UNIVERSITÀ DEGLI STUDI DI VERONA

30° Anniversario 1987-2017
Fondazione Teresa Camplani
Casa di Cura Domus Salutis

LA RIABILITAZIONE INTERDISCIPLINARE

della disabilità complessa
fra presente e futuro

La nutrizione nelle malattie cardio-respiratorie: dalla valutazione funzionale alla prescrizione

Mauro Zamboni

Clinica Geriatrica

Università di Verona

24 novembre 2017

Centro congressi "Auditorium Monsignor Capretti"

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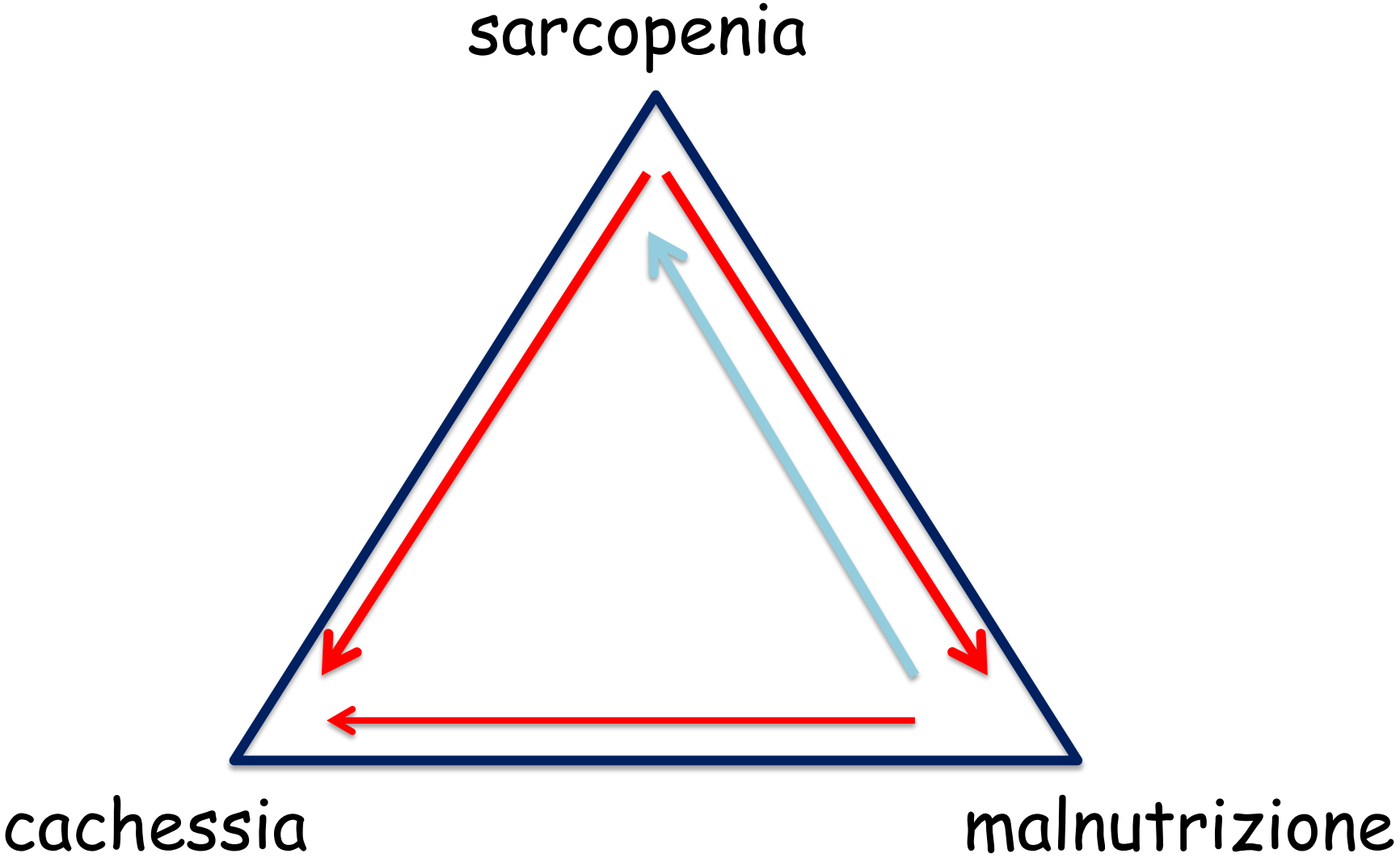
Alterazioni Nutrizionali nelle Malattie Cardiorespiratorie



"Sarcopenia is a term that denotes the decline in muscle mass and strength that occurs with healthy aging."

Rosenberg, Am J Clin Nutr 1989

" Sarcopenia is part of normal aging
and does not require a disease to occur,
although it is accellerated by chronic diseases."

Roubenoff et al, J Gerontol 2000

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Definition

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

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

Update 1999 American Thoracic Society

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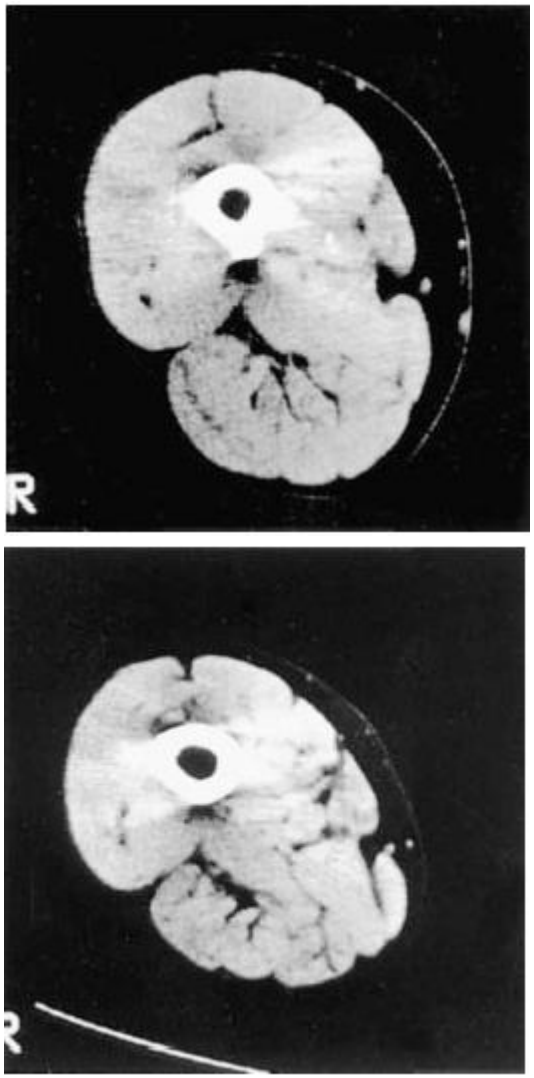
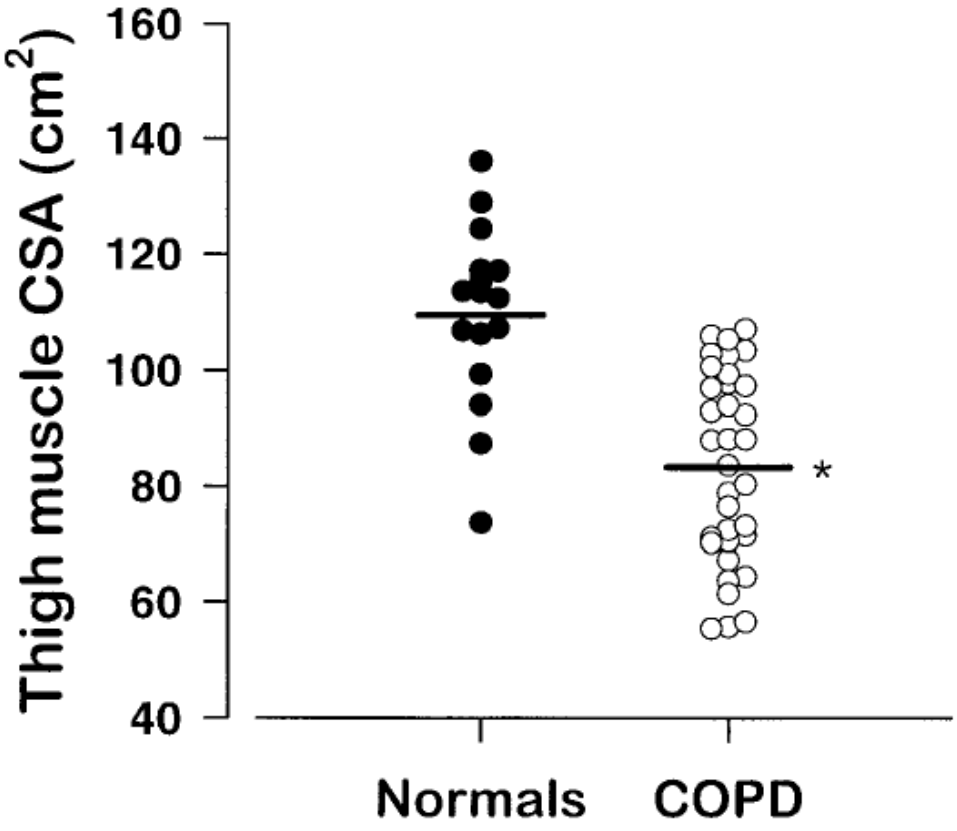
Thigh muscle cross sectional area in COPD and control subjects





Am J Respir Crit Care Med Vol 158. pp 629-634, 1998

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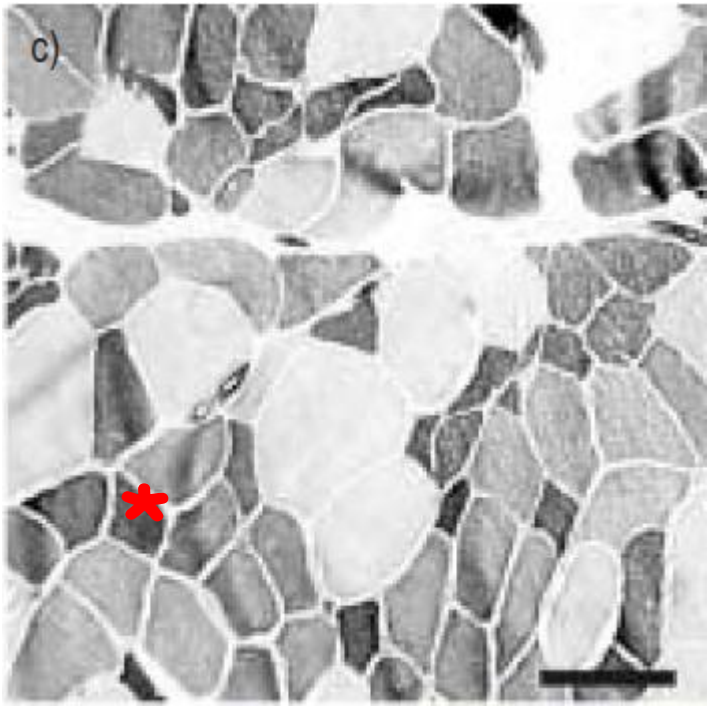
Vastus lateralis biopsies of 15 COPD moderate-severe weight-stable patients and healthy age -matched controls



Type 1 fibers (oxidative)

Type IIX fibers (glycolitic)
* (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

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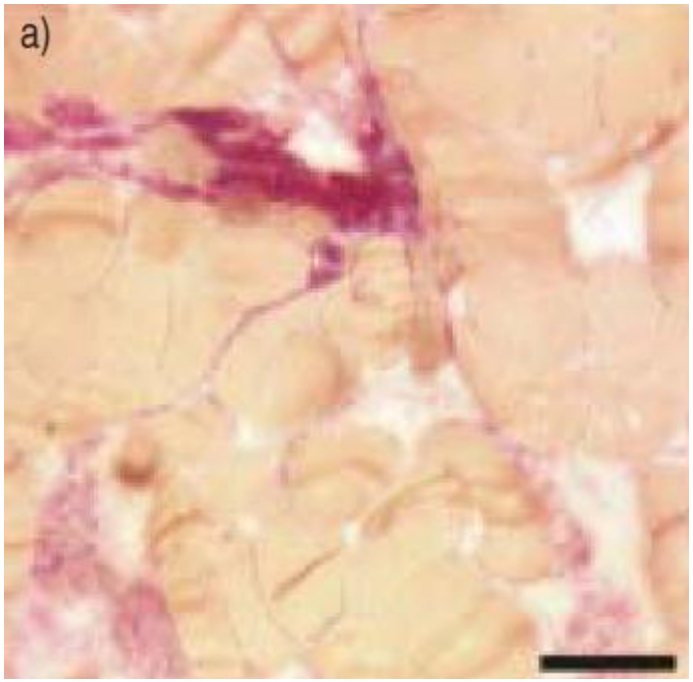
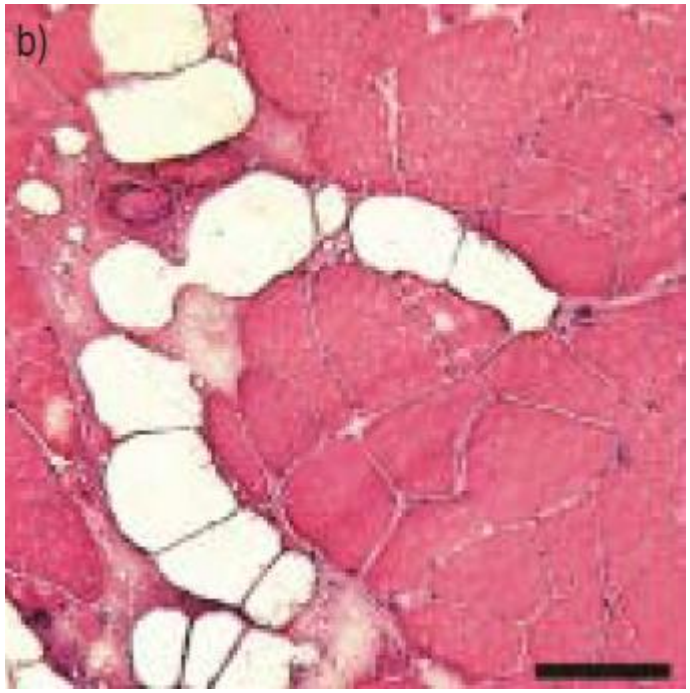
Vastus lateralis biopsies of COPD weight-stable patients





Fybrosis

Fat infiltration

Eur Resp J 2003; 22: 280-85

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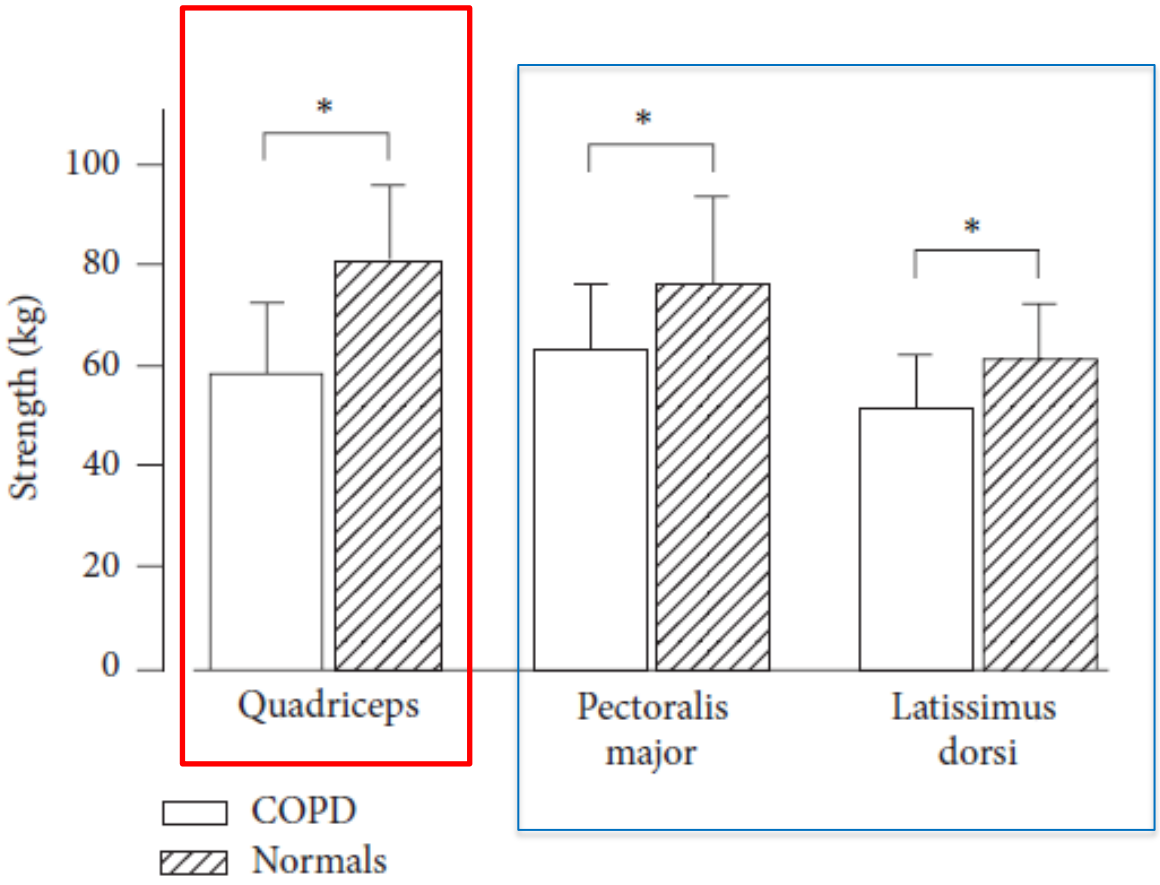
muscle strength in patients with COPD compared to normal subjects



Am J Respir Crit Care Med Vol 158. pp 629-634, 1998

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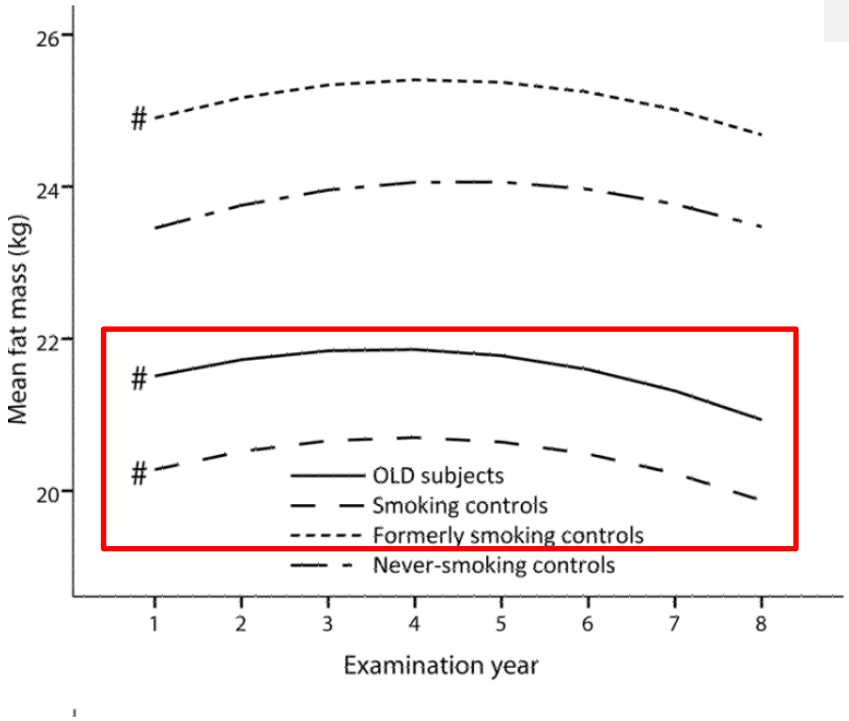
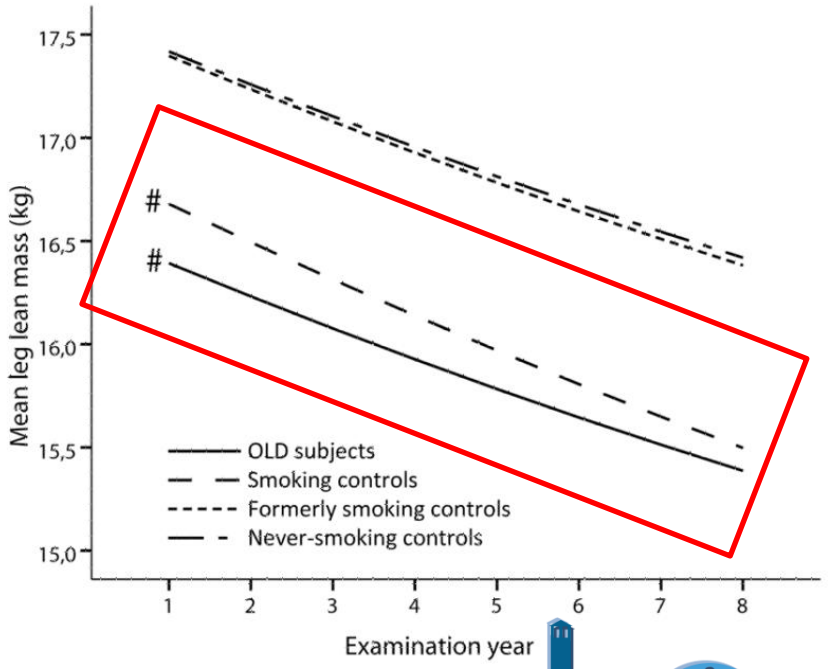
Body composition changes in COPD: 7 –years longitudinal data from the Health ABC Study

Fat mass



Leg Fat Free mass



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

Thorax. 2011 November ; 66(11): 961–969.

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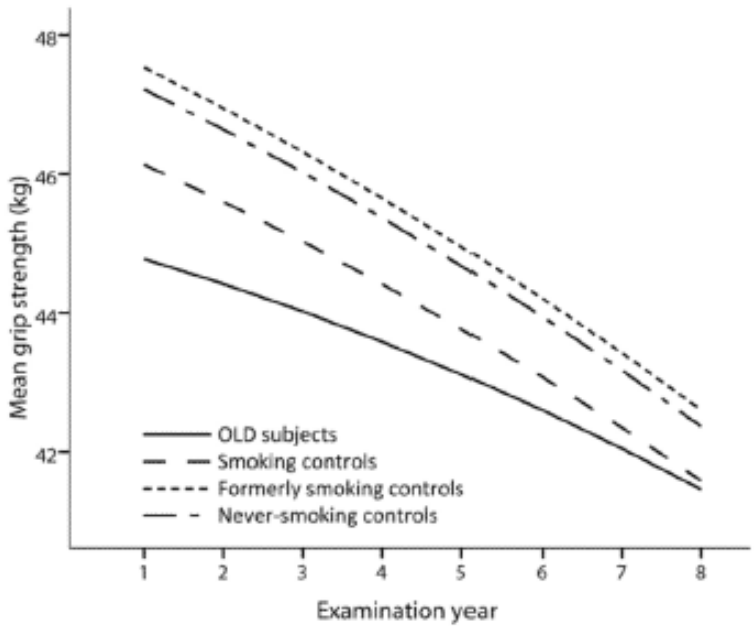
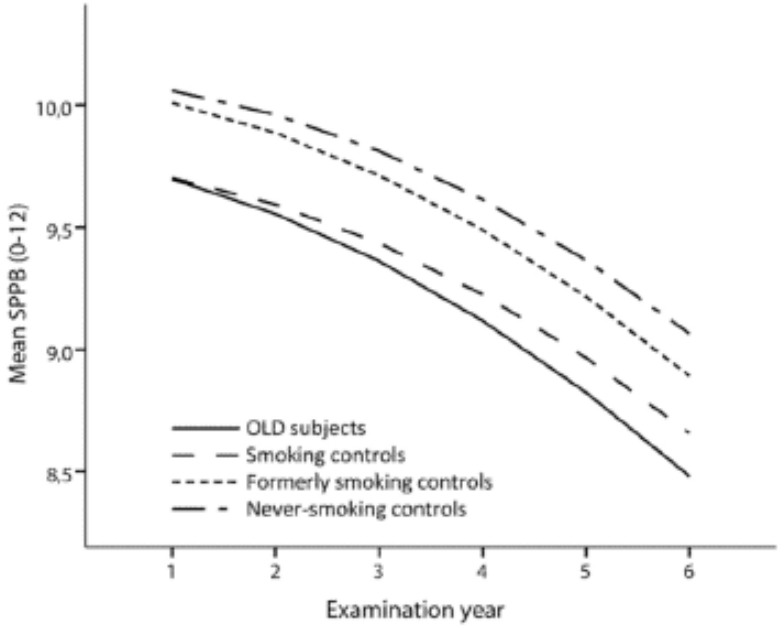
Body composition changes in COPD: 7 –years longitudinal data from the Health ABC Study





Thorax. 2011 November ; 66(11): 961–969.

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

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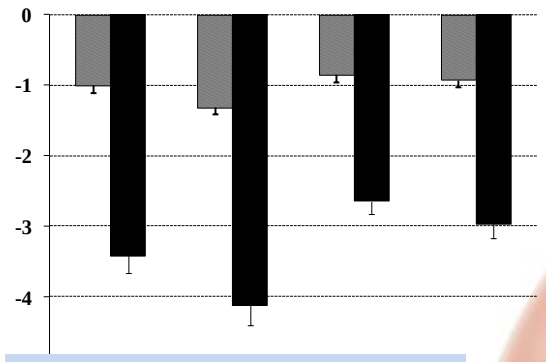
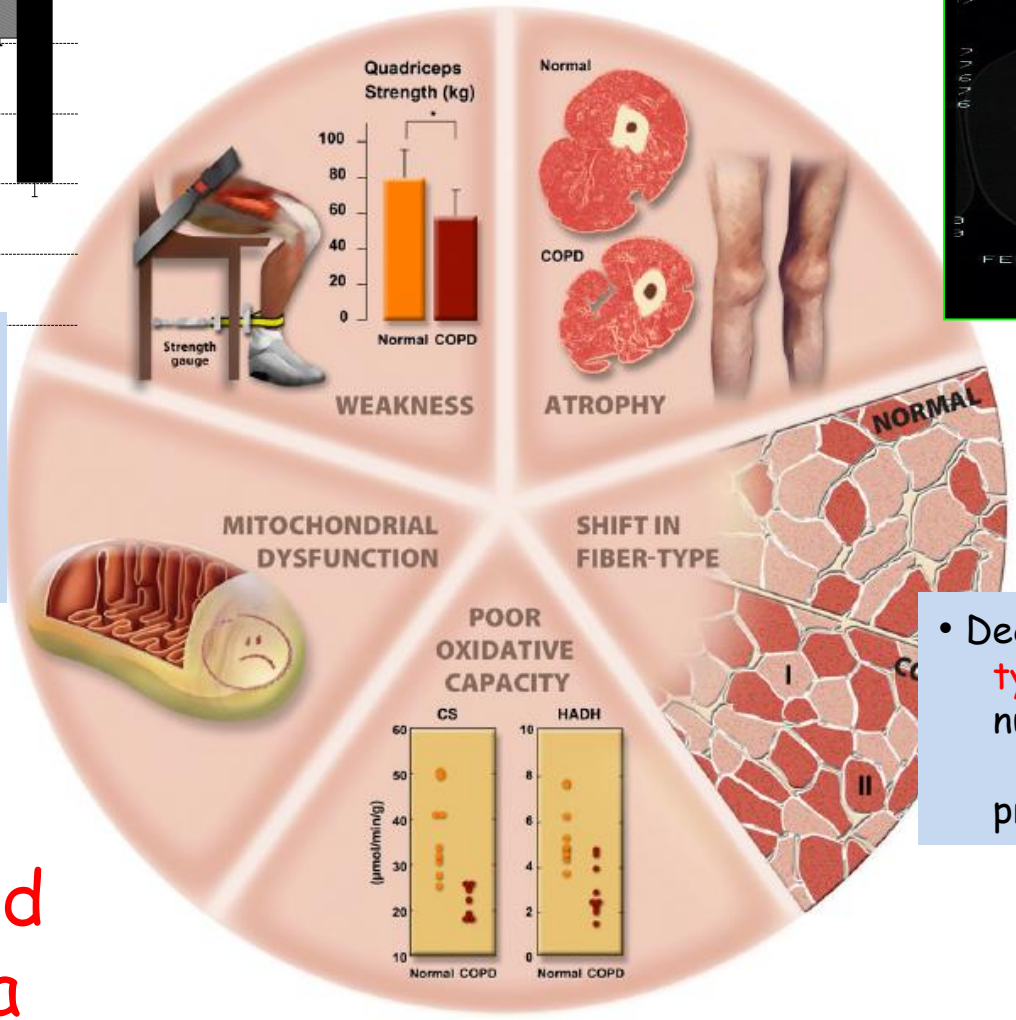
Morphological and structural alterations in limb muscles in COPD patients



3-y Loss of leg lean mass (hatched bar) and muscle strength (black bar) in older adults HABC study



- Decrease in type II fibers number , size
  mithocondria
  protein myosin

Age related sarcopenia

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

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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

REPORT

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People
ALFONSO J. CRUZ-JENTOFT[1], JEAN PIERRE BAEYENS[2], JÜRGEN M. BAUER[3], YVES BOIRIE[4], TOMMY CEDERHOLM[5], FRANCESCO LANDI[6], FINBARR C. MARTIN[7], JEAN-PIERRE MICHEL[8], YVES ROLLAND[9], STÉPHANE M. SCHNEIDER[10], EVA TOPINKOVÁ[11], MAURITS VANDEWOUDE[12], MAURO ZAMBONI[13]

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

Assenza di perdita di peso

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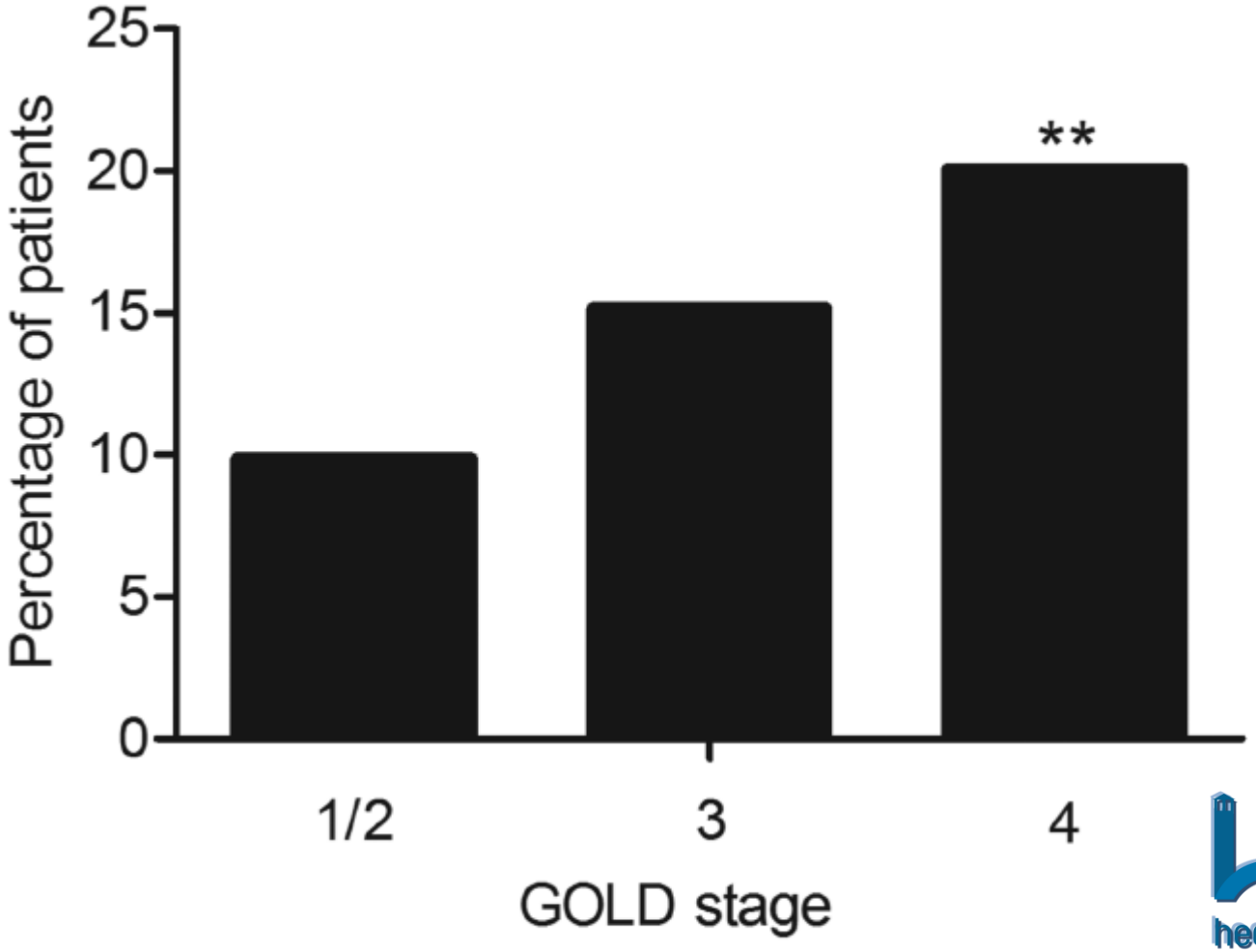
Prevalence of Sarcopenia according to EWGSOP criteria by GOLD stage in 622 subjects with stable COPD

Jones SE et al, Thorax 2015



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Muscle wasting in heart failure: An overview☆

Stephan von Haehling[a,b,*], Lisa Steinbeck[a], Wolfram Doehner[a,c], Jochen Springer[a,b,d], Stefan D. Anker[a,e]

The International Journal of Biochemistry & Cell Biology 45 (2013) 2257–2265

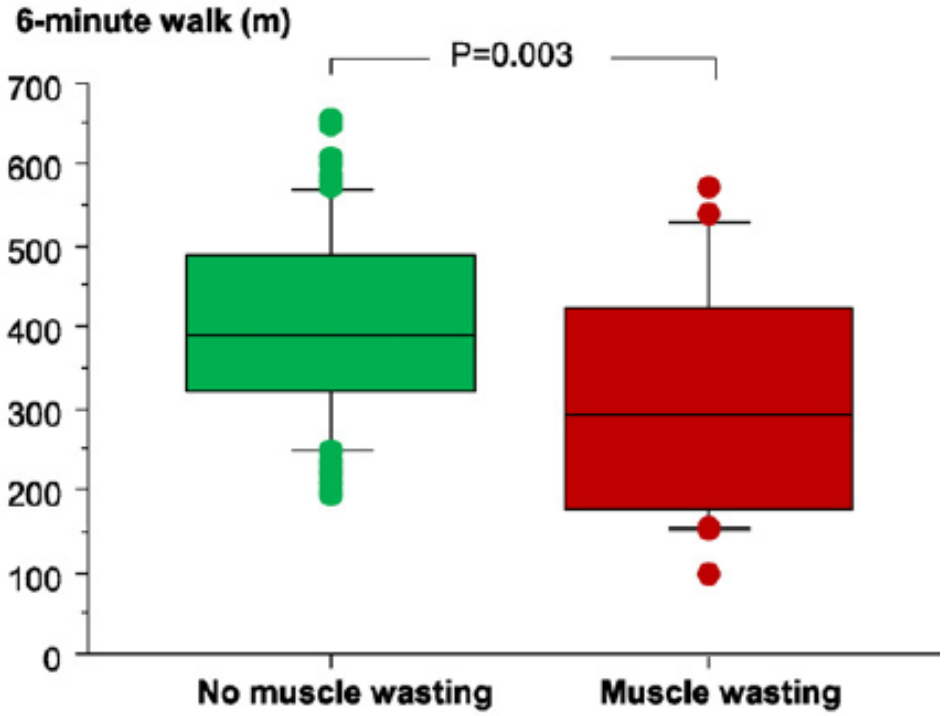
Our group recently studied the clinical effects of muscle wasting in patients with HF as defined using the criteria of sarcopenia (Fülster et al., 2013), *i.e.* appendicular lean mass corrected for height squared of 2 standard deviations or more below the mean of young healthy persons. Patients were prospectively enrolled as part of the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF) (von Haehling et al., 2010). Of 200 patients (mean age 66.9 ± 10.4 years, New York Heart Association class 2.3 ± 0.5, left ventricular ejection fraction 38.9 ± 13.5, body mass index 28.8 ± 5.1), 39 (19.5%) fulfilled the criteria of muscle wasting as assessed by DEXA scan. Patients with muscle wasting had significantly lower values for handgrip and quadriceps strength,

Sarcopenia in patients with heart failure with preserved ejection fraction: Impact on muscle strength, exercise capacity and quality of life

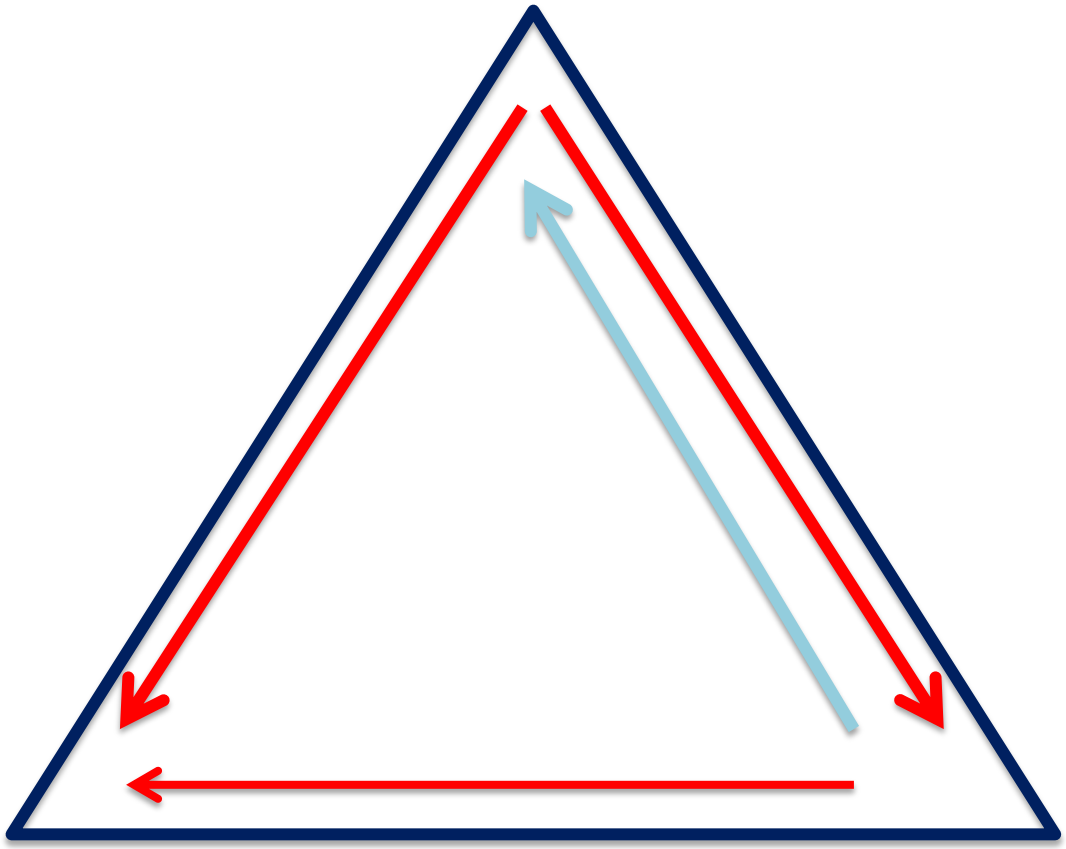
International Journal of Cardiology 222 (2016) 41–46

19.5%

All patients % (n = 117)	Patients with muscle wasting % (n = 23)	Patients without muscle wasting % (n = 94)

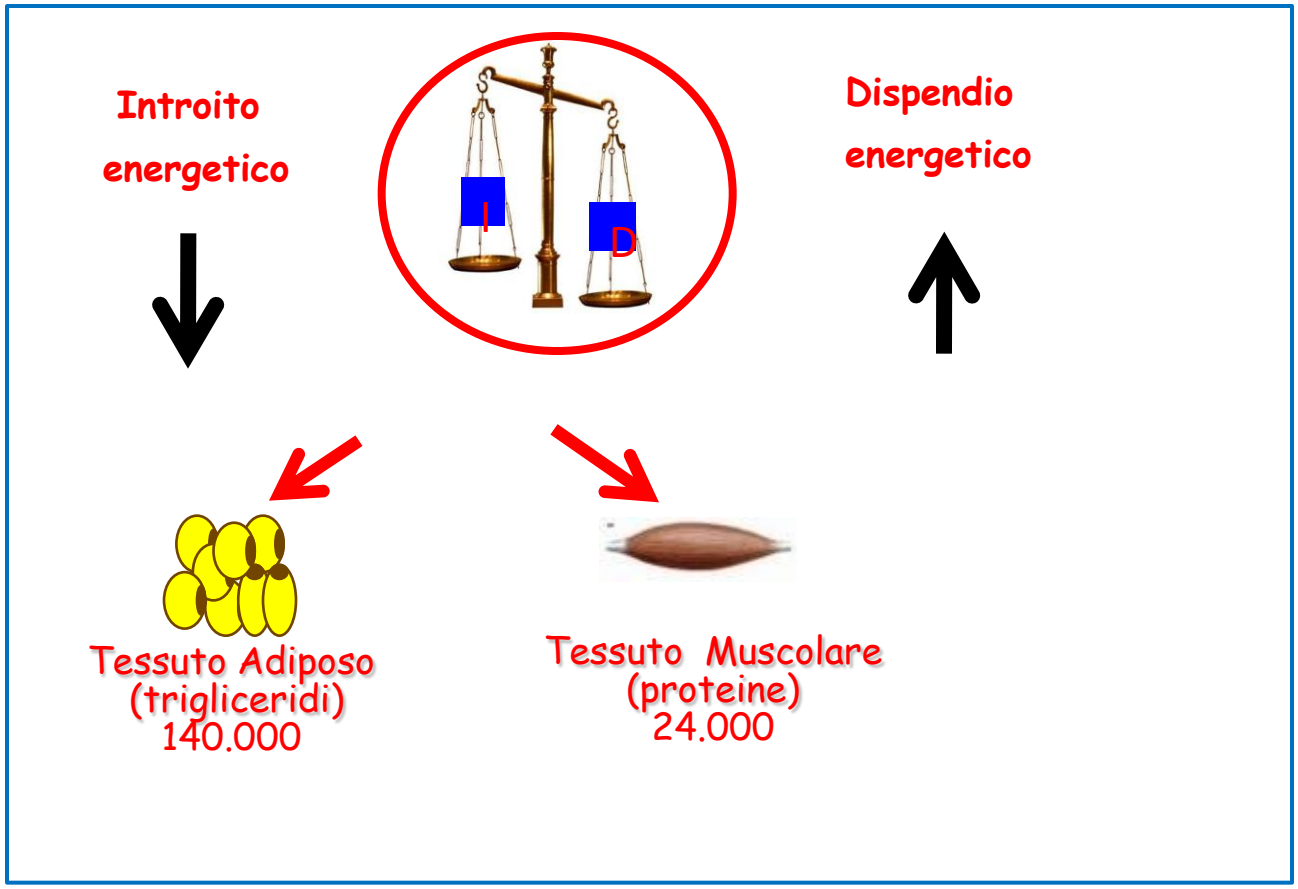


Alterazioni Nutrizionali nelle Malattie Cardiorespiratorie



Energy or Energy Protein Malnutrition

is present when insufficent energy or protein is available to meet metabolic demands, may develop because ofpoor dietary protein calorie intake, increased metabolic demands



Weight loss

With a decline in
Fat mass
Muscle mass
Visceral protein

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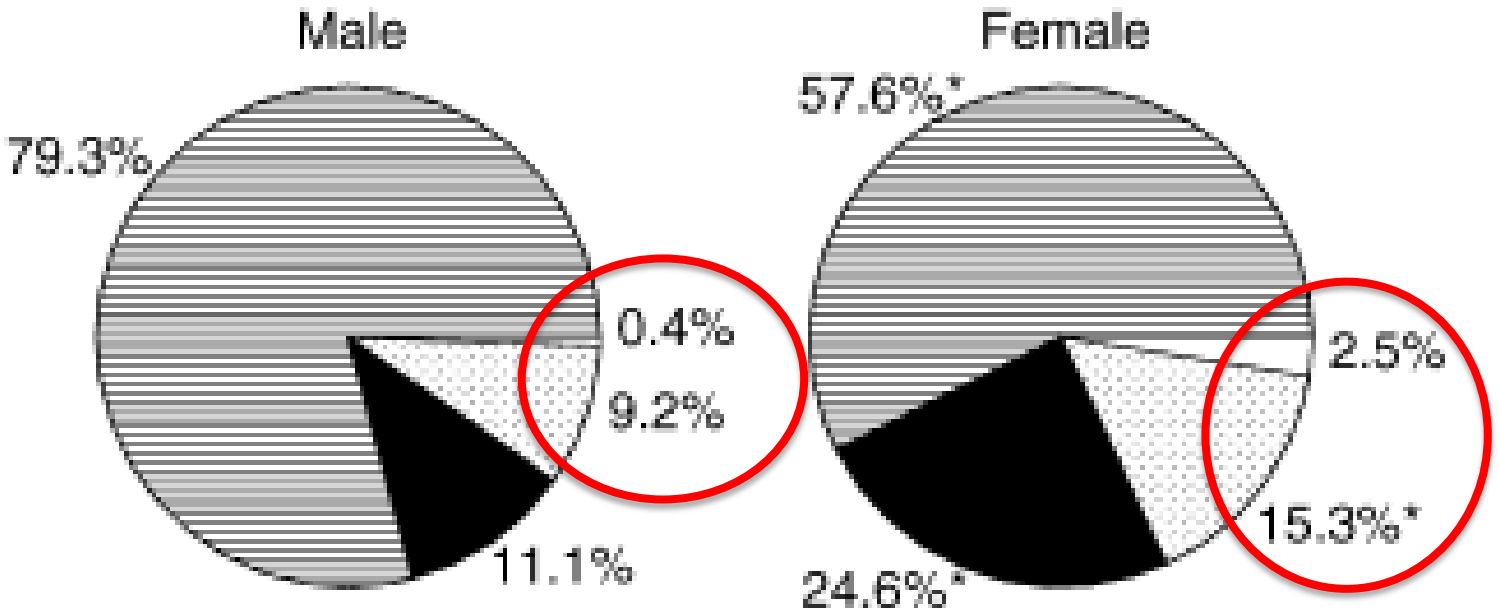
Prevalence of nutritional depletion in a large out-patient population of patients with COPD



39 out-patient centers
389 patients with moderate to svere COPD
Age 40-75 years

Black: BMI normal FFM depletion
White:BMI depletion and normal FFM
Dots : BMI and FFM depletion

Respiratory Medicine (2006) 100, 1349–1355

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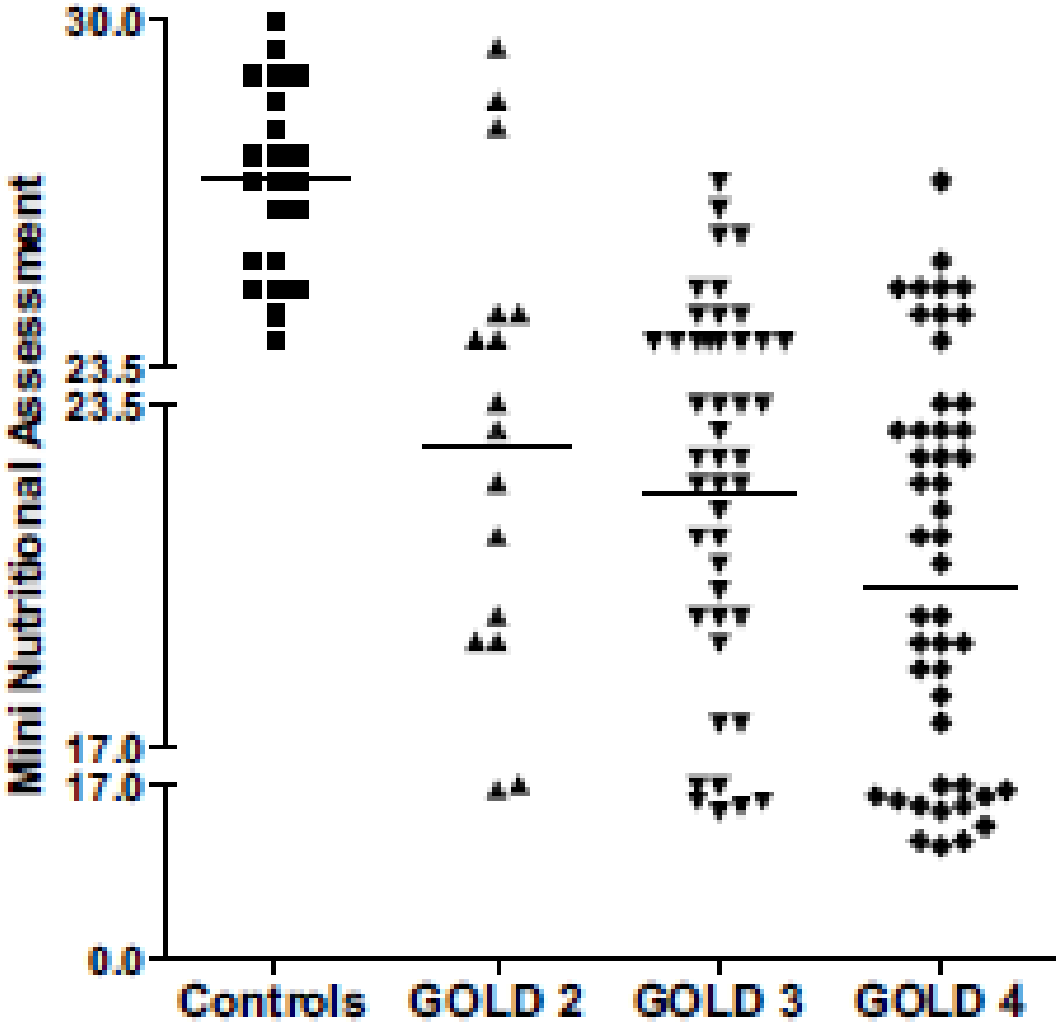

Respiratory Medicine (2006) **100**, 1349–1355

Factors Leading to Sarcopenia in COPD patients

American Thoracic Society (mod)

Disuse

Inflammation

Oxidative Stress- Smoking

Exacerbations

Corticosteroids

Malnutrition

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

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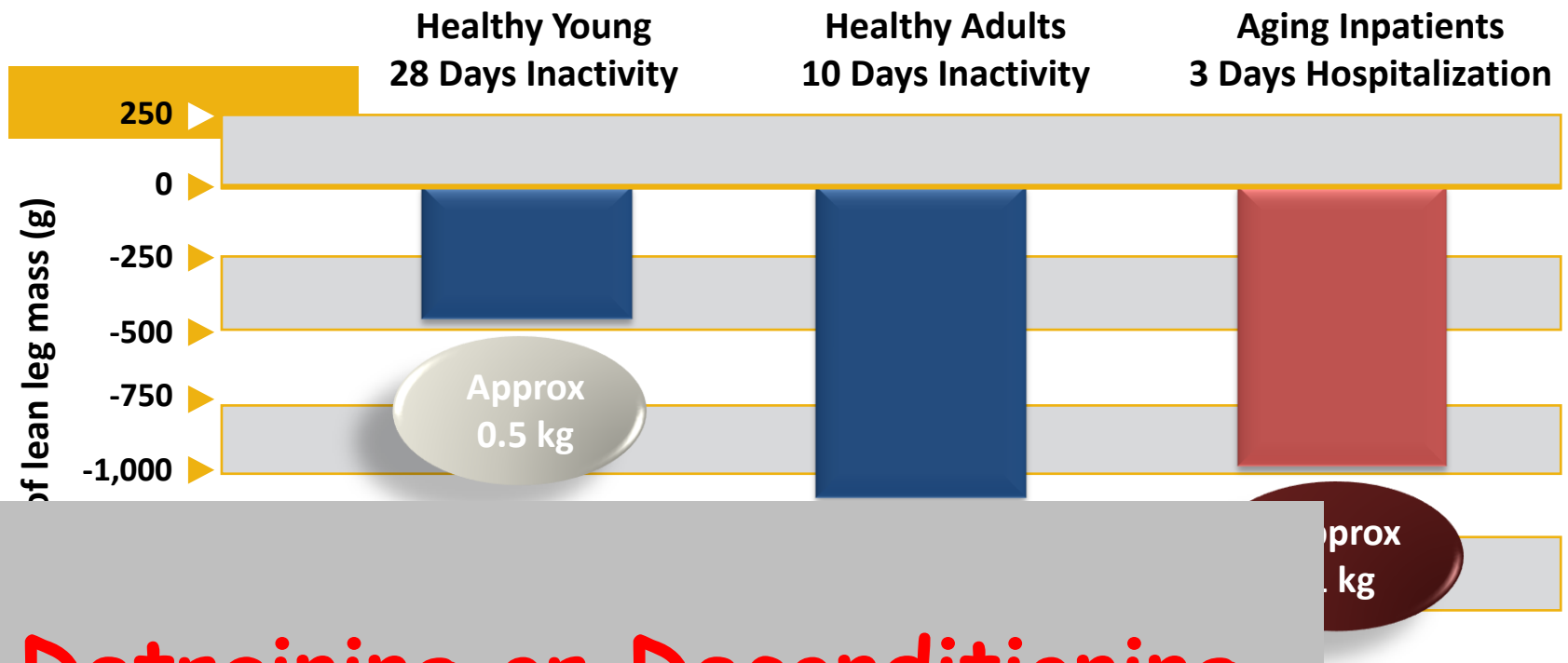
Bed rest and muscle mass-2



Detraining or Deconditioning characterize COPD

Bossenbroek et al, 2011

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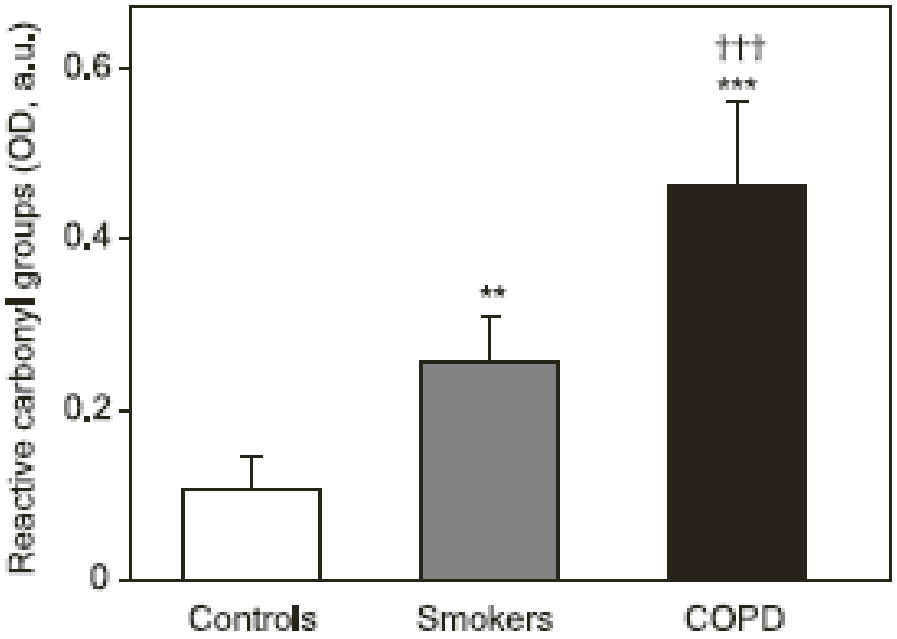
Cigarette Smoke–induced Oxidative Stress

A Role in Chronic Obstructive Pulmonary Disease Skeletal Muscle Dysfunction

Esther Barreiro[1,2], Víctor I. Peinado[2,3], Juan B. Galdiz[4], Elisabet Ferrer[2,3], Judith Marin-Corral[1], 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 induce oxidative modifications of key muscle biological structures

Am J Respir Crit Care Med Vol 182. pp 477–488, 2010

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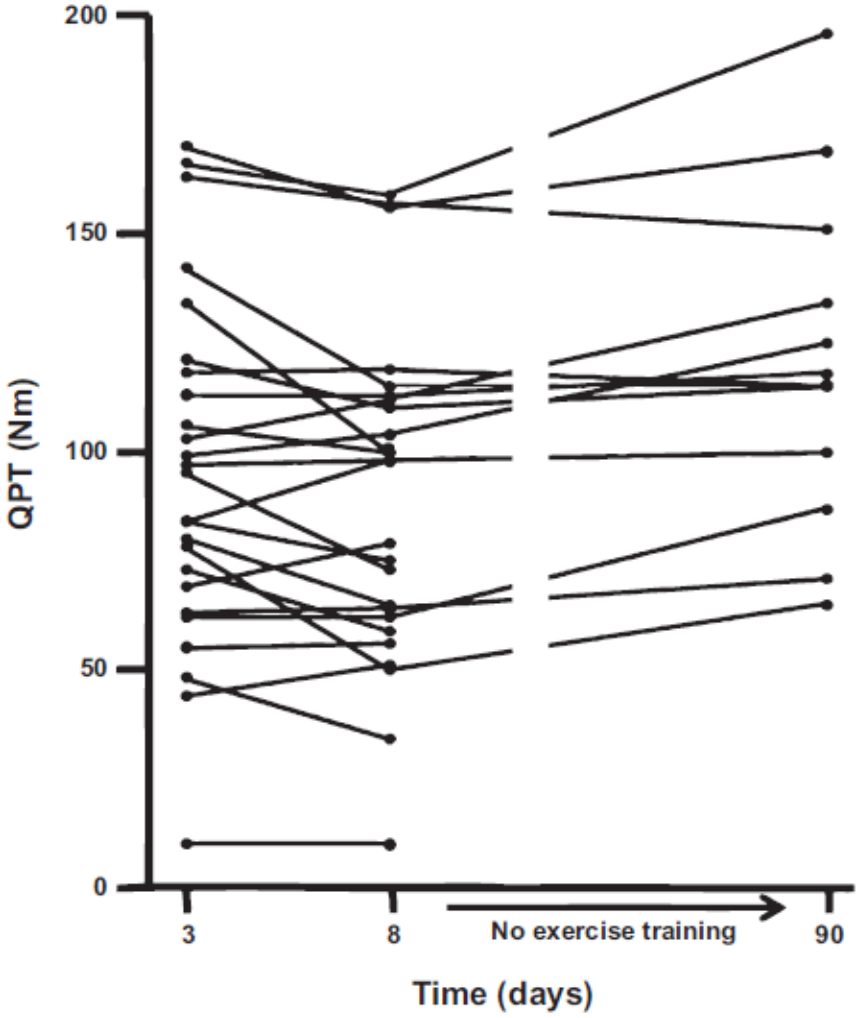
Quadriceps peak torque in patients with acute exacerbations and after 90 days of follow-up



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

After 3 months only partial recovery

J Appl Physiol 114: 1291–1299, 2013.

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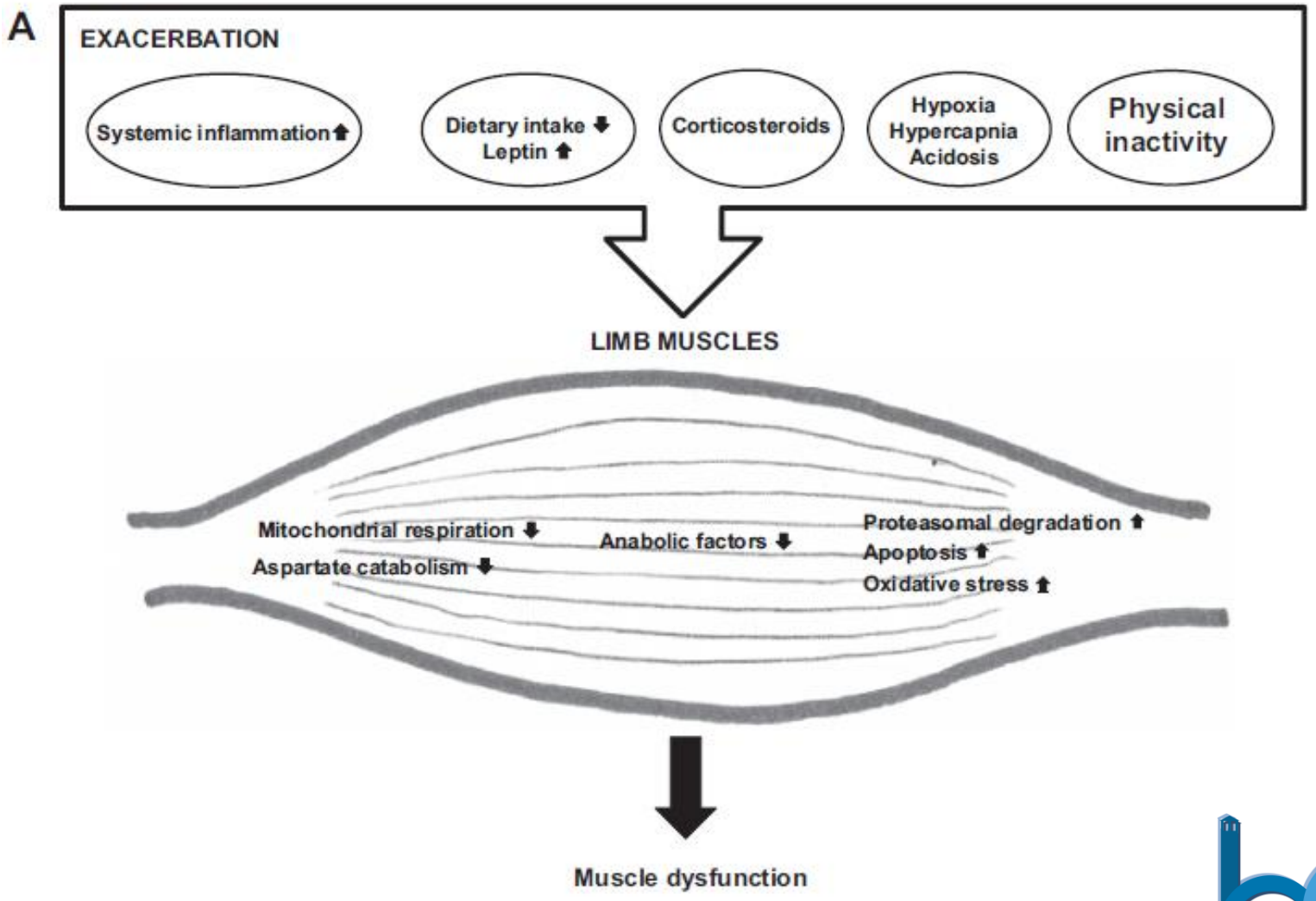
Mechanisms leading to muscle dysfunction in acute exacerbations



J Appl Physiol 114: 1291–1299, 2013.

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Steroid induced myopathy

Acute

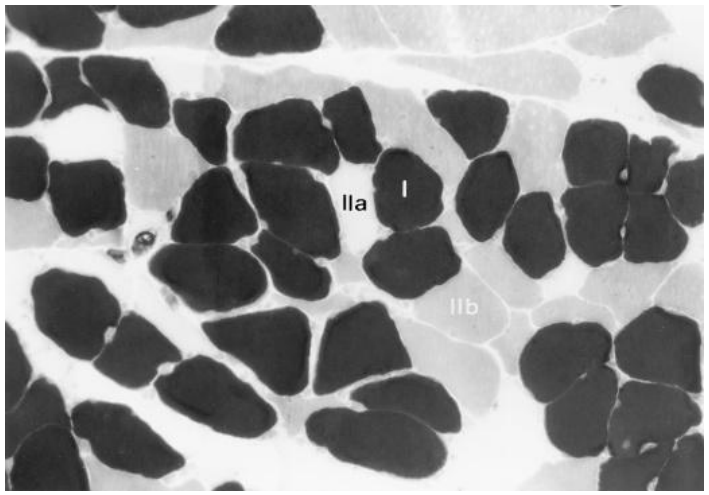
-Proximal and distal muscle weakness after 5-7 days of high dose intravenous treatment

-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 patiens with COPD



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

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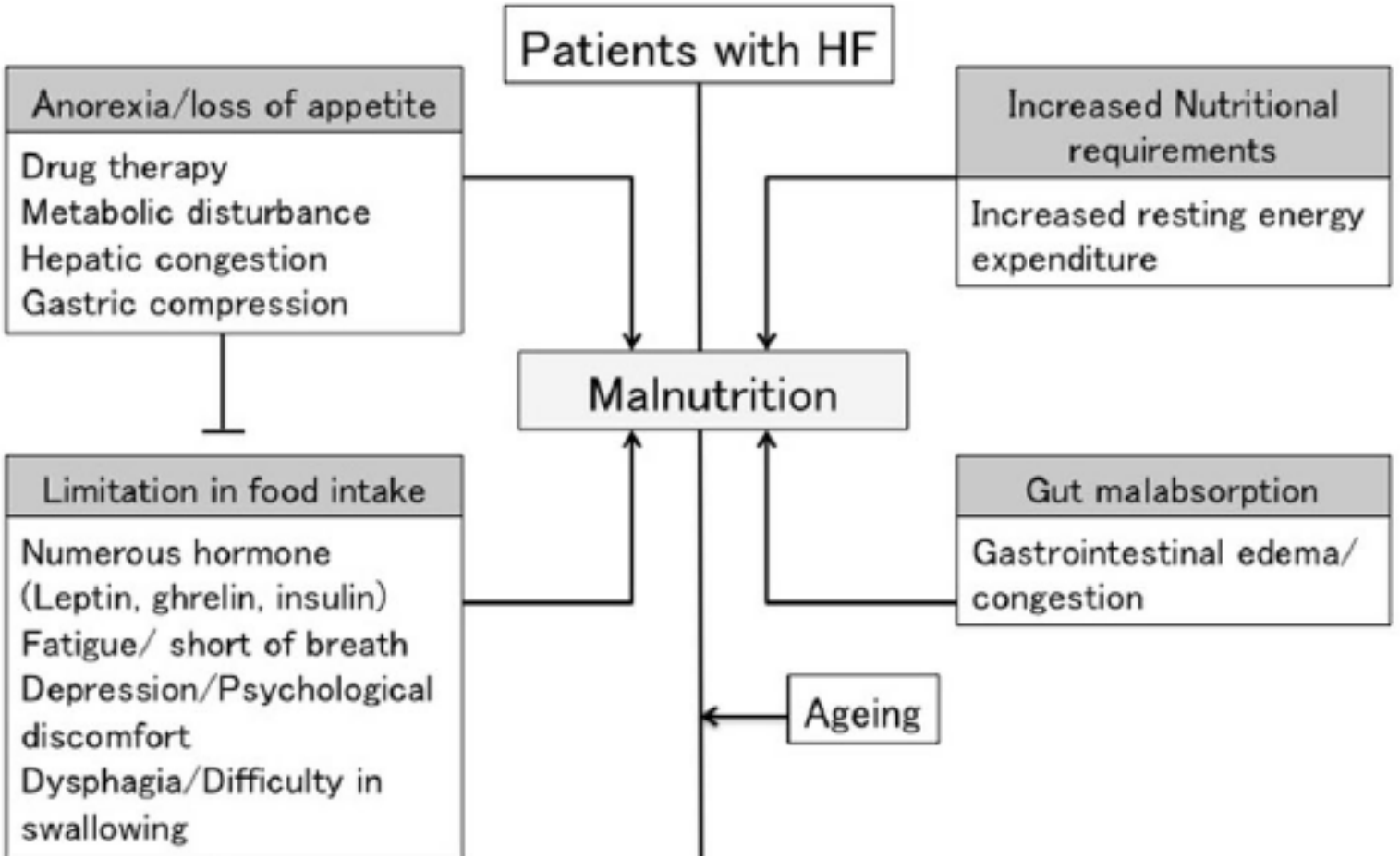

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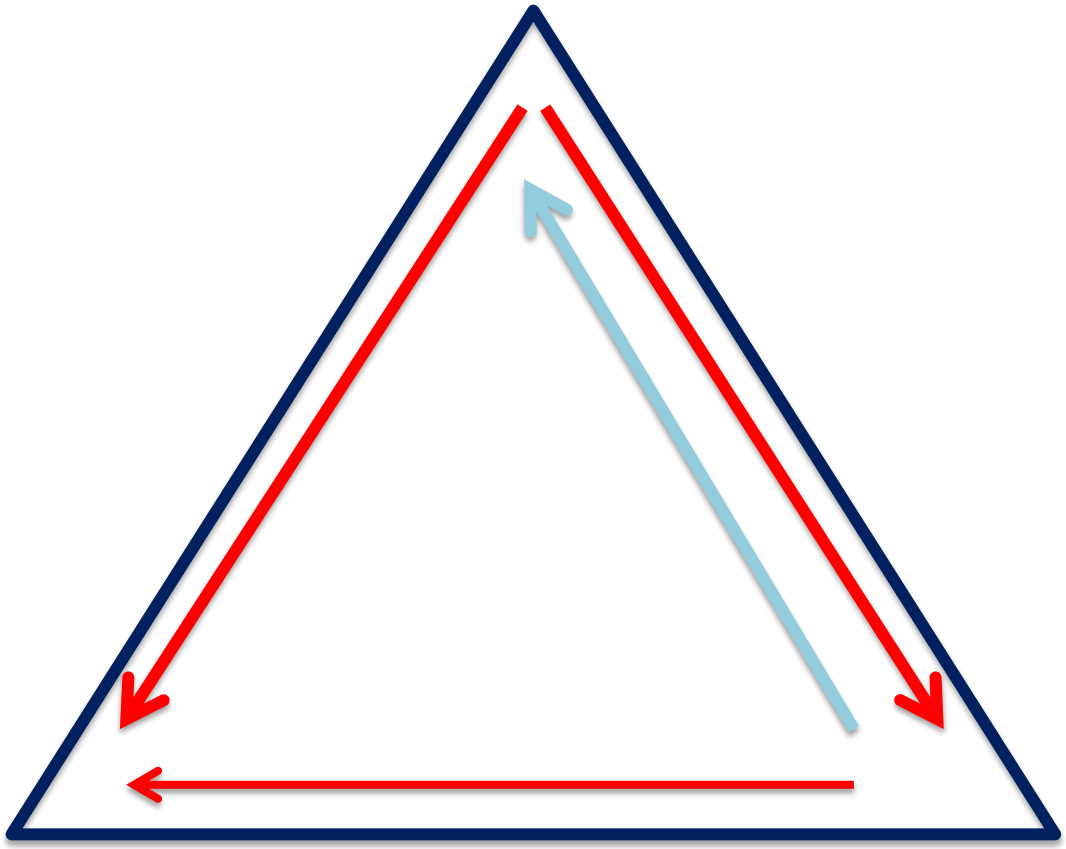


Cachexia definition

Fearon KC et al Clin Nutr 2006

Complex syndrome combining:

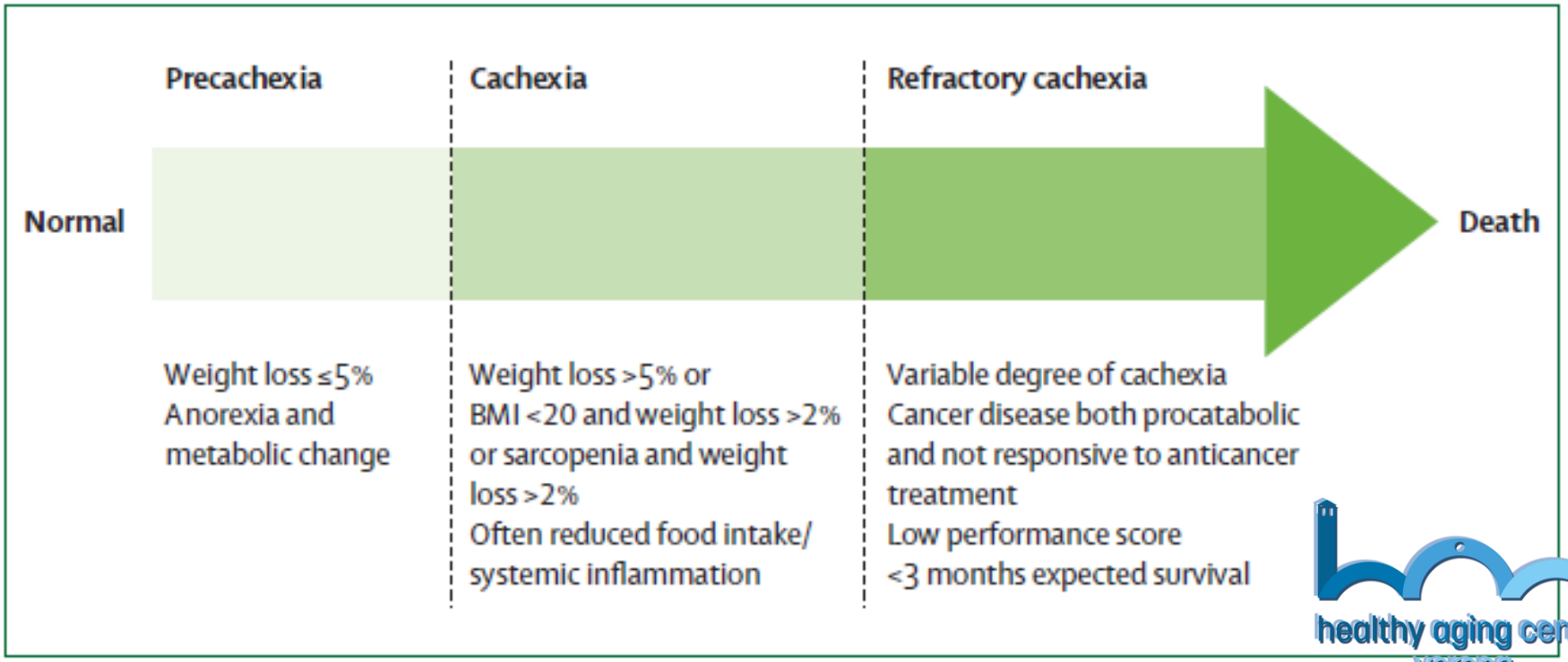
-Weight loss (> 10%)

-Reduced food intake (< 1'500 Kcal /day)

-Systemic inflammation (CRP > 10 mg / l)

+ Anorexia & Weakness

www.thelancet.com/oncology **Vol 12 May 2011**



The number of persons in the United States with cachexia[1]

Disease	No. with disease	Cachexia	No. needing treatment
		%	
AIDS[2]	900 000	35	315 000
Cancer	1 368 000	30	410 400
COPD	16 000 000	20	3 200 000
Kidney failure	375 000	40	150 000
Rheumatoid arthritis	2 100 000	10	210 000
Heart failure	4 800 000	20	960 000
Nursing home	1 600 000	20	320 000

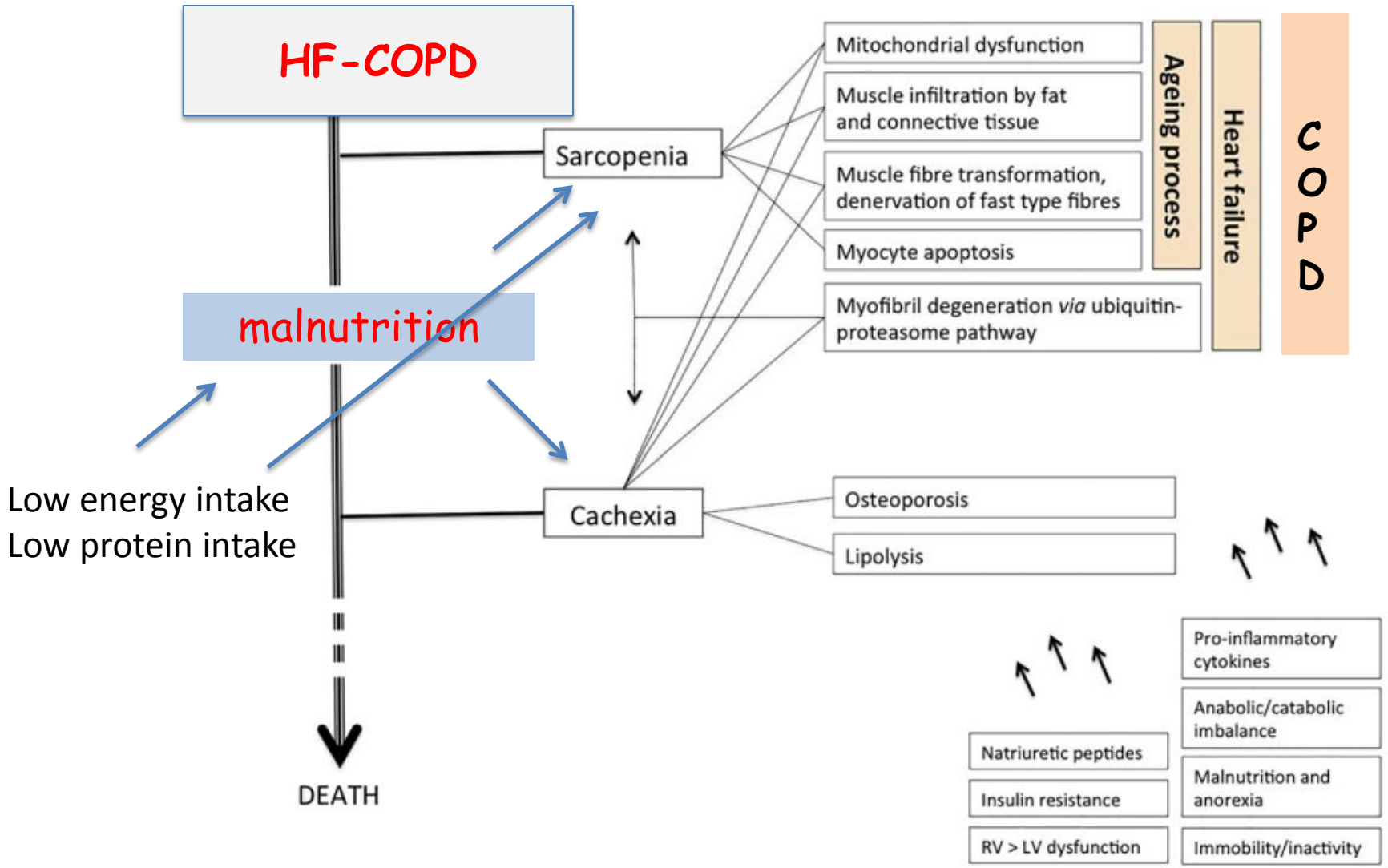
[1] The numbers are based on generally reported prevalences of disease and literature estimations of unintentional weight loss in these conditions. COPD, chronic obstructive pulmonary disease.

[2] The values may be too high in the era of the use of highly active antiretroviral therapy; some authors believe that 10% may be more appropriate.

Morley, J. E et al., 2006

The American Journal of CLINICAL NUTRITION

The wasting continuum in HF and COPD: from sarcopenia to cachexia



Proceedings of the Nutrition Society (2015), **74**, 367–377

S von Haeling (mod)

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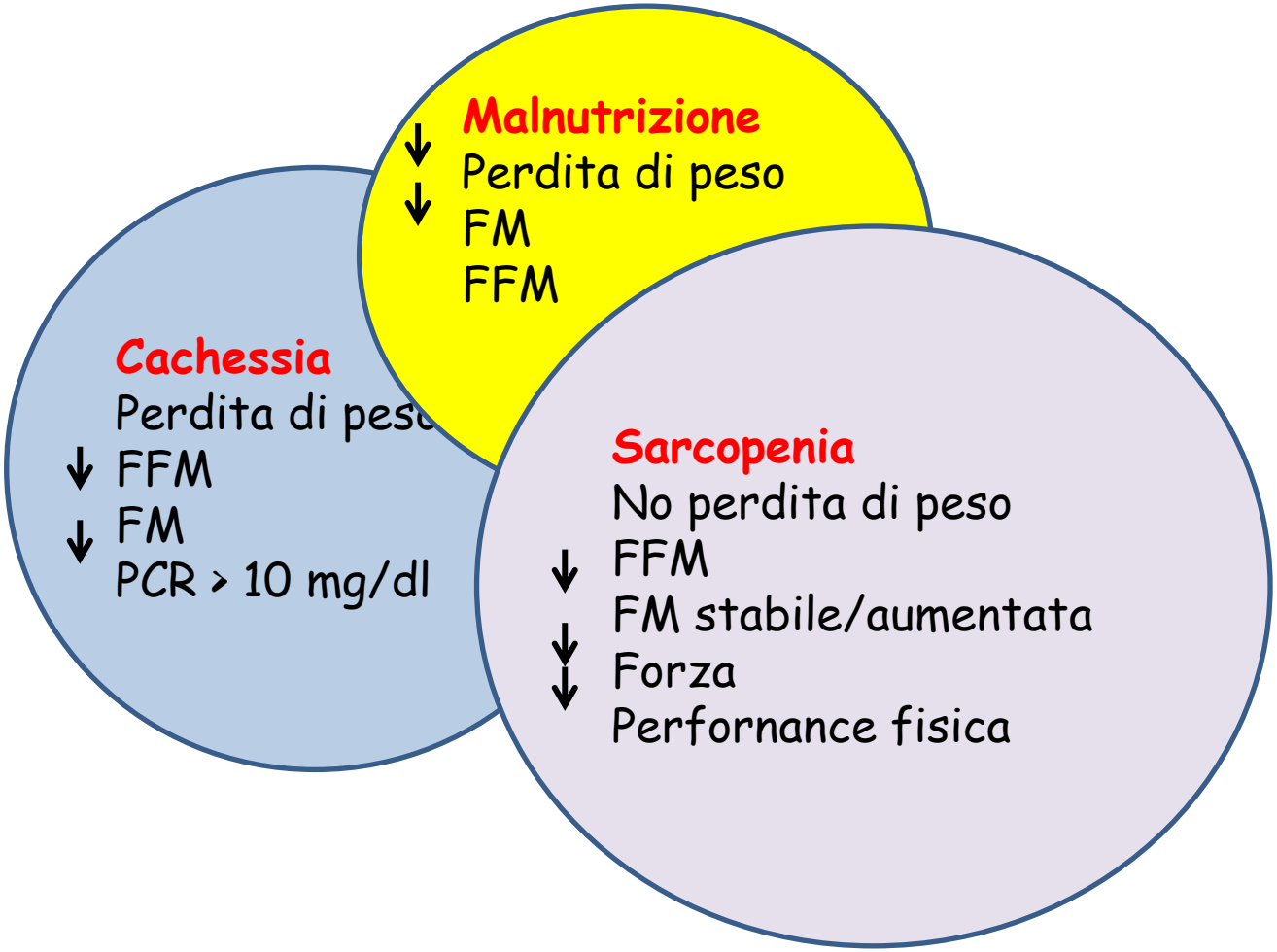
Overlap Cachexia, Starvation and sarcopenia



Modificata da: Thomas Clinical Nutrition 2007,
ESPEN Initiative for Diagnostic Criteria for Undernutrition 2014

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Definition

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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

*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.

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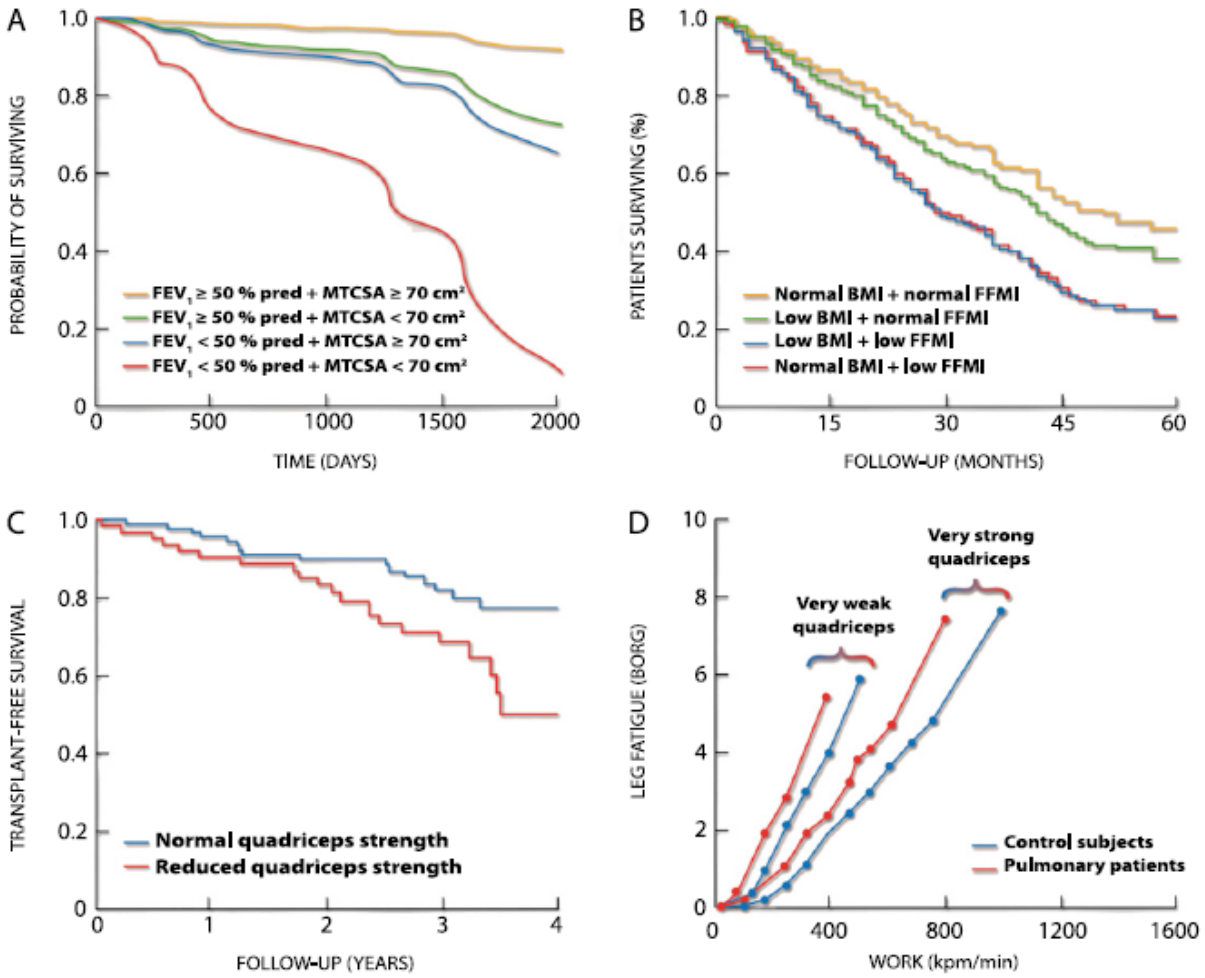
Relation between muscle mass and strength and clinical outcomes in patients with COPD



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Sarcopenia
Treatment options in HF and COPD patients

Disuse

Inflammation

Smoking

Exacerbations

Malnutrition

Corticosteroids

Vitamin D deficency

Protein/Energy supplementation

Supplementation with exercise training
Neuromuscular stimulation

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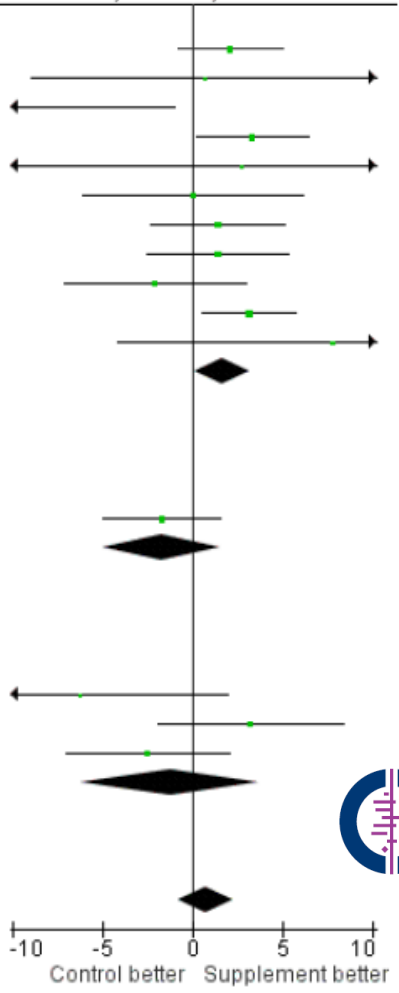
Nutritional supplementation for stable chronic obstructive pulmonary disease (Review)

Cochrane Database of Systematic Reviews 2012, Issue 12

Nutritional supplementation vs placebo: final weight

Study or Subgroup	Supplement Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.2.1 Undernourished								
DeLetter 1991	58.87	4.94	18	56.8	3.81	17	11.9%	2.07 [-0.84, 4.98]
Efthimiou 1988	48.8	11.6	7	48.1	6.1	7	2.3%	0.70 [-9.01, 10.41]
Fuenzalida 1990	60.1	6.01	5	70.48	7.94	4	2.4%	-10.38 [-19.78, -0.98]
Lewis 1987	53.3	3.05	10	50	4.15	11	11.3%	3.30 [0.20, 6.40]
Otte 1989	47.7	21.3	13	45	18.2	15	1.0%	2.70 [-12.10, 17.50]
Rogers 1992	54.5	10.05	15	54.5	6.2	12	4.8%	0.00 [-6.18, 6.18]
Schols 1995	56.6	7.2	39	55.2	7.6	25	9.3%	1.40 [-2.34, 5.14]
Sugawara 2010	47.9	5.4	17	46.5	5.9	15	8.8%	1.40 [-2.54, 5.34]
van Wetering 2010	64.2	8.6	16	66.3	5.3	14	6.4%	-2.10 [-7.15, 2.95]
Weekes 2009	55.7	4.93	30	52.6	5	25	12.9%	3.10 [0.46, 5.74]
Whittaker 1990	52.8	8.9	6	45	9.8	4	1.5%	7.80 [-4.16, 19.76]
Subtotal (95% CI)			**176**			**149**	**72.6%**	**1.65 [0.14, 3.16]**
Heterogeneity: Tau² = 1.06; Chi² = 12.06, df = 10 (P = 0.28); I² = 17%								
Test for overall effect: Z = 2.14 (P = 0.03)								
1.2.2 Nourished								
Schols 1995	71.6	6	33	73.3	8	38	10.7%	-1.70 [-4.97, 1.57]
Subtotal (95% CI)			**33**			**38**	**10.7%**	**-1.70 [-4.97, 1.57]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.02 (P = 0.31)								
1.2.3 Combined population of undernourished and nourished								
Knowles 1988	57	9.75	13	63.25	11	12	3.0%	-6.25 [-14.42, 1.92]
Steiner 2003	68.03	9.97	25	64.82	10.32	35	6.2%	3.21 [-1.98, 8.40]
Sugawara 2012	52.1	8.3	17	54.6	4.3	14	7.4%	-2.50 [-7.04, 2.04]
Subtotal (95% CI)			**55**			**61**	**16.7%**	**-1.28 [-6.27, 3.72]**
Heterogeneity: Tau² = 10.75; Chi² = 4.53, df = 2 (P = 0.10); I² = 56%								
Test for overall effect: Z = 0.50 (P = 0.62)								
Total (95% CI)			**264**			**248**	**100.0%**	**0.69 [-0.86, 2.24]**
Heterogeneity: Tau² = 3.04; Chi² = 22.25, df = 14 (P = 0.07); I² = 37%								
Test for overall effect: Z = 0.88 (P = 0.38)								
Test for subgroup differences: Chi² = 4.11, df = 2 (P = 0.13), I² = 51.4%								



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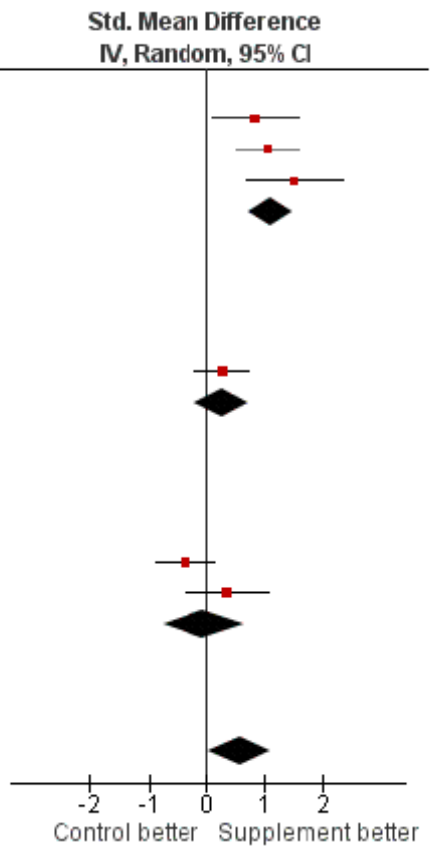
Nutritional supplementation for stable chronic obstructive pulmonary disease (Review)

Cochrane Database of Systematic Reviews 2012, Issue 12

Nutritional supplementation vs placebo: FFM

Study or Subgroup	Std. Mean Difference	SE	Supplement Total	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.8.1 Undernourished						
Sugawara 2010 (1)	0.8329	0.3713	17	15	15.5%	0.83 [0.11, 1.56]
Schols 1995 (2)	1.0495	0.2735	39	25	17.9%	1.05 [0.51, 1.59]
van Wetering 2010 (3)	1.5066	0.4282	15	14	14.1%	1.51 [0.67, 2.35]
Subtotal (95% CI)			**71**	**54**	**47.5%**	**1.08 [0.70, 1.47]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.45$, df = 2 (P = 0.48); $I^2 = 0\%$						
Test for overall effect: Z = 5.54 (P < 0.00001)						
1.8.2 Adequately nourished						
Schols 1995	0.2651	0.239	33	38	18.7%	0.27 [-0.20, 0.73]
Subtotal (95% CI)			**33**	**38**	**18.7%**	**0.27 [-0.20, 0.73]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.11 (P = 0.27)						
1.8.3 Combined population of undernourished and nourished patients						
Steiner 2003	-0.3712	0.2642	25	35	18.1%	-0.37 [-0.89, 0.15]
Sugawara 2012 (4)	0.3532	0.3641	17	14	15.7%	0.35 [-0.36, 1.07]
Subtotal (95% CI)			**42**	**49**	**33.8%**	**-0.05 [-0.76, 0.65]**
Heterogeneity: $Tau^2 = 0.16$; $Chi^2 = 2.59$, df = 1 (P = 0.11); $I^2 = 61\%$						
Test for overall effect: Z = 0.15 (P = 0.88)						
Total (95% CI)			**146**	**141**	**100.0%**	**0.57 [0.04, 1.09]**
Heterogeneity: $Tau^2 = 0.33$; $Chi^2 = 22.28$, df = 5 (P = 0.0005); $I^2 = 78\%$						
Test for overall effect: Z = 2.11 (P = 0.03)						
Test for subgroup differences: $Chi^2 = 11.33$, df = 2 (P = 0.003), $I^2 = 82.3\%$						



(1) this is FFMI (kg/m²)
(2) used bio-electrical resistance to measure FFM, data sent by author (Dr Schols)
(3) this is FFMI (kg/m²)
(4) FFM, kg

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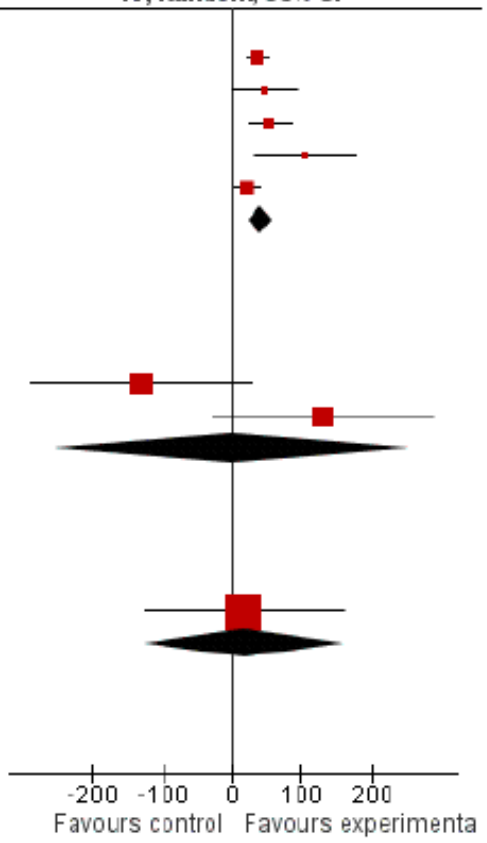
Nutritional supplementation for stable chronic obstructive pulmonary disease (Review)

Cochrane Database of Systematic Reviews 2012, Issue 12

Nutritional supplementation vs placebo: change in function

Study or Subgroup	Mean Difference	SE	Experimental Total	Control Total	Weight	Mean Difference IV, Random, 95% CI
1.13.1 6-minute walk test						
DeLetter 1991 (1)	36.58	8.7393	18	17	33.1%	36.58 [19.45, 53.71]
Efthimiou 1988 (2)	47	23.3421	7	7	11.1%	47.00 [1.25, 92.75]
Sugawara 2010 (3)	54.12	15.1764	17	13	20.0%	54.12 [24.37, 83.87]
Sugawara 2012 (4)	105	37.5965	17	14	5.0%	105.00 [31.31, 178.69]
van Wetering 2010 (5)	21.5	9.6125	16	14	30.9%	21.50 [2.66, 40.34]
Subtotal (95% CI)			**75**	**65**	**100.0%**	**39.96 [22.66, 57.26]**
Heterogeneity: $Tau^2 = 159.25$; $Chi^2 = 7.30$, df = 4 (P = 0.12); $I^2 = 45\%$						
Test for overall effect: Z = 4.53 (P < 0.00001)						
1.13.2 12-minute walk test						
Otte 1989	-130.3	79.9521	13	15	50.1%	-130.30 [-287.00, 26.40]
Rogers 1992	130.49	80.3839	15	12	49.9%	130.49 [-27.06, 288.04]
Subtotal (95% CI)			**28**	**27**	**100.0%**	**-0.04 [-255.61, 255.53]**
Heterogeneity: $Tau^2 = 27578.76$; $Chi^2 = 5.29$, df = 1 (P = 0.02); $I^2 = 81\%$						
Test for overall effect: Z = 0.00 (P = 1.00)						
1.13.3 Incremental shuttle walk test						
Steiner 2003 (6)	17.4	73.3717	42	43	100.0%	17.40 [-126.41, 161.21]
Subtotal (95% CI)			**42**	**43**	**100.0%**	**17.40 [-126.41, 161.21]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.24 (P = 0.81)						



Test for subgroup differences: $Chi^2 = 0.19$, df = 2 (P = 0.91), $I^2 = 0\%$

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