Società Italiana di Gerontologia e Geriatria

Lunch Symposium: La Medicina basata sulle prove di efficacia: Quali evidenze in nutrizione clinica?
29 novembre 2013

Fragilità e osteoporosi: ruolo della nutrizione medica nella riabilitazione del paziente fragile

Giuseppe Bellelli

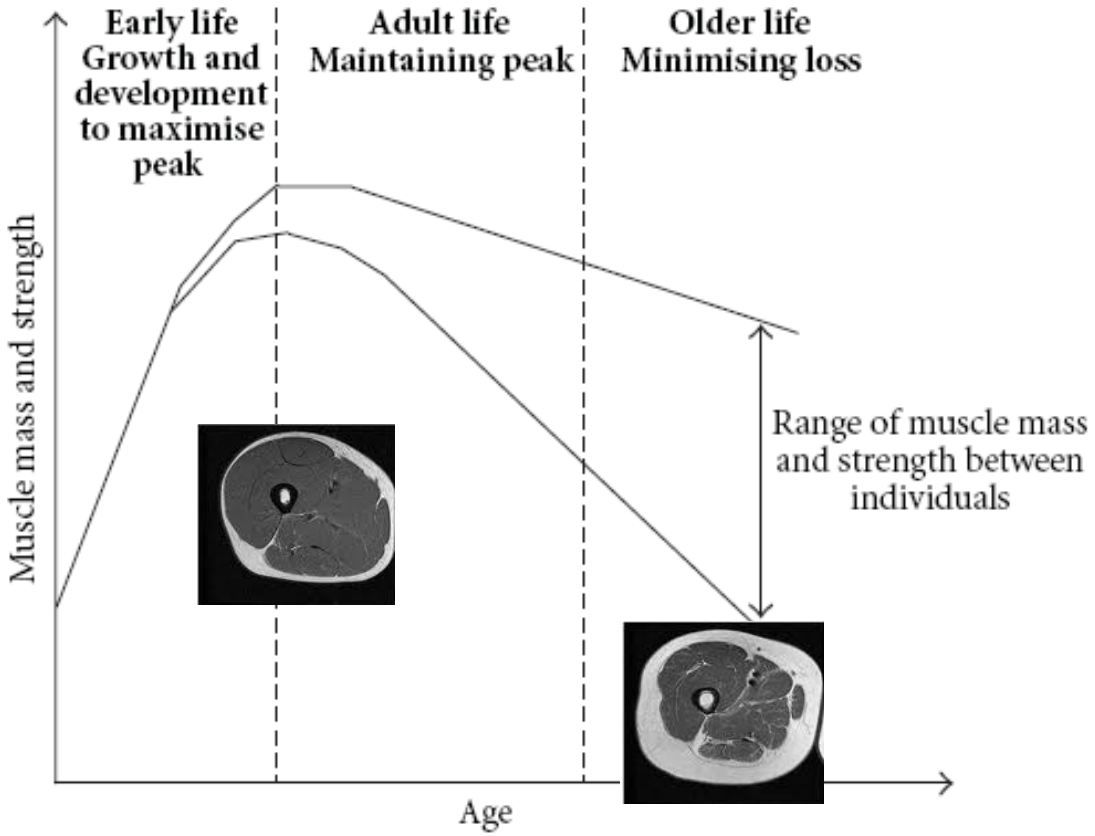
Clinica Geriatrica, Università Milano-Bicocca

Gruppo di Ricerca Geriatrica, Brescia

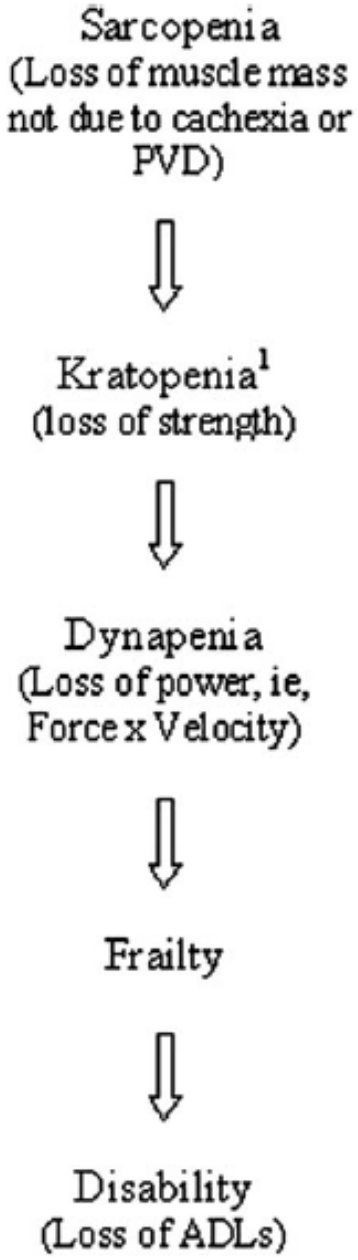
Gruppo di ricerca geriatrica

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

A life course model of sarcopenia (sarχ - carne- e πένιά –perdita)



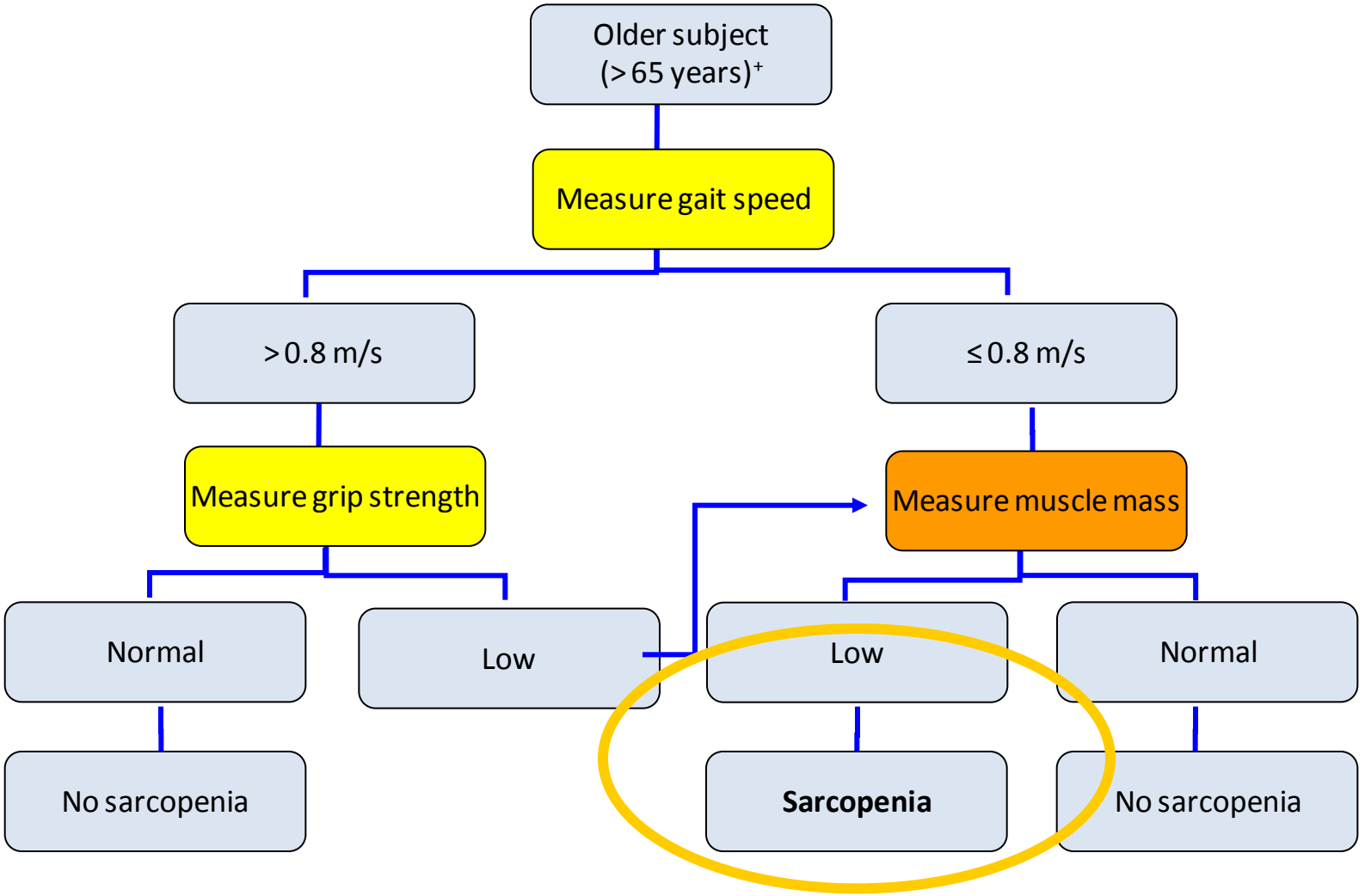
Robinson S, J Aging Research 2012



Pathway from sarcopenia to disability

Morley JE. Sarcopenia: diagnosis and treatment. JNHA. 2008

EWGSOP suggested algorithm for sarcopenia case finding in older individuals*



* Sarcopenia: European Consensus on Definition and Diagnosis
Report of the European Working Group on Sarcopenia in Older People

Sarcopenia: Prevalence and prognostic significance in hospitalized patients

Salah Gariballa [a,b,*], Awad Alessa [a]

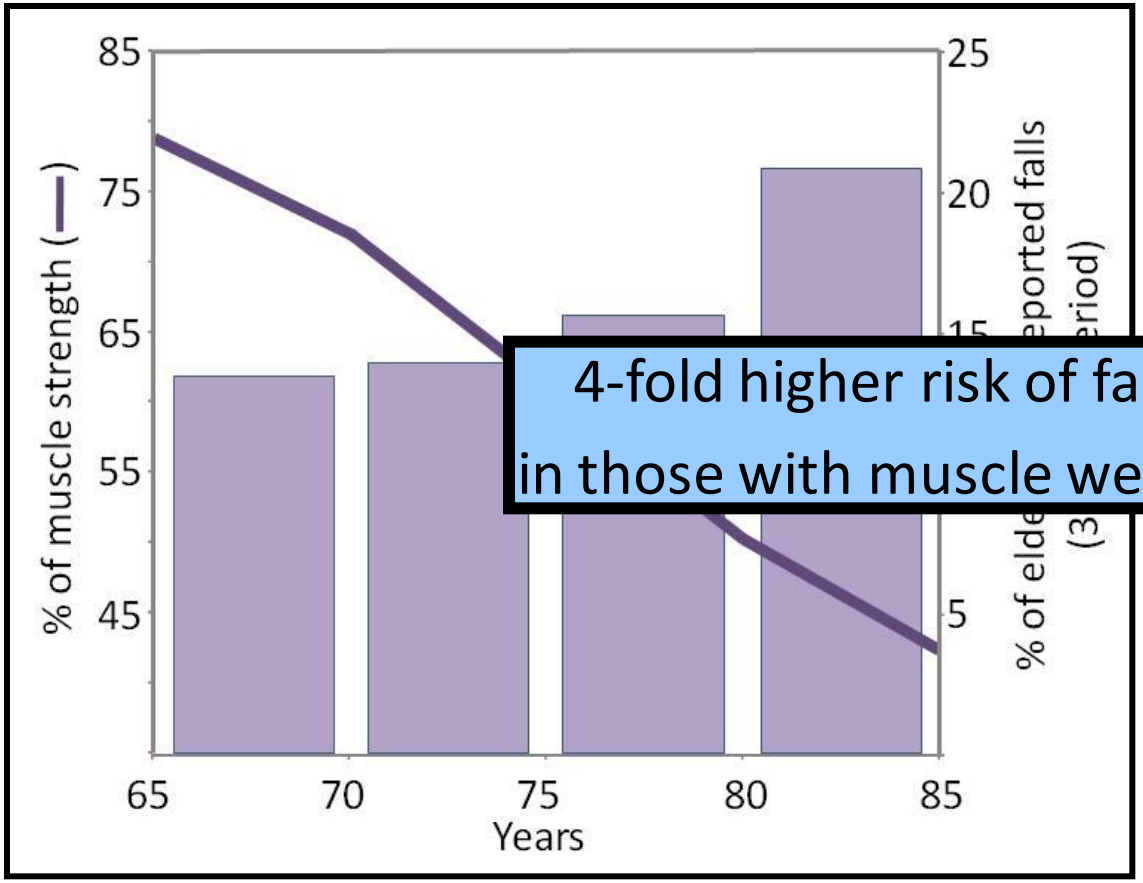
Baseline characteristics of subjects according to presence or absence of sarcopenia.

Variable		Sarcopenia ($n = 44$)	Not sarcopenia ($n = 388$)
Age (SD) *		79 (7)	77 (6)
Gender, female		29 (66)	176 (45)
Smoking	Never smoked	17 (39)	118 (30)
	Ex smoker	16 (36)	200 (52)
	Current smoker	11 (25)	70 (18)
Alcohol $\geq$ 14 units		5 (11)	51 (13)
Barthel score		15.3 (4.8)	16.1 (4.6)
Geriatric depression score *		21.2 (4)	20 (3)
SF-36 score		75 (19)	80 (21)
C-reactive protein mg/L		51 (59)	52 (74)
Haemoglobin g/dl		12.3 (2)	12.7 (2)
Albumin g/L *		35.5 (5)	38 (5)
Transferrin g/L		2.03 (.58)	2.17 (.49)

*$P < 0.05$.

Clinical Nutrition 2013

Consequences of sarcopenia
Risk of falls and fractures

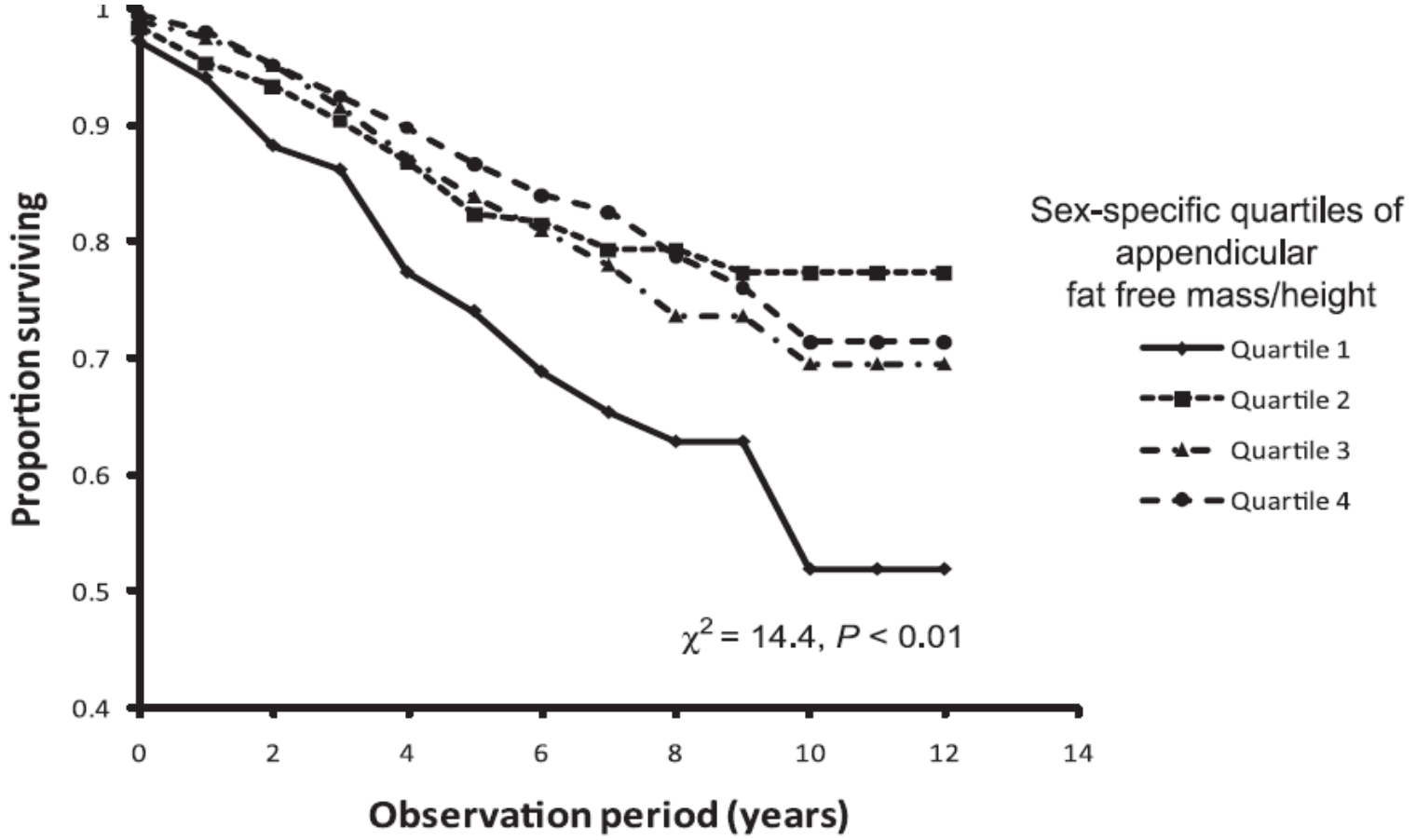


4-fold higher risk of falling
in those with muscle weakness

Perell et al, JGMS 2001; Evans J Nutr 1997; Stevens et al., J Safety Res 2008; AGS, JAGS 2001

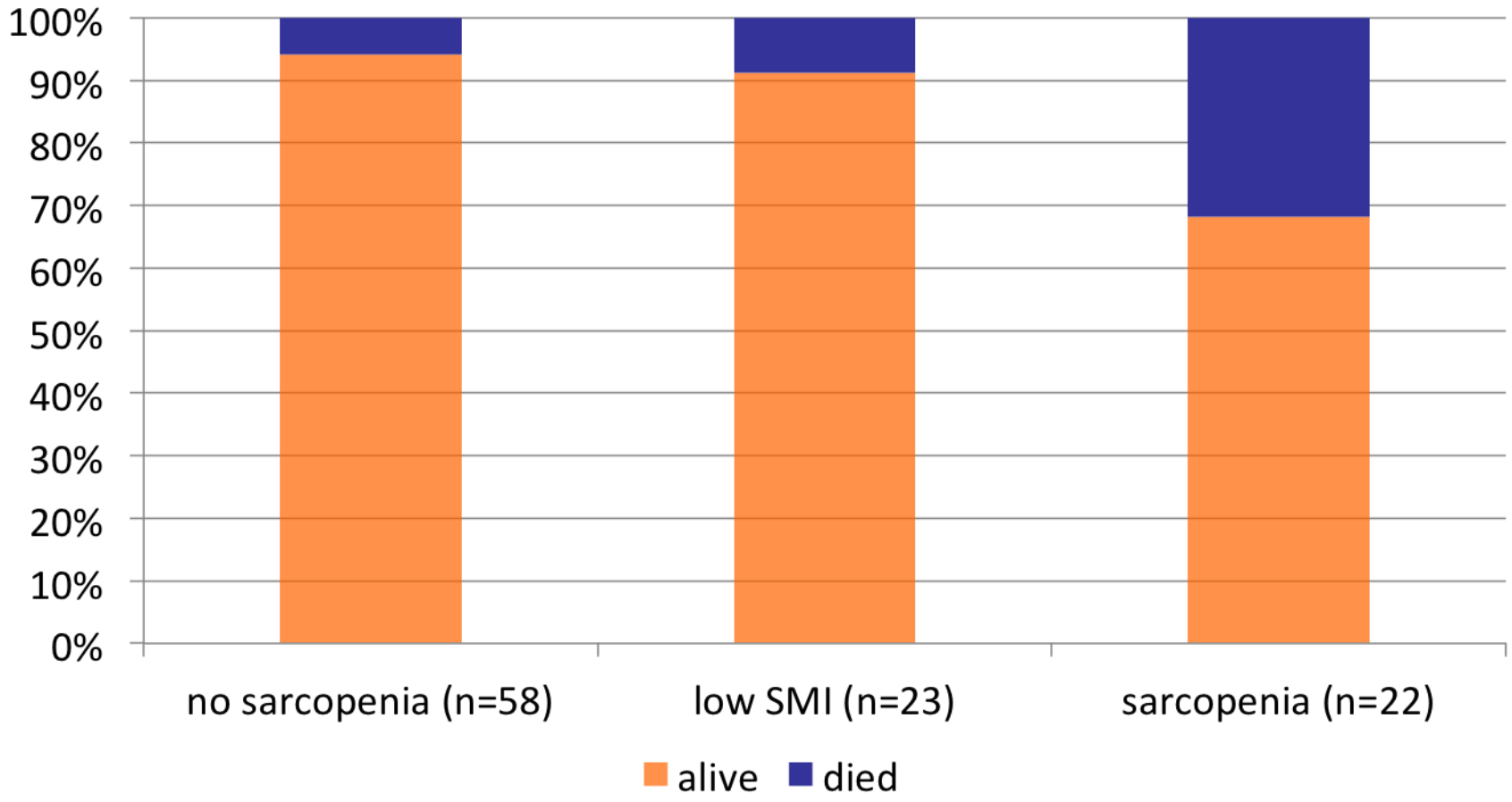
Mortalità nei community dwellers

Sopravvivenza a 12 anni di un gruppo di anziani (n=1413 healthy community dwellers) suddivisi in base a quartili genere-specifici del parametro ALM/h



Bunout D. Australas J Ageing 2011;30:89-92

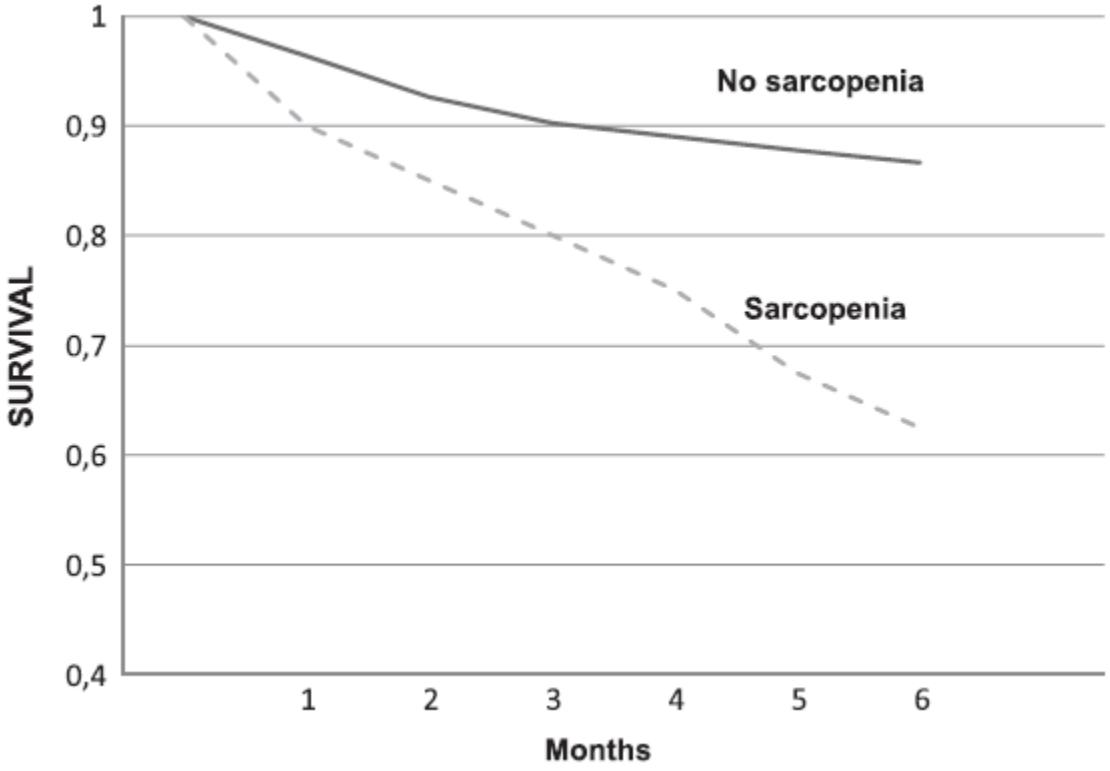
Rate of mortality at 3 months in 103 patients discharged from an acute Geriatric Unit



Cerri AP et al, unpublished data

Sarcopenia e mortalità in RSA

122 pazienti di età >70 aa residenti in RSA (RSA Santa Maria della Pace, Roma; 40 con sarcopenia, 82 senza sarcopenia) (p<.001)



Landi F. JAMDA 2012;13:121-6

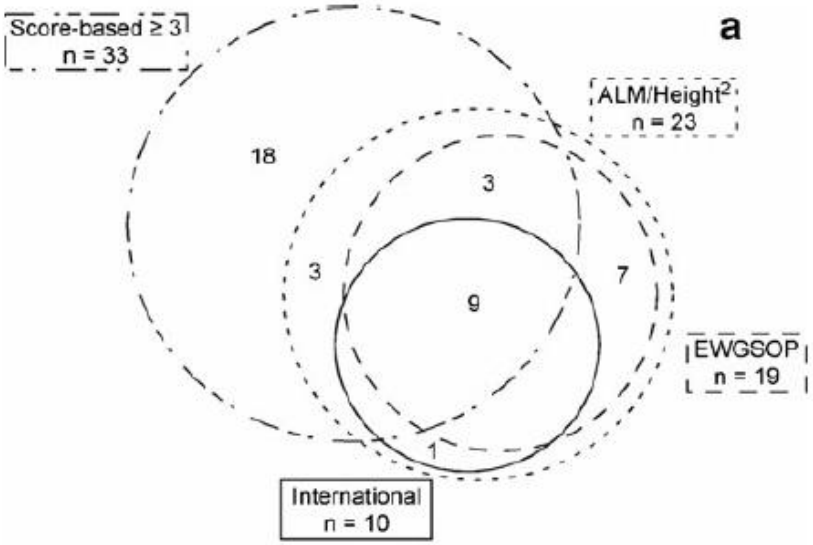
Sarcopenia is commonly associated with disability and has been estimated to cost the US health system ≈$18.4 billion a year

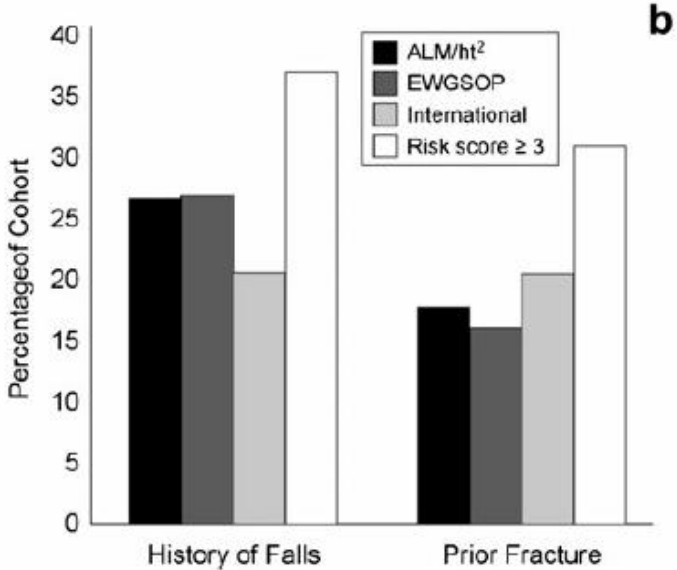
Jansenn I, Appl. Physiol. Nutr. Metab. ***35****: 707–712 (2010)*

Costs of managing osteopenia, osteoporosis and femur fractures were 411 million USD in 2010 . Total costs will be 19.2 % higher in 2015, and by 2020, the figures will have increased by 41.7 %

Carlos F, Arch Osteoporosis. ***8****(1-2):125 (2013)*

What's in a name revisited: should osteoporosis and sarcopenia be considered components of "dysmobility syndrome?"

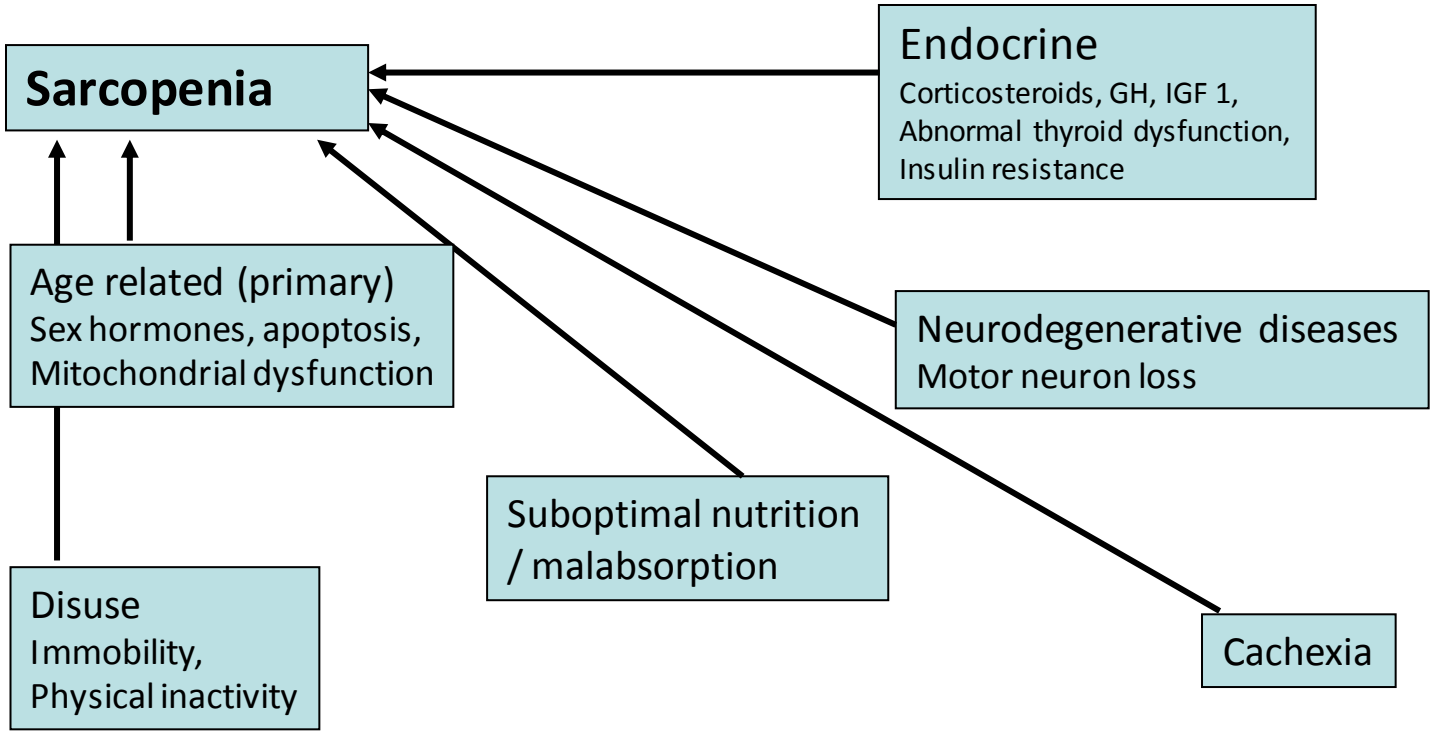




Osteoporos Int (2013) 24:2955–2959

Causes of sarcopenia

Sarcopenia is multi-factorial in cause

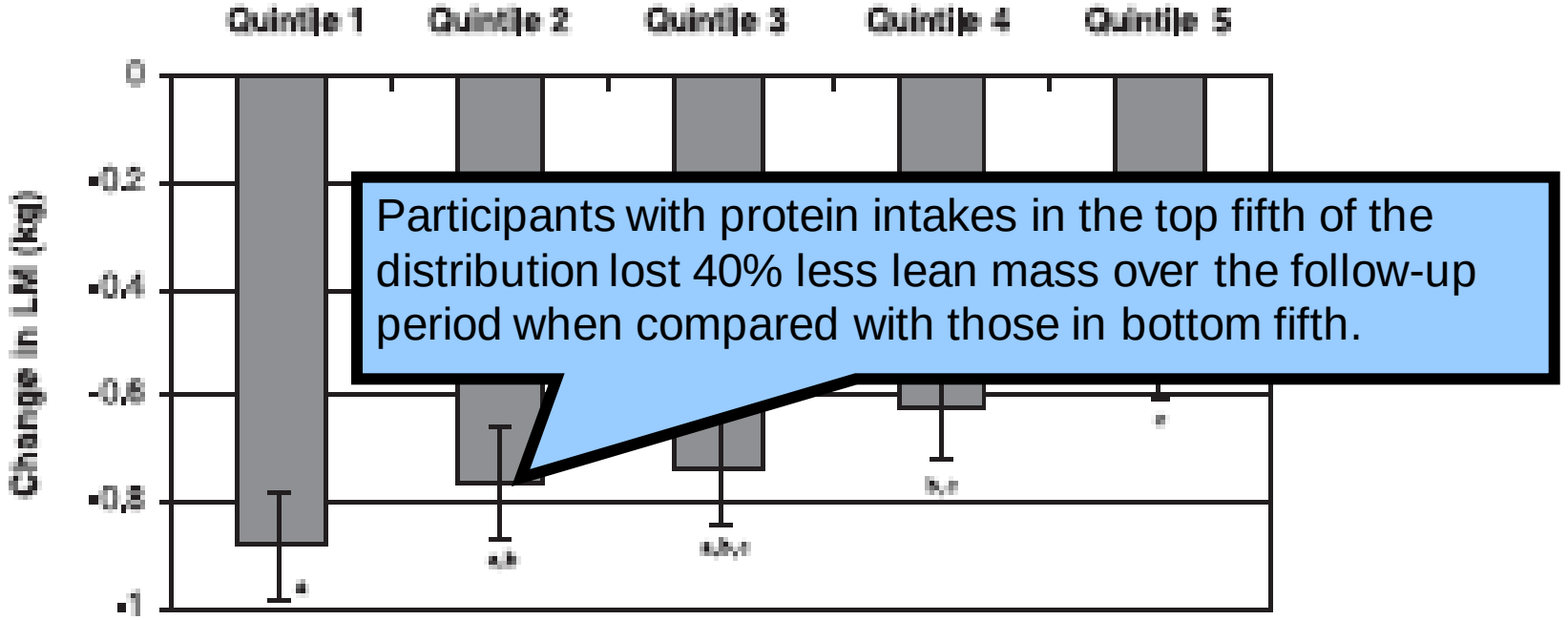


Cruz-Jentoft et al,. Age Aging 2010

Management of sarcopenia: Nutritional management

Contributory factors related to nutrition	Nutritional management strategies
Inadequate protein intake	Increase protein intake (1-1.5g/kg)
Increased splanchnic extraction of amino acids	Consume high quality or “fast” proteins. AA supplementation
Decreased muscle response to anabolic stimuli	Increase EAA, in particular leucine, intake
Vitamin D deficiency	Increase Vitamin D intake

Adjusted lean mass (LM) loss by quintile of energy-adjusted total protein intake (*n*=2066)



Houston D, Am J Clin Nutr 2008;87:150 –5

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Whey protein stimulates postprandial muscle protein accretion more effectively than do casein and casein hydrolysate in older men[1–3]

Bart Pennings, Yves Boirie, Joan MG Senden, Annemie P Gijsen, Harm Kuipers, and Luc JC van Loon

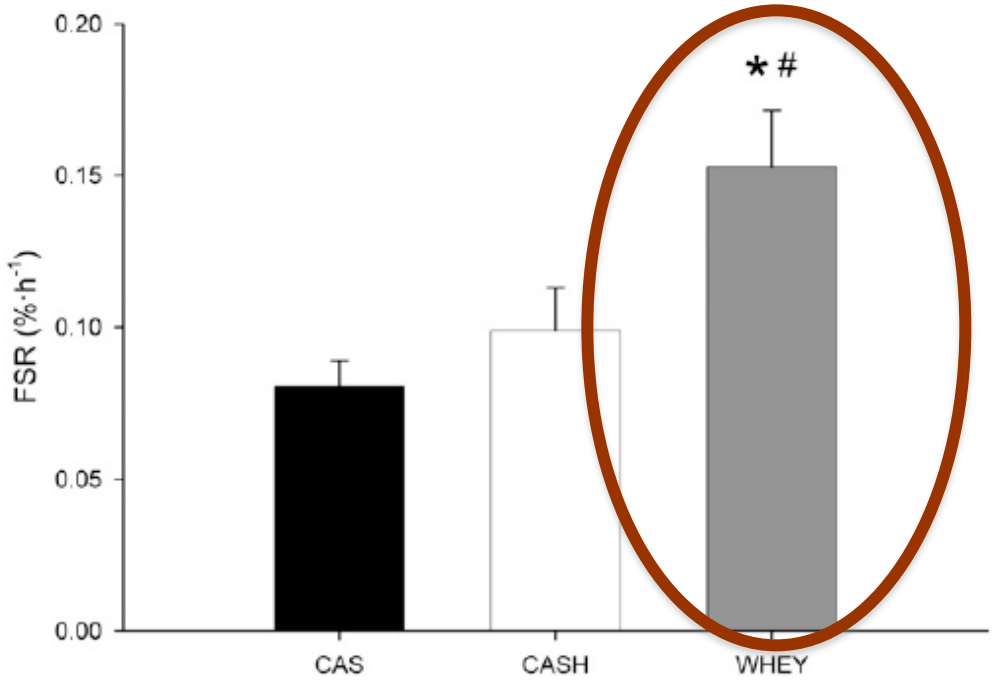

FIGURE 5. Mean (±SEM) mixed muscle protein fractional synthetic rates (FSR), with tissue-free L-[1-^{13}C]phenylalanine enrichments as precursor, after ingestion of casein (CAS; n = 16), casein hydrolysate (CASH; n = 16), and whey (WHEY; n = 16). Data were analyzed with ANOVA with Bonferroni correction. *WHEY significantly different from CAS, $P < 0.01$. #WHEY significantly different from CASH, $P < 0.05$.

Am J Clin Nutr, 2011, 10.3945/ajcn.110.008102

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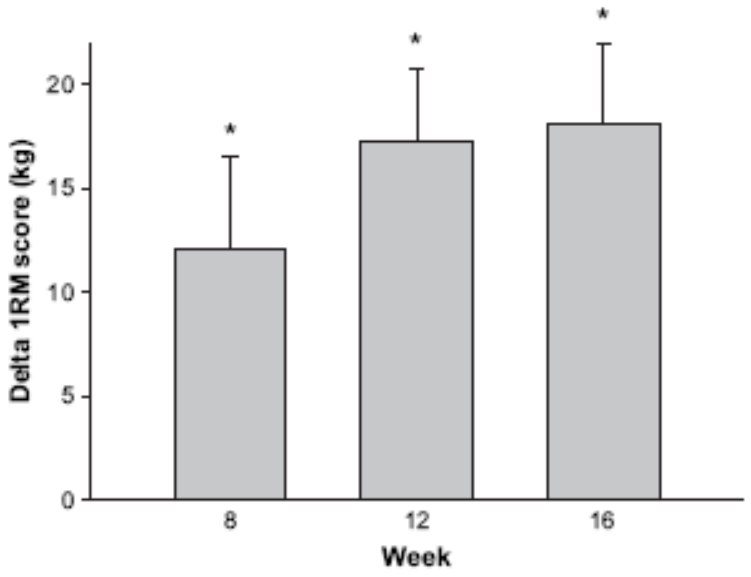
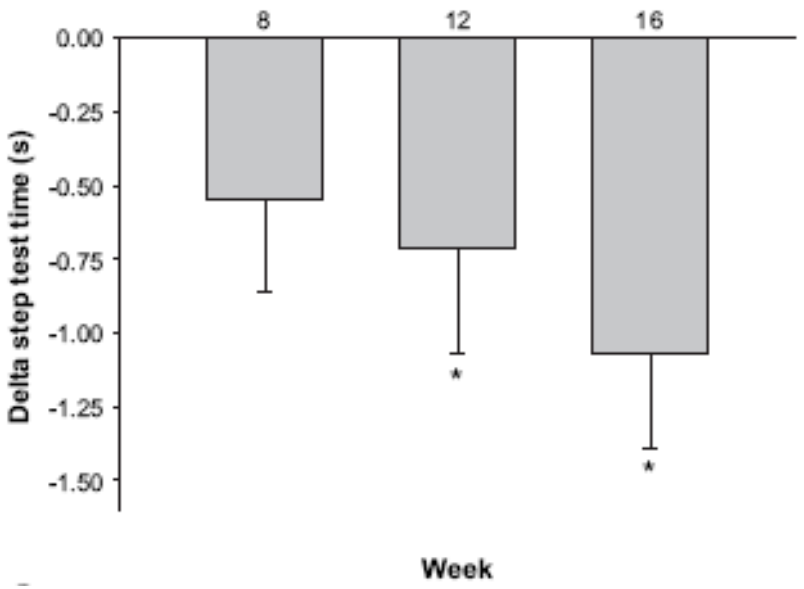
Supplementation of EAA, rich in leucine increases muscle strength and function in the elderly

Maximum strength



Time to perform 5-step test



22g EAA; 7.9g Leucine/day; non-controlled trial

Borsheim et al, 2008; 27: 189–195.

Management of sarcopenia: Nutritional guidelines

The Society of Sarcopenia, Cachexia and Wasting Disease recommend that a **leucine-enriched balanced essential amino acid mix** should be used to slow muscle loss in sarcopenic patients

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Nutritional Recommendations for the Management of Sarcopenia

John E. Morley, MB, BCh, Josep M. Argiles, PhD, William J. Evans, MD, Shalender Bhasin, MD, David Cella, PhD, Nicolaas E. P. Deutz, MD, PhD, Wolfram Doehner, MD, PhD, Ken C. H. Fearon, MD, Luigi Ferrucci, MD, PhD, Marc K. Hellerstein, MD, PhD, Kamyar Kalantar-Zadeh, MD, PhD, Herbert Lochs, MD, Neil MacDonald, MD, Kathleen Mulligan, PhD, Maurizio Muscaritoli, MD, Piotr Ponikowski, MD, PhD, Mary Ellen Posthauer, RD, CD, LD, Filippo Rossi Fanelli, MD, Morrie Schambelan, MD, Annemie M. W. J. Schols, PhD, Michael W. Schuster, MD, and Stefan D. Anker, MD, PhD, The Society for Sarcopenia, Cachexia, and Wasting Disease

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Morley et al., J Am Med Dir Assoc 2010 11: 391-396

Management of sarcopenia: Nutritional management

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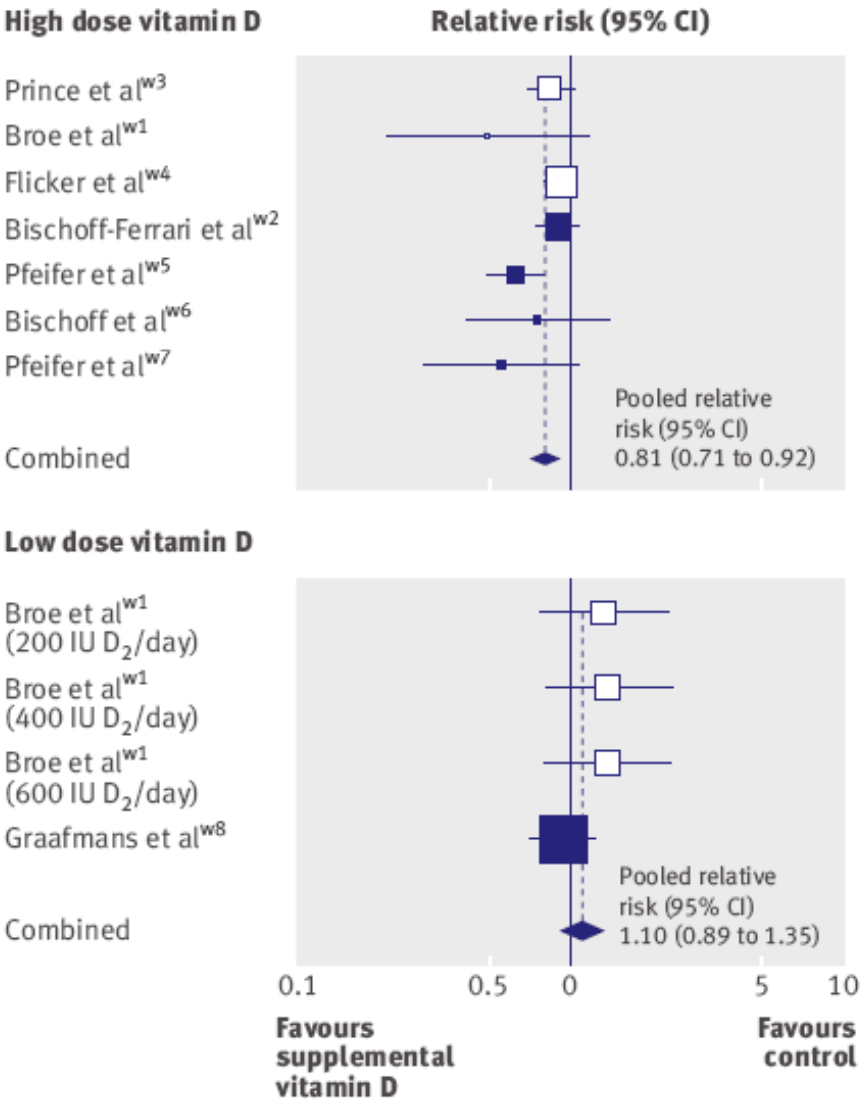
Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials

H A Bischoff-Ferrari, director of centre on aging and mobility

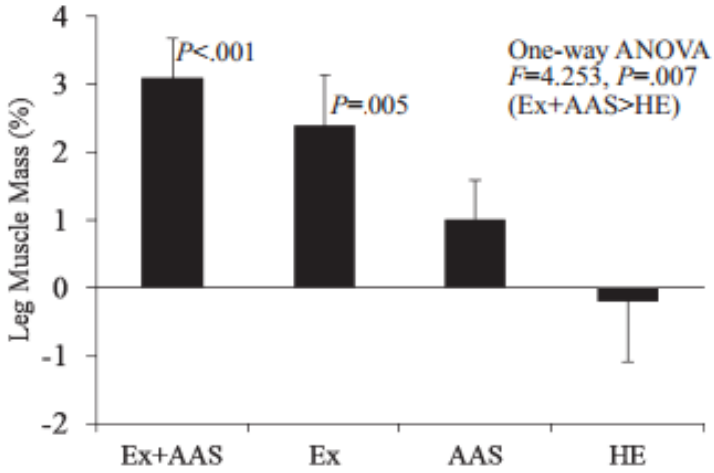


- Supplemental vitamin D (700–1000 IU per day) reduced the risk of falling by 19%.

BMJ 2009;339:b3692

Effects of Exercise and Amino Acid Supplementation on Body Composition and Physical Function in Community-Dwelling Elderly Japanese Sarcopenic Women: A Randomized Controlled Trial

Hun Kyung Kim, PhD,[*] Takao Suzuki, MD, PhD,[†] Kyoko Saito, PhD,[*] Hideyo Yoshida, MD, PhD,[*] Hisamine Kobayashi, DVM,[‡] Hiroyuki Kato, MS,[‡] and Miwa Katayama, DVM[‡]



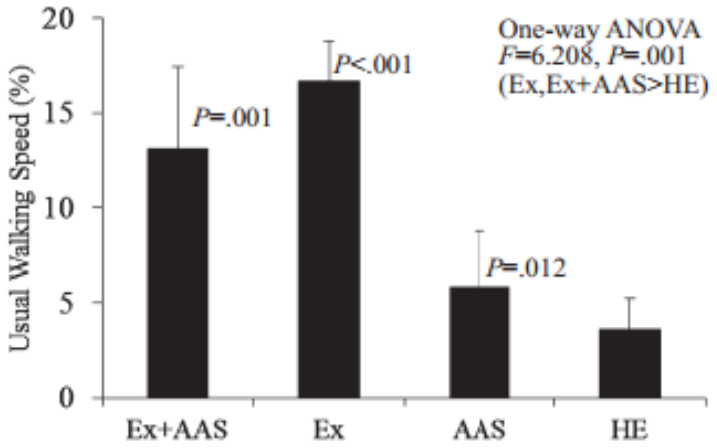


Table 3. Change in Leg Muscle Mass and Functional Fitness After Intervention According to Study Group

Dependent Variable*	Adjusted Odds Ratio (95% Confidence Interval)		
	AAS	Exercise	Exercise + AAS
Change in leg muscle mass and knee extension strength	1.99 (0.72–5.65)	2.61 (0.88–8.05)	4.89 (1.89–11.27)
Change in leg muscle mass and usual walking speed	1.35 (0.45–4.08)	2.41 (0.79–7.58)	4.11 (1.33–13.68)

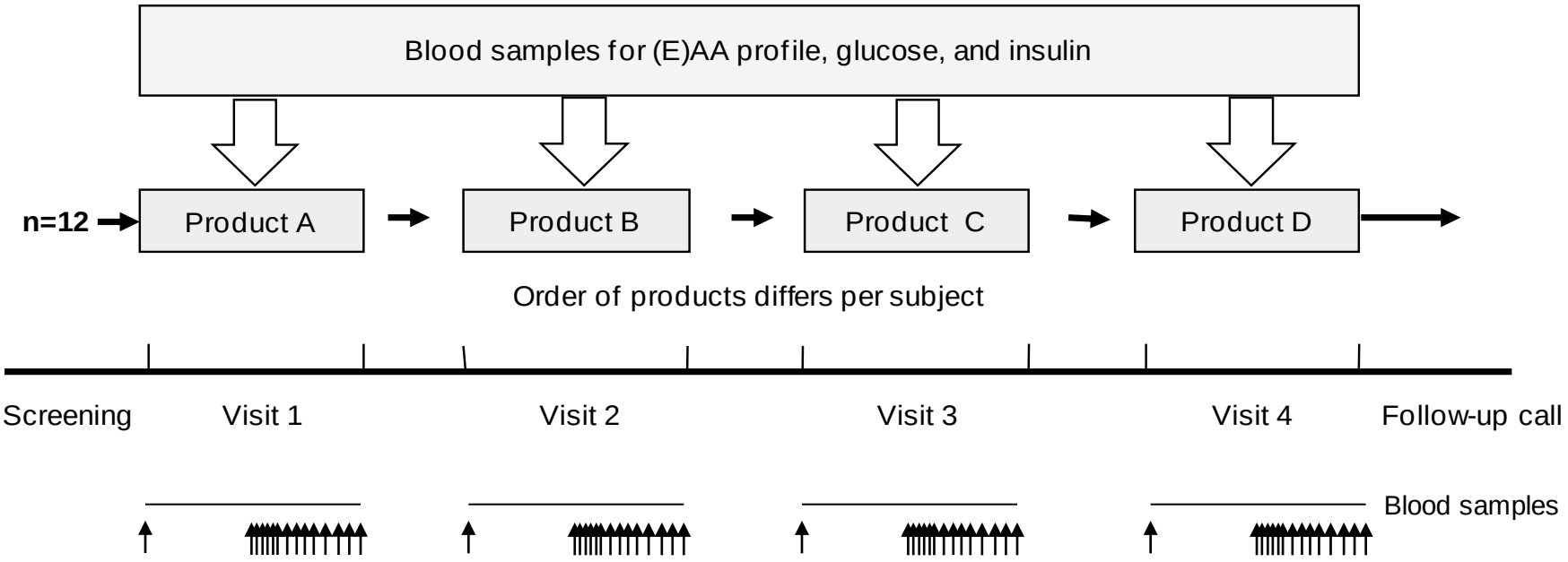
JAGS 2012; 60:16-23

FortiFit: Key nutritional features

Whey protein 20 g	Fast AA bioavailability required for muscle protein synthesis
Essential AA 10 g	Adequate amount of substrate for muscle health in elderly
Leucine 3 g	Additional trigger to overcome the age-related anabolic response
Vitamin D 800IU	To maintain muscle function
Calcium 500 mg	To support bone health
Low caloric 150 Kcal	To support fast and high availability of EAA to enhance muscle protein synthesis
Antioxidants (vit E, C, A, carotenoids, zinc, selenium)	To address the age-related oxidative stress and deficiencies
Other micronutrients (vit B6, Folic Acid, vit B12, magnesium)	To address the age-related deficiency for specific micronutrient

Evidence – ArenA study

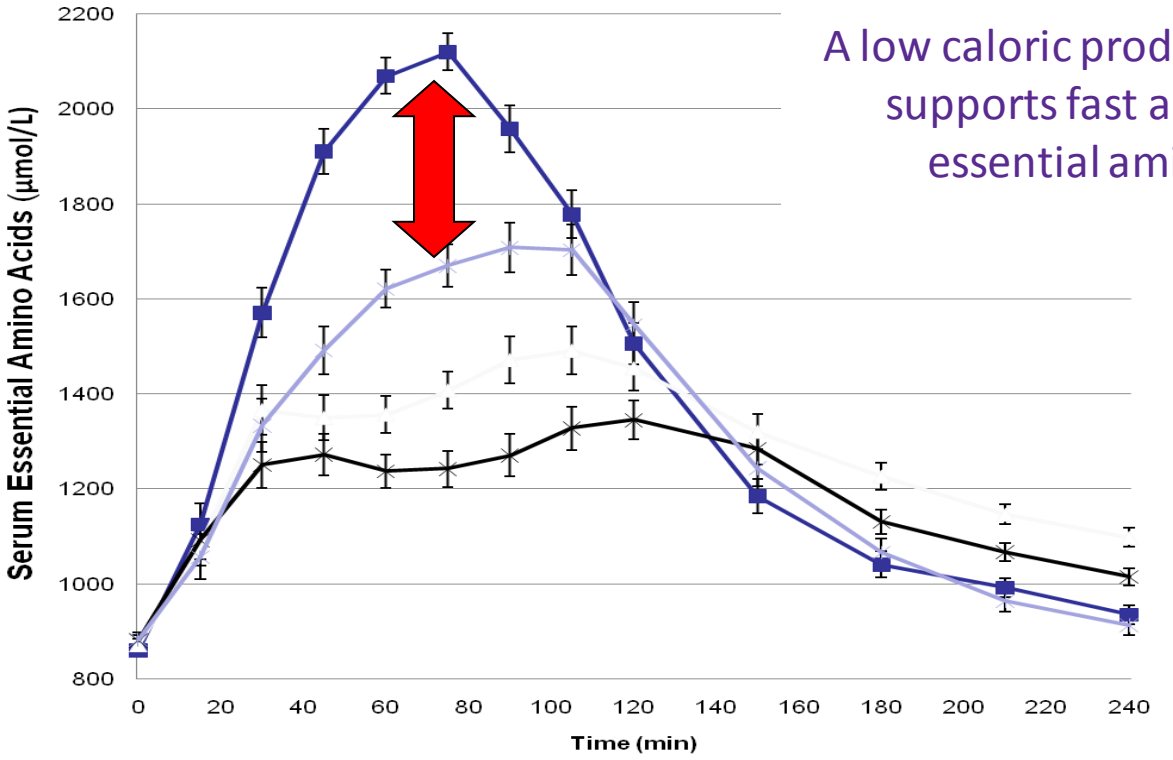
To study the superior effect of the protein/amino acid blend in FortiFit and its low-caloric density on the serum amino acid profile.



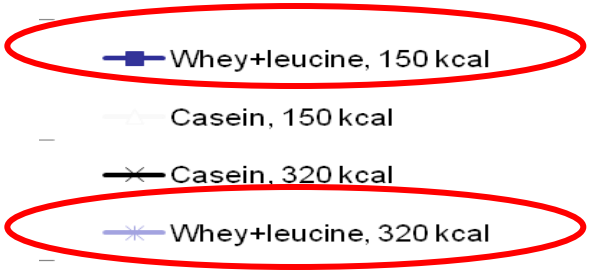
Luiking, Y. et al A high whey-protein leucine enriched low-caloric supplement results in higher and faster rise in serum amino acid levels than a casein containing or high caloric supplement equivalent. Clin Nutr. 2010; 5(Suppl 2); p. 102.

Low caloric supplement- Arena Study

A low caloric product increases post-prandial circulating EAA availability; high EAA availability is important for stimulation of muscle protein synthesis



A low caloric product with fast (whey) protein supports fast and high levels circulating essential amino acids in the **elderly**



Luiking et al., Clin Nutr 2010

FortiFit: Evidence – PROVIDE trial (proof of principle)

To assess the effect of FortiFit on muscle strength and physical performance in sarcopenic elderly

Study population

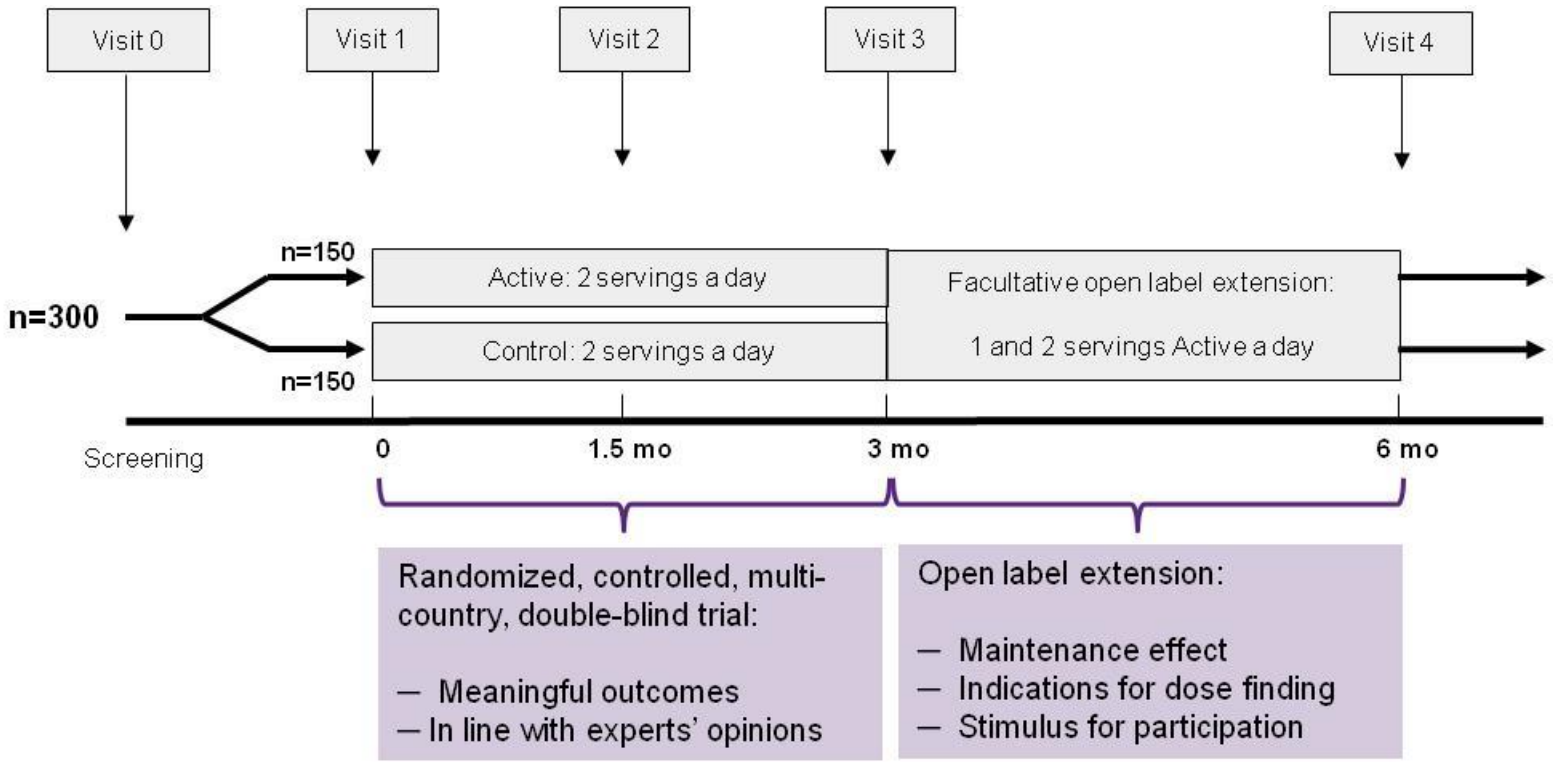
Eligible

- 65+
- Impaired mobility (Performance score 4-9)
- Sarcopenia (defined by BIA)
- BMI 20-30
- No inflammation disease
- No high levels of vitamin D or calcium intake

Not eligible

- BMI > 30
- No cognitively impaired
- No depressed
- No chronic diseases
- Not willing to participate

FortiFit: Evidence – PROVIDE trial (proof of principle)



Status: Ongoing - Results expected in 2013

Take home messages

- La sarcopenia è un problema emergente in ambito geriatrico, gravato da un elevato tasso di complicanze, disabilità e costi
- Sono necessari approcci alimentari specifici (leucina e vit D), disegnati per il trattamento nutrizionale della sarcopenia e per ridurre il rischio di cadute nell'anziano fragile
- In generale i prodotti devono essere a base di "high quality protein" e basso contenuto di calorie per aumentare la biodisponibilità sierica degli amminoacidi essenziali
- Per produrre evidenze cliniche sono in corso studi clinici disegnati secondo i crismi della sperimentazione clinica.