

**Il decondizionamento
muscolare nelle malattie
respiratorie croniche:
il caso della BPCO**

Prof Mauro Zamboni
Università di Verona

7
APRILE
8

**OTTICA
RESPIRO**
VERONA **2017**
CROWNE PLAZA

Skeletal Muscle Dysfunction in Chronic Obstructive Pulmonary Disease. A Statement of the American Thoracic Society and European Respiratory Society

American Journal of Respiratory and Critical Care Medicine, Vol. 159,
Skeletal Muscle Dysfunction in Chronic Obstructive Pulmonary Disease 1999



AMERICAN THORACIC SOCIETY DOCUMENTS

An Official American Thoracic Society/European Respiratory Society Statement: Update on Limb Muscle Dysfunction in Chronic Obstructive Pulmonary Disease

François Maltais, Marc Decramer, Richard Casaburi, Esther Barreiro, Yan Burelle, Richard Debigaré, P. N. Richard Dekhuijzen, Frits Franssen, Ghislaine Gayan-Ramirez, Joaquim Gea, Harry R. Gosker, Rik Gosselink, Maurice Hayot, Sabah N. A. Hussain, Wim Janssens, Micheal I. Polkey, Josep Roca, Didier Saey, Annemie M. W. J. Schols, Martijn A. Spruit, Michael Steiner, Tanja Taivassalo, Thierry Troosters, Ioannis Vogiatzis, and Peter D. Wagner; on behalf of the ATS/ERS Ad Hoc Committee on Limb Muscle Dysfunction in COPD

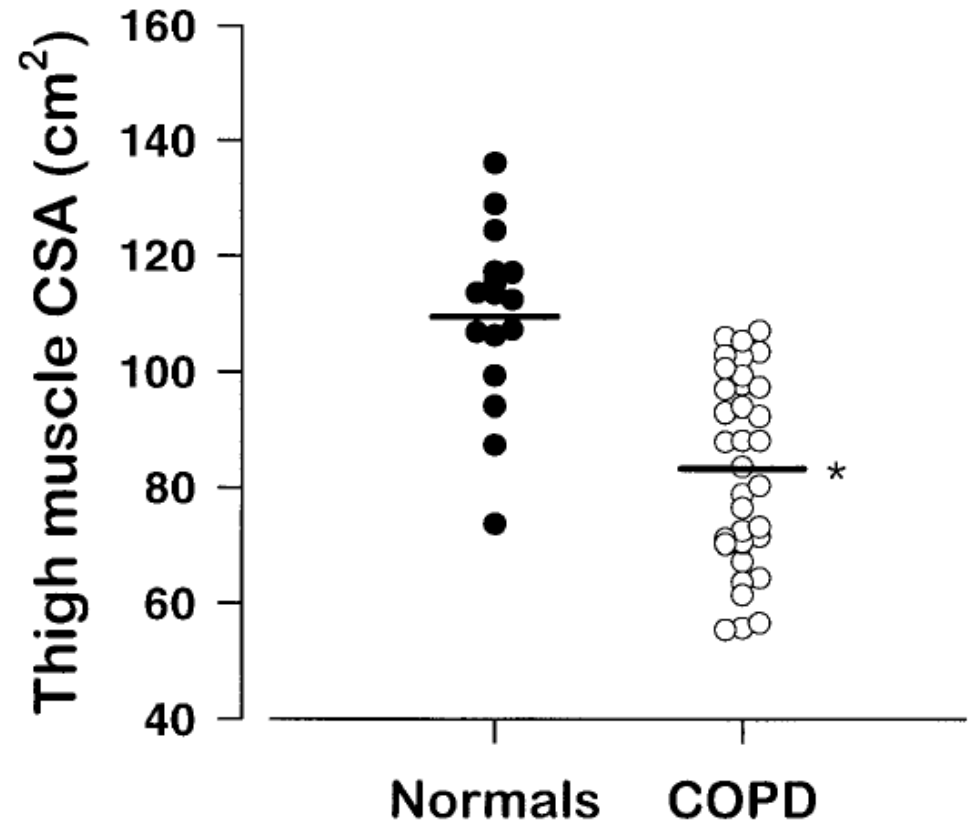
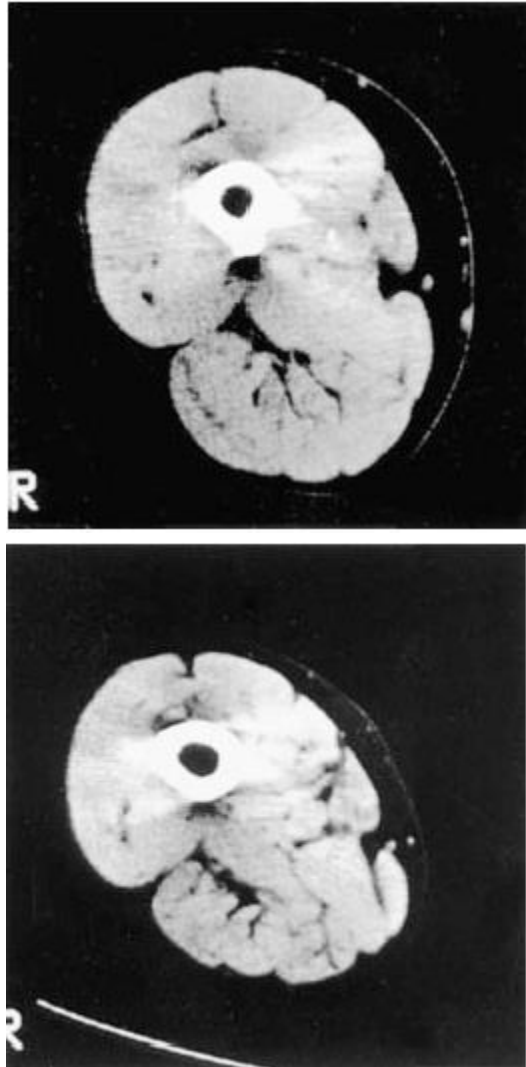
Am J Respir Crit Care Med Vol 189, Iss 9, pp e15–e62, May 1, 2014

Definition

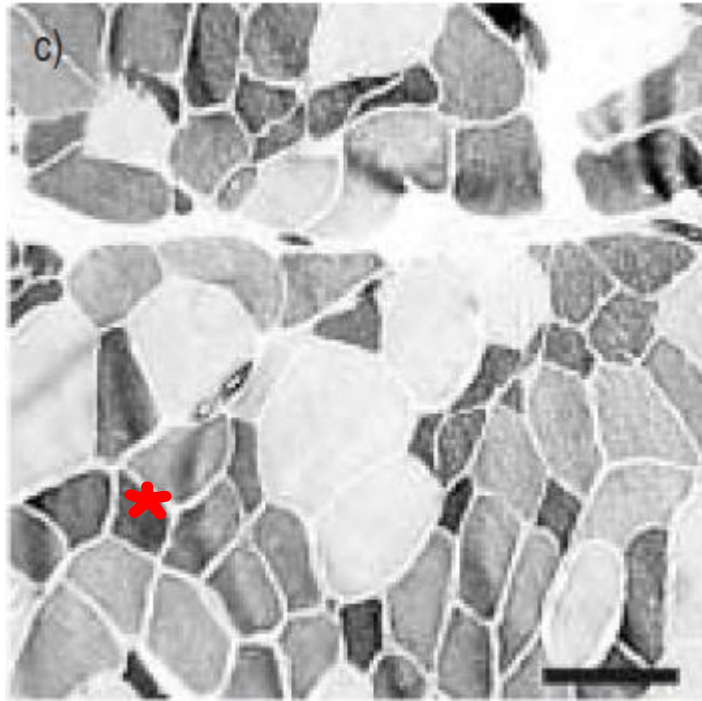


Limb muscle dysfunction is defined as the **morphological** and **functional changes** that are seen **in limb muscles** in patients with COPD

Thigh muscle cross sectional area in COPD and control subjects



Vastus lateralis biopsies of COPD weight-stable patients and healthy age -matched controls



Type 1 fibers (oxidative)

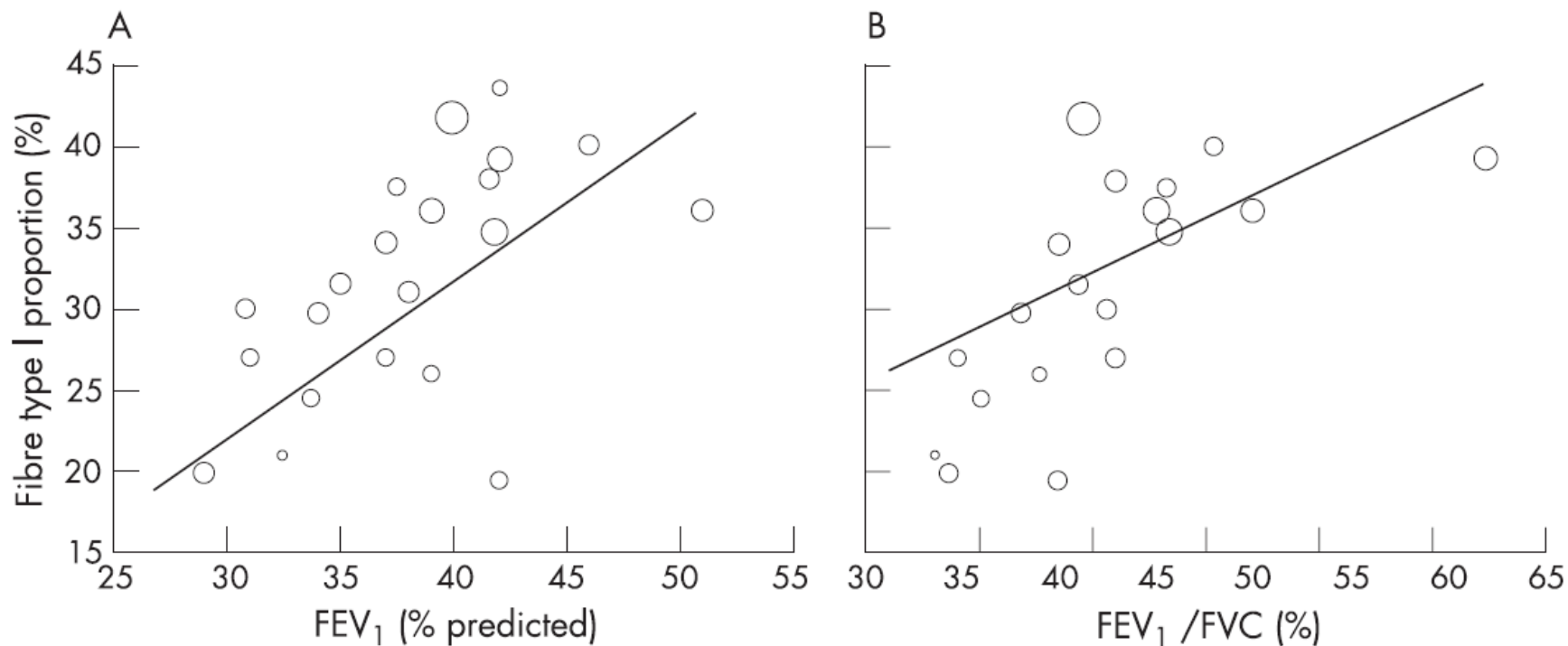


Type IIX fibers (glycolytic)
* (atrophic)

Muscle biopsy	Controls	COPD
Proportion of type-I fibres %	43.4±12.6	19.4±14.0***
Proportion of type-IIA fibres %	29.4±12.1	34.8±11.9
Proportion of type-IIX fibres %	27.2±12.3	45.8±18.9***
CSA of type-IIX fibres μm^2	4248±1300	2566±1137**

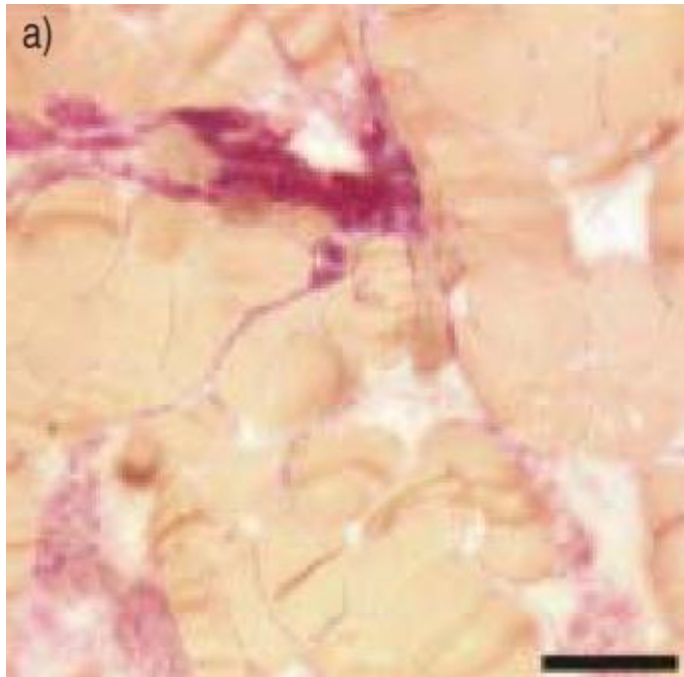
Eur Resp J 2003; 22: 280-85

Muscle fibre type shifting in the vastus lateralis of patients with COPD is associated with disease severity: a systematic review and meta-analysis

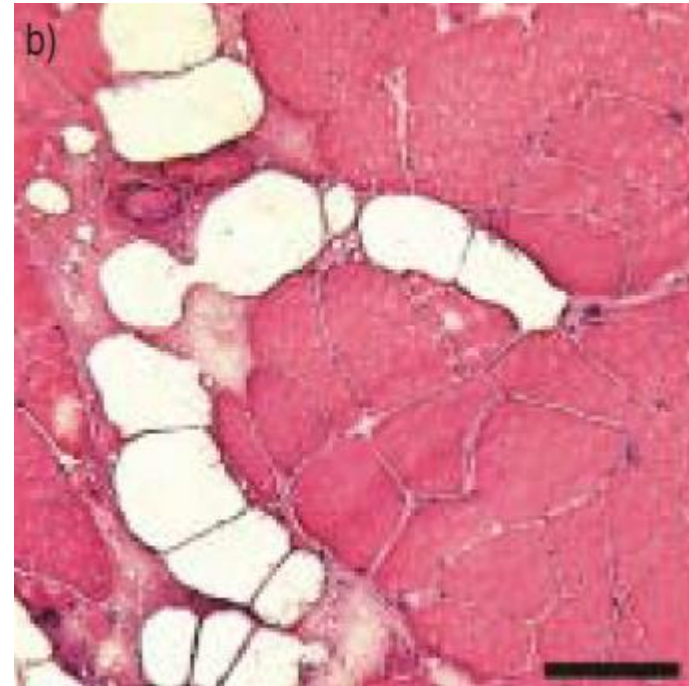


Gosker et al, 2007

Vastus lateralis biopsies of COPD weight-stable patients

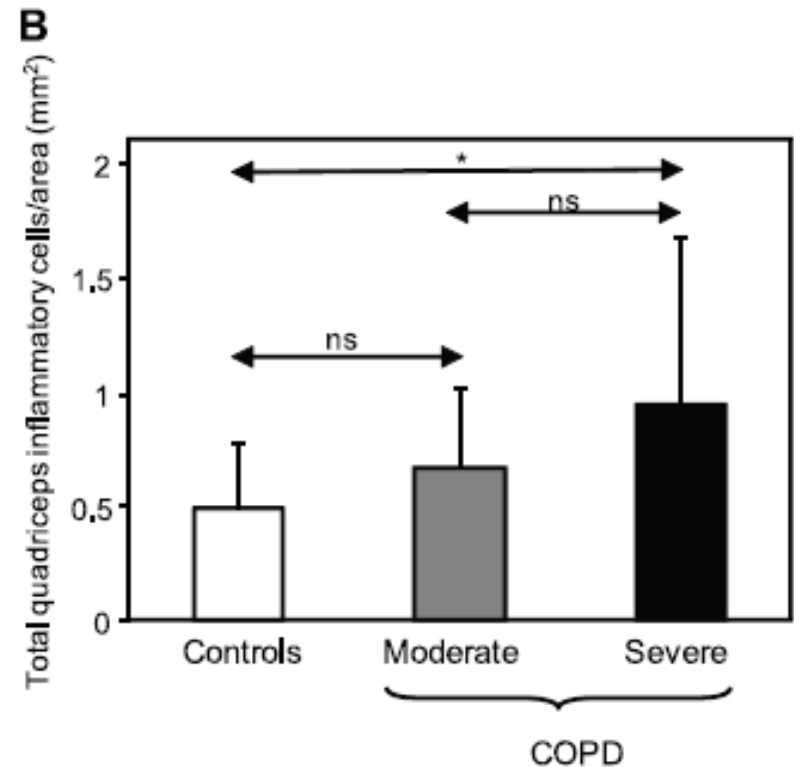
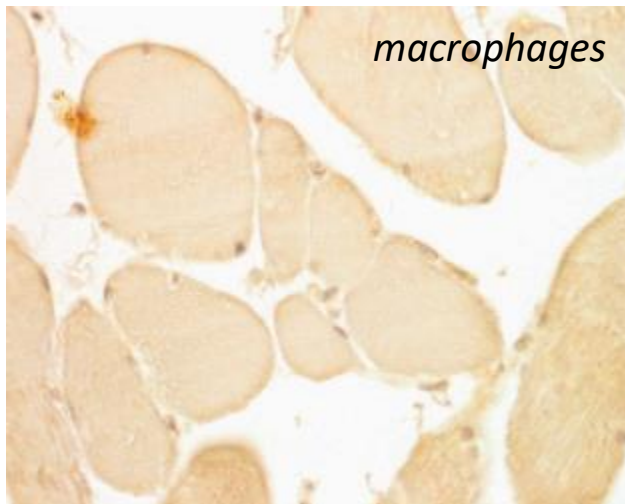
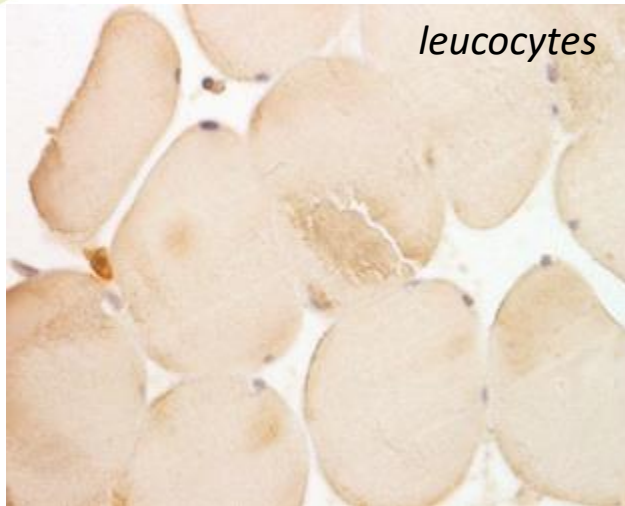


Fybrosis

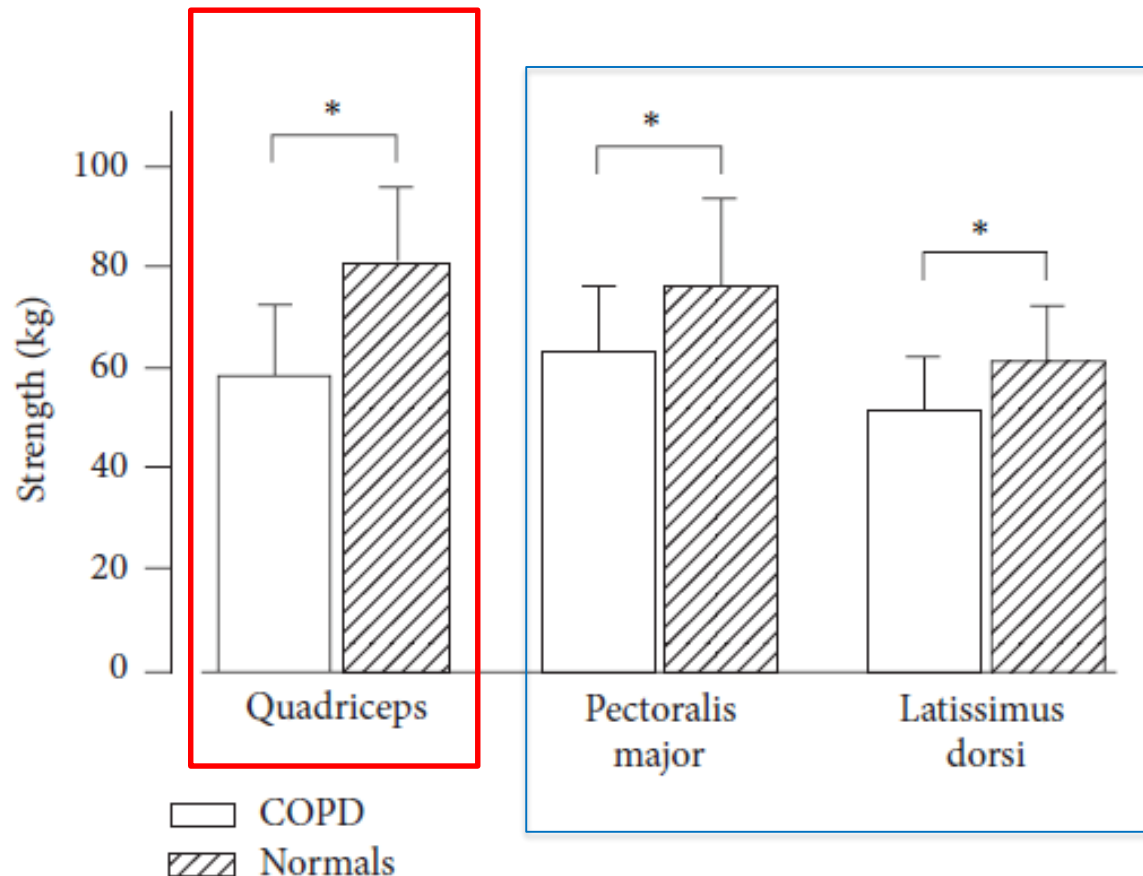


Fat infiltration

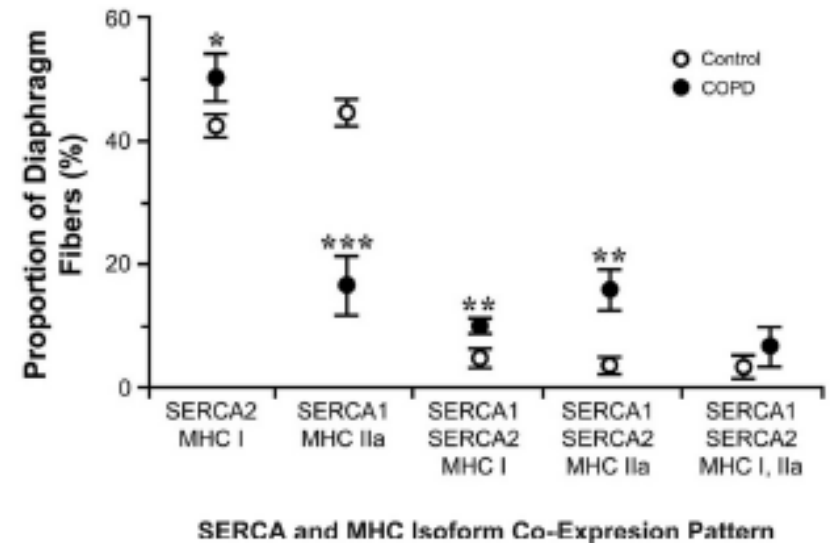
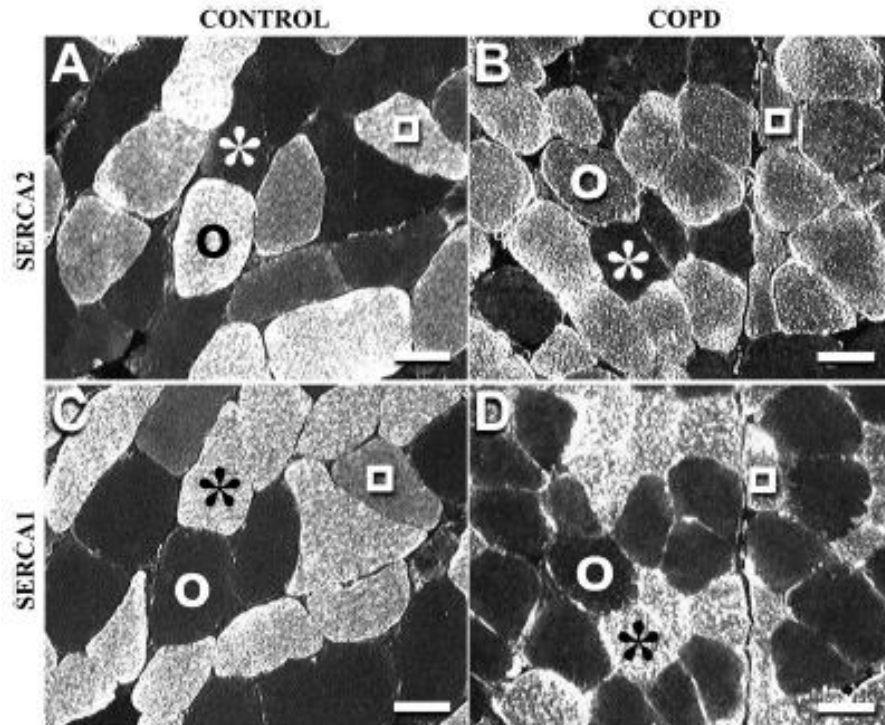
Inflammatory cells in limb muscles of patients with COPD



muscle strength in patients with COPD compared to normal subjects



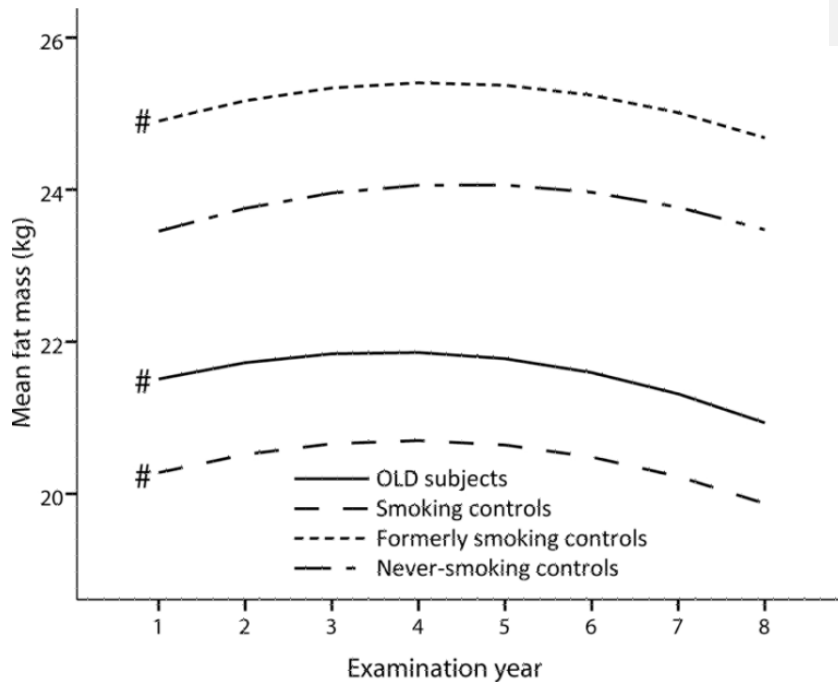
COPD elicits remodelling of the diaphragm and vastus lateralis muscle in Humans



Levine S et al, J Appl Physiol 2012

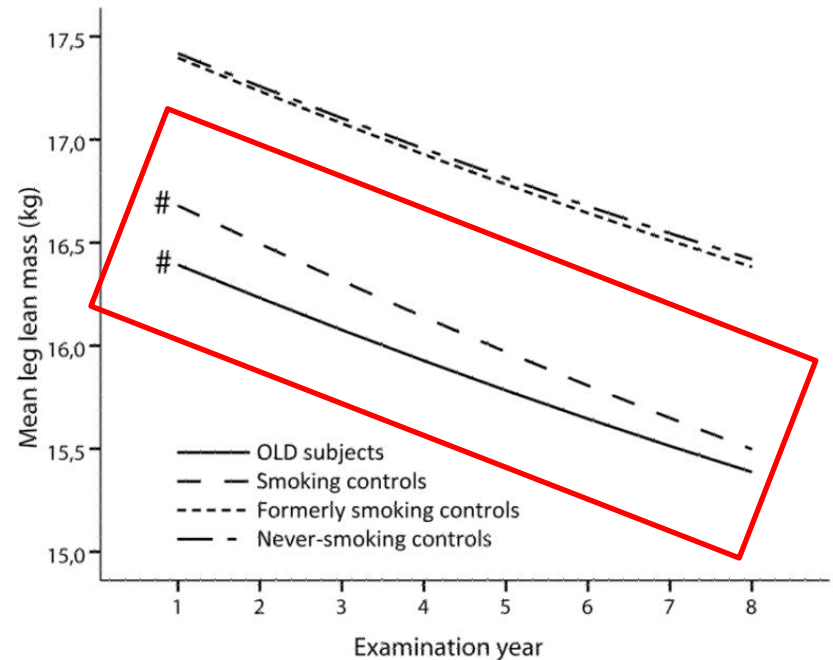
**Body composition changes in COPD:
7 -years longitudinal data from
the Health ABC Study**

Fat mass

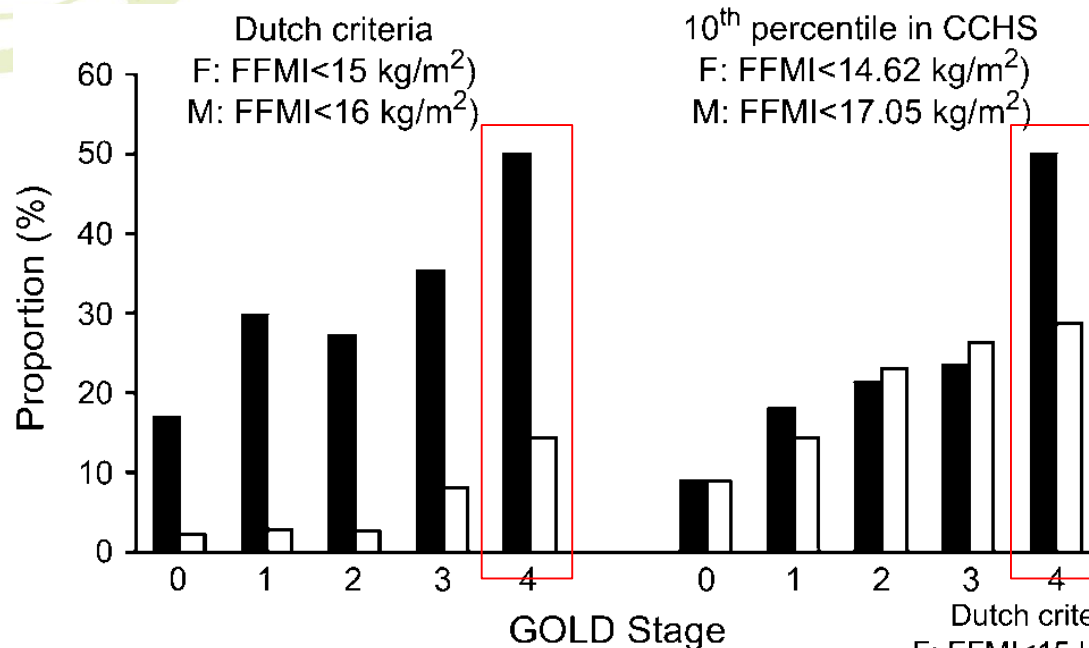


260 OLD patients
157 smoking controls
866 formerly smoking controls
891 never smoking controls
OLD: obstructive lung disease

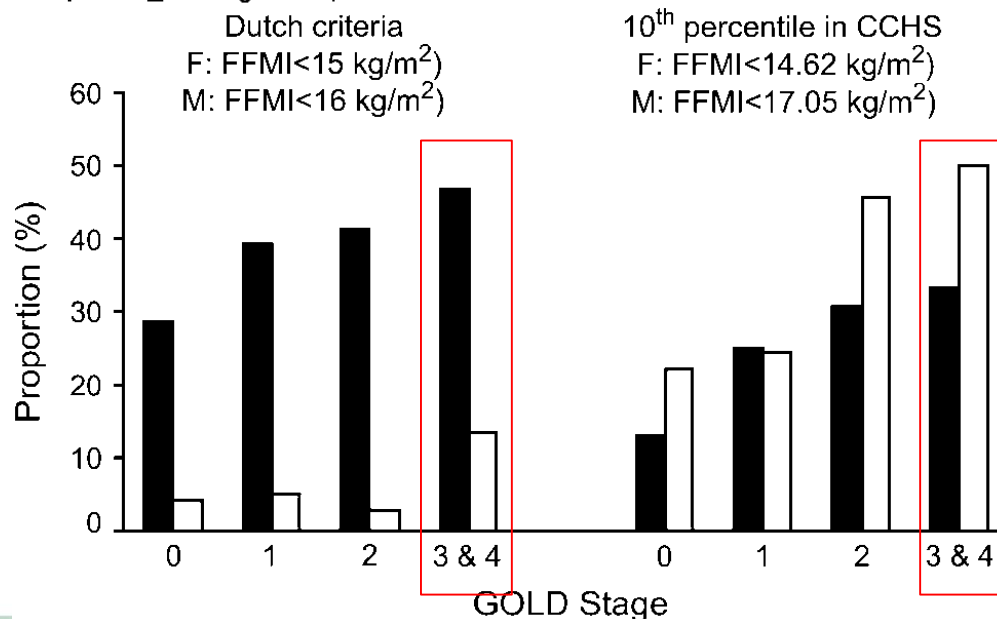
Leg Fat Free mass



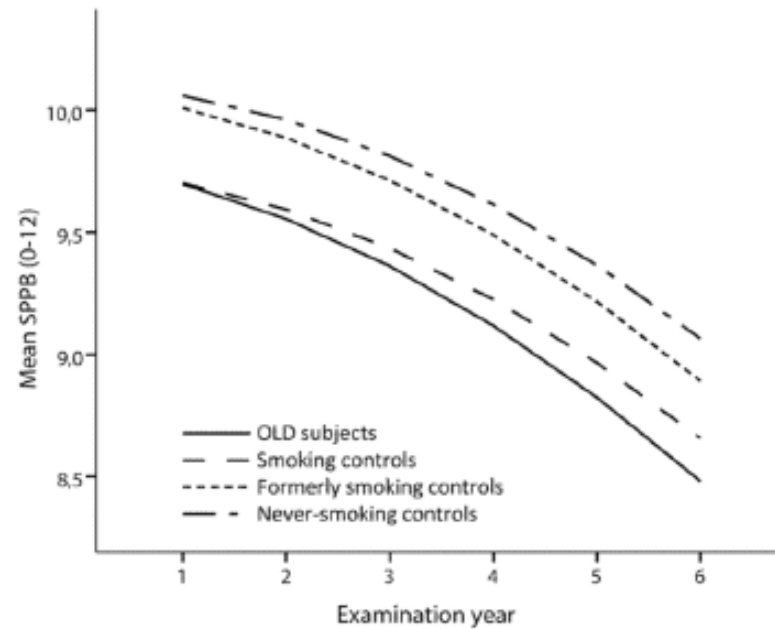
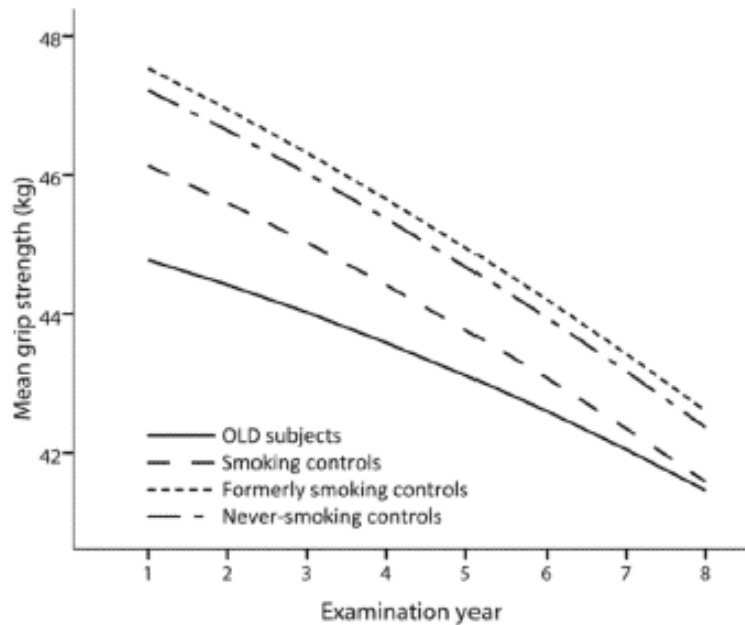
Body composition and COPD: The Copenhagen City Heart Study (n 1898 patients with COPD)



**Only in patients
with normal BMI**

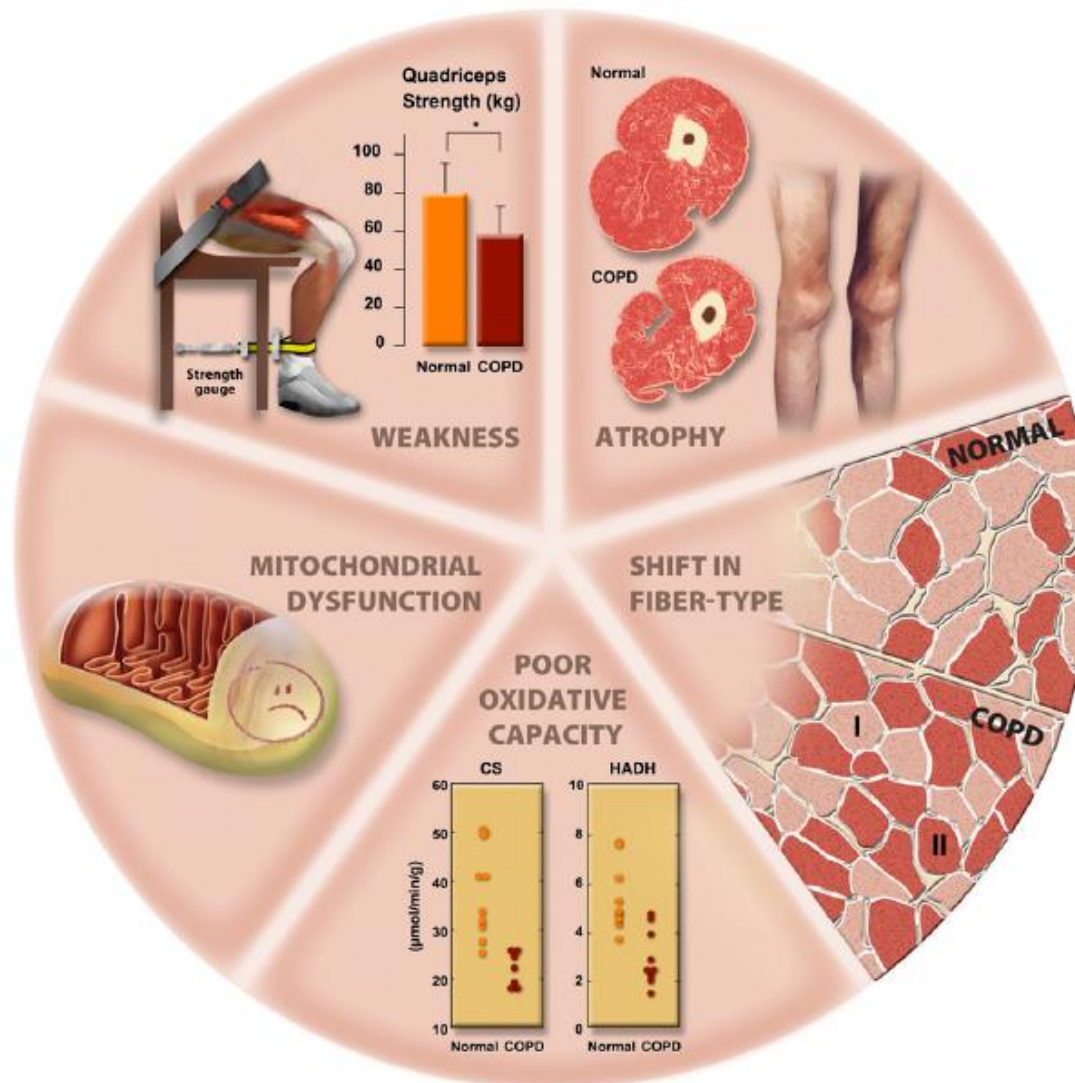


**Body composition changes in COPD:
7 -years longitudinal data from
the Health ABC Study**



260 OLD patients
157 smoking controls
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OLD: obstructive lung disease

Morphological and structural alterations in limb muscles in COPD patients



Muscle changes observed in COPD meets the criteria of Sarcopenia

Age and Ageing 2010; 39: 412–423
doi: 10.1093/ageing/afq034
Published electronically 13 April 2010

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any medium, provided the original work is properly cited.



REPORT

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People

ALFONSO J. CRUZ-JENTOFT¹, JEAN PIERRE BAEYENS², JÜRGEN M. BAUER³, YVES BOIRIE⁴,
TOMMY CEDERHOLM⁵, FRANCESCO LANDI⁶, FINBARR C. MARTIN⁷, JEAN-PIERRE MICHEL⁸,
YVES ROLLAND⁹, STÉPHANE M. SCHNEIDER¹⁰, EVA TOPINKOVÁ¹¹, MAURITS VANDEWOUDE¹²,
MAURO ZAMBONI¹³

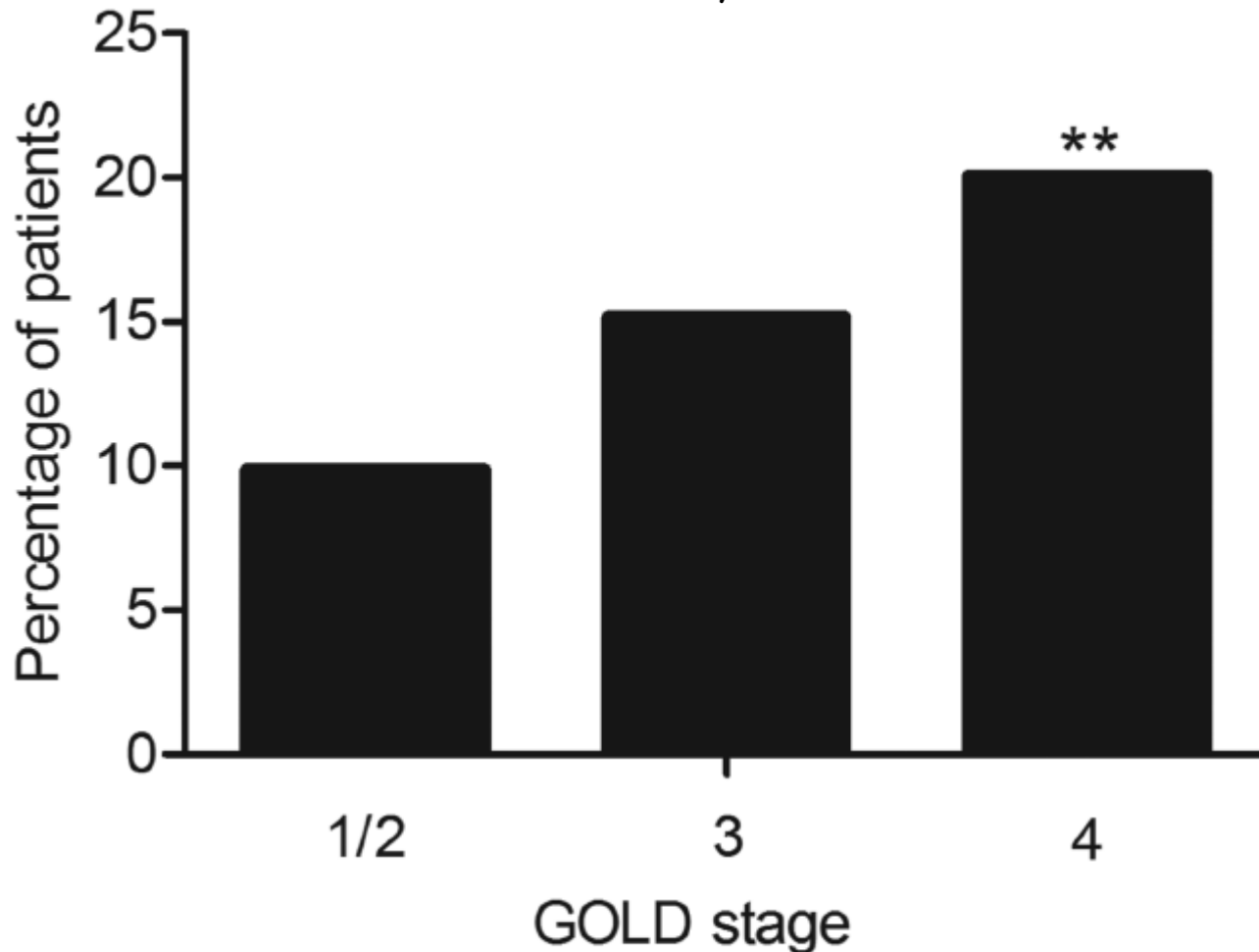
Table 1. Criteria for the diagnosis of sarcopenia

Diagnosis is based on documentation of criterion 1 plus (criterion 2 or criterion 3)

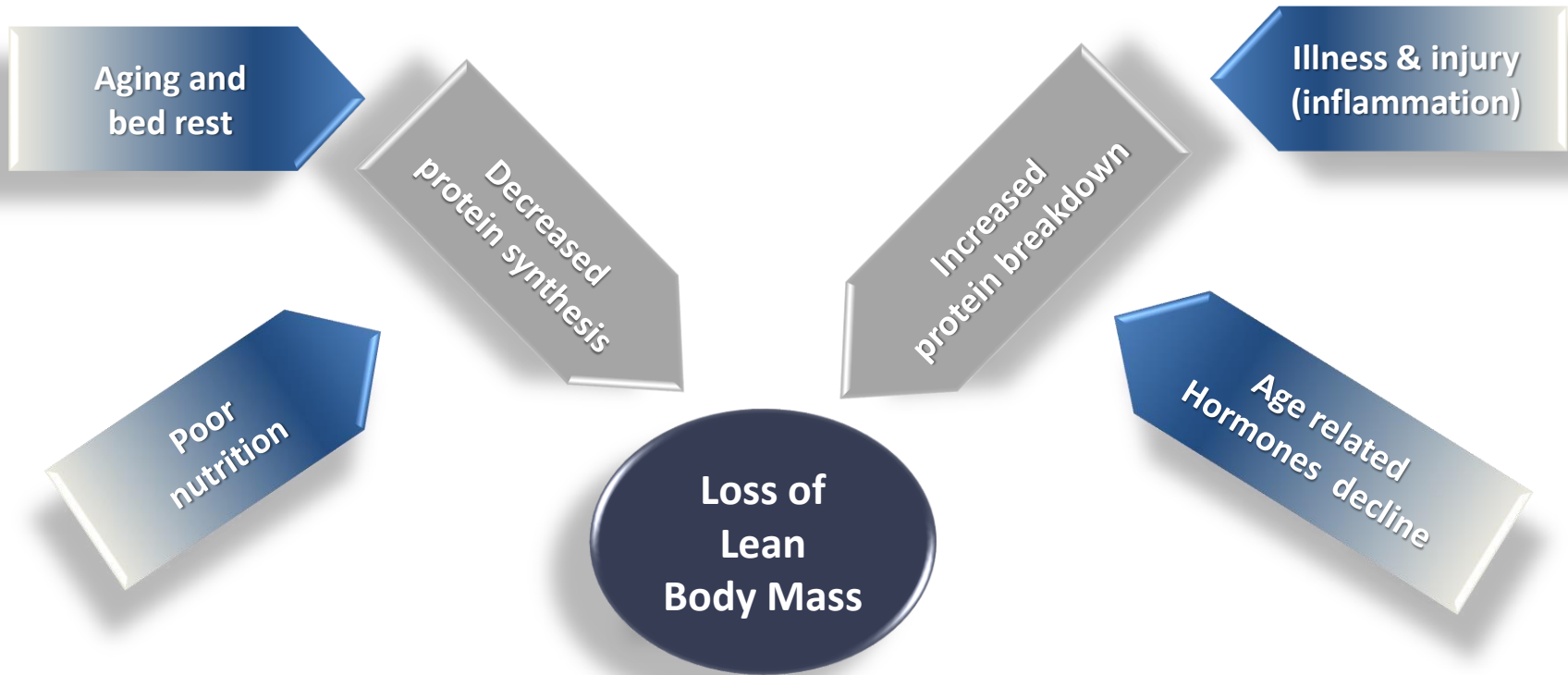
1. Low muscle mass
2. Low muscle strength
3. Low physical performance

Prevalence of Sarcopenia according to EWGSOP criteria by GOLD stage in 622 subjects with stable COPD

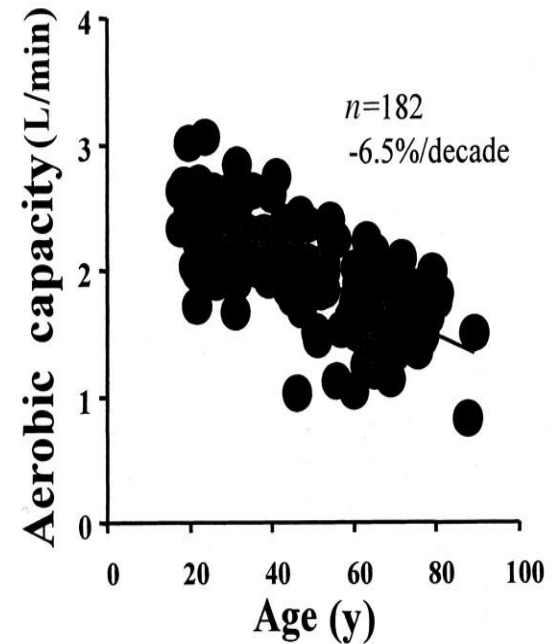
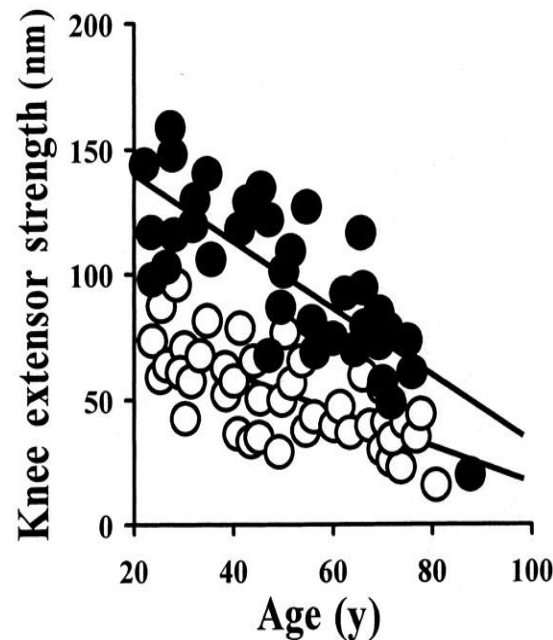
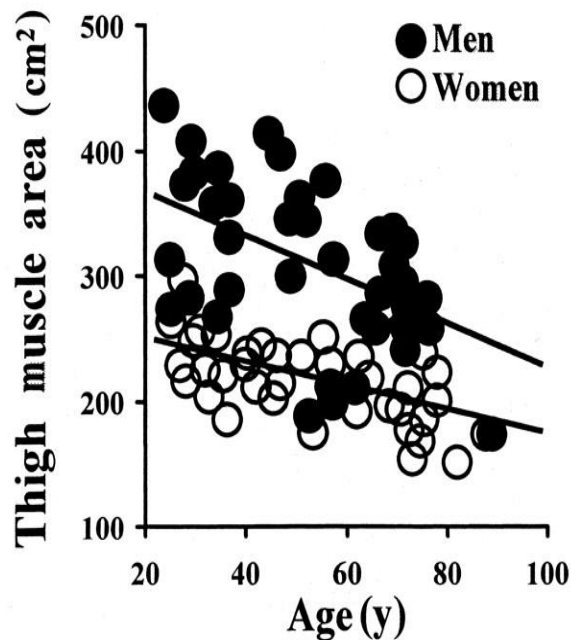
Jones SE et al, Thorax 2015



Drivers of lean body mass loss



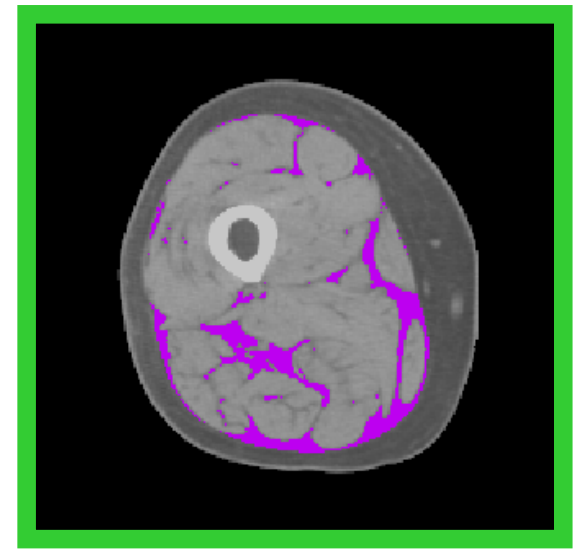
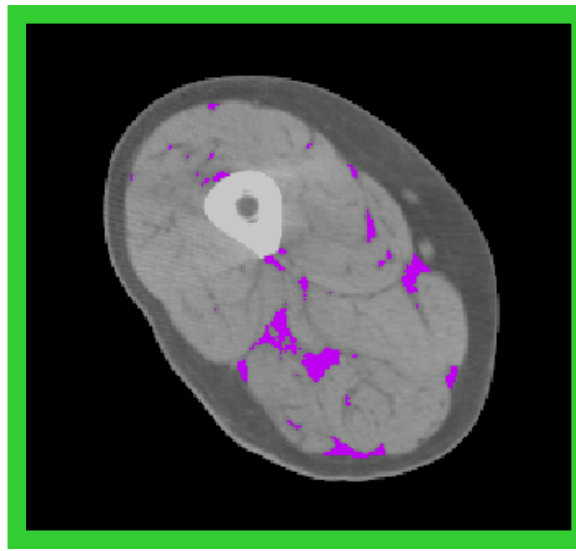
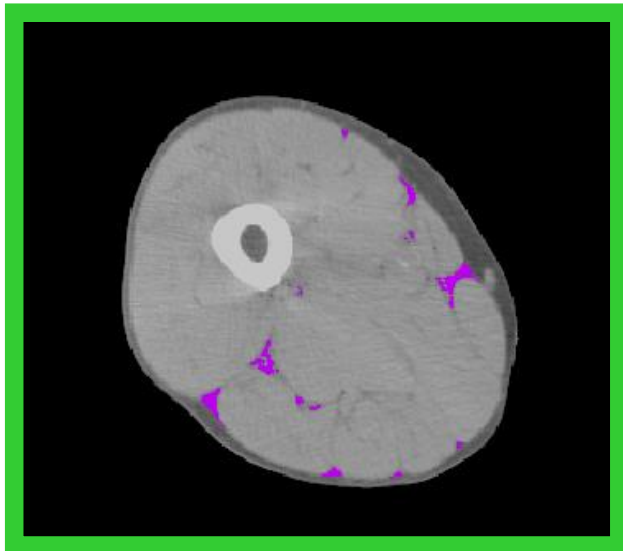
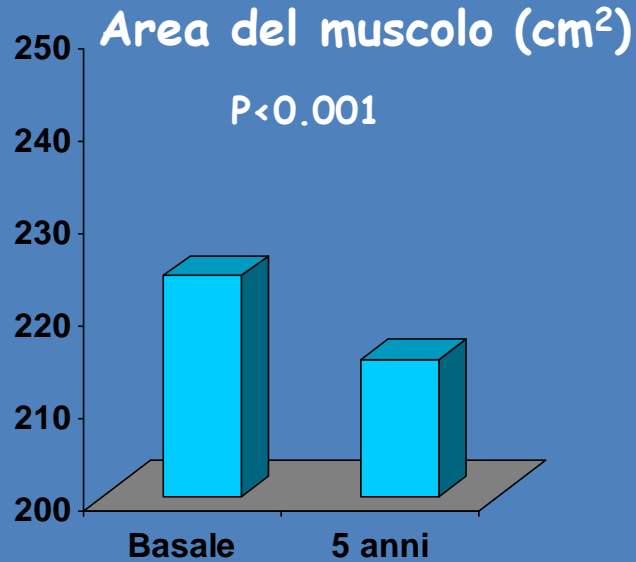
Age-related decrease in muscle area, knee extensor strenght and aerobic capacity in 78 healthy persons



Nair KS, Am J Clin Nutr 2005

Effetto dell'età sull'infiltrazione lipidica del muscolo (n=1981): 5 anni di follow-up

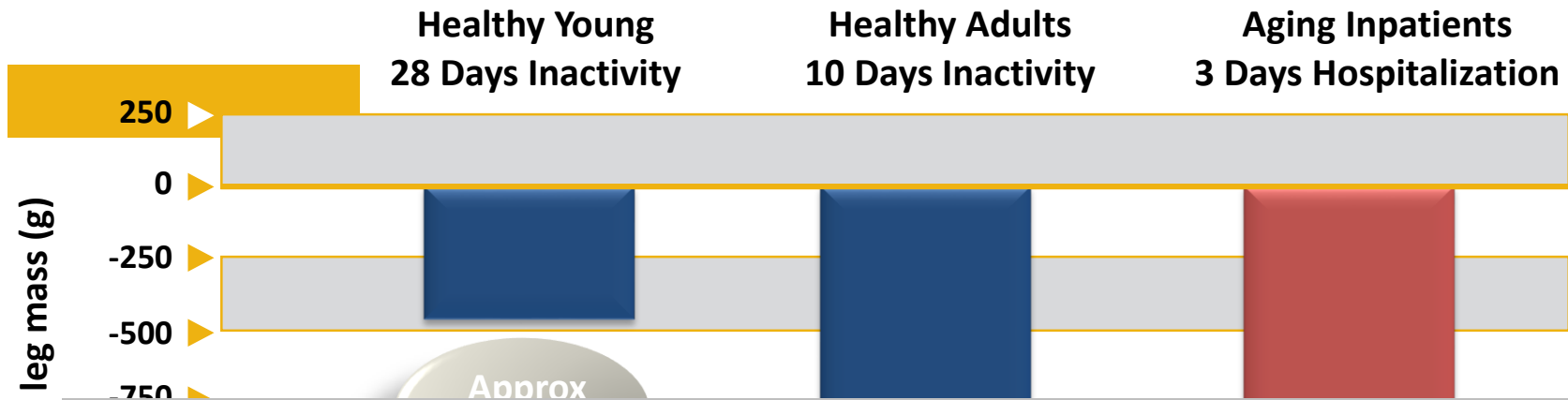
Rossi AP et al. J Geront 2011



Factors Leading to COPD Sarcopenia American Thoracic Society (mod)

Disuse
Inflammation
Oxidative Stress- Smoking
Exacerbations
Malnutrition
Corticosteroids
Vitamin D deficiency

Bed rest and muscle mass-2



Detraining or Deconditioning
characterize COPD

Bossenbroek et al, 2011

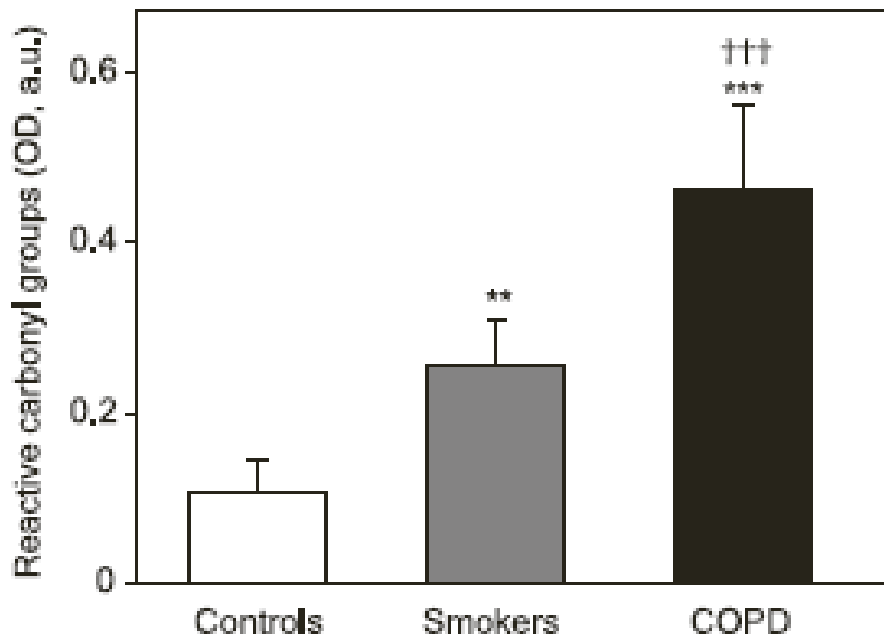
Cigarette Smoke-induced Oxidative Stress

A Role in Chronic Obstructive Pulmonary Disease Skeletal Muscle Dysfunction

Esther Barreiro^{1,2}, Víctor I. Peinado^{2,3}, Juan B. Galdiz⁴, Elisabet Ferrer^{2,3}, Judith Marin-Corral¹, Francisco Sánchez^{1,2}, Joaquim Gea^{1,2}, and Joan Albert Barberà^{2,3}, on behalf of the ENIGMA in COPD Project



Muscle proteins oxidation levels

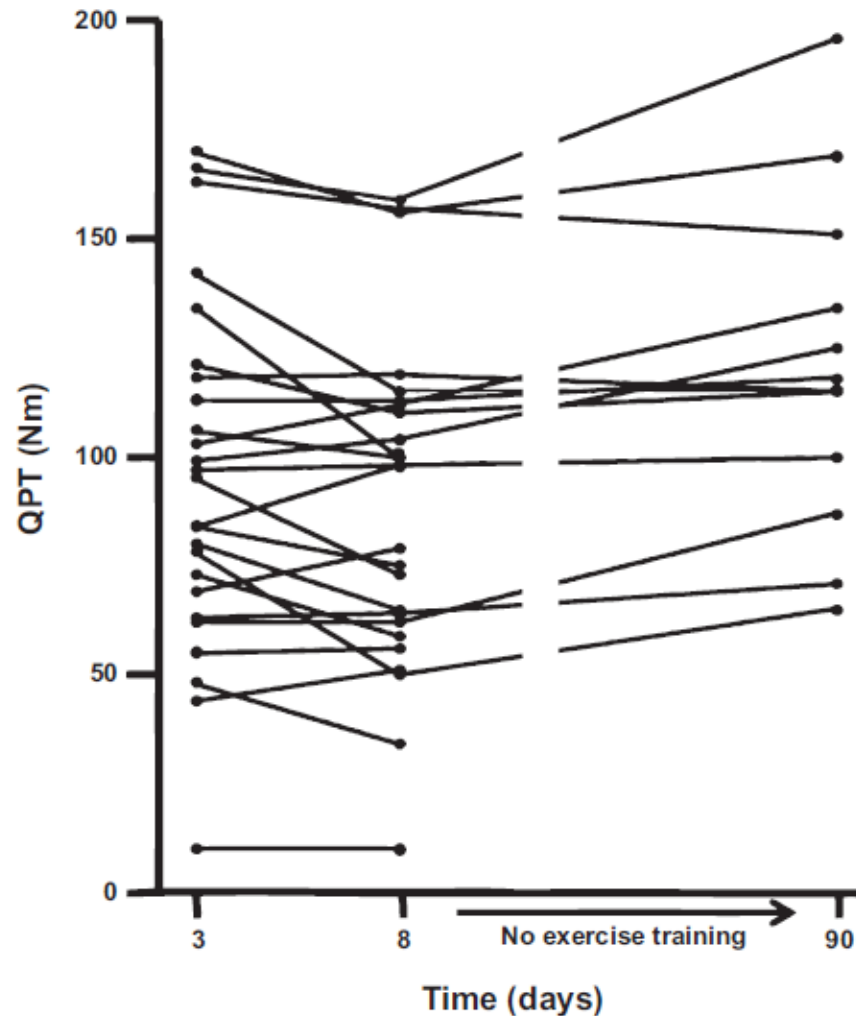


Oxidative stress is a contributor to COPD muscle dysfunction



Oxidants contained in cigarette smoke induce oxidative modifications of key muscle biological structures

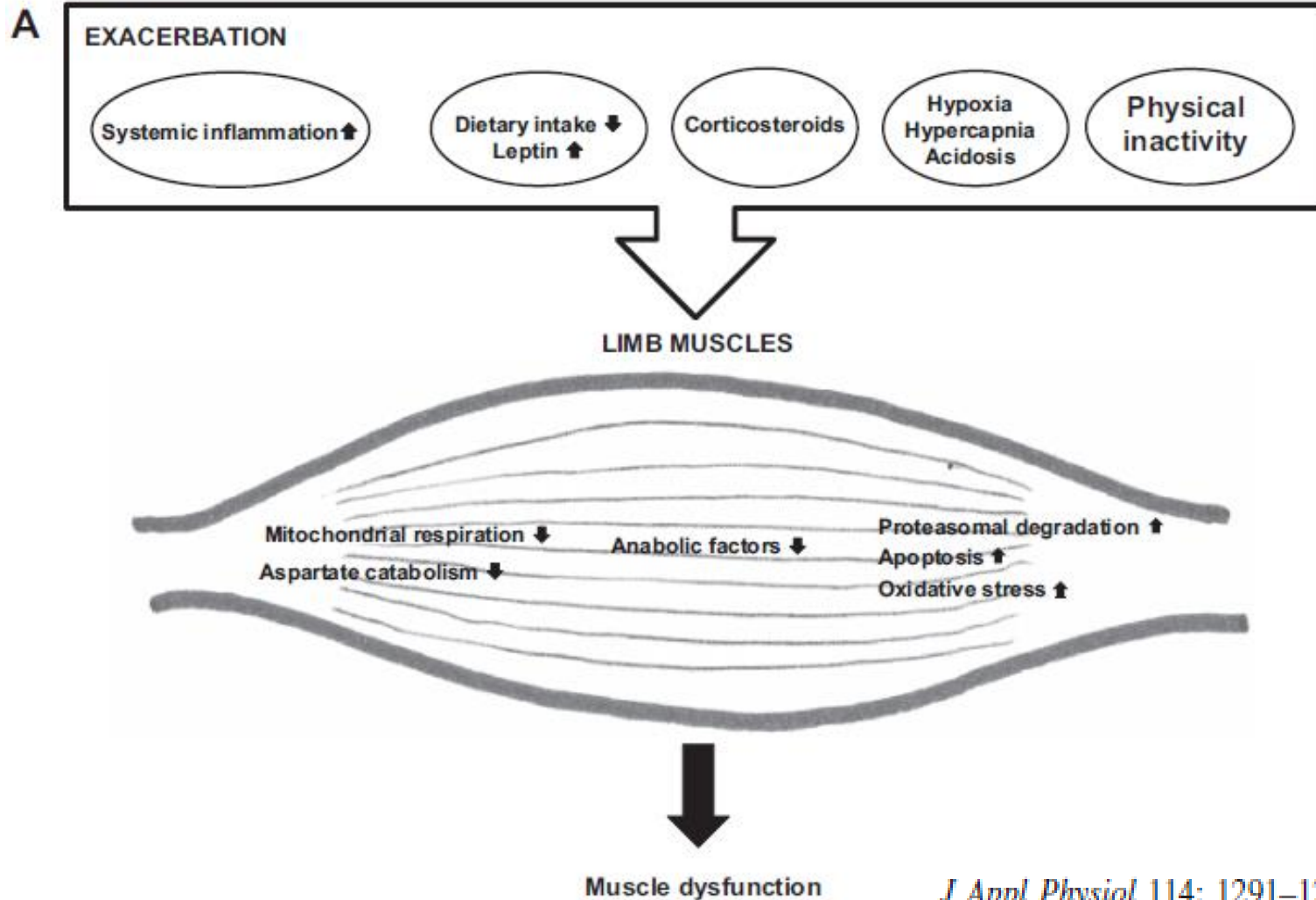
Quadriceps peak torque in patients with acute exacerbations and after 90 days of follow-up



Decrease in quadriceps strength by 5% after 5 days of hospitalization

After 3 months only partial recovery

Mechanisms leading to muscle dysfunction in acute exacerbations



J Appl Physiol 114: 1291–1299, 2013.

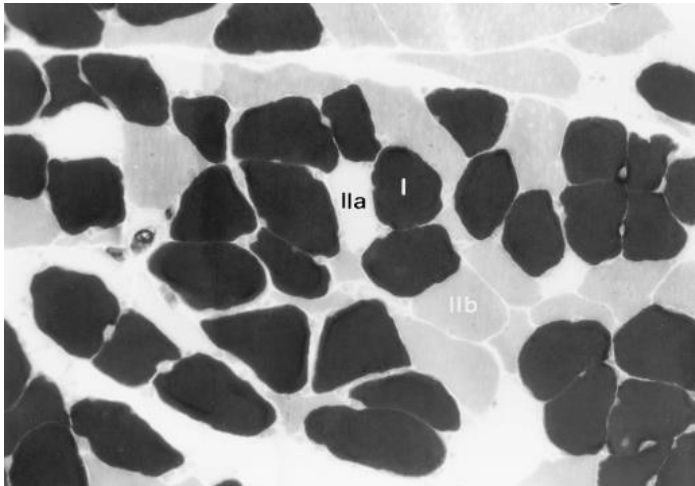
Steroid induced myopathy

Acute

- Proximal and distal muscle weakness after 5-7 days of high dose intravenous treatment
- Recovery after treatment cessation prolonged up to 6 months

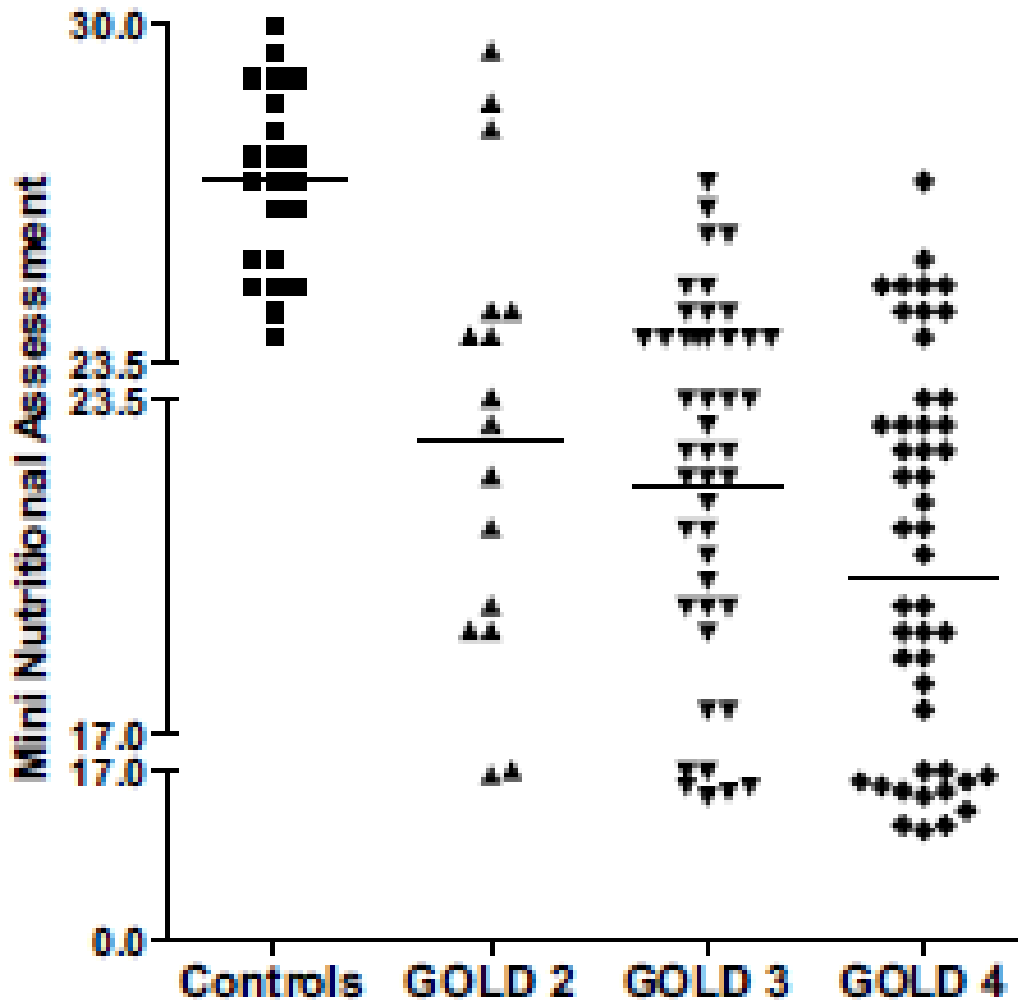
Chronic

- Proximal muscle weakness after long-term treatment with low doses of oral corticosteroids
- prognostic negative factor on survival in patients with COPD

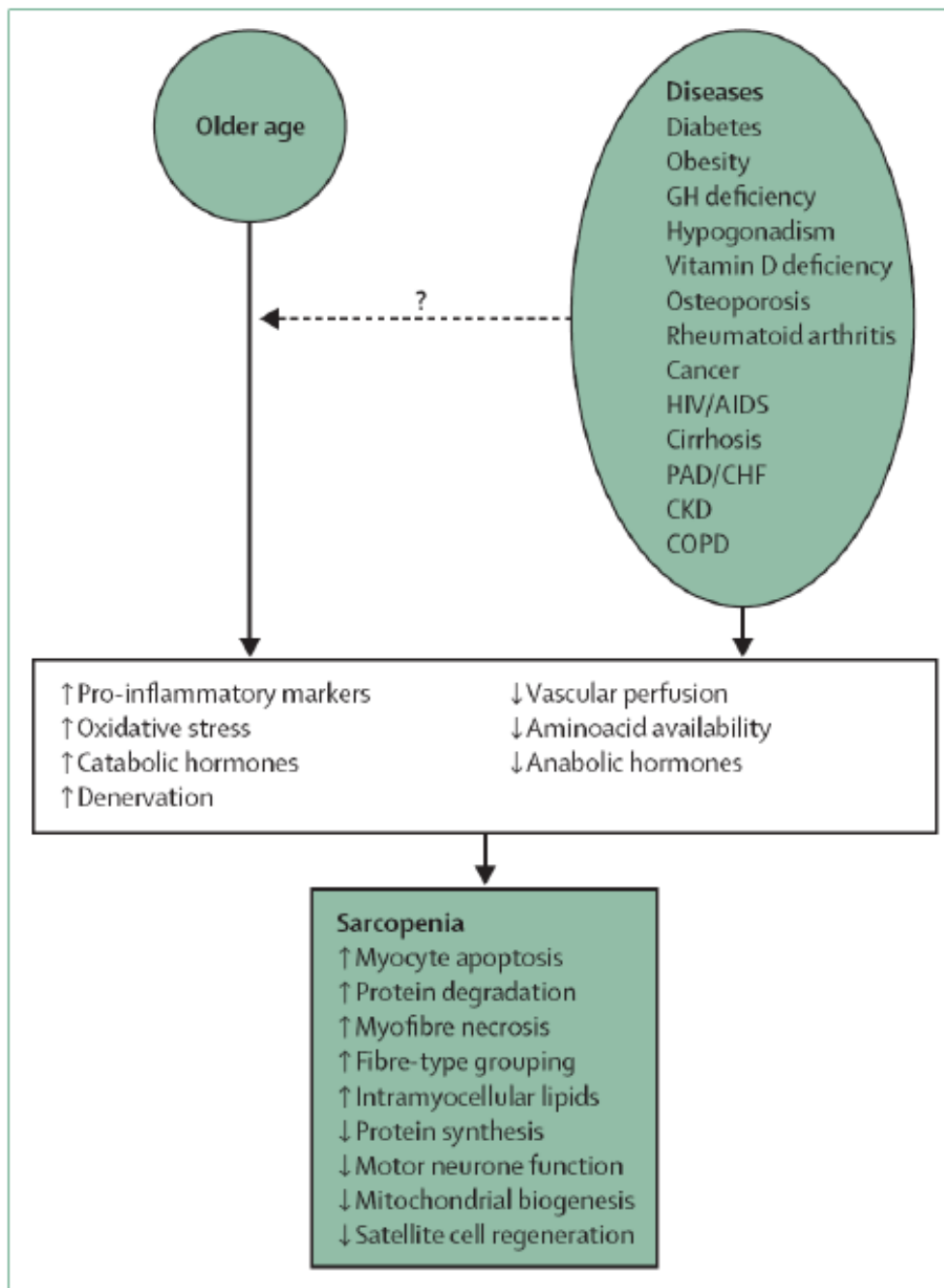


Atrophy of type II fibres
(IIx)
with less or no impact in
type I fibres

Malnutrition risk and COPD



overlap
malnutrition
and sarcopenia





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An Official American Thoracic Society/European Respiratory Society Statement: Update on Limb Muscle Dysfunction in Chronic Obstructive Pulmonary Disease

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Am J Respir Crit Care Med Vol 189, Iss 9, pp e15–e62, May 1, 2014

Definition

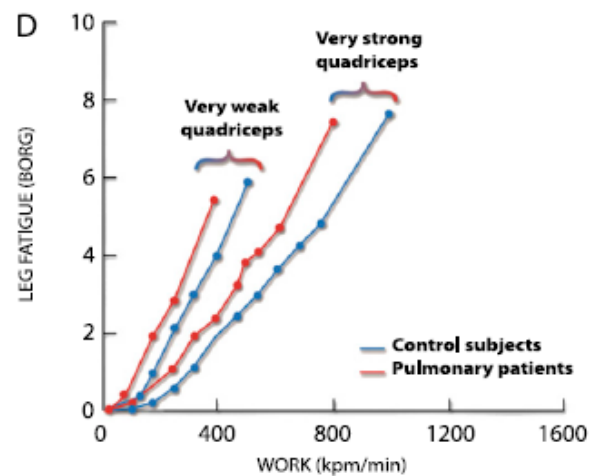
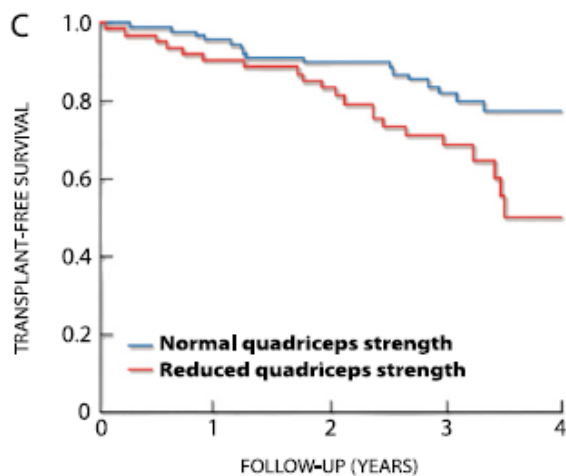
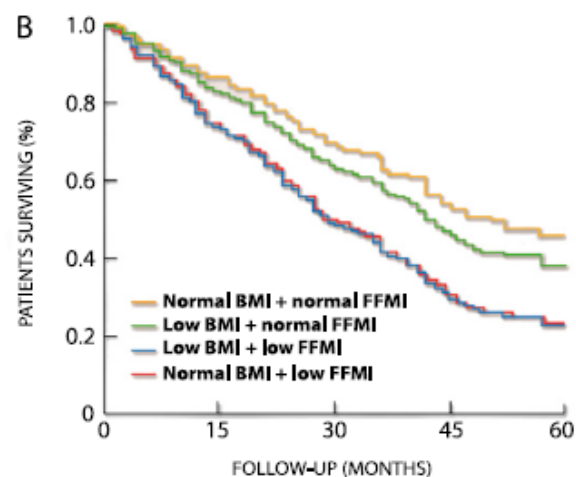
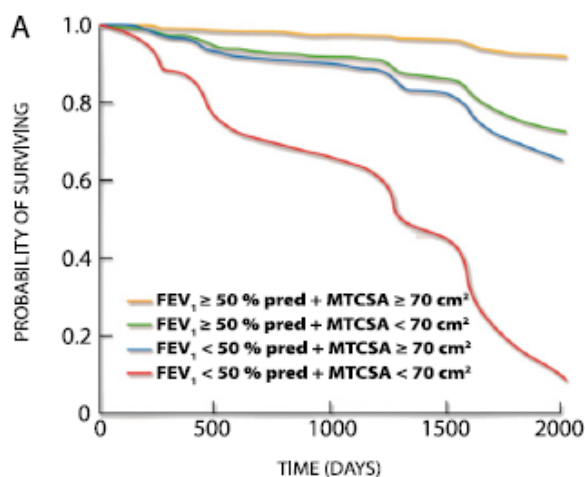


*Limb muscle dysfunction is defined as the **morphological** and **functional** changes that are seen in limb muscles in patients with COPD*

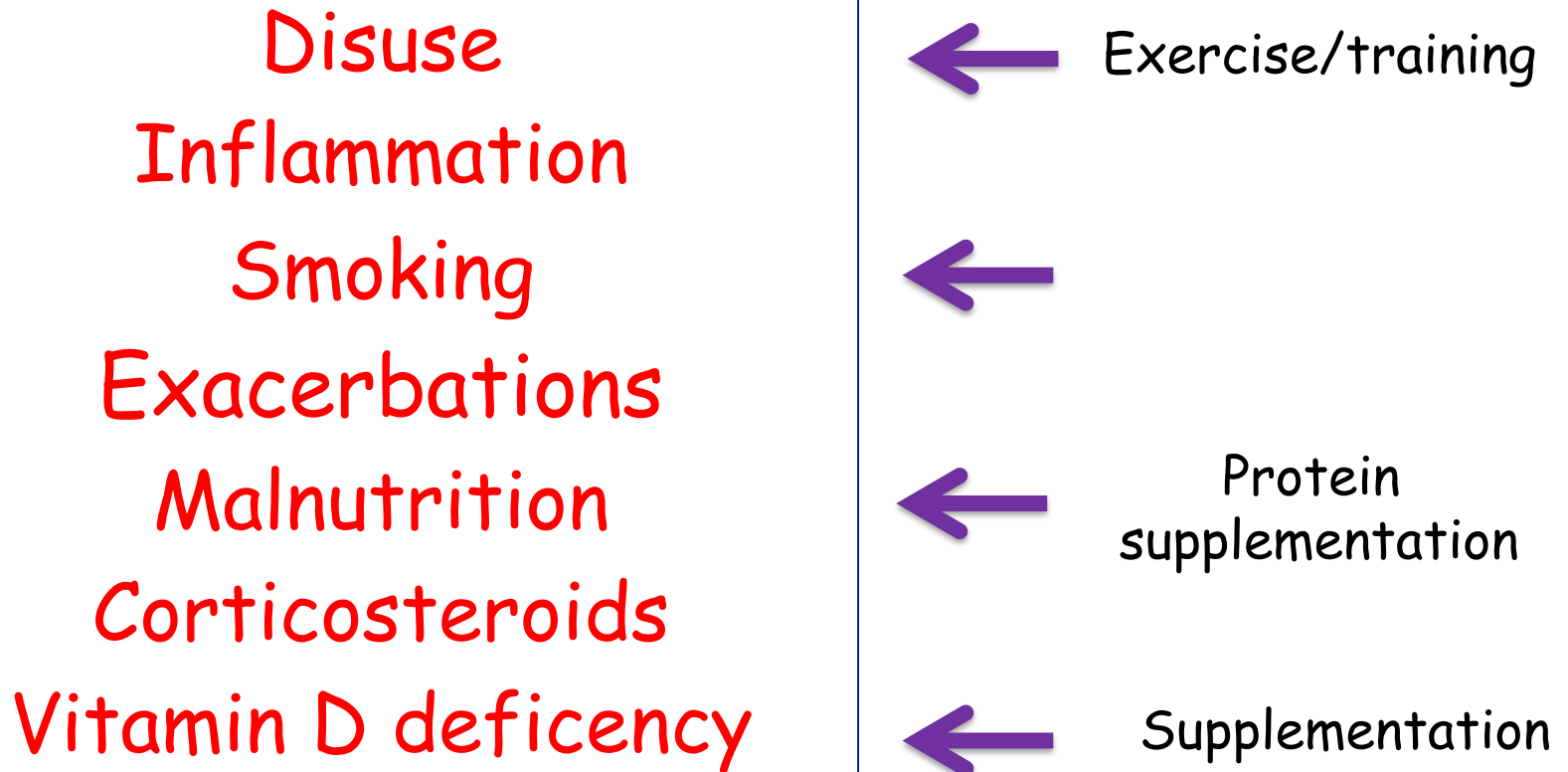


Limb muscle dysfunction is an important systemic consequence of COPD, because of its impact on physical activity, exercise tolerance, quality of life, and even survival.

Relation between muscle mass and strength and clinical outcomes in patients with COPD



COPD Sarcopenia: Treatment options

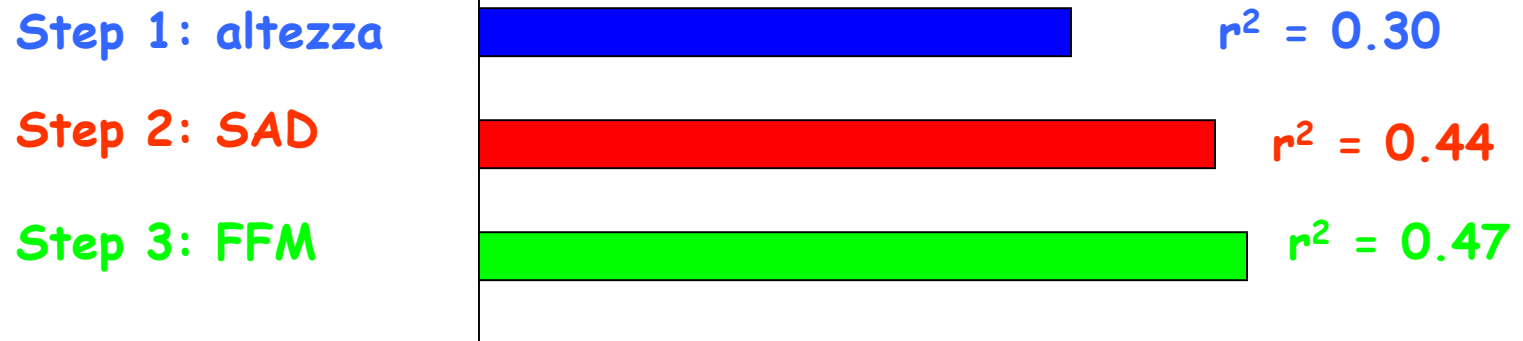


Supplementation with exercise training
Neuromuscular stimulation

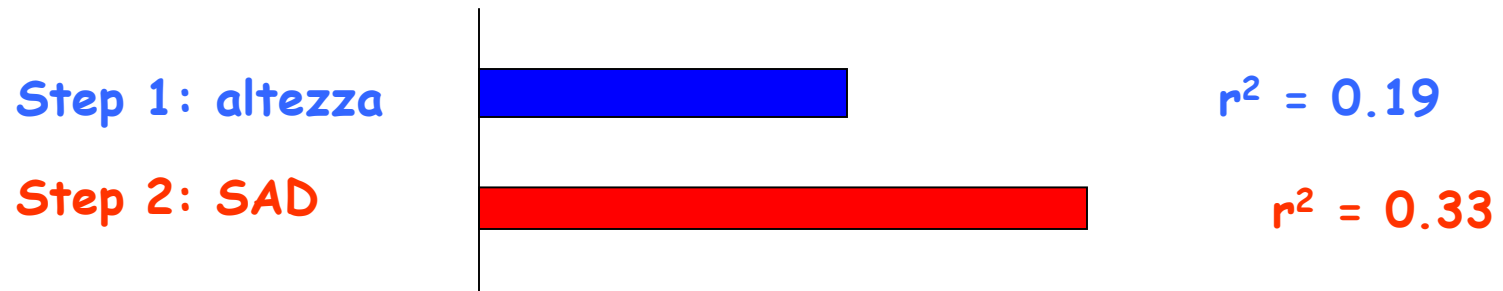
Non solo Sarcopenia

Predittori di FVC e FEV₁
in maschi con età compresa tra 67-78 anni
Verona ABC Study

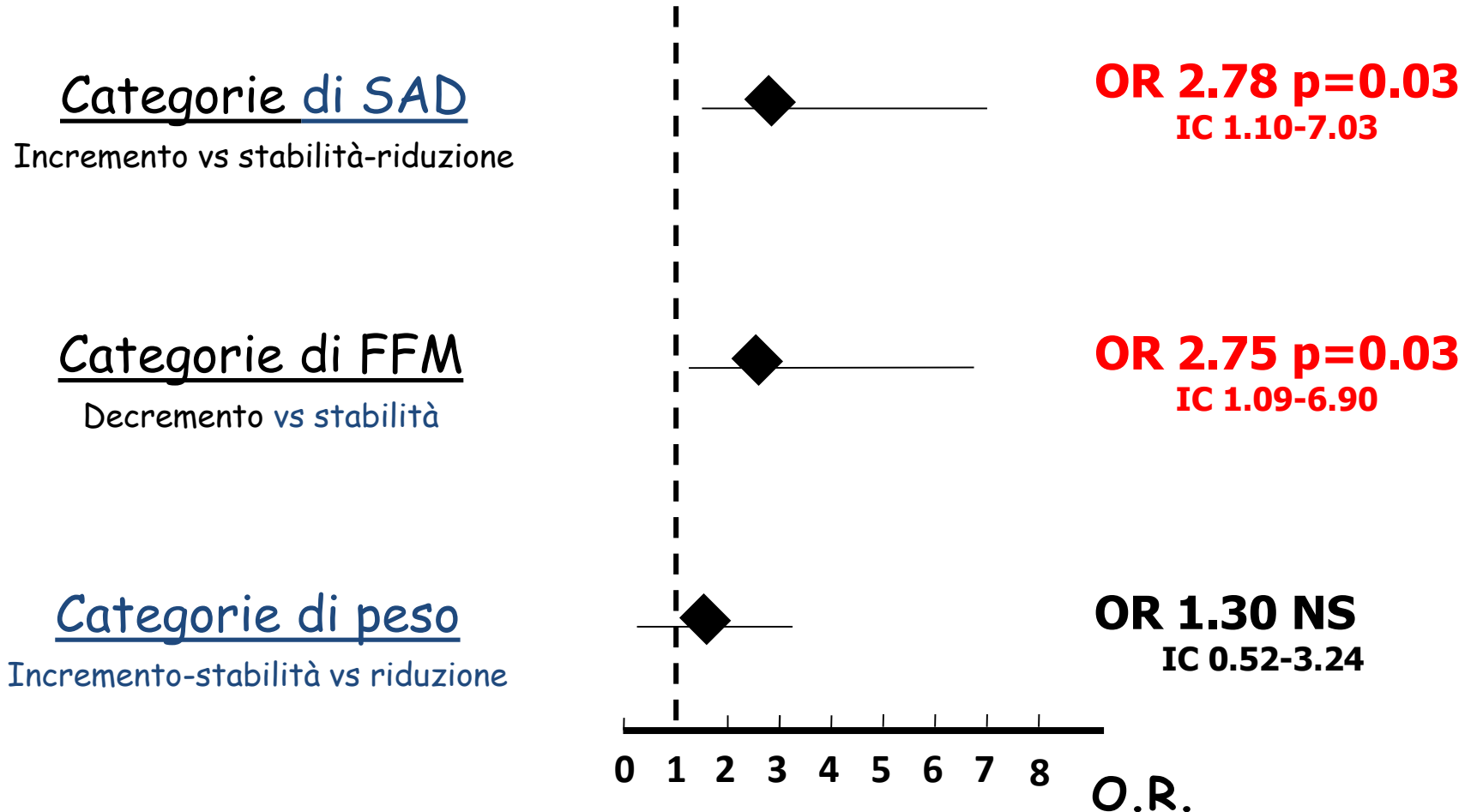
FVC



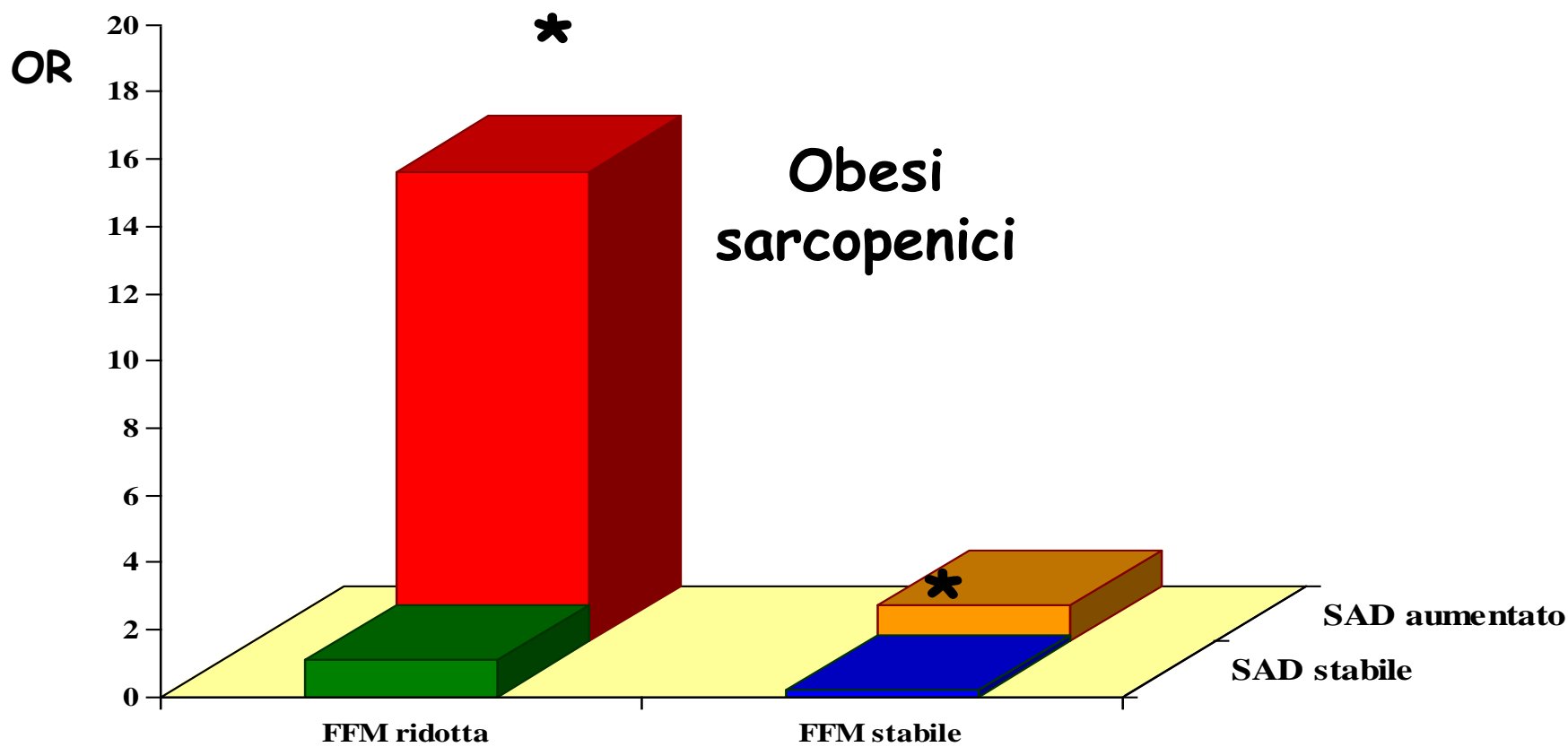
FEV₁



**Rischio relativo di peggioramento di FEV1 in relazione
alle categorie di composizione corporea
dopo aggiustamento per sesso e fumo**



peggioramento del FEV1 in base alla modificazione della composizione corporea dopo aggiustamento per sesso e fumo



* $p < 0.05$

Rossi et al, Int J Obes 2008