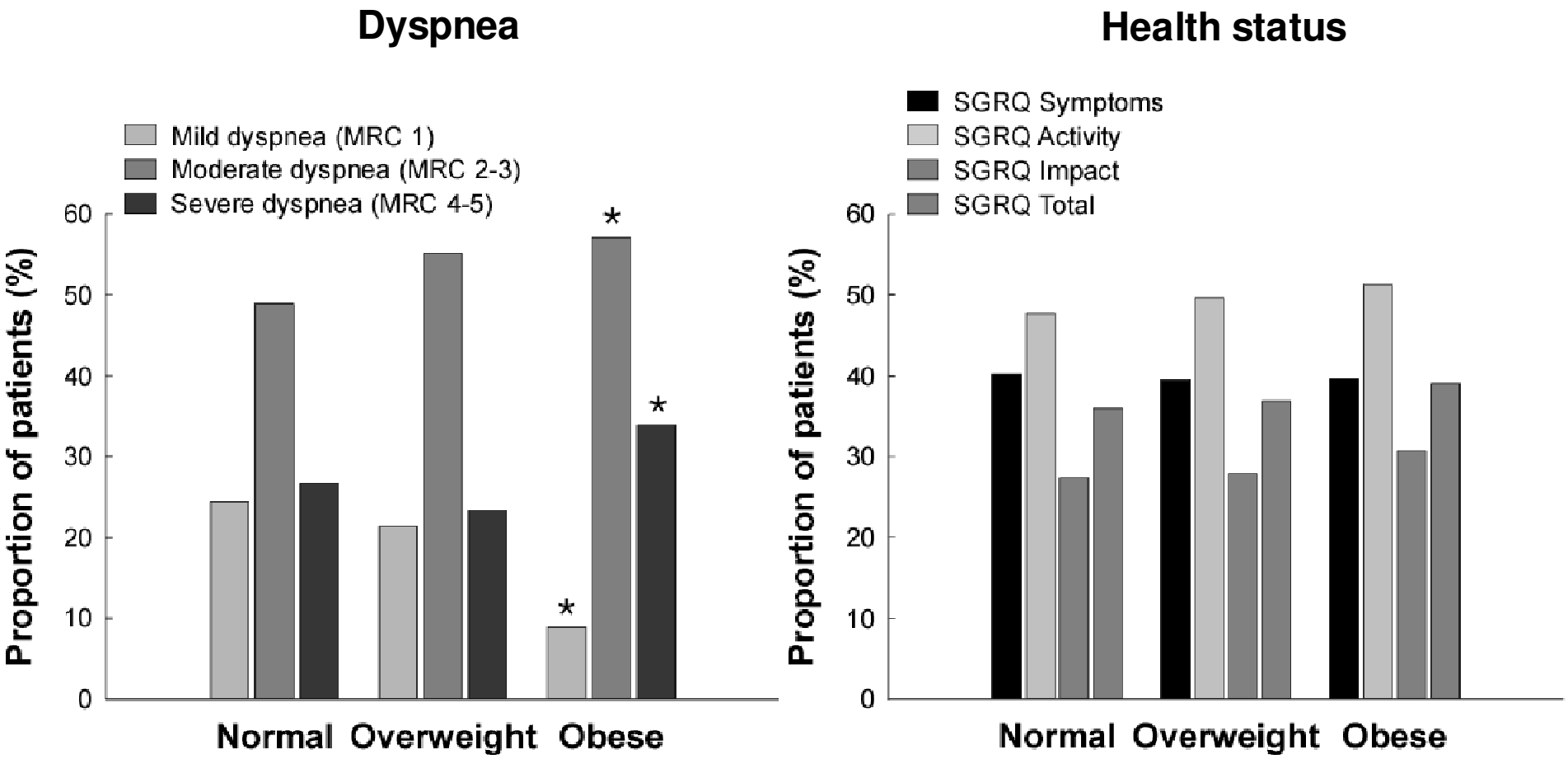
Obesity is a risk factor for overtreatment of COPD

Among subjects without chronic airflow limitation, overweight and obese subjects were less likely to have therapy de-escalated or remain off therapy



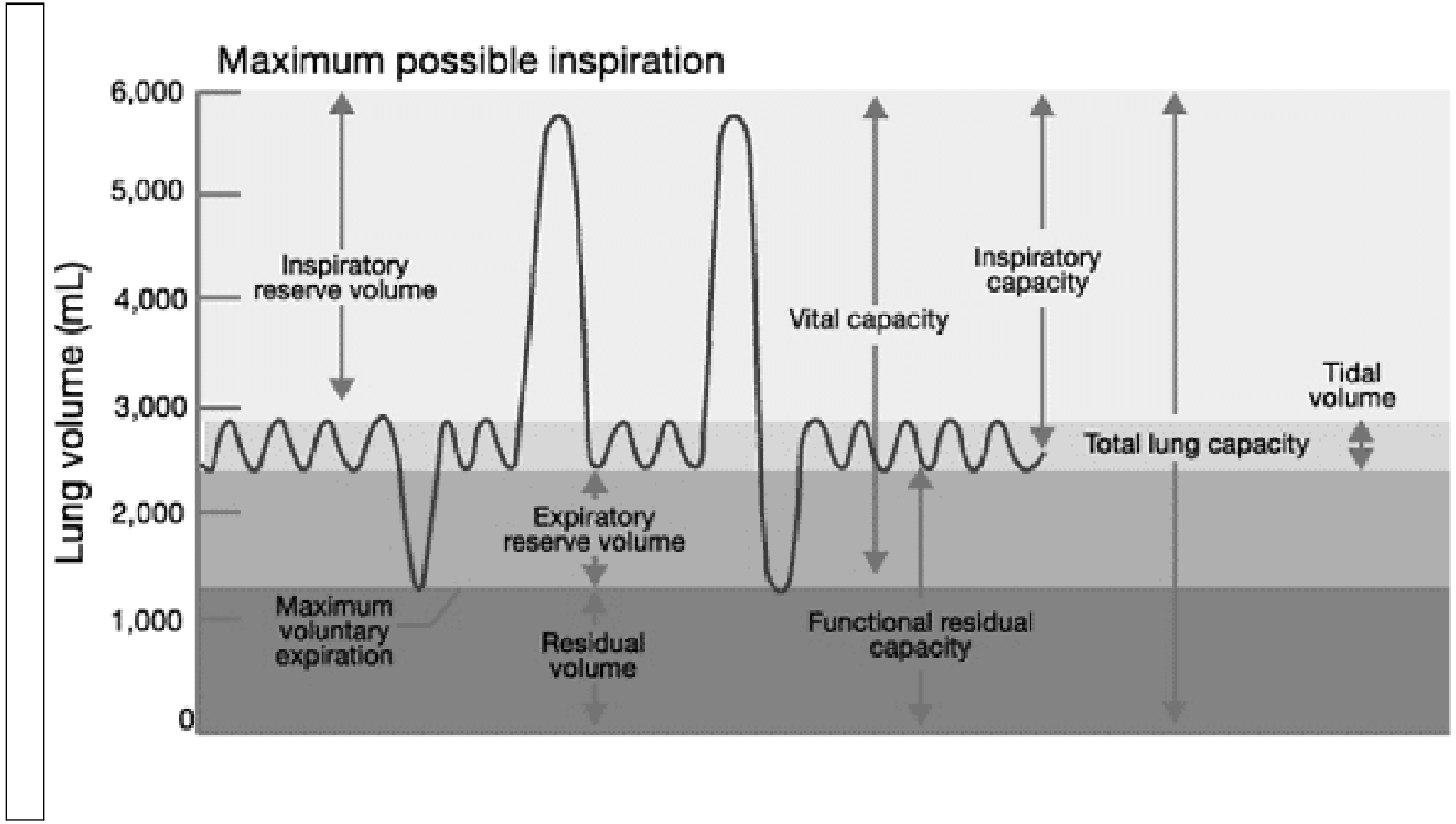
Collins et al., Chest 2014; Franssen FM, Chest 2014

COPD and obesity: symptoms and health status

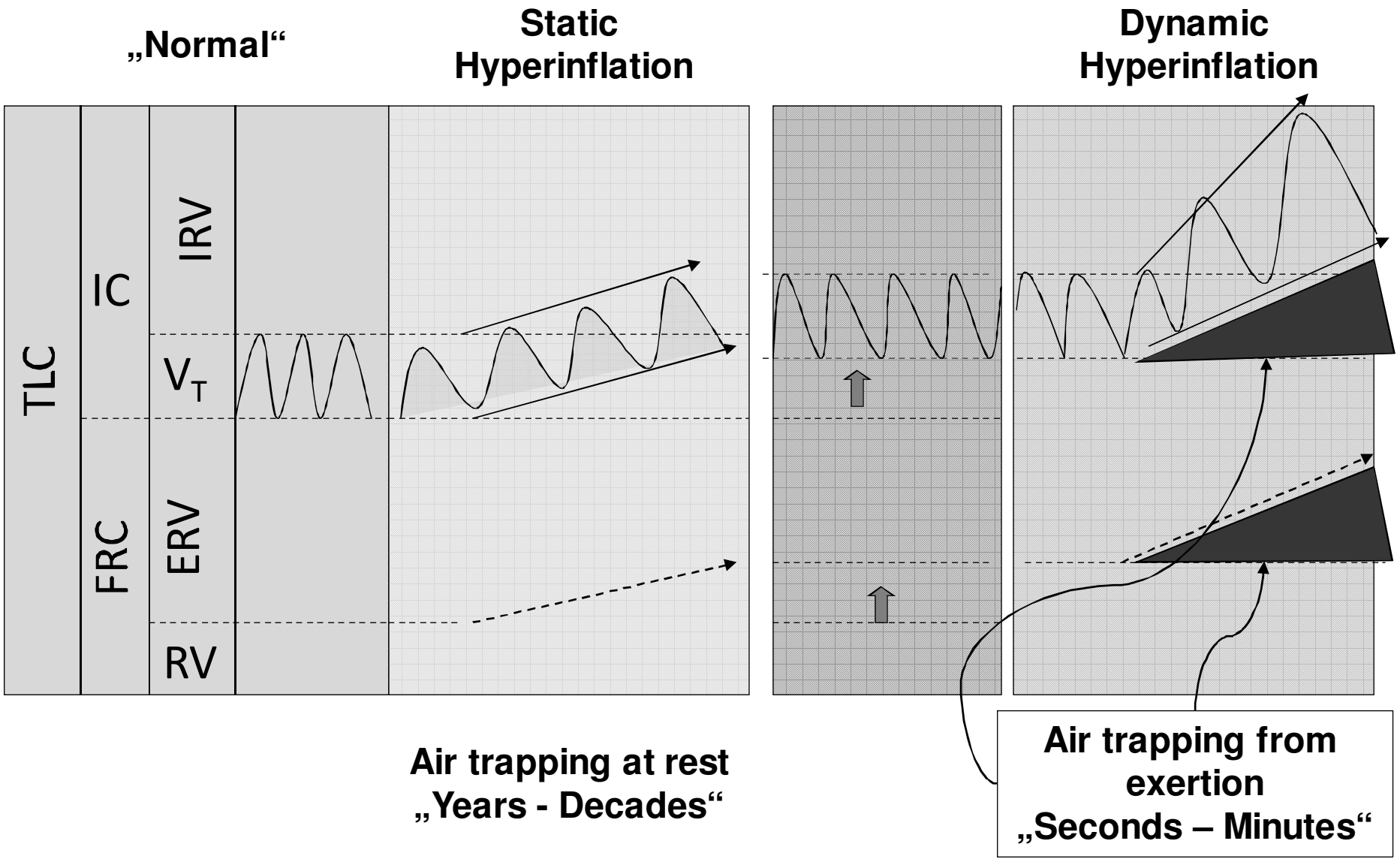


Cecere et al., COPD 2011

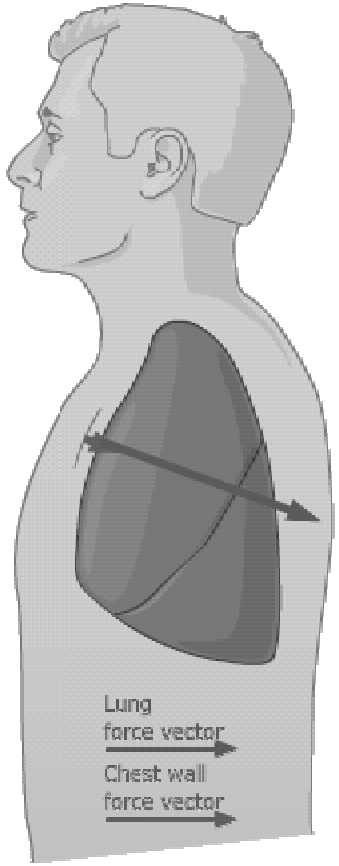
Normal lung volumes



Static and dynamic hyperinflation in COPD



Lung function in obesity



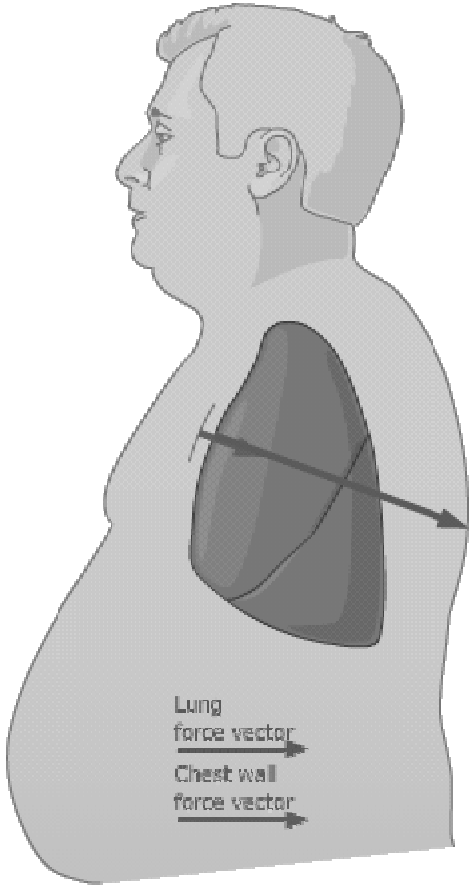
Lean

Obesity

Decreased lung compliance

Decreased FRC and ERV, preserved TLC and VC

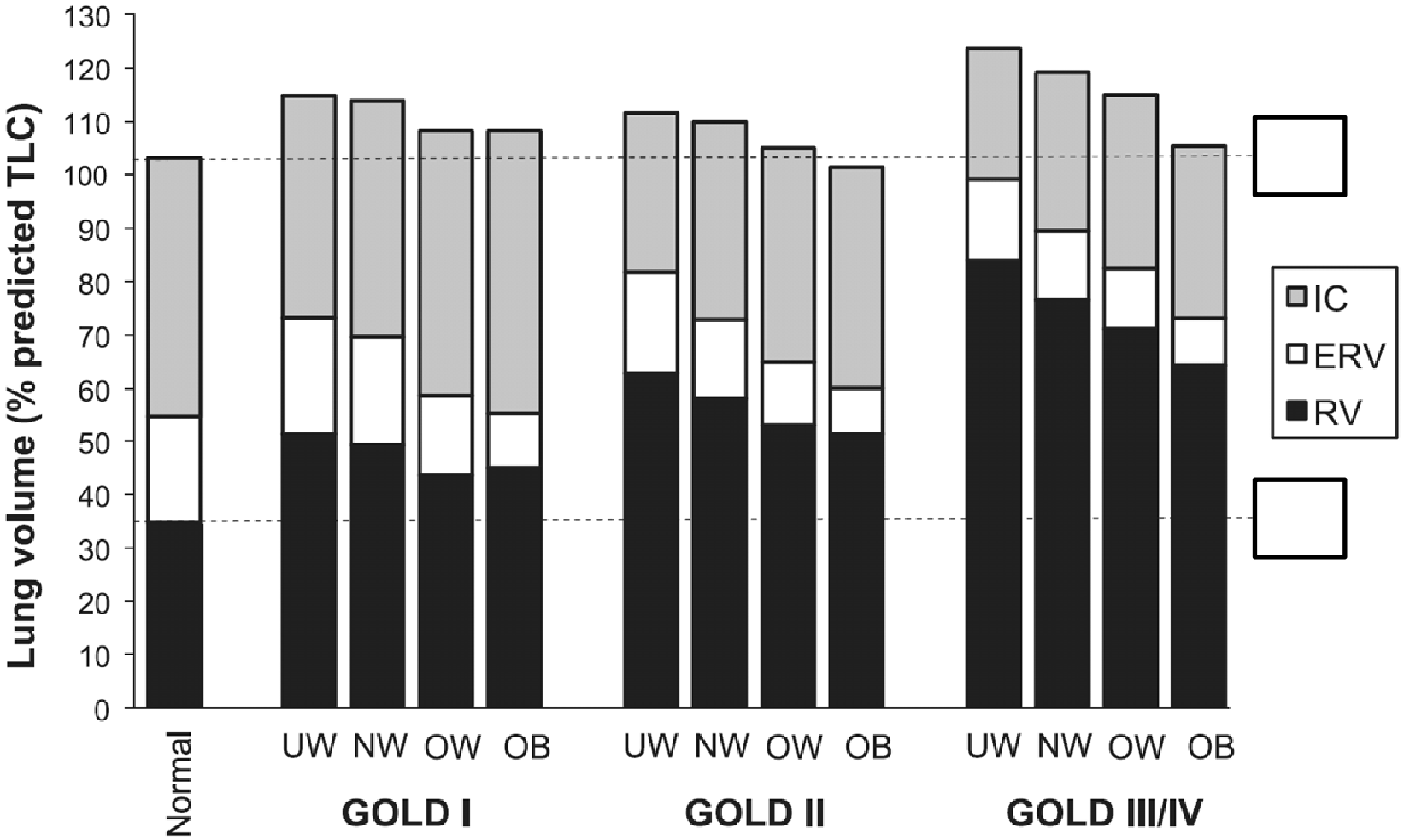
Impact on symptoms, lung function and exercise performance in COPD?



Obese

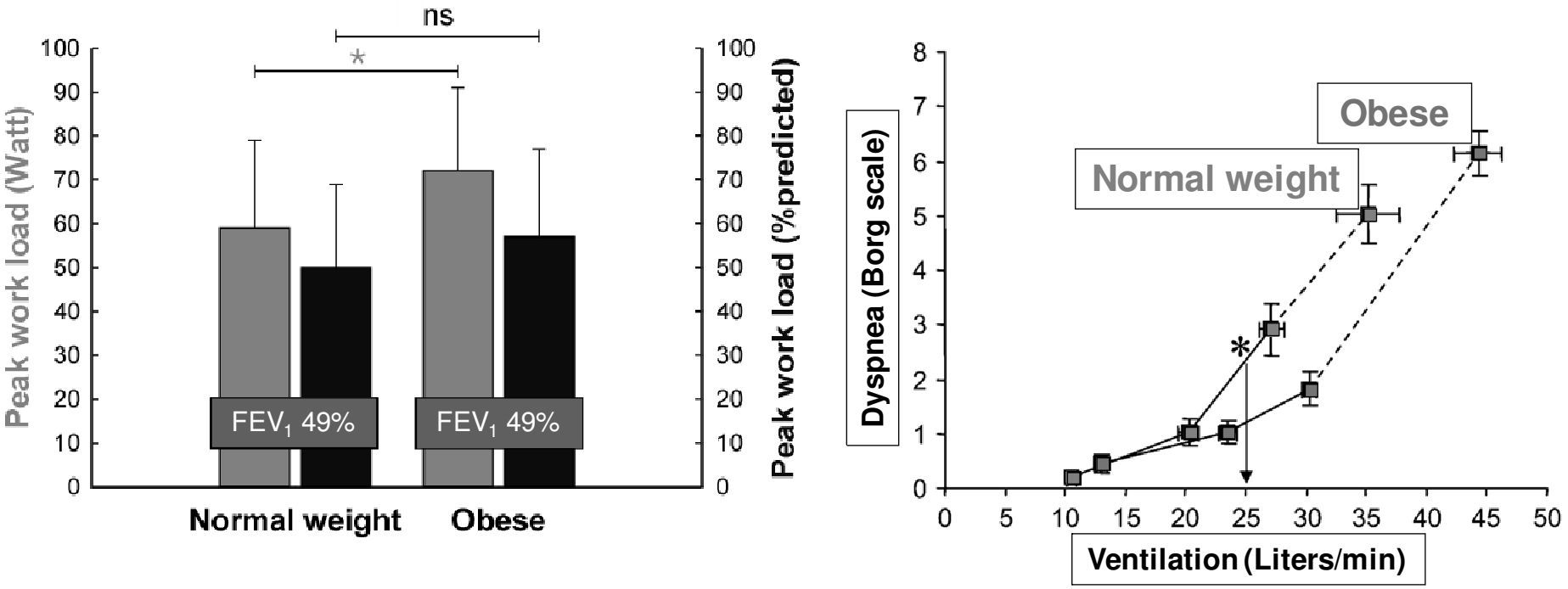
Franssen et al., Thorax 2008
Gifford et al., Chest 2010

Combined effects of obesity and COPD: lung function at rest



O'Donnell et al., Chest 2011

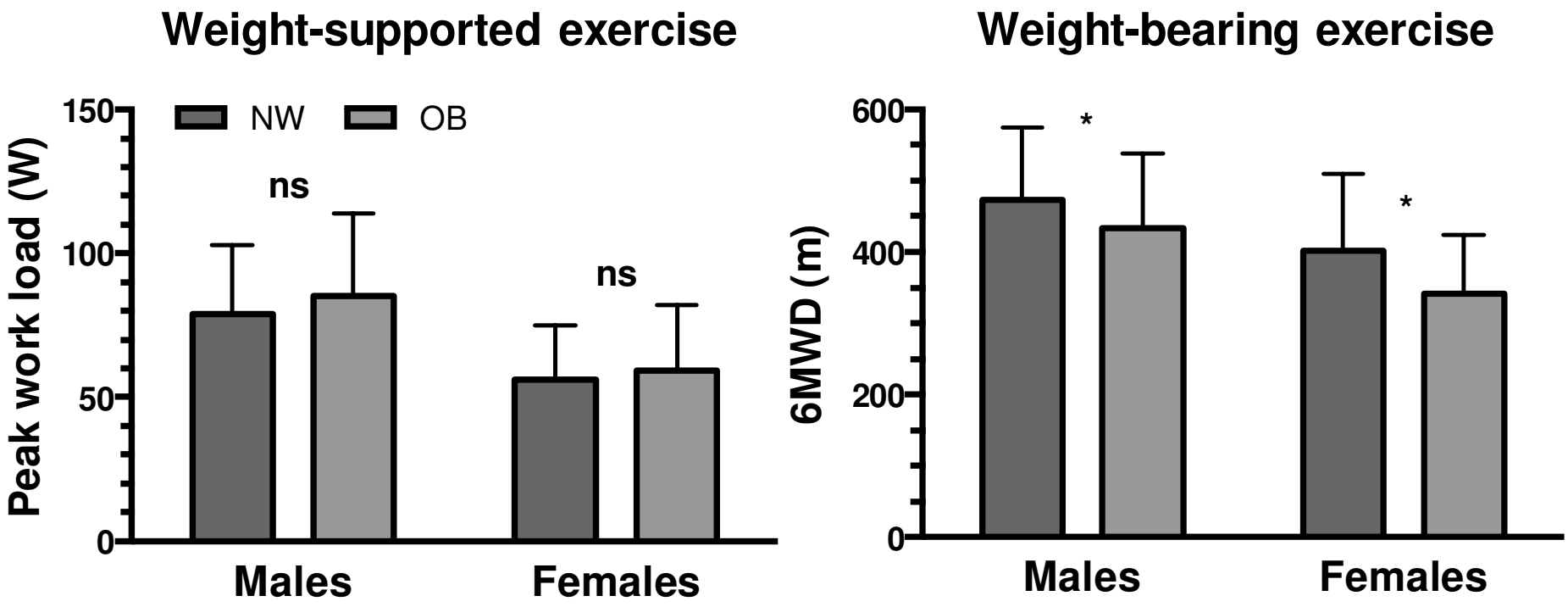
Exercise capacity in normal weight and obese COPD patients



Obese COPD patients do not experience greater exercise limitation and dyspnea than normal weight patients during peak cycle ergometry.

Ora et al., Am J Respir Crit Care Med 2009

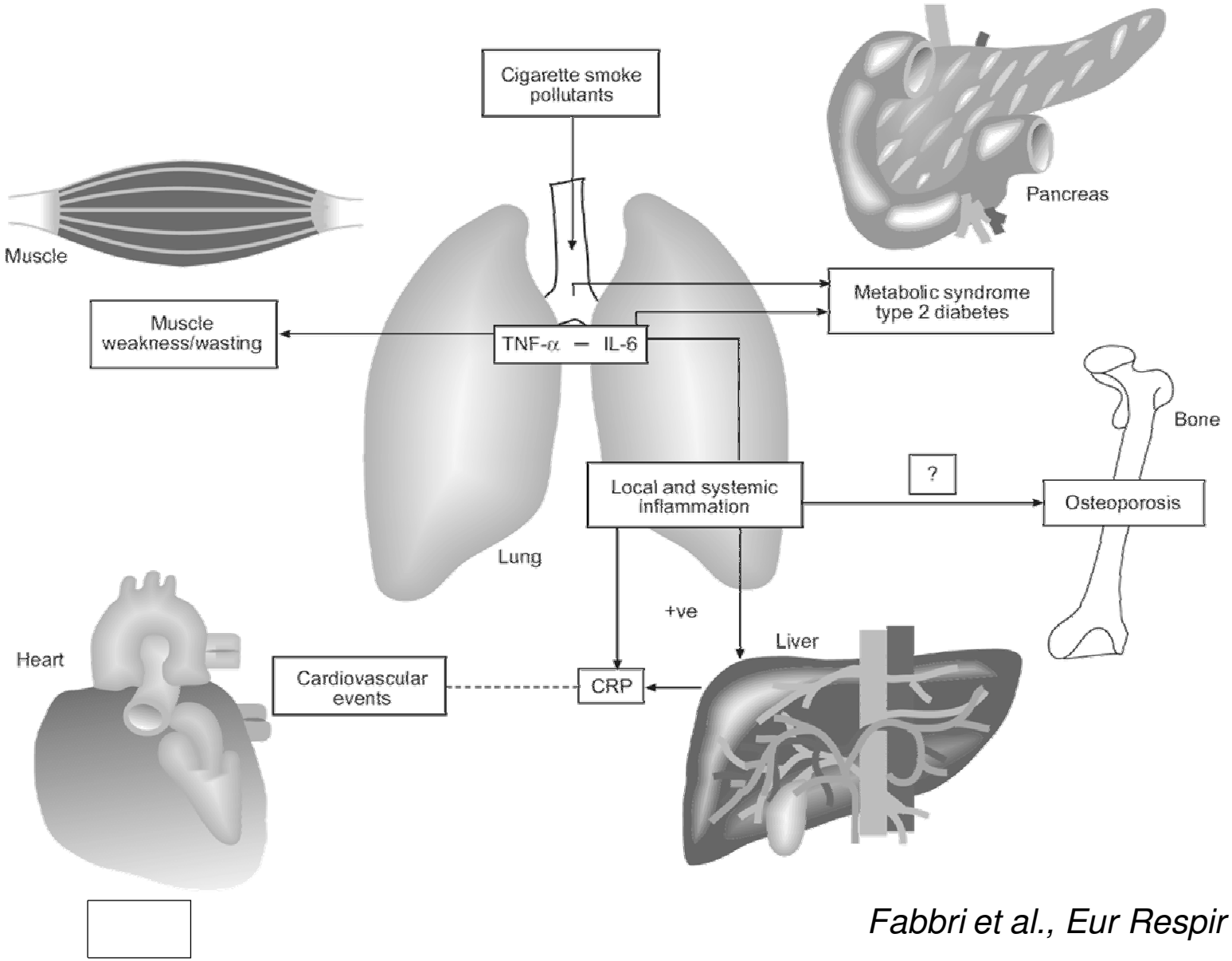
Effects of obesity on weight-bearing vs. weight-supported exercise testing in COPD



In contrast to cycle ergometry, six minute walking distance is shorter in obese COPD patients compared with non-obese patients, **matched for gender, age and FEV_1**

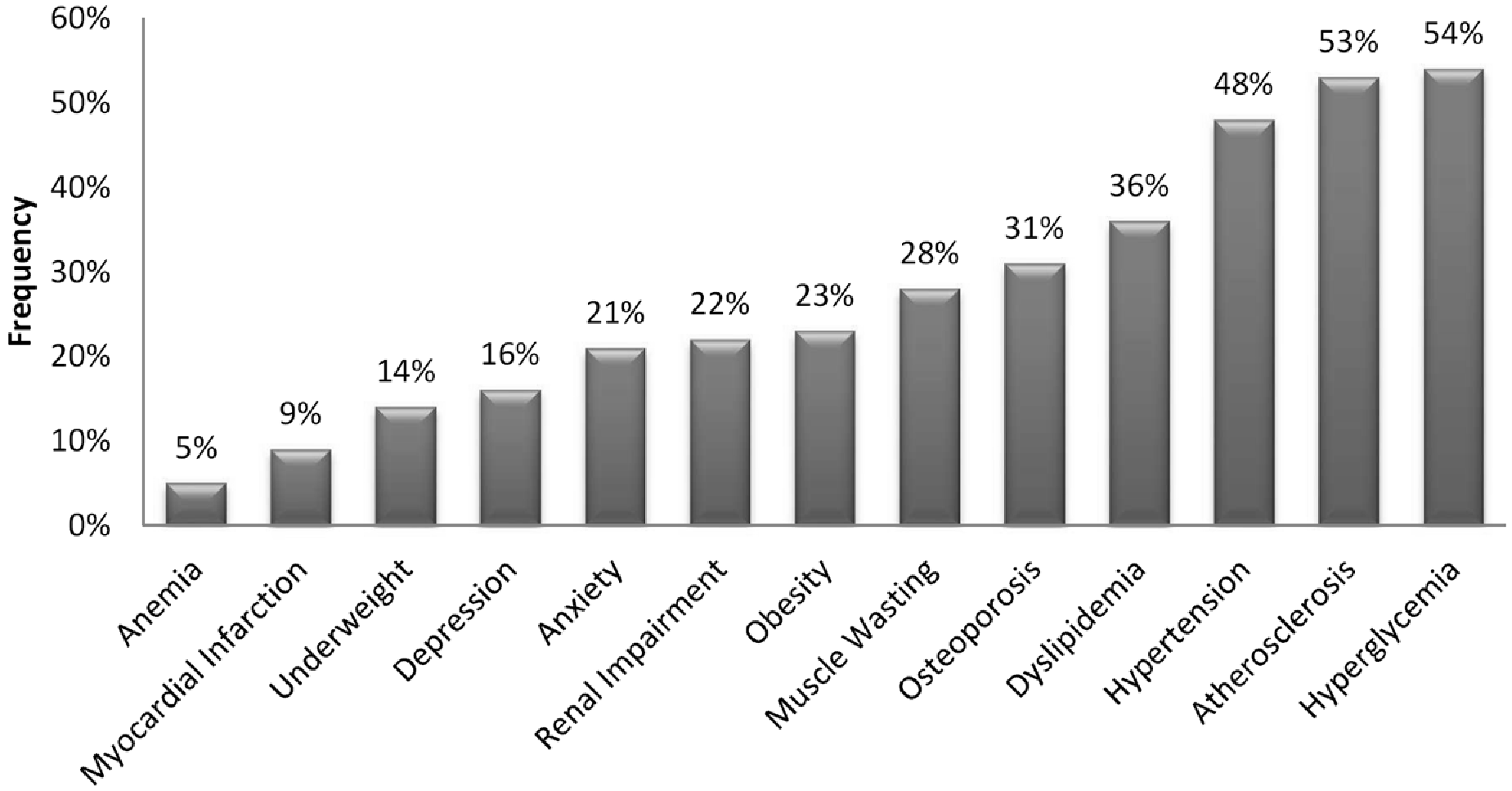
Maatman et al., Respirology 2016

Combined effects of obesity and COPD: systemic consequences



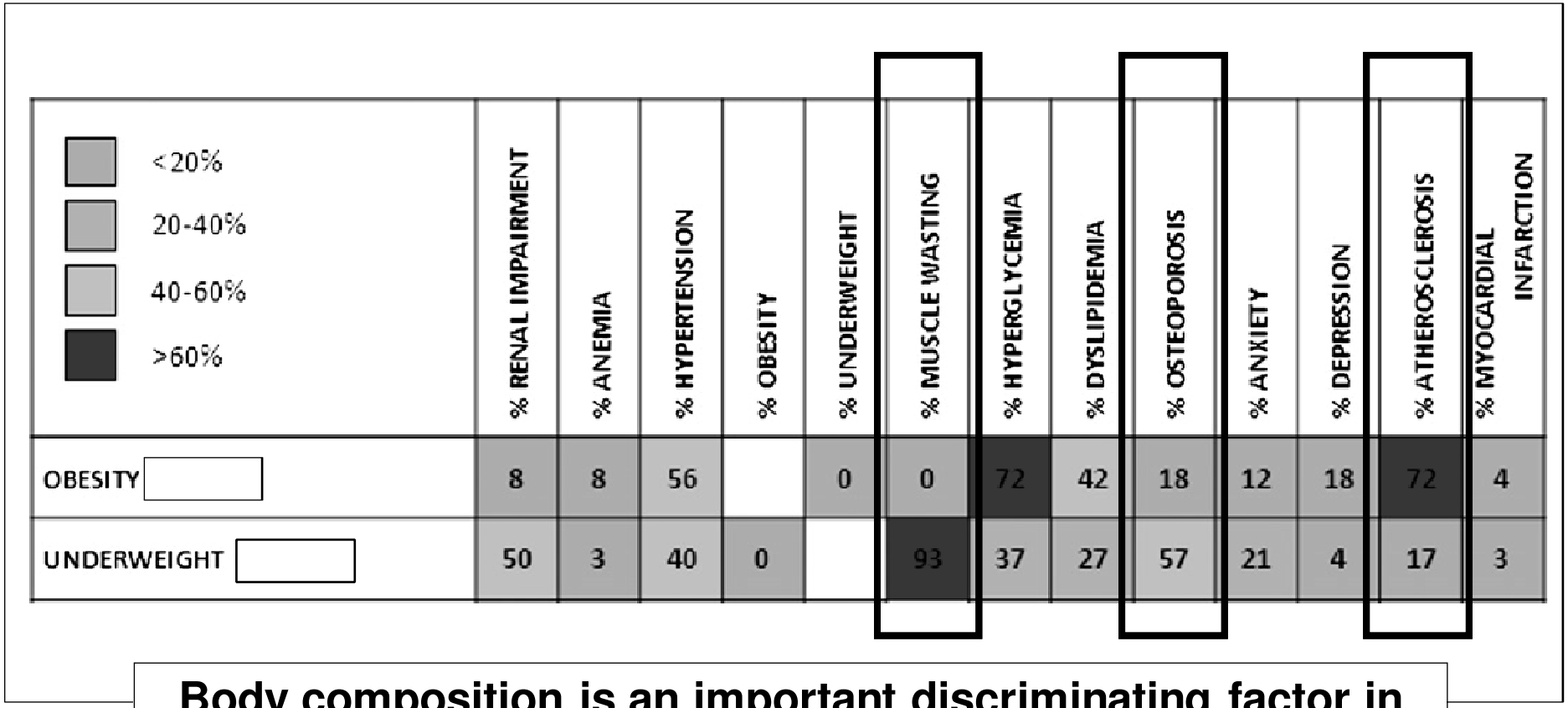
Fabbri et al., Eur Respir J 2008

Frequencies of objectively identified comorbidities



Vanfleteren et al., Am J Respir Crit Care Med 2013

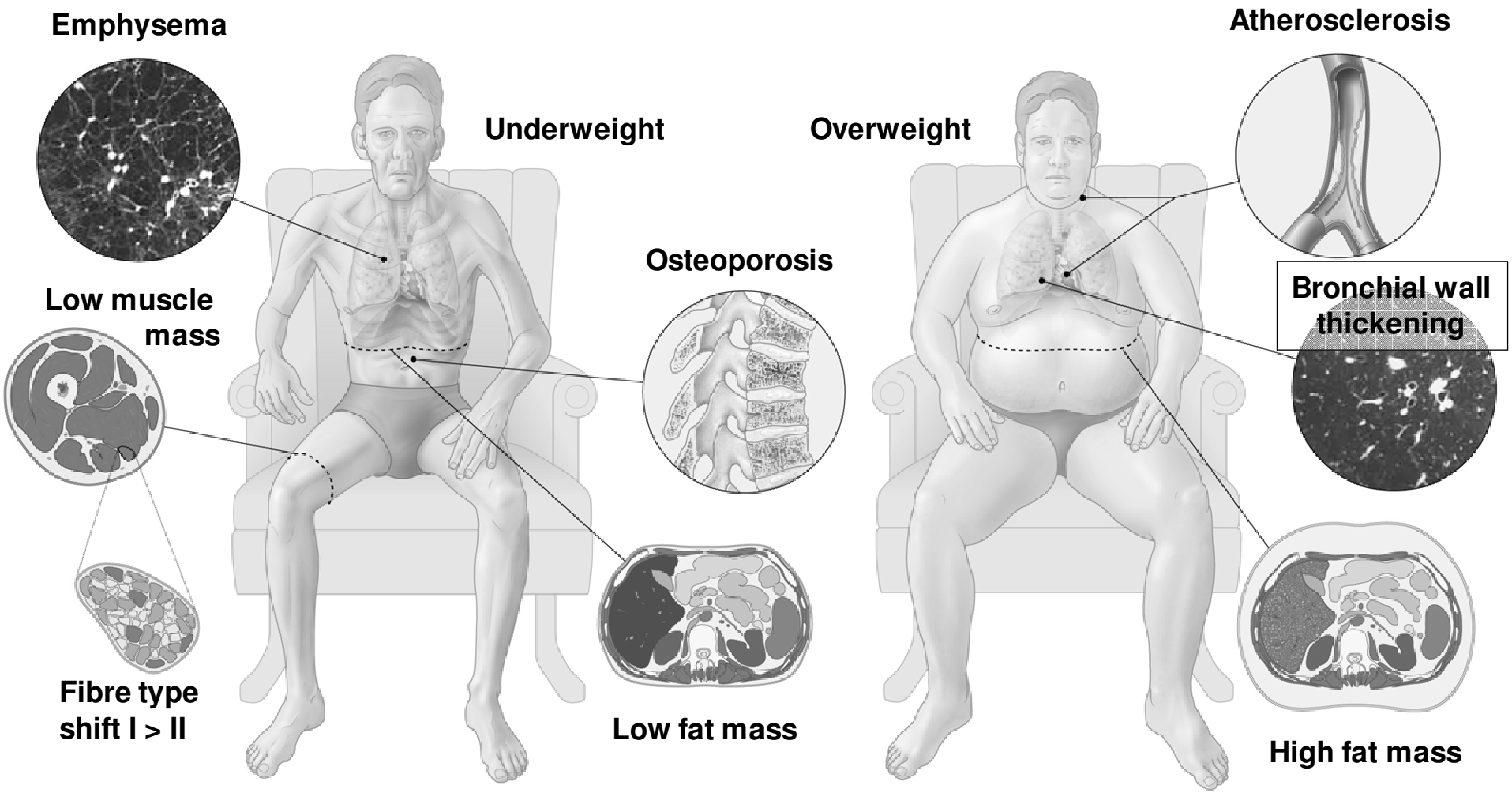
Clustering of objectively identified comorbidities in COPD



Body composition is an important discriminating factor in unbiased clustering of COPD

Vanfleteren et al., Am J Respir Crit Care Med 2013

Classical COPD phenotypes revisited



Cachectic phenotype

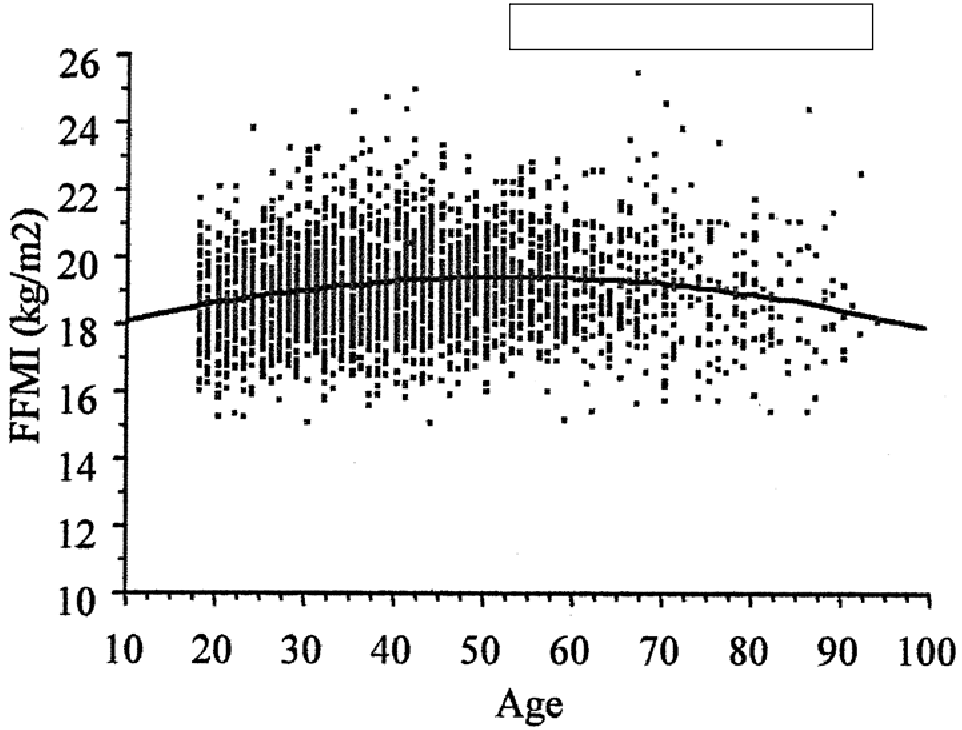
Metabolic phenotype

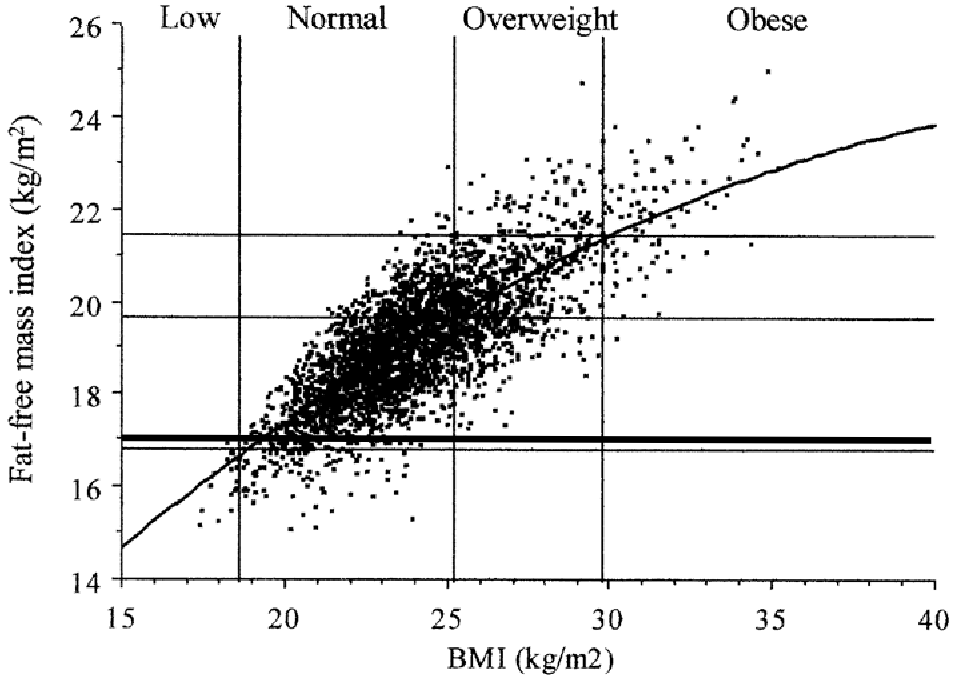
ERS Taskforce 'Nutrition in COPD', Eur Respir J 2014

Assessing low fat-free mass: the impact of aging and BMI

Above the age of 60, fat-free mass index declines

Fat-free mass index is positively correlated with BMI





There is a rationale for gender-, age- and BMI specific cut-offs

Kyle et al., Nutrition 2003

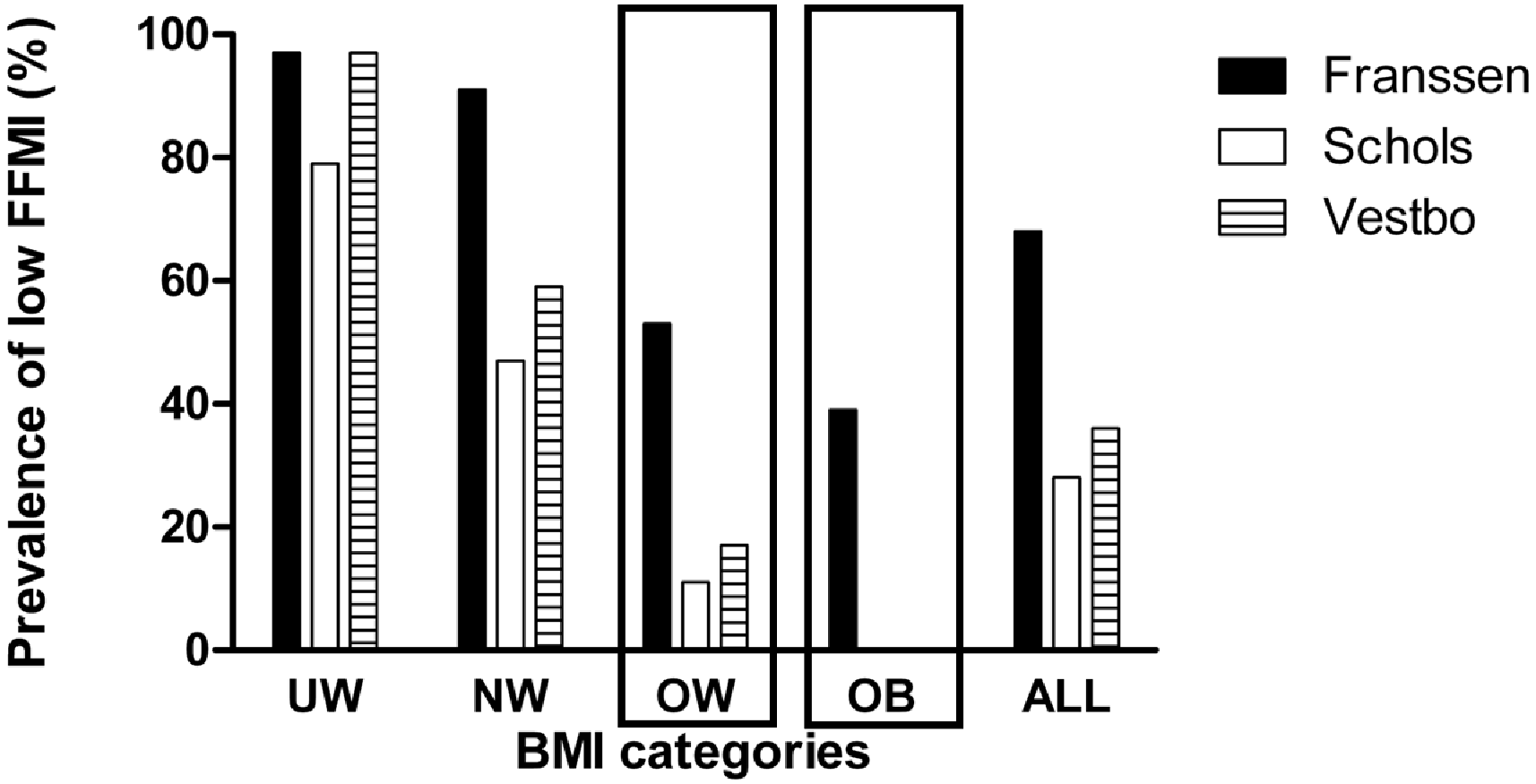
New reference values for fat-free mass index: results from the UK Biobank (n = 186,975)

		Men				Women			
Age, y	BMI, kg/m^2	P5	P10	P25	P50	P5	P10	P25	P50
45–59	<18.50	14.0	14.9	15.3	15.7	12.9	13.3	13.7	14.1
	18.50–24.99	17.0	17.5	18.1	18.9	14.3	14.6	15.1	15.7
	25.00–29.99	19.0	19.3	19.9	20.6	15.5	15.8	16.3	16.9
	≥30.00	20.9	21.3	21.8	22.6	16.9	17.2	17.7	18.3
60–69	<18.50	14.5	14.9	15.2	15.8	12.7	13.0	13.6	14.2
	18.50–24.99	16.8	17.2	17.9	18.6	14.2	14.5	15.0	15.5
	25.00–29.99	18.6	18.9	19.5	20.2	15.4	15.7	16.1	16.7
	≥30.00	20.4	20.7	21.3	22.1	16.7	17.0	17.5	18.1

Body composition data from the general population indicate that in overweight and obese populations higher cut-off values for low fat-free mass should be applied

Franssen et al., JAMDA 2014

The prevalence of low muscle mass in overweight and obese COPD patients

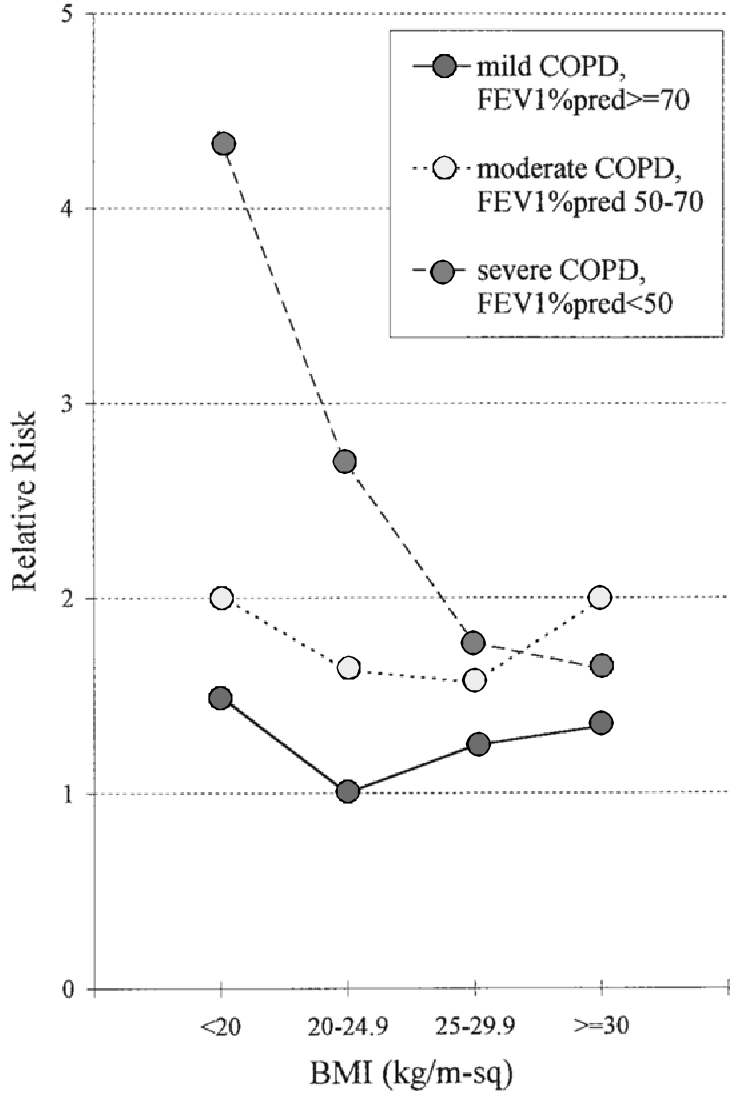


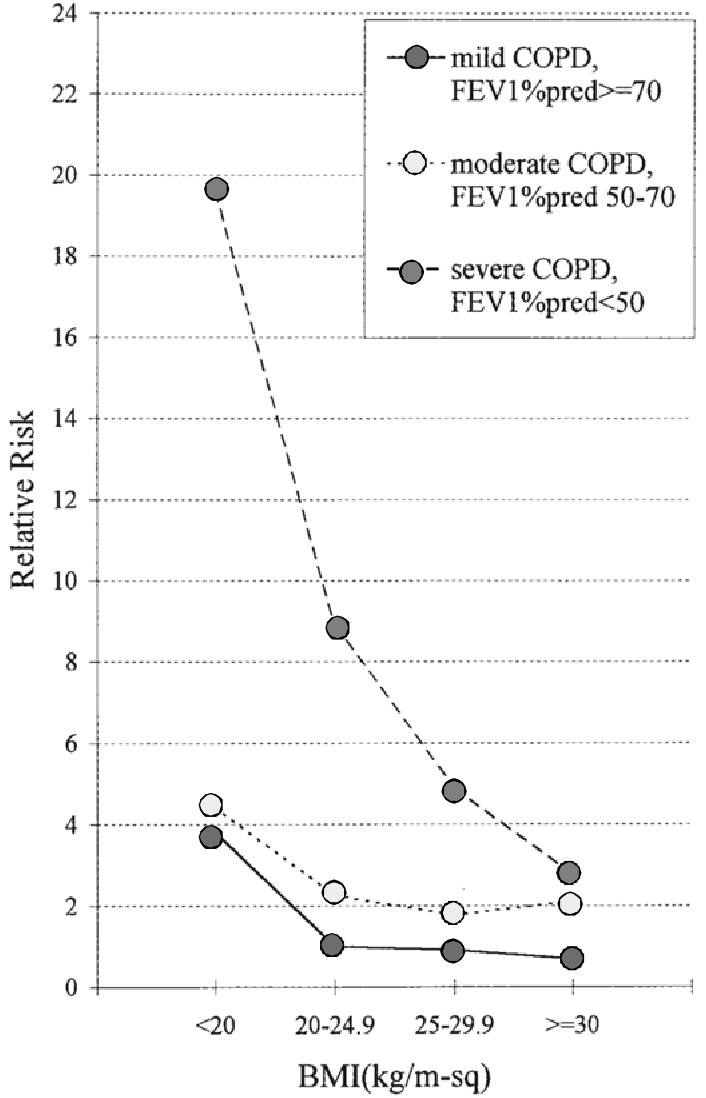
A large proportion of overweight and obese patients with COPD fulfull the new criteria for low fat-free mass

Franssen et al., in preparation

Combined effects of obesity and COPD: obesity paradox

All-cause mortality

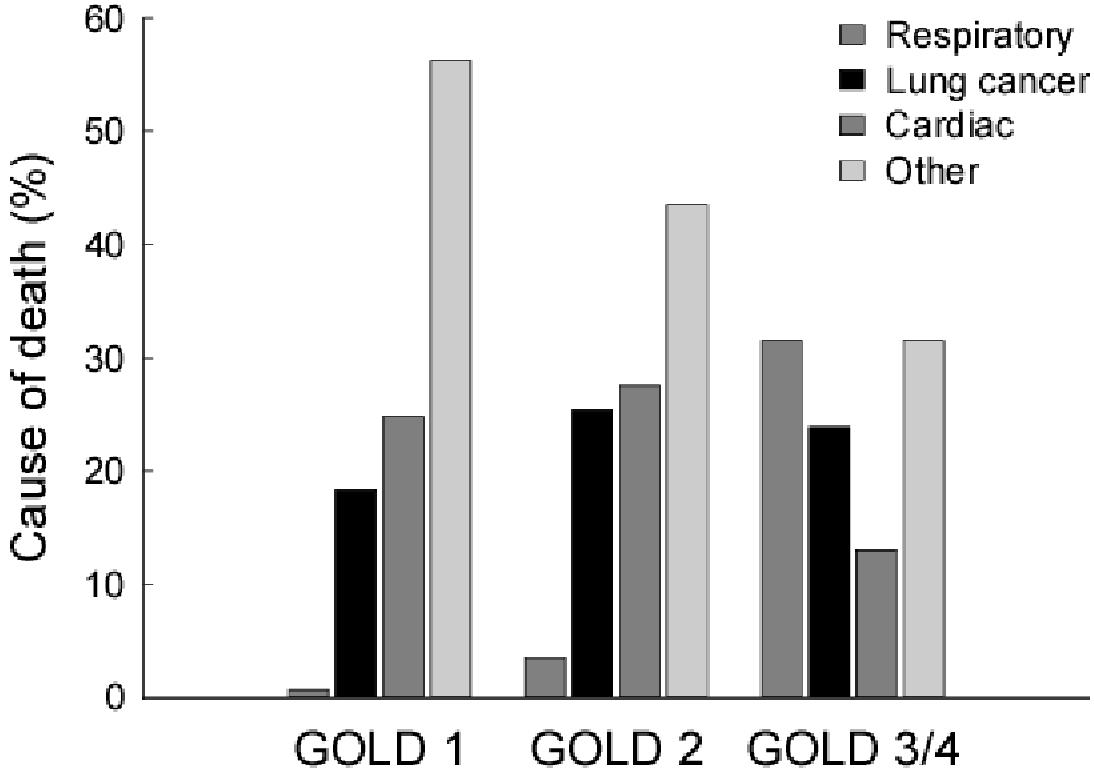




COPD related mortality

Landbo et al., Am J Respir Crit Care Med 1999

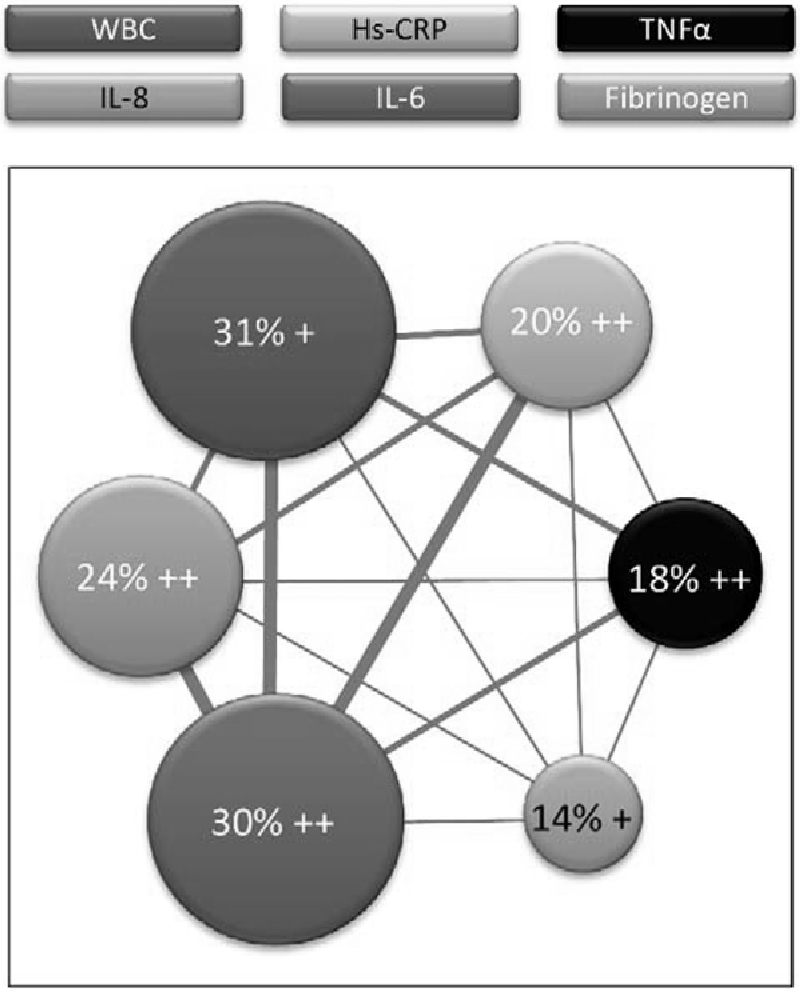
Causes of death in COPD



Only a minority of COPD patients die from this disease

Mannino et al., Respir Med 2006

Persistent systemic inflammation in COPD

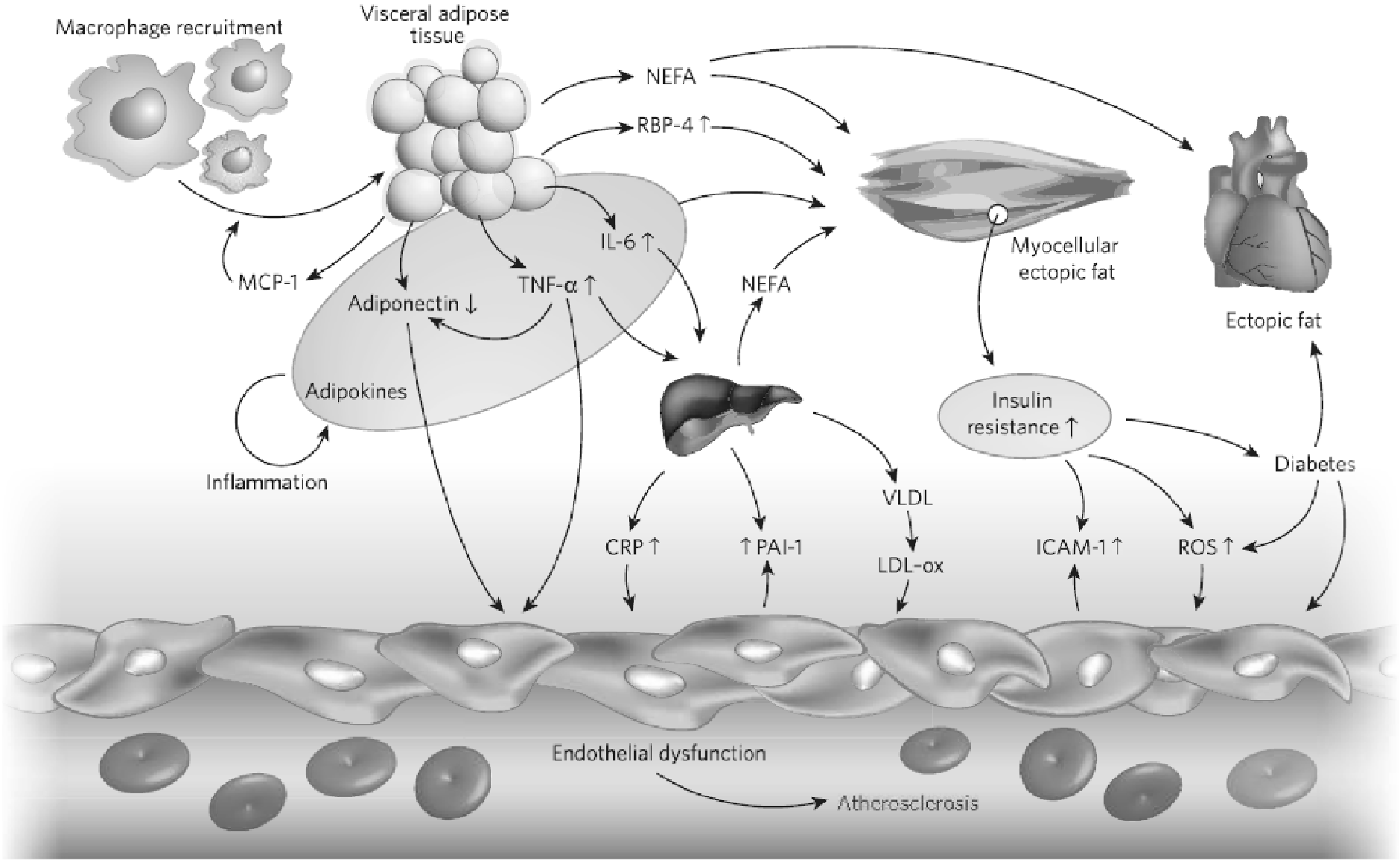


30% of patients do not have systemic inflammation, whereas only 16% have persistent systemic inflammation

Age, **high BMI**, current smoking, poor health status and airflow limitation were independent risk factors for persistent systemic inflammation

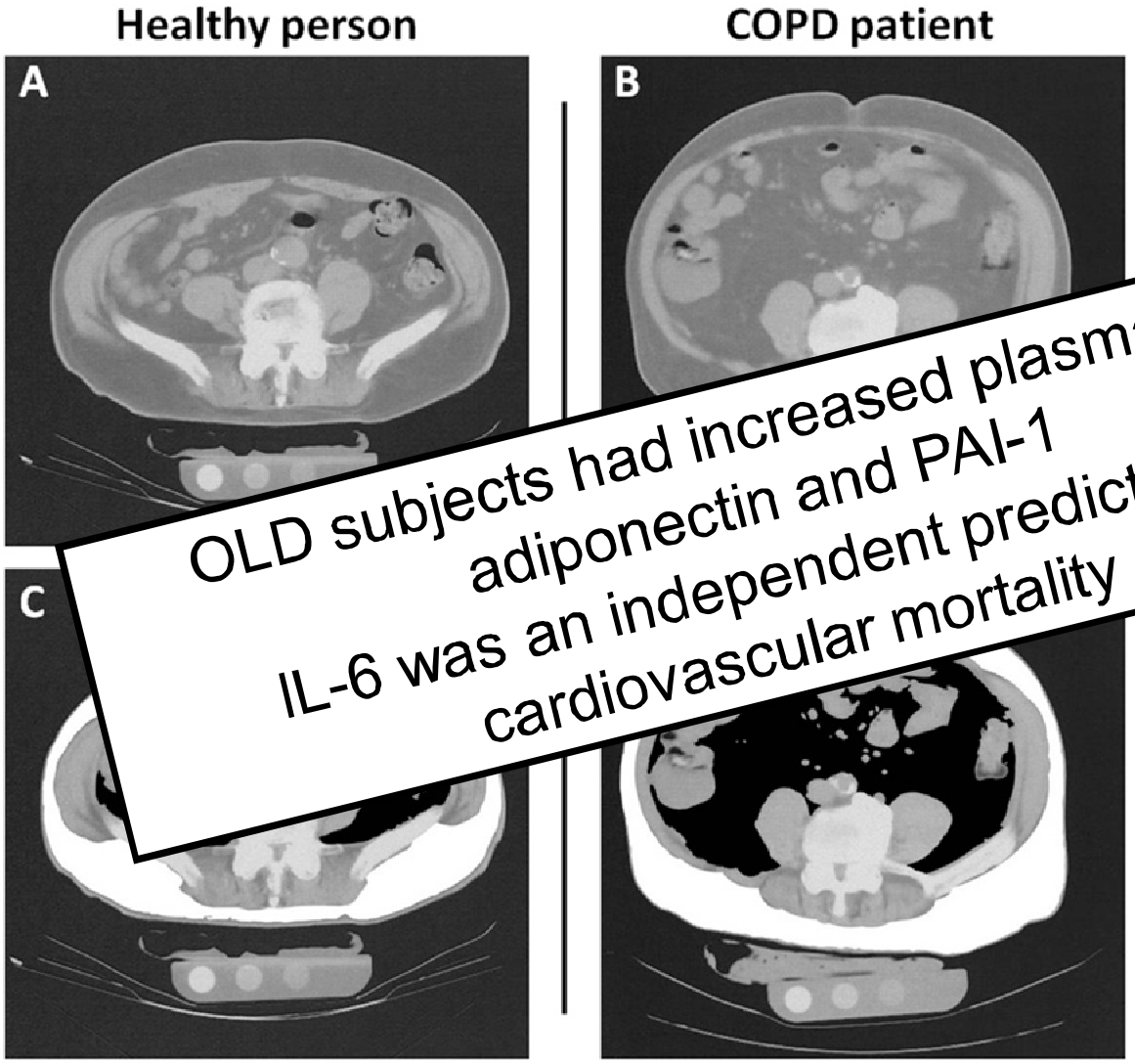
Agusti et al., PloS One 2012

Adipocyte dysfunction, systemic inflammation and cardiovascular risk



Van Gaal et al., Nature 2006

Excessive visceral fat accumulation in COPD



BMI

OLD subjects had increased plasma IL-6, adiponectin and PAI-1
IL-6 was an independent predictor for cardiovascular mortality

Visceral fat ↑

Subcutaneous fat ↔

van den Borst et al., Am J Respir Crit Care Med 2013

Considerations for treatment of obesity in COPD

PRO:

- Increased dyspnea at rest
- Reduce cardiovascular risk
- Improve physical functioning
- Reduce mortality in non-severe COPD
- Improve glucocorticosteroid responsiveness

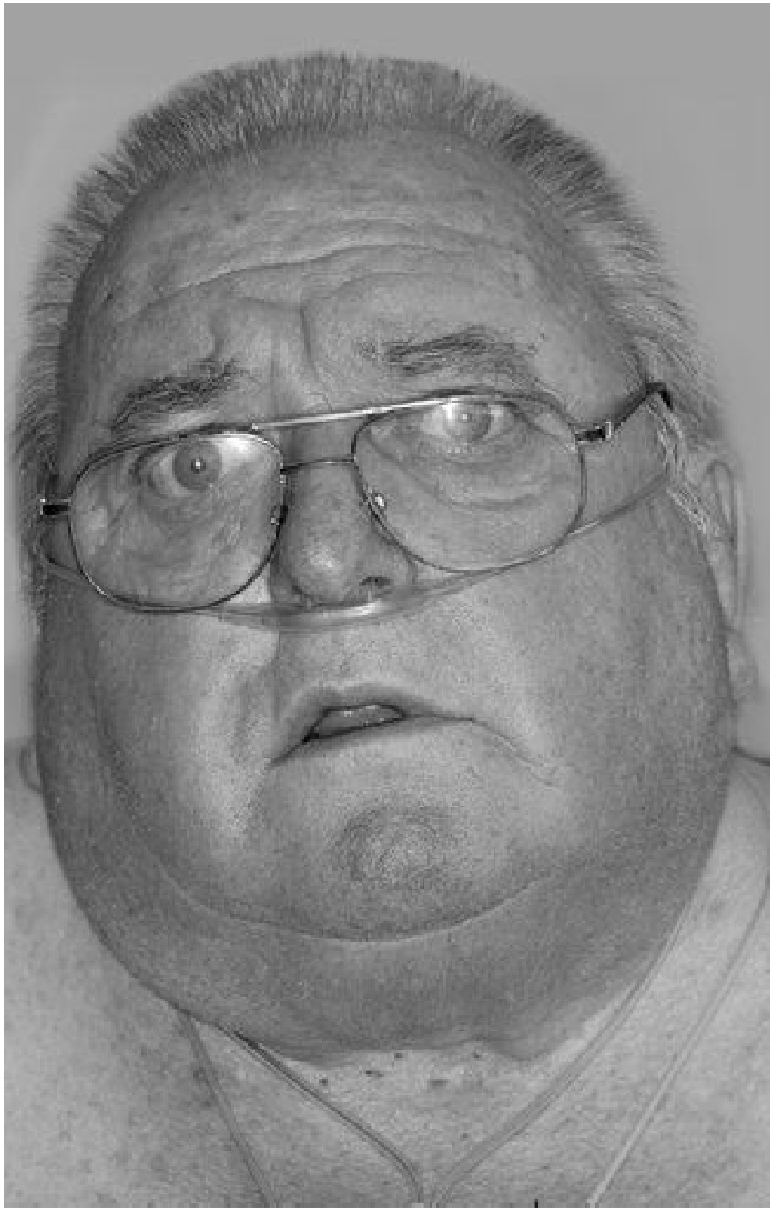
CON:

- Reduced static lung volumes
- Preserved non-weight bearing exercise tolerance
- Comparable exercise-related symptoms
- Lower prevalence of muscle wasting
- Lower prevalence of reduced bone mineral density
- Better prognosis in severe COPD

Management of obesity in COPD

WHY?

- CV risk factors?
- Comorbidities?
- Symptoms?
- Performance?
- Mortality?



HOW?

- VLCD?
- Acti
- r?
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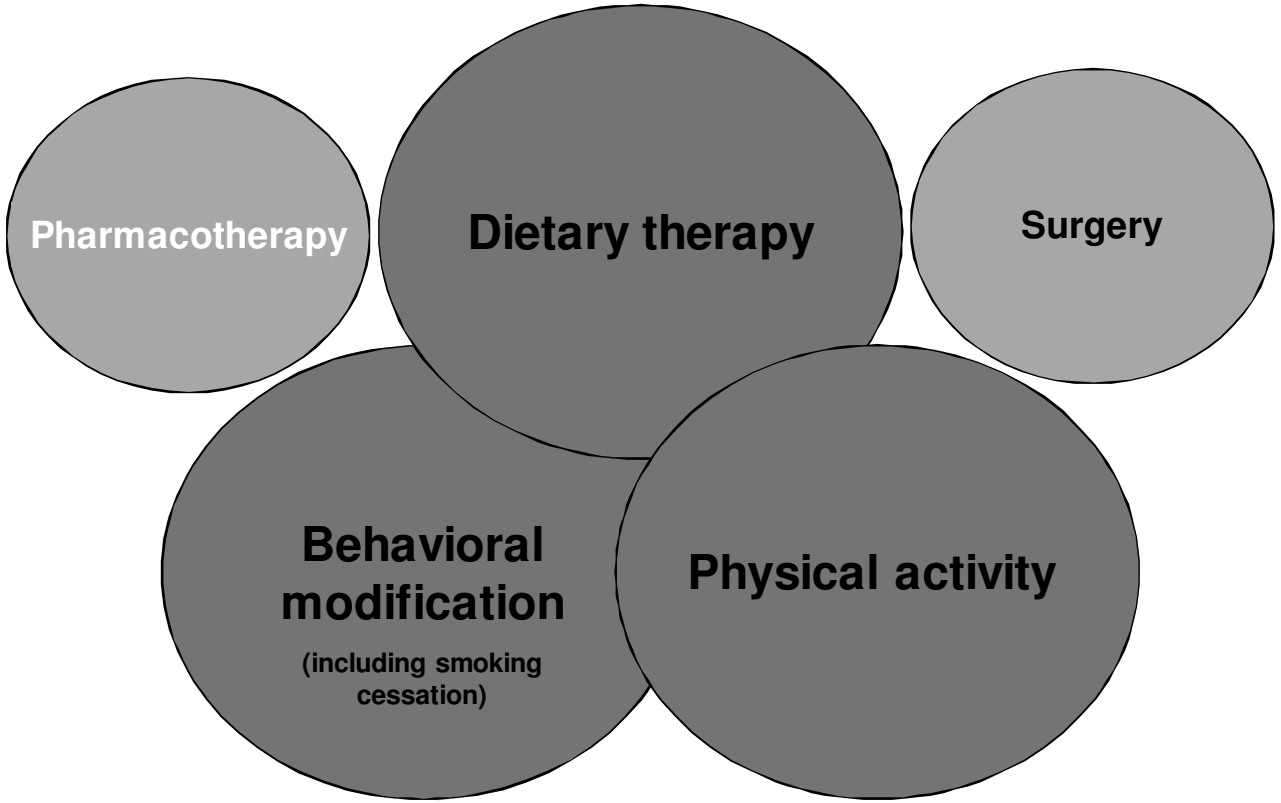
NO STUDIES IN COPD

Multidimensional treatment of adult obesity

Intitial goal: loss of 10% of baseline weight after six months at a rate of 0.5 - 1.0 kg per week



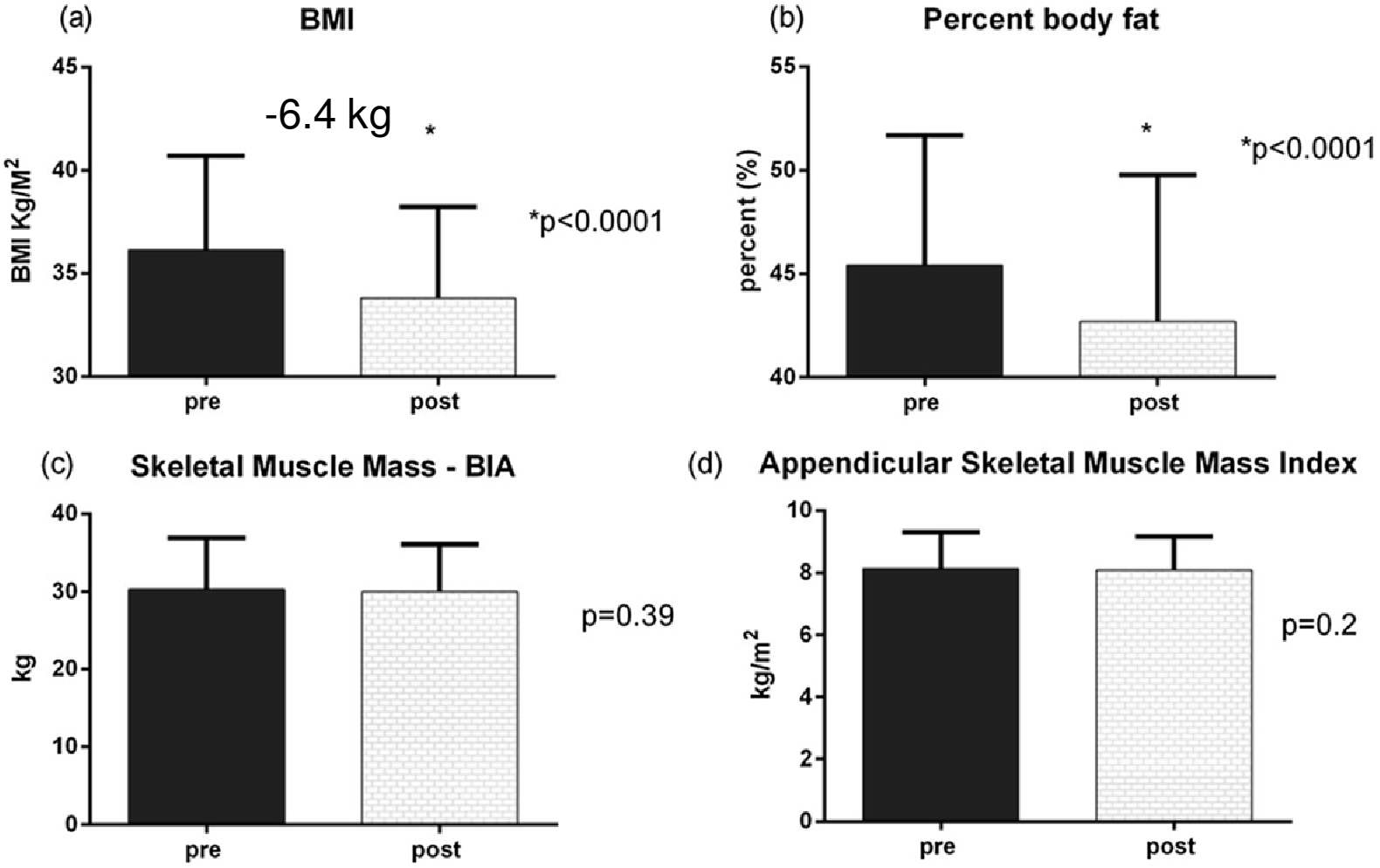
Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults, National Institute of Health, 1998

Treating obesity in COPD

Inclusion:	COPD, BMI > 30 kg/m^2, FEV_1 < 80%, clinically stable
Exclusion:	Current smoking, cardiac disease, insulin users, significant orthopaedic problems
Program:	- Low-energy diet, 2 meal replacements, high-protein intake - Home-based strength training 3 days/week - Two weekly treatment visit, two weekly phone call - 12 weeks

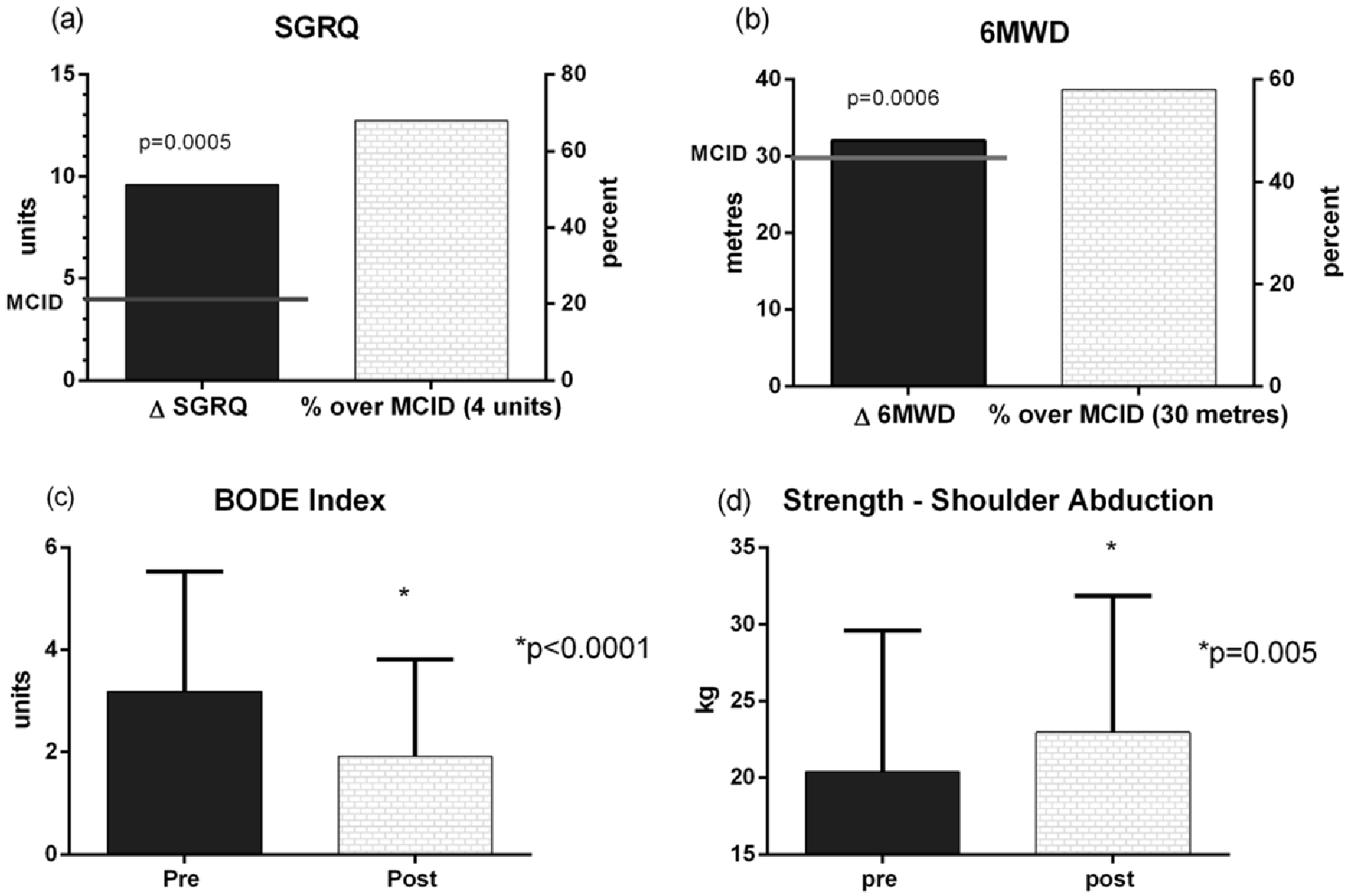
et al., Respirology 2016

Treating obesity in COPD



McDonald et al., Respirology 2016

Treating obesity in COPD



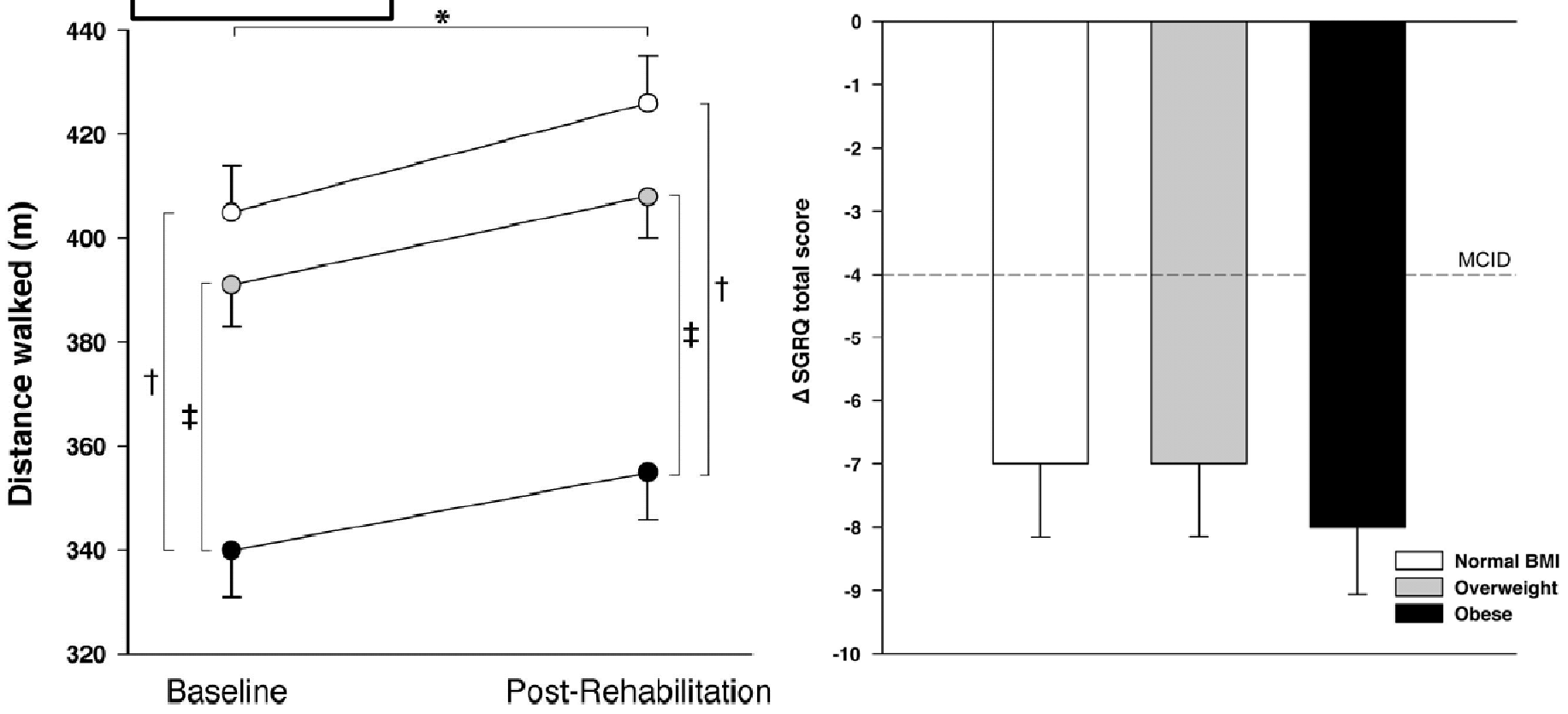
McDonald et al., Respirology 2016

Treating obesity in COPD

Pulmonary function	n	Pre	Post	p value
Post-bronchodilator FEV1 (L), mean (SD)	28	1.7 (0.5)	1.8 (0.5)	0.4112
Post-bronchodilator FVC (L), mean (SD)	**28**	**2.8 (0.8)**	**3.0 (0.8)**	**0.0033**
FEV1/FVC ratio, mean (SD)	28	61.7 (12.6)	60.4 (13.2)	0.1886
Functional residual capacity (L), mean (SD)	14	3.4 (1.1)	3.5 (1.0)	0.19
Residual volume (L), mean (SD)	14	2.5 (0.9)	2.4 (0.8)	0.42
End residual volume (L), mean (SD)	14	0.95 (0.4)	1.1 (0.5)	0.15
Total lung capacity (L), mean (SD)	14	5.6 (1.3)	5.7 (1.4)	0.27

Mc Donald et al., Respirology 2016

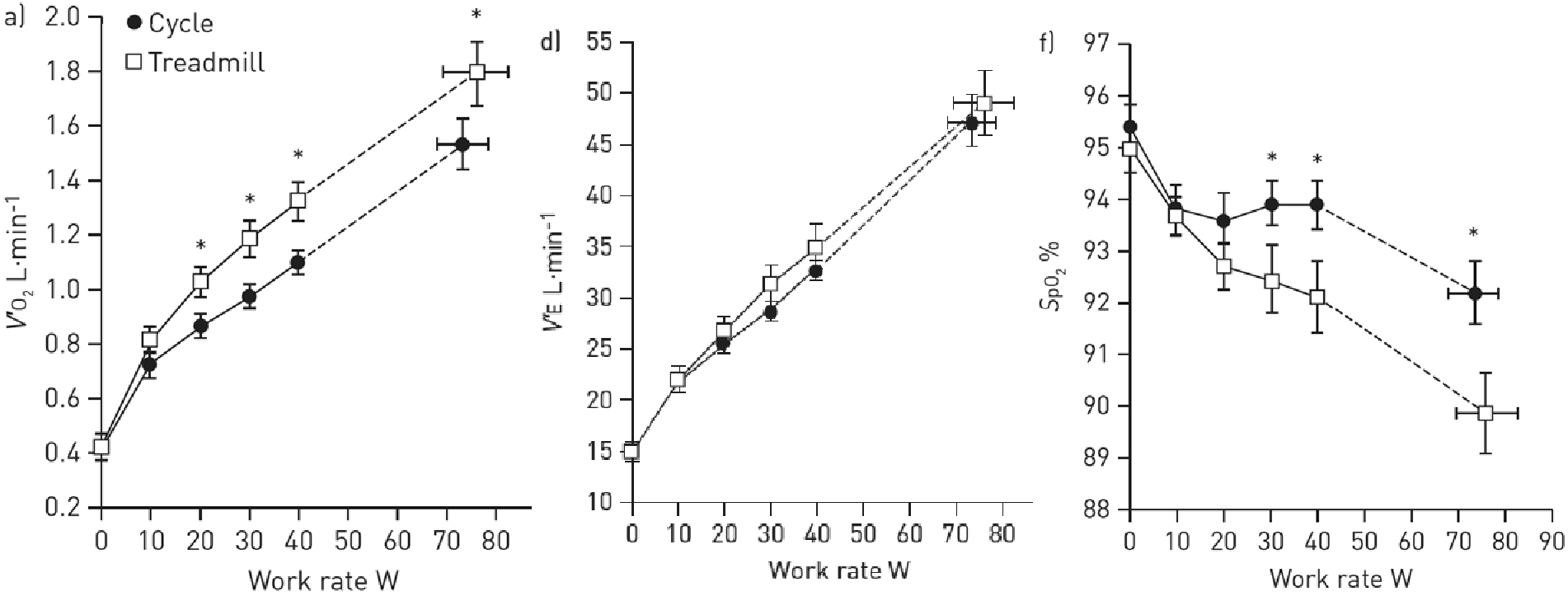
The impact of obesity on response to pulmonary rehabilitation in COPD



Obesity and overweight do not influence the magnitude of improvement after pulmonary rehabilitation

Sava et al., BMC Pulm Med 2010

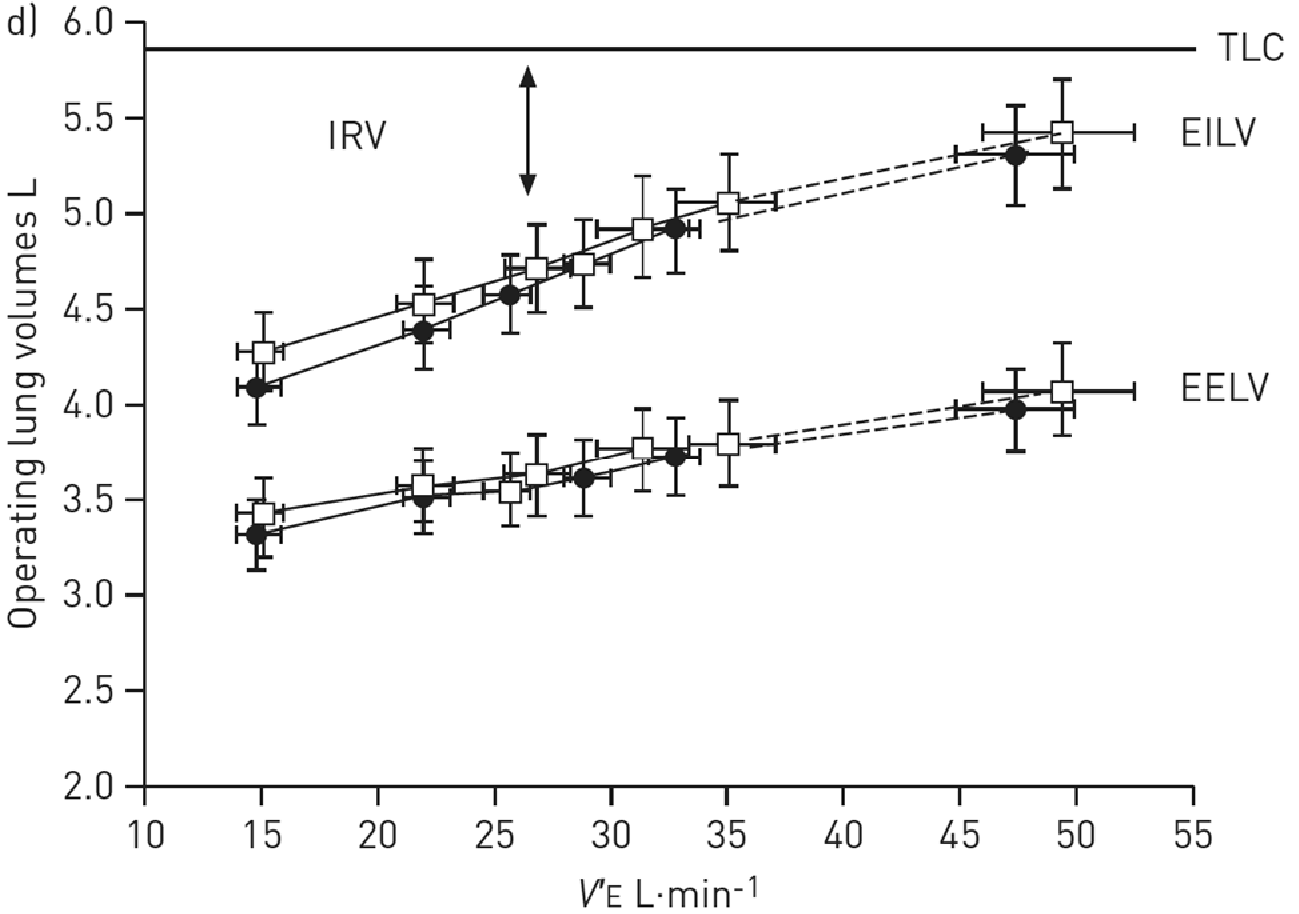
The impact of exercise modality on physiological responses and dyspnea in obese COPD patients



Compared with cycling, treadmill walking is associated with higher oxygen uptake and greater desaturation in obese COPD patients

Ciavaglia et al., Eur Respir J 2014

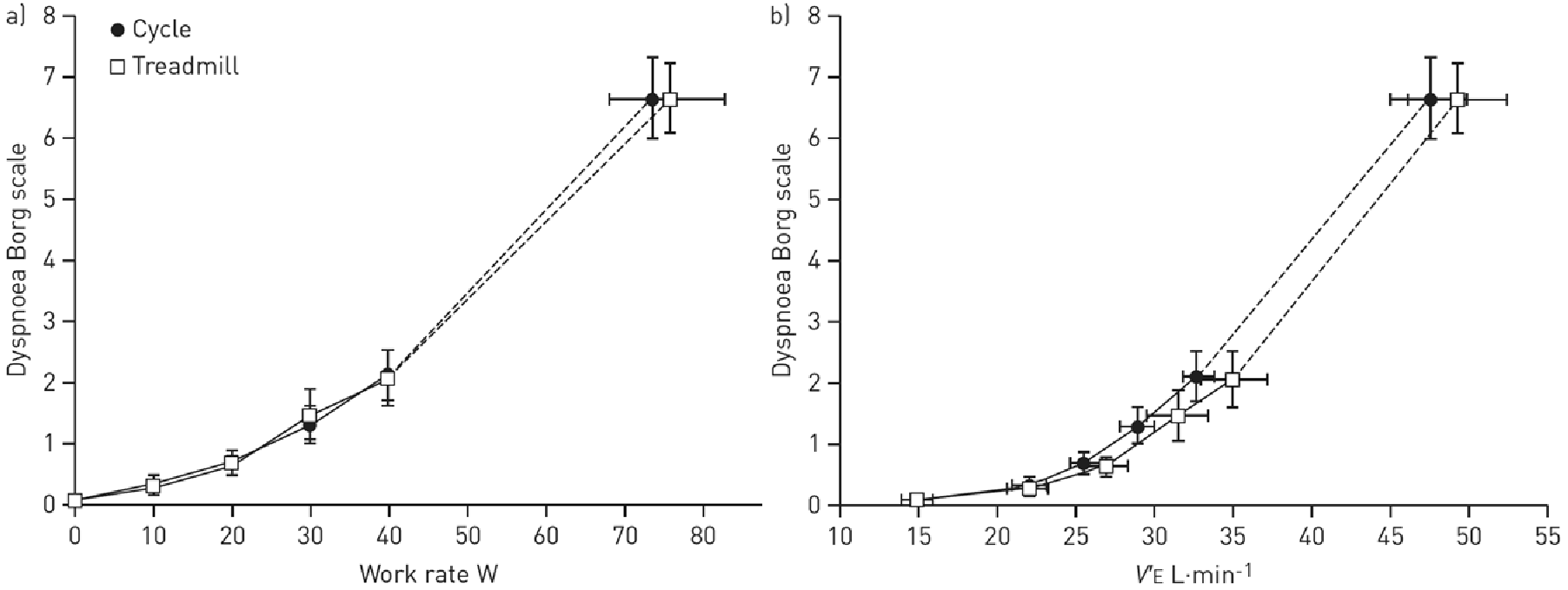
The impact of exercise modality on physiological responses and dyspnea in obese COPD patients



Operating lung volumes are similar cycling and treadmill walking in obese patients with COPD

Ciavaglia et al., Eur Respir J 2014

The impact of exercise modality on physiological responses and dyspnea in obese COPD patients



Exercise modality has no effect on dyspnea/work rate or dyspnea/ventilation relationships in obese patients with COPD

Ciavaglia et al., Eur Respir J 2014

Special considerations for pulmonary rehabilitation in patients with COPD and obesity

Water-based exercise training was more effective than land-based exercise training in increasing exercise capacity and health status in COPD patients and co-morbidities (42% obesity)

McNamara et al., Eur Respir J 2012

COPD and obesity: summary

1) The number of COPD patients with obesity is expected to increase, in line with the obesity pandemic.
2) For accurate clinical assessment and disease management it is essential to understand the effects of excessive fat mass in patients in which COPD and obesity collide.
3) Contrary to expectations, obesity is not necessarily associated with worse patient-related outcomes in COPD.
4) The role of adipose tissue dysfunction in COPD pathophysiology and increased cardiovascular risk is a hot research topic.
5) The effects of weight loss and the optimal BMI for obese patients with COPD are currently unkwown.
6) The presence of comorbid obesity in a patient with COPD may warrant specific programme adaptations during pulmonary rehabilitation

@fritsfranssen