CONVEGNO
LA GERIATRIA IN EMILIA ROMAGNA 2016
Convegno Congiunto SIGG - SIGOT - AGE
Regione Emilia Romagna

Diagnosi e Trattamento della Sarcopenia nell'Anziano

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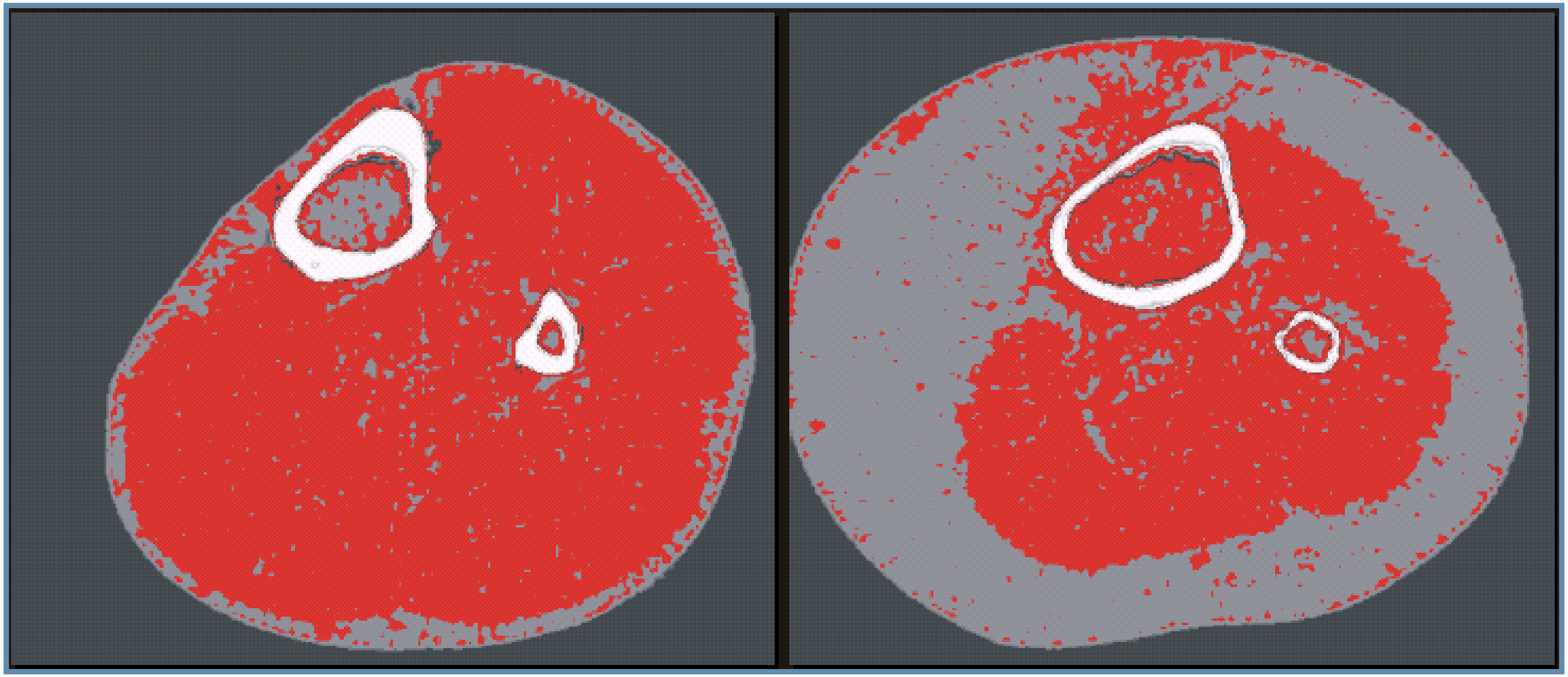
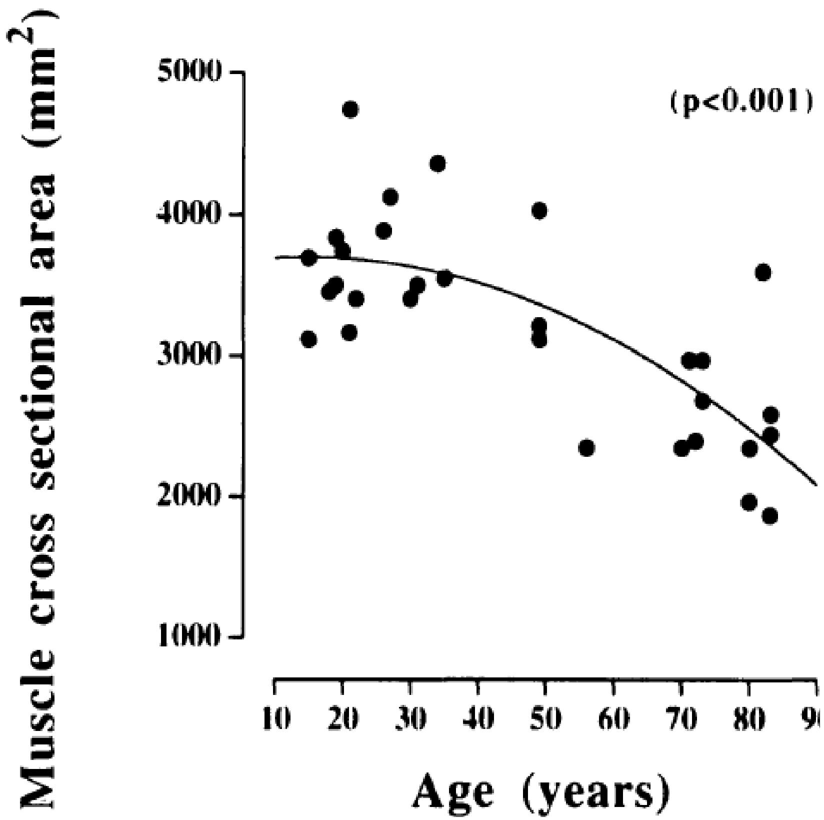
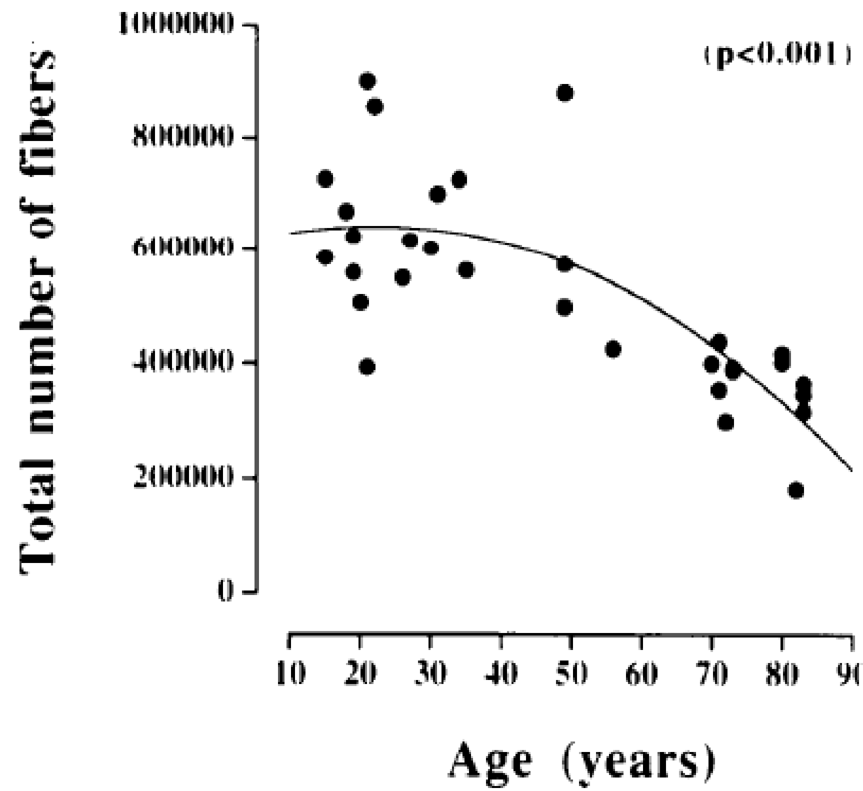
Sarcopenia *(sarx penia)*

Age related decline in skeletal muscle mass



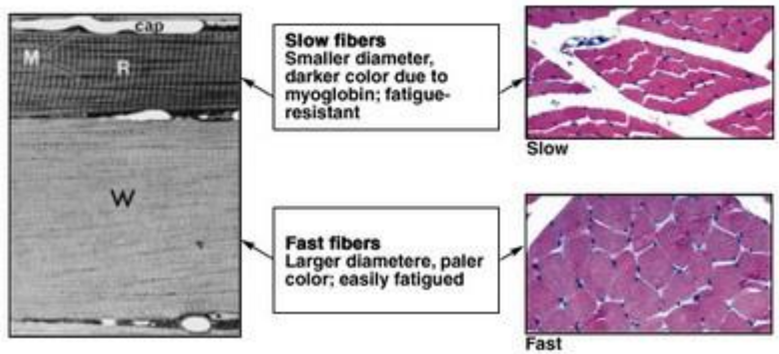
Relationship between age, muscle cross-sectional area, and total numbers of fibers





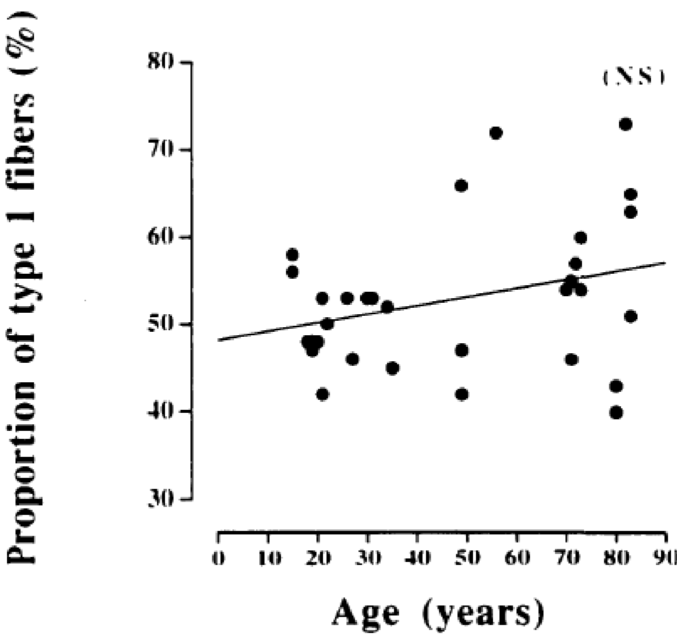
Lexell J. JGMS 50A, 11-16, 1995

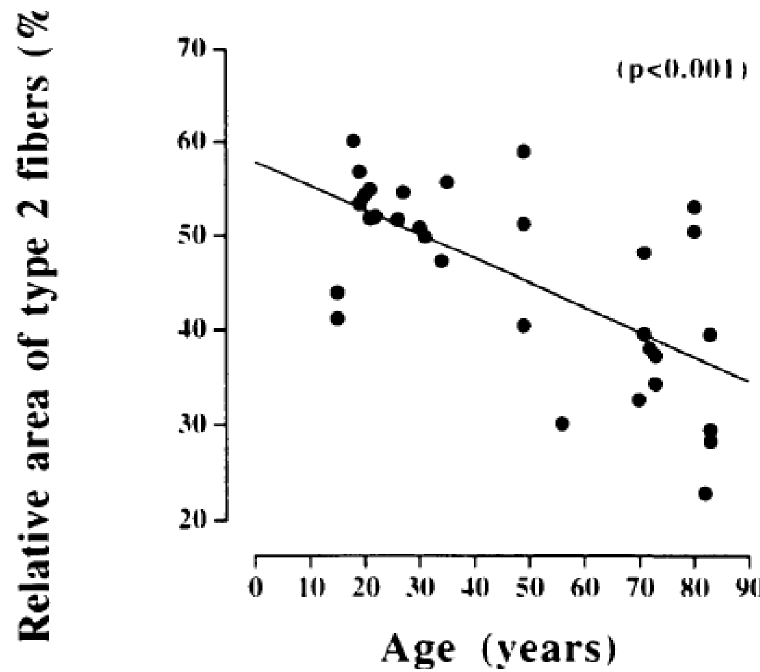
Relationship between age proportion of type 1 fibers and and relative area of type 2 fibers



Type I

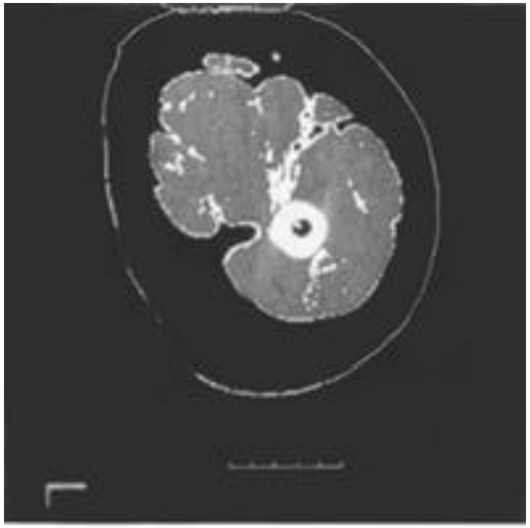
Type II (a,b)



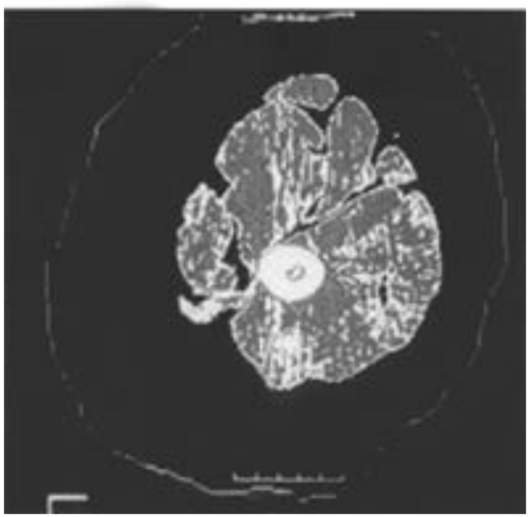


Lexell J. JGMS 50A, 11-16, 1995

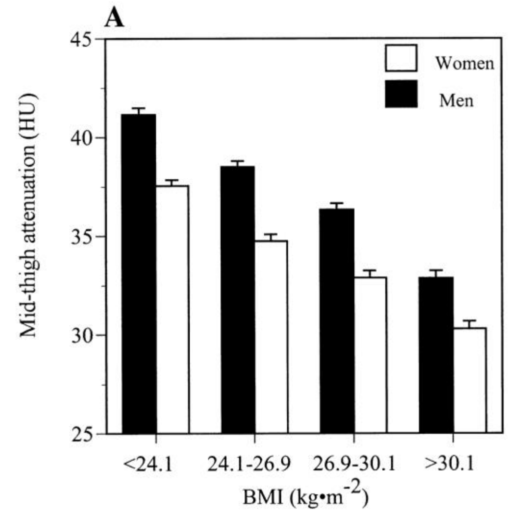
Association between age, BMI and skeletal muscle adipose tissue infiltration

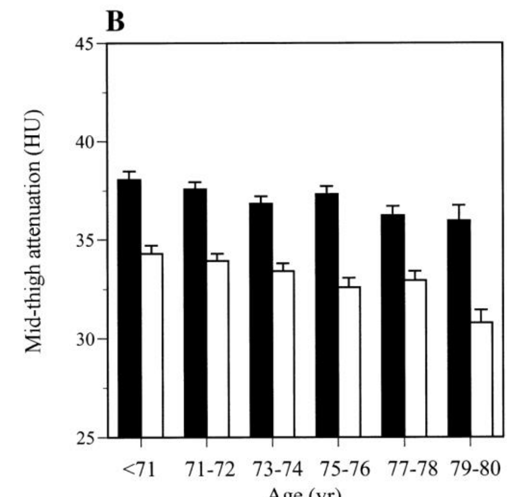


Lean volunteer



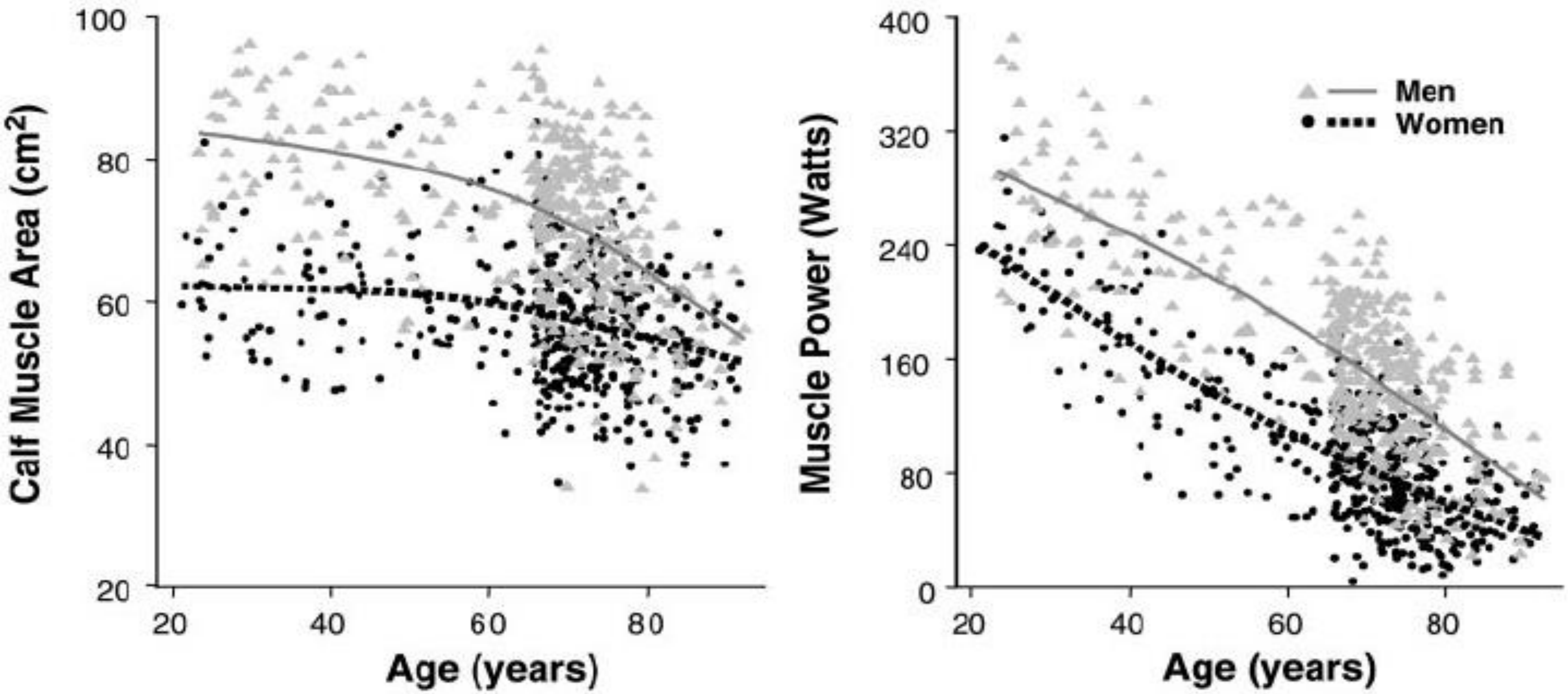
Obese volunteer





Goodpaster B et al, ANYAS; 2000:904:18-24; JAP; 2001;90:2157-2165

Relationship of age, muscle area and muscle power (InCHIANTI)



Lauretani, F. et al. J Appl Physiol 95: 1851-60, 2003

Sarcopenia: consensus definitions

- 2010 – **S**pecial **I**nterest **G**roup

  …condition characterized by loss of muscle mass and muscle strength…

- 2010 – **E**uropean **W**orking **G**roup on **S**arcopenia in **O**lder **P**eople

  …syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death…

- 2011 – **I**nternational **W**orking **G**roup on **S**arcopenia …Sarcopenia is the age-associated loss of skeletal muscle mass and function. Sarcopenia is a complex syndrome that is associated with muscle mass loss alone or in conjunction with increased fat mass.…

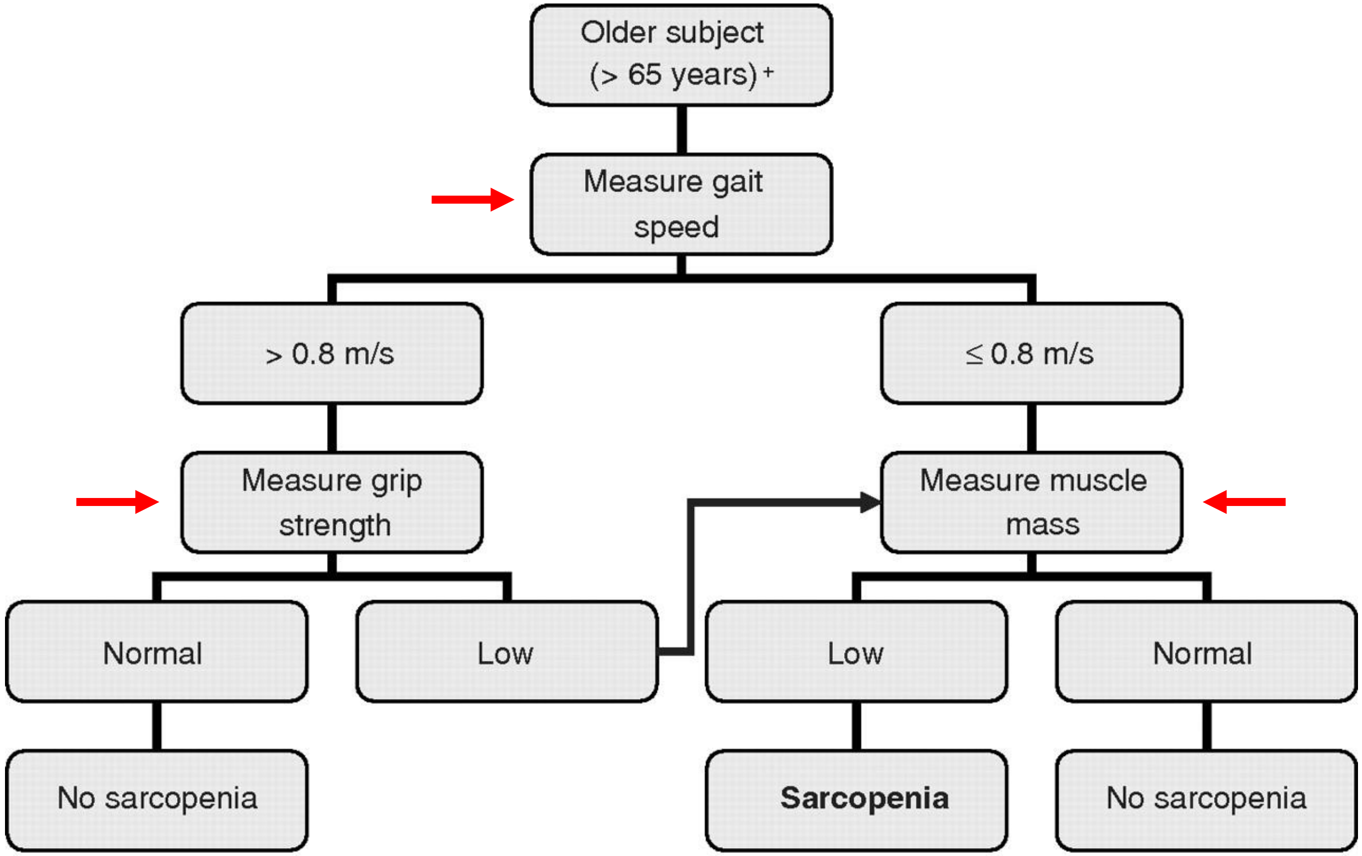
- 2014 – FNIH Sarcopenia Project: …functional limitation in the presence of weakness as a consequence of reduced skeletal muscle mass…

SIG. 2010: Clinical Nutrition 2010;29:154-159.
EWGSOP : Age Ageing 2010;39:412-23.
IWGS: JAMDA 2011;12:249-256
FNIH: JGMS 2014;69:547-558

Operational definitions

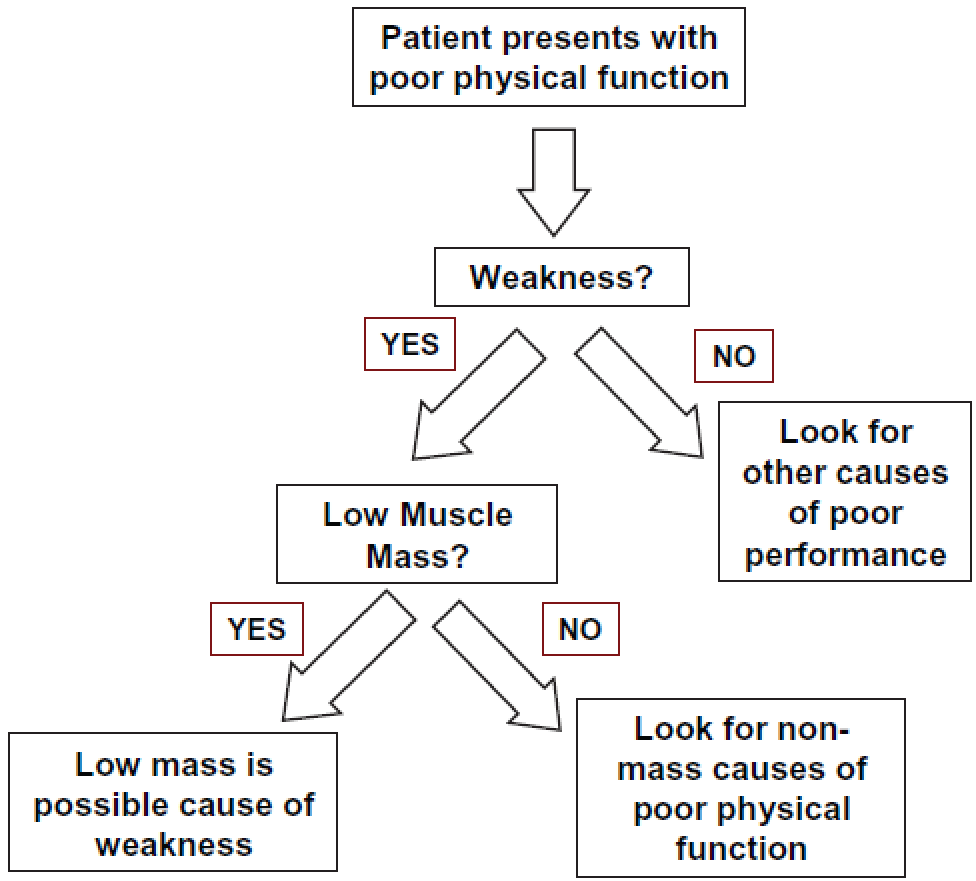
Consensus	Definition	Method	Criteria
SIG (2010)	Muscle Mass	Not definded	≥2 SD below mean according to gender and race
	Physical function	Walking speed	<0.8 m/s
EWGSOP (2010)	Muscle Mass	DXA; BIA Anthropometry	According to methods and gender
	Strength	Grip strength	According to gender and BMI
	Physical function	Walking speed	≤0.8 m/s
IWGS (2011)	Muscle mass aLM/h^2	DXA	W ≤ 5.67 kg/m^2 M≤ 7.25 kg/m^2
	Physical function	Walking speed	≤1.0 m/s
FNIH (2014)	Physical function	Walking speed	≤0.8 m/s
	Strength	Grip strength	M<26 kg ; W<16 g
	Muscle Mass ALM; ALM_{BMI}	DXA	M < 0.789 W <0.512

EWGSOP: diagnostic algorithm



Cruz-Jentoft A J et al. Age Ageing 2010;39:412-423

The FNIH sarcopenia project: clinical algorithm



Studensky et al. JGMS 2014;69:547-558

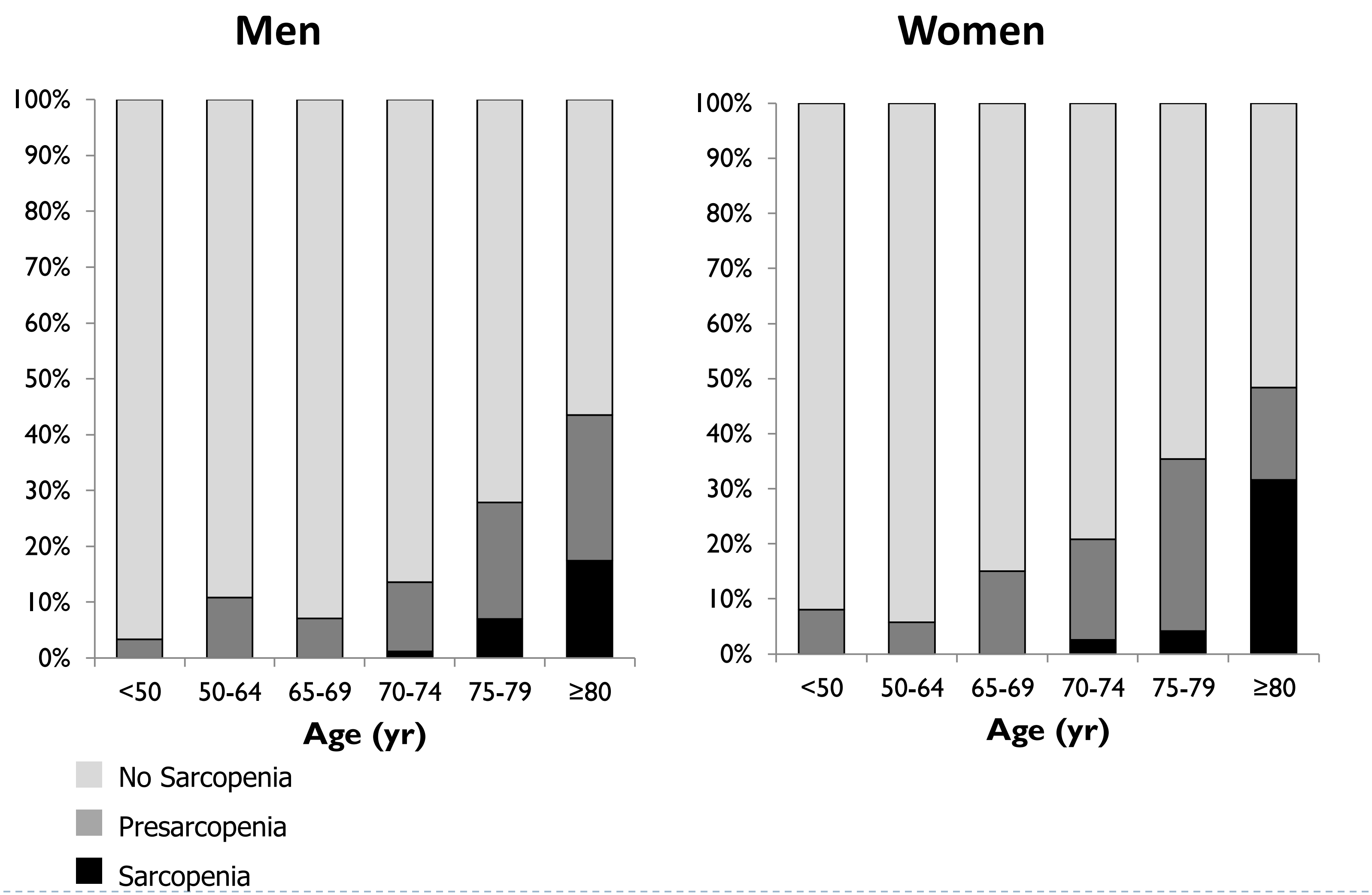
Prevalence of sarcopenia in older adults: Report of the International Sarcopenia Initiative

Criteria	Operational Definition: Physical Performance	Operational Definition: Muscle Strength	Operational Definition: ALM	Prevalence (%): Men (n = 7,113)	Prevalence (%): Women (n = 2,950)
Foundation of NIH Sarcopenia Project					
Weakness and low lean mass	—	Grip strength Men: <26 kg Women: <16 kg	ALM_{BMI} Men: <0.789 Women: <0.512	1.3	2.3
Slowness with weakness and low lean mass	Gait speed: ≤0.8 m/s	Grip strength Men: <26 kg Women: <16 kg	ALM_{BMI} Men: <0.789 Women: <0.512	0.5	1.8
International Working Group	Gait speed: <1.0 m/s	—	ALM/ht^2 Men: ≤7.23 kg/m² Women: ≤5.67 kg/m²	5.1	11.8
European Working Group on Sarcopenia Older Persons					
Sarcopenia	Gait speed: <0.8 m/s or Grip strength Men: <30 kg Women: <20 kg		ALM/ht^2 Men: ≤7.23 kg/m² Women: ≤5.67 kg/m²	5.3	13.3
Severe sarcopenia	Gait speed: <0.8 m/s	Grip strength Men: <30 kg Women: <20 kg	ALM/ht^2 Men: ≤7.23 kg/m² Women: ≤5.67 kg/m²	0.7	2.9

Note: ALM_{BMI} = ratio of appendicular lean mass over body mass index; ALM/ht^2 = ratio of appendicular lean mass over height squared.

Cruz-Jentoft A J et al. Age Ageing 2014;43:748-759

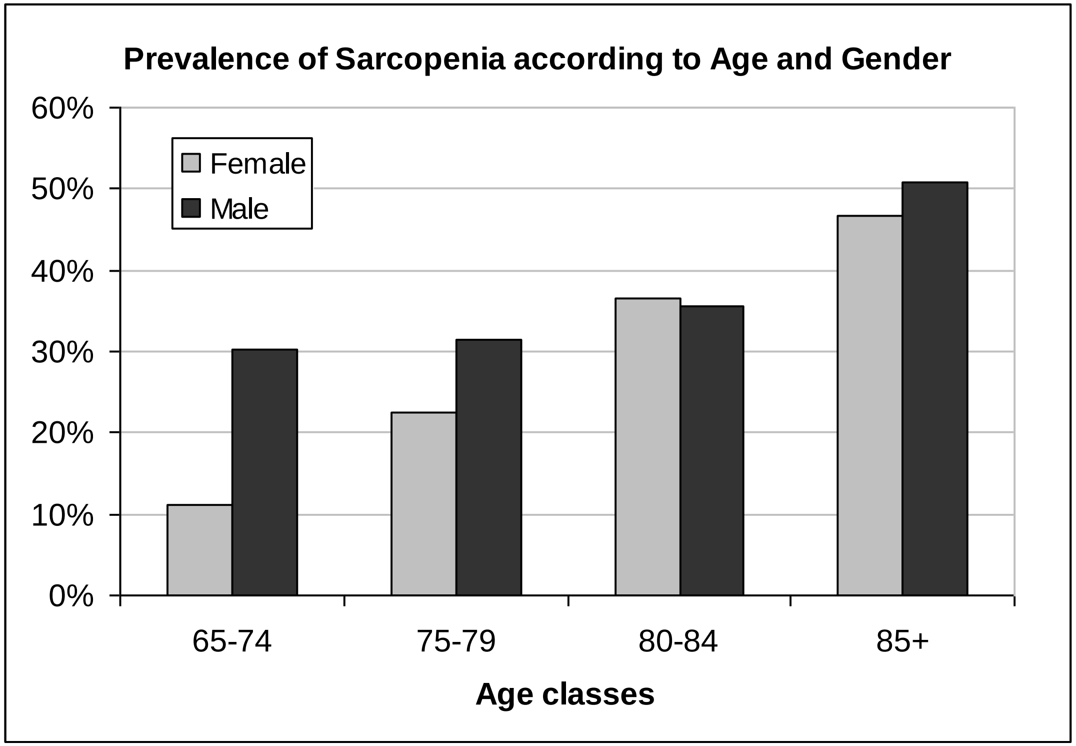
Prevalence of Sarcopenia and pre-sarcopenia: EWGSOP definition, InCHIANTI Study



Volpato S et al. JGMS 2014;69:438-46

Gruppo Lavoro Italiano Sarcopenia – Trattamento e Nutrizione

EWGSOP definition



Diagnostic criteria for Cachexia in adults

1. Weight loss ≤5% in 12 months in the presence of underlying illness (or BMI <20)

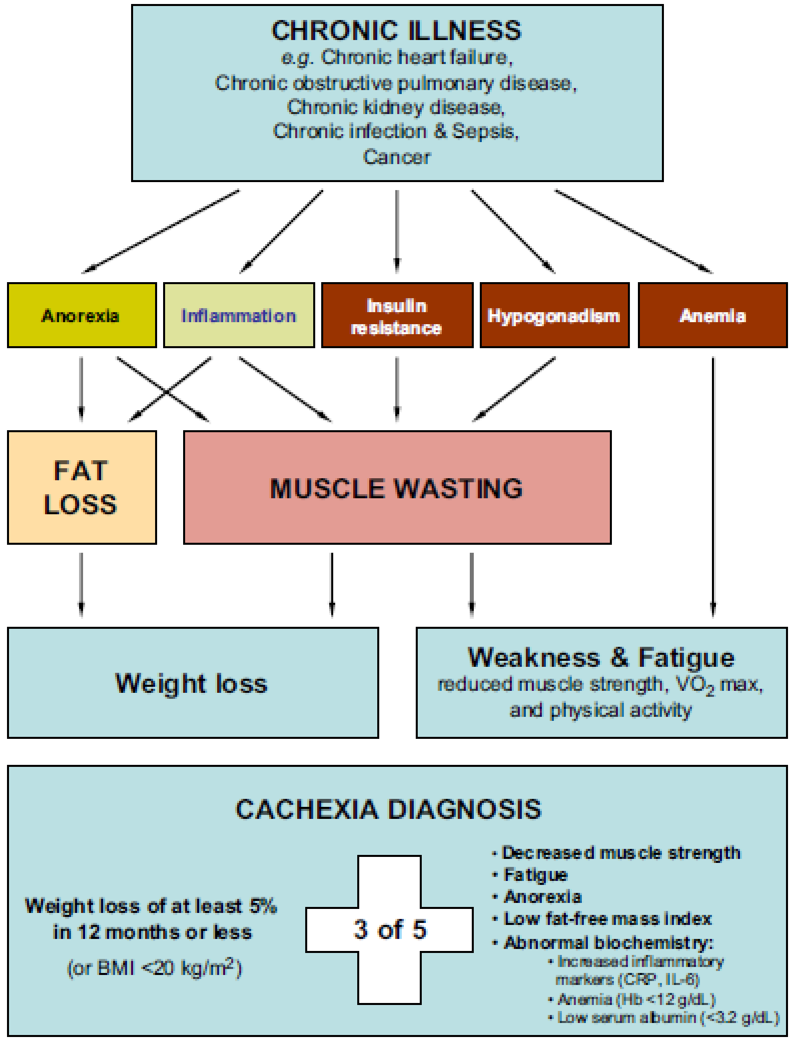
+

3 (any 3 of the following):

a) Decrease muscle strength
b) Fatigue
c) Anorexia
d) Low fat-free mass index
e) Abnormal biochemistry
   - Increased inflammatory markers (PCR> 5mg/l)
   - Anemia
   - Low albumin (<3.2 g/dl)

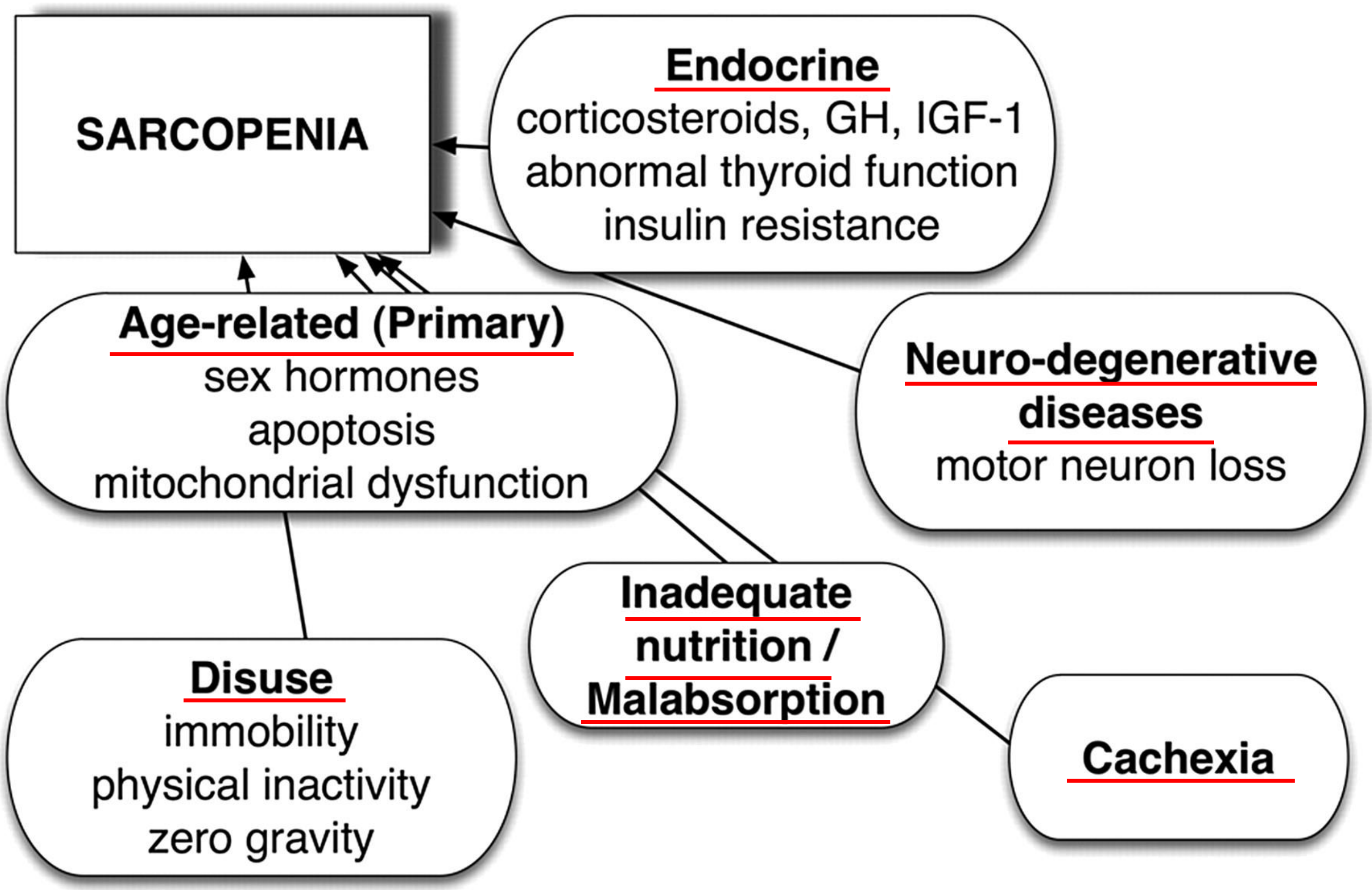
Evans WJ, et al. Clin Nutr 2008; 27:793–9

Conceptual representation of the chachexia definition



Evans WJ, et al. Clin Nutr 2008; 27:793–9.

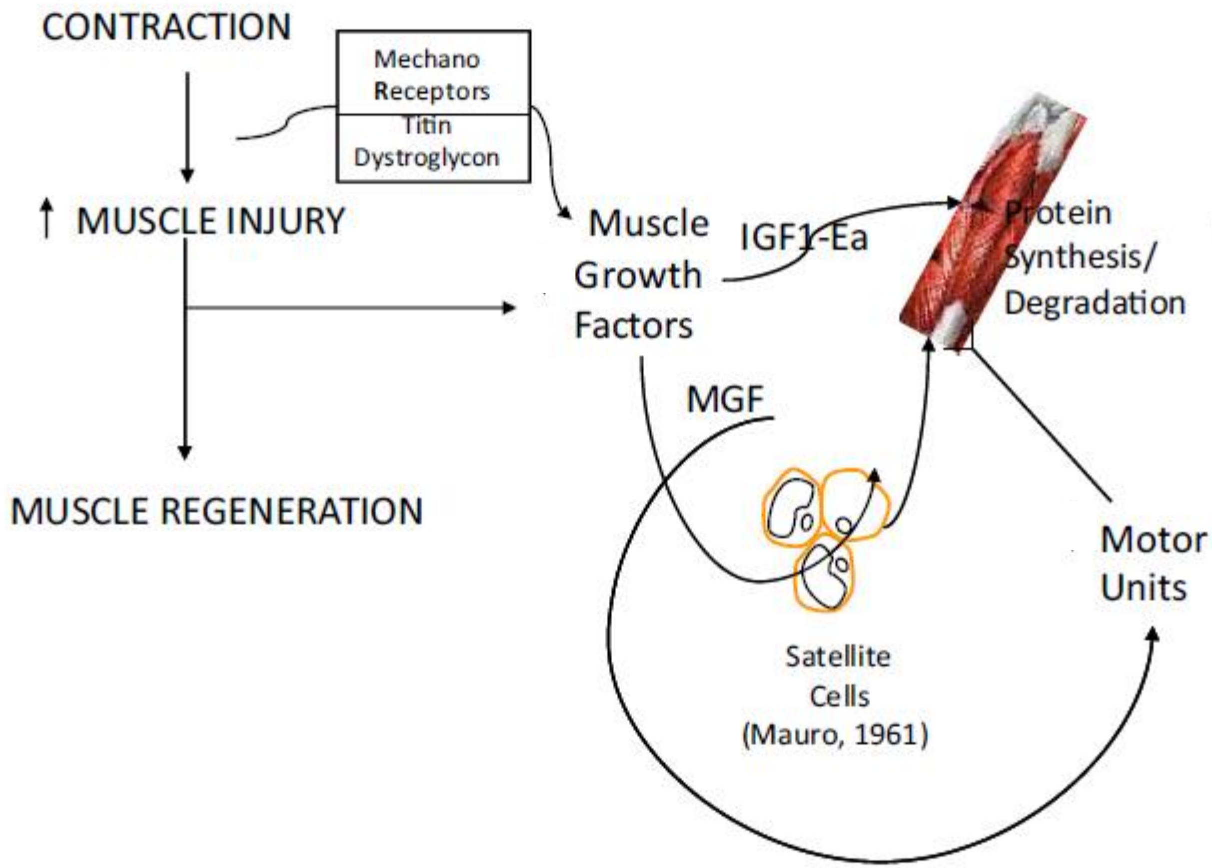
Mechanisms of sarcopenia



Cruz-Jentoft A J et al. Age Ageing 2010;39:412-423

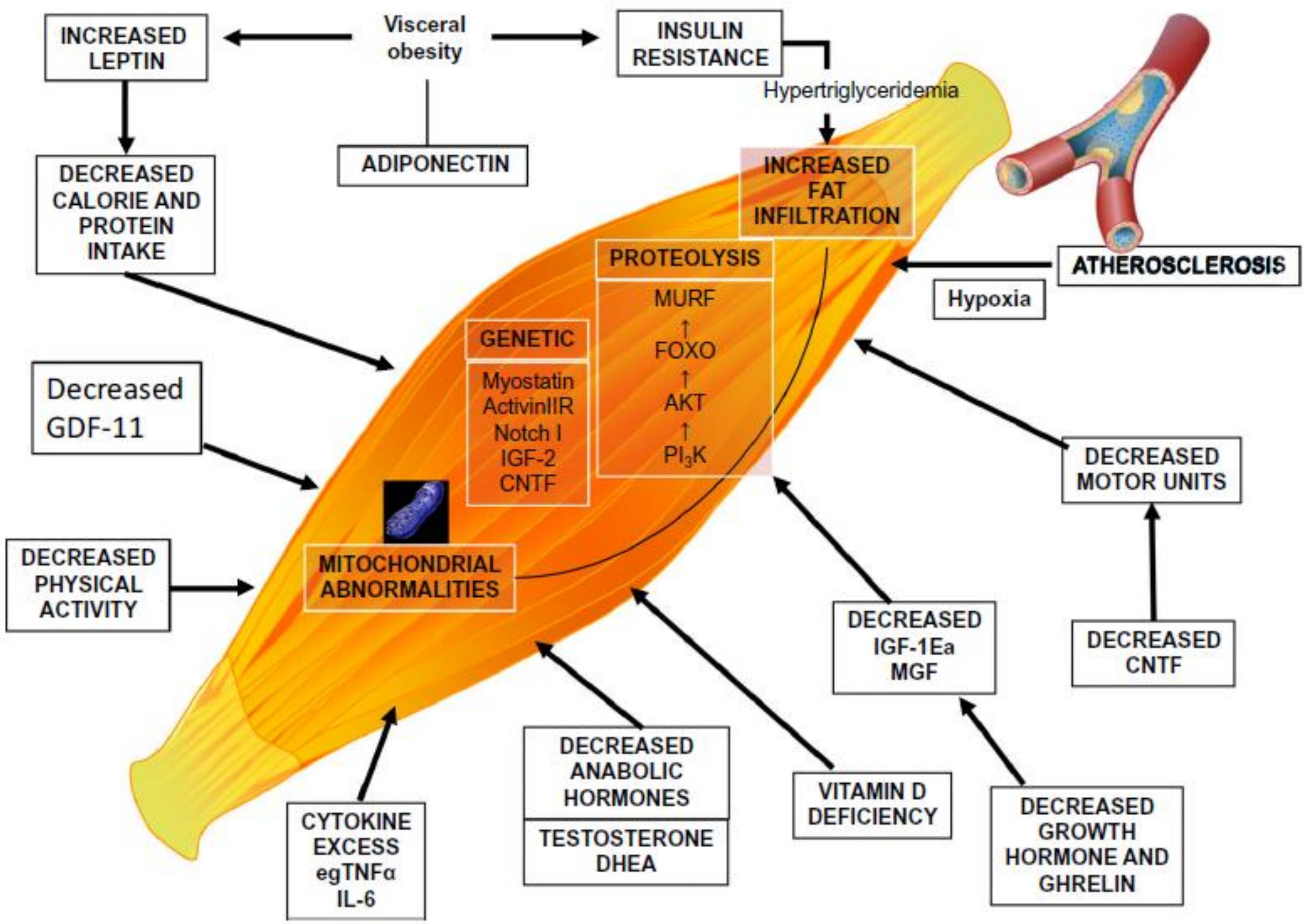
The Pathophysiology of Sarcopenia

Age-realted increased muscle injury with a decrease in muscle regeneration and function



Morley JE. Calcif Tissue Int. 2016; 98:319–333

The Pathophysiology of Sarcopenia



Morley JE. Calcif Tissue Int. 2016; 98:319–333

Current and future options for the prevention and treatment of sarcopenia

Modality	Effect	Side effects
Resistance exercise	Increase muscle mass, strength, and power	Potential for falls; muscle injuries
Protein (essential amino acids)	Increase muscle mass; synergy with exercise to increase muscle strength and power	Minimal increased creatinine levels

Resistance and aerobic exercise

- Resistance exercise improved strength and decreased frailty in very old persons. Fiatarone et al, N Engl J Med 1994; Fiatarone et al, JAMA 1990; Marini et al, Ital J Anat Embryol 2008; Morganti et al, 1995; Stasser B et al, Wien Klin Wochenschr 2009.
  - These effects can be maintained for at least 1 year. Capodaglio et al, Age Ageing 2005; Capodaglio et al, Eur J Appl Physiol 2007.
  - Strength training improved distance walked in 6 minutes and gait speed. Morley, JAMDA 2010.
  - Resistance exercise increases type II muscle fiber size and improves satellite muscle recruitment in older persons. Harber et al, Am J Physiol Regul Integr Comp Physiol 2009; Snijders et al, Ageing Res Rev 2009.
- Aerobic exercise remodels myofibers and increases muscle strength. van Swearingen et al, J Gerontol A Biol Sci Med Sci 2009.
  - In older persons, aerobic exercise improves gait speed, quality of life years (QALY), and is cost effective. Bulthius et al, Arthritis Rheum 2008; Baker et al, Age Ageing 2007; Mian et al, Eur J Appl Physiol 2007.

Effect of Structured Physical Activity on Prevention of Major Mobility Disability in Older Adults: The LIFE Study Randomized Clinical Trial

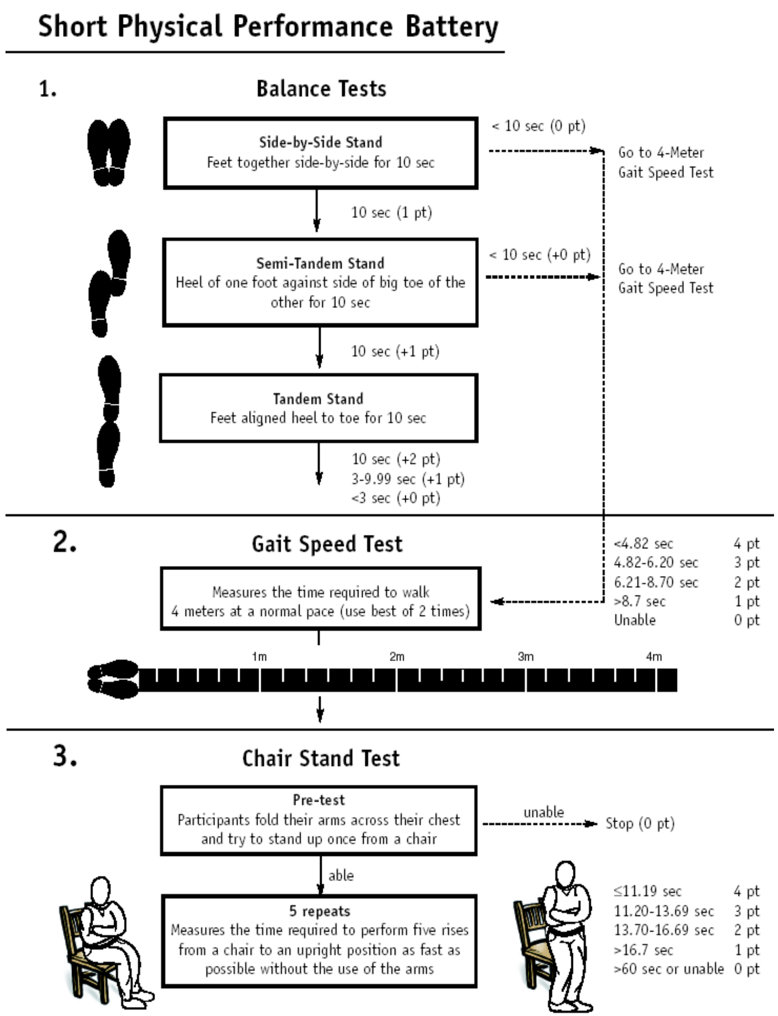


Table 1. Baseline Characteristics of the Participants

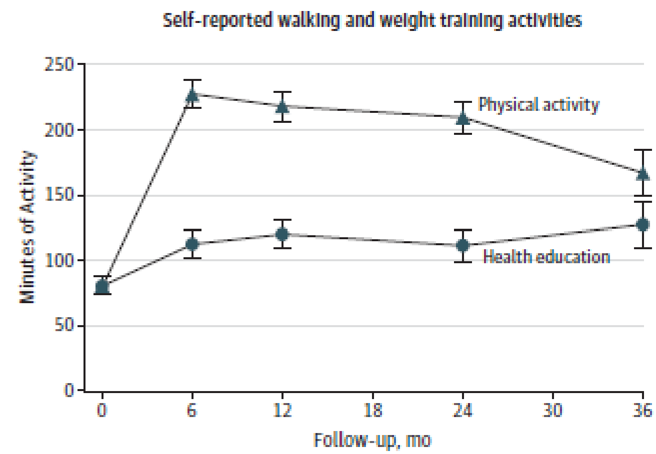
Characteristic	No. (%)[a] Physical Activity (n = 818)	Health Education (n = 817)
Age, mean (SD), y	78.7 (5.2)	79.1 (5.2)
Women	547 (66.9)	551 (67.4)
Ethnicity/race		
Hispanic	31 (3.8)	30 (3.7)
White	604 (73.8)	635 (77.7)
African American	163 (19.9)	125 (15.3)
SPPB score		
Mean (SD)	7.4 (1.6)	7.3 (1.6)
<8	353 (43.3)	378 (46.2)
400-m walking speed, mean (SD), m/s	0.83 (0.17)	0.82 (0.17)
BMI, mean (SD)	30.1 (5.7)	30.3 (6.2)
Walking/weight training activities, mean (SD), min/wk[b]	75.1 (125.6)	86.7 (134.5)
Median (IQR)	0 (0-105)	30 (0-105)
Accelerometry of moderate physical activity, mean (SD), min/wk[c]	193.7 (155.3)	202.1 (186.5)
Median (IQR)	161 (80-257) (n = 590)	153 (85-266) (n = 581)
3MSE score, 0-100 scale, mean (SD)	91.5 (5.5)	91.6 (5.3)
Conditions, No./total (%)		
Hypertension[b]	573/813 (70.5)	578/808 (71.5)
Diabetes[b]	199/815 (24.4)	216/813 (26.6)
Myocardial infarction[b]	60/815 (7.4)	69/812 (8.5)
Stroke[b]	57/814 (7.0)	52/814 (6.4)
Cancer[b]	178/814 (21.9)	192/815 (23.6)
Chronic pulmonary disease[b]	130/815 (16.0)	123/812 (15.2)

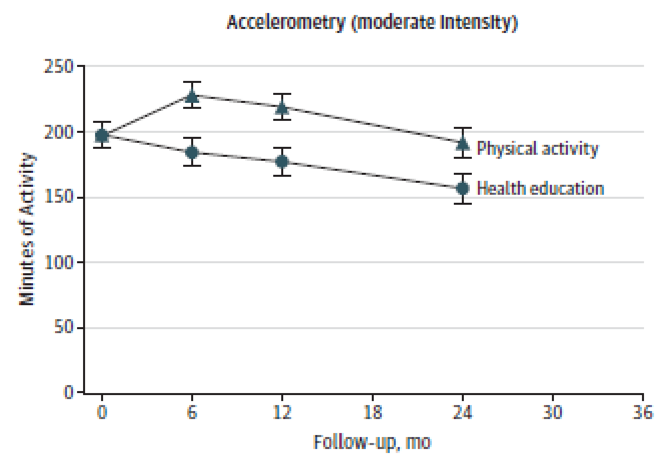
Pahor M. et al JAMA. 2014;doi:10.1001/jama.2014.5616

Effect of Structured Physical Activity on Prevention of Major Mobility Disability in Older Adults: The LIFE Study Randomized Clinical Trial

Table 3. Physical Activity Intervention Schedule

Phase	Center-Based Physical Activity
Adoption: Weeks 1–52	Two times each week; progressing to 40 min walking, 10 min strength training, 10 min balance
Maintenance: Weeks 53 to enc	Two times each week; progressing to 40 min walking, 10 min strength training, 10 min balance
Phase	**Home-Based Physical Activity**
Adoption: Weeks 1–52	One time per week (weeks 1–4); two times per week (weeks 4–8); up to three to four times per week (weeks 8–52)
Maintenance: Weeks 53 to end	Up to three to four times per week





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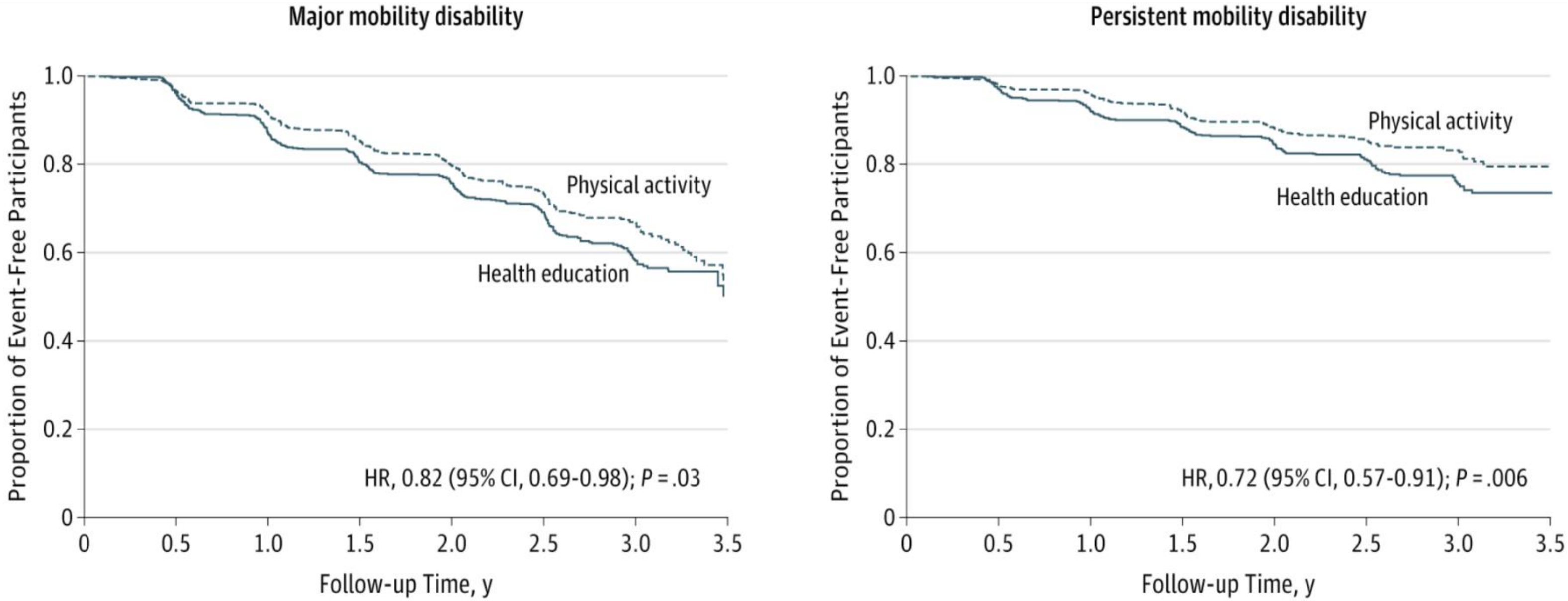
Effect of Structured Physical Activity on Prevention of Major Mobility Disability in Older Adults: The LIFE Study Randomized Clinical Trial

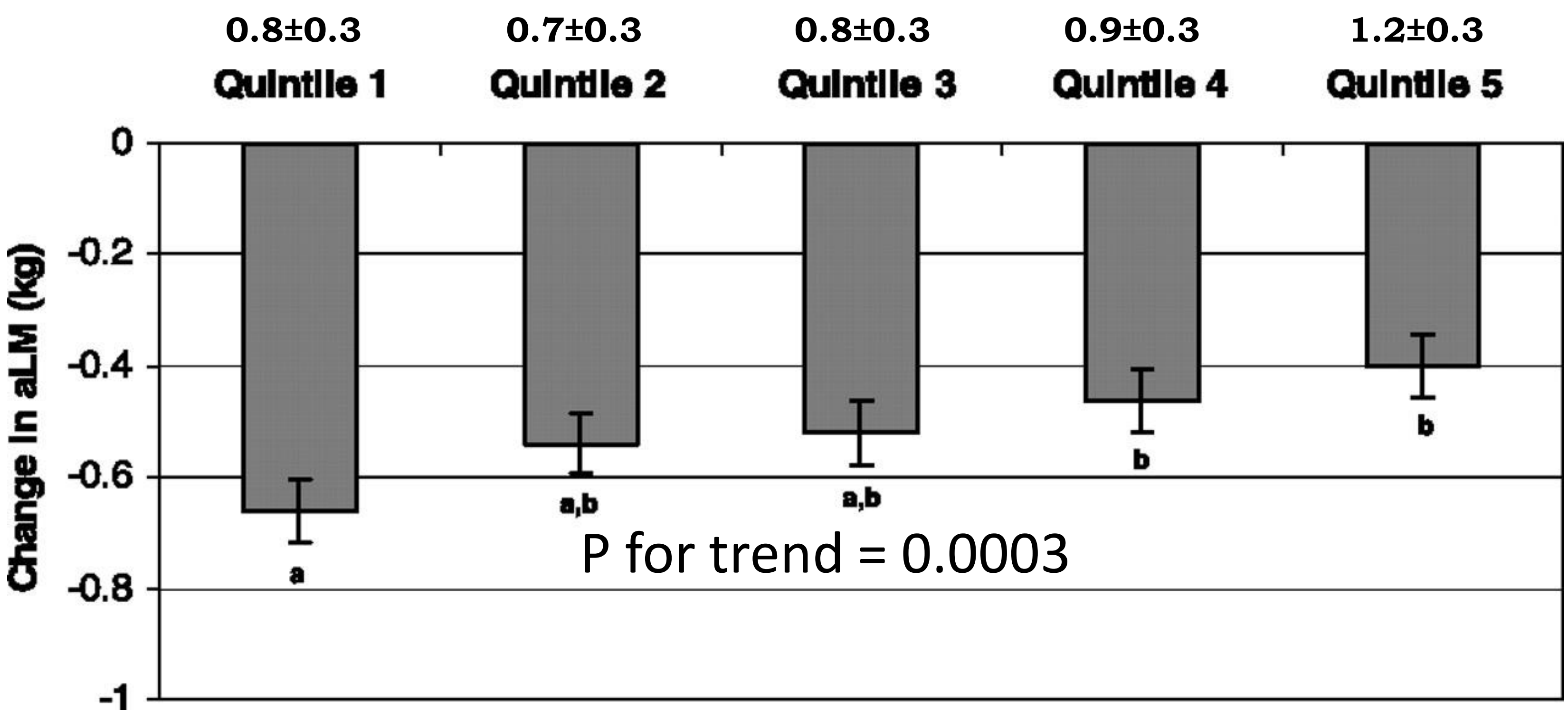


	Major mobility disability								Persistent mobility disability							
Follow-up Time, y	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5
No. at risk																
Physical activity	818	758	706	646	559	378	182	11	818	761	726	673	579	393	188	12
Health education	817	765	680	617	540	358	162	13	817	762	707	655	567	371	178	10
Events																
Physical activity	0	29	67	115	155	197	224	246	0	18	32	64	88	104	113	120
Health education	0	33	105	155	190	232	277	286	0	25	64	91	118	138	158	162

Pahor M. et al JAMA. 2014;doi:10.1001/jama.2014.5616

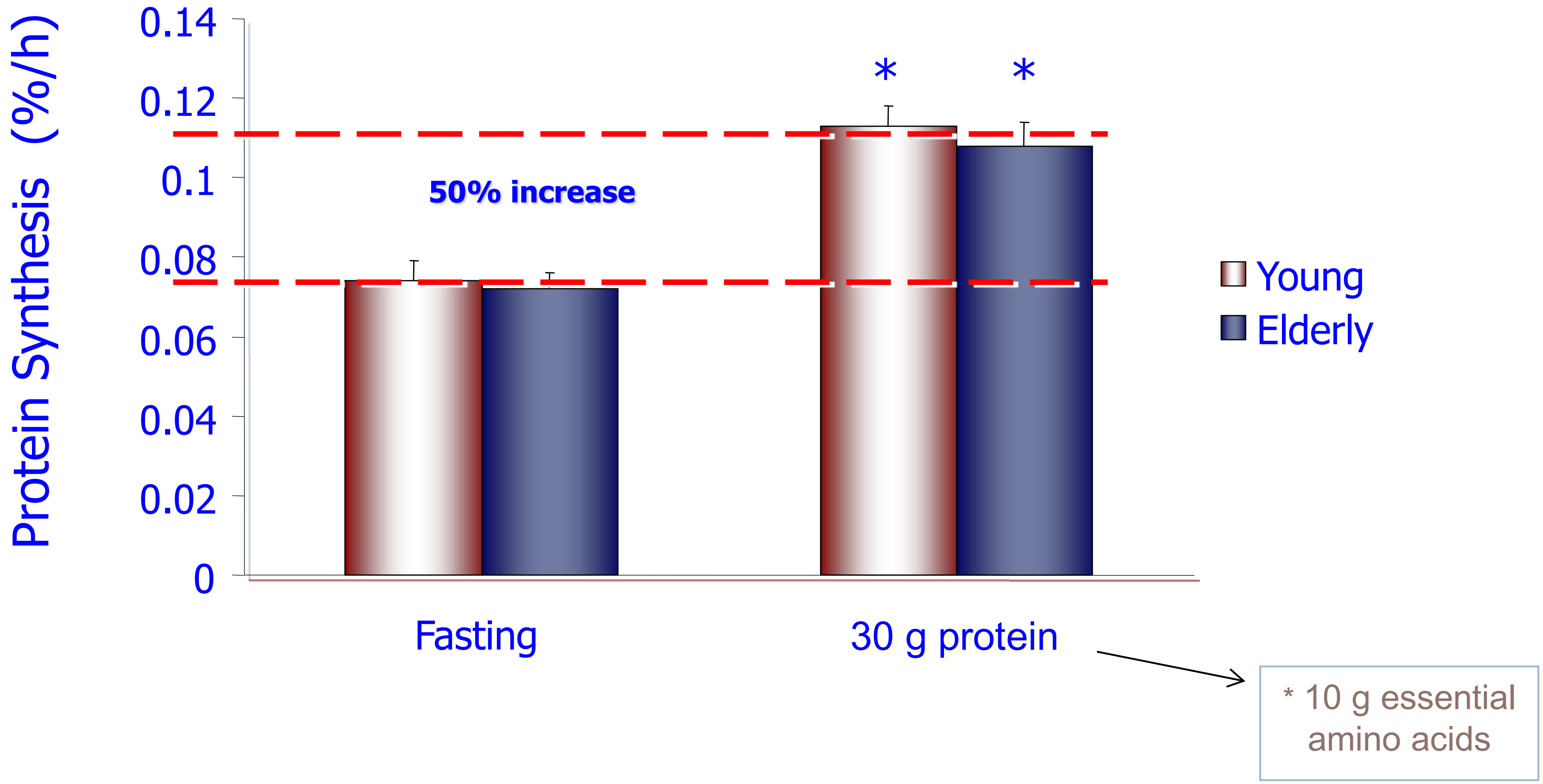
Dietary protein intake is associated with lean mass change in older adults (HABC Study)

Energy-adjusted total protein intake



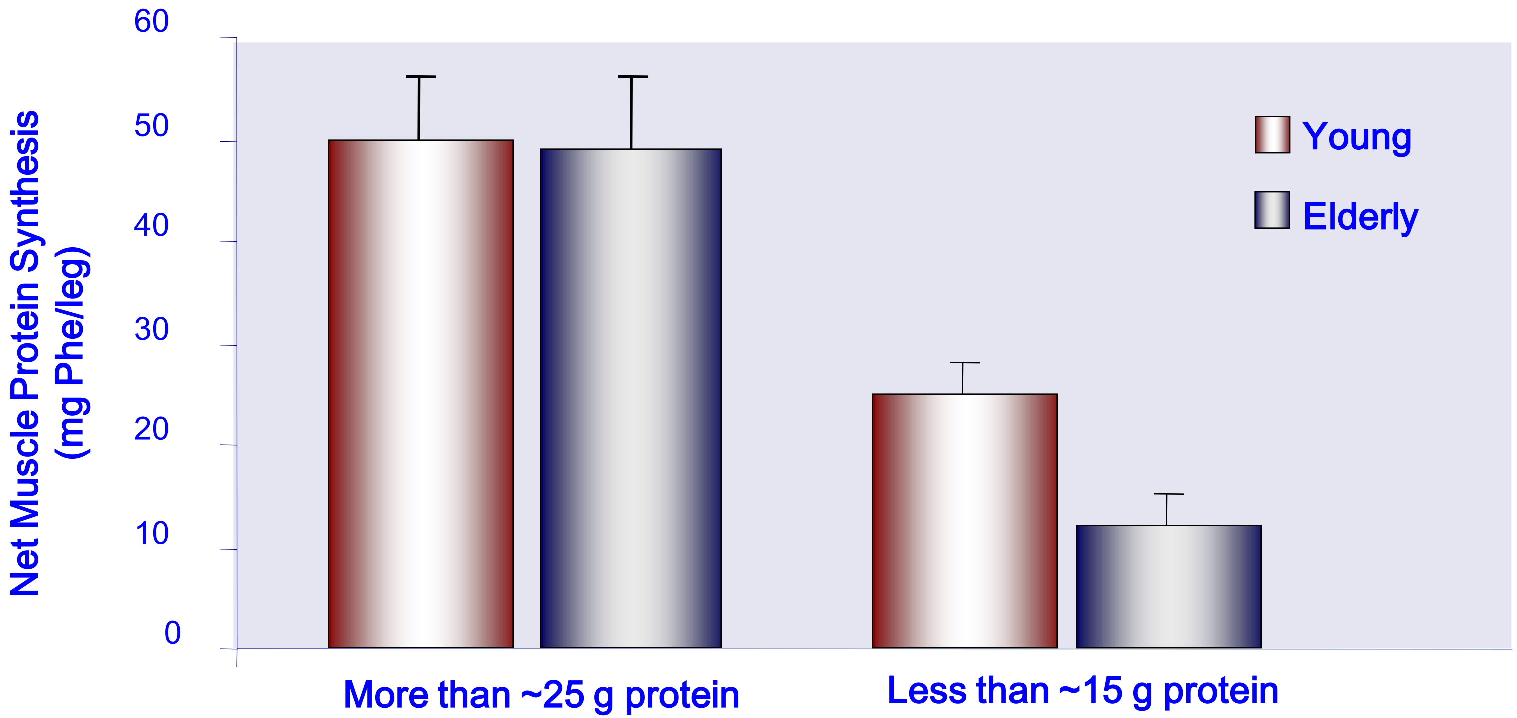
Houston D K et al. Am J Clin Nutr 2008;87:150-155

Ageing and muscle protein synthesis in response to protein intake



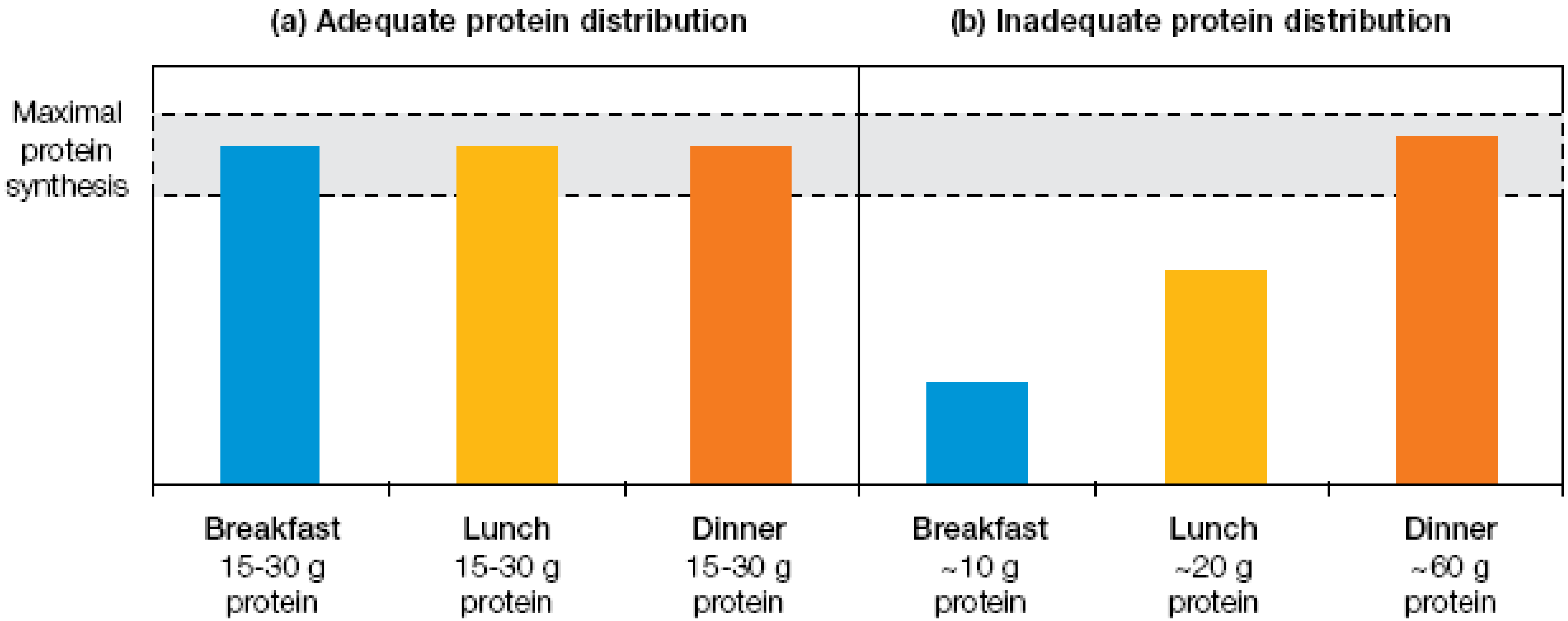
Symons et. al. AJCN, 2007

Ageing and muscle protein synthesis in response to protein intake



Katsanos et. al. AJCN, 2005

Protein intake distribution and protein synthesis

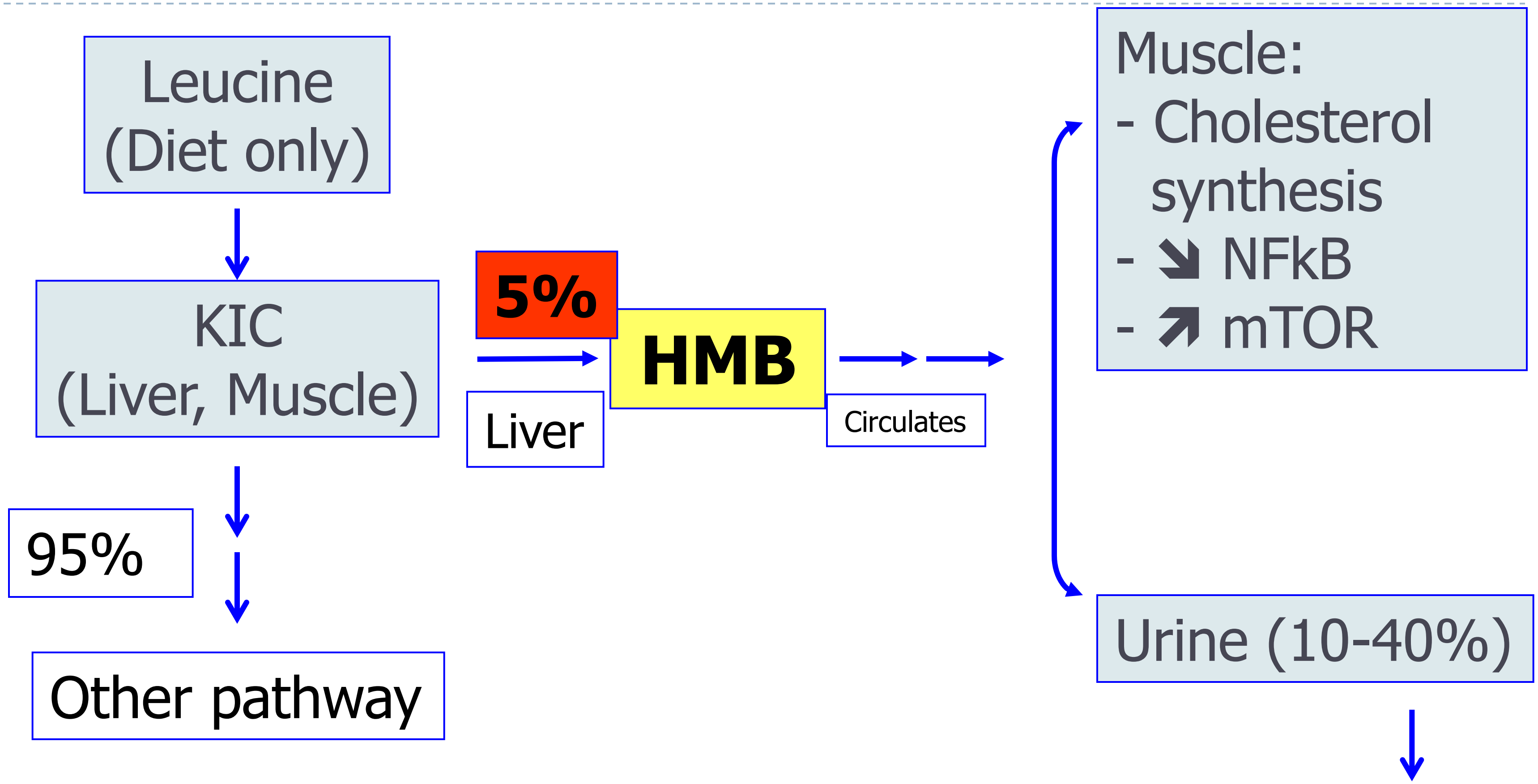


Adapted from Paddon-Jones, 2009

Options to optimize post-prandial anabolic action of dietary proteins

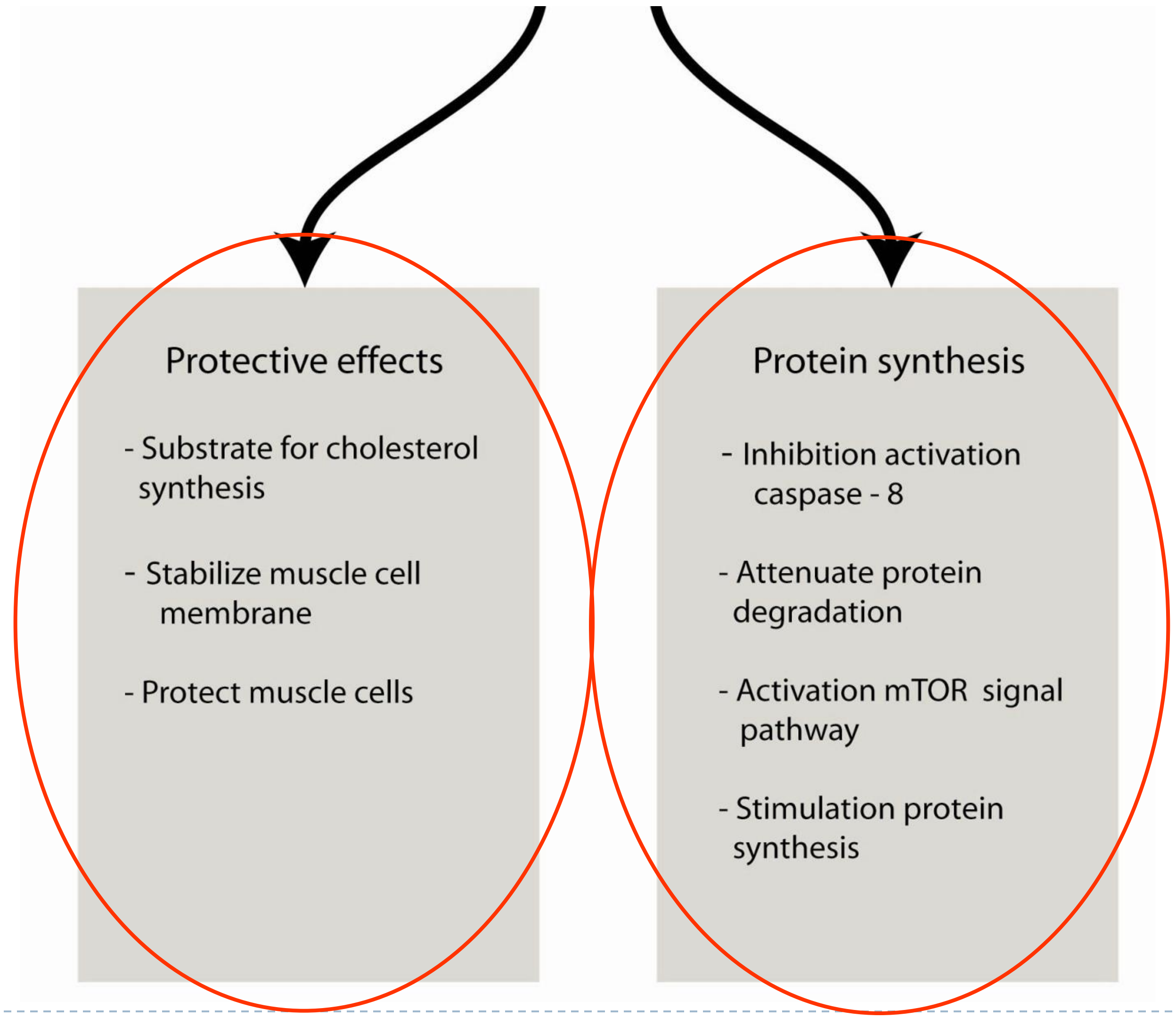
- Increase protein intake
  - Age-specific RDAs
- Increase amino acid bioavailability
  - Distribution of protein intake
  - Digestion rate
- Use specific substrates
  - Leucine
  - **ß-hydroxy-ß-methylbutyrate (HMB)**

Leucine-ß-hydroxy-ß-methylbutyrate Metabolic Pathway



The is an amino acid metabolite that occurs naturally in human muscle cells. Traditionally, HMB has been used by athletes to enhance performance and build muscle mass. Recent studies have focused on the use of HMB to preserve or rebuild muscle mass.

Role of HMB on muscle function



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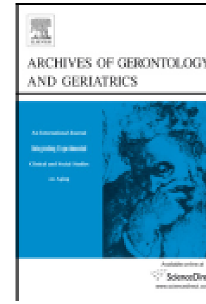


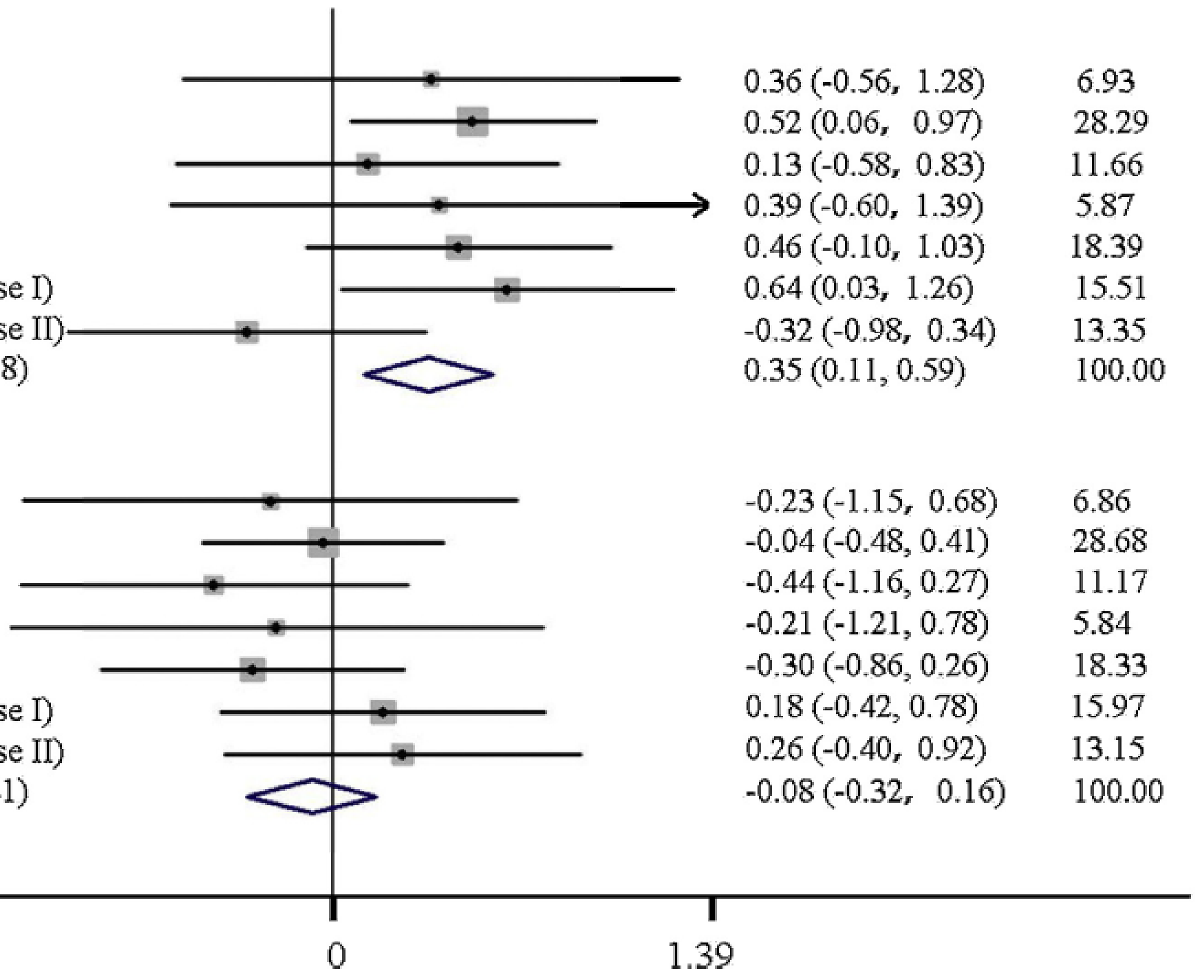
Effect of beta-hydroxy-beta-methylbutyrate supplementation on muscle loss in older adults: A systematic review and meta-analysis

CrossMark

Hongmei Wu, Yang Xia, Jin Jiang, Huanmin Du, Xiaoyan Guo, Xing Liu, Chunlei Li, Guowei Huang, Kaijun Niu*

Nutritional Epidemiology Institute and School of Public Health, Tianjin Medical University, Tianjin, China

Effect of HMB supplementation on muscle and fat mass



Author	SMD (95% CI)	Weight (%)
Muscle mass		
Deutz, N. E. et al 2013	0.36 (-0.56, 1.28)	6.93
Baier, S. et al 2009	0.52 (0.06, 0.97)	28.29
Vukovich, M. D. et al 2001	0.13 (-0.58, 0.83)	11.66
May, P. E. et al 2002	0.39 (-0.60, 1.39)	5.87
Flakoll, P. et al 2004	0.46 (-0.10, 1.03)	18.39
Stout, J. R. et al 2013 (phase I)	0.64 (0.03, 1.26)	15.51
Stout, J. R. et al 2013 (phase II)	-0.32 (-0.98, 0.34)	13.35
Overall ($I^2 = 0.0\%$, P = 0.438)	0.35 (0.11, 0.59)	100.00
Fat mass		
Deutz, N. E. et al 2013	-0.23 (-1.15, 0.68)	6.86
Baier, S. et al 2009	-0.04 (-0.48, 0.41)	28.68
Vukovich, M. D. et al 2001	-0.44 (-1.16, 0.27)	11.17
May, P. E. et al 2002	-0.21 (-1.21, 0.78)	5.84
Flakoll, P. et al 2004	-0.30 (-0.86, 0.26)	18.33
Stout, J. R. et al 2013 (phase I)	0.18 (-0.42, 0.78)	15.97
Stout, J. R. et al 2013 (phase II)	0.26 (-0.40, 0.92)	13.15
Overall ($I^2 = 0.0\%$, P = 0.741)	-0.08 (-0.32, 0.16)	100.00

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Randomized control trials

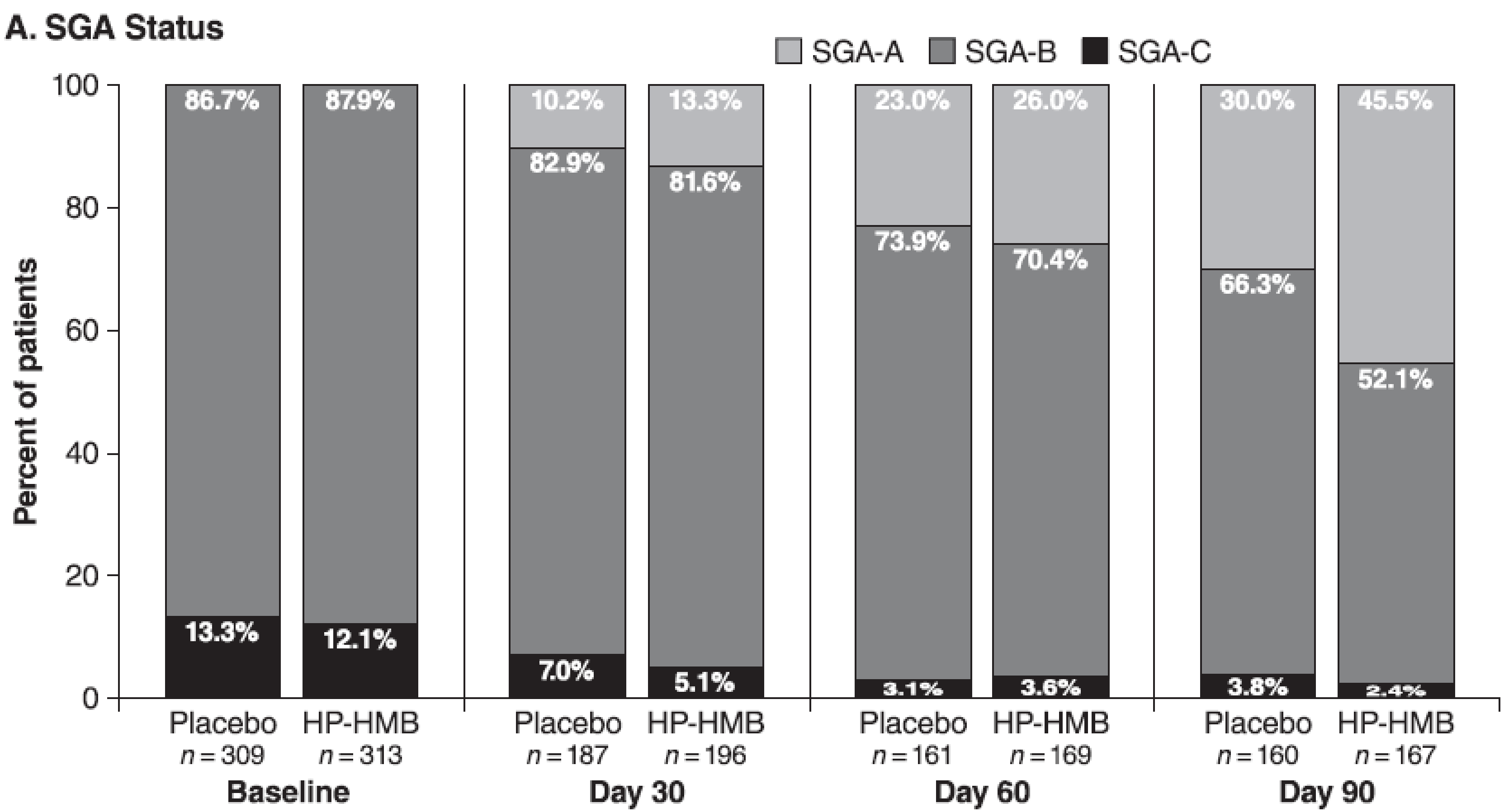
Readmission and mortality in malnourished, older, hospitalized adults treated with a specialized oral nutritional supplement: A randomized clinical trial

Nicolaas E. Deutz [a, *], Eric M. Matheson [b], Laura E. Matarese [c], Menghua Luo [d], Geraldine E. Baggs [d], Jeffrey L. Nelson [d], Refaat A. Hegazi [d], Kelly A. Tappenden [e], Thomas R. Ziegler [f], on behalf of the NOURISH Study Group

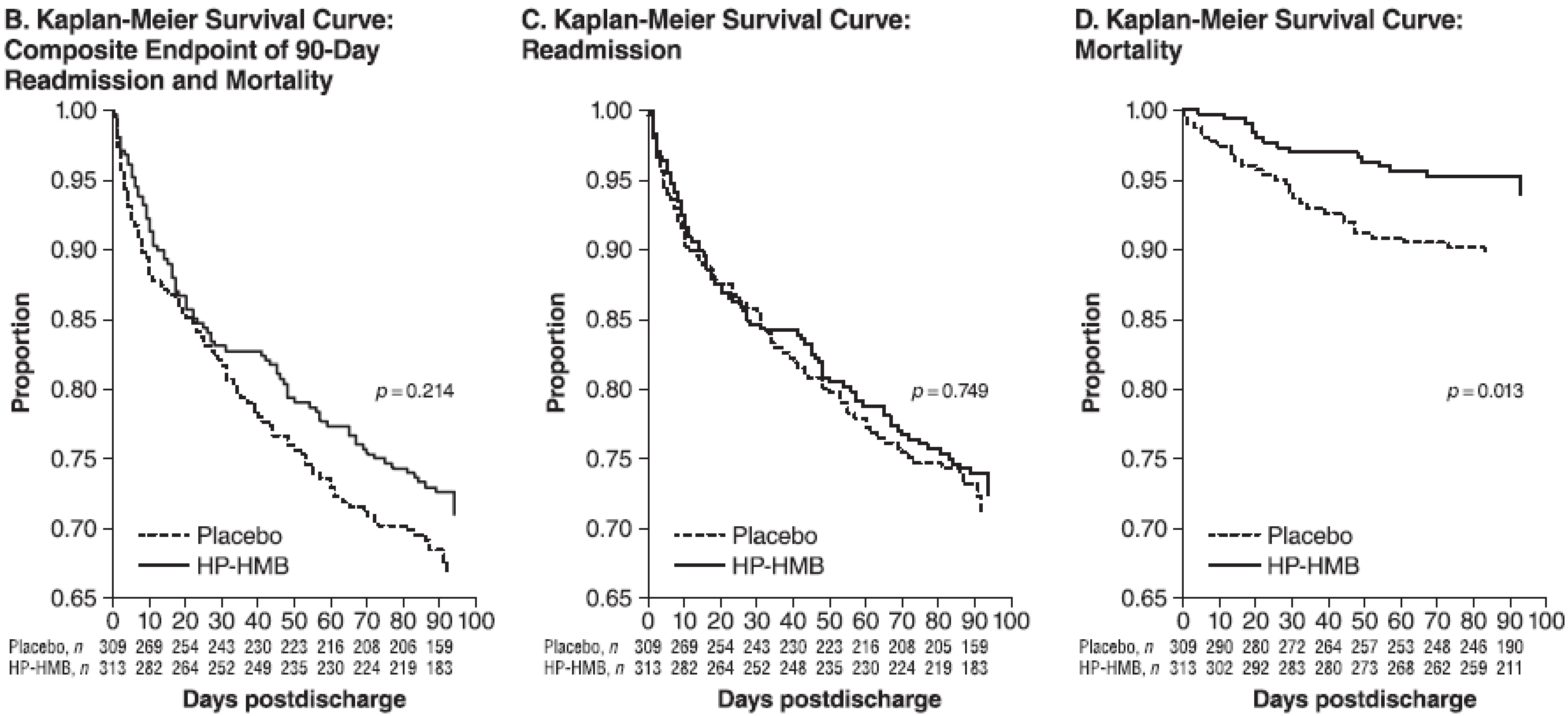
HP-HMB was a specialized, nutrient-dense ready-to-drink liquid with 350 kcal plus:

- ✓ 20 g protein,
- ✓ 11 g fat,
- ✓ 44 g carbohydrate,
- ✓ 1.5 g calcium-HMB,
- ✓ 160 IU vitamin D and other essential micronutrients

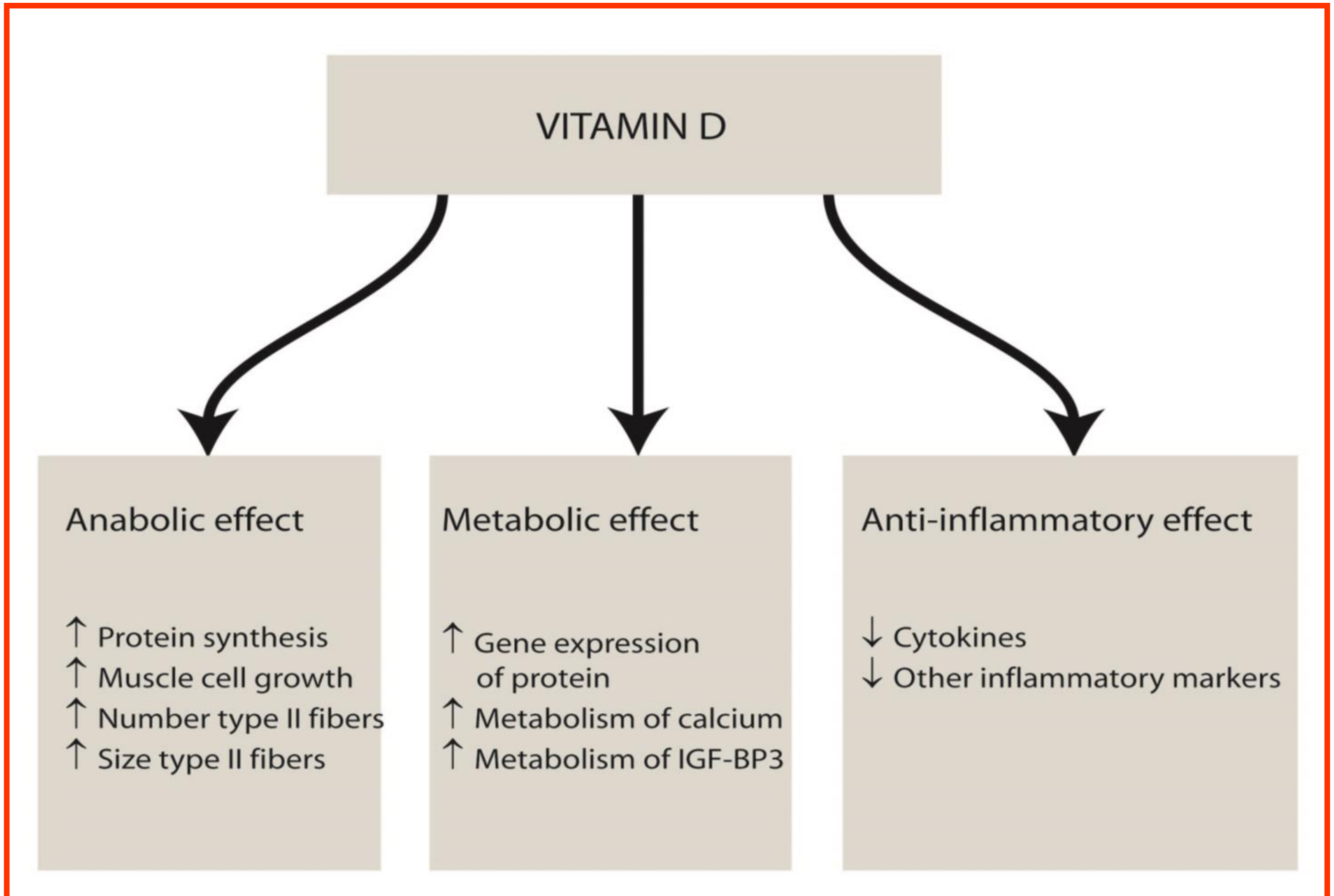
HP-HMB and Nutritional (SGA) status



Effect on hospital readmission and mortality



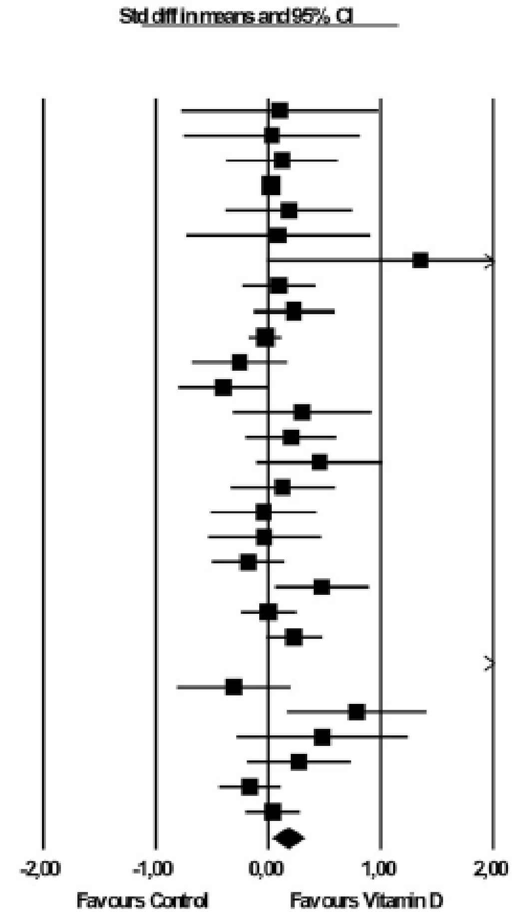
Role of Vitamin D on muscle function



The Effects of Vitamin D on Skeletal Muscle Strength, Muscle Mass, and Muscle Power: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Effect of vitamin D supplementation on global muscle strength

Study name	Std diff in means	Lower limit	Upper limit	p-Value
Barker et al. 2012	0,099	-0,778	0,976	0,824
Binder E. 1995	0,030	-0,759	0,820	0,940
Bischoff et al. 2003	0,123	-0,376	0,622	0,629
Brunner et al. 2008	0,026	-0,055	0,107	0,526
Bunout et al. 2006	0,183	-0,384	0,750	0,527
Carrillo et al. 2012	0,087	-0,738	0,911	0,837
Close et al. 2012	1,353	-0,021	2,727	0,054
Dhesi et al. 2004	0,093	-0,240	0,425	0,585
El-Hajj Fuleihan et al. 2006	0,226	-0,138	0,589	0,224
Glendenning et al. 2012	-0,028	-0,178	0,122	0,715
Goswami et al. 2012	-0,257	-0,682	0,167	0,235
Grady et al.	-0,403	-0,803	-0,003	0,048
Gupta et al. 2010	0,300	-0,324	0,923	0,346
Hara et al. 2013	0,203	-0,203	0,609	0,328
Hornickx et al. 2012	0,455	-0,113	1,022	0,116
Janssen et al. 2010	0,126	-0,343	0,595	0,599
Kampman et al. 2012	-0,042	-0,518	0,434	0,863
Kenny et al. 2003	-0,038	-0,544	0,469	0,884
Knutsen et al. 2014	-0,179	-0,504	0,146	0,280
Kukuljan et al. 2009	0,476	0,055	0,897	0,027
Latham et al. 2003	0,000	-0,251	0,251	1,000
Pfeifer et al. 2009	0,228	-0,025	0,480	0,078
Sato et al. 2005	2,741	2,183	3,298	0,000
Smedshaug et al. 2007	-0,308	-0,818	0,202	0,237
Songpatanasilp et al. 2009	0,786	0,158	1,414	0,014
Verhaar et al. 2000	0,481	-0,285	1,246	0,218
Ward et al. 2010	0,273	-0,191	0,737	0,249
Wood et al. 2014	-0,166	-0,446	0,115	0,248
Zhu et al. 2010	0,038	-0,205	0,281	0,759
	0,170	0,031	0,310	0,017



(A) Heterogeneity : Q-value 125.37 ; Df(Q) 28 ; p-value 0.001; I^2 : 77.67

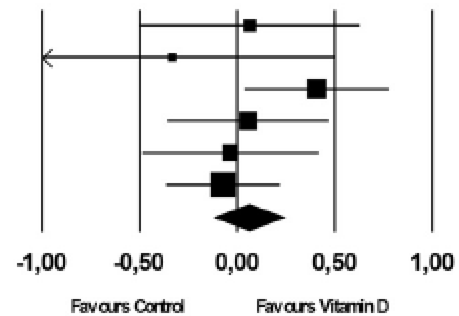
Beaudart et al. JECM 2014;99:4336-45

The Effects of Vitamin D on Skeletal Muscle Strength, Muscle Mass, and Muscle Power: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Effect of vitamin D supplementation on muscle mass

Study name	Std diff in means	Lower limit	Upper limit	p-Value
Bunout et al. 2006	0,064	-0,502	0,629	0,826
Carrillo et al. 2013	-0,333	-1,163	0,497	0,431
El-Hajj Fuleihan et al. 2005	0,408	0,035	0,781	0,032
Kukuljan et al. 2009	0,055	-0,361	0,471	0,796
Manios et al. 2009	-0,034	-0,487	0,419	0,882
Wood et al. 2014	-0,073	-0,366	0,220	0,624
	0,058	-0,118	0,233	0,520

Std diff in means and 95% CI

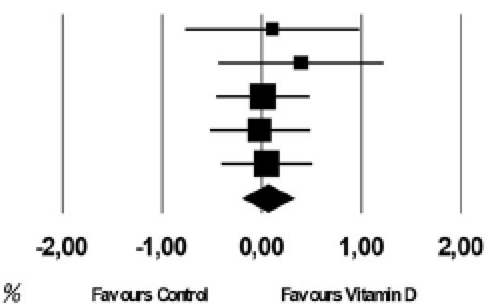


(B) Heterogeneity : Q-value 5.17 ; Df(Q) 5 ; p-value 0.39; I^2 : 3.34

Effect of Vitamin D supplementation on muscle power

Study name	Std diff in means	Lower limit	Upper limit	p-Value
Barker et al. 2012	0,105	-0,772	0,982	0,814
Carrillio et al. 2013	0,392	-0,441	1,224	0,356
Janssen et al. 2009	0,010	-0,459	0,479	0,967
Kenny et al. 2003	-0,020	-0,527	0,486	0,938
Ward et al. 2010	0,050	-0,412	0,512	0,832
	0,057	-0,194	0,308	0,657

Std diff in means and 95% CI



(C) Heterogeneity : Q-value 0.76 ; Df(Q) 4 ; p-value 0.94; I^2 : 0.00 %

Beaudart et al. JECM 2014;99:4336-45

Effects of a Vitamin D and Leucine-Enriched Whey Protein Nutritional Supplement on Measures of Sarcopenia in Older Adults, the PROVIDE Study: A Randomized, Double-Blind, Placebo-Controlled Trial

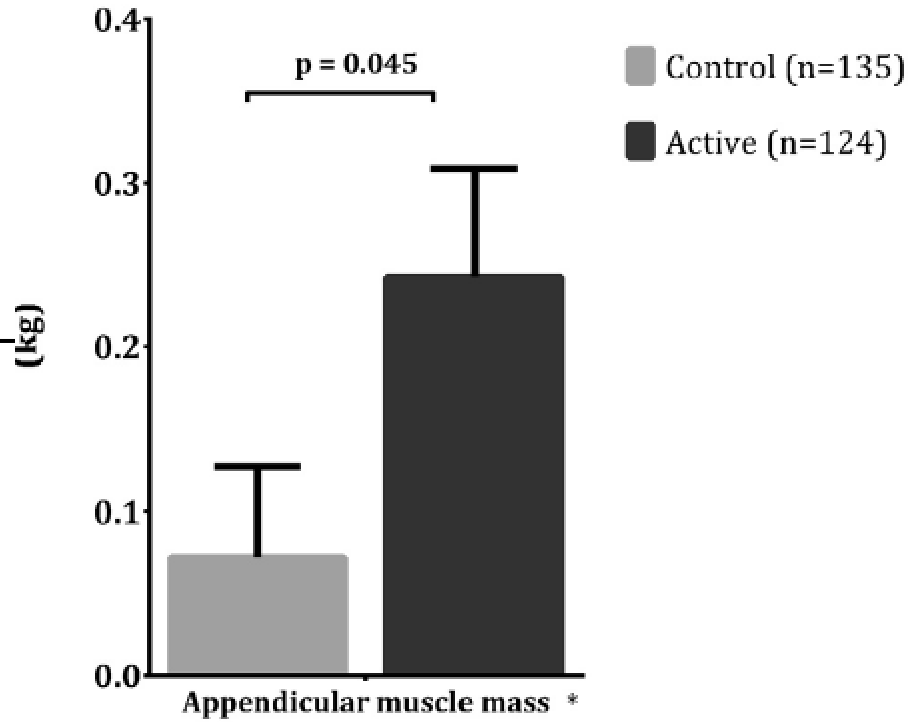
Design: A multicenter, randomized, controlled, double-blind, 2 parallel-group trial among 380 sarcopenic primarily independent-living older adults with Short Physical Performance Battery (SPPB; 0–12) scores between 4 and 9, and a low skeletal muscle mass index. The active group (n = 184) received a vitamin D and leucine-enriched whey protein nutritional supplement to consume twice daily for 13 weeks. The control group (n = 196) received an iso-caloric control product to consume twice daily for 13 weeks.

Primary outcomes of handgrip strength and SPPB score, and secondary outcomes of chair-stand test, gait speed, balance score, and appendicular muscle mass (by DXA) were measured at baseline, week 7, and week 13 of the intervention.

Bauer JM, JAMDA 2015;16: 740-747

Effects of a Vitamin D and Leucine-Enriched Whey Protein Nutritional Supplement on Measures of Sarcopenia in Older Adults, the PROVIDE Study: A Randomized, Double-Blind, Placebo-Controlled Trial

	Mean (SD)	Change From Baseline, Mean (SD)		Estimated Between-Group DifferenceMean (95% CI)Active − Control	P*
	Baseline	Week 7	Week 13		
Handgrip strength, kg					
Active[†]	20.9 (7.9)	0.20 (3.2)	0.79 (3.6)[‡]	0.30[§] (−0.46–1.05)	.44
Control[‖]	20.6 (7.5)	0.34 (2.8)	0.54 (3.2)		
SPPB					
Active[¶]	7.5 (1.9)	0.50 (1.26)	0.86 (1.38)[**]	0.11[§] (−0.21–0.42)	.51
Control[††]	7.5 (2.0)				
Chair-stand time, s[‡‡]					
Active[§§]	17.1 (15.2, 21.2)			o −0.19)	.018
Control[‖‖]	17.6 (14.6, 20.6)				
Balance test[¶¶]					
Active[¶]	3.0 (2.0, 4.0)				.89
Control[††]	3.0 (2.0, 4.0)				
Gait speed, m/s					
Active[¶]	0.8 (0.2)			0.04)	.46
Control[***]	0.8 (0.2)				



Bauer JM, JAMDA 2015;16: 740-747

Current and future options for the prevention and treatment of sarcopenia

Modality	Effect	Side effects
Resistance exercise	Increase muscle mass, strength, and power	Potential for falls; muscle injuries
Protein (essential amino acids)	Increase muscle mass; synergy with exercise to increase muscle strength and power	Minimal increased creatinine levels
Testosterone	Increase muscle mass, strength, power, and function	Fluid retention; increased hematocrit; short term worsening of sleep apnea; effects on prostate cancer; possible increase in cardiovascular events
Selective androgen receptor modulators (SARMS)	Increase muscle mass; small increase in power	Increased cardiac failure
Growth hormone	Increase nitrogen retention; increase muscle mass	Arthralgia; muscle pain; edema; carpal tunnel syndrome; hyperglycemia
Ghrelin agonists	Increased muscle mass and appetite	Fatigue; atrial fibrillation; dyspnea
Myostatin antibodies	Increased lean body mass and handgrip	Urticaria; aseptic meningitis; diarrhea; confusion; fatigue
Activin 11R antagonists	Increase thigh muscle volume, muscle mass, and 6-min walk distance	Acne; involuntary muscle contractions
Angiotensin converting enzyme inhibitor (perindopril)	Increased distance walked; decreased hip fracture	Hypotension; hyperkalemia; muscle cramps; numbness
Espindolol (B_1/B_2 adrenergic receptor antagonist)	Maintains muscle mass; increased hand grip strength	?
Fast skeletal muscle troponin activators (Tirasemtiv)	Improves muscle function	?

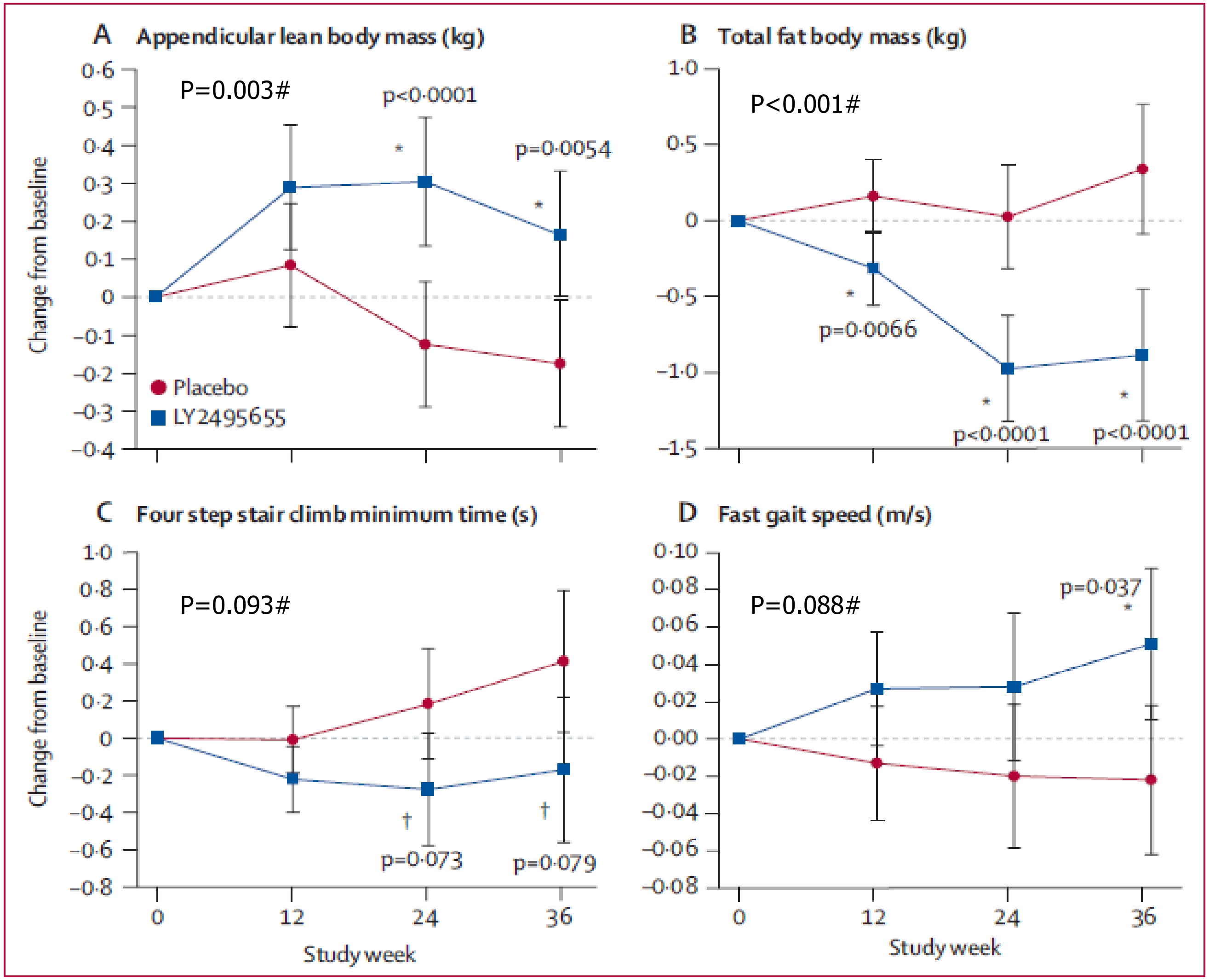
Myostatin antibody (LY2495655) in older weak fallers: a proof-of-concept, randomised, phase 2 trial

Clemens Becker, Stephen R Lord, Stephanie A Studenski, Stuart J Warden, Roger A Fielding, Christopher P Recknor, Marc C Hochberg, Serge L Ferrari, Hubert Blain, Ellen F Binder, Yves Rolland, Serge Poiraudeau, Charles T Benson, Stephen L Myers*, Leijun Hu*, Qasim I Ahmad*, Kelli R Pacuch, Elisa V Gomez, and Olivier Benichou, on behalf of the STEADY Group†*

	Placebo group (n=99)	LY2495655 group (n=102)
Age (years)	83 (75–99)	82 (75–96)
Women	65 (66%)	75 (74%)
White	98 (99%)	101 (99%)
Weight (kg)	69·3 (13·7)	69·1 (13·4)
Height (cm)	161·4 (10·2)	161·3 (10·6)
Appendicular lean body mass/height²	6·02 (0·8)	6·1 (0·8)
Sarcopenia*	29 (31%)	25 (26%)
BMI (kg/m²)	26·5 (4·0)	26·4 (3·8)
Number of pre-existing conditions	8·8 (6·9)	11·5 (8·1)
Number of concomitant drugs (mean per patient)	8·6 (4·9)	9·3 (5·1)
Number of falls between visit one (screening) and visit two (randomisation; mean per patient)	0·15	0·23
Previous fractures (total number per group)	61	105
Number of patients with previous fractures (%)	32 (33%)	41 (40%)
Pre-existing osteoporosis† (%)	33 (33%)	48 (47%)
Patients with 25-hydroxyvitamin D <20 ng/mL before the first dose (%)	20 (20%)	28 (28%)
Chair rise test without arms (s)	16·4 (4·9)	16·8 (5·8)
Patients performing chair rise test without arms (%)	78 (79%)	76 (75%)
Hand grip strength (kg)	19·9 (7·7)	20·0 (7·2)

Lancet Diab Endocr 2015;3:948-57

Change from baseline in body composition and performance-based measures



#: p value for overall treatment effect

Lancet Diab Endocr 2015;3:948-57

Myostatin antibody in older weak fallers: a proof-of-concept randomised, phase 2 trial: Adverse Events

	Placebo (N=99)	315 mg LY (N=102)	p-value
Deaths	0	1 (1%)	1·000
Serious adverse events	18 (18%)	26 (26%)	0·235
Early treatment discontinuation	14 (14%)	20 (20%)	0·351
Adverse events leading to treatment discontinuation	6 (6%)	10 (10%)	0·436
Injection site reactions			
Mild	8 (8%)	22 (22%)	<0·001*
Moderate	1 (1%)	8 (8%)	
Severe	0	1 (1%)	
Patients with ≥1 fracture	6 (6%)	10 (10%)	0·403
Patients with ≥1 TEAE considered by investigators as possibly related to study drug	23 (23%)	42 (41%)	0·007
All TEAEs considered by investigators as possibly related to study drug (by frequency and alphabetic order):			
Injection site pain	5 (5%)	20 (20%)	0·002
Blood creatine phosphokinase increased	0	5 (5%)	0·060
Fatigue	1 (1%)	3 (3%)	0·621
Injection site bruising	0	4 (4%)	0·121
Injection site erythema	1 (1%)	3 (3%)	0·621
Rash	0	4 (4%)	0·121
Diarrhoea	1 (1%)	2 (2%)	1·000
Injection site rash	0	3 (3%)	0·246
Anaemia	2 (2%)	0	0·241
Constipation	0	2 (2%)	0·498
Dysgeusia	2 (2%)	0	0·241

Lancet Diab Endocr 2015;3:948-57