VII CONGRESSO NAZIONALE B&M 2018

IV SESSIONE

Prof. Rocco Barazzoni

Professore associato di Medicina Interna,
Università degli Studi di Trieste
Segretario Generale Società ESPEN dal 2012 al 2016.

BRAIN AND MALNUTRITION
Chronic Diseases Association ONLUS

ESPEN

Obesità e Sarcopenia

Rocco Barazzoni

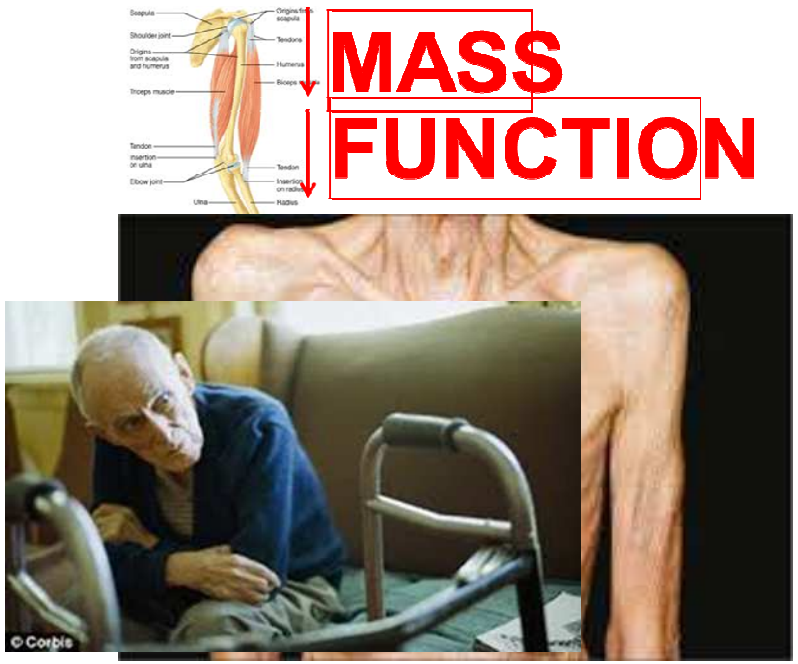
Dept of Medical, Surgical and Health Sciences
University of Trieste - Italy

REPORT

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People

Cruz-Jentoft et al, Age Ageing 2010



SARCOPENIA: a complex MULTIFACTORIAL Syndrome

SENESCENCE

- MOTONEURON DYSFUNCTION
- Satellite CELLS

NUTRITION

- ANOREXIA
- MALABSORPTION

ENDOCRINE

- ↓SEX HORMONES
- ↓ VITAMIN D
- ↓ GH-IGF1

MUSCLE DISUSE

- IMMOBILITY
- SEDENTARY Lifestyle

METABOLISM

AGING

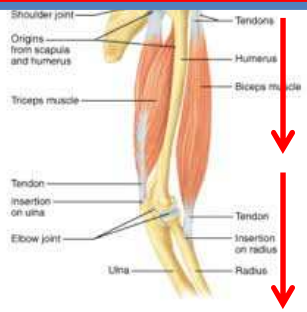
A PERFECT METABOLIC STORM

AGING

A PERFECT METABOLIC STORM

OX STRESS ⟷ **INFLAMMATION**

PROTEIN DEGRADATION

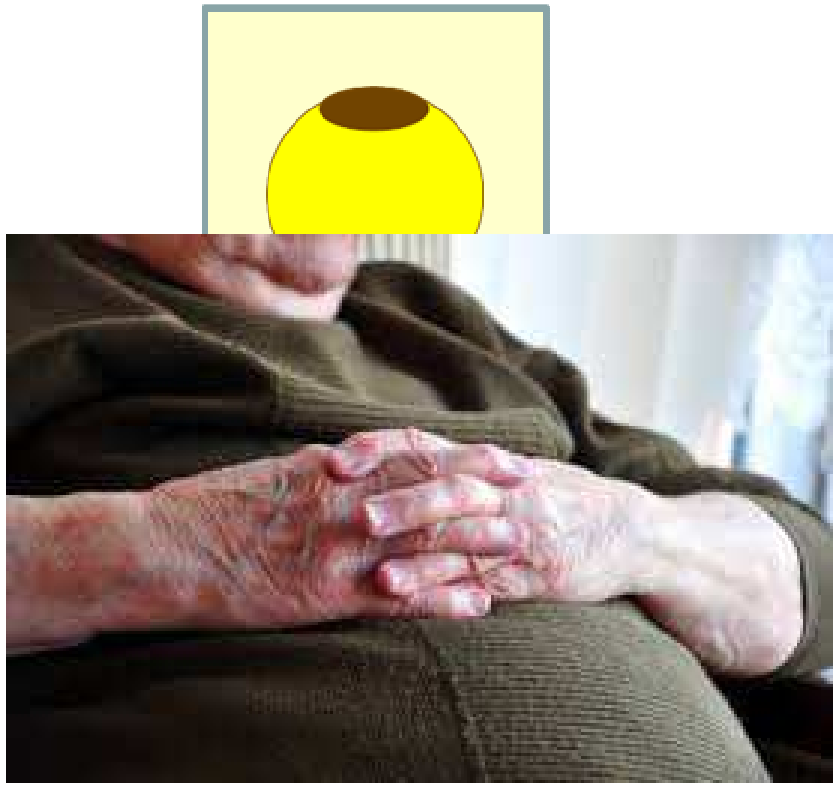


MASS

FUNCTION

\+ (INSULIN RESISTANCE) +

INSULIN RESISTANCE



OVERWEIGHT and OBESITY

"Chronic conditions characterized by abnormal-excess fat accumulation leading to excess morbidity" (WHO)

Clinical = BMI > 30 kg/m^2

OBESITY per se

A PERFECT MUSCLE METABOLIC STORM

OX STRESS ⟷ **INFLAMMATION**

PROTEIN DEGRADATION

MASS

FUNCTION

\+ (INSULIN RESISTANCE) +

INSULIN RESISTANCE

COMPLICATED OBESITY

A PERFECT MUSCLE METABOLIC STORM

OX STRESS ⟷ **INFLAMMATION**

METABOLIC SYNDROME DIABETES

\+

MASS

FUNCTION

\+

INSULIN RESISTANCE

ACUTE and CHRONIC DISEASE

A PERFECT MUSCLE METABOLIC STORM

OX STRESS ⟷ **INFLAMMATION**

\+

PROTEIN DEGRADATION

MASS

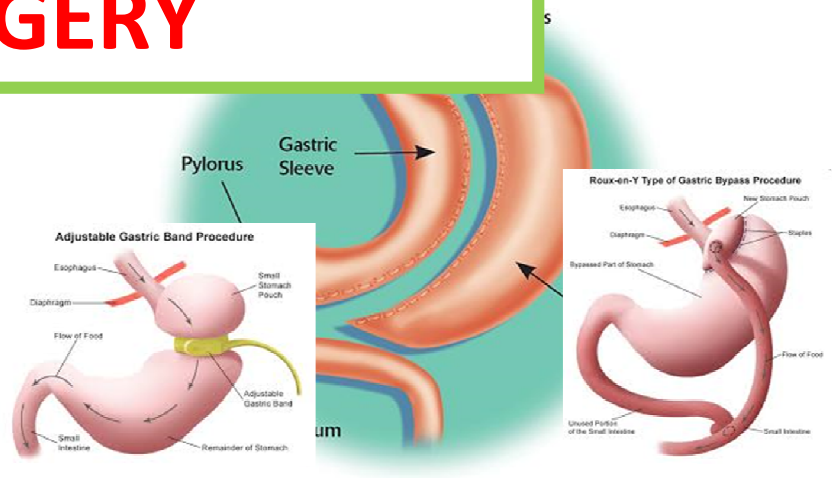
FUNCTION

\+

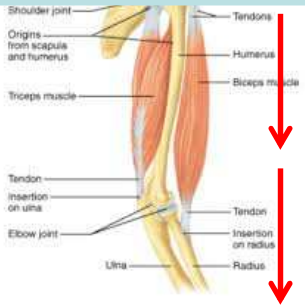
INSULIN RESISTANCE

THERAPEUTIC WEIGHT LOSS BARIATRIC SURGERY

-Deficiencies



PROTEIN DEGRADATION



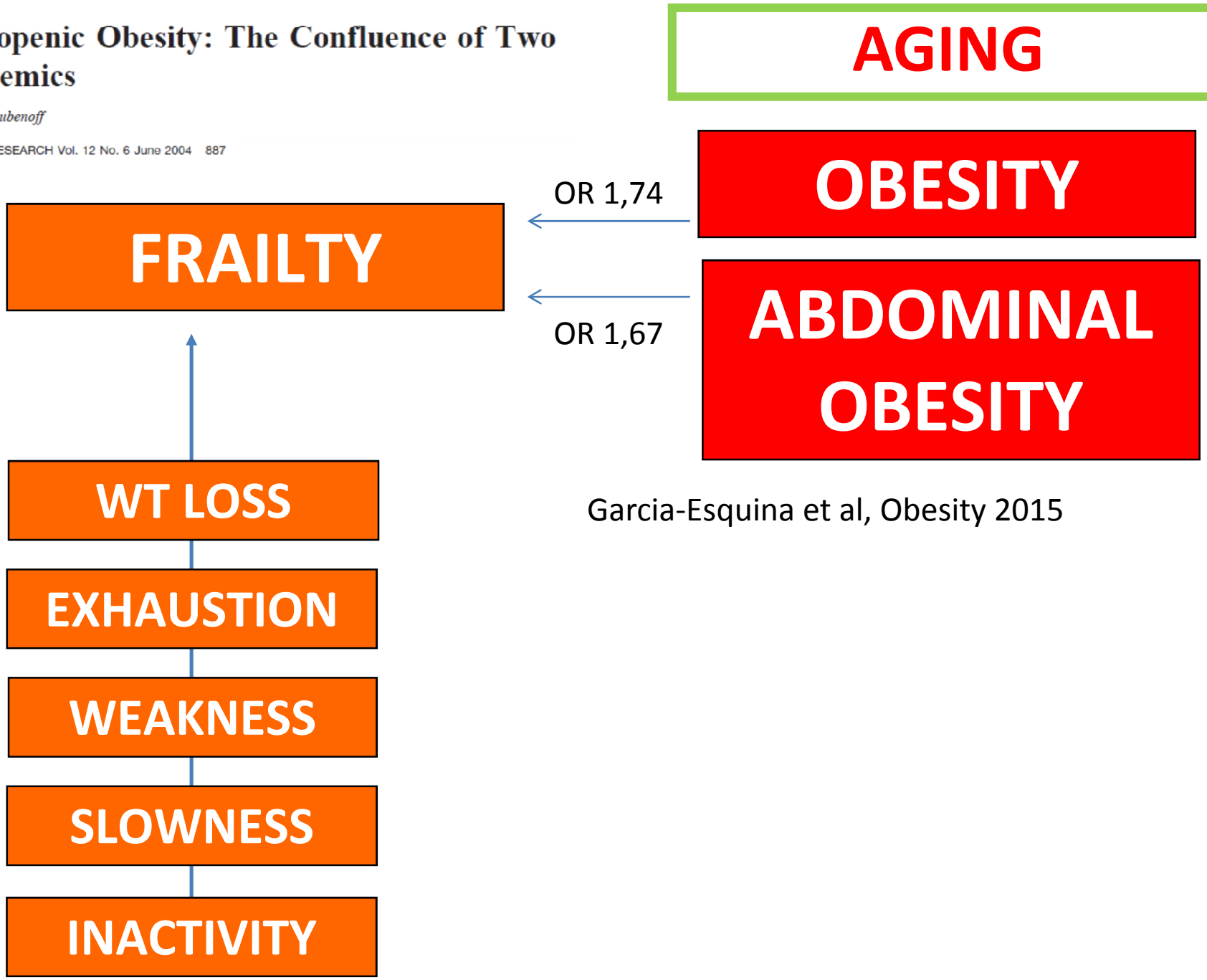
MASS

FUNCTION

Sarcopenic Obesity: The Confluence of Two Epidemics

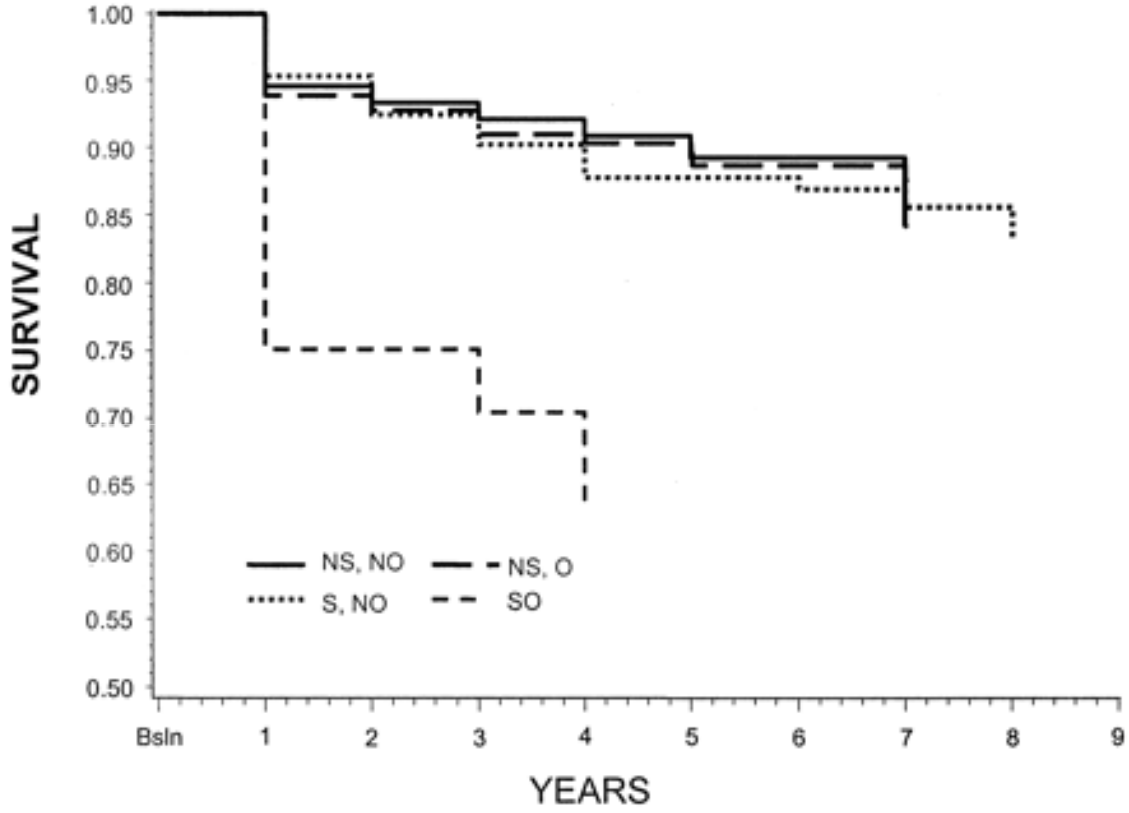
Ronenn Roubenoff

OBESITY RESEARCH Vol. 12 No. 6 June 2004 887



Garcia-Esquina et al, Obesity 2015

Increased frailty in obese individuals with lower muscle mass

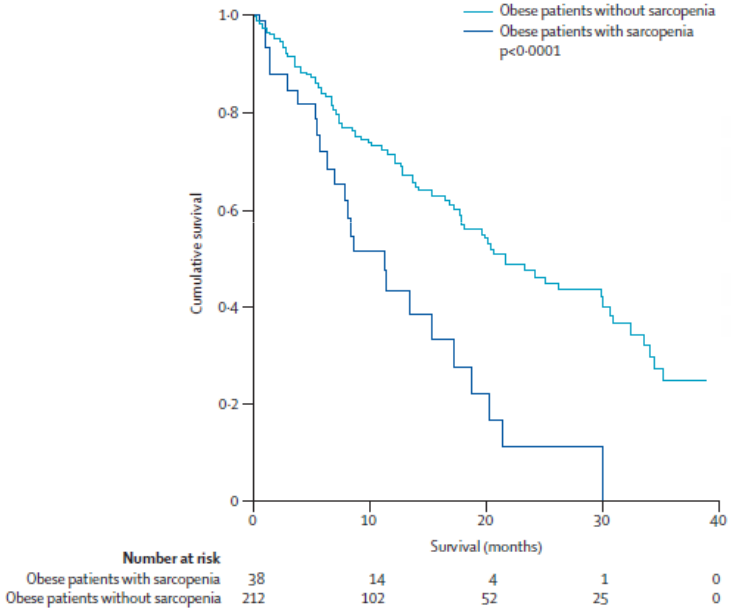


Baumgartner et al, Ob Res 2004

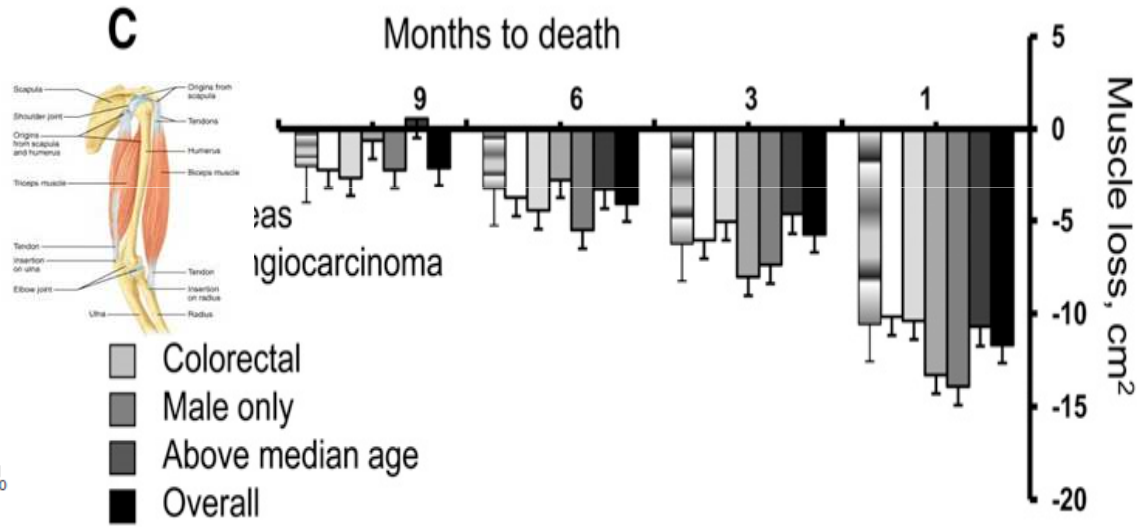
Beyond BMI

BODY COMPOSITION

Low Lean Mass and Lean Mass loss predict mortality in OBESE CANCER patients



Prado et al, Lancet Oncol 2008



Prado et al, Am J Clin Nutr 2013

AWARENESS!!
Malnutrition!!

ESPEN

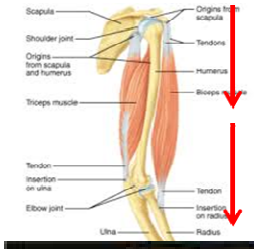
THE EUROPEAN SOCIETY FOR CLINICAL NUTRITION AND METABOLISM

ESPEN guidelines on definitions and terminology of clinical nutrition

T. Cederholm [a, *], R. Barazzoni [b], P. Austin [c, y], P. Ballmer [d], G. Biolo [e], S.C. Bischoff [f], C. Compher [g, 1], I. Correia [h, 1], T. Higashiguchi [i, 1], M. Holst [j], G.L. Jensen [k, 1], A. Malone [l, 1], M. Muscaritoli [m], I. Nyulasi [n, 1], M. Pirlich [o], E. Rothenberg [p], K. Schindler [q], S.M. Schneider [r], M.A.E. de van der Schueren [s, z], C. Sieber [t], L. Valentini [u], J.C. Yu [v, 1], A. Van Gossum [w], P. Singer [x]

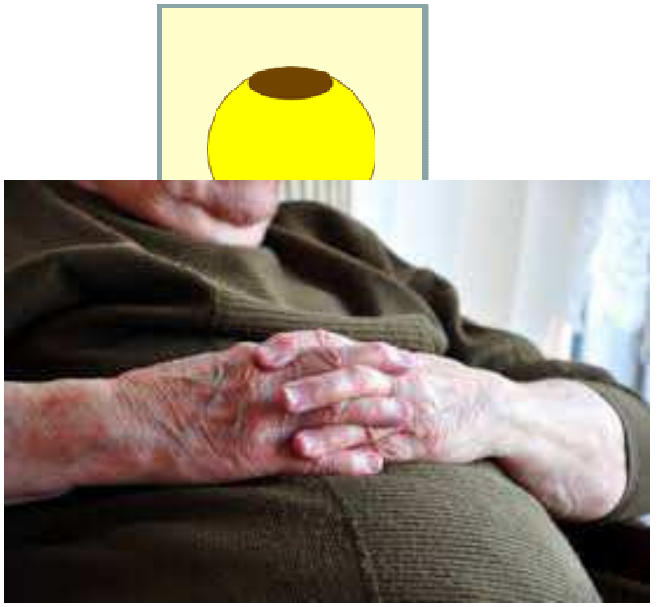
Clin Nutr 2016

Currently, there are no commonly accepted criteria for sarcopenic obesity beyond those for sarcopenia and obesity separately.



MASS

FUNCTION



Validity and Reliability of Tools to Measure Muscle Mass, Strength, and Physical Performance in Community-Dwelling Older People: A Systematic Review

Mijnarends et al, JAMDA 2013

MUSCLE PERFORMANCE

MUSCLE STRENGTH

Chest press[27]
Dumbbell[69]
Elastic bands[69]

Handheld dynamometer[18–26]

MUSCLE MASS

BIA
Single frequency
Multifrequency[7]

BOD POD[74]
Calf circumferen
CT[13,17,83]

DXA[14–17,78–81]
Equation for LBM
MRI[17]
Skin-fold thickne
Ultrasonography[13]
4-C model[76,83]

SARCOPENIA

VARIABLE DEF

OBESITY

% Body Fat

- **26**-fold VARIATION in SO prevalence
- Elderly population

Batsis et al, J Am Geriatr Soc 2013

Manual muscle testing[19]
Vigorimeter[20]

Plate with spring gauge[28]
Pull down[29]

Continuous scaled physical functional performance[30]

Figure-8 walk[30]

Fullerton Functional Fitness Test battery[47,*]
Functional reach[52,*]

GAITRite mat (4.6-m mat with sensor)[46,*]
Gait speed (2 m to 1 km)[21,26,27,40,42,43,49,52–55,*]

yeed (5 min)[32,37,38,51,56,*]

ty assessment tool-SF[53,*]

cation scale: chair rise, stair
lt, kneel, supine rise[44]
al capacity evaluation:
ing speed, grip, etc.[35,*]
al performance test
em)[57]
al performance test
em)[33]

ported physical function
tems)[31]

37,40,50,54,*]

Sit to stand 5 times[31,34,40,42,43,49]

Sit to stand 10 times[48]

Sit to stand 30 sec[41,45]

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ESPEN suggestion for diagnostic criteria for malnutrition

Step 1. Risk screening by a validated instrument , e.g. NRS-2002, MUST, MNA(-SF), SNAQ, ...

i.e. BMI, Weight loss, Reduced food intake, Disease severity

Step 2. Diagnosis is confirmed by

- **BMI <18.5 kg/m^2**

or

- **Weight loss >10%** (indefinite time)/**>5%** last 3 mo

combined with either

- **BMI <20** (<70 y)/**<22** (>70 y) or
- **FFMI <15** and **17** kg/m^2 in women and men, respect.

Cederholm et al Clin Nutr 2015

Global Leadership Initiative in Malnutrition

Core committee

ASPEN:	GL Jensen / C Compher
ESPEN:	T Cederholm / A Van Gossum
FELANPE:	I Correia / MC Gonzalez
PENSA:	R Fukushima / T Higashiguchi

Working group

G Baptista, R Barazzoni, R Blaauw, A Crivelli, D Evans, L Gramlich, V Fuchs, S Jones, H Keller, A Malone, K Mogensen, M Muscaritoli, M Pirlich, V Pisprasert, M de van der Schueren, S Siltharm, P Singer, K Tappenden, D Waitzberg, NV Fuentes, L Lido, P Yamwong, J Yu, I Nyulasi

ESPEN
THE EUROPEAN SOCIETY FOR CLINICAL NUTRITION AND METABOLISM

aspen
American Society for Parenteral and Enteral Nutrition

FELANPE

PENSA
PARENTERAL AND ENTERAL NUTRITION SOCIETY OF ASIA

JSPEN

ALGORYTHM FOR MALNUTRITION DIAGNOSIS

Screening

At risk for Malnutrition

- Use validated screening tools

Diagnosis

Assessment Criteria

- **Phenotype**
  - Weight loss
  - ↓BMI (underweight)
  - ↓ Muscle Mass
- **Etiology**
  - ↓ Food intake (or absorption)
  - ↑ Inflammation - Disease

YES

AT LEAST

- 1 Phenotype Criterion

AND

- 1 Etiology Criterion

Cut-Offs and SURROGATES:

THE FINAL HURDLE?

- ↓ MUSCLE MASS

E.G: fat free mass index (FFMI, kg/m^2) by DEXA or BIA, CT, MRI.
Ethnicity adaptation NEEDED
ALTERNATIVES: when not available or by regional preference:

- physical exam
- standard anthropometric measures
- functional assessments (e.g. hand-grip strength) may be considered as a SUPPORTIVE measure.

**Acute disease/injury-related with severe inflammation.
E.G: major infection, burns, trauma or closed head injury
***Chronic disease-related with chronic or recurrent mild to moderate inflammation.
E.G:: malignant disease, COPD, CHF, CKD or any disease with chronic or recurrent Inflammation.
C-reactive protein may be used as a supportive laboratory measure.

CLINICAL approach
SARCOPENIC OBESITY

OBESITY

COMPLICATIONS

COMORBIDITIES

+

THERAPEUTIC WEIGHT LOSS

BARIATRIC SURGERY

SARCOPENIC OBESITY

↓OUTCOME

AGING

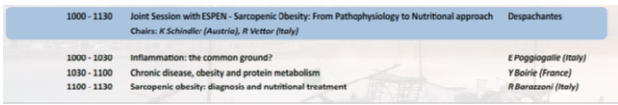
CANCER

CHRONIC DISEASE

ESPEN

THE EUROPEAN SOCIETY FOR CLINICAL NUTRITION AND METABOLISM

ECO 2017



1000 - 1130	Joint Session with ESPEN - Sarcopenic Obesity: From Pathophysiology to Nutritonal approach *Chairs: K Schindler (Austria), R Vettor (Italy)*	Despachantes
1000 - 1030	Inflammation: the common ground?	*E Poggiogalle (Italy)*
1030 - 1100	Chronic disease, obesity and protein metabolism	*Y Boirie (France)*
1100 - 1130	Sarcopenic obesity: diagnosis and nutritional treatment	*R Barazzoni (Italy)*

ESPEN-EASO Position paper

Sarcopenic Obesity: Time to meet the challenge

Barazzoni et al, Clin Nutr in press 2018

TREATMENT: multimodal approach

- **NUTRITION**
- **EXERCISE (PA)**
- **HORMONAL - PHARMACOLOGICAL**

LITTLE DATA FUCUSING on

OBESE-SARCOPENIC OBESE INDIVIDUALS!!

OBESITY!!

A PERFECT METABOLIC STORM

OX STRESS ⟷ **INFLAMMATION**

PROTEIN

ANABOLIC RESISTANCE

+

MASS

FUNCTION

+

INSULIN RESISTANCE

NUTRITION QUANTITY

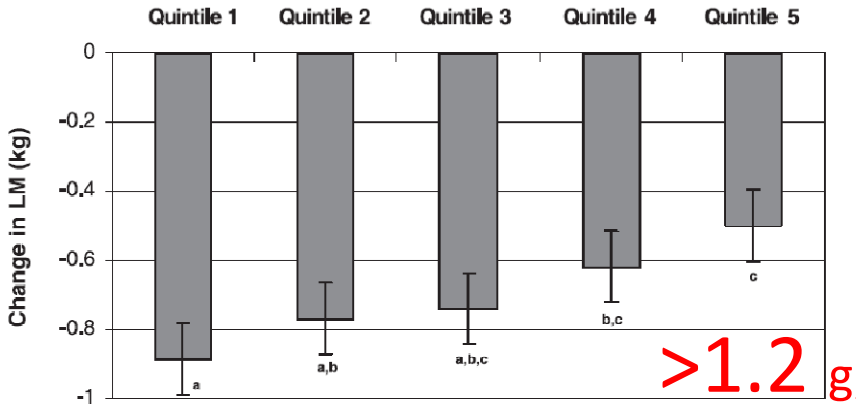
PROTEIN DEGRADATION

MASS

FUNCTION

↑PROTEIN ?

Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study[1–3]



>1.2 g/kg·day

Taku et al, Am J Clin Nutr 2007

INCREASING PROTEIN INTAKE

(gr / kg BW · day OR PERCENT energy/day)

- ↑LEAN MASS
- ↓SARCOPENIA
- ↑PHYSICAL
- ↑MUSCLE STRENGTH

Beasley et al, J Am Geriatr Soc 2013; Farsijani et al, Am J Clin Nutr 2016; Chorong et al, Nutrition 2016; Isanejad et al, Br J Nutr 2016

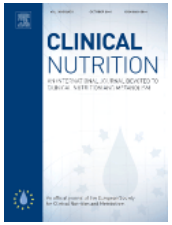
PROTEIN DEGRADATION

MASS

FUNCTION

HEALTHY OLDER ADULTS

CLINICAL NUTRITION



ESPEN endorsed recommendation

Protein intake and exercise for optimal muscle function with aging: Recommendations from the ESPEN Expert Group

Nicolaas E.P. Deutz [a,*], Jürgen M. Bauer [b], Rocco Barazzoni [c], Gianni Biolo [c], Yves Boirie [d], Anja Bosy-Westphal [e], Tommy Cederholm [f,g], Alfonso Cruz-Jentoft [h], Zeljko Krznariç [i], K. Sreekumaran Nair [j], Pierre Singer [k], Daniel Teta [l], Kevin Tipton [m], Philip C. Calder [n,o]

Clin Nutr 2015

1-1.2 **g/kg · day**

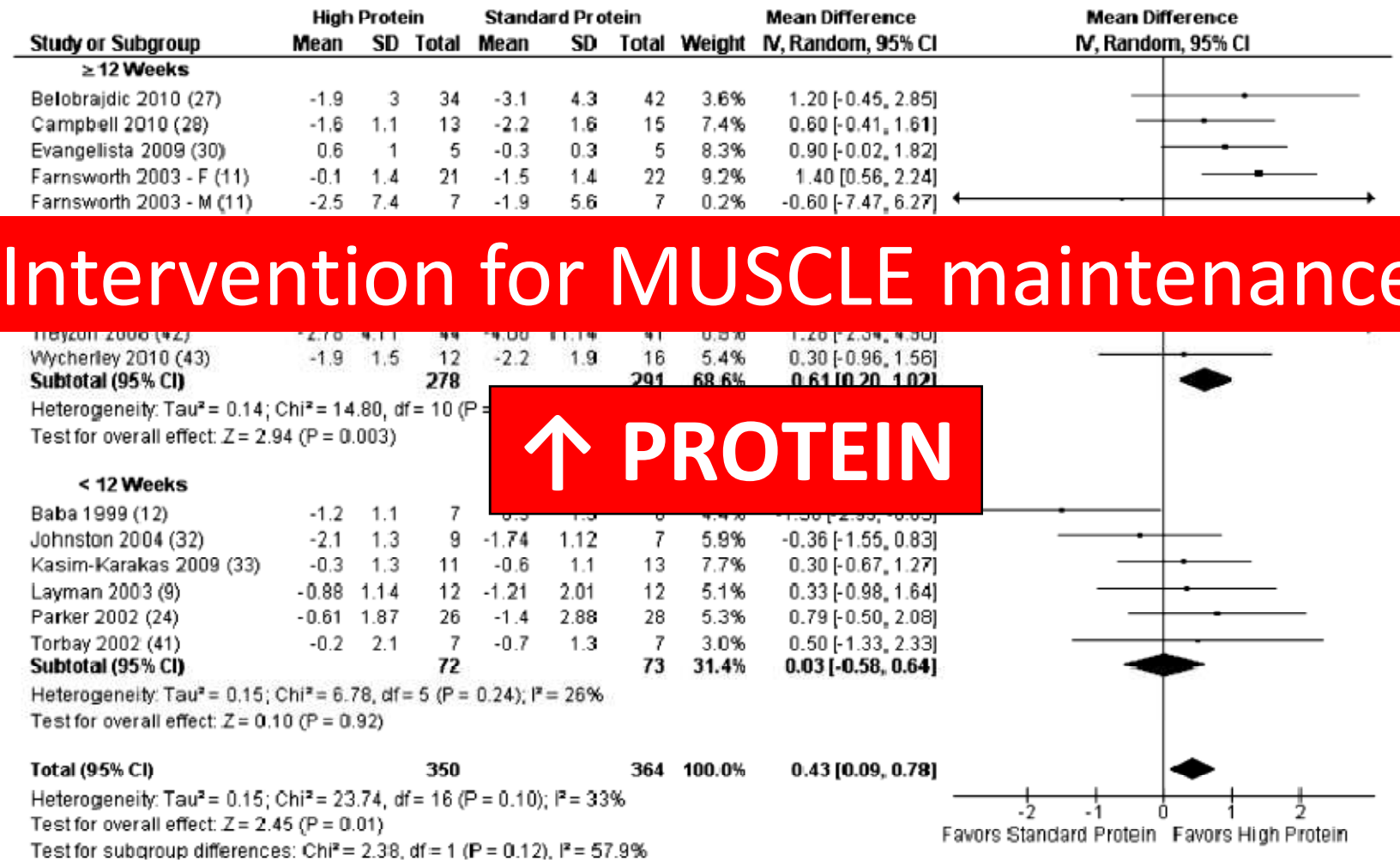
CHRONIC KIDNEY DISEASE

HEMODIALYSIS – PERITONEAL DIALYSIS

ESPEN GLs: 1,2-1,4 g/kg BW

Cano et al, Clin Nutr 2009

LOW-CALORIE DIET



Intervention for MUSCLE maintenance

↑ PROTEIN

FIGURE 5. Meta-analysis for changes in fat-free mass (kg) in randomized controlled trials that compared high-protein, low-fat diets with isocalorically prescribed standard-protein, low-fat, energy-restricted diets. IV, inverse variance.

Wycherley et al, Am J Clin Nutr 2012

OBESITY + DISEASE

GUIDELINES INTENSIVE CARE
(ASPEN)

NUTRITIONAL SUPPORT

PROTEIN: Very High-Protein

BMI < 40: 2 g/kg IBW

BMI > 40: 2.5 g/kg IBW

McClave et al, JPEN 2016

OBESITY + DISEASE

GUIDELINES INTENSIVE CARE
(ASPEN)

NUTRITIONAL SUPPORT

CALORIE

- DO NOT OVERFEED
- PROVIDE ADEQUATE CALORIES
- PREVENT METABOLIC COMPLICATIONS

↓

PERMISSIVE UNDERFEEDING (65-70%)

BMI < 50: 11-14 kcal/kg actual BW
BMI > 50: 22-25 kcal/kg IBW

McClave et al, JPEN 2016

«GENERAL» OBESITY GUIDELINES ?

2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society

3b. Prescribe a calorie-restricted diet, for obese and overweight individuals who would benefit from weight loss, based on the patient's preferences and health status, and preferably refer to a nutrition professional* for counseling. A variety of dietary approaches can produce weight loss in overweight and obese adults, as presented in CQ3, ES2. — A (Strong)

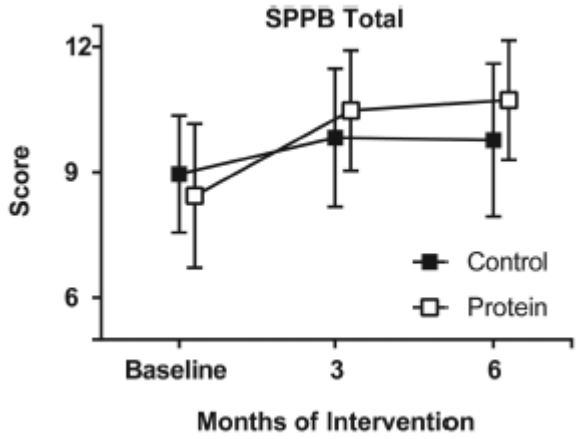
- Higher-protein diet (25% of total calories from protein, 30% of total calories from fat, and 45% of total calories from carbohydrate), with provision of foods that realize an energy deficit.
- Higher-protein Zone™-type diet (5 meals/d, each with 40% of total calories from carbohydrate, 30% of total calories from protein, and 30% of total calories from fat) without formal prescribed energy restriction but with a realized energy deficit.

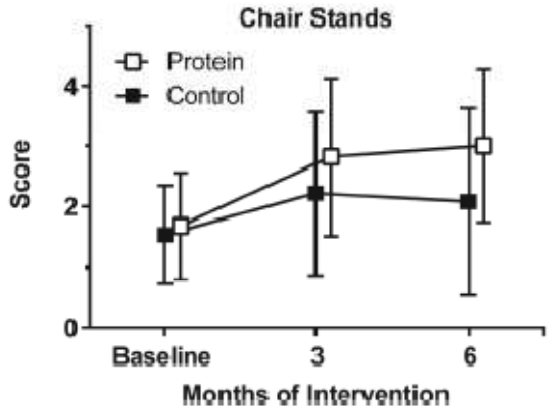
SARCOPENIC OBESITY

IF SEEKING WEIGHT LOSS :

-Preserve MUSCLE MASS (↑protein, exercise)

Improved Function With Enhanced Protein Intake per Meal: A Pilot Study of Weight Reduction in Frail, Obese Older Adults Porter Starr et al, J Gerontol Med Sci 2016





High-Protein Diet
SAFETY - FEASIBILITY

Protein and Chronic Kidney Disease

Protein Intake Quart ↓

Change in Estimated GFR	
Participants with Normal Renal Function (n = 1135)‡	Participants with Mild Renal Insufficiency (n = 489)§
mL/min per 1.73 m²	
0 (referent)	0 (referent)
2.45 (−0.98 to 5.88)	−2.51 (−6.25 to 1.23)
1.82 (−1.77 to 5.41)	−0.10 (−4.06 to 3.86)
2.23 (−1.66 to 6.12)	−0.32 (−4.50 to 3.86)
0.46 (−3.83 to 4.75)	−4.77 (−9.52 to −0.02)

Knight et al, Ann Int Med 2003

Higher Protein intake NOT indicated in elderly individuals if GFR<30

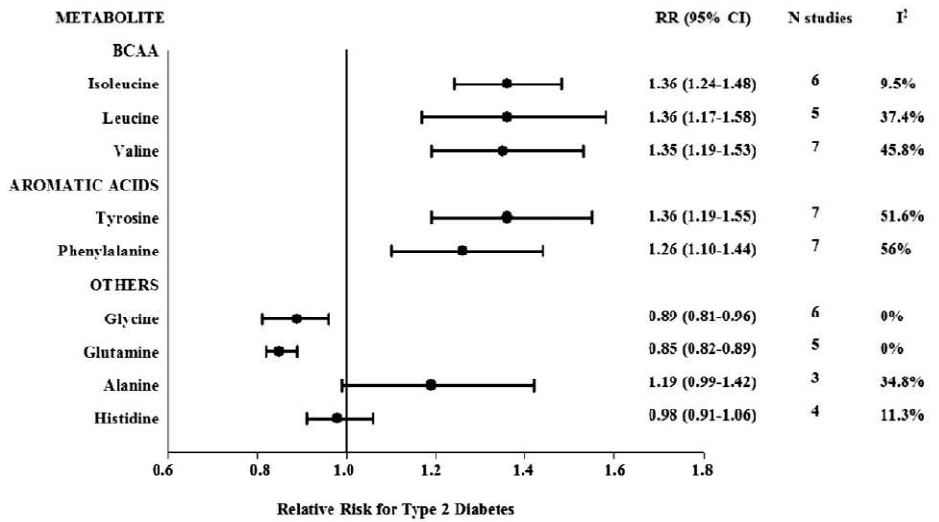
Bauer et al, JAMDA 2013

↓

OBESITY ?

Protein and
Chronic Metabolic Complications

Excess Plasma AMINO ACIDS predict INSULIN RESISTANCE and DIABETES



Guasch-Ferre et al, Diabetes Care 2016

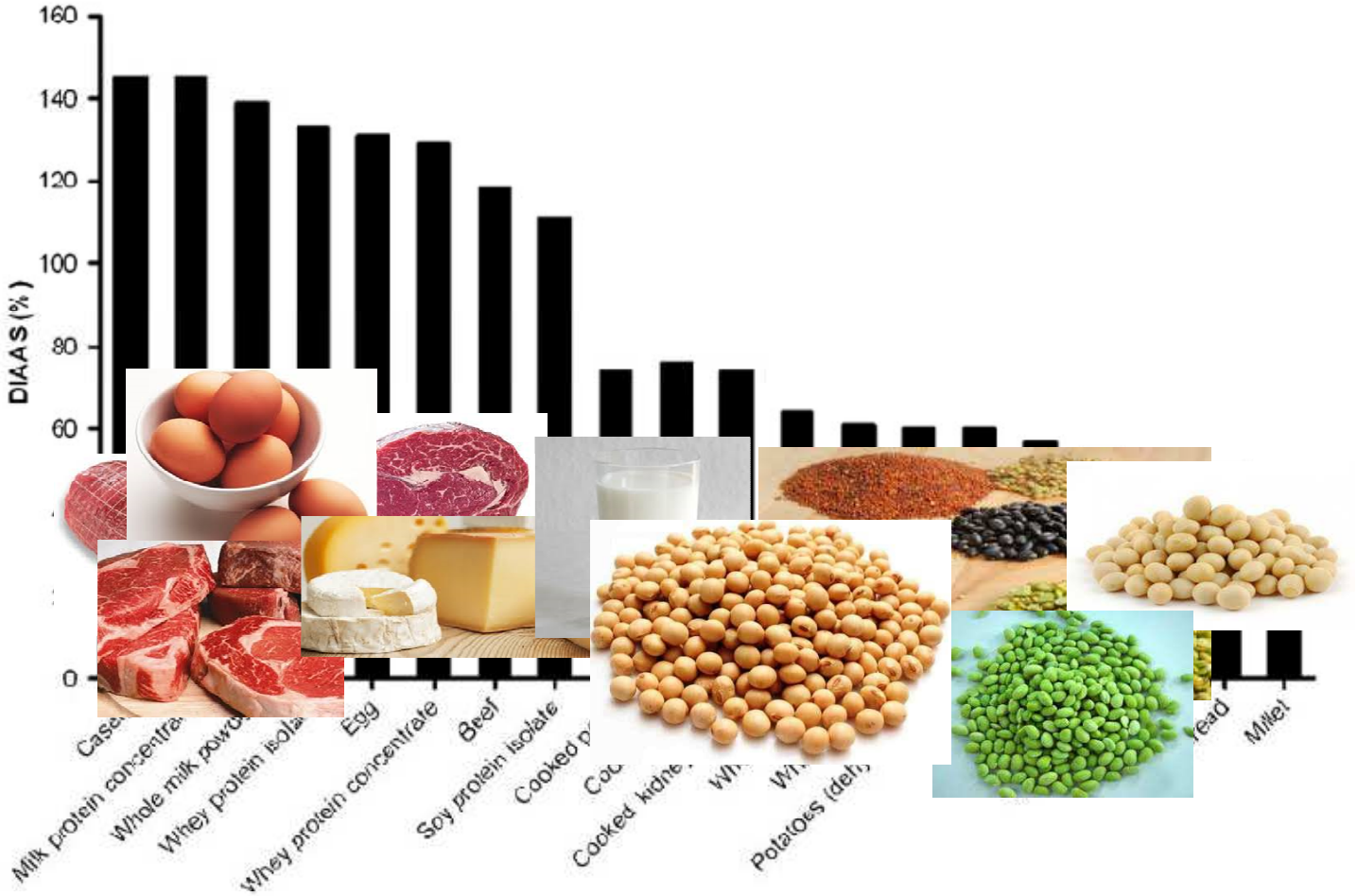
Protein Ingestion Induces Muscle Insulin Resistance Independent of Leucine-Mediated mTOR Activation

Smith et al, Diabetes 2015

RISK-BENEFIT evaluation
(statins)

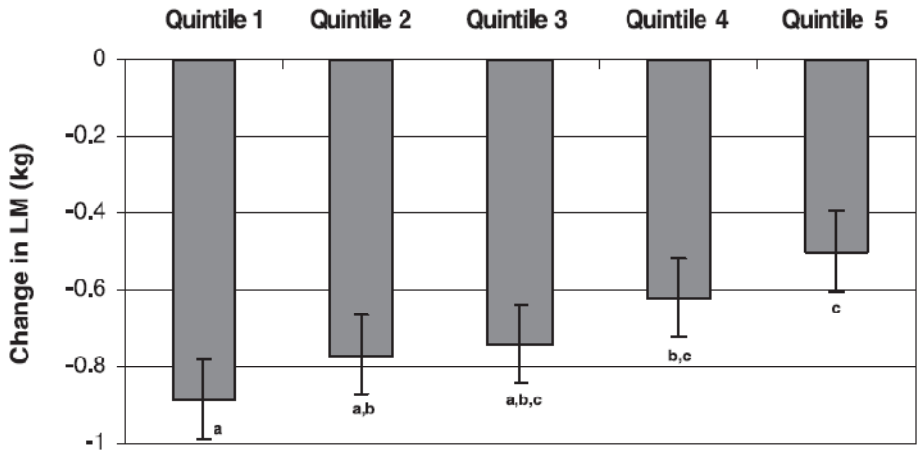
Protein QUALITY

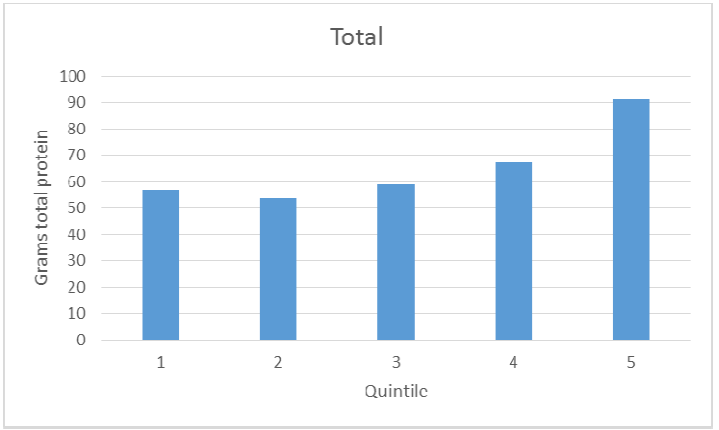
Animal/Vegetable

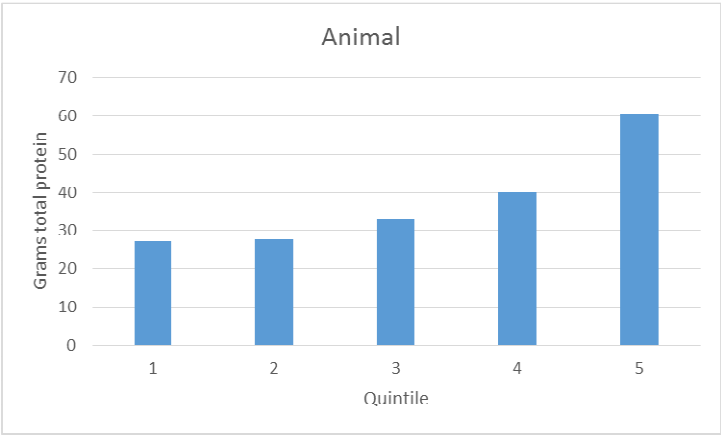


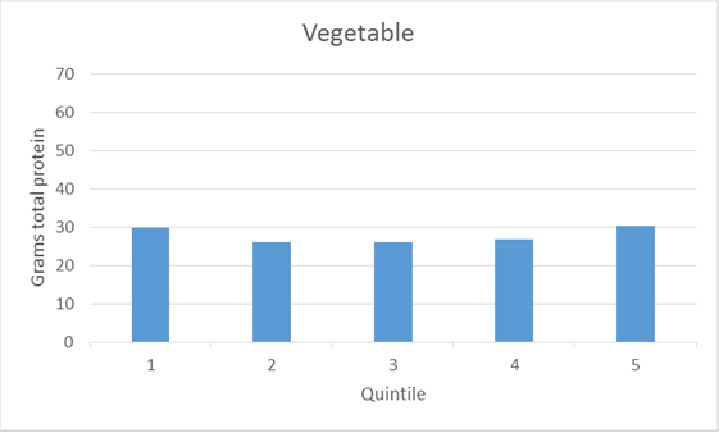
DIAAS Digestible Indispensable AA Score

Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study[1–3]





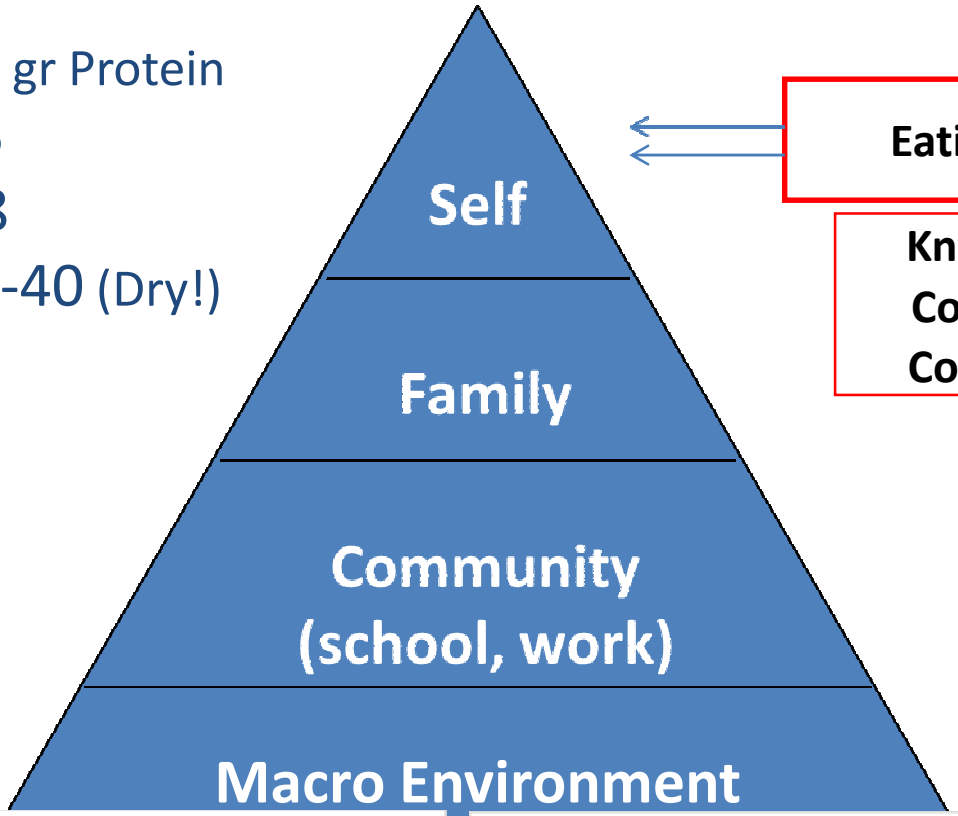




Taku et al, Am J Clin Nutr 2007

Influences on Food Choices

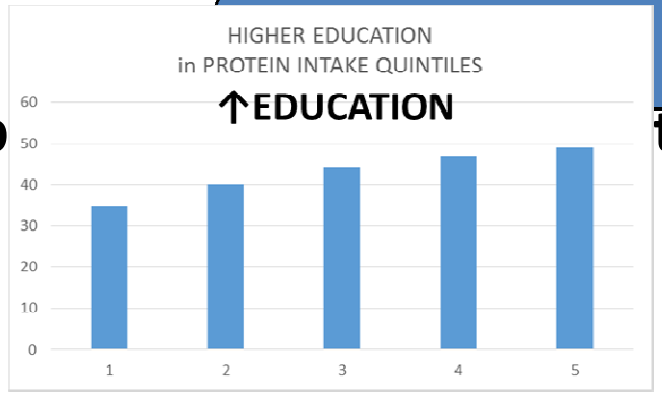
100 gr MEAT: 25-30 gr Protein
100 gr DAIRY: 20-25
100 gr FISH: 15-18
100 gr LEGUMES: 30-40 (Dry!)

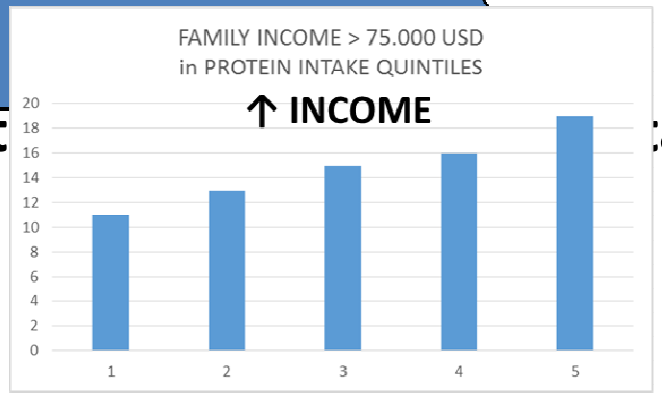


Eating PATTERNS

Knowledge
Cost-Access
Convenience

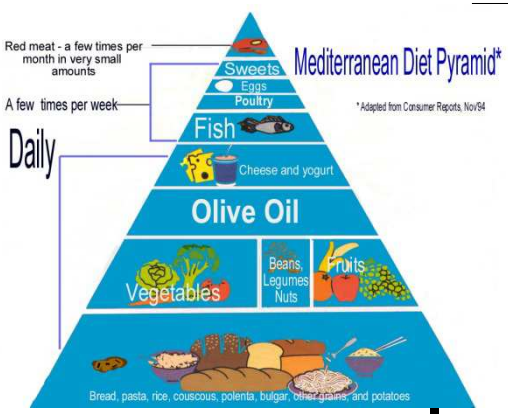
(pub t ation)





NUTRITION QUALITY

OX STRESS ⟷ **INFLAMMATION**



↑ ANTI-OXIDANT | OXIDANT

↑ ANTI-INFLAMMATORY | PRO-INFLAMMATORY

+

INSULIN RESISTANCE

MED DIET

PUFA

MUFA

ANTI-OXIDANTS

FIBRE

Eur J Nutr. 2017 Mar 16. doi: 10.1007/s00394-017-1422-2. Association of the Baltic Sea and Mediterranean diets with indices of sarcopenia in elderly women, OSPTRE-FPS study. Isanejad M1,2, Sirola J3,4, Mursu J5, Rikkonen T3, Kröger H3,4, Tuppurainen M6, Erkkilä AT5.

Measurements of skeletal muscle mass and power are positively related to a Mediterranean dietary pattern in women

Kelaiditis et al, Osteoporosis Int 2016

Table 2 Measures of muscle mass, muscle strength, and inflammation by quartile of Mediterranean diet score in 2570 females aged 18–79 years

	Model	Q1	Q2	Q3	Q4	Q4-Q1	*P* trend
Mediterranean diet score (points)	–	0–3	4	5	6–9	–	–
Fat-free mass (%)	*n*=	897	538	461	674	–	–
	1	60.9 ± 0.3	60.6 ± 0.3	61.3 ± 0.3	61.6 ± 0.3	0.7 ± 0.4	0.021
	2	60.7 ± 0.2	60.6 ± 0.3	61.6 ± 0.3	61.6 ± 0.2	0.9 ± 0.3	<0.001
	3	60.7 ± 0.2	60.6 ± 0.3	61.6 ± 0.3	61.7 ± 0.2	1.0 ± 0.3	<0.001
Fat-free mass index (kg/m^2)	*n*=	897	538	461	674	–	–
	1	14.9 ± 0.1	15.0 ± 0.1	15.2 ± 0.1	15.1 ± 0.1	0.1 ± 0.1	0.050
	2	15.0 ± 0.1	15.0 ± 0.1	15.1 ± 0.1	15.1 ± 0.1	0.1 ± 0.1	0.076
	3	15.0 ± 0.1	15.0 ± 0.1	15.1 ± 0.1	15.1 ± 0.1	0.1 ± 0.1	0.086
Grip strength[a] (kg)	*n*=	303	214	188	244	–	–
	1	28.6 ± 0.4	28.2 ± 0.5	28.8 ± 0.4	29.4 ± 0.4	0.8 ± 0.5	0.470
	2	28.9 ± 0.3	28.6 ± 0.4	28.8 ± 0.4	28.7 ± 0.3	−0.1 ± 0.5	0.855
	3	28.8 ± 0.3	28.6 ± 0.4	28.8 ± 0.4	28.7 ± 0.3	−0.1 ± 0.5	0.855
Arm muscle quality[a] (kg/kg)	*n*=	303	214	188	244	–	–
	1	13.3 ± 0.2	13.1 ± 0.2	13.6 ± 0.2	13.7 ± 0.2	0.4 ± 0.2	0.077
	2	13.4 ± 0.1	13.2 ± 0.2	13.5 ± 0.2	13.5 ± 0.2	0.1 ± 0.2	0.472
	3	13.4 ± 0.1	13.2 ± 0.2	13.5 ± 0.2	13.5 ± 0.2	0.1 ± 0.2	0.472
Leg explosive power[b] (watts/kg)	*n*=	662	410	340	502	–	–
	1	87.4 ± 1.5	90.3 ± 1.8	92.6 ± 2.0	94.7 ± 1.8	7.3 ± 2.3	0.001
	2	86.8 ± 1.4	90.8 ± 1.8	92.5 ± 1.9	95.0 ± 1.7	8.2 ± 2.2	<0.001
	3	86.8 ± 1.4	90.7 ± 1.8	92.7 ± 1.9	95.1 ± 1.7	8.3 ± 2.2	<0.001
C-reactive protein[c] (mg/L)	*n*=	497	359	315	487	–	–
	1	1.6 (1.5, 1.8)	1.6 (1.4, 1.8)	1.6 (1.5, 1.8)	1.6 (1.4, 1.7)	–	0.644
	2	1.6 (1.5, 1.8)	1.6 (1.4, 1.7)	1.6 (1.5, 1.8)	1.6 (1.5, 1.7)	–	0.879
	3	1.6 (1.5, 1.8)	1.6 (1.4, 1.7)	1.6 (1.4, 1.8)	1.6 (1.5, 1.7)	–	0.842

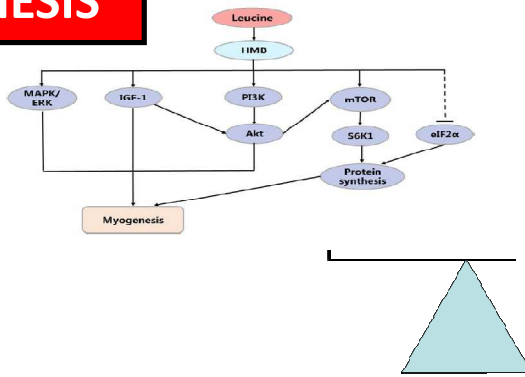
NUTRACEUTICALS

overcome-reduce anabolic resistance!

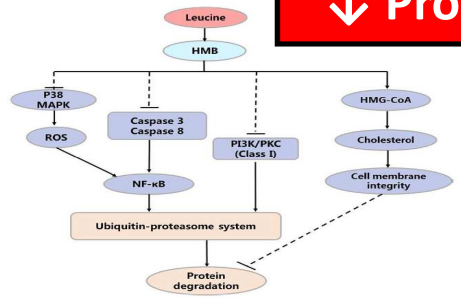
ANABOLIC SUBSTRATES
ANTIINFLAMMATORY
ANTIOXIDANTS

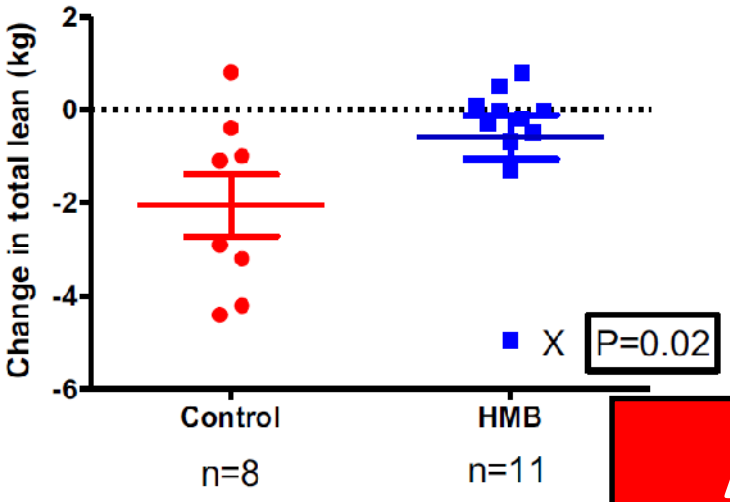
ESSENTIAL AMINO ACIDS and METABOLITES
(Leucine: HYDROXY-METHYL BUTYRATE)

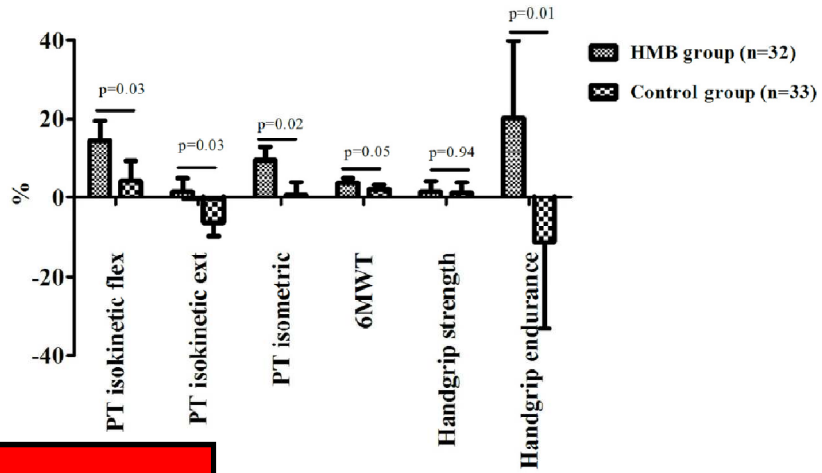
↑ Prot SYNTHESIS



↓ Prot DEGRADATION







AGING

Deutz et al, Clin Nutr 2013

Berton et al, PLoS One 2015

VITAMIN D

Vitamin D Deficiency-Induced Muscle Wasting Occurs through the Ubiquitin Proteasome Pathway and Is Partially Corrected by Calcium in Male Rats

Mehrajuddin Bhat, Ramesh Kalam, Syed SYH Qadri , Seshacharyulu Madabushi, and Ayesha Ismail

Endocrinology 2013

Vitamin D deficiency down-regulates Notch pathway contributing to skeletal muscle atrophy in old wistar rats

Carla Domingues-Faria[1,2,4], Audrey Chanet[2,4], Jérôme Salles[2,4], Alexandre Berry[2,4], Christophe Giraudet[2,4], Véronique Patrac[2,4], Philippe Denis[3,4], Katia Bouton[2,4], Nicolas Goncalves-Mendes[1], Marie-Paule Vasson[1,5], Yves Boirie[2,6] and Stéphane Walrand[2,4*]

Nutr Metab 2014

COMBINED SUPPLEMENTATIONS

A high whey protein–, leucine-, and vitamin D–enriched supplement preserves muscle mass during intentional weight loss in obese older adults: a double-blind randomized controlled trial[1–3]

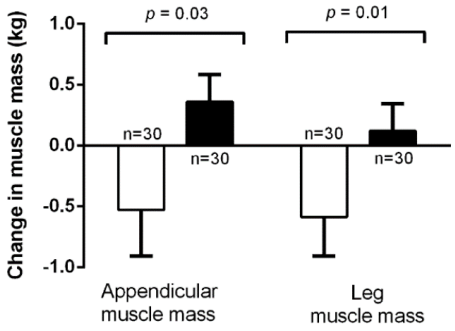
Verreijen et al, AJCN 2015

Whey protein, amino acids, and vitamin D supplementation with physical activity increases fat-free mass and strength, functionality, and quality of life and decreases inflammation in sarcopenic elderly[1,2]

Rondanelli et al, Am J Clin Nutr 2016

- «FAST» protein
- Essential-BCAA
- Hydroxy-Methyl-Butirate (HMB)
- Vitamin D

↑ EFFECTIVENESS



NUTRACEUTICALS

CALORIE

PROTEIN

GLUCOSE - FAT

NO STRONG DATA FUCUSING on OBESE-SARCOPENIC OBESE INDIVIDUALS!!

Conclusions

1) SARCOPENIC OBESITY is potentially a major clinical and prognostic feature in the heterogeneous and growing obese patient population;
2) A large body of work is needed to increase AWARENESS and improve its clinical DEFINITION;
3) Nutrition should be a therapeutic cornerstone both in prevention and treatment of low muscle mass and function; quality of DIETARY PATTERNS and adequate PROTEIN INTAKE appear to be key nutritional tools;
4) A number of nutritional-nutraceutical supplements could play beneficial therapeutic roles including ESSENTIAL and BC AMINO ACIDS, N-3 PUFA, VITAMIN D and ANTIOXIDANTS;
5) A large effort in high-quality CLINICAL RESEARCH will be mandatory to define optimal nutritional treatment tools in obese and sarcopenic obese individuals

Thank you for your attention