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Supplementazione nutrizionale sistematica: quali nuove evidenze cliniche e farmacoeconomiche?

27 - 29 novembre 2025

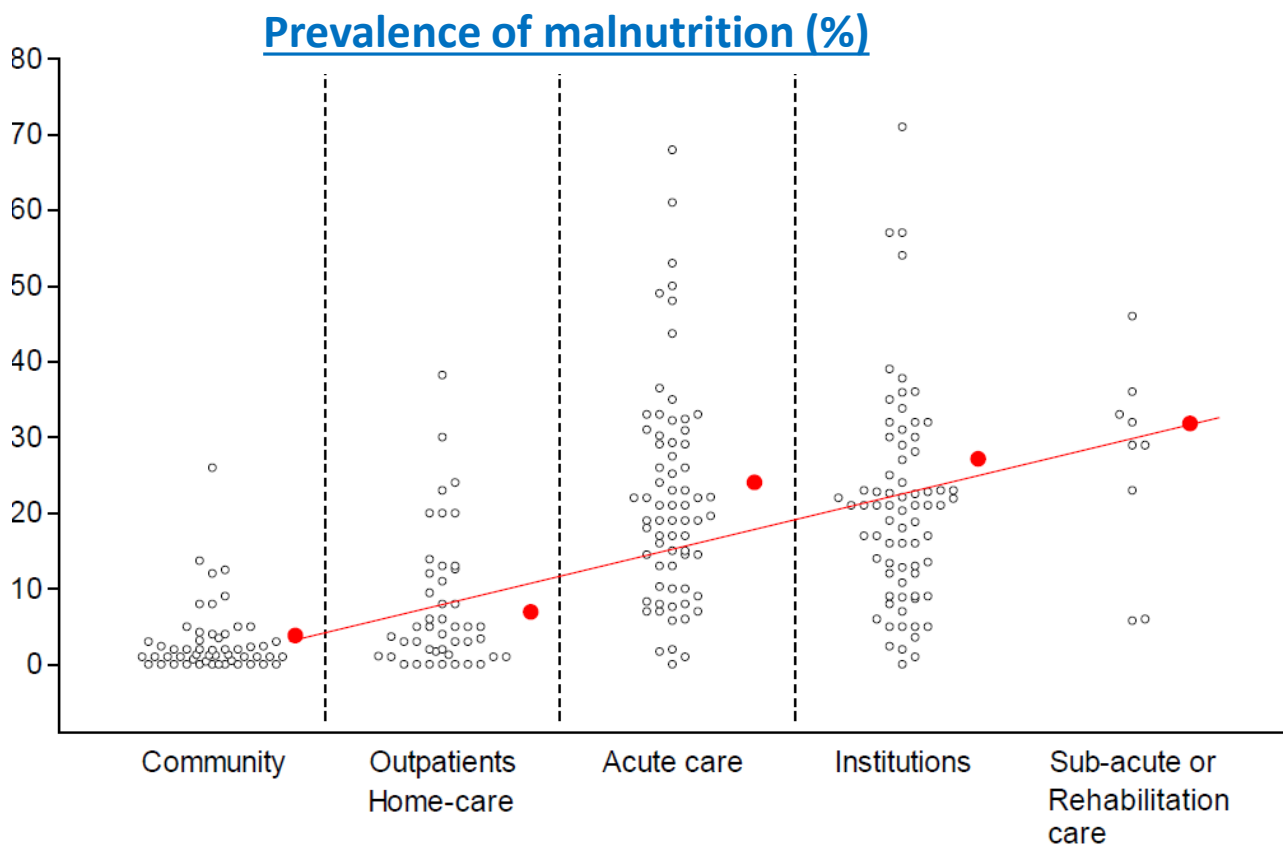
Padova Congress
Via Carlo Goldoni 8, Cancello C – Padova

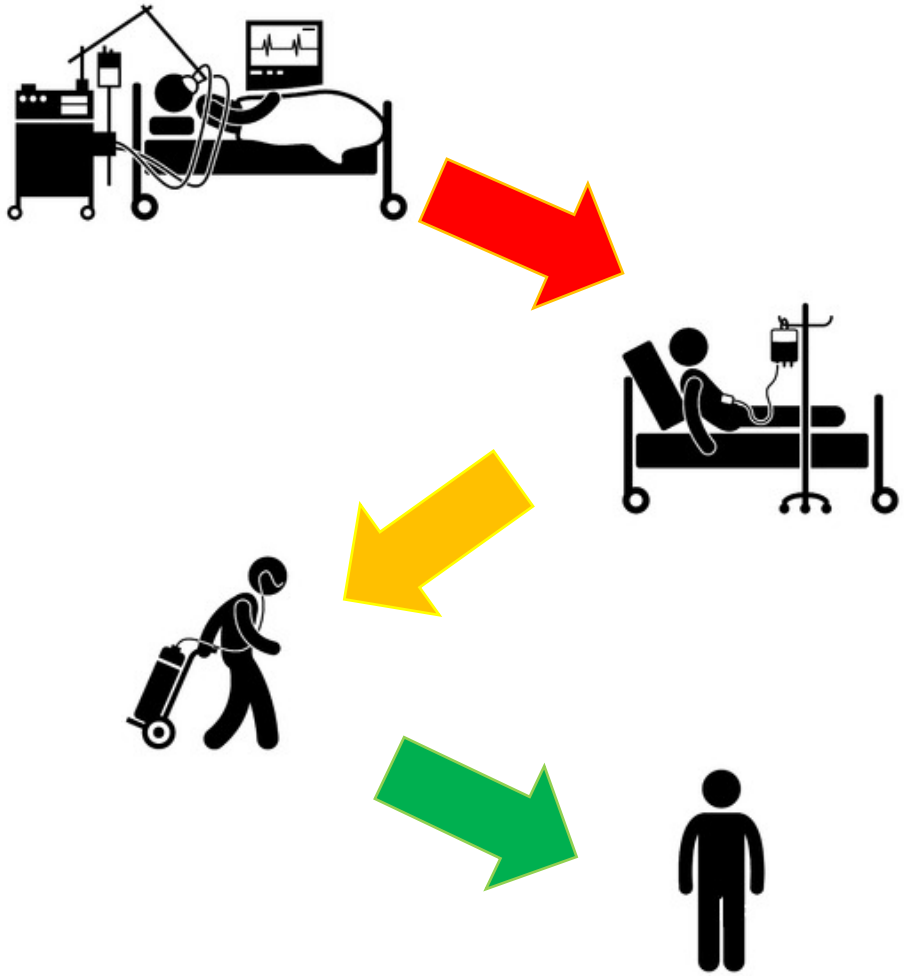
SCANSIONA IL QR CODE PER SCOPRIRE LE NUOVE EVIDENZE SULL'USO SISTEMATICO DI ONS ALL'OSPEDALIZZAZIONE

DANONE | NUTRICIA
LIFE-TRANSFORMING NUTRITION

Let’s treat and identify early high risk conditions!

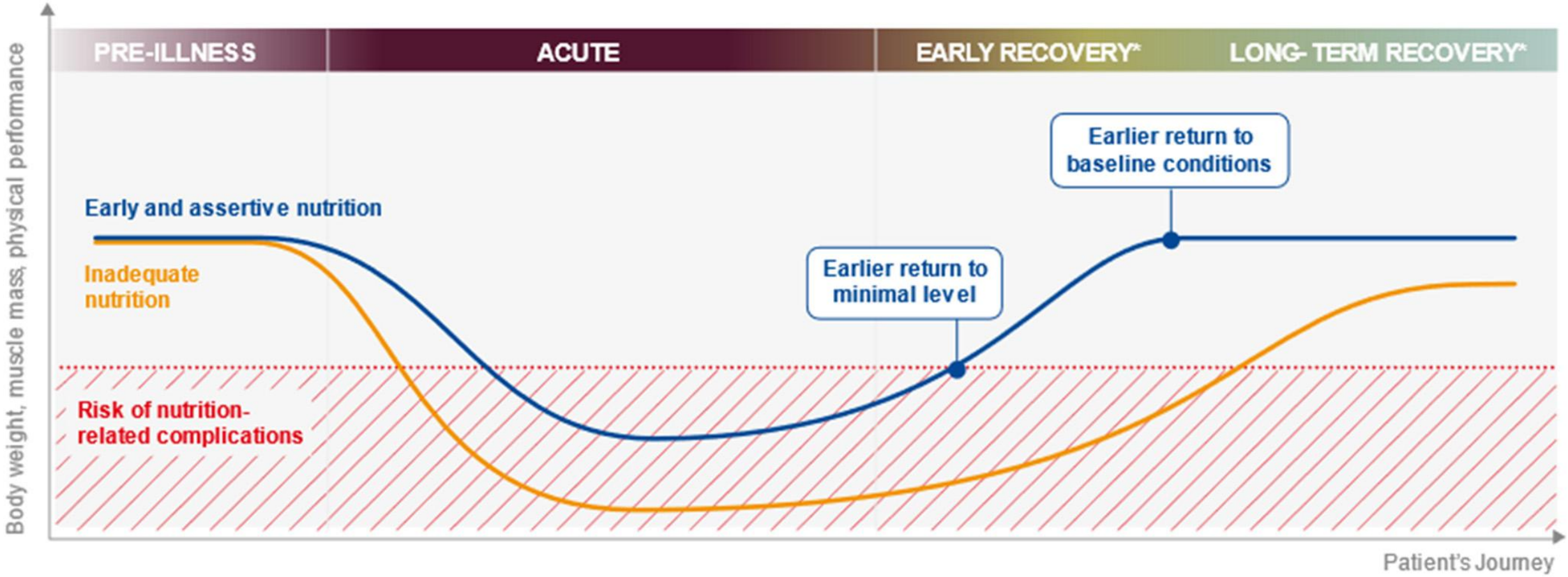
Addressing the patient's journey assertively to avoid the worsening of nutritional status





Cereda E. Curr Opin Clin Nutr Metab Care 2012, 15:29–41

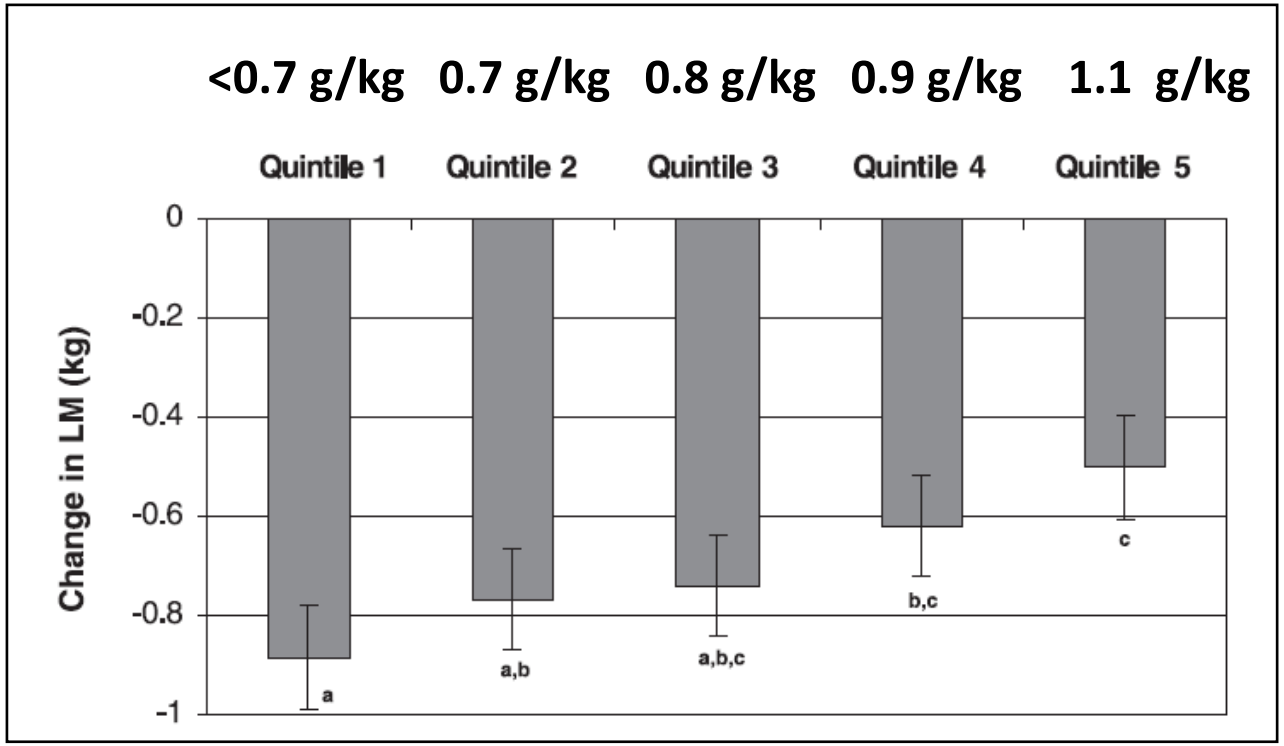
Assertive nutrition is aimed to optimize patient's recovery



Cereda E et al. Nutrients. 2021 Sep 21;13(9)3293

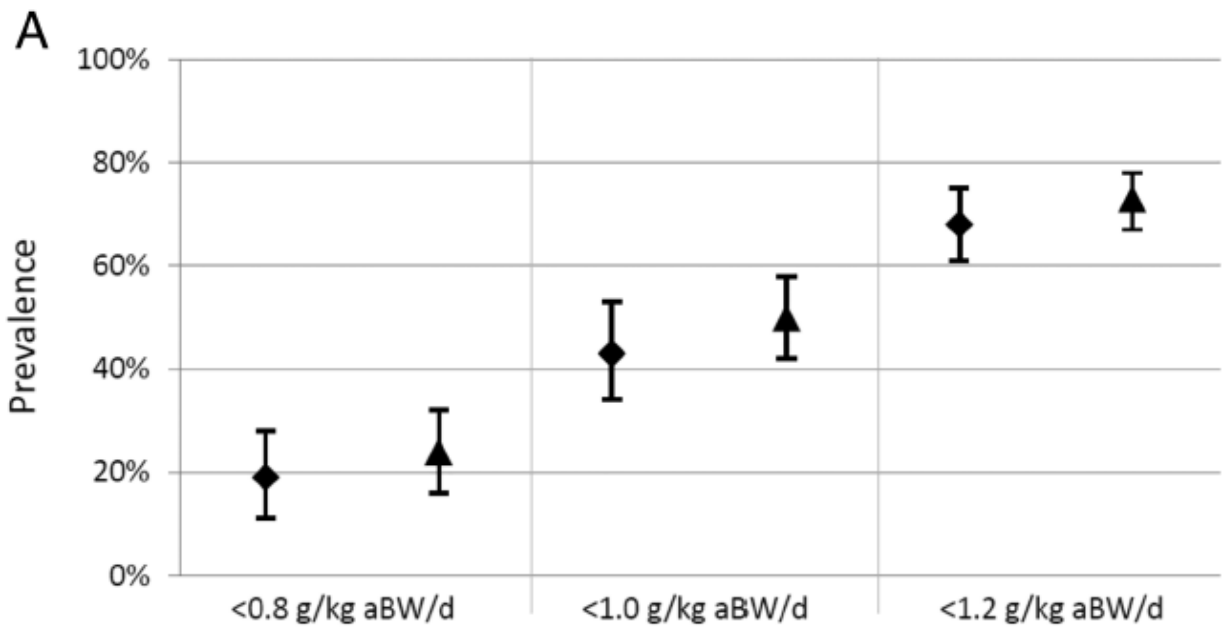
Low protein intake is associated with disability trajectories and loss of muscle mass

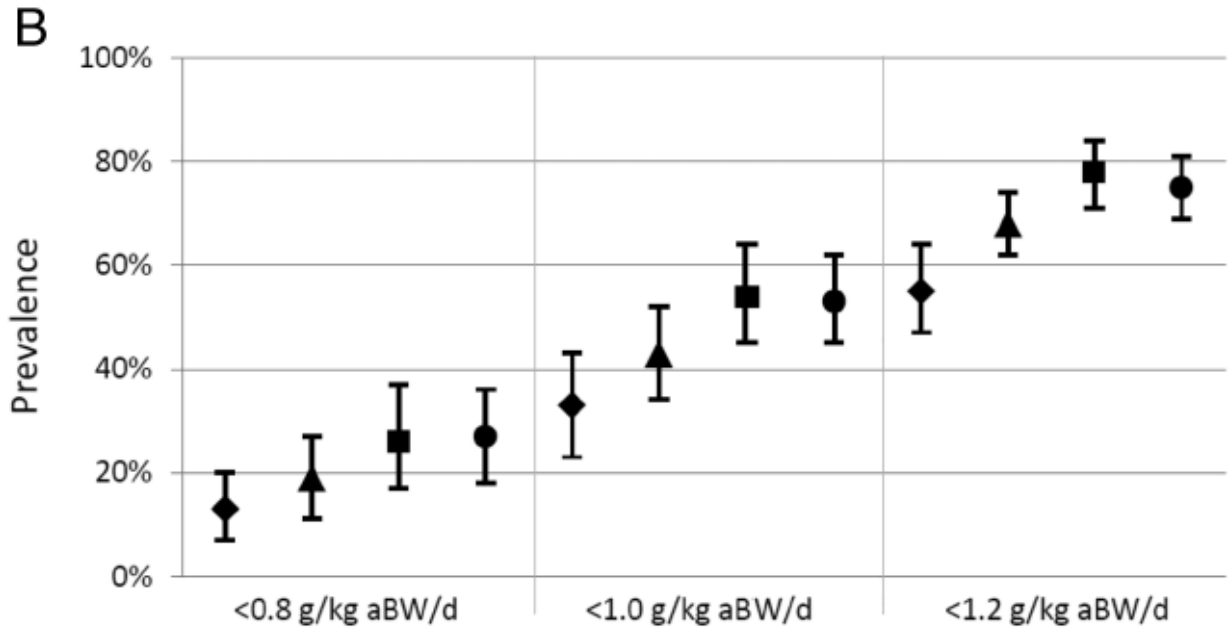
Trajectory	Odds ratio (95%CI)
Constant very low disability (n = 74)	7.97 (1.96–32.43) .004
Low increasing to mild disability (n = 260)	3.28 (1.09–9.87) .03
Mild increasing to moderate disability (n = 244)	1.49 (0.54–4.16) .44



Houston DK et al. Am J Clin Nutr 2008;87:150 –5.
Mendonça N et al. J Am Geriatr Soc 2019;67:50–56.

Protein intake below recommended in community-dwelling older adults (PROMISS consortium analysis)



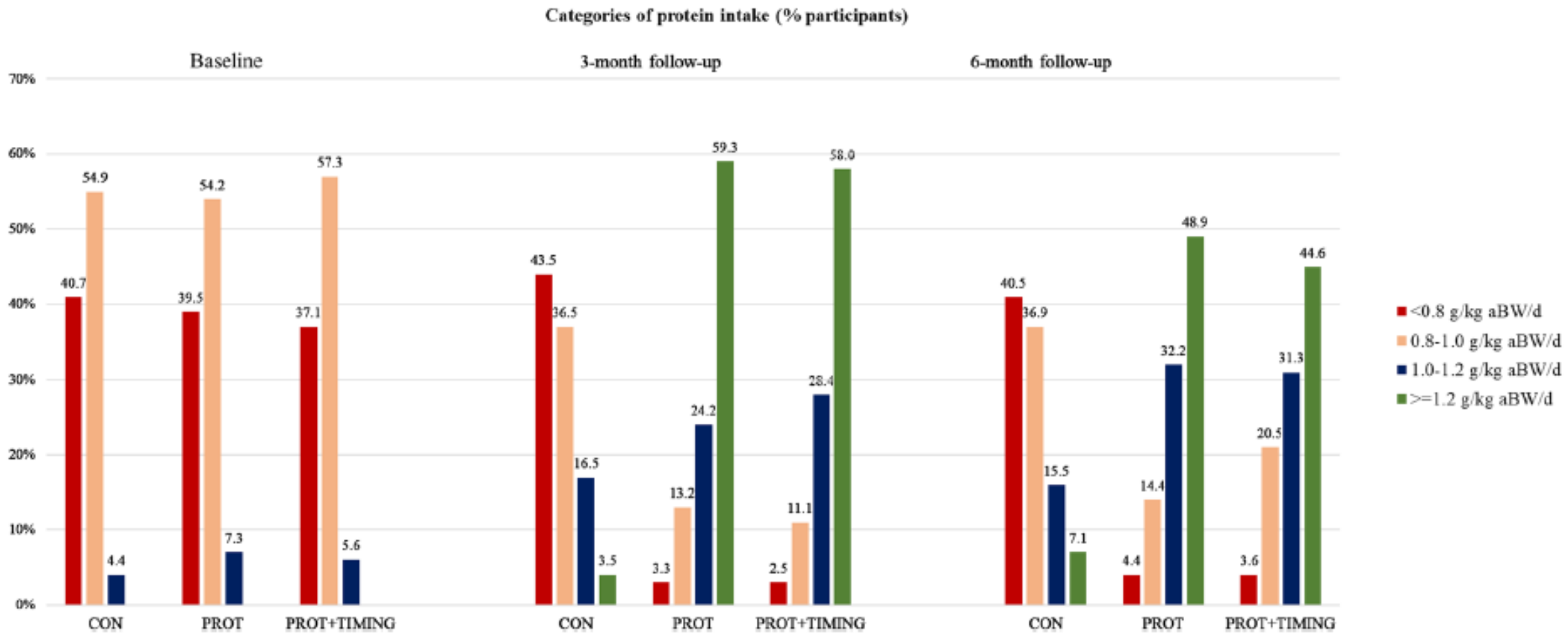


Gender (B; ♦ female, ▲ male)

Body mass index (♦ <22, ▲ 22–27, ■ 27–30, ● ≥30 kg/m^2)

Hengeveld LM et al. J Cachexia Sarcopenia Muscle 2020; 11: 1212–1222

Dietary advice increases intake in older adults with lower habitual protein intake



Reinders I et al. Neurology. European Journal of Nutrition (2022) 61:505–520

Acute hospitalization

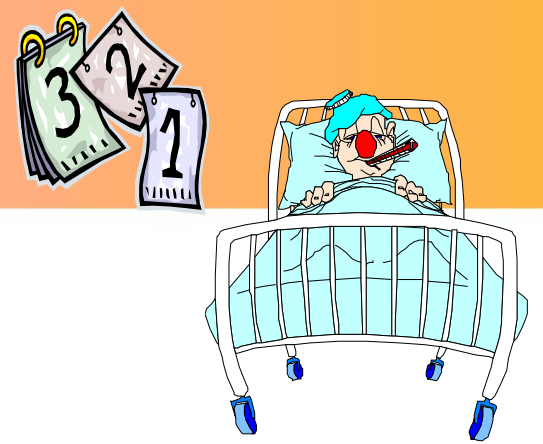
Inpatients are likely to present since admission, and to experience during their stay, a significant impairment of the protein-calorie balance.

Increased needs (underlying disease [inflammation])

Reduced food intake (underlying disease, polymorbidity and polypharmacy, fasting for diagnostic procedures as well as the unpleasant feeding experience mainly due to the environment and the quality of food)

Norman K et al. Clin Nutr. 2008;27(1):5-15
Thibault R et al. Clin Nutr. 2021;40(12):5684-5709

Hospitalization: deterioration?



All these factors contribute to nutritional deterioration

Weight loss

Unavoidable bed rest
(+++ in the old adults)

+++ Muscle mass
(up to 1 kg over 3 days)

It impairs protein anabolism even in presence of adequate calorie provision, while calorie restriction enhances the catabolic response to inactivity

Di Girolamo FG et al. Front Nutr. 2021;8:633987

How to cope with the patient's needs?

The strategies to be implemented are the following (in order):

Dietary counselling with food fortification

The use of ONS
[high-protein & energy-dense])

Nutritional counselling

Artificial nutrition

Wunderle C et al. Clin Nutr. 2023;42(9):1545-1568
Thibault R et al. Clin Nutr. 2021;40(12):5684-5709

Be pro-active, not reactive!

Although no clear recommendation exists, a more pro-active – rather than reactive – approach should be considered.

Guideline-based recommendations

Calorie and protein targets, are frequently hard to be achieved only with standard hospital food.

EFFORT trial
and
literature synthesis

Calories: 30 kcal/kg/day
Proteins: 1.2-1.5 g/kg/day

Wunderle C et al. Clin Nutr. 2023;42(9):1545-1568
Thibault R et al. Clin Nutr. 2021;40(12):5684-5709
Volkert D et al. Clin Nutr. 2022;41(4):958-989

The value of ONSs in daily practice

ONSs are a valuable treatment strategy to improve protein-calorie intake but evidence on the timing they should be provided along with nutritional counselling is lacking.

We designed the present trial to evaluate the efficacy of a systematic use of high-protein energy-dense ONS since hospital admission.

COMPACT-BIVA: Trial design (NCT02763904)

Fondazione IRCCS Policlinico San Matteo, Pavia

Hospital admission

Excluded:

- Indication for artificial nutrition
- Severe hypophagia (<50% of dietary requirements) or indication to fasting
- Scheduled for surgery
- Contraindication to ONS or indication to the use of disease specific ONS
- Terminal illness

Included:

- Patients with NRS-2002≥3
- Age ≥18 years
- Expected LOS ≥7 days
- Assessed within 48 hours

Randomization (1:1)

n=110

Experimental arm:
Nutritional counselling + systematic ONS* provision (twice a day) since admission

Weekly consultation with Dietitians

n=110

Control arm:
Nutritional counselling + ONS* provision on demand (since day 8) *

* in case of incapacity of meeting the estimated dietary requirements

* Fortimel Compact Protein

Cereda E et al. Clin Nutr. 2025; In publication

COMPACT-BIVA: Trial design (NCT02763904)

- Body composition
- Anthropometry
- Dietary intakes
- Muscle strength

- Dietary intake

- Body composition
- Anthropometry
- Dietary intake
- Muscle strength

- Body composition
- Anthropometry
- Dietary intake
- Muscle strength
- Length of hospital stay
- Risk of infections

OUTCOMES

PRIMARY: Body composition (Bioimpedence, PhA)

SECONDARY:

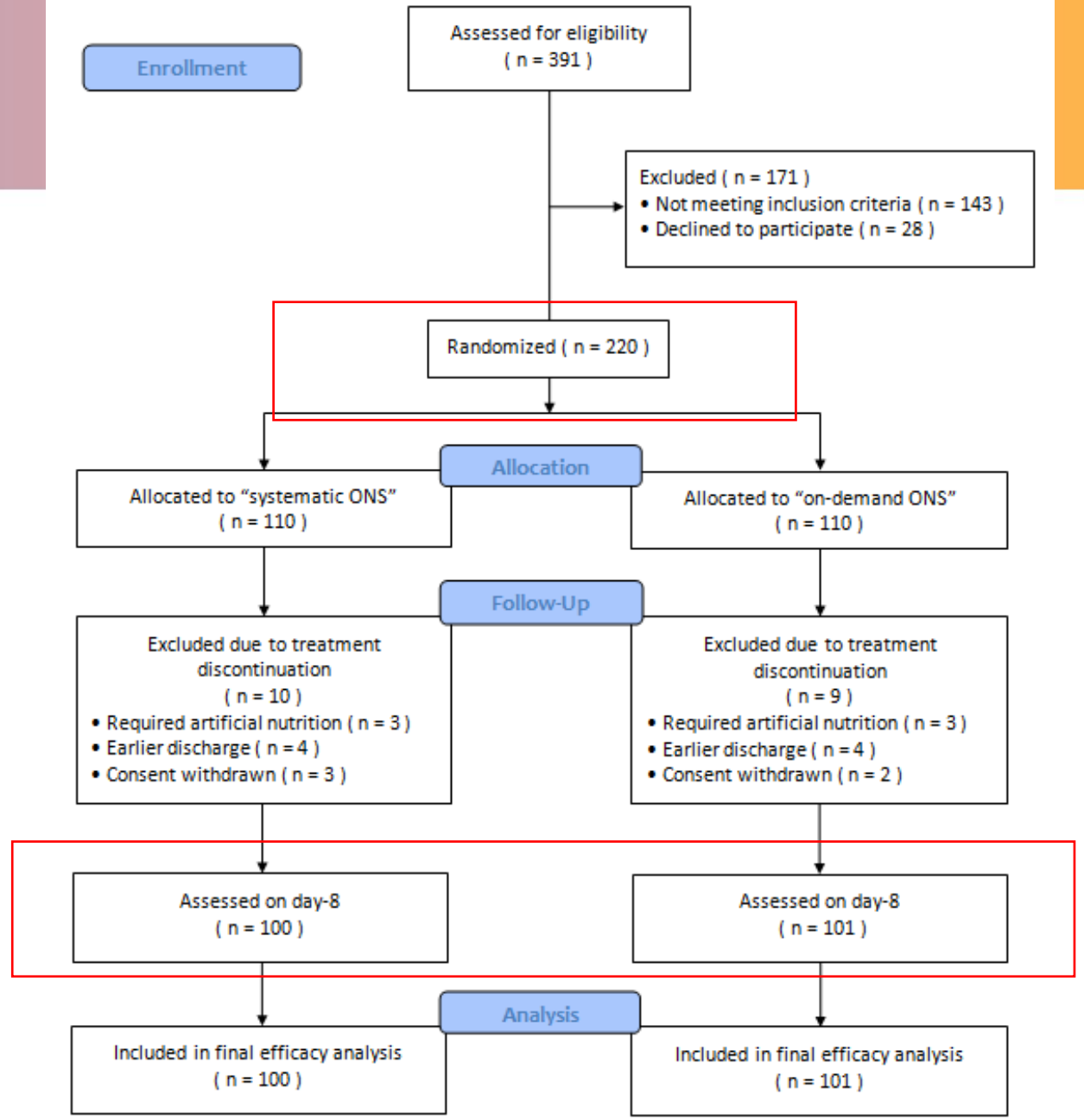
- **Anthropometry** (body weight, BMI)
- **Dietary intake** (proteins and calories)
- **Muscle strength** (hand-grip strength)
- **Length of hospital stay**
- **Risk of infections**

Primary efficacy evaluation

Cereda E et al. Clin Nutr. 2025; In publication

COMPACT-BIVA: Results

Study flow diagram



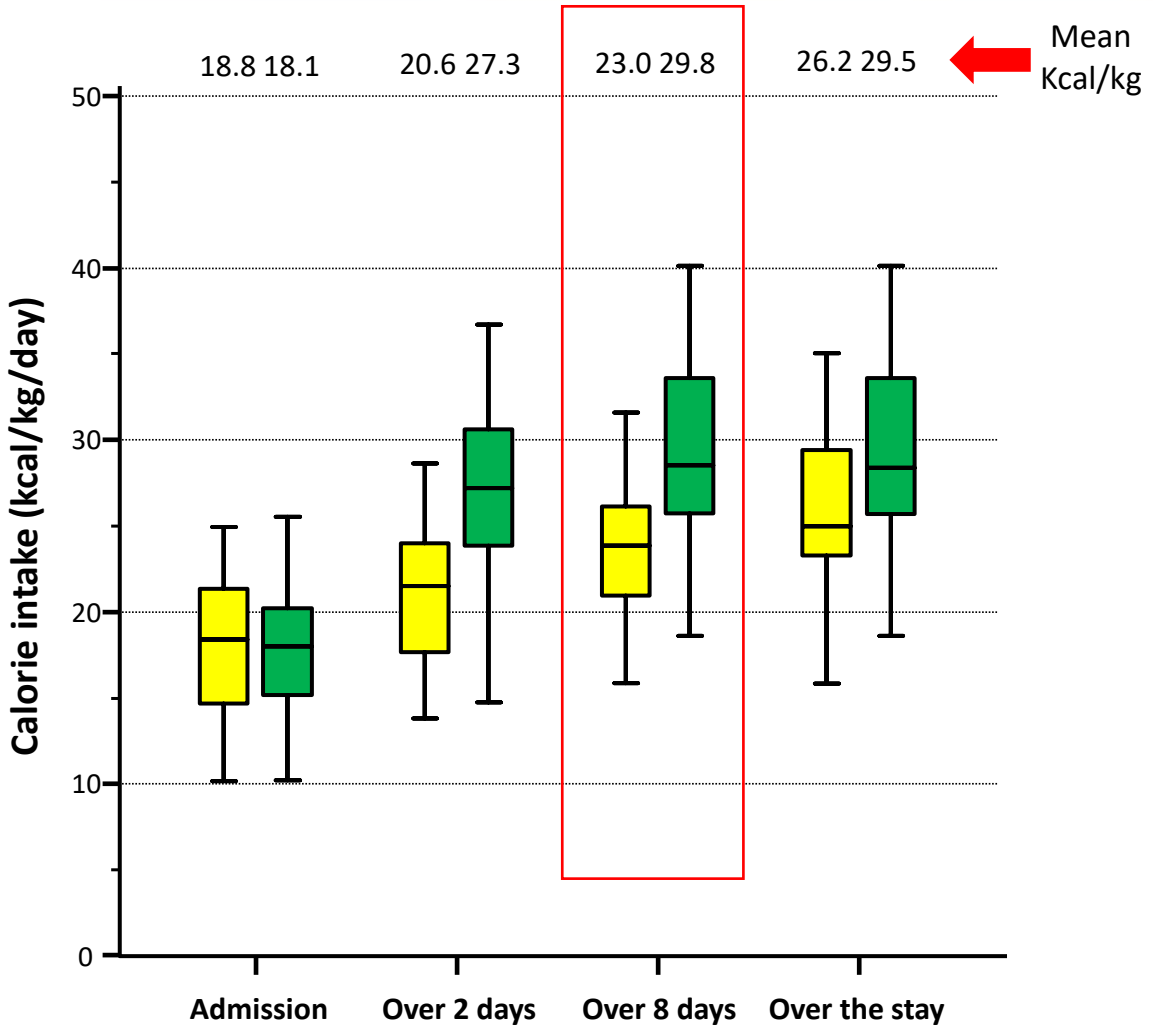
Cereda E et al. Clin Nutr. 2025; In publication

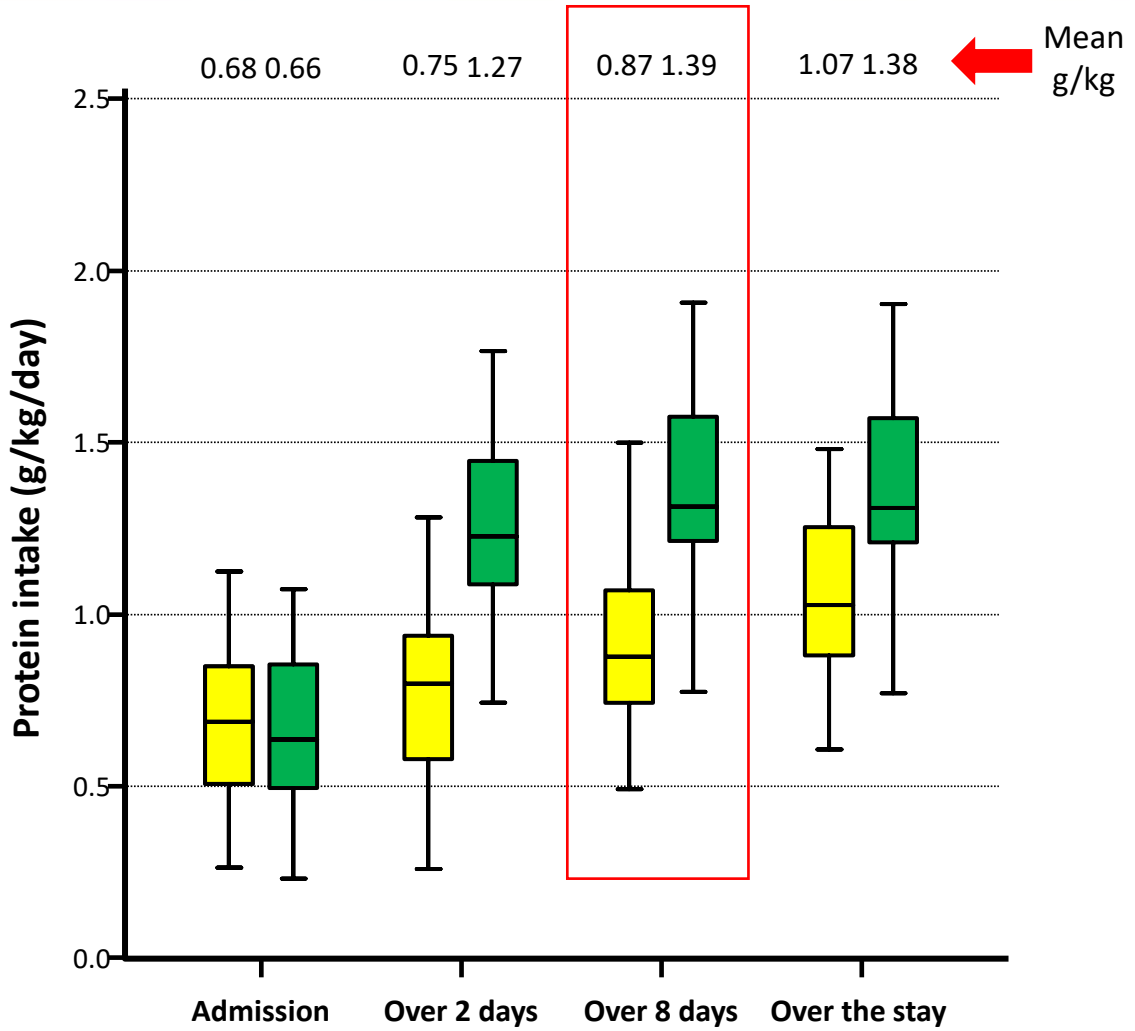
COMPACT-BIVA: Results

	Whole randomized population		Modified intention-to-treat population	
Characteristic	On-demand ONS (N=110)	Systematic ONS (N=110)	On-demand ONS (N=101)	Systematic ONS (N=100)
Sex (male), N (%)	78 (77.2)	74 (74.0)	69 (68.3)	68 (68.0)
Age (years), Mean (SD)	72.9 (11.9)	72.2 (13.0)	72.1 (11.9)	71.5 (13.2)
Admission diagnosis, N (%)				
General internal medicine	10 (9.1)	12 (10.9)	9 (8.9)	11 (11.0)
Respiratory	45 (40.9)	40 (36.4)	43 (42.6)	39 (39.0)
Infectious disease	13 (11.8)	15 (13.6)	12 (11.9)	13 (13.0)
Oncology/hematology	15 (13.6)	17 (15.5)	12 (11.9)	14 (14.0)
Cardiology	13 (11.8)	15 (13.6)	11 (10.9)	13 (13.0)
Gastroenterology	7 (6.4)	6 (5.5)	7 (6.9)	5 (5.0)
Others	7 (6.4)	5 (4.5)	7 (6.9)	5 (5.0)
Body mass index (kg/m^2), Mean (SD)	21.5 (3.9)	20.8 (3.8)	21.6 (3.8)	21.0 (3.8)
Weight loss (%), Mean (SD)	11.6 (7.6)	11.9 (8.1)	11.0 (6.9)	11.6 (7.3)
Energy intake (kcal/Kg/day), Mean (SD)	18.1 (6.2)	18.1 (6.1)	18.8 (6.0)	18.1 (6.0)
Protein intake (g/Kg/day), Mean (SD)	0.67 (0.29)	0.66 (0.30)	0.68 (0.29)	0.66 (0.29)
NRS-2002 (score), Mean (SD)	4.4 (0.8)	4.4 (0.7)	4.3 (0.8)	4.4 (0.6)
Malnutrition (GLIM criteria), N (%)	105 (95.5)	108 (98.2)	96 (95.0)	100 (100.0)
Phase angle (°), Mean (SD)	3.59 (0.89)	3.57 (1.01)	3.58 (0.91)	3.58 (1.00)
Handgrip strength (kg), Mean (SD)	16.5 (8.9)	16.3 (9.7)	15.7 (8.5)	16.8 (9.6)

Cereda E et al. Clin Nutr. 2025; In publication

COMPACT-BIVA: Results





ONS on demand Systematic ONS

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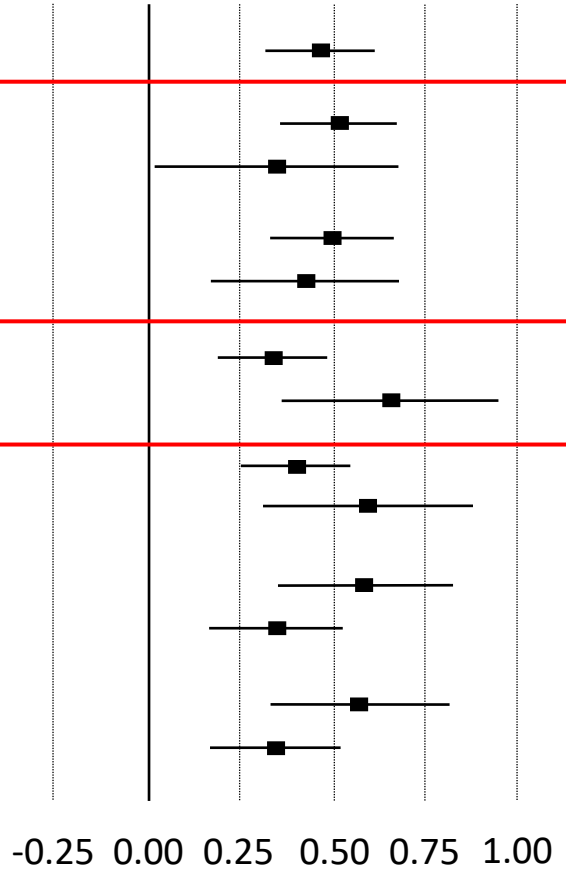
COMPACT-BIVA: Results

Groups	Mean difference in PhA (°) at day-8 (95% confidence interval)		P-value for interaction
Overall	0.47	(0.31-0.62)	--
Men	0.52	(0.36-0.68)	0.30
Women	0.35	(0.02-0.68)	
Age <75 years	0.50	(0.33-0.67)	0.65
Age ≥75 years	0.43	(0.17-0.69)	
NRS-2002 = 3-4	0.34	(0.19-0.49)	0.040
NRS-2002 = 5-6	0.66	(0.36-0.96)	
No sarcopenia	0.39	(0.24-0.54)	0.22
Sarcopenia	0.58	(0.30-0.86)	
Calorie intake ≤18 Kcal/kg/day	0.59	(0.35-0.83)	0.14
Calorie intake >18 Kcal/kg/day	0.35	(0.17-0.53)	
Protein intake ≤0.66 g/kg/day	0.58	(0.34-0.82)	0.13
Protein intake >0.66 g/kg/day	0.35	(0.17-0.53)	



Cereda E et al. Clin Nutr. 2025; In publication

COMPACT-BIVA: Results

	Day 8				Discharge			
	On demand ONS (N=101)	Systematic ONS (N=100)	Treatment effect [a]	P-value [c]	On demand ONS (N=101)	Systematic ONS (N=100)	Treatment effect [a]	P-value [c]
Primary outcome								
Δ Phase angle (°)	-0.02 [0.40]	0.45 [0.66] [b]	0.47 (0.31, 0.62)	**<0.001**	0.33 [0.40] [b]	0.82 [0.66] [b]	0.49 (0.33, 0.64)	**<0.001**
Secondary outcomes								
Δ Handgrip strength (kg)	1.3 [2.5] [b]	1.8 [2.8] [b]	0.5 (-0.2, 1.3)	0.13	2.9 [2.5] [b]	3.7 [2.8] [b]	0.8 (0.1, 1.5)	**0.042**
Δ Calorie intake (kcal/kg)	4.2 [4.6] [b]	11.7 [5.8] [b]	7.5 (6.2, 9.2)	**<0.001**	8.5 [6.1] [b]	11.4 [5.7] [b]	2.9 (1.3, 4.5)	**0.001**
Δ Protein intake (g/kg)	0.19 [0.22] [b]	0.73 [0.34] [b]	0.54 (0.37, 0.62)	**<0.001**	0.54 [0.35] [b]	0.72 [0.32] [b]	0.18 (0.09, 0.27)	**<0.001**
Δ Body weight (kg)	-0.1 [1.1]	0.3 [0.6] [b]	0.4 (0.2, 0.7)	**<0.001**	0.0 [1.1]	0.4 [0.7] [b]	0.4 (0.2, 0.7)	**<0.001**
Δ Length of stay (days)	--	--	--	--	14 [11-18]	12 [8-17]	-2 (-3, 0)	**0.044**
New infections, N [%]	--	--	--	--	3 [3.0]	2 [2.0]	-1 (-3.3, 5.3)	0.66

[a] Data are provided as mean or median difference and (95%CI).
[b] Within-group change Vs. baseline significant at the 5% level.

COMPACT-BIVA: Results

Exploratory endpoints

	Day 8			Discharge		
	Δ Calorie intake	**Δ Protein intake**	**Δ Handgrip**	**Δ Calorie intake**	**Δ Protein intake**	**Δ Handgrip**
Δ Phase angle	0.37 (P<0.001)	0.46 (P<0.001)	0.21 (P=0.004)	0.22 (P<0.002)	0.20 (P=0.006)	0.22 (P=0.002)
Δ Handgrip	0.30 (P<0.001)	0.18 (P=0.013)	--	0.24 (P<0.001)	0.20 (P=0.004)	--

Safety

Adverse Event	Systematic ONS (N=110)	Adverse Event leading to discontinuation	On-demand ONS (N=80)	Adverse Event leading to discontinuation
Sense of fullness, N (%)	12	--	8	--
Nausea, N (%)	2	2	1	1
Sense of fullness, N (%)	1	1	--	--

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COMPACT-BIVA: Discussion

Although we have limited the inclusion to moderately hypophagic patients (reasonably less complicated than others requiring artificial nutrition) ….

The study:

- confirmed the value of nutritional counselling and tailoring of dietary interventions as standard of care in patients at nutritional risk (a significant improvement in almost all nutritional parameters was observed in both groups).
- provided a solution to the established difficulties in satisfying the estimated requirements – particularly of proteins - which the recommended adaptations of food did not appear to be effective to cope with.

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COMPACT-BIVA: Discussion

The importance of timing in addressing the patient's needs has been further emphasized by the subgroup analysis showing a higher benefit in patients at higher nutritional risk.

Finally, although a formal health economic analysis was not performed, taking into account the cost of one day of ONS treatment (~3-4 €) and of hospital stay (~700-800 €), we can argue that systematic ONS provision is a cost-effective intervention in the examined setting.

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COMPACT-BIVA: Conclusions

In moderately **hypophagic adults** at **nutritional risk** and **hospitalized for acute care conditions**, the consumption of **energy-dense high-protein ONS since admission** improved the **patient journey body composition**, **muscle strength**, **protein-calorie intake**, as well as **body weight**, and **reduced the LOS**.

IMPROVEMENT IN NUTRITIONAL INTAKE

The systematic use of ONS leads to an increased **energy and protein intake**

IMPROVEMENT IN MUSCLE FUNCTION

Systematic use of ONS is associated with **higher handgrip strength**

IMPROVEMENT IN BODY COMPOSITION

Systematic use of ONS is associated with **improved body composition** as demonstrated by significant increase in **phase angle** and **body weight** in the **systematic ONS group**

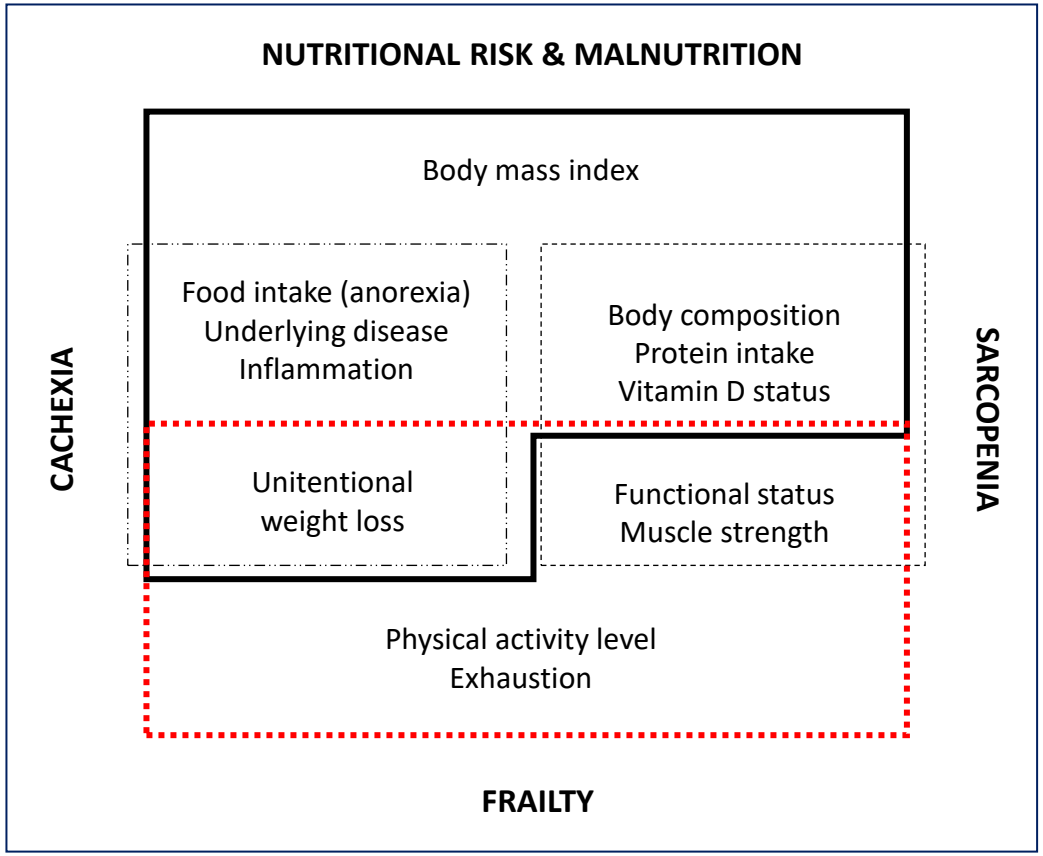
REDUCTION IN LENGTH OF STAY

Systematic use of ONS is associated with lower length of **hospital stay by 2 days**

In this setting a "*don't delay, start today*" approach is beneficial to patients.

Cereda E et al. Clin Nutr. 2025; In publication

Going beyond the treatment of malnutrition



EWGSOP2

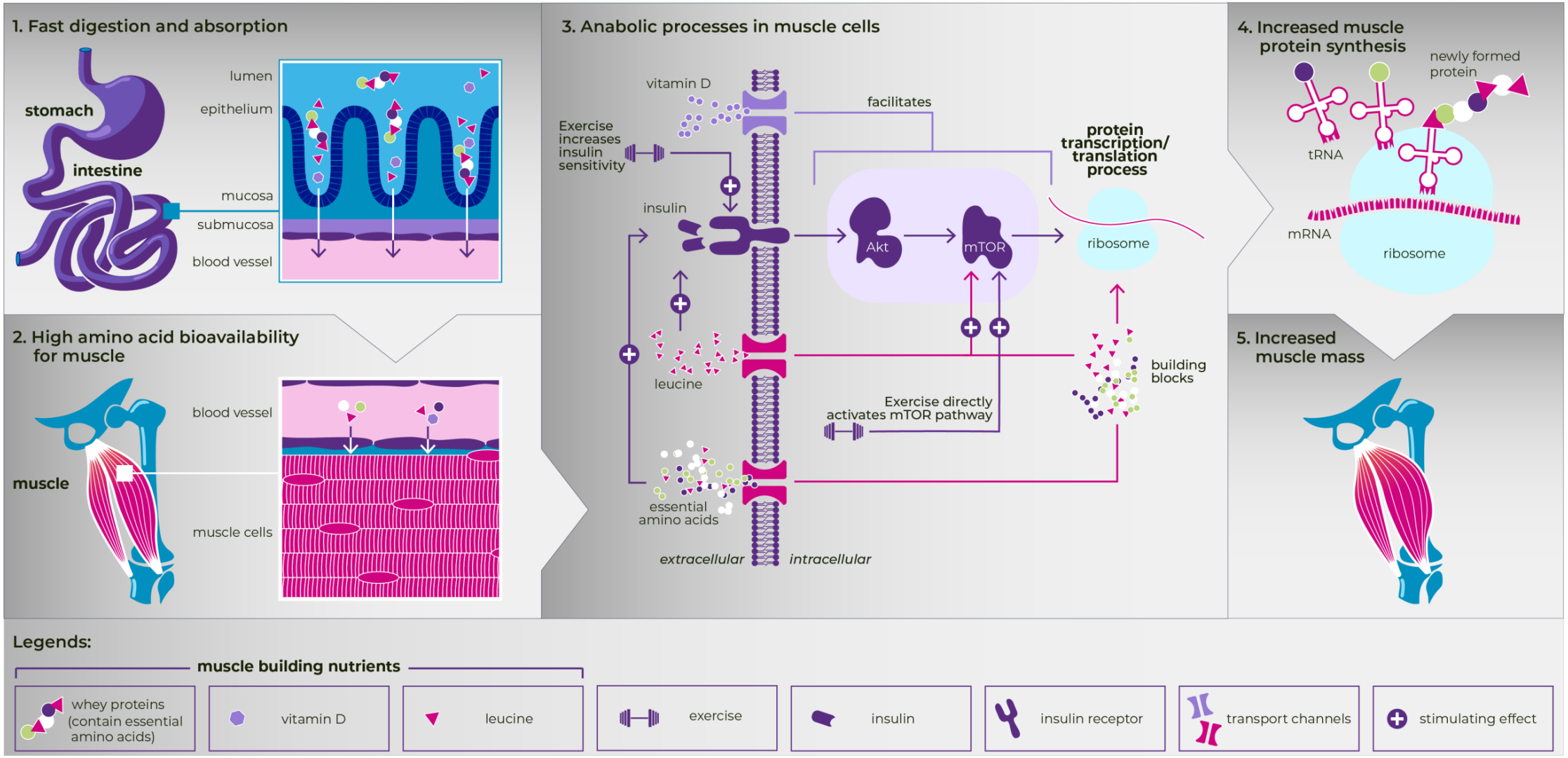
- Physical exercise, such as resistance training)
- Optimization of protein intake
- Vitamin D supplementation

PROT-AGE Study Group

- Protein intake of at least 1.2 g/kg/day
- Per-meal anabolic threshold of protein/amino acid intake of ~25-30 g (containing ~2.5-2.8 g of leucine)
- High-quality protein (e.g. whey)
- Adequate intake of vitamin D

Cereda E et al. Curr Opin Clin Nutr Metab Care 2018, 21:24–29
Bauer et al. J Am Med Dir Assoc 2013;14:542-59
Deutz et al. Clin Nutr 2014;33:929-36
Cruz-Jentoft AJ et al. Age Ageing. 2019;48:16-31.

Muscle-targeted supplementation



Cereda E et al. Nutrients. 2022 Apr 6;14(7):1524

Muscle-targeted supplementation with high-quality proteins, leucine and vitamin D (IRIS study)

Rondanelli M, Cereda E et al. J Cachexia Sarcopenia Muscle 2020;11(6):1535-1547.

(NCT03120026)

Sarcopenic older adults
Randomized
(1:1)
N= 140

N= 70 → **Experimental group**

- Hospital diet
  - FortiFit (2x/day): Fortifit® powder containing 20 g whey protein, 2.8 g total leucine, 800 IU vitamin D, and 500 mg calcium/serve
- Individualized physical rehabilitation program

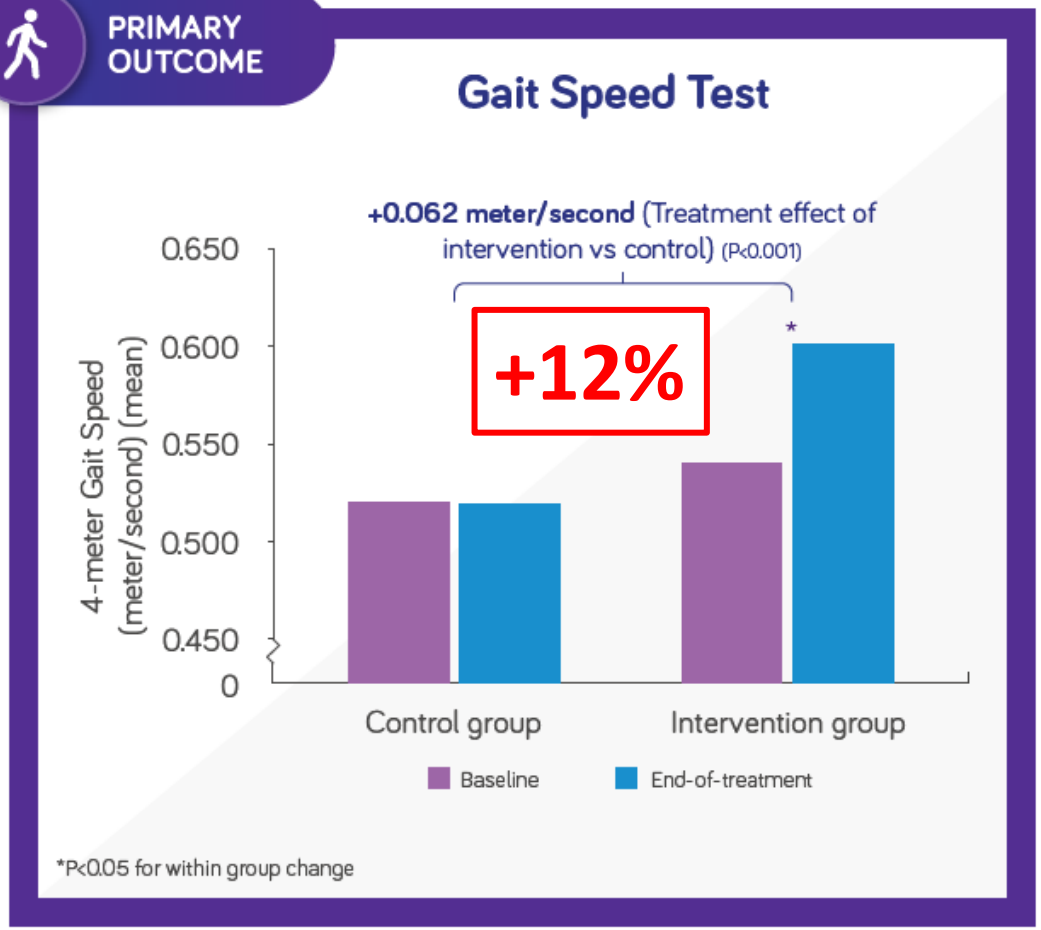
INTERVENTION formula
given **≥4 weeks, ≤8 weeks** (minimum and maximum duration of the rehabilitation)

N= 70 → **Control group**

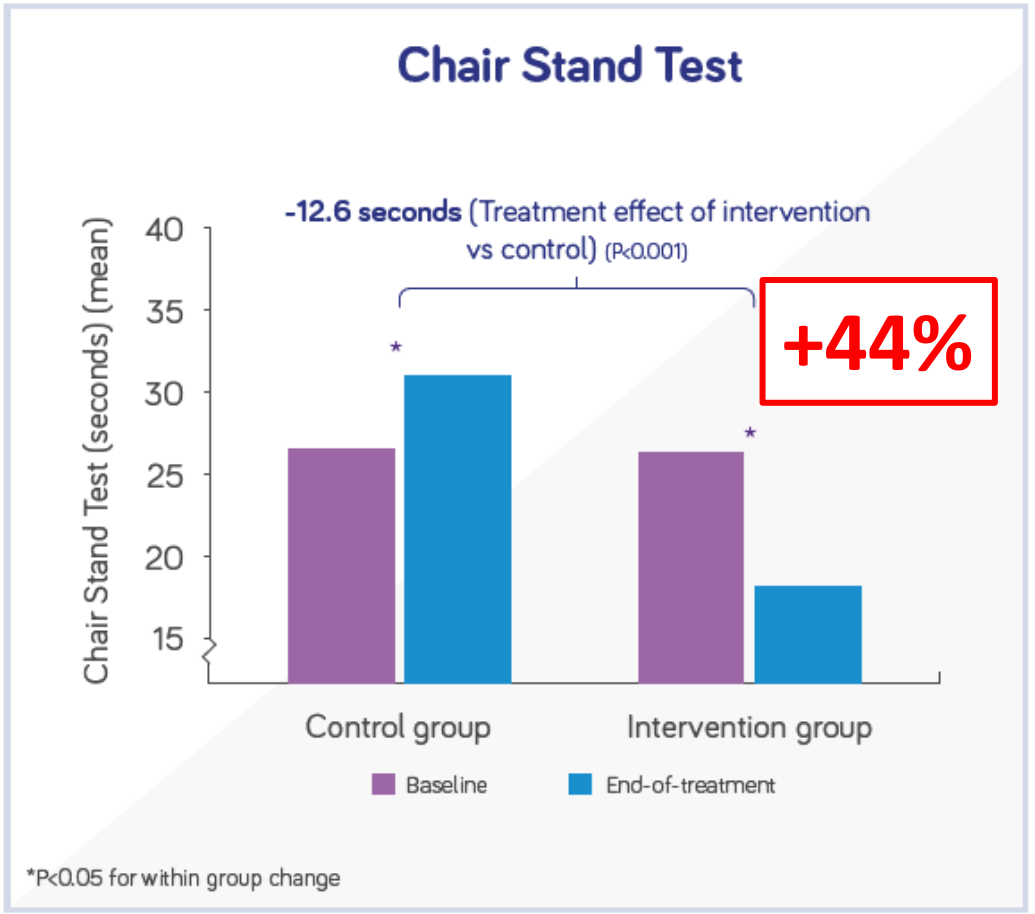
- Hospital diet
  - Iso-caloric control intervention (2x/day)
- Individualized physical rehabilitation program

Muscle-targeted supplementation with high-quality proteins, leucine and vitamin D (IRIS study)

PRIMARY OUTCOME



Physical performance



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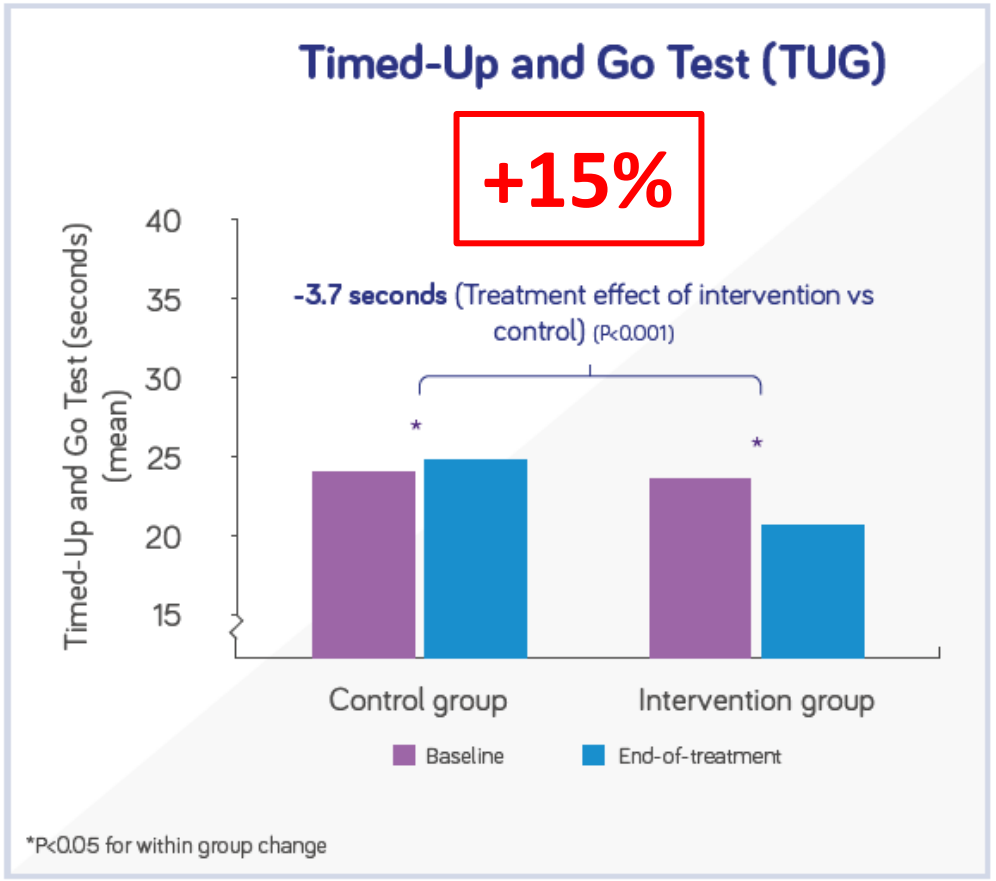
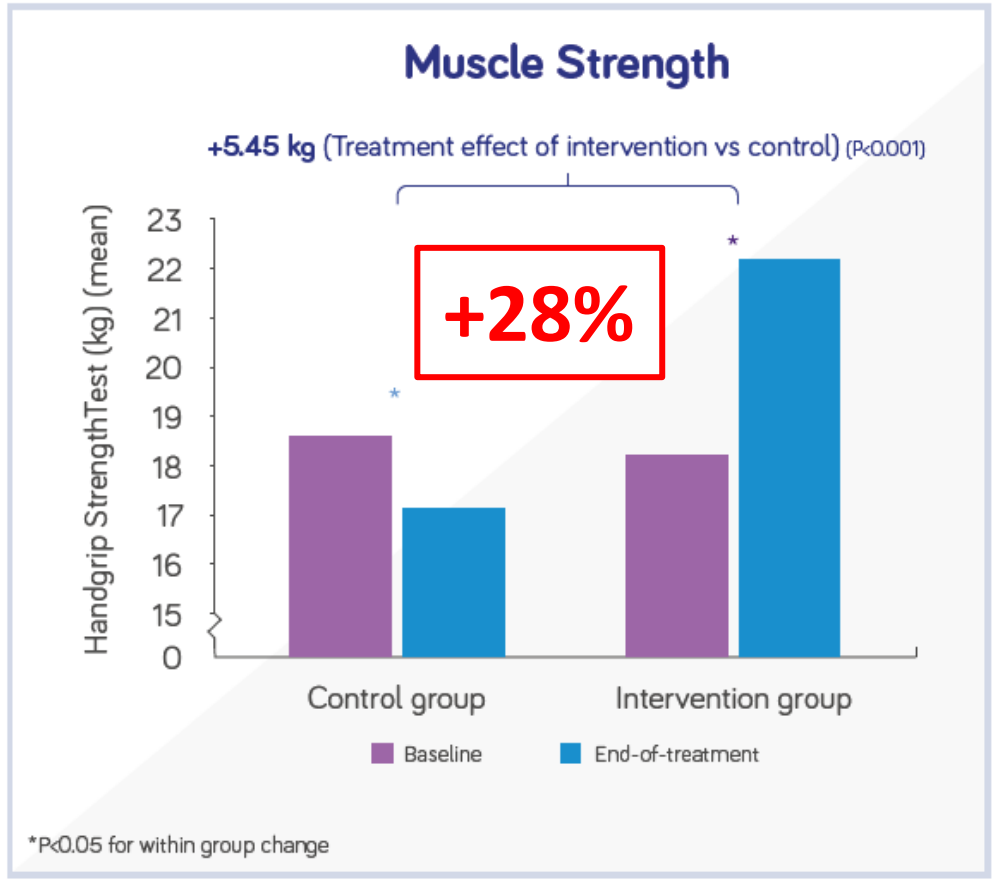
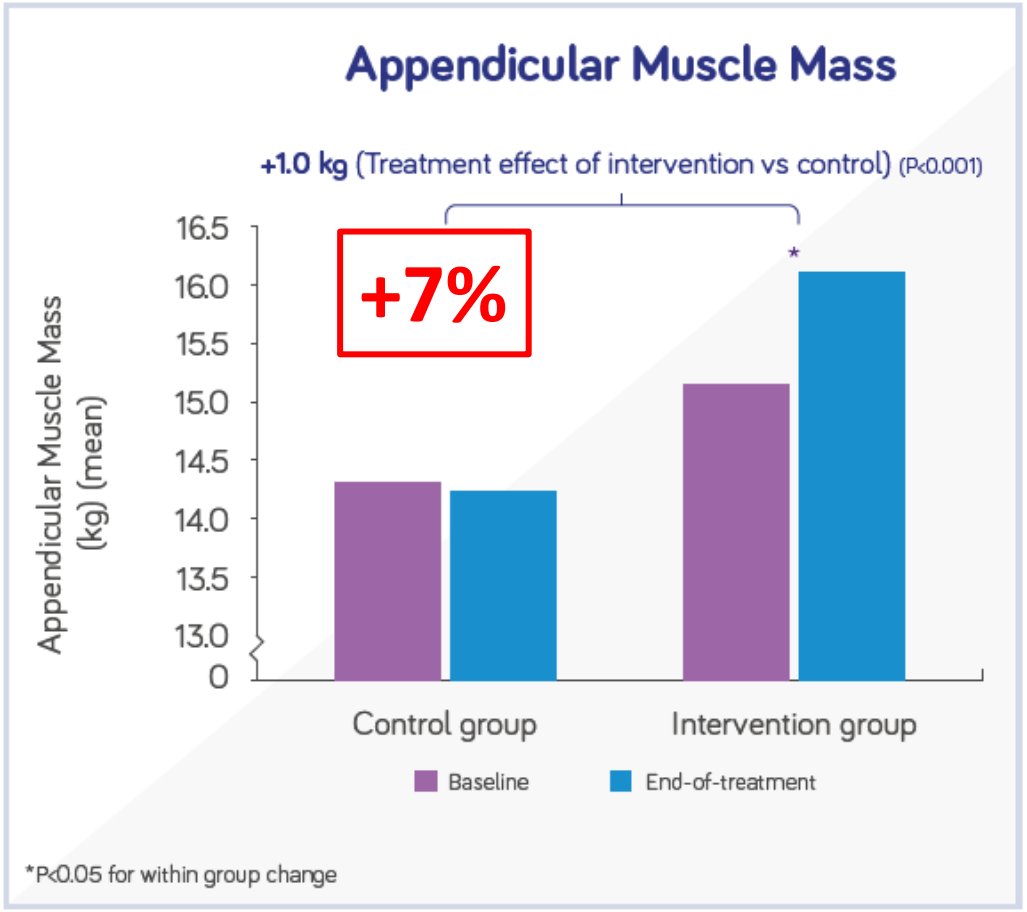


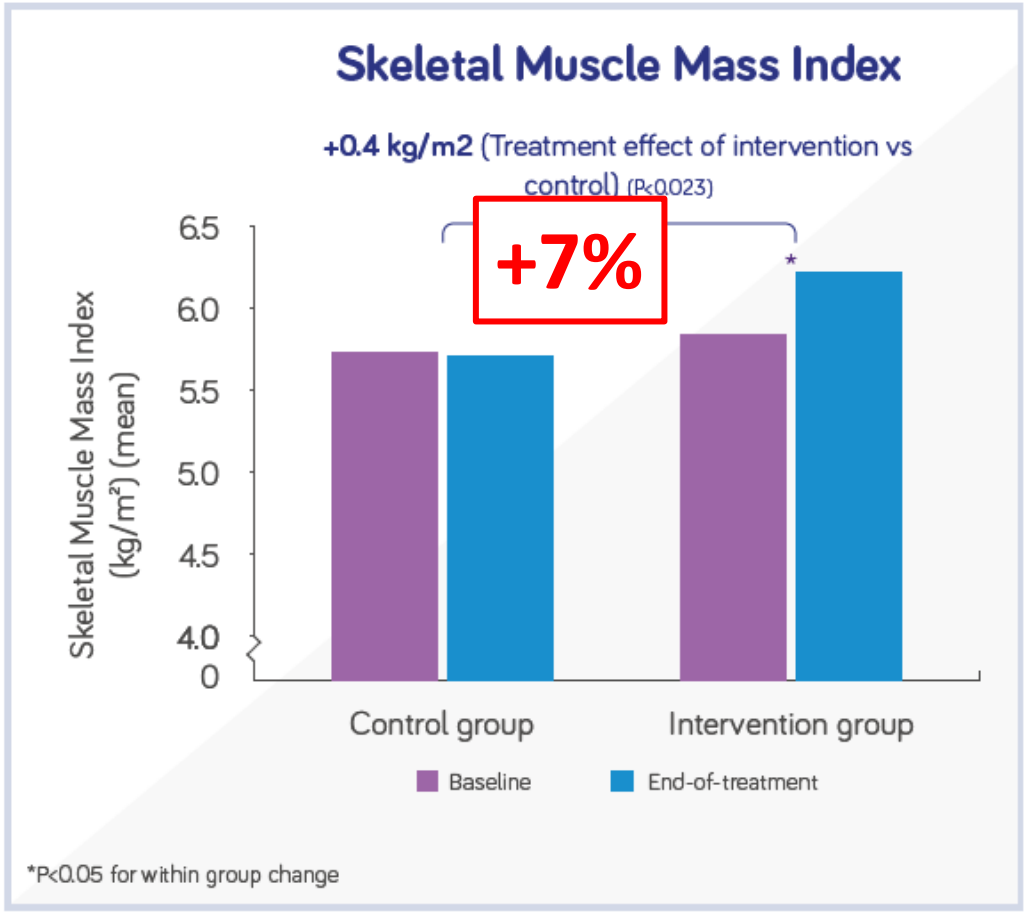
Functional status



Muscle-targeted supplementation with high-quality proteins, leucine and vitamin D (IRIS study)

Body composition



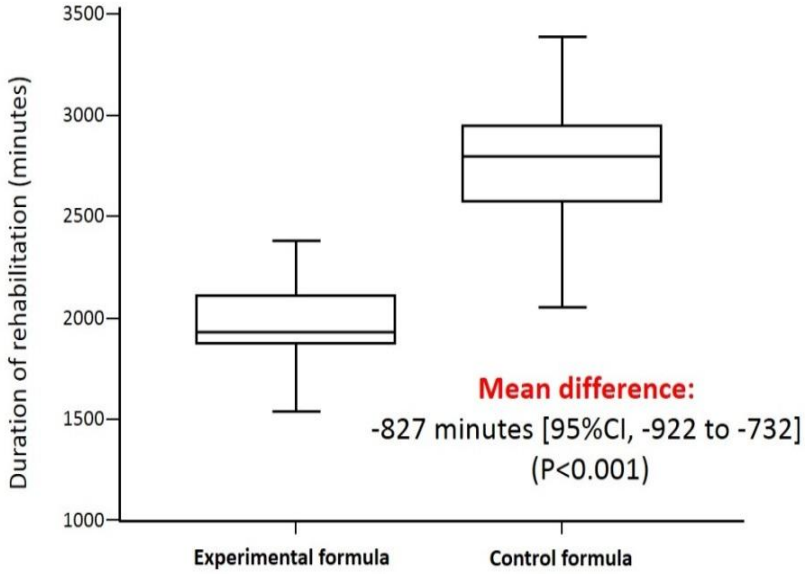


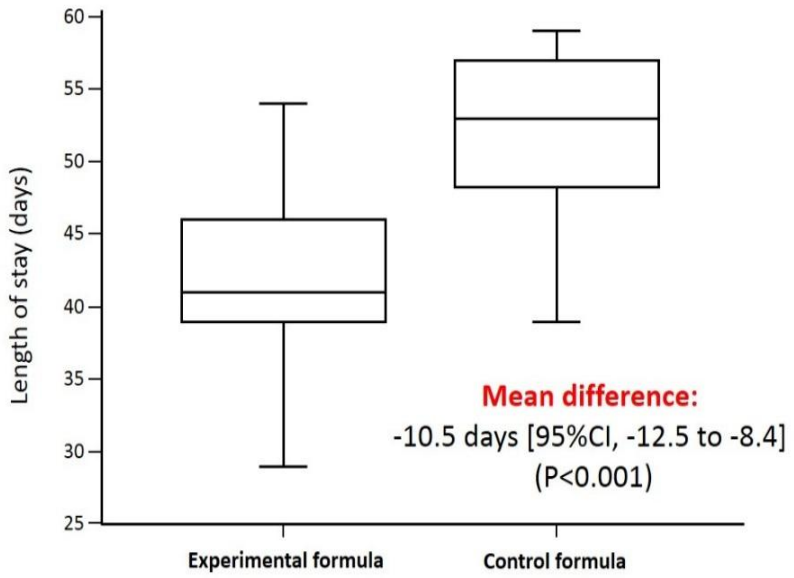
Rondanelli M, Cereda E et al. J Cachexia Sarcopenia Muscle 2020;11(6):1535-1547.

Muscle-targeted supplementation with high-quality proteins, leucine and vitamin D (IRIS study)

- **A greater proportion of patients went home** instead of being transferred to an institution: **84.3% vs. 60.3%**
  Treatment difference, +**24.0%** [95%CI, 9.1 to 39.1], (P=0.002)

- **A greater proportion of patients experienced a reduction in intensity of care:** **85.9% vs. 63.5%**
  Treatment difference, +**22.5%** [95%CI, 7.8 to 37.1], (P=0.003)





Rondanelli M, Cereda E et al. J Cachexia Sarcopenia Muscle 2020;11(6):1535-1547.

Budget impact analysis of a muscle-targeted nutritional intervention for sarcopenia (IRIS study)

Budget impact analysis of a muscle-targeted nutritional intervention for sarcopenia☆

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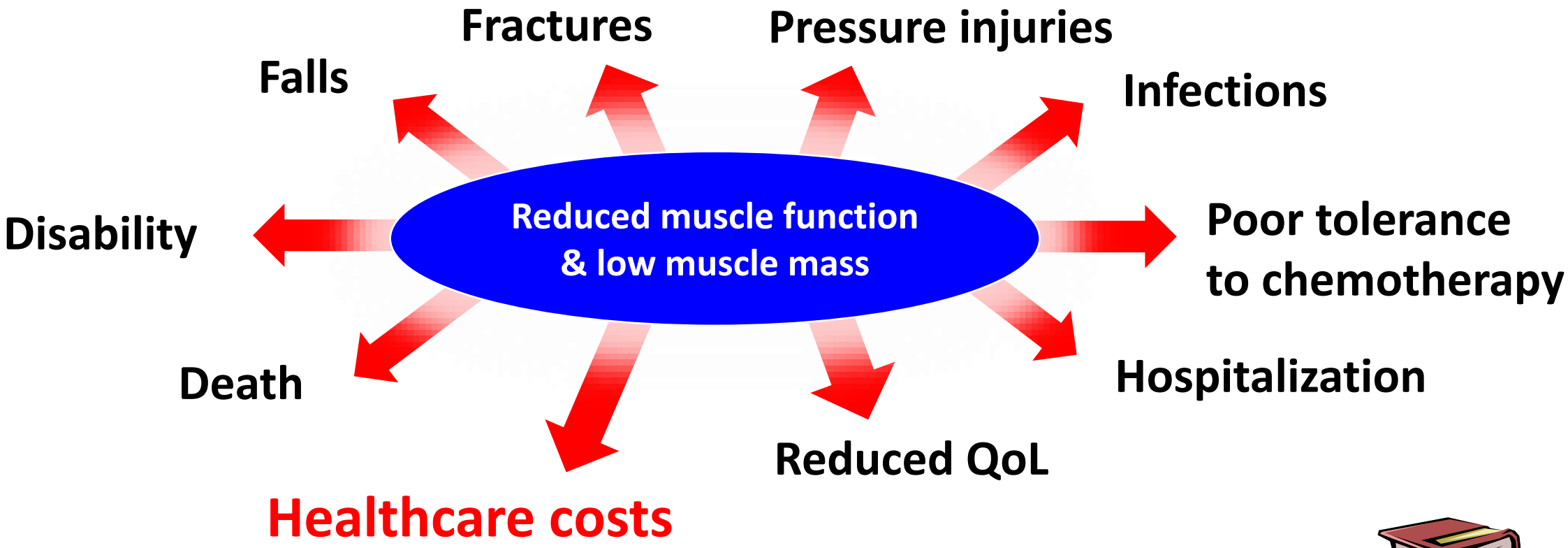
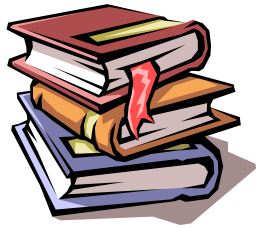
Three different payer perspectives:

(1) hospital, including only nutrition and rehabilitation costs;
(2) third-party payer (TPP), including also the economic consequences of patients discharged to an institution;
(3) societal perspective, including also the economic impact on families due to home assistance.

Cereda E et al. Clin Nutr. 2025 Nov 1;55:162-169.

Budget impact analysis of a muscle-targeted nutritional intervention for sarcopenia (IRIS study)





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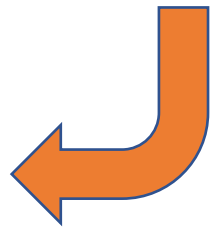
Budget impact analysis of a muscle-targeted nutritional intervention for sarcopenia (IRIS study)

Direct and indirect healthcare unit costs

Unit cost		Perspective		
		Hospital	**TPP**	**Society**
Treatment (daily cost)	Active	€ 6.2	€ 6.2	€ 6.2
	Placebo	€ 3.2	€ 3.2	€ 3.2
Rehabilitation	Based on perspective	€ 156.0 per day	€ 1,943.0 for LOS≤ 37 days, then € 147.0 for every extra day	€ 1,943.0 for LOS≤ 37 days, then € 147.0 for every extra day
Institution	Daily cost	NA	€ 125.3	€ 208.9
Home	Daily cost	NA	NA	Based on ADL score

ADL score - Disability	Formal caregiver (weight %)	Unpaid work (weight %)
0	€ 60.42 (100 %)	€ 0.00 (0 %)
1–2	€ 42.27 (75 %)	€ 7.29 (25 %)
3–4	€ 28.18 (50 %)	€ 14.57 (50 %)
5	€ 12.65 (25 %)	€ 21.86 (75 %)
6	€ 0.00 (0 %)	€ 29.15 (100 %)



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Budget impact analysis of a muscle-targeted nutritional intervention for sarcopenia (IRIS study)

Average total cost per patient in each perspective

Perspective	Costs	Placebo	Active	Savings
Hospital	Average total cost per patient	8,313.8	6,777.7	-1,536.1
	Hospital treatment	167.1	262.3	95.2
	Hospital rehabilitation	8,146.7	6,515.4	-1,631.2
	12-month post discharge	NA	NA	NA
TPP	Average total cost per patient	€ 19,785.2	€ 9,245.7	-€ 10,539.5
	Hospital treatment	€ 167.1	€ 262.3	€ 95.2
	Hospital rehabilitation	€ 4,180.7	€ 2,772.2	-€ 1,408.5
	12-month post discharge	€ 15,437.5	€ 6,211.3	-€ 9,226.2
Society	Average total cost per patient	38,534.6	24,172.1	-14.362,5
	Hospital treatment	€ 167.1	€ 262.3	€ 95.2
	Hospital rehabilitation	€ 4,180.7	€ 2,772.2	-€ 1,408.5
	12-month post discharge	34,186.9	21,137.7	-13,049.2

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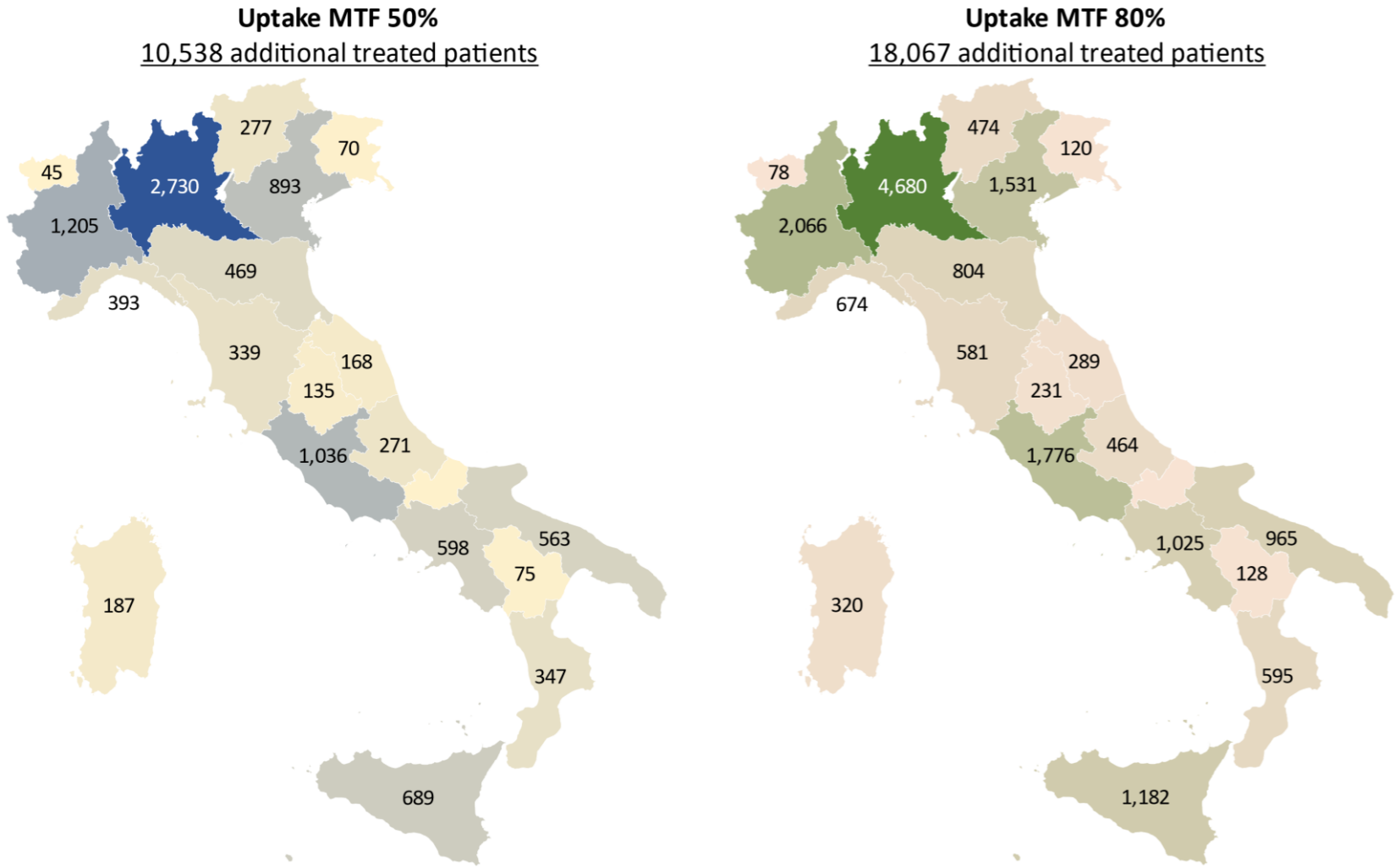
Budget impact analysis of a muscle-targeted nutritional intervention for sarcopenia (IRIS study)

About
495.214 – 792.342
bed days could be saved



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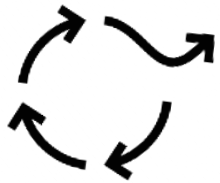
TAKE HOME MESSAGES (& PRACTICES)



1. Break the cycle with assertive nutrition - more patients will progress more quickly to a state of frailty if they are not managed properly

2. Meeting the gap on protein intakes is mandatory (diet may be not enough!)

3. Muscle-targeted interventions to optimize recovery in specific conditions (sarcopenia) are evidence-based!

4. Maybe screening is not even necessary if obvious that a patient is at risk!

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