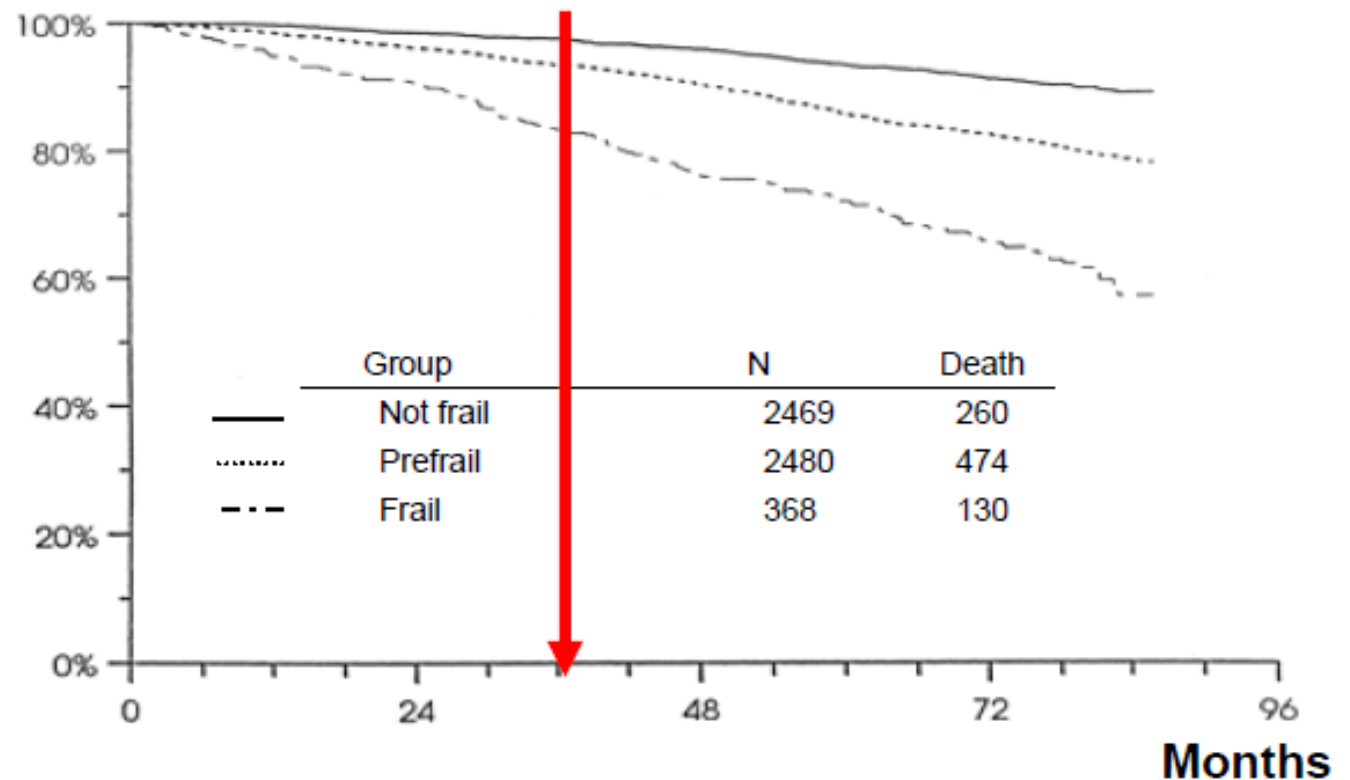


Ruolo della nutrizione clinica nella gestione del paziente anziano fragile con riduzione di forza fisica

**Roberto Pisati, MD
Medical, Regulatory
and Public Affairs**

Frailty and survival

Mortality



Fried et al., J Gerontol Med Sci 2001;56A:M146-M156

Gait Speed and Survival in Older Adults

Stephanie Studenski, MD, MPH

Subashan Perera, PhD

Kushang Patel, PhD

Caterina Rosano, MD, PhD

Kimberly Faulkner, PhD

Marco Inzitari, MD, PhD

Jennifer Brach, PhD

Julie Chandler, PhD

Peggy Cawthon, PhD

EP 14B, JGIM, MD

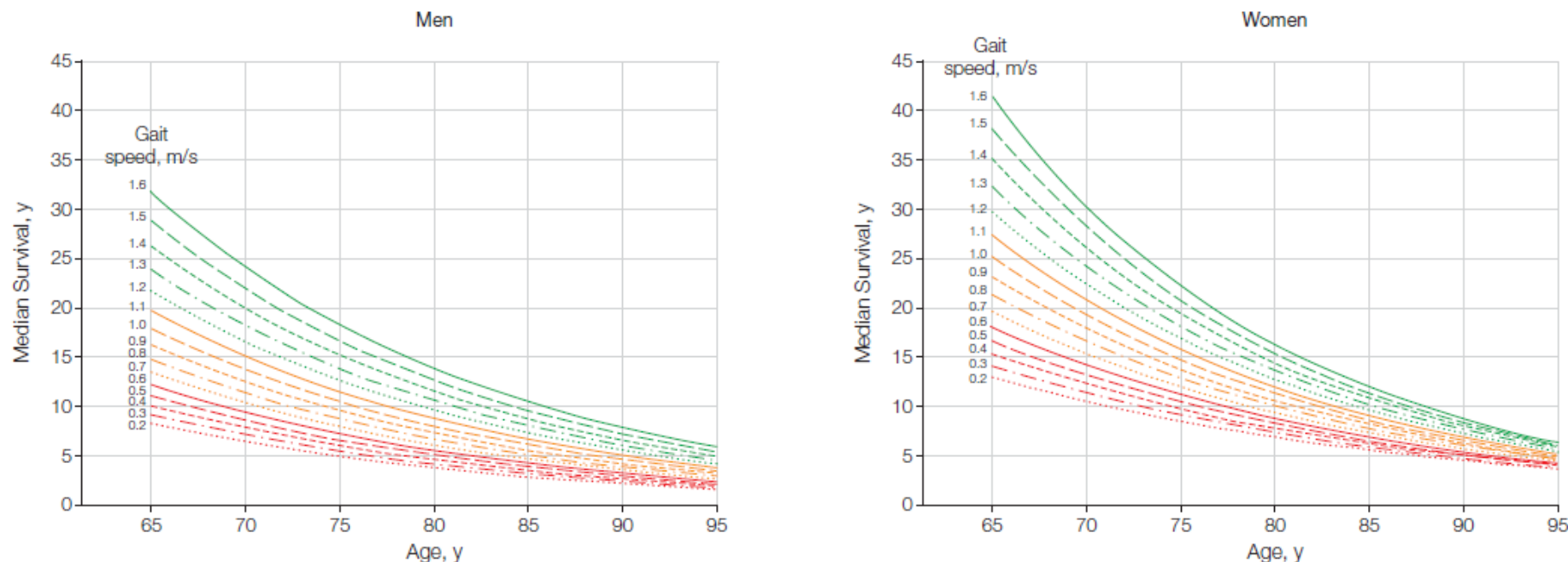
Context Survival estimates help individualize goals of care for geriatric patients, but life tables fail to account for the great variability in survival. Physical performance measures, such as gait speed, might help account for variability, allowing clinicians to make more individualized estimates.

Objective To evaluate the relationship between gait speed and survival.

Design, Setting, and Participants Pooled analysis of 9 cohort studies (collected between 1986 and 2000), using individual data from 34 485 community-dwelling older adults aged 65 years or older with baseline gait speed data, followed up for 6 to 21 years. Participants were a mean (SD) age of 73.5 (5.9) years; 59.6%, women; and 79.8%, white; and had a mean (SD) gait speed of 0.92 (0.27) m/s.

Main Outcome Measures Survival rates and life expectancy.

Figure 2. Predicted Median Life Expectancy by Age and Gait Speed



Balance and gait impairment: major features of frailty

Balance and gait impairment: risk factors for falls

Frailty in elderly people

Andrew Clegg, John Young, Steve Iliffe, Marcel Olde Rikkert, Kenneth Rockwood

Panel 1: Frequent clinical presentations of frailty

Non-specific

Extreme fatigue, unexplained weight loss, and frequent infections.

Falls

Balance and gait impairment are major features of frailty, and are important risk factors for falls. A so-called hot fall is related to a minor illness that reduces postural balance below a crucial threshold necessary to maintain gait integrity. Spontaneous falls occur in more severe frailty when vital postural systems (vision, balance, and strength) are no longer consistent with safe navigation through undemanding environments. Spontaneous falls are typically repeated and are closely associated with the psychological reaction of fear of further falls that causes the patient to develop severely impaired mobility.

Delirium

Delirium (sometimes called acute confusion) is characterised by the rapid onset of fluctuating confusion and impaired awareness. Delirium is related to reduced integrity of brain function and is independently associated with adverse outcomes. Roughly 30% of elderly people admitted to hospital will develop delirium, and the point prevalence estimate for delirium for patients in long-term care is 15%.

Fluctuating disability

Fluctuating disability is day-to-day instability, resulting in patients with "good", independent days, and "bad" days on which (professional) care is often needed.

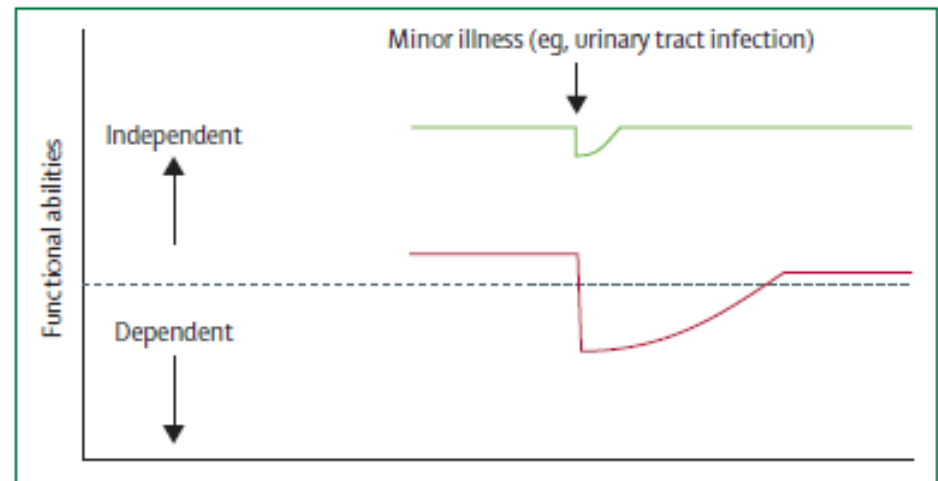


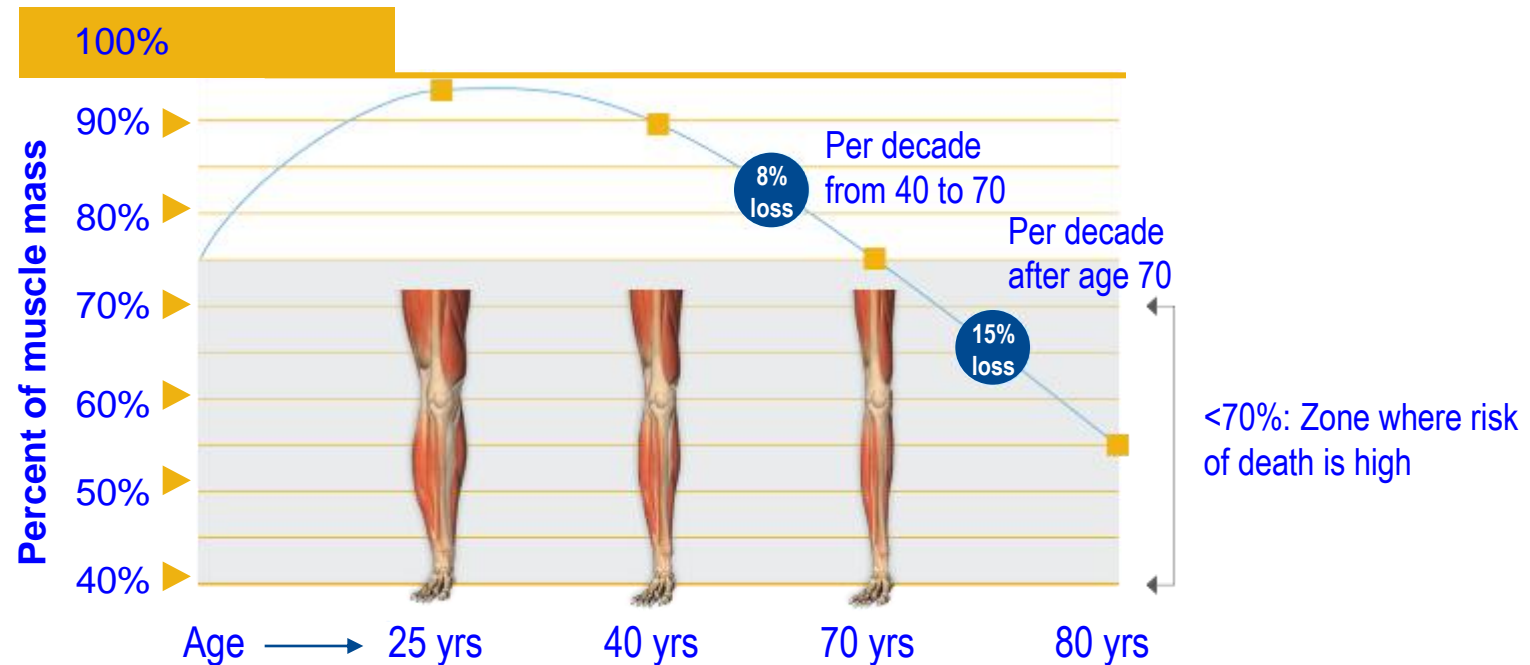
Figure 1: Vulnerability of frail elderly people to a sudden change in health status after a minor illness

The green line represents a fit elderly individual who, after a minor stressor event such as an infection, has a small deterioration in function and then returns to homeostasis. The red line represents a frail elderly individual who, after a similar stressor event, undergoes a larger deterioration, which may manifest as functional dependency, and who does not return to baseline homeostasis. The horizontal dashed line represents the cutoff between dependent and independent.

Frail elderly people -> vulnerable to minor illnesses (2013)

Progressive loss of LBM / muscle mass occurs naturally with age

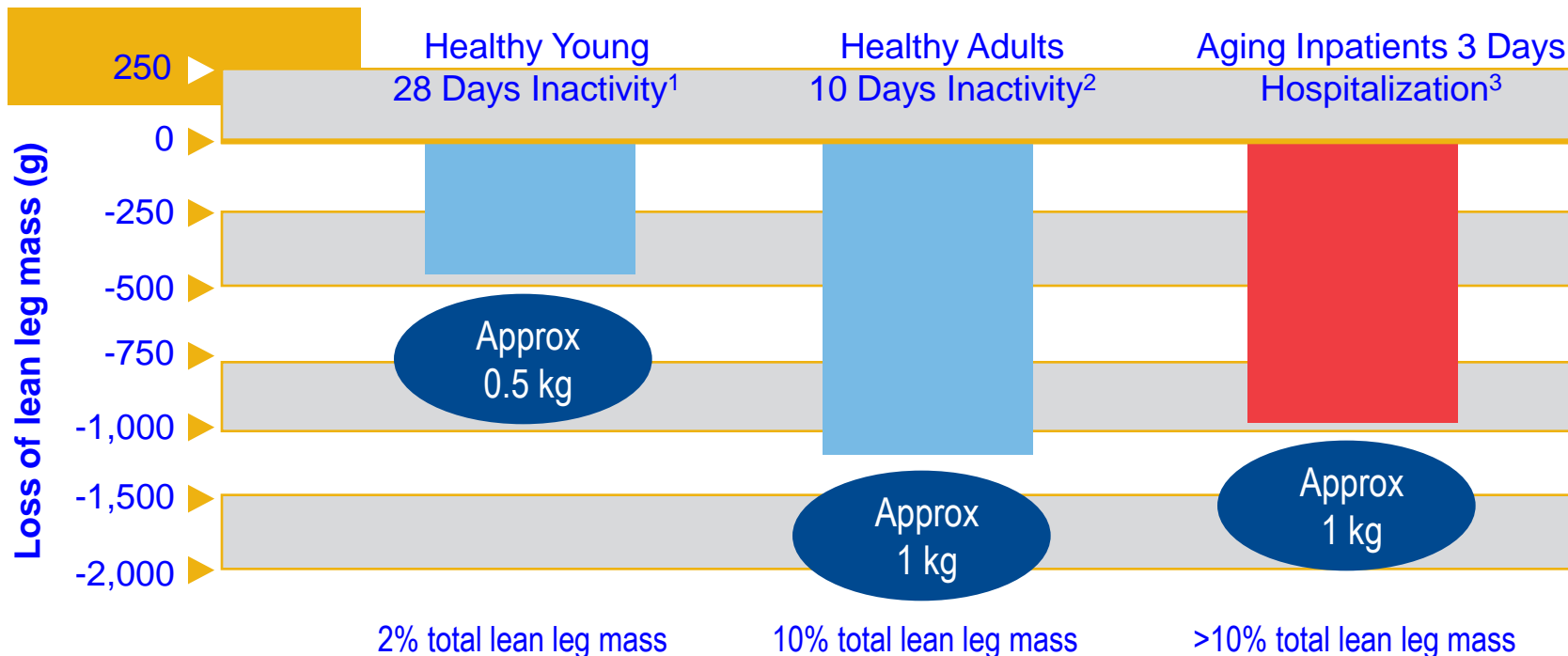
► AVERAGE LOSS OF MUSCLE MASS WITH AGE



Age-related loss of muscle mass, strength and/or functionality is called Sarcopenia

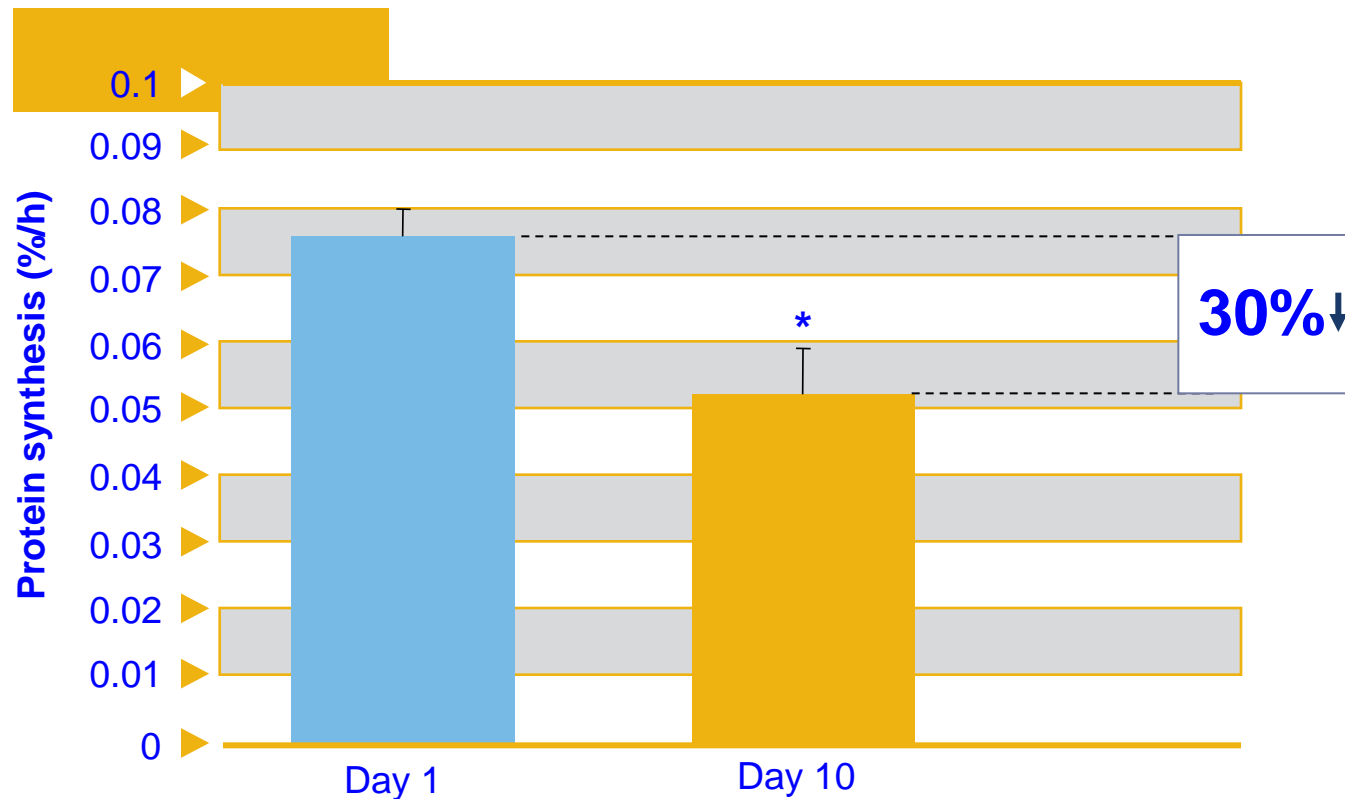
Bed rest or hospitalization is associated with significant loss of muscle mass

► LBM LOSS ASSOCIATED WITH BED REST OR HOSPITALIZATION IN HEALTHY YOUNG ADULTS, HEALTHY AGING ADULTS, AND HOSPITALIZED OLDER PATIENTS¹



Inactivity reduces muscle protein synthesis in older adults

► 24-HOUR MUSCLE PROTEIN SYNTHESIS DURING 10 DAYS OF INACTIVITY IN ELDERLY (STABLE ISOTOPE METHODOLOGY)¹



Nell'invecchiamento concomitanti fattori riducono la crescita muscolare

ALIMENTAZIONE



1

Inadeguato
apporto proteico

TRATTO GASTROINTESTINALE



digestione

2

Ridotto
assorbimento

CIRCOLAZIONE SANGUIGNA

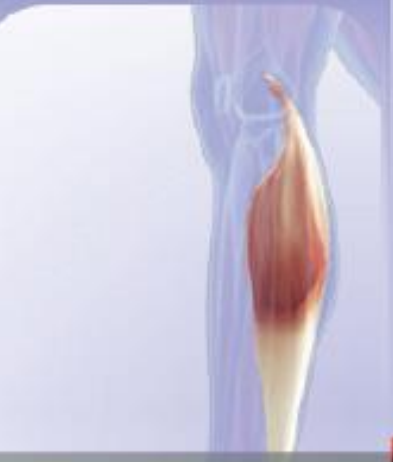


aminoacidi

3

Ridotta
disponibilità
di aminoacidi
a livello muscolare

MUSCOLO



sintesi proteica

4

Ridotto effetto
anabolico degli
aminoacidi

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, PhDⁱ, Daniel Teta MD, PhD^j, Renuka Visvanathan MBBS, PhD^k, Elena Volpi MD, PhD^l, Yves Boirie MD, PhD^m

Recommended Protein Intake for Healthy Older People: Current Recommendations and Evolving Evidence

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

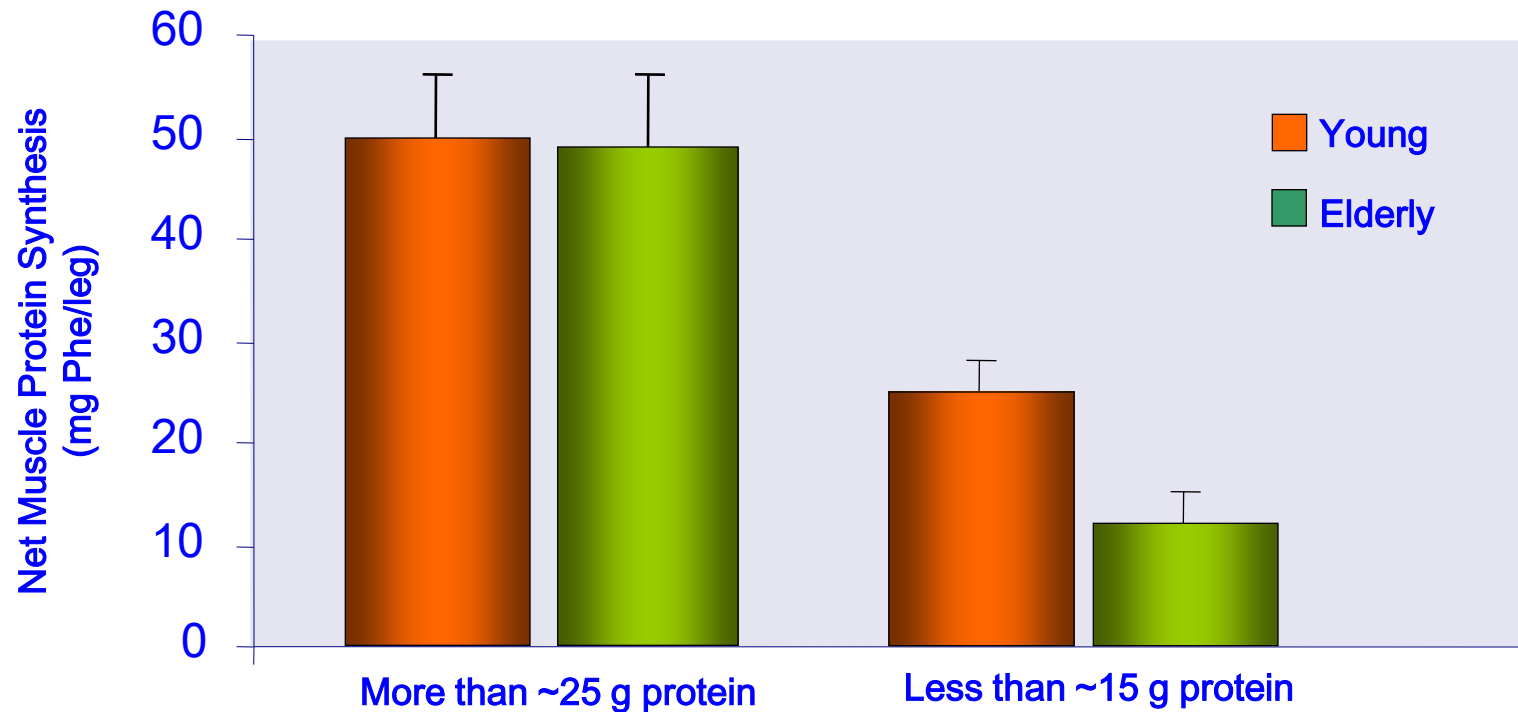
- To maintain and regain muscle, older people need more dietary protein than do younger people; older people should consume an average daily intake in the range of 1.0 to 1.2 g/kg BW/d.
- The per-meal anabolic threshold of dietary protein/amino acid intake is higher in older individuals (ie, 25 to 30 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.

Proteins needs in healthy elderly:

- 1.0-1.2 g/Kg/die
- 25-30 g protein per meal
- 2.5-2.8 g leucine per meal

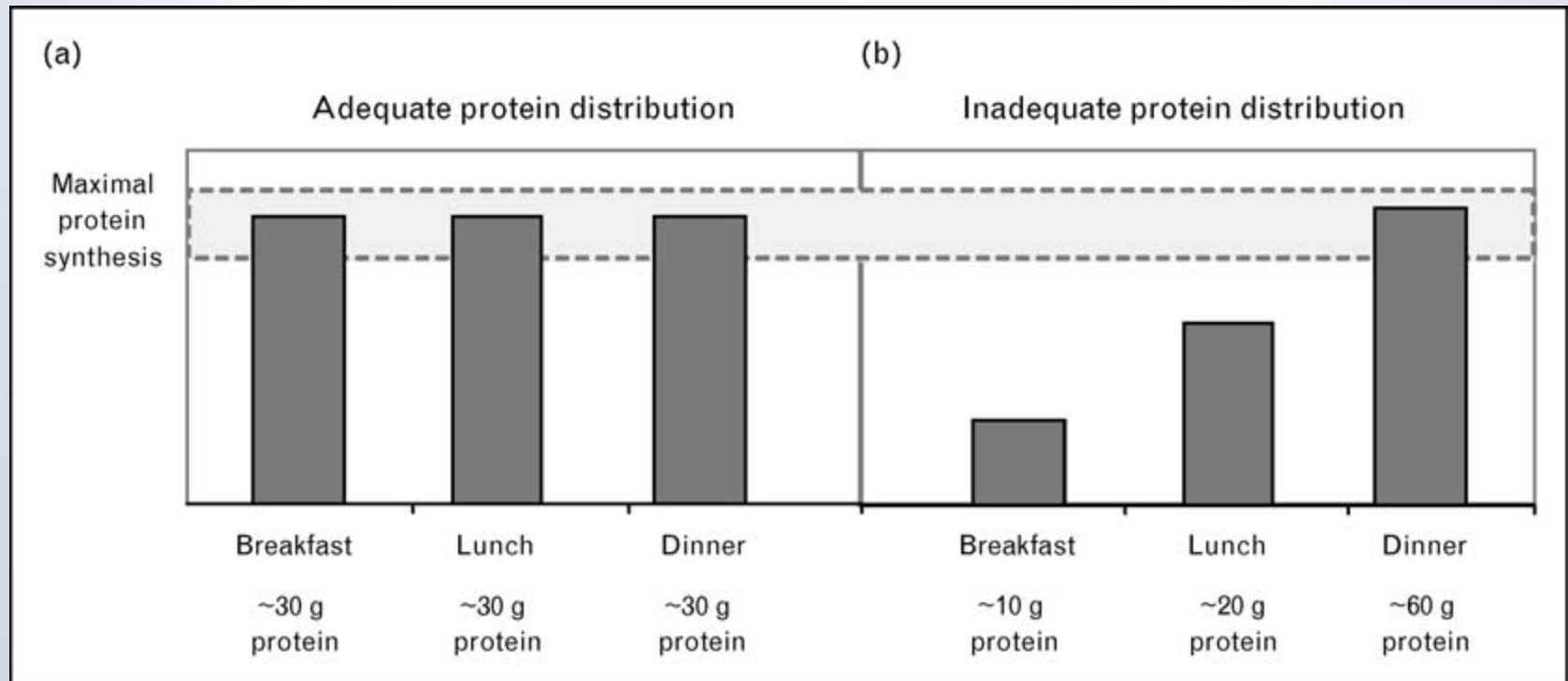
**Up to 1.2 -1.5 g/Kg/die during
acute or chronic diseases**

Age-related dose-response



Ageing and muscle protein synthesis

- Ageing is associated with a reduced ability to synthesize muscle proteins
- 25-30 g high quality protein (~10g EAA) per meal or supplementation with leucine to maximize muscle protein synthesis



The effectiveness of leucine on muscle protein synthesis, lean body mass and leg lean mass accretion in older people: a systematic review and meta-analysis

British Journal of Nutrition (2015), **113**, 25–34

Zhe-rong Xu¹, Zhong-ju Tan¹, Qin Zhang¹, Qi-feng Gui¹ and Yun-mei Yang^{2*}

In the present study, we performed a meta-analysis to assess the ability of leucine supplementation to increase the muscle protein fraction synthetic rate and to augment lean body mass or leg lean mass in elderly patients. A literature search was conducted on Medline, Cochrane, EMBASE and Google Scholar databases up to 31 December 2013 for clinical trials that investigated the administration of leucine as a nutrient that affects muscle protein metabolism and muscle mass in elderly subjects. The included studies were randomised controlled trials. The primary outcome for the meta-analysis was the protein fractional synthetic rate. Secondary outcomes included lean body mass and leg lean mass.

A total of nine studies were included in the meta-analysis.

These findings suggest that leucine supplementation is useful to address the age-related decline in muscle mass in elderly individuals, as it increases the muscle protein fractional synthetic rate.

Vitamin D supplementation improves neuromuscular function in older people who fall

JUGDEEP K. DHESI¹, STEPHEN H. D. JACKSON², LINDSAY M. BEARNE³, CAJE MONIZ⁴, MICHAEL V. HURLEY³, CAMERON G. SWIFT², THERESA J. ALLAIN⁵

Abstract

Background: vitamin D supplementation reduces the incidence of fractures in older adults. This may be partly mediated by effects of vitamin D on neuromuscular function.

Objective: to determine the effects of vitamin D supplementation on aspects of neuromuscular function known to be risk factors for falls and fractures.

Design: randomised, double-blind, placebo-controlled study.

Conclusions: vitamin D supplementation, in fallers with vitamin D insufficiency, has a significant beneficial effect on functional performance, reaction time and balance, but not muscle strength. This suggests that vitamin D supplementation improves neuromuscular or neuroprotective function, which may in part explain the mechanism whereby vitamin D reduces falls and fractures.

Key points

- Impaired neuromuscular function is related to an increased risk of falls and fractures in the older population.
- Previous cross-sectional work suggests that neuromuscular function is related to vitamin D status.
- Our study demonstrates that vitamin D supplementation has beneficial effects on functional performance, balance and reaction time but not on muscle strength.
- Vitamin D supplementation improves neuromuscular co-ordination, rather than muscle strength *per se*, and may reduce falls and thereby fractures.

A Pooled Analysis of Vitamin D Dose Requirements for Fracture Prevention

Heike A. Bischoff-Ferrari, M.D., Dr.P.H., Walter C. Willett, M.D., Dr.P.H.,
Endel J. Orav, Ph.D., Paul Lips, M.D., Pierre J. Meunier, M.D.,
Ronan A. Lyons, M.D., M.P.H., Leon Flicker, M.D., John Wark, M.D., Ph.D.,
Rebecca D. Jackson, M.D., Jane A. Cauley, Dr.P.H.,
Haakon E. Meyer, M.D., Ph.D., Michael Pfeifer, M.D., Kerrie M. Sanders, Ph.D.,
Hannes B. Stähelin, M.D., Robert Theiler, M.D., and Bess Dawson-Hughes, M.D.

CONCLUSIONS

High-dose vitamin D supplementation (≥ 800 IU daily) was somewhat favorable in the prevention of hip fracture and any nonvertebral fracture in persons 65 years of age or older. (Funded by the Swiss National Foundations and others.)

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

For these reasons it is recommended that older persons ingest between 1.0 and 1.5 g of protein/kg/d.

Essential amino acids appear to be the primary stimulus of protein synthesis.⁴³ Leucine appears to be the most potent of these amino acids.

Essential amino acids act synergistically with exercise to increase fractional protein synthesis.

Replacement of vitamin D in persons with low levels increases strength and function and decreases falls.⁸⁰ Vitamin D replacement is associated with less mortality.⁸¹



Nutritional management of Ageing/Frailty

Contributory factors related to nutrition

- Inadequate protein intake
- Increased splanchnic extraction of amino acids
- Decreased muscle response to anabolic stimuli
- Vitamin D deficiency

Nutritional management strategies

- Increase protein intake (1-1.5g/kg)
- Consume high quality or “fast” proteins. AA supplementation
- Increase EAA, in particular leucine, intake
- Increase Vit D intake



FortiFit: Key nutritional features

FortiFit contains per serving

Whey protein
20g



Fast amino acid bioavailability **required for muscle protein synthesis**

contains Essential AA
10g



Adequate amount of substrate **for muscle health in elderly**

Leucine
3g



Additional trigger **to overcome the age-related decreased anabolic response**

Vitamin D 800IU



To maintain **muscle function**

+ Calcium 500mg



To support **bone health**



FortiFit: Key nutritional features

FortiFit contains per serving

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

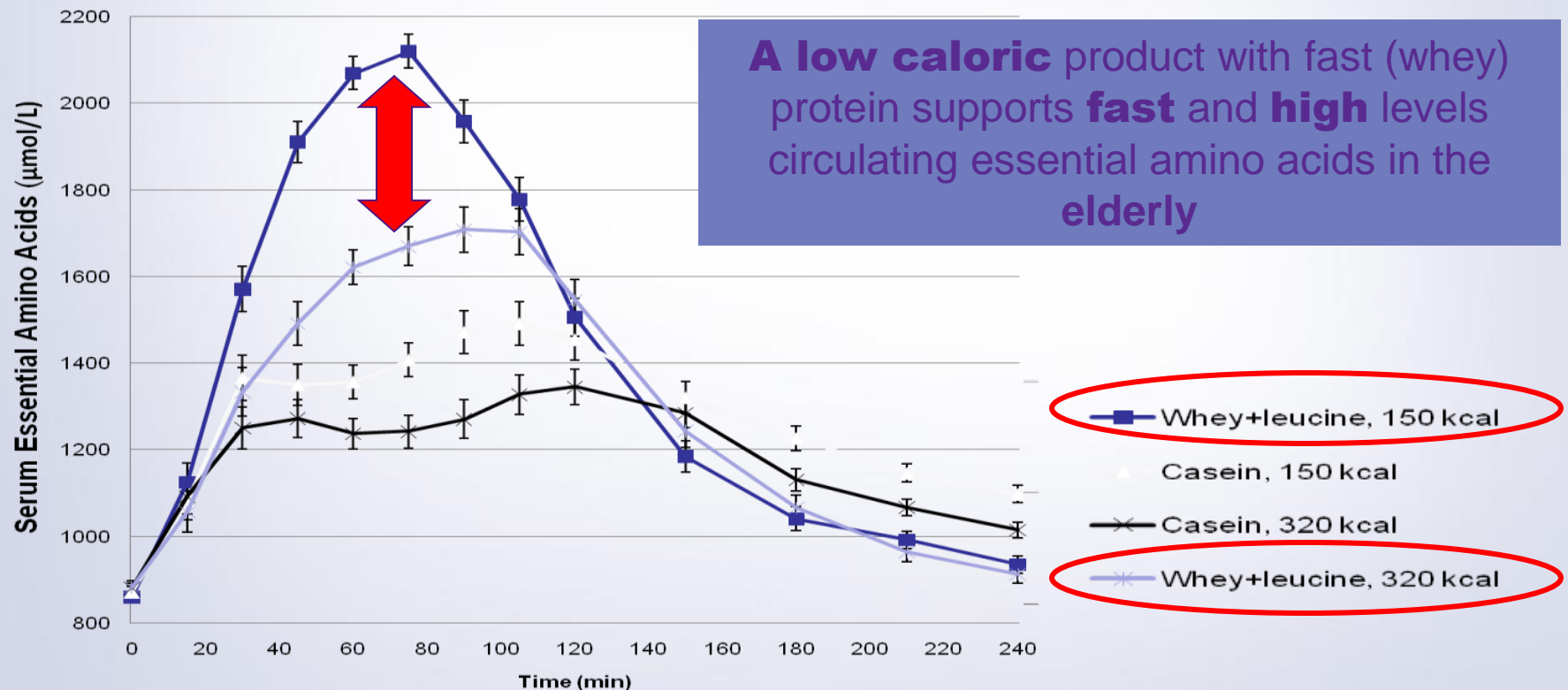
Vit B6, Folic acid, Vit B12,
magnesium



To address the **age-related deficiency** for specific micronutrients

FortiFit: Low caloric

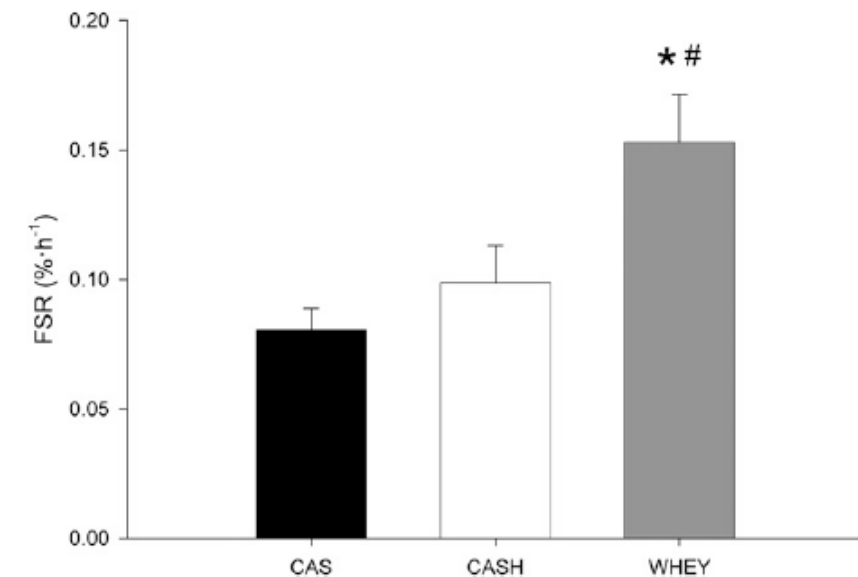
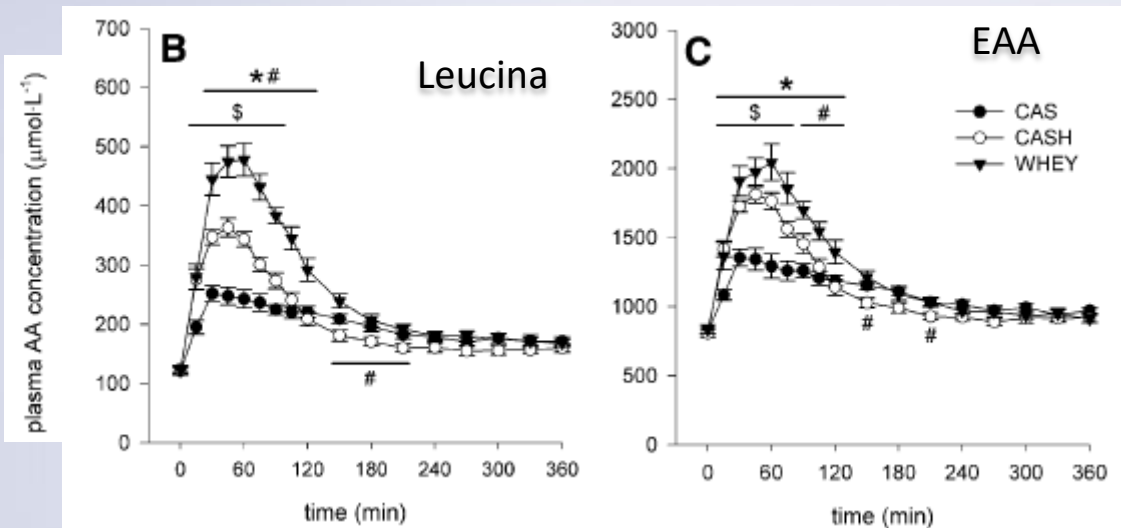
A low caloric product increases post-prandial circulating EAA availability; high EAA availability is important for stimulation of muscle protein synthesis



Whey protein stimulates postprandial muscle protein accretion more effectively than do casein and casein hydrolysate in older men¹⁻³

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

The American Journal of Clinical Nutrition



Le **sieroproteine** (20 g) stimolano la sintesi muscolare postprandiale in maniera **più efficace** rispetto alla caseina e alla caseina idrolisata negli anziani, grazie ad una **più rapida cinetica di assorbimento** e una più alta concentrazione di leucina

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

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Robert G Memelink (robert.memelink@nutricia.com)

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Robert R Wolfe (rwolfe2@uams.edu)

Methods

Utilizing a randomized, controlled, double blind study design, healthy older adults received a single bolus of a high whey protein, leucine-enriched supplement (EXP: 20g whey protein, 3g total leucine, 150kcal; n = 9) or an iso-caloric milk protein control (Control: 6g milk protein; n = 10), immediately after unilateral resistance exercise. Postprandial mixed muscle protein fractional synthesis rate (FSR) was measured over 4h using a tracer infusion protocol with L-[ring- $^{13}\text{C}_6$]-phenylalanine and regular blood and muscle sampling.

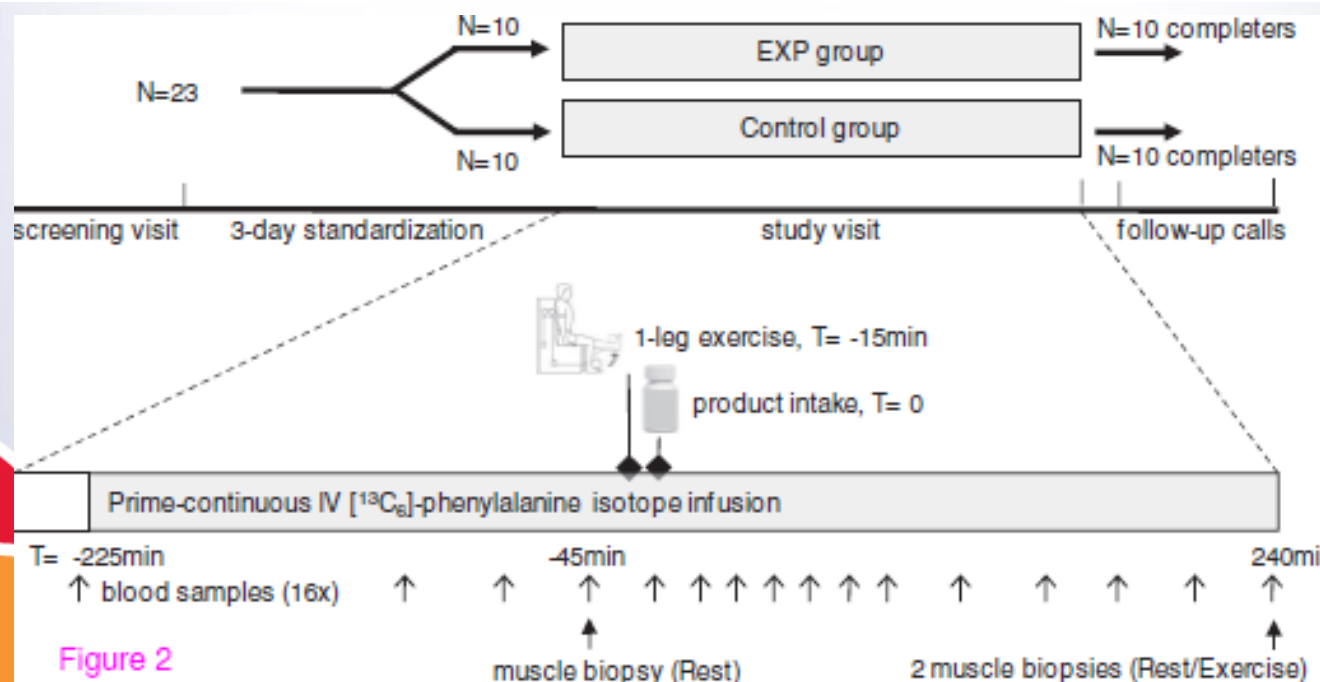


Figure 2

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

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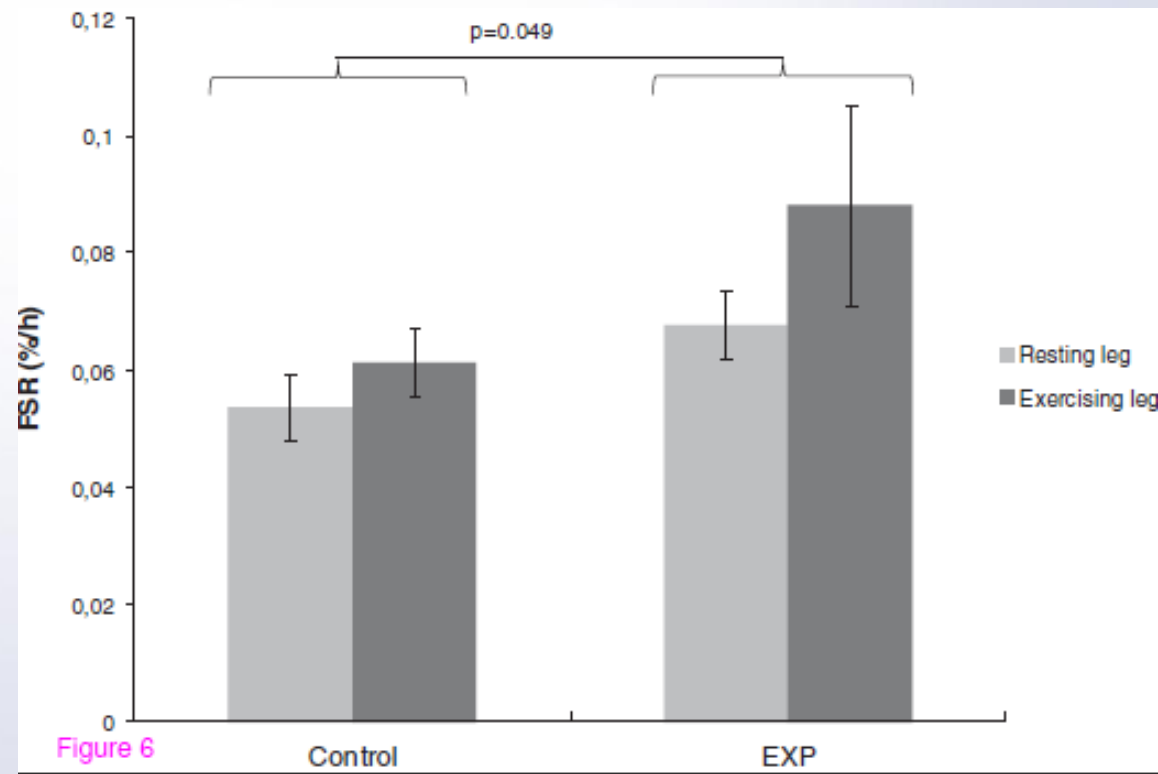
Robert R Wolfe (rwolfe2@uams.edu)

Results

FSR was significantly higher overall after EXP (0.0780 ± 0.0070 %/h) vs Control (0.0574 ± 0.0066 %/h (EMM \pm SE)) ($p = 0.049$). No interaction between treatment and exercise was observed ($p = 0.519$). Higher postprandial concentrations of EAA and leucine are possible mediating factors for the FSR response, while plasma insulin increase did not dictate the FSR response. Moreover, when the protein intake from the supplements was expressed per kg leg lean mass (LLM), a significant correlation was observed with resting postprandial FSR ($r = 0.48$, $P = 0.038$).

Conclusion:

Ingestion of a high whey protein, leucine enriched supplement resulted in a larger overall postprandial muscle protein synthesis rate in healthy older subjects compared with a conventional dairy product.



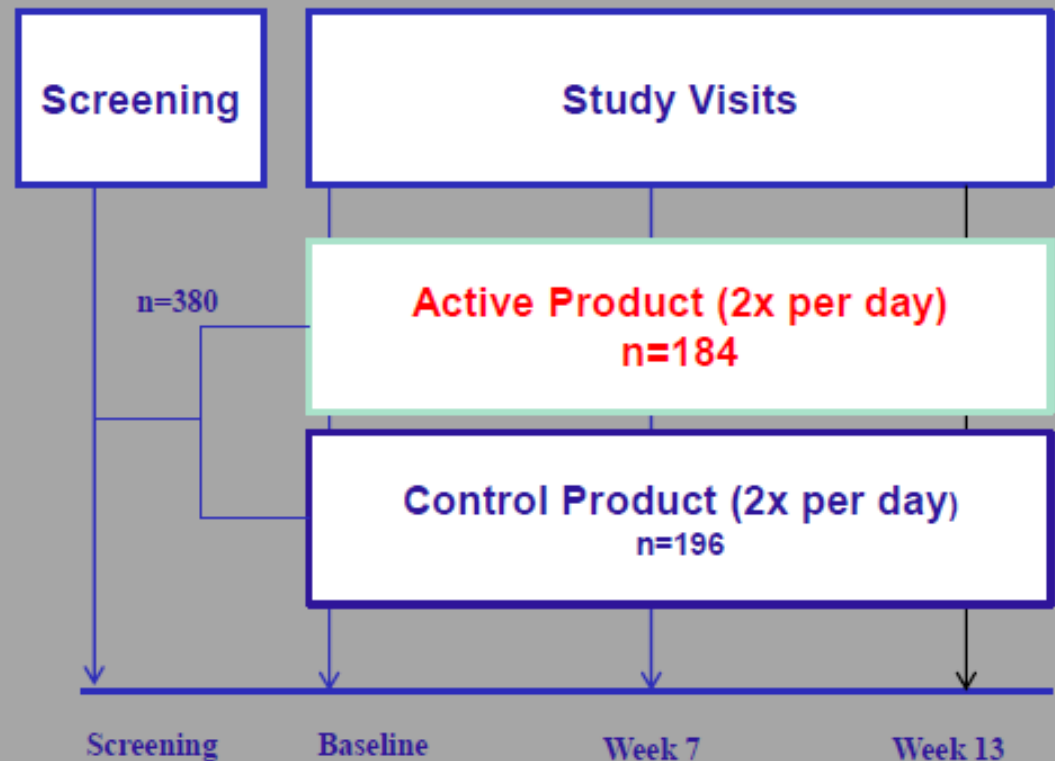
Original Study

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, PhDⁱ,
Gilbert Donders MD, PhD^j, Michael Drey MD^k, Carolyn Greig PhD^l,
Ulf Holmbäck PhD^m, Marco Narici PhDⁿ, Jamie McPhee PhD^o,
Eleonora Poggialle 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

Study design

- Randomized controlled trial
- Multicentre (18 sites in BE, DE, IE, IT, SE, UK)
- Parallel groups
- Double-blind
- 13 week duration



Active and control products

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

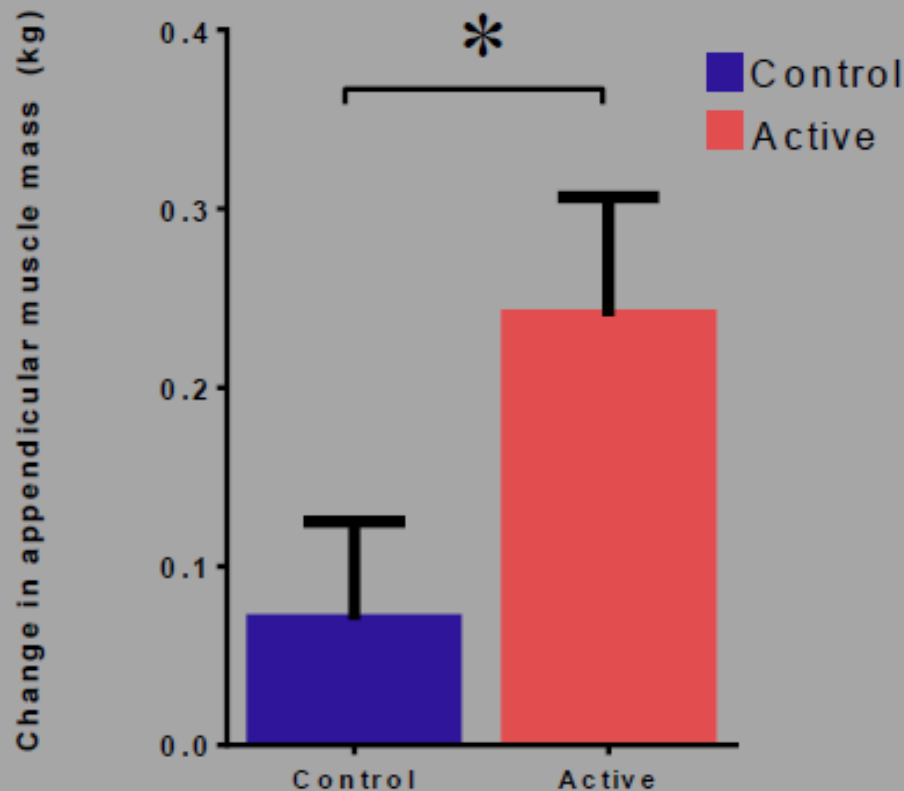
*40g dry powder / serving
150ml re-constituted

SUBJECT CHARACTERISTICS

	Active n=184	Control n=196
Age, mean (SD), years	77.3 (6.7)	78.1 (7.0)
Sex, female	120 (65.2)	129 (65.8)
Living Independently, n (%)	162 (88.0)	167 (85.2)
BMI, mean (SD), kg/m ²	26.0 (2.5)	26.2 (2.8)
MNA 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)
Serum calcidiol (vitamin D), median (IQR), nmol/L	48.0 (34.0 – 66.0)	49.0 (34.0 – 65.0)
Protein intake, mean (SD), g/kg BW/day	1.04 (0.56)	1.01 (0.29)
SPPB, mean (SD)	7.48 (1.91)	7.46 (1.96)
Gait speed, mean (SD)	0.78 (0.22)	0.75 (0.20)
Chair-stand time, median (IQR)	17.1 [15.2 - 21.2]	17.6 [14.6 - 20.6]
Balance score, median (IQR)	3.0 [2.0 – 4.0]	3.0 [2.0 – 4.0]
Handgrip-strength, males, median (IQR), kg	26.8 [22.0 – 30.8]	27.1 [22.0 – 32.1]
Handgrip-strength, females, median (IQR), kg	16.5 [13.5 – 21.5]	16.8 [14.2 – 20.5]

PRO

Greater increase in appendicular muscle mass in active than control



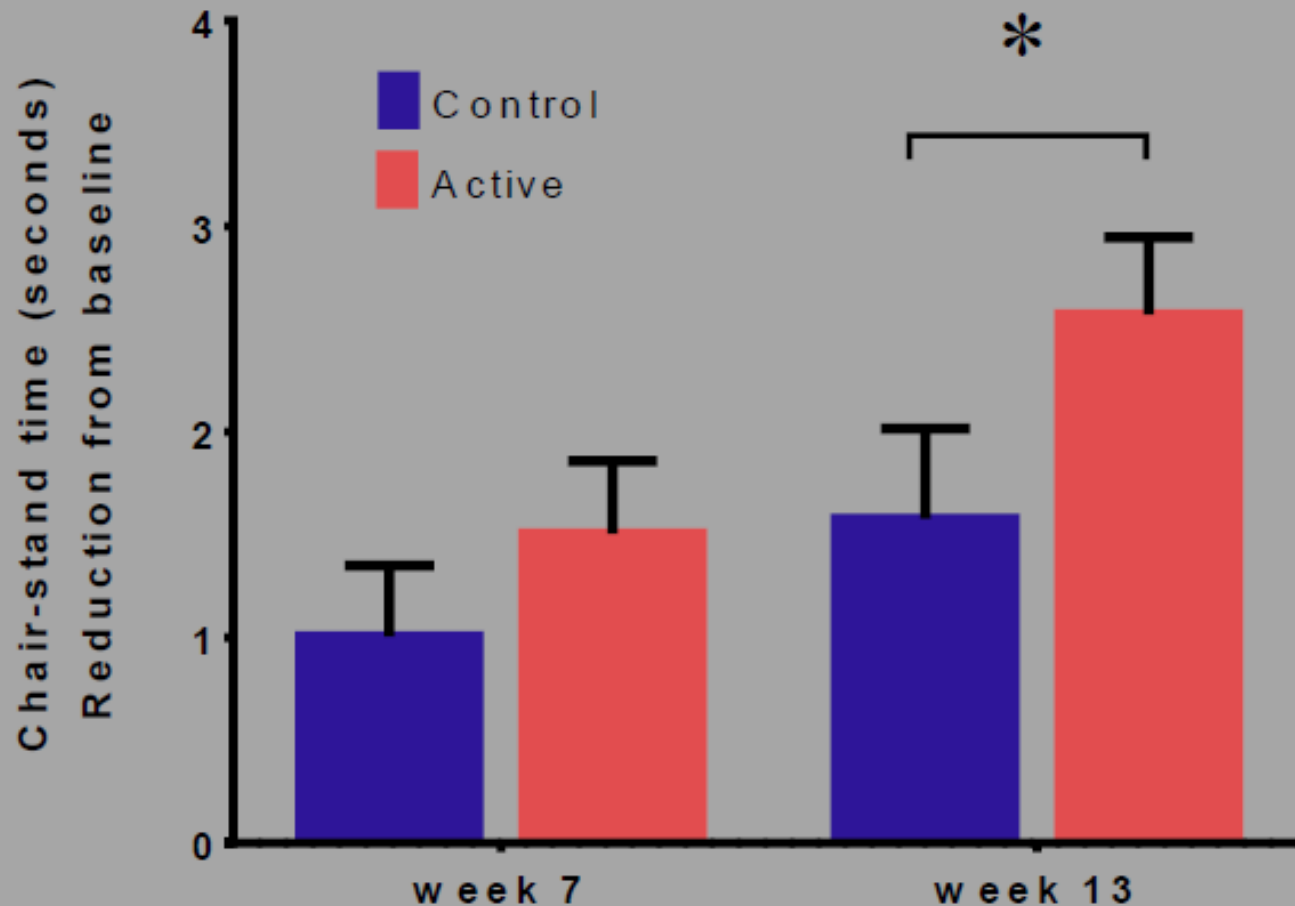
Baseline appendicular muscle mass (kg) Mean (SEM)	
Control	17.5 (0.30)
Active	17.9 (0.31)
Predicted mean effect size [95% CI] ²	
0.17 kg [0.01 – 0.34]; p=0.044	

*P<0.01



PROVIDE

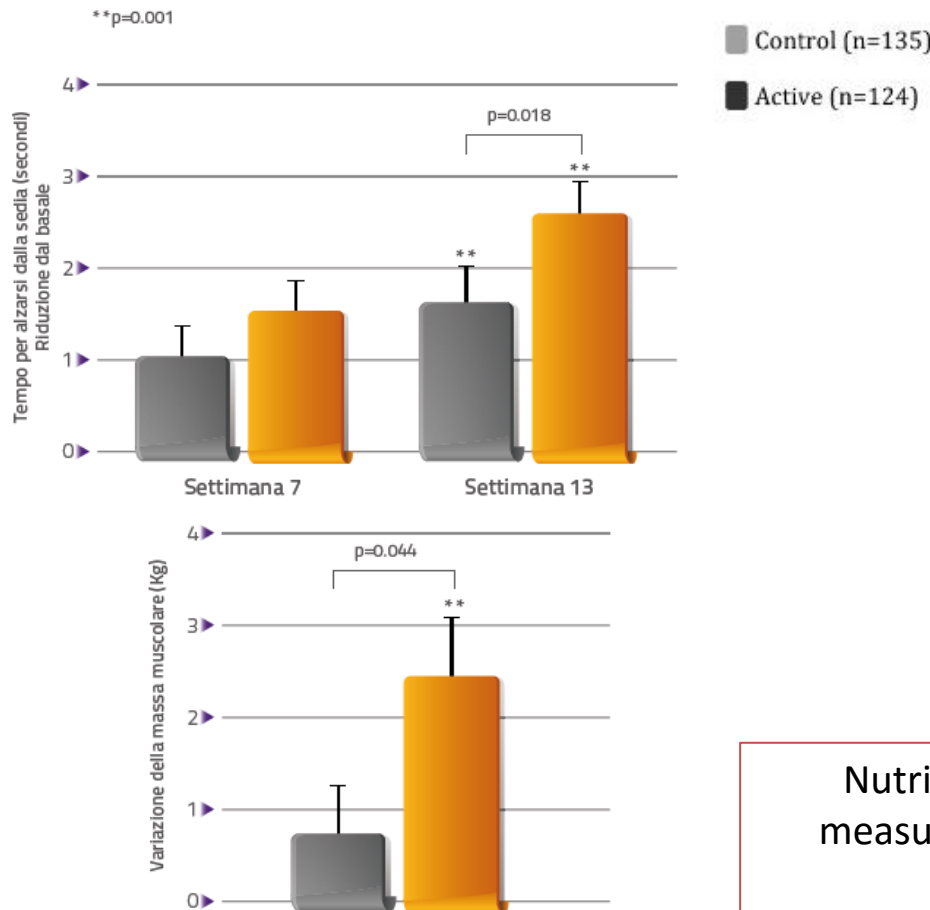
Greater Improvement in Chair-Stand Time in active than control



* $P < 0.01$

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



Key Findings:

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, especially relevant for those who are unable to exercise

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

Nutritional Supplementation and Sarcopenia: The Evidence Grows

John E. Morley MB, BCh *

Divisions of Geriatric Medicine and Endocrinology, Saint Louis University School of Medicine, St Louis, MO

In this issue of your *Journal* we publish a trail-breaking study showing that persons with early frailty (based on the Short Physical Performance Battery [SPPB]) and loss of muscle mass can improve both muscle mass and chair-stand time over a period of 13 weeks.¹

field.^{34–38} The evidence for the supplement of dietary protein is based on the decreased sensitivity of old muscles leading to the need for the protein to be given at least twice a day.^{39,40} Essential amino acids activate mammalian target of rapamycin, thus increasing the accumulation into muscle.⁴¹ Splanchnic protein synthesis is a priority with aging, resulting in a need for higher essential amino acid plasma levels to maintain the rate of muscle protein synthesis.⁴² The new

Another component of the nutritional supplement was 800 IU of vitamin D.¹ Most older persons and particularly those in nursing homes, are vitamin D deficient.^{57–63} A meta-analysis has shown that vitamin D replacement can improve muscle function.⁶⁴ Persons with lower 25(OH) vitamin D levels have better responses.^{65,66} There does not appear to be an advantage of giving more than 1000 IU vitamin D daily.

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. Verdijk¹, Henrike M. Hamer¹, Sjors Verlaan², Yvette Luiking², Imre W.K. Kouw¹, Joan M. Senden¹, Janneau van Kranenburg¹, Annemarie P. Gijsen¹, Martijn Poeze^{1,3}, Luc J.C. van Loon¹

Methods: A total of 45 non-sarcopenic older men (age: 69 ± 1 y; BMI: 25.7 ± 0.3 kg/m²) were randomly assigned to ingest 21 g of leucine-enriched whey protein with carbohydrate (9 g) and fat (3 g) (Pro-En), an isonitrogenous amount of 21 g of leucine-enriched whey protein without carbohydrate and fat (Pro), or an isocaloric mixture (628 kJ) containing carbohydrate and fat only (En). Stable isotope tracer methodology was applied to assess basal as well as postprandial muscle protein synthesis rates in the three groups.

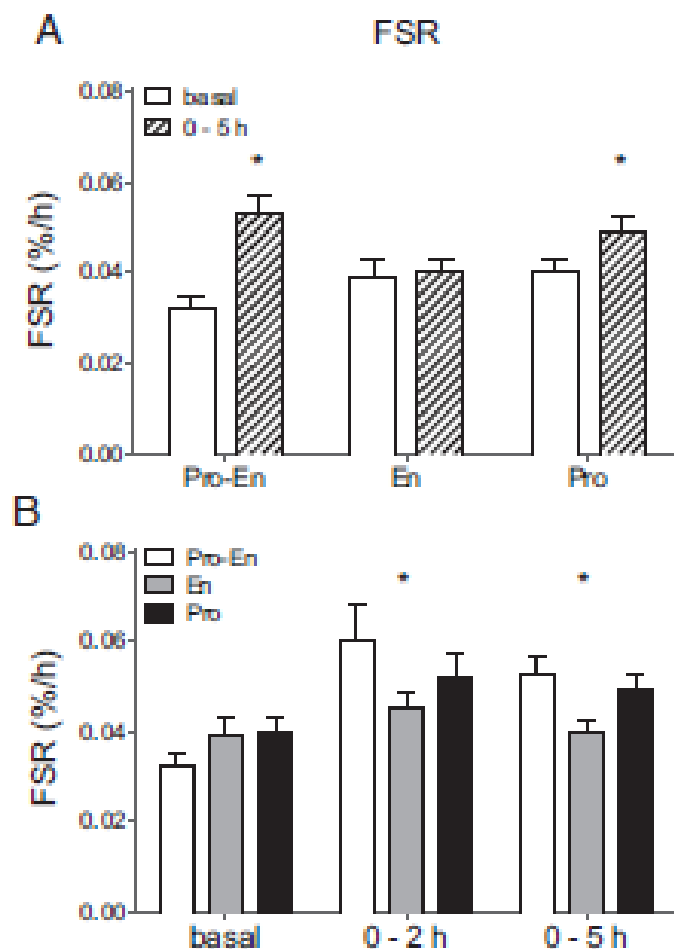
Results: Ingestion of protein in the Pro-En and Pro groups significantly increased muscle protein synthesis rates when compared with basal rates (from 0.032 ± 0.003 to 0.053 ± 0.004 and 0.040 ± 0.003 to 0.049 ± 0.003 %/h, respectively; $P < 0.05$), whereas ingestion of carbohydrate and fat did not increase muscle protein synthesis rates in the En group (from 0.039 ± 0.004 to 0.040 ± 0.003 %/h; $P = 0.60$). Despite the greater postprandial rise in circulating insulin concentration in the Pro-En group, no significant differences were observed in postprandial muscle protein synthesis rates between the Pro-En and Pro groups ($P = 0.32$). Postprandial muscle protein synthesis rates were higher in the Pro-En vs En group ($P = 0.01$).

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

ORIGINAL ARTICLE

JCEM THE JOURNAL OF CLINICAL
ENDOCRINOLOGY & METABOLISM

Irene Fleur Kramer^{1,3}, Lex B. Verdijk¹, Henrike M. Hamer¹, Sjors Verlaan², Yvette Luiking², Imre W.K. Kouw¹, Joan M. Senden¹, Janneke van Kranenburg¹, Annemarie P. Gijzen¹, Martijn Poeze^{1,3}, Luc J.C. van Loon¹



- **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.

Alimentazione o supplementazione?

Impact of protein pulse feeding on lean mass in malnourished and at-risk hospitalized elderly patients: A randomized controlled trial[☆]

Olivier Bouillanne^{a,d,*}, Emmanuel Curis^e, Brigitte Hamon-Vilcot^a, Ioannis Nicolis^e, Pascale Chrétien^f, Nathalie Schauer^a, Jean-Pierre Vincent^b, Luc Cynober^{d,g}, Christian Aussel^{c,d}

Results: Protein pulse feeding was significantly more efficacious than protein spread feeding in improving LM index (mean changes from baseline for PD group: +0.38 kg/m²; 95% confidence interval (CI), [0; 0.60]; for SD group: -0.21 kg/m²; 95% CI, [-0.61; 0.20]; $p = 0.005$ between the two groups), ASMM index (+0.21 kg/m²; 95% CI, [0; 0.34] and -0.11 kg/m²; 95% CI, [-0.20; 0.09]; $p = 0.022$), BCM index (+0.44 kg/m²; 95% CI, [0.08; 0.52] and -0.04 kg/m²; 95% CI, [-0.09; 0.10]; $p = 0.004$). There was no significant effect for hand-grip strength or ADL score.

In conclusion, this study demonstrates for the first time that a protein pulse feeding strategy can improve lean mass in malnourished and at-risk hospitalized elderly patients. This nutritional strategy is especially well-adapted to elderly patients in a rehabilitation unit, and is well-accepted, being perceived as following natural eating patterns, unlike oral supplements or pharmaconutrient treatments.

Applied nutritional investigation

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

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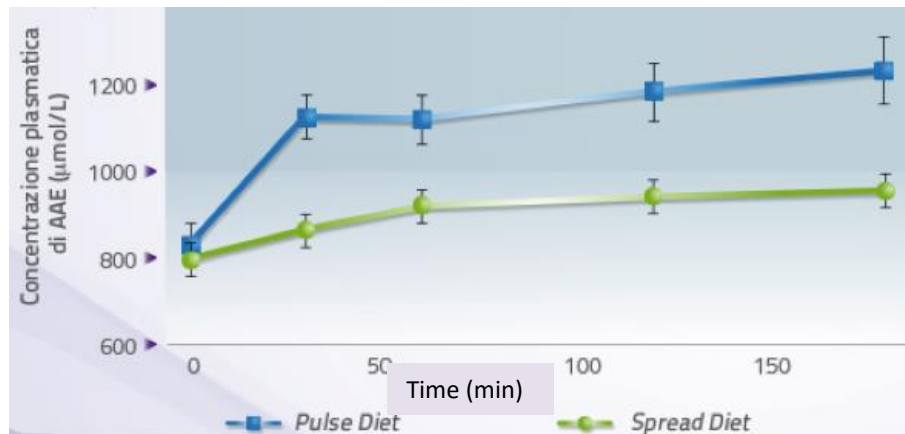
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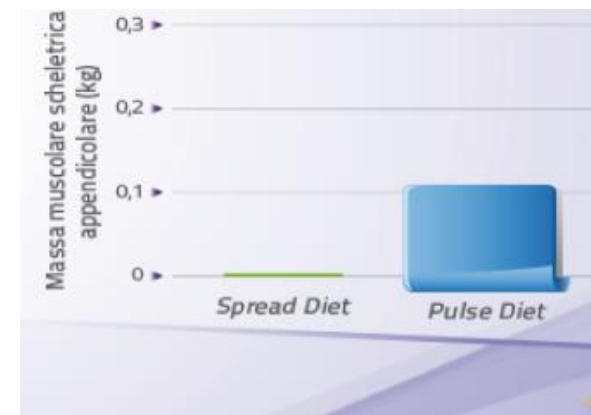
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- **In a spread diet (SD):** dietary protein was spread over the four daily meals.
- **In a pulse diet (PD):** 72% of dietary protein (averaging 1.31 g/kg body weight daily) was consumed in one meal at noon.

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



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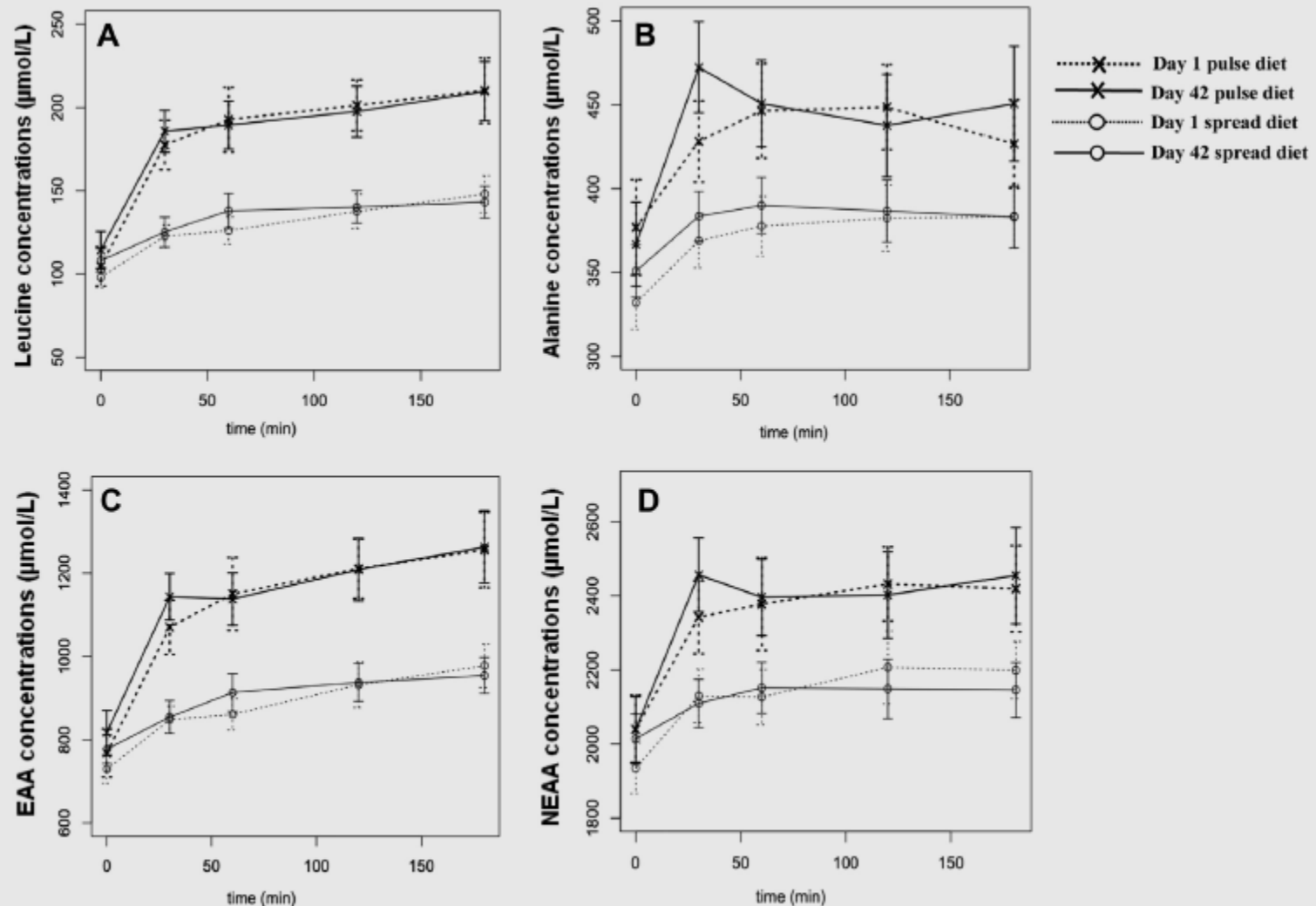


Fig 1. Plasma leucine (A), alanine (B), essential amino acid (EAA) (C), and non-essential amino acid (NEAA) (D) concentrations at day 1 (---) and day 42 (—) in the pulse diet group (x) and in the spread diet group (o), just before the beginning of the midday meal and at +30 min, +60 min, +120 min, and +180 min after the meal. Values expressed in μmol/L are means ± SEM.

Interaction exercise and protein



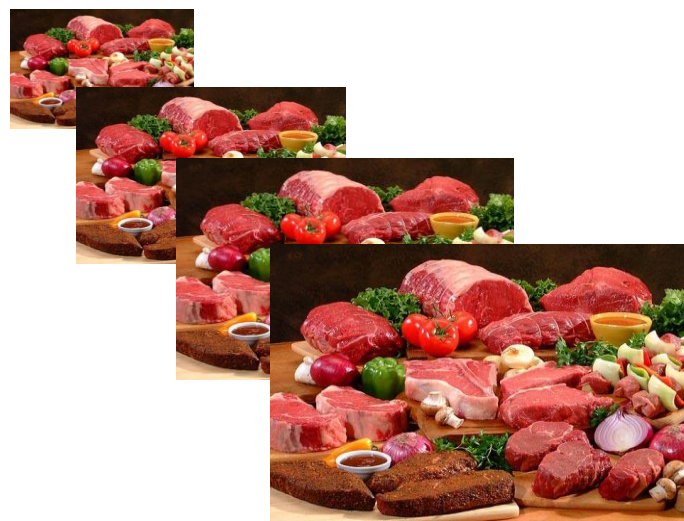
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Perspective: Protein: What Kind, How Much, When?

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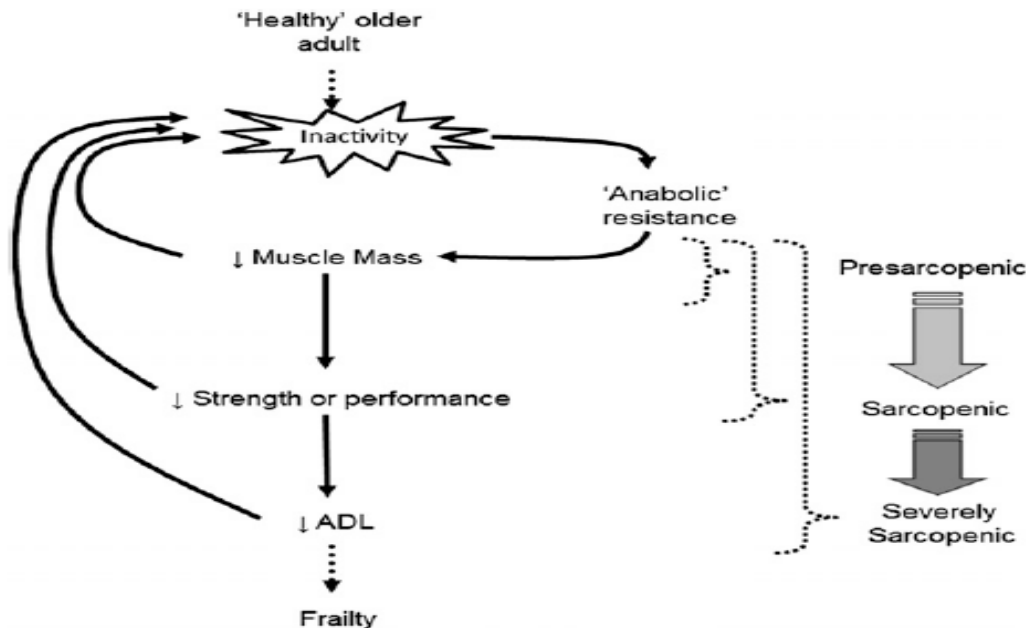
Keeping Older Muscle “Young” through Dietary Protein and Physical Activity^{1,2}

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ABSTRACT

Sarcopenia is characterized by decreases in both muscle mass and muscle function. The loss of muscle mass, which can precede decrements in muscle function, is ultimately rooted in an imbalance between the rates of muscle protein synthesis and breakdown that favors a net negative balance (i.e., synthesis < breakdown). A preponderance of evidence highlights a blunted muscle protein synthetic response to dietary protein, commonly referred to as “anabolic resistance,” as a major underlying cause of the insipid loss of muscle with age. Dietary strategies to overcome this decreased dietary amino acid sensitivity include the ingestion of leucine-enriched, rapidly digested proteins and/or greater protein ingestion in each main meal to maximally stimulate muscle anabolism. Anabolic resistance is also a hallmark of a sedentary lifestyle at any age. Given that older adults may be more likely to experience periods of reduced activity (either voluntarily or through acute illness), it is proposed that inactivity is the precipitating factor in the development of anabolic resistance and the subsequent progression from healthy aging to frailty. However, even acute bouts of activity can restore the sensitivity of older muscle to dietary protein. Provided physical activity is incorporated into the daily routine, muscle in older adults should retain its capacity for a robust anabolic response to dietary protein comparable to that in their younger peers. Therefore, through its ability to “make nutrition better,” physical activity should be viewed as a vital component to maintaining muscle mass and function with age. *Adv. Nutr.* 5: 599S–607S, 2014.



Physical activity: a tool to help
«**make nutrition better**»
(greater protein intake, rapidly
digested, leucine-enriched
protein sources) to maintain/
enhance musculo-skeletal
health with age

Fighting Sarcopenia in Older Frail Subjects: Protein Fuel for Strength, Exercise for Mass

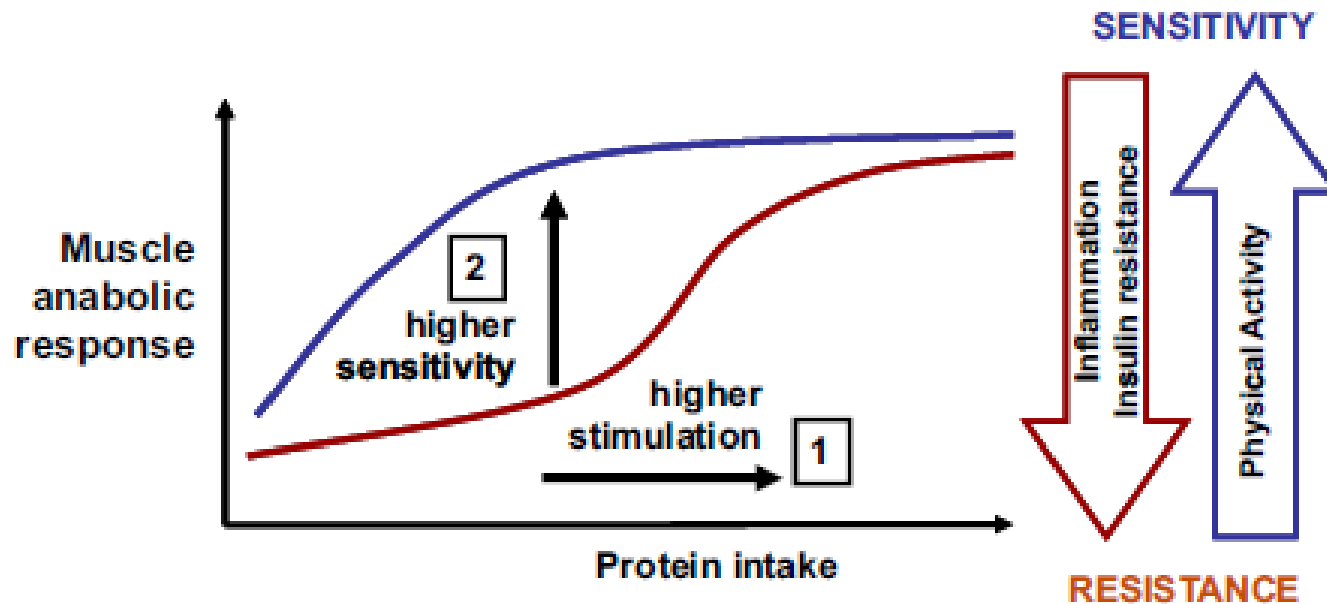
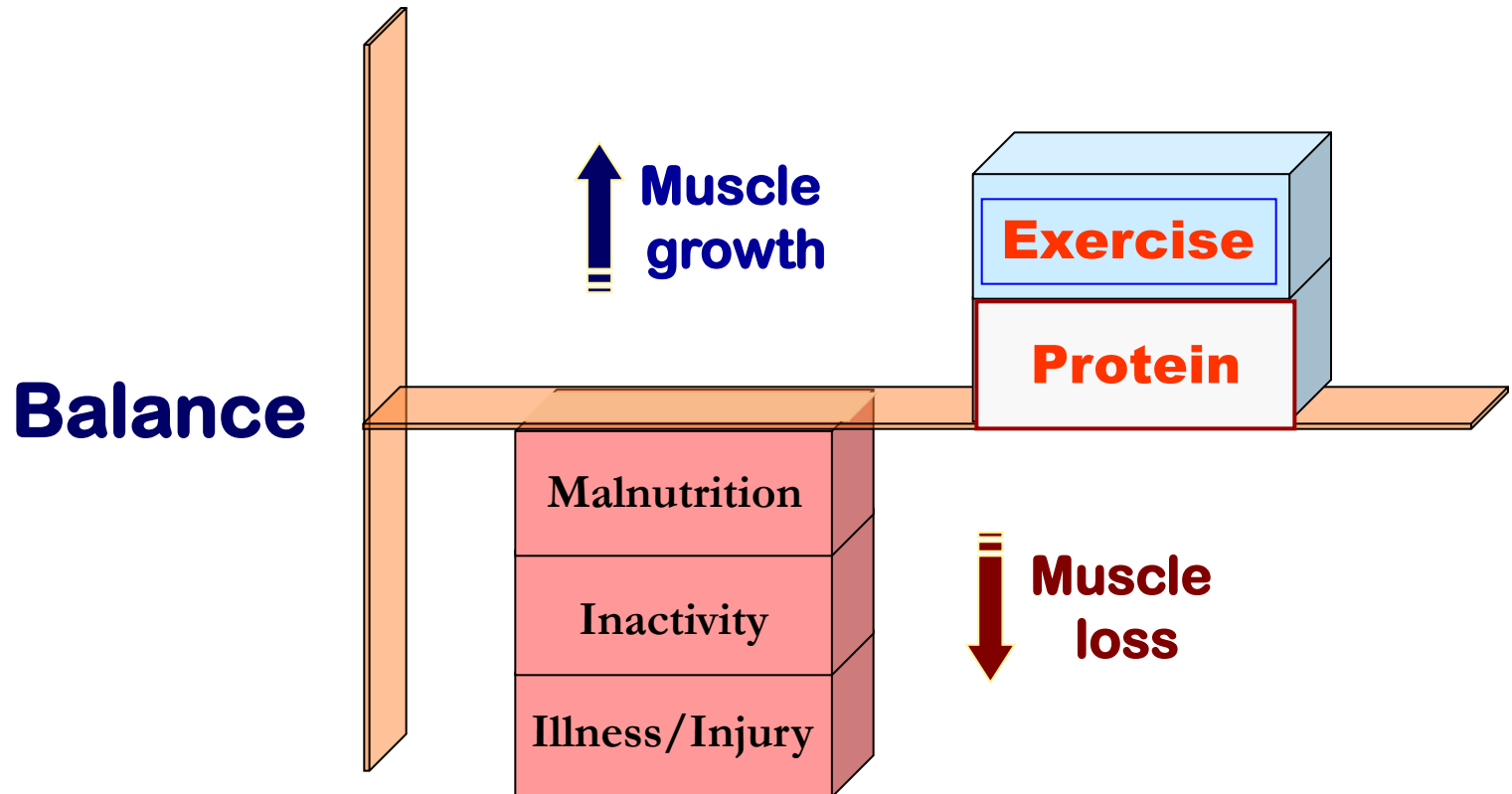


Fig. 2. Schematic representation of muscle anabolic response according to protein intake and exercise in older subjects. In situation of frailty, a lower muscle response may be restored by improving quantitative or qualitative aspects of protein consumption (box 1). Physical activity may potentiate the sensitivity of muscle protein synthesis to dietary protein (box 2).

Maintaining Muscle Mass and Function



Interaction exercise and protein



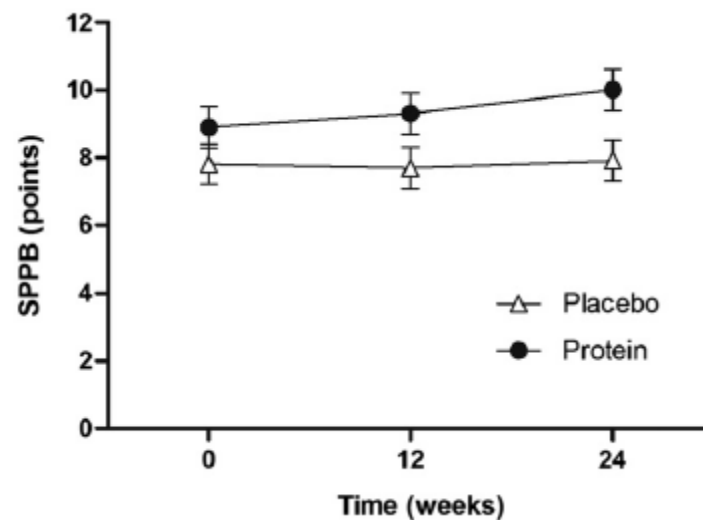
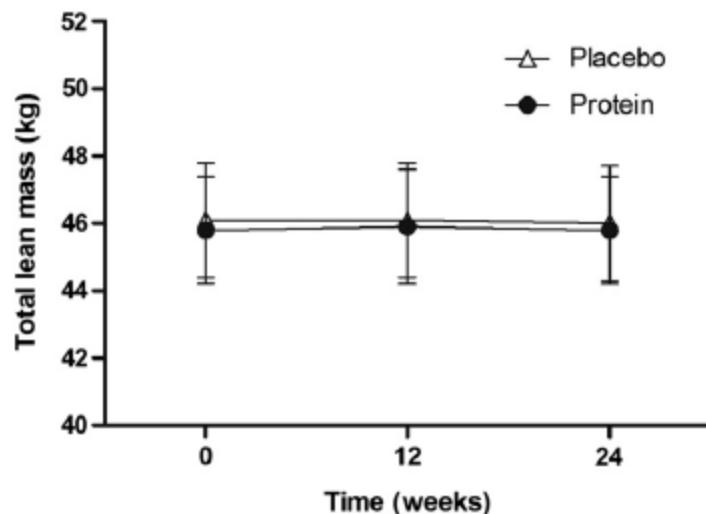
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Original Study

Protein Supplementation Improves Physical Performance in Frail Elderly People:
A Randomized, Double-Blind, Placebo-Controlled Trial



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Interaction exercise and protein

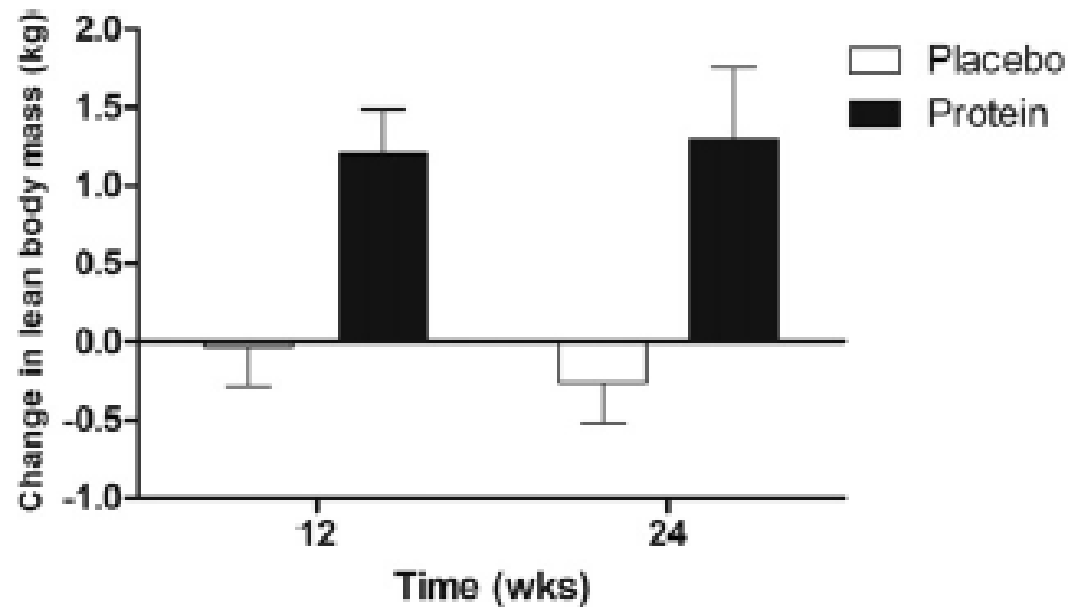


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Original Study

Protein Supplementation Increases Muscle Mass Gain During Prolonged Resistance-Type Exercise Training in Frail Elderly People: A Randomized, Double-Blind, Placebo-Controlled Trial



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Conclusion

- Sarcopenia/Osteopenia/Dysmobility/Frailty: hot and clinically relevant areas of medicine
- Physiology/Pathophysiology of muscle protein synthesis in the elderly: peculiarities to consider
- The right protein, the right AA, the right dose at the right moment, the right level of calories, Vit. D to have the best possible effects on muscle protein synthesis and protection from fractures in the elderly patient
- Physical exercise + clinical nutrition = the «magic bullet» in successful management of Sarcopenia/Osteopenia/Dysmobility/Frailty