Management nutrizionale della sarcopenia

Lorenzo M Donini

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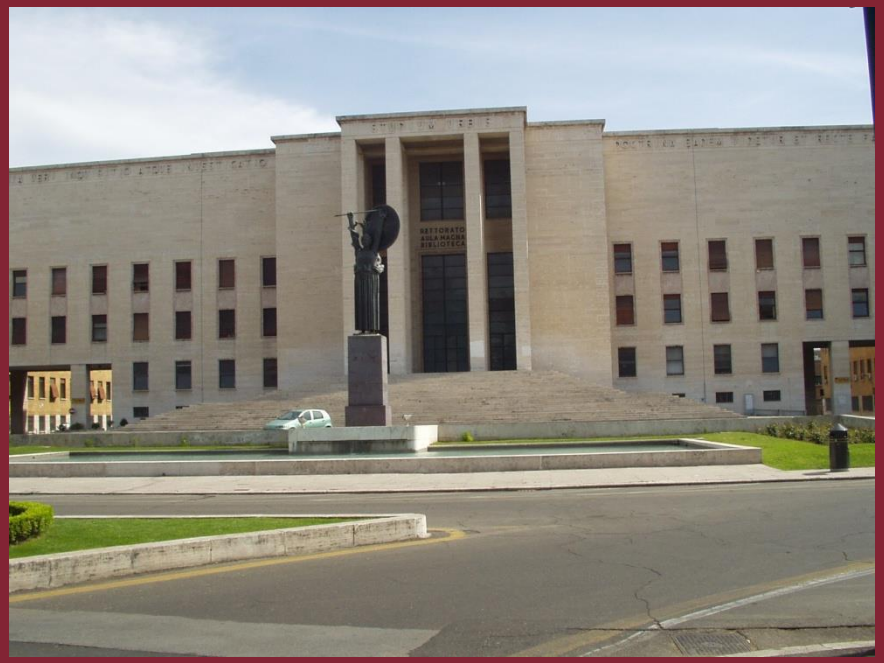
Sezione di Fisiopatologia Medica, Scienza dell'Alimentazione ed Endocrinologia



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La sarcopenia in età geriatrica:
- etiopatogenesi
- conseguenze cliniche e funzionali

Linee di intervento

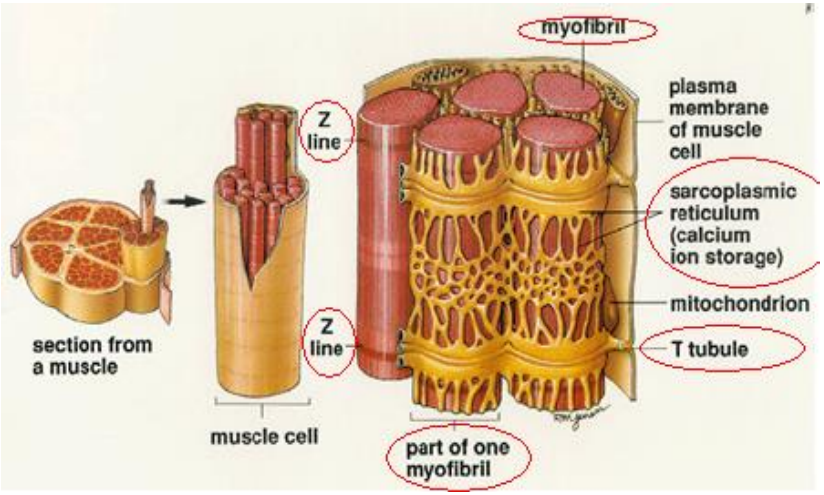
Il progetto PROVIDE

La sarcopenia in età geriatrica:
- etiopatogenesi
- conseguenze cliniche e funzionali

Linee di intervento

Il progetto PROVIDE

The Aging Body



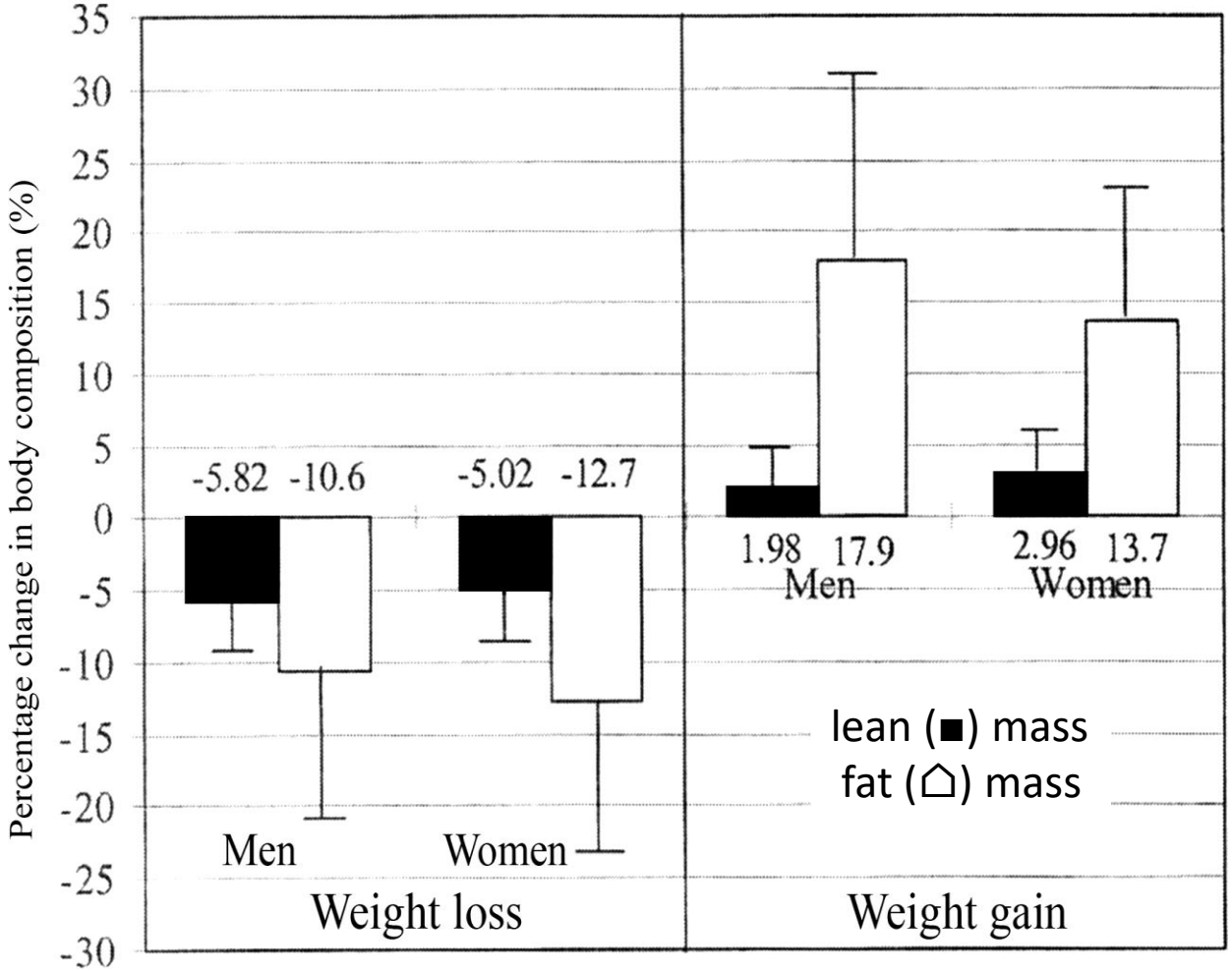
- Body Weight peaks during 5th-6th decade of life and is stable until 65-70 years old[2]
- Typically, with age comes a *loss in lean mass and a gain in fat mass*
  - Resulting from innate metabolic changes and increase in sedentary life
- Muscle cell mass declines to the greatest of body cell mass
  - Skeletal muscle begins to decline around 45-55 years old
  - After this age, muscle declines 12-15% per decade until 80
- Bone weakens as a result of aging and corresponds with a decrease in muscle

1. *Roubenoff, R. "Sarcopenia: A major modifiable cause of frailty in the elderly." Journal of Nutrition, Health and Aging. 4(3):1. 2000.*
2. *Kinney, John. "Nutritional frailty, sarcopenia and falls in the elderly." Current Opinion in Clin Nutr and Metab Care. 7:15-20. 2004*
3. *Kamel, Hosam. "Sarcopenia and Aging." Nutrition Reviews. 61(5): 157-167. 2003.*

Weight change and the conservation of lean mass in old age: the Health, Aging and Body Composition Study[1–3]

Am J Clin Nutr 2005;82:872–8.

Anne B Newman, Jung Sun Lee, Marjolein Visser, Bret H Goodpaster, Stephen B Kritchevsky, Frances A Tylavsky, Michael Nevitt, and Tamara B Harris



Factors that may influence the loss of LBM: **sex hormone steroids, insulin-like growth factor, protein intake, physical activity**.

LBM is associated with muscle strength, bone density, and physical functioning and therefore to disability in old age.

Mean (±SD) percentage changes in lean (▪) and fat (□) compartments with weight loss and weight gain over a 4-y period in the Health, Aging and Body Composition Study cohort (n = 2163).

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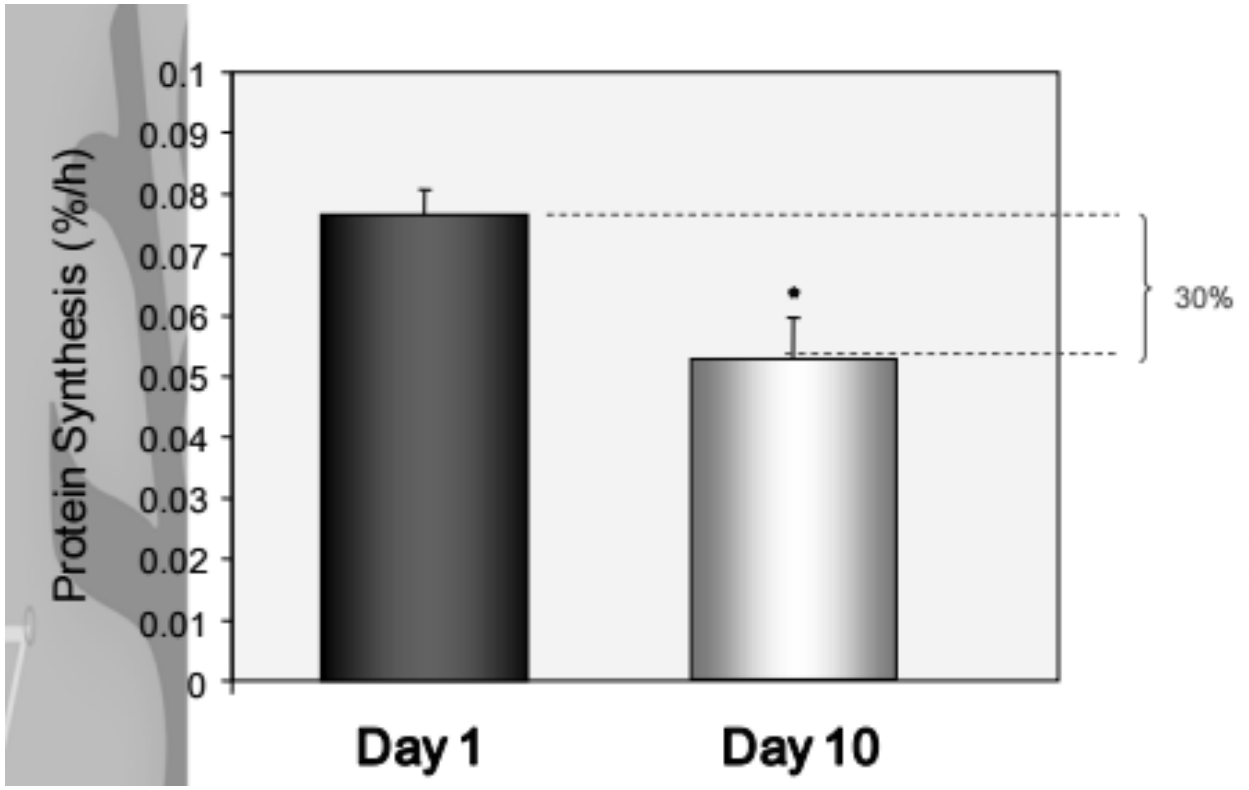
RESEARCH LETTER

Effect of 10 Days of Bed Rest on Skeletal Muscle in Healthy Older Adults

Kortebein, P. et al. JAMA 2007



24 h muscle protein synthesis during 10 day of inactivity in elderly (stable isotope methodology)

large loss of skeletal muscle as a result of bed rest, (particularly from the lower extremities)

⇐ decline in protein synthesis and strength

⇐ negative N balance (before bed rest despite being on a diet with the RDA for protein, increased during bed rest)

" the pronounced effect of bed rest alone on skeletal muscle mass and function combined with the physiological stress associated with hospitalization (⇒ nutritional compromise, inflammation) may result in a more substantial loss of muscle size and function for many older adults during hospitalization"

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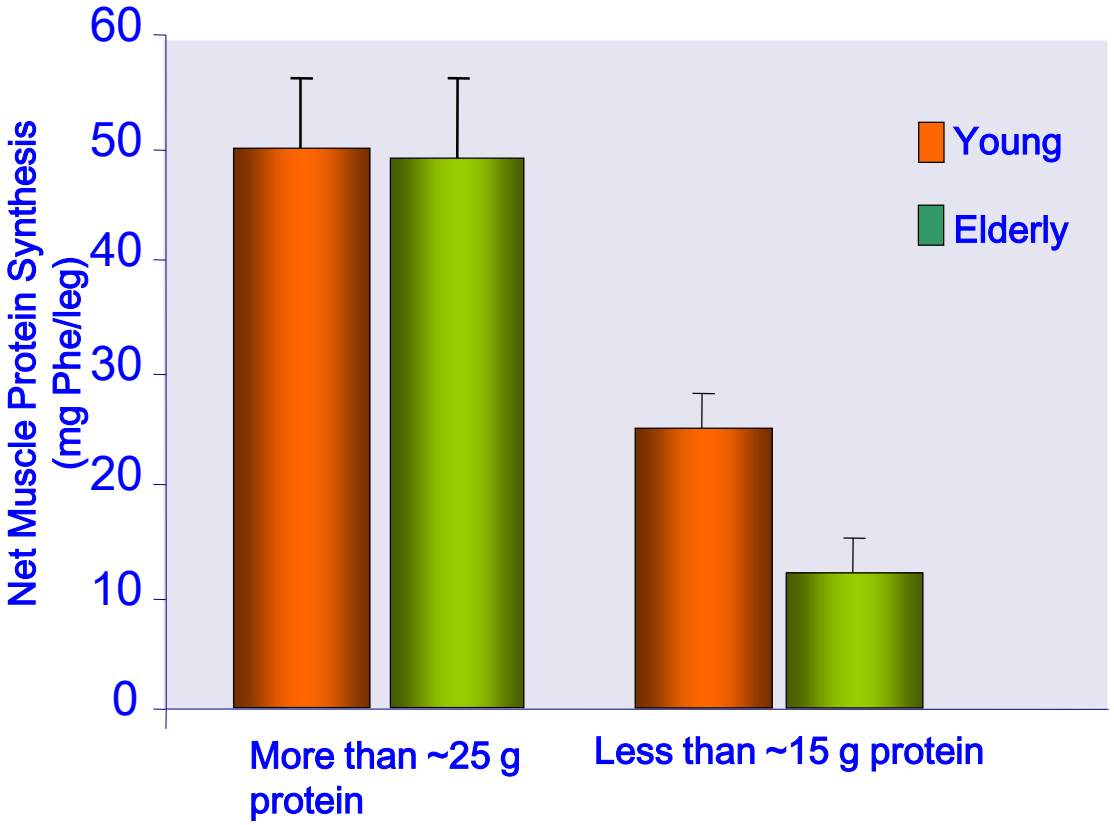
Aging is associated with diminished accretion of muscle proteins after the ingestion of a small bolus of essential amino acids[1–3]

Christos S Katsanos, Hisamine Kobayashi, Melinda Sheffield-Moore, Asle Aarsland, and Robert R Wolfe

Am J Clin Nutr 2005;82:1065–73



ingestion of a small bolus of EAAs results in diminished muscle protein accretion in elderly persons when compared with young persons.

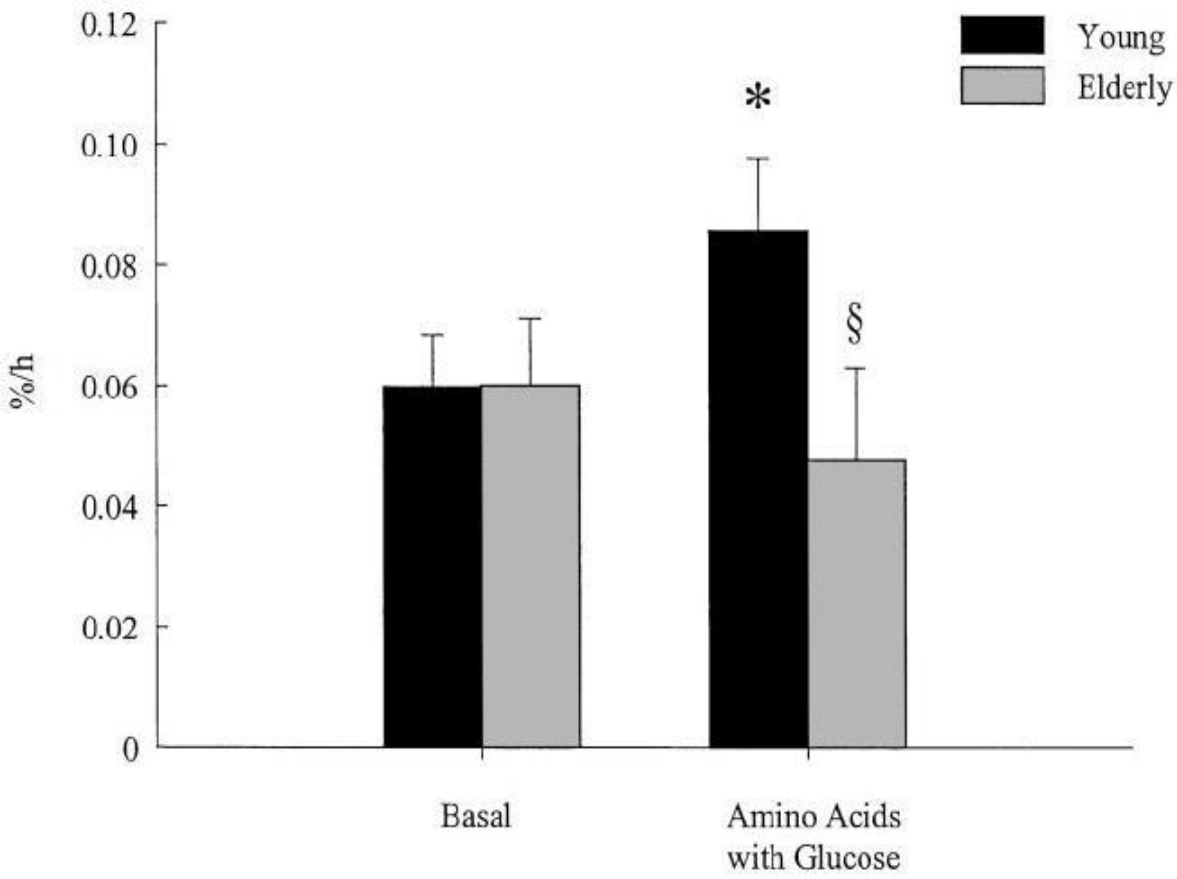
⇒ important role of the amount of AA ingested in a single occasion, not only the amount of amino acids ingested during the course of a time period (eg, 1 d), as a cause of age-associated muscle protein loss.

0021-972X/00/$03.00/0
The Journal of Clinical Endocrinology & Metabolism

Vol. 85, No. 12
Printed in U.S.A.

The Response of Muscle Protein Anabolism to Combined Hyperaminoacidemia and Glucose-Induced Hyperinsulinemia Is Impaired in the Elderly*

ELENA VOLPI†, BETTINA MITTENDORFER, BLAKE B. RASMUSSEN, AND ROBERT R. WOLFE



AA alone stimulate muscle protein synthesis in the elderly.
However, mixed nutritional supplementation failed to improve muscle mass.

The failure of mixed nutritional supplementation to increase muscle mass in the elderly depends on specific alterations in the response of muscle to the combined effects of exogenous AA and endogenous insulin.

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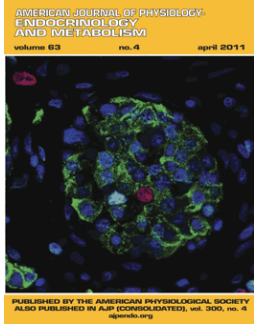
A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly

Christos S. Katsanos,[1] Hisamine Kobayashi,[2] Melinda Sheffield-Moore,[3] Asle Aarsland,[4] and Robert R. Wolfe[1]

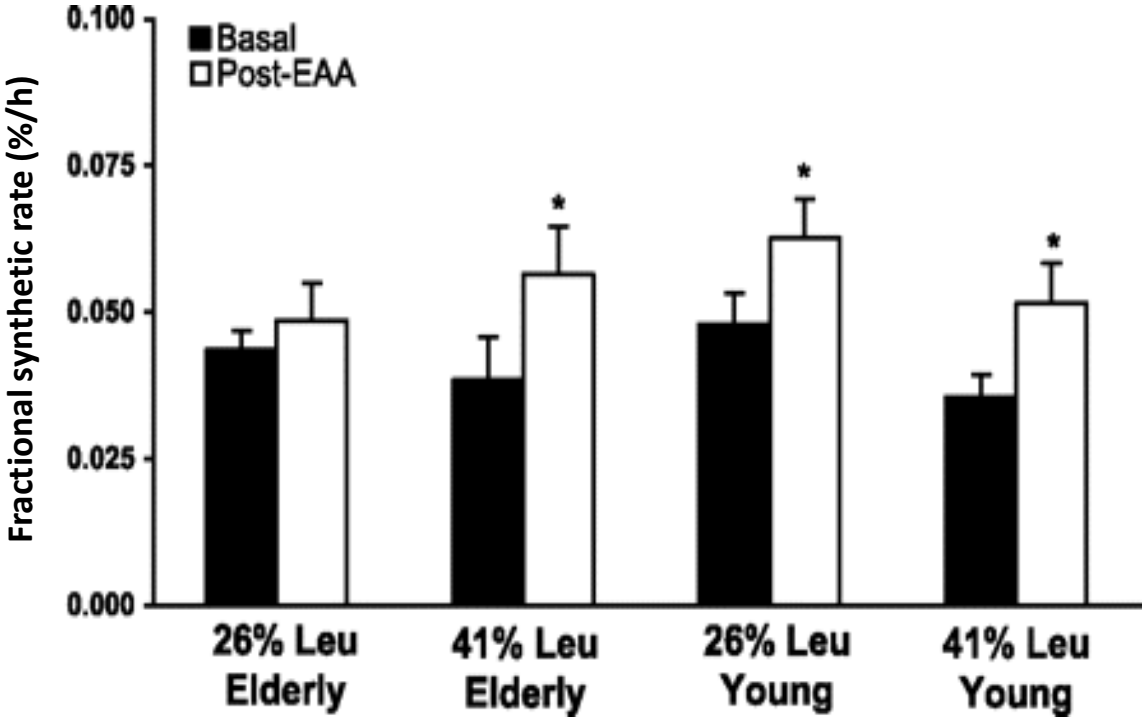
Departments of [1]Surgery and Shriners Hospitals for Children-Galveston, [3]Internal Medicine, and [4]Anesthesiology, University of Texas Medical Branch, Galveston, Texas; and [2]AminoScience Laboratories, Ajinomoto Company, Incorporated, Kawasaki, Japan

Am J Physiol Endocrinol Metab 291: E381–E387, 2006.
First published February 28, 2006; doi:10.1152/ajpendo.00488.2005.



In the elderly an higher dose of leucine is necessary to stimulate muscle protein synthesis

- Of EAAs, leucine is the most potent stimulator of muscle protein synthesis
- As with EAAs, the **elderly are less responsive to the stimulatory effect of leucine**



JAMDA 14 (2013) 542–559

ELSEVIER

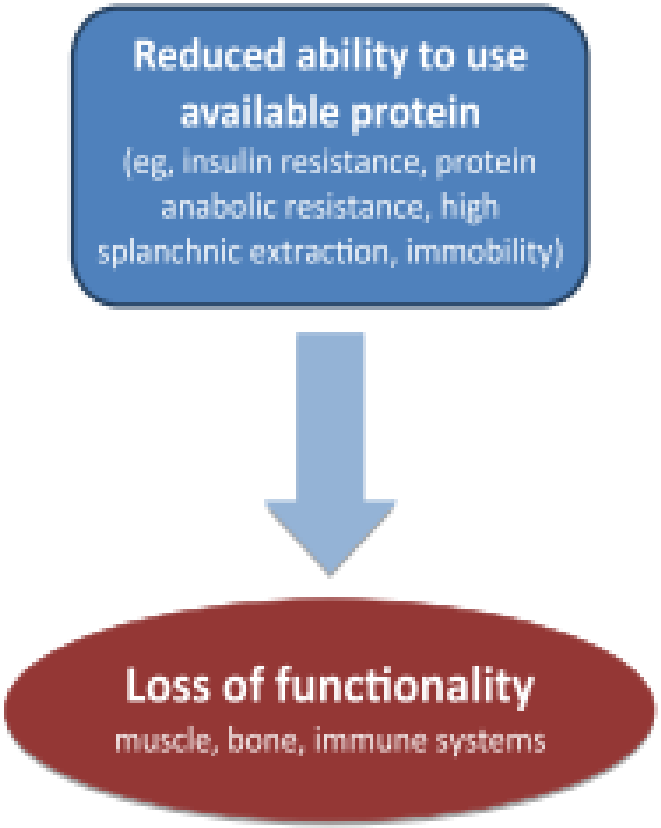
JAMDA

journal homepage: www.jamda.com

Special Article

Evidence-Based Recommendations for Optimal Dietary Protein Intake in Older People: A Position Paper From the PROT-AGE Study Group

Jürgen Bauer MD [a,*], Gianni Biolo MD, PhD [b], Tommy Cederholm MD, PhD [c], Matteo Cesari MD, PhD [d], Alfonso J. Cruz-Jentoft MD [e], John E. Morley MB, BCh [f], Stuart Phillips PhD [g], Cornel Sieber MD, PhD [h], Peter Stehle MD, PhD [i], Daniel Teta MD, PhD [j], Renuka Visvanathan MBBS, PhD [k], Elena Volpi MD, PhD [l], Yves Boirie MD, PhD [m]



Aging-related causes of protein shortfall. Such protein deficits have adverse consequences, including impairment of muscular, skeletal, and immune function.

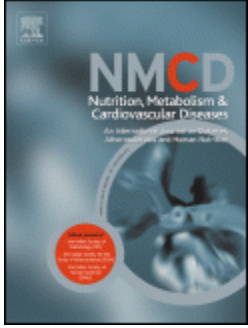
Nutrition, Metabolism & Cardiovascular Diseases (2011) 21, 922–932

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/nmcd

Nutrition, Metabolism & Cardiovascular Diseases



The third Italian National Food Consumption Survey, INRAN-SCAI 2005–06 – Part 1: Nutrient intakes in Italy

S. Sette*, C. Le Donne, R. Piccinelli, D. Arcella, A. Turrini, C. Leclercq, On Behalf of the INRAN-SCAI 2005–06 Study Group[1]

adults (18–64.9 years)	Males (n. 1068)					Females (n. 1245)				
	Mean	SD[a]	Median	5th[b]	95th[b]	Mean	SD[a]	Median	5th[b]	95th[b]
Protein (g/kg body weight)[c]	1.20	0.36	1.15	0.71	1.83	1.25	0.36	1.23	0.71	1.90

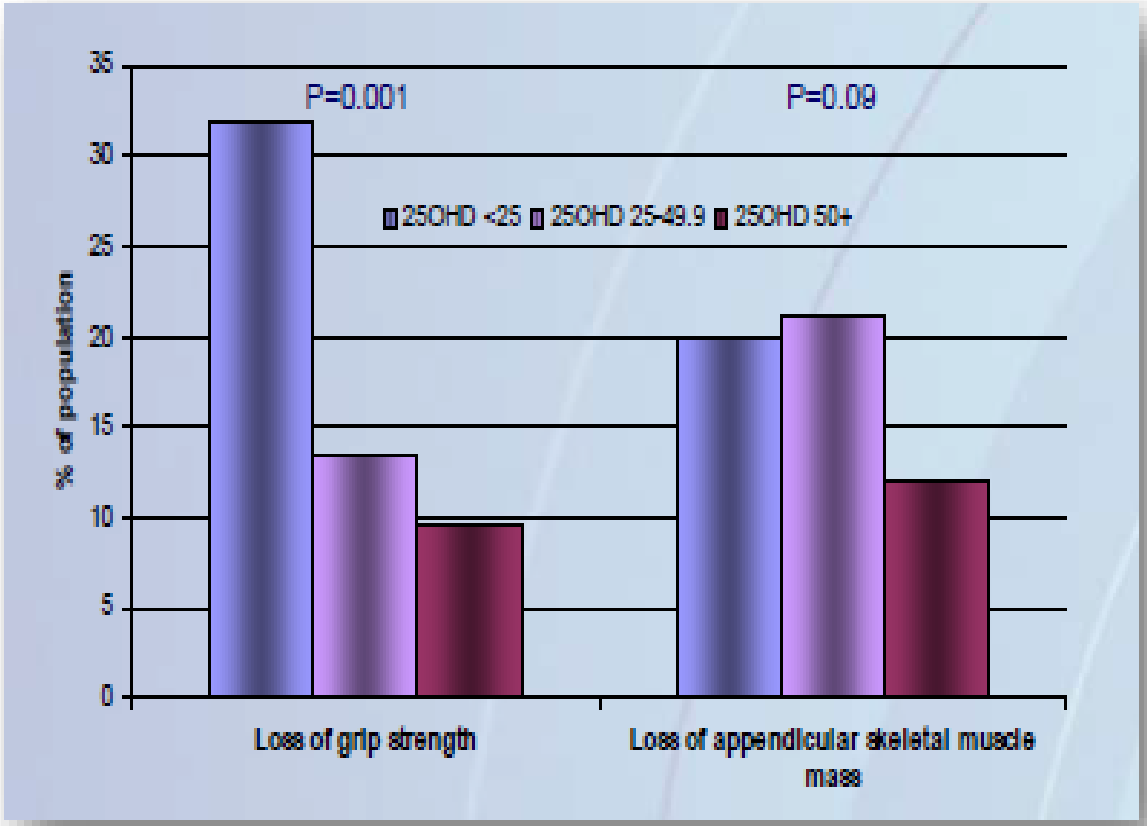
elderly (65 years and above)	Males (n. 202)					Females (n. 316)				
	Mean	SD[a]	Median	5th[b]	95th[b]	Mean	SD[a]	Median	5th[b]	95th[b]
Protein (g/kg body weight)	1.15	0.30	1.12	0.70	1.67	1.12	0.32	1.11	0.63	1.69

Mean **protein intake in gram per kilogram** of reported body weight decreased with age.

An independent association between low vitamin D levels and sarcopenia exists

Low vitamin D levels have been associated with:

- reduced muscle mass and strength
- gait impairments
- decreased balance
- increased risk of falls
- long term decline in physical performance



Especialli when 25OHD levels are <75nmol/l

Visser et al., J Clin Endocrinol Metab. 2003; Rolland et al,. J Nutr Health Aging 2008; Bischoff-Ferrari, Best Pract Res Cl Rh. 2009; Visvanathan and Chapman, Maturitas 2010; Ceglia, Curr Opin Clin Nutr Metab Care. 2009; Wicherts et al., J Clin Endocrinol Metab 2007

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Bone 80 (2015) 89–94

Contents lists available at ScienceDirect

Bone

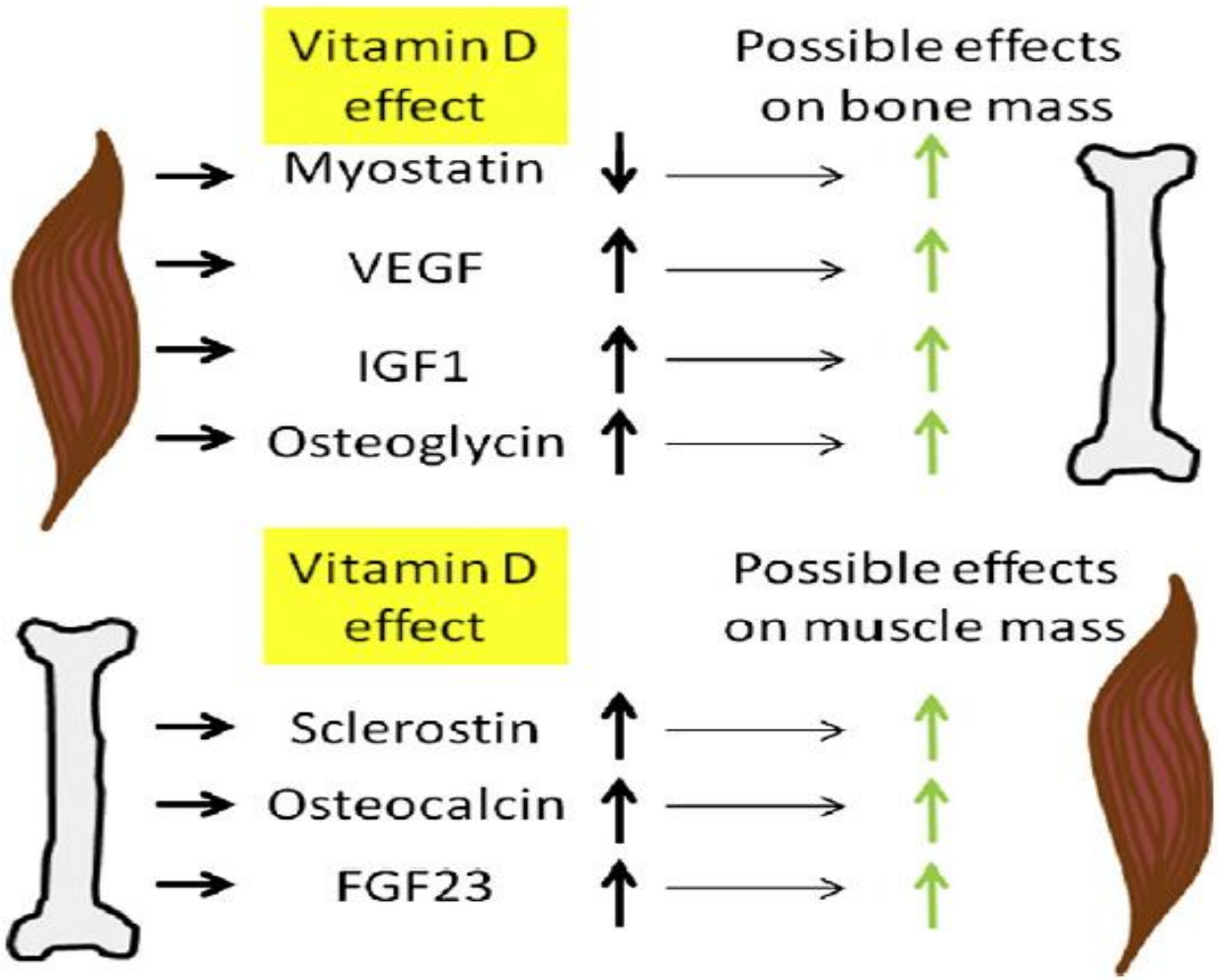
journal homepage: www.elsevier.com/locate/bone

Review

Bone muscle interactions and vitamin D

Jenny E. Gunton [a,b,c,d,e,*], Christian M. Girgis [a,b,c,d], Paul A. Baldock [b,e], Paul Lips [f]

- **FGF: fibroblast growth factor**
- **VEGF: vascular endothelial growth factor**



Nutrition, Metabolism & Cardiovascular Diseases (2011) 21, 922–932

available at www.sciencedirect.com

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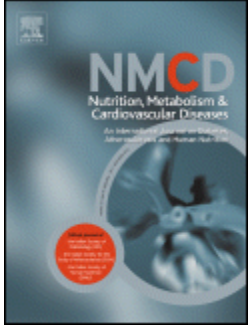
Nutrition, Metabolism & Cardiovascular Diseases



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S. Sette*, C. Le Donne, R. Piccinelli, D. Arcella, A. Turrini, C. Leclercq, On Behalf of the INRAN-SCAI 2005–06 Study Group[1]

adults (18–64.9 years)	Males (n. 1068)					Females (n. 1245)				
	Mean	SD[a]	Median	5th[b]	95th[b]	Mean	SD[a]	Median	5th[b]	95th[b]
Vitamin D (μg)	2.6	2.3	1.9	0.7	7.7	2.3	2.2	1.5	0.4	7.3

elderly (65 years and above)	Males (n. 202)					Females (n. 316)				
	Mean	SD[a]	Median	5th[b]	95th[b]	Mean	SD[a]	Median	5th[b]	95th[b]
Vitamin D (μg)	2.5	2.4	1.9	0.5	7.5	1.8	1.7	1.4	0.3	6.2

Mean intakes were found to decrease with age from teenagers to adults and to the elderly for phosphorus, zinc, thiamine, riboflavin, vitamin B6, vitamin E, **vitamin D** and vitamin B12.

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The Influence of Energy Intake on Protein Metabolism

By H. N. MUNRO and D. J. NAISMITH
Biochemistry Department, The University, Glasgow

Biochem J. 1953 May; 54(2): 191–197.

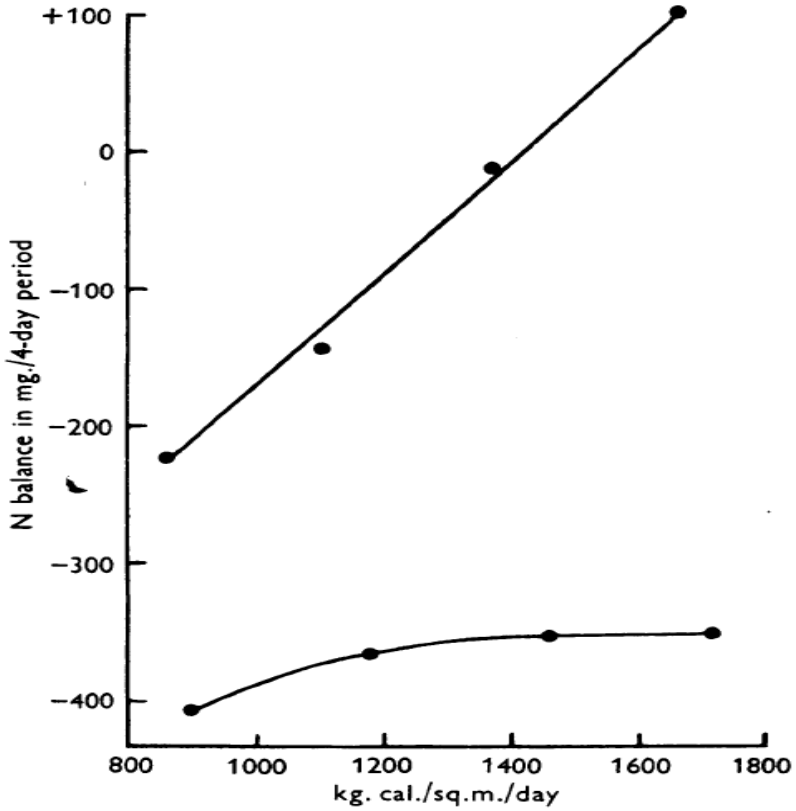


Fig. 1. The effect on nitrogen balance of changes in energy intake produced by alterations in dietary carbohydrate. Upper regression line, protein-containing diet (Exp. 1). Lower line (drawn freehand through points), protein-free diet (Exp. 3). Each point is the mean result obtained with four rats.

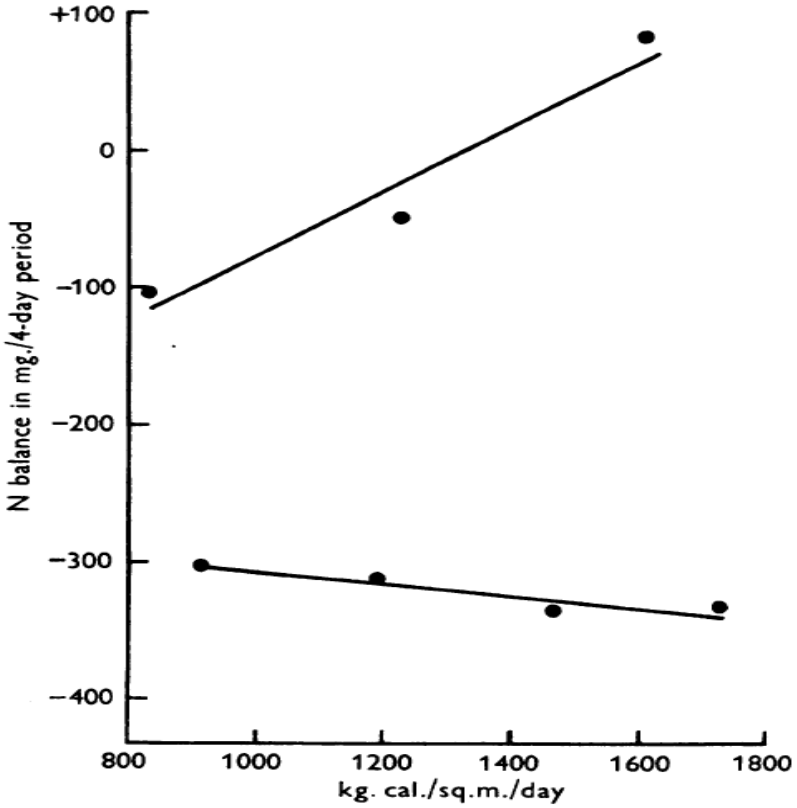


Fig. 2. The effect on nitrogen balance of changes in energy intake produced by alterations in dietary fat. Upper regression line, protein-containing diet (Exp. 2). Lower regression line, protein-free diet (Exp. 4). Each point is the mean result obtained with five rats (Exp. 2) or four rats (Exp. 4).

Produced by: Agriculture and Consumer Protection

Title: PROTEIN REQUIREMENTS FOR THE ELDERLY...

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS	ESN:FAO/WHO/UNU EPR/81/37 August 1981
WORLD HEALTH ORGANIZATION	
THE UNITED NATIONS UNIVERSITY	

Provisional Agenda Item 3.3.4

Joint FAO/WHO/UNU Expert Consultation on Energy and Protein Requirements

Rome, 5 to 17 October 1981

PROTEIN REQUIREMENTS FOR THE ELDERLY

Energy intake is of considerable importance in determining an adequate allowance of protein for the elderly: N balance is affected by E balance as well as by protein intake, thus complicating determinations of protein needs from N balance data.

original communications

Comparative nitrogen balance study between young and aged adults using three levels of protein intake from a combination wheat-soy-milk mixture[1–3]

Anthony H. R. Cheng, Ph.D., Ariel Gomez, M.S., James G. Bergan, Ph.D., Tung-Ching Lee, Ph.D., Fernando Monckeberg, M.D., and C. O. Chichester, Ph.D.


The American Journal of
CLINICAL NUTRITION
A Publication of the American Society for Nutrition
DECEMBER 2010 • VOLUME 92 • NUMBER 6

- **However, it is accepted that older people need smaller E intake and thus the provision of the same caloric intake for older people could lead to a more favorable E balance of the older men that would allow them to retain dietary protein better and thus could mask a greater need.**

Review Journal of the American College of Nutrition, Vol. 23, No. 6, 601S–609S (2004)

Protein Nutrition, Exercise and Aging

William J. Evans, PhD

- **L'esercizio fisico di potenza** determina un incremento della massa muscolare derivante dall'aumento relativo della sintesi di proteine rispetto alla loro degradazione.
- Questa risposta all'esercizio fisico di potenza è **ridotta nell'anziano** rispetto al giovane con conseguente riduzione dell'ipertrofia muscolare secondaria all'allenamento.

- in soggetti anziani sottoposti ad esercizio fisico di potenziamento muscolare, si ha una **riduzione del 10-15% dell'escrezione di N** rispetto ai sedentari
- ciò avviene per assunzioni proteica sia di 0.8 g/kg/die che di 1.6 g/kg/die, ad indicare che l'effetto dell'allenamento di potenza sull'utilizzo proteico è indipendente dall'introito proteico stesso.
- Da notare però che nello stesso studio i soggetti con il maggior introito proteico (1.6 g/kg/die), presentavano al termine dell'allenamento **maggiore risposta di tipo ipertrofico**, rispetto al gruppo con introito usuale di proteine (0.8 g/kg/die).

Review

Dietary Protein and Resistance Training Effects on Muscle and Body Composition in Older Persons

Wayne W. Campbell, PhD, and Heather J. Leidy, PhD

NUTRITION

- resistance exercise and a diet that includes adequate amounts of high-quality proteins are important to reduce the progression of sarcopenia
- resistance training can help improve strength, FFM, muscle mass balance and physical functioning capacities for frail elderly persons
- **older persons may experience a loss of FFM and muscle mass (and therefore subtle metabolic and physiological accommodation responses) with long-term ingestion of 0.8 g /kg/d for protein**, even when they performed resistance training

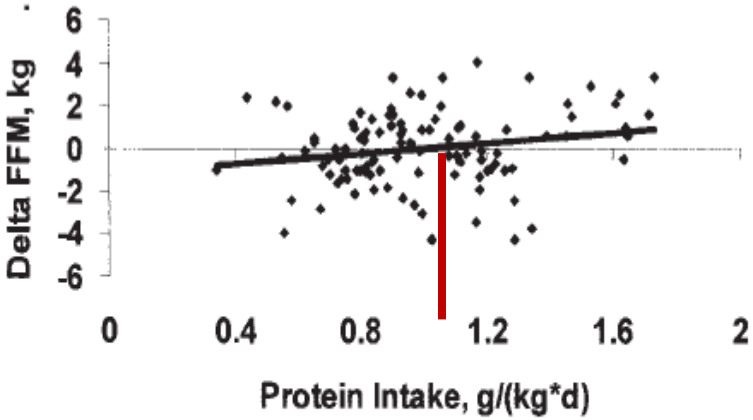


Fig. 1. Protein intake and fat-free mass changes after three months of resistance training in 50–80 year-old people. Regression equation: $\Delta FFM = (1.19955 \times \text{protein intake (kg)}) - 1.172$; $r = 0.202$, $P = 0.038$, $n = 106$ men and women.

Frailty in the Elderly: Contributions of Sarcopenia and Visceral Protein Depletion

Theodore B. VanItallie

Metabolism, Vol 52, No 10, Suppl 2 (October), 2003

Sarcopenia (gradual loss of both motor nerves and muscle fibers, particularly of the fast-twitch [IIa] fibers, with impaired function of the surviving myocytes)

⇐ **TBP declines** curvilinearly with age, with an accelerated decrease after 65 years (⇐ loss of skeletal muscle protein, visceral protein depletion) (Hansen RD, 2000)

⇐ involutional effects of aging-related **hormone changes**

⇐ **disuse** arising for the most part from chronic physical inactivity

⇐ **inadequate intake of protein and calories** (physiologic anorexia of aging, increase in the level of circulating cytokines, alterations of and release and activity of cholecystokinin)

⇒ **increased risk of falling, physical frailty, and disability.**

La sarcopenia in età geriatrica:

- etiopatogenesi
- **conseguenze cliniche e funzionali**

Linee di intervento

Il progetto PROVIDE

Frailty in the Elderly: Contributions of Sarcopenia and Visceral Protein Depletion

Theodore B. VanItallie

Metabolism, Vol 52, No 10, Suppl 2 (October), 2003

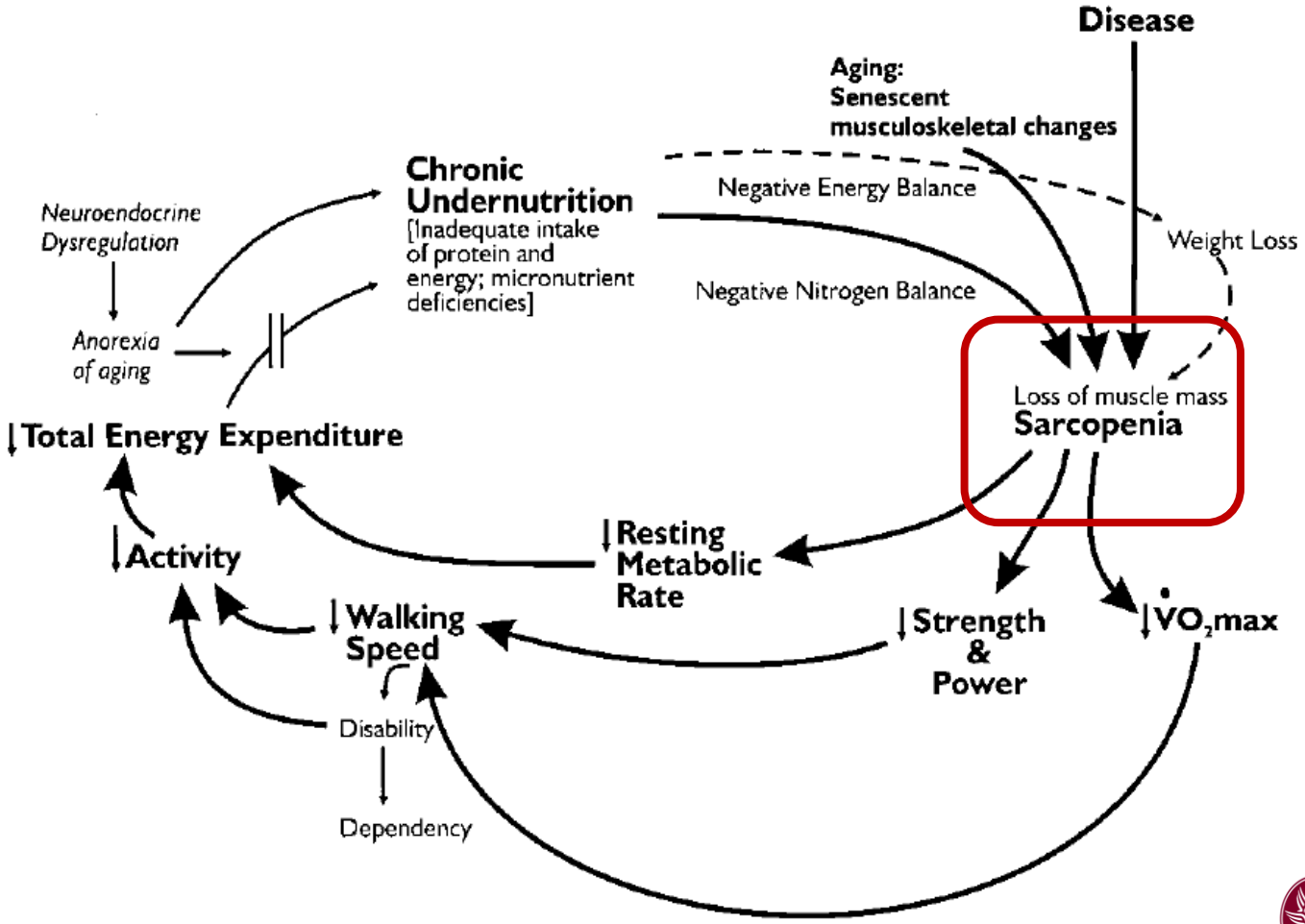
- "frailty is characterized by generalized **weakness**, impaired mobility and balance and poor endurance. **Loss of muscle strength** is an important factor in the process of frailty, and is the limiting factor for an individual's chances of living an independent life until death." (van den Beld AW, 2000)

- potential causes of frailty include **sarcopenia**, neuroendocrine decline, and immune dysfunction; frailty involves problems or difficulties in different functional domains: physical, **nutritive**, cognitive, and sensory (Strawbridge WJ, 1998)

Journal of Gerontology: MEDICAL SCIENCES
2001, Vol. 56A, No. 3, M146–M156

Frailty in Older Adults: Evidence for a Phenotype

Linda P. Fried,[1] Catherine M. Tangen,[2] Jeremy Walston,[1] Anne B. Newman,[3] Calvin Hirsch,[4] John Gottdiener,[5] Teresa Seeman,[6] Russell Tracy,[7] Willem J. Kop,[8] Gregory Burke,[9] and Mary Ann McBurnie[2] for the Cardiovascular Health Study Collaborative Research Group



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Musculoskeletal Frailty: A Geriatric Syndrome at the Core of Fracture Occurrence in Older Age

Calcif Tissue Int (2012) 91:161–177

E. Gielen · S. Verschueren · T. W. O'Neill · S. R. Pye · M. D. L. O'Connell · D. M. Lee · R. Ravindrarajah · F. Claessens · M. Laurent · K. Milisen · J. Tournoy · M. Dejaeger · F. C. Wu · D. Vanderschueren · S. Boonen

FRAILTY

Intrinsic ageing of the organ systems

- musculoskeletal system (sarcopenia and osteoporosis)
- non musculoskeletal systems

Functional deficits

Comorbidity

FRAILTY-syndrome

Clinical expression of frailty

- Reduced mobility
- Walking instability
- Recurrent falls
- Loss of strength
- Exhaustion
- Inactivity
- Confinement to bed

- Reduced appetite
- Malnutrition
- Weight loss
- Incontinence
- Cognitive deterioration
- Delirium
- Dependence

BMC Geriatrics

BMC Geriatrics 2008, 8:34

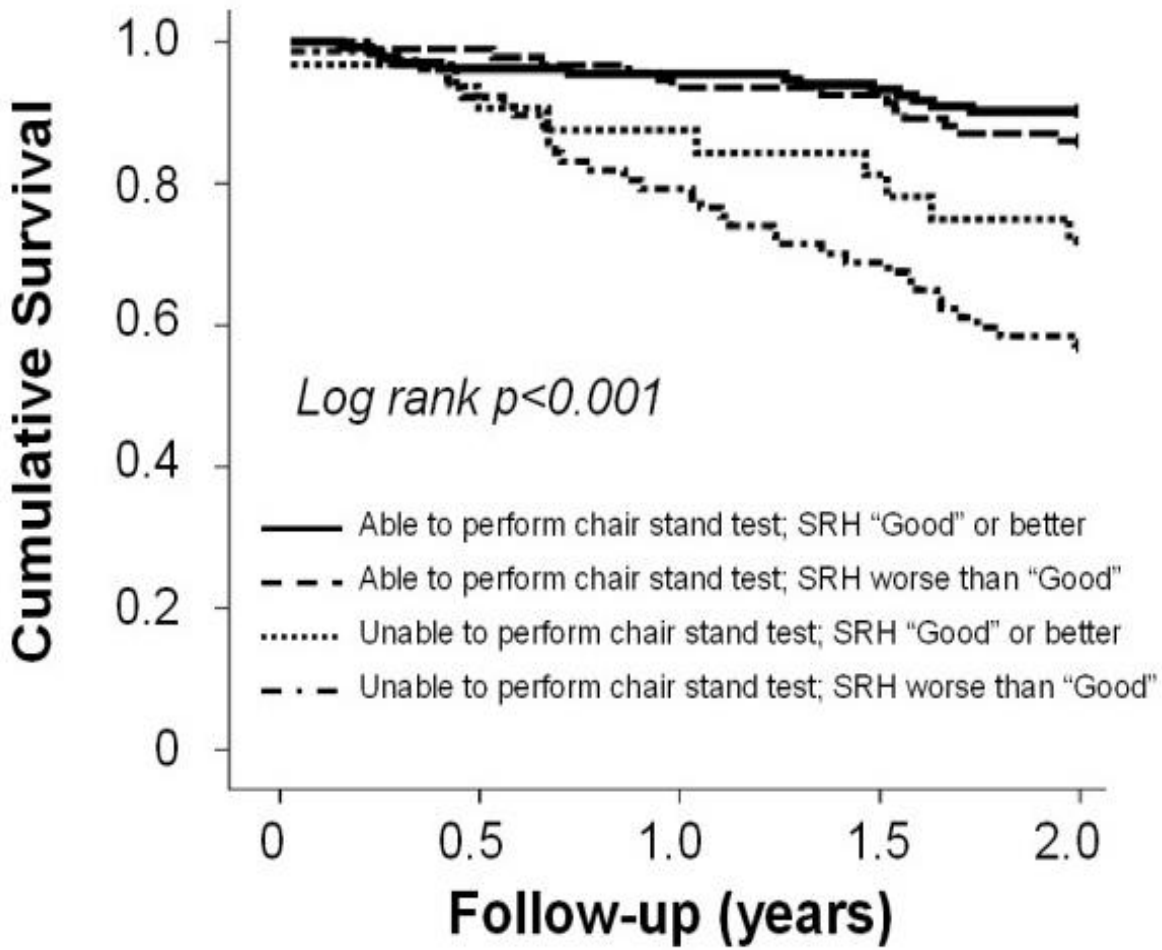
BioMed Central

Research article

Open Access

Physical function and self-rated health status as predictors of mortality: results from longitudinal analysis in the ilSIRENTE study

Matteo Cesari*[1,2], Graziano Onder[1], Valentina Zamboni[1], Todd Manini[2], Ronald I Shorr[2,3], Andrea Russo[1], Roberto Bernabei[1], Marco Pahor[2] and Francesco Landi[1]



Kaplan-Meier survival curves for mortality according to the ability to perform the chair stand test and self-rated health (SRH) score.

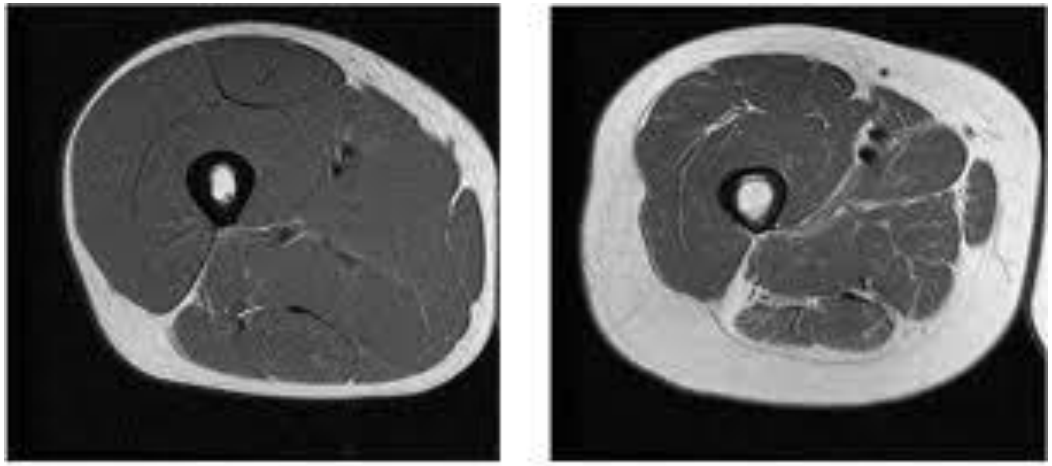
The Healthcare Costs of Sarcopenia in the United States

Ian Janssen, PhD,† Donald S. Shepard, PhD,§ Peter T. Katzmarzyk, PhD,†‡ and Ronenn Roubenoff, MD, MHS**

J Am Geriatr Soc 52:80–85, 2004.

The healthcare costs of sarcopenia were estimated based on the effect of sarcopenia on increasing physical disability risk in older persons

$ 18.5 billion/year
($10.8 billion in M, $7.7 billion in F)
1.5% of total healthcare expenditures for that year



Age 25 Age 63

La sarcopenia in età geriatrica:
- etiopatogenesi
- conseguenze cliniche e funzionali

Linee di intervento

Il progetto PROVIDE

How nutritional approach should be characterized to optimize post-prandial anabolic action of dietary proteins?

Increase protein intake	• Meet the age-specific RDAs
Increase amino acid bioavailability	• Distribution of protein intake • Digestion rate
Use specific substrates	• Leucine • Vitamin D

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Nutrition

journal homepage: www.nutritionjrnl.com

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Applied nutritional investigation

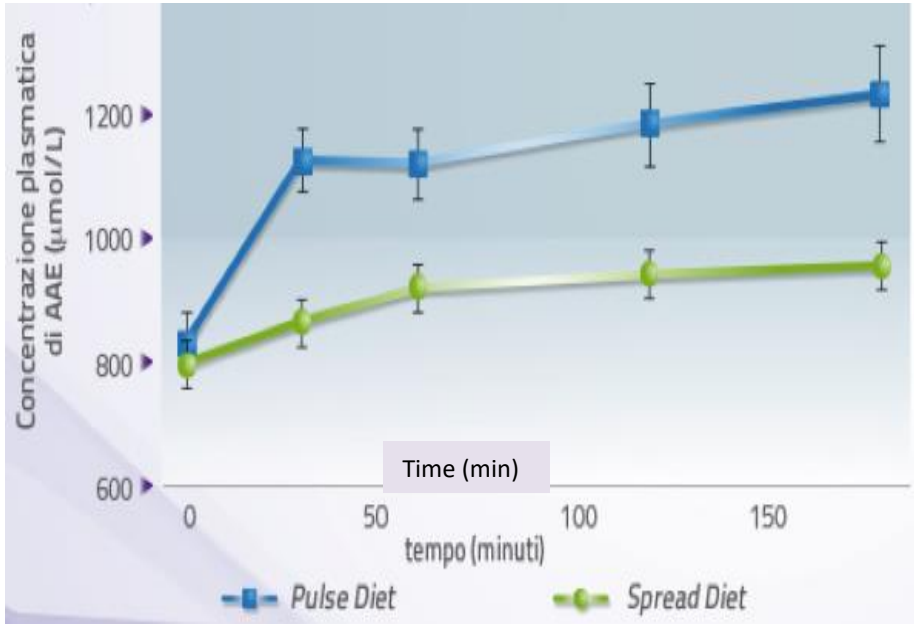
Long-lasting improved amino acid bioavailability associated with protein pulse feeding in hospitalized elderly patients: A randomized controlled trial

Olivier Bouillanne M.D., Ph.D. [a,b,*], Nathalie Neveux Pharm. D., Ph.D. [b,c], Ioannis Nicolis Ph.D. [d], Emmanuel Curis Pharm. D., Ph.D. [d], Luc Cynober Pharm. D., Ph.D. [b,c], Christian Aussel Pharm. D., Ph.D. [b,e]

[a] Service de Gérontologie 2, Hôpital Émile-Roux, AP-HP, Limeil-Brévannes, France
[b] Laboratoire de Biologie de la Nutrition, Université Paris Descartes, Paris, France
[c] Service Interhospitalier de Biochimie, AP-HP, Hôpitaux Cochin et Hôtel-Dieu, Paris, France
[d] Laboratoire de Biomathématiques, Université Paris Descartes, Faculté de Pharmacie, Paris, France
[e] Unité de Nutrition, PUI, AP-HP, Hôpital Henri-Mondor, Créteil, France

- **In a spread diet (SD):** dietary protein was spread over the four daily meals.
- **In a pulse diet (PD):** 72% of dietary protein (averaging 1.31 g/kg body weight daily) was consumed in one meal at noon.

Protein pulse feeding was more efficient than protein spread feeding at increasing plasma postprandial AA concentrations,

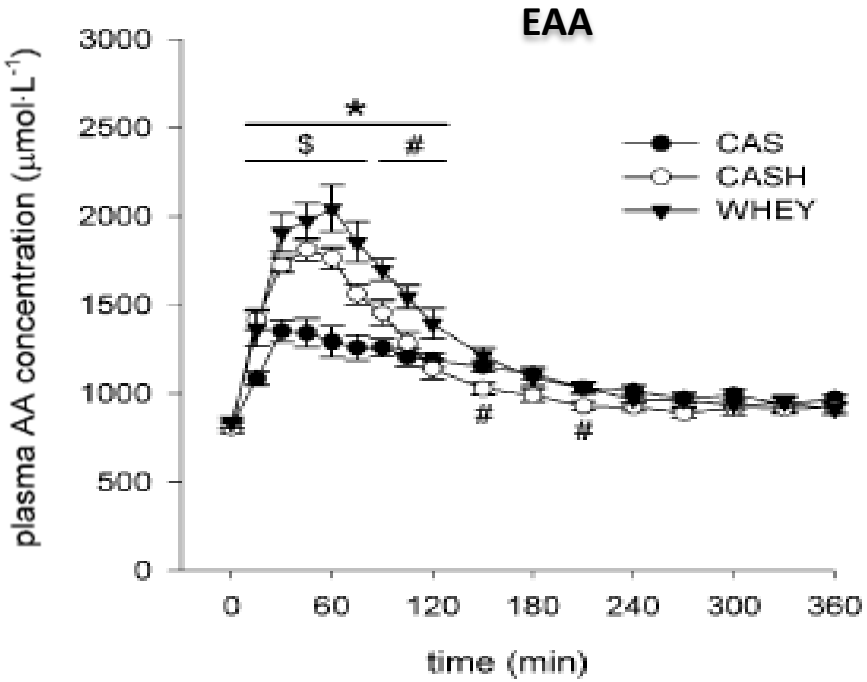


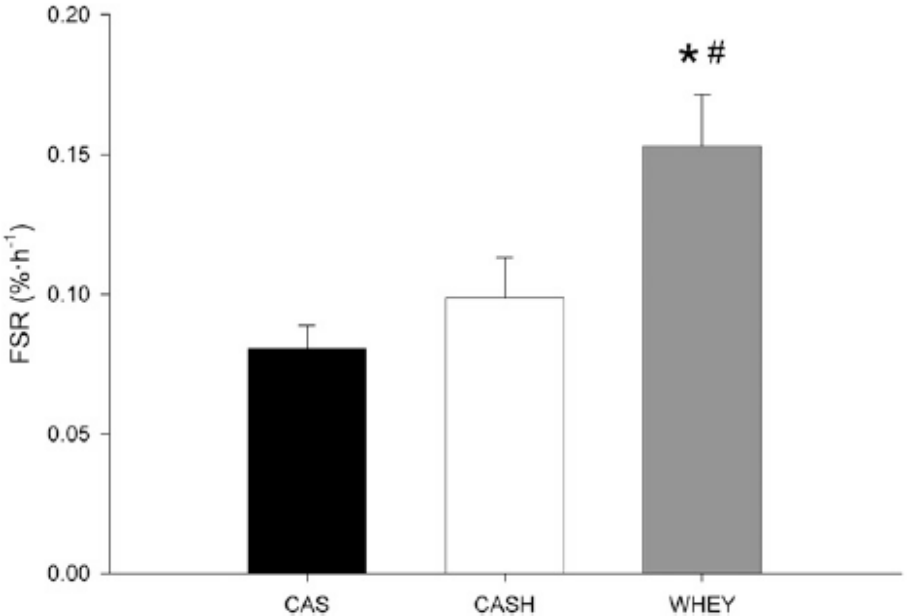
Protein pulse feeding was significantly more efficacious than protein spread feeding in improving LM index

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

Am J Clin Nutr. 2011 May;93(5):997-1005.

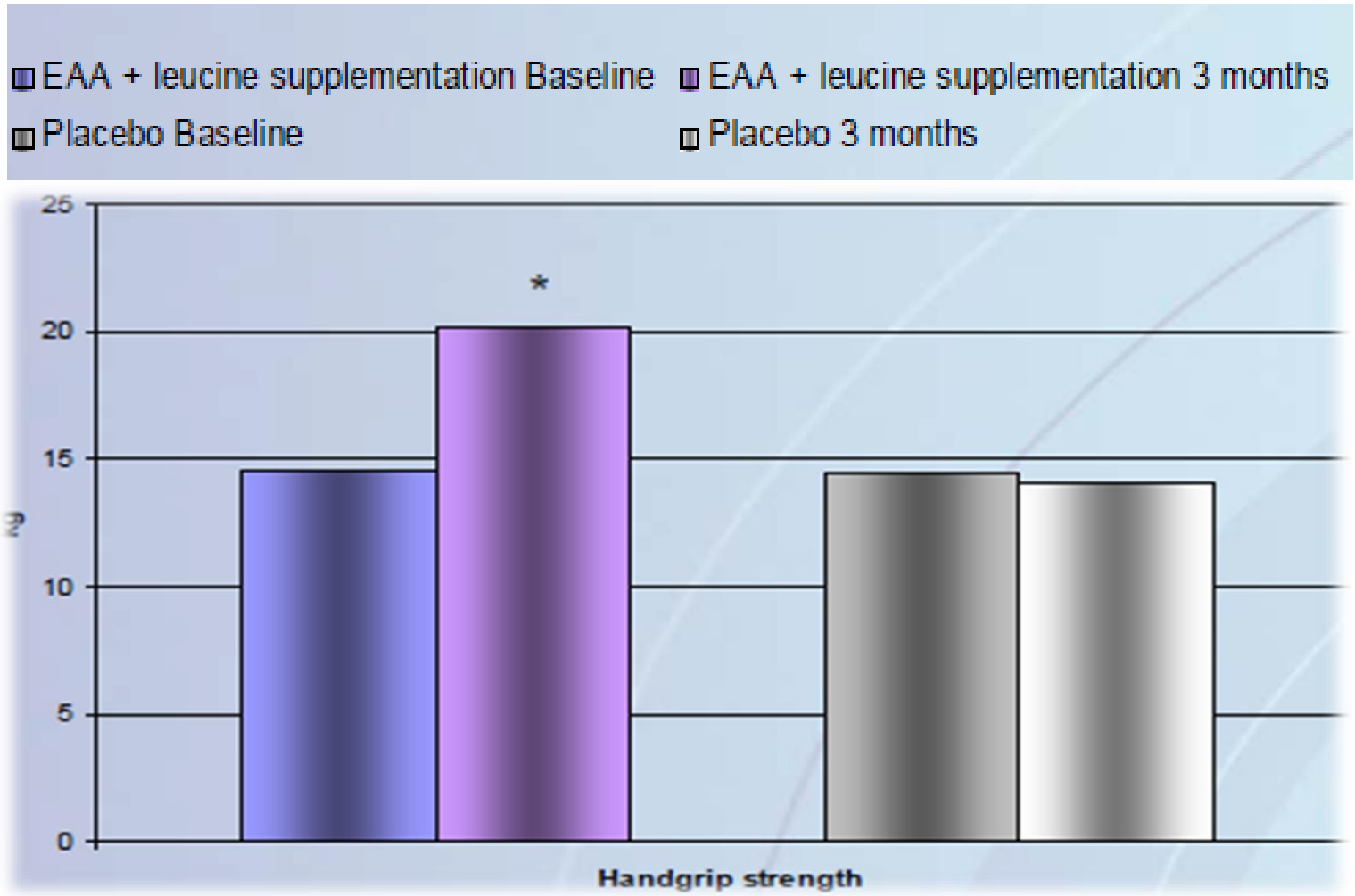




Whey protein stimulates postprandial muscle protein accretion more effectively than do casein and casein hydrolysate in older men. This effect is attributed to a combination of whey's faster digestion and absorption kinetics and higher leucine content.

Supplementation of leucine (with EAA) significantly increases muscle strength (handgrip strenght)

11, 5 g EAA
3.0 g Leucine



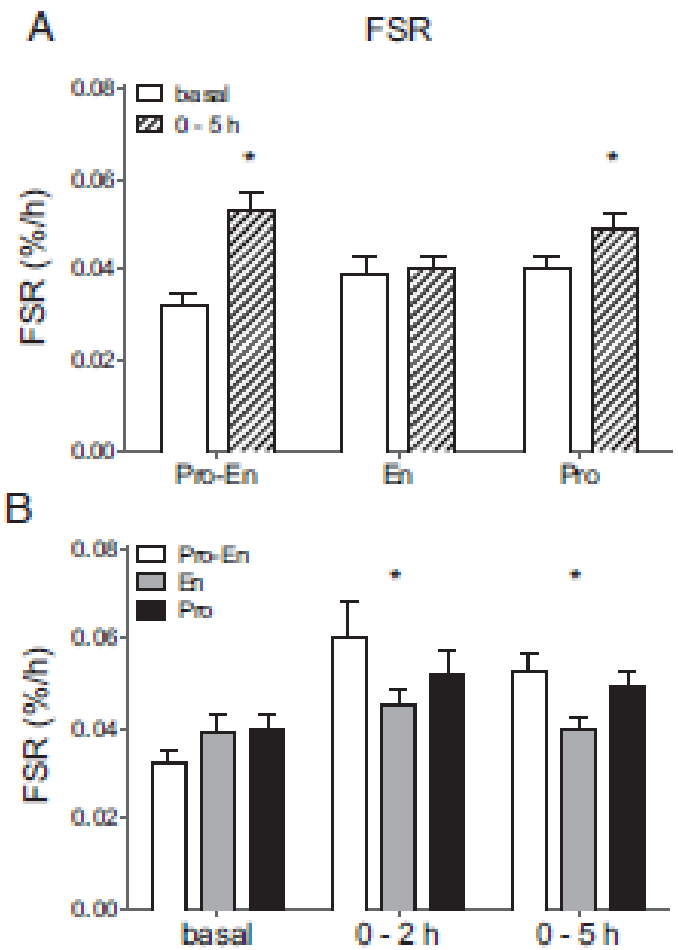
Scognamiglio et al., Aging Clin Exp Res 2004; Scognamiglio et al., Gerontology 2005; Borsheim et al., Clin Nutr 2008

Impact of the macronutrient composition of a nutritional supplement on muscle protein synthesis rates in older men: a randomized, double blind, controlled trial

Irene Fleur Kramer[1,3], Lex B. Verdijk[1], Henrike M. Hamer[1], Sjors Verlaan[2], Yvette Luiking[2], Imre W.K. Kouw[1], Joan M. Senden[1], Janneau van Kranenburg[1], Annemarie P. Gijsen[1], Martijn Poeze[1,3], Luc J.C. van Loon[1]

ORIGINAL ARTICLE

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM



- **Pro-En:** 21 g of leucine-enriched whey protein with carbohydrate (9 g) and fat (3g)
- **Pro:** isonitrogenous amount of 21 g of leucine-enriched whey protein without carbohydrate and fat
- **En:** an isocaloric mixture (628 kJ) containing carbohydrate and fat only

Supplementation of an adequate amount of dietary protein could be essential to preserve muscle mass in elderly, independent of additional energy.

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JAMDA 14 (2013) 542e559

journal homepage: www.jamda.com

Special Article

Evidence-Based Recommendations for Optimal Dietary Protein Intake in Older People: A Position Paper From the PROT-AGE Study Group

Jürgen Bauer MD [a,*], Gianni Biolo MD, PhD [b], Tommy Cederholm MD, PhD [c], Matteo Cesari MD, PhD [d], Alfonso J. Cruz-Jentoft MD [e], John E. Morley MB, BCh [f], Stuart Phillips PhD [g], Cornel Sieber MD, PhD [h], Peter Stehle MD, PhD [i], Daniel Teta MD, PhD [j], Renuka Visvanathan MBBS, PhD [k], Elena Volpi MD, PhD [l], Yves Boirie MD, PhD [m]

PROT-AGE recommendations for dietary protein intake in *healthy* older adults

- To maintain and regain muscle, older people need more dietary protein than do younger people; older people should consume an average daily intake in the range of 1.0 to 1.2 g/kg BW/d.
- The per-meal anabolic threshold of dietary protein/amino acid intake is higher in older individuals (ie, 25 to 30 g protein per meal, containing about 2.5 to 2.8 g leucine) in comparison with young adults.
- Protein source, timing of intake, and amino acid supplementation may be considered when making recommendations for dietary protein intake by older adults.
- More research studies with better methodologies are desired to fine tune protein needs in older adults.

Up to 1.2 -1.5 g/Kg/die during acute or chronic diseases

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PROT-AGE recommendations on dietary protein and amino acid quality for older people

- The list of indispensable amino acids s qualitatively identical for young and old adults.
- There is no evidence that protein digestion and absorption capacities change significantly with aging.
- "Fast" proteins may have some benefits over "slow" proteins in muscle protein metabolism.
- Dietary enrichment with leucine or a mixture of branched-chain amino acids may help enhance muscle mass and muscle function, but further studies are needed to support specific recommendations.
- β-HMB may attenuate muscle loss and increase muscle mass and strength in older people, but further studies are needed to support specific recommendations.
- Creatine supplementation may be justified for older people, especially those who are creatine-deficient or at high risk of deficiency.

Vitamin D and Sarcopenia/Falls

Joan M. Lappe,[*,1] *and Neil Binkley*[2]

Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. 18, no. 4, 478–482, 2015

- Some small prospective studies do find **vitamin D supplementation to increase type II muscle fiber number and cross-sectional area**.
- In contrast, others find no association of 25(OH)D with muscle mass or strength.
- Meta-analyses are conflicting, finding supplemental vitamin D to have beneficial effects on strength and balance or no effect on strength .
- It is not surprising that meta-analyses have failed to clarify the role of vitamin D inadequacy with muscle function.
  - This lack of clarity likely reflects multiple confounders and design concerns in existing studies.
  - An important limitation of most studies is nonrecognition that the serum 25(OH)D response to vitamin D supplementation is highly variable. It is self-evident that individuals who receive vitamin D supplementation but do not alter their serum 25(OH)D would not be expected to experience a biologic effect.

More than healthy bones: a review of vitamin D in muscle health

S. Bobo Tanner and Susan A. Harwell

Ther Adv Musculoskel Dis

2015, Vol. 7(4) 152–159

- Experimental techniques have allowed detection of the **VDR on skeletal muscle** and in cerebellar tissue

- These data suggest that **vitamin D supplementation** may contribute to the health and maintenance of muscle function.

- The role of vitamin D in muscle health and function remains an exciting and growing area of research with substantial clinical implications.

Nutritional management of Ageing/Frailty

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 Vit D intake

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La sarcopenia in età geriatrica:
- etiopatogenesi
- conseguenze cliniche e funzionali

Linee di intervento

Il progetto PROVIDE

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Original Study

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

Jürgen M. Bauer MD, PhD [a,*], Sjors Verlaan MSc [b,c], Ivan Bautmans PhD [d], Kirsten Brandt PhD [e], Lorenzo M. Donini MD, PhD [f], Marcello Maggio MD, PhD [g], Marion E.T. McMurdo MD, PhD [h], Tony Mets MD, PhD [d], Chris Seal PhD [e], Sander L. Wijers PhD [b], Gian Paolo Ceda MD [g], Giuseppe De Vito MD, PhD [i], Gilbert Donders MD, PhD [j], Michael Drey MD [k], Carolyn Greig PhD [l], Ulf Holmbäck PhD [m], Marco Narici PhD [n], Jamie McPhee PhD [o], Eleonora Poggiogalle MD [f], Dermot Power MD, PhD [p], Aldo Scafoglieri PhD [d], Ralf Schultz MD, PhD [q], Cornel C. Sieber MD [r], Tommy Cederholm MD, PhD [m]

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[n] *Faculty of Medicine, MRC ARUK Centre for Musculoskeletal Ageing Research, Royal Derby Hospital, University of Nottingham, Derby, United Kingdom*
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Original Study

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- Multicenter, randomized, controlled, double-blind, 2 parallel-group trial among 380 sarcopenic primarily independent-living older adults
- SPPB 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**.

Table 1
Baseline Demographic and Clinical Characteristics

	Active n = 184	Control n = 196
Age, mean (SD), y	77.3 (6.7)	78.1 (7.0)
Sex, female n (%)	120 (65.2)	129 (65.8)
Living situation, n (%)		
Institutionalized	18 (9.8)	19 (9.7)
Home care	4 (2.2)	10 (5.1)
Living independently	162 (88.0)	167 (85.2)
Mini Mental State Examination, median (IQR)	29.0 (27.0–30.0)	29.0 (28.0–30.0)
Hemoglobin concentration, median (IQR), mmol/L	8.4 (7.9–8.9)	8.5 (8.0–8.9)
BMI, mean (SD), kg/m^2	26.0 (2.5)	26.2 (2.8)
Mini Nutritional Assessment Short-Form (MNA-SF), n (%)		
Malnutrition	1 (0.5)	1 (0.5)
Risk of malnutrition	15 (8.2)	19 (9.7)
No malnutrition	168 (91.3)	176 (89.8)
Protein intake, median (IQR), g/kg body weight/day	1.0 (0.9–1.2)	1.0 (0.8–1.2)
Fasting glucose concentration, median (IQR), mmol/L	5.2 (4.9–5.8)	5.2 (4.9–5.7)
Fasting insulin concentration, median (IQR), mU/L	9.0 (5.0–13.0)	9.0 (6.0–14.0)
Handgrip strength male, median (IQR), kg	26.8 (22.0–30.8)	27.1 (22.0–32.1)
<30 kg, n (%)	45 (70.3)	45 (69.2)
Handgrip strength female, median (IQR), kg	16.5 (13.5–21.5)	16.8 (14.2–20.5)
<20 kg n, (%)	80 (69.6)	94 (74.0)
Gait speed n (%), <0.8 m/s	101 (54.9)	109 (55.6)
SMI (BIA), n (%)		
Normal SMI	0 (0)	0 (0)
Class I sarcopenia*	154 (84)	164 (84)
Class II sarcopenia†	30 (16)	32 (16)
Appendicular muscle mass (DXA), mean (SD), kg	17.9 (4.1)	17.5 (3.8)

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Per serving *	Unit	Active	Control
Energy	kcal	150	150
Protein (from whey protein source) *Essential amino acids* *Leucine*	g *g* *g*	21 *10* *3*	0 *0* *0*
Carbohydrates	g	9.4	31.4
Fat	g	3	3
Vitamin D	IU	800	0
Calcium	mg	500	0

Luiking *et al. Nutrition Journal* 2014, **13**:9
http://www.nutritionj.com/content/13/1/9

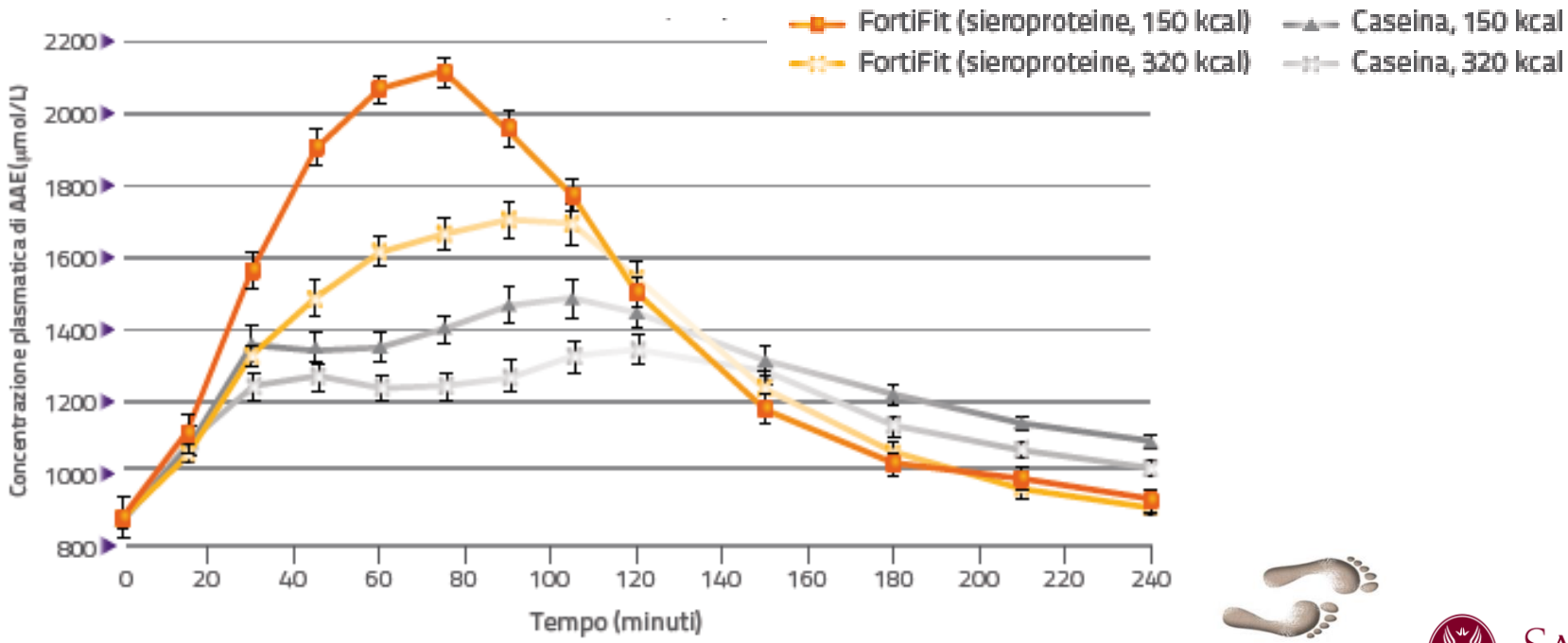
NUTRITION JOURNAL

RESEARCH Open Access

Postprandial muscle protein synthesis is higher after a high whey protein, leucine-enriched supplement than after a dairy-like product in healthy older people: a randomized controlled trial

Yvette C Luiking[1,2], Nicolaas EP Deutz[2], Robert G Memelink[1], Sjors Verlaan[1] and Robert R Wolfe[3*]

- **Prodotto A (W150):** a base di sieroproteine, leucina, 150 Kcal per dose (FortiFit)
- **Prodotto B (W320):** a base di sieroproteine, leucina, 320 Kcal per dose
- **Prodotto C (C150):** a base di caseina, 150 Kcal per dose
- **Prodotto D (C320):** a base di caseina, 320 Kcal per dose



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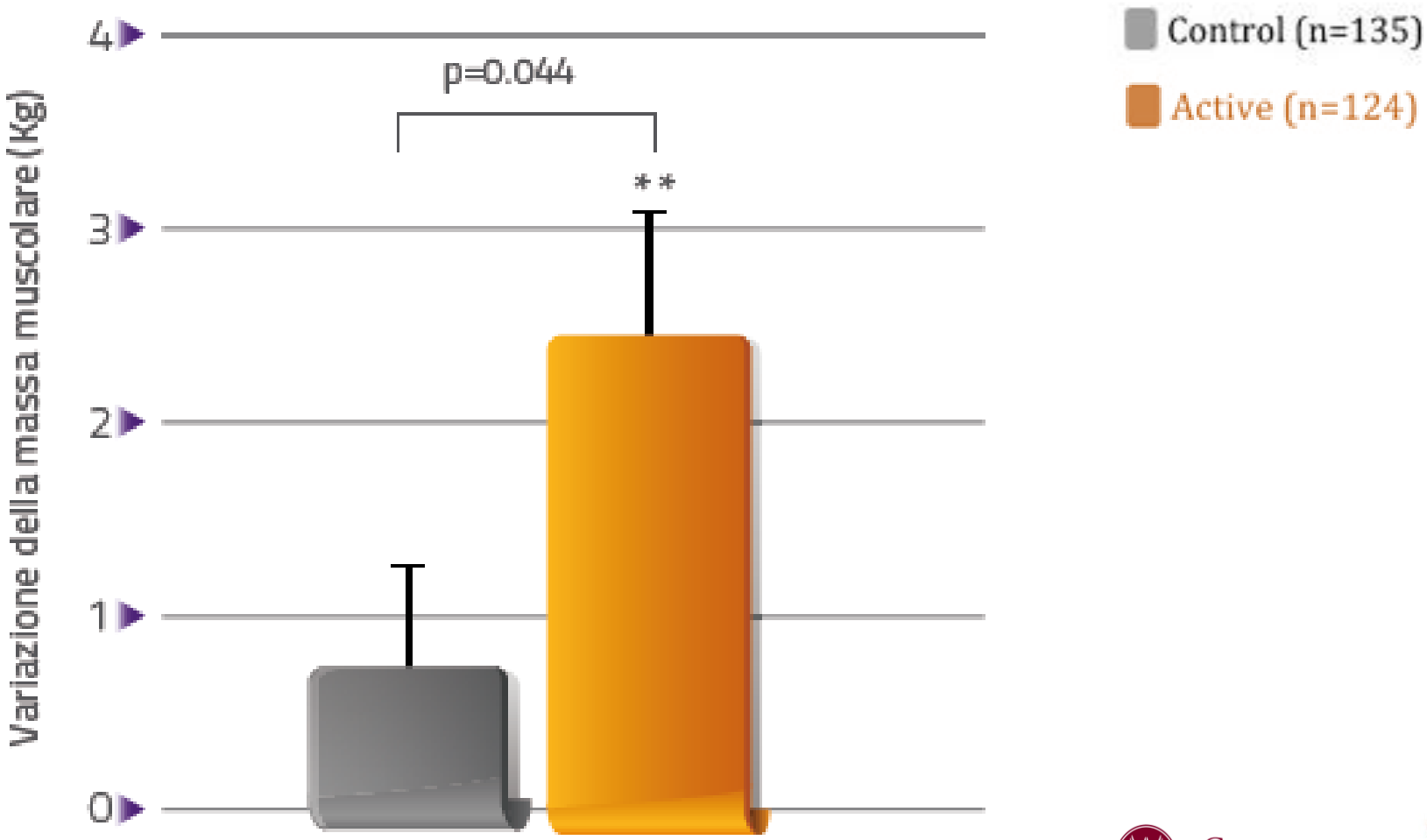

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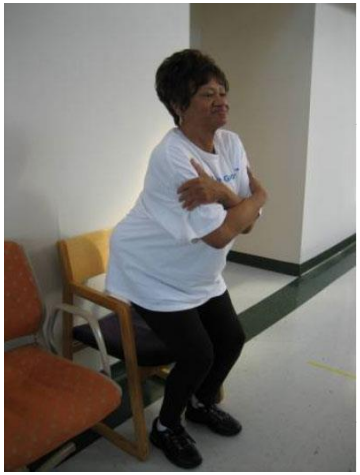

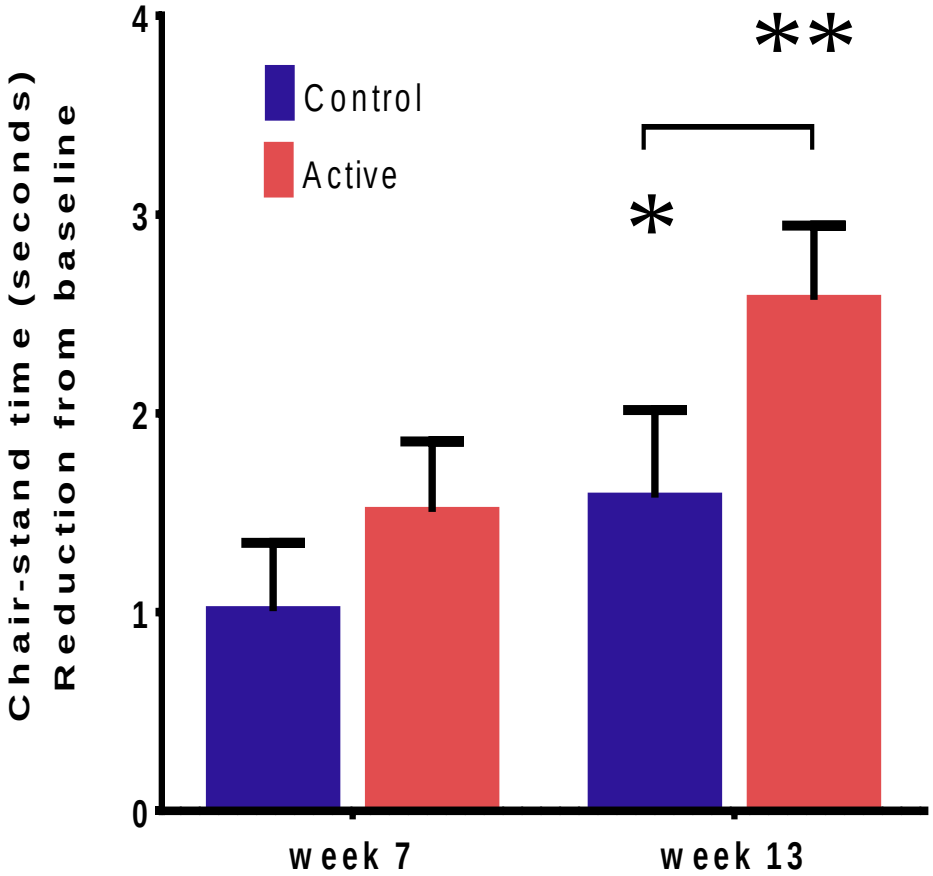

**p<0.001

	Mean (SD)	Change From Baseline, Mean (SD)	
	Baseline	Week 7	Week 13
Chair-stand time, s[††]			
Active[§§]	17.1 (15.2, 21.2)	−1.4 (−3.3–0.4)	−2.5 (−4.2 to −0.6)**
Control[‖‖]	17.6 (14.6, 20.6)	−1.0 (−3.0–1.1)	−1.2 (−3.3–0.8)**

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In sarcopenic older adults, 13-week intervention of a vitamin D and leucine-enriched whey protein oral nutritional supplement is effective in improving:

- **Appendicular skeletal muscle mass**
- **Lower-extremity function**

- A specific nutritional supplementation alone might benefit geriatric patients, <u>especially relevant for those who are unable to exercise</u>

- **Nutritional supplementation positively influence measures of sarcopenia and could prevent mobility disability.**

La sarcopenia in età geriatrica:
- etiopatogenesi
- conseguenze cliniche e funzionali

Linee di intervento

Il progetto PROVIDE

Conclusione

Clinical Nutrition (2006) 25, 330–360

ELSEVIER

Clinical Nutrition

http://intl.elsevierhealth.com/journals/clnu

ESPEN GUIDELINES

ESPEN Guidelines on Enteral Nutrition: Geriatrics ☆

D. Volkert[a,*,1], Y.N. Berner[b], E. Berry[c], T. Cederholm[d], P. Coti Bertrand[e], A. Milne[f], J. Palmblad[g], St. Schneider[h], L. Sobotka[i], Z. Stanga[j], DGEM: ☆☆ R. Lenzen-Grossimlinghaus, U. Krys, M. Pirlich, B. Herbst, T. Schütz, W. Schröer, W. Weinrebe, J. Ockenga, H. Lochs

The administration of ONS has been reported to

- **increase in E and nutrient intake**
- have positive effects on **nutritional status** irrespective of the main diagnosis (even in demented subjects)
- improve **functional status** and **quality of life**
- reduce the risk of developing **pressure ulcers** functional improvements (in several studies)
- reduce **complications** in geriatric patients after hip fracture and orthopaedic surgery
- have significant benefit with respect to **hospital stay** (in some studies)
- increase in **survival**

Impact of Oral Nutritional Supplementation on Hospital Outcomes

VOL. 19, NO. 2 FEBRUARY 2013 ■ THE AMERICAN JOURNAL OF MANAGED CARE ■

Tomas J. Philipson, PhD; Julia Thornton Snider, PhD; Darius N. Lakdawalla, PhD; Benoit Stryckman, MA; and Dana P. Goldman, PhD

	Regression Specification					
	(1)	(2)	(3)	(4)	(5)	(6)
Subset of Matched Sample Analyzed	**All**	**All**	**Follow-up at least 1 d**	**Follow-up 1 d to 3 y**	**Follow-up 1 d to 2 y**	**Follow-up 1 d to 1 y**
Model	OLS	IV	IV	IV	IV	IV
Effect of any ONS use on LOS, d (SE)	2.879[b] (0.0432)	−2.291[b] (0.0657)	−1.714[b] (0.0721)	−2.299[b] (0.0843)	−2.407[b] (0.0892)	−2.585[b] (0.103)
Predicted LOS without ONS, d	8.30	10.88	10.5	10.93	11.07	11.32
Predicted LOS with ONS, d	11.18	8.59	8.79	8.63	8.66	8.74
Change due to ONS use	34.7%	−21.0%	−16.3%	−21.0%	−21.8%	−22.8%
Observations, n	1,160,088	1,160,088	862,960	735,636	670,823	566,682

IV indicates instrumental variable; LOS, length of stay; OLS, ordinary least squares; ONS, oral nutritional supplement; SE, standard error.
[a]Regression results were from a sample of ONS episodes matched 1:1 to non-ONS episodes on propensity to receive ONS. Terminal episodes and tube-fed episodes were excluded. The instrument was the fraction of episodes in a given hospital in a given quarter involving ONS use. Standard errors took into account repeated observations of the same individual.
[b]Significant at the 1% level.

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frontiers in PHARMACOLOGY

ORIGINAL RESEARCH ARTICLE
published: 04 May 2012
doi: 10.3389/fphar.2012.00078

The budget impact of oral nutritional supplements for disease related malnutrition in elderly in the community setting

***Karen Freijer*[1]*, *Mark J. C. Nuijten*[2] *and Jos M. G. A. Schols*[3]**

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[2] *Ars Accessus Medica, Jisp, Netherlands*
[3] *CAPHRI – School for Public Health and Primary Care, Department of General Practice and Department of Health Services Research, Maastricht University, Maastricht, Netherlands*

Table 2 | Costs of DRM in elderly (>60 years) per illness category in community in the Netherlands in 2009 (million Euros)*.

Illness category	Residential home	Home care	Total
Infectious diseases	720.000	1.160.000	1.880.000
Cancer	1.816.765	16.083.713	17.900.478
Endocrinology	971.757	3.215.000	4.186.757
Diabetes	1.228.387	3.215.000	4.443.387
Hematology	230.000	1.520.000	1.750.000
Psychiatry	83.775.896	11.047.385	94.823.280
Neurology	997.523	4.782.222	5.779.745
Dementia	1.394.273	10.294.199	11.688.472
Spinal cord injury	1.193.333	7.173.333	8.366.667
Eye/ear	0	0	0
Cardiovascular	10.206.524	15.590.556	25.797.080
CVA, hemiparesis	13.288.667	16.026.517	29.315.184
Respiratory	3.709.924	8.221.544	11.931.468
Gastro-intestinal	913.889	7.731.331	8.645.220
Urogenital	904.896	0	904.896
Dermatology	436.739	2.446.434	2.883.173
Musculoskeletal	2.976.678	32.377.870	35.354.549
Congenital	0	0	0
Traumata – intoxications	4.849.538	5.143.498	9.993.036
Hip replacement	0	0	0
Total	109.730.125	146.028.603	275.643.390

**Based on cost of care per illness of the Dutch National Institute for Public Health and the Environment (RIVM; Slobbe et al., 2006) indexed to 2009.*

Table 3 | Results of the base case analysis: budget impact of ONS (without and with ONS) in elderly with DRM in the community in the Netherlands in 2009 (million Euros).

	Without ONS	With ONS	Savings
Costs of DRM	€ 275.643	€ 205.322	€ 70.321
Costs of ONS	€ 0	€ 57.335	–€ 57.335
Budget impact	€ 275.643	€ 262.657	€ 12.986

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La vieillesse n’est pas si mauvais quand vous considérez l’alternative.

Maurice Chevalier

(Paris, 1888-1972)