Sarcopenia:
Challenges & Strategies for Prevention & Management

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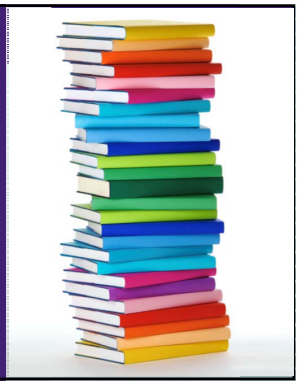

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Disclosures

- Honorarium provided by Nutricia
- No other related disclosures

- ***No conflict of interest for this presentation***

The opinions reflected in this presentation are those of the speaker and independent of Nutricia North America

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Learning Objectives

- After a quick background review, Participants will:
  - 1: Gain an understanding of the evolving definitions of sarcopenia, including recent definitions of sarcopenic obesity
  - 2: Identify the challenges related to prevention & management of sarcopenia, including sarcopenic obesity
  - 3: Characterize essential nutritional & non-nutritional components of 'state of the art' interventions for the management of sarcopenia

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What is Sarcopenia & does it really matter?

- Loss of skeletal muscle mass (SMM) concurrent to the process of aging or secondary to other causes
  - Involuntary loss
- Does this change in body composition impact health?
- Is this a significant problem?

Morley JE. Sarcopenia in the elderly. *Fam Pract*. 2012;29 Suppl 1:i44-i48.

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Global demographics & sarcopenia

- Globally by 2025 more than 1.2 billion people will be ≥ 60 years old
  - No consistent pattern for risk factors
  - Wide variance in prevalence due to varied definitions
  - Multifactorial pathogenesis
    - Process of aging as etiology is **primary sarcopenia**
  - Secondary:
    - **Secondary sarcopenia** = other factors driving muscle mass loss
    - Insufficient dietary intake of total calories and protein, increased nutritional losses, increased nutritional requirements, malnutrition

Supriya R, et al. A Multifactorial Approach for Sarcopenia Assessment: A Literature Review. *Biology (Basel)*. 2021;10(12):1354

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Numerous organizations focused on sarcopenia research

- European Working Group on Sarcopenia (EWGS),
- Asian Working Group on Sarcopenia, (AWGS),
- International working group, (IWG), on Sarcopenia,
- NIH-Sarcopenia Project

Supriya R, et al. A Multifactorial Approach for Sarcopenia Assessment: A Literature Review. *Biology (Basel)*. 2021;10(12):1354

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Yes, sarcopenia matters….

**2016: WHO classified as a disease in the International Classifications of diseases (ICD-10).
Now has a billable code.**

Morley JE. Editorial: Sarcopenia: 2020. J Nutr Health Aging. 2021;25(3):278-280

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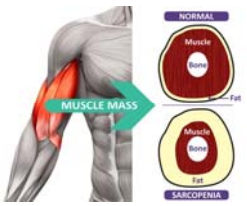
Generically: What is Sarcopenia?

- Age-related loss of skeletal muscle mass **(SMM)** with the normal process of aging
  - Involuntary loss
  - Even if unchanged total body weight throughout adult life, composition of body weight changes
    - Lose muscle mass, gain fat mass



Morley JE. Sarcopenia in the elderly. *Fam Pract*. 2012;29 Suppl 1:i44-i48.

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Understanding Sarcopenia

- Muscle mass peaks between 20-35 years of age
  - Muscle mass loss occurs at a rate of 3-8% decrease per decade thereafter
    - After age 60, muscle mass is lost quicker
    - Numerous factors impact rate of progression
- **Sarcopenia is a major** cause of disability, falls, fractures, frailty, functional decline, ↑hospitalizations in elderly population

Morley JE. Sarcopenia in the elderly. *Fam Pract*. 2012;29 Suppl 1:i44-i48.; Rockwood K, et al. Fifteen years of progress in understanding frailty and health in aging. *BMC Med*. 2018;16(1):220

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Metabolic impact of Sarcopenia (altered body composition):

- Decreased muscle mass:
  - Loss of muscle strength (grip strength –60%)
  - Decreased independent physical activity
  - Altered endurance
  - Increased issues of "dis-use"
  - Increased frailty/risk of falls
- Declines in basal metabolic rate (BMR)
- Combined changes in BMR & ↓ activity=
- Reduced caloric intake
- Negative impact on glucose homeostasis and immunity
- Increased morbidity and mortality

Barkoukis, H. Muscle Building and Maintenance in the Elderly: the Use of Protein. *Curr Nutr Rep* 2016;5:77–83

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Skeletal muscle mass becomes a determinant in survival & recovery in critical illness

Muscle mass LOSS % of total	Complications Related to loss	Associated mortality (%)
10 %	Impaired immunity Increased infection	10%
20 %	↓ healing; increased weakness	30%
30%: more than this	↑ Pressure sores & pneumonia; no healing	50% / 100%

Hanna JS. Sarcopenia and critical illness: a deadly combination in the elderly. *JPEN J Parenter Enteral Nutr*. 2015;39(3):273-281

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High body fat & low muscle mass….

- Obesity rates have risen
- WHO definition: **BMI** ≥ 30 kg/m²and waist circumference ≥ 102 cm men; ≥ 88 women;
  - Other definition uses body composition: body fat mass 38%/27% men/women
- Sarcopenia + obesity = sarcpenic obesity syndrome
  - Accelerates functional decline, increases co-morbidities, 'fat-frail' situation

Prokopidis K, et al. Impact of Protein Intake in Older Adults with Sarcopenia and Obesity: A Gut Microbiota Perspective. *Nutrients*. 2020;12(8):2285.

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1: Gain an understanding of the evolving definitions of sarcopenia, including recent definitions of sarcopenic obesity

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Early definitions of sarcopenia

Early Definitions focused exclusively on quantifying muscle mass

Loss of muscle mass was primary focal point

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Sarcopenia seen as a 'disease' state

- Baumgartner defined sarcopenia as:

$$\frac{\text{Appendicular skeletal mass (ASM)}}{\text{Height}^2}$$

Cutoff defined: 2 SD below mean ASM/H^2 for reference sample of young/middle-aged healthy individuals from Rosetta Study-

Quantified by DXA (dual x-ray absorptiometry)

Baumgartner RN, et al. Epidemiology of sarcopenia among the elderly in New Mexico [published correction appears in Am J Epidemiol 1999 Jun 15;149(12):1161]. *Am J Epidemiol*. 1998;147(8):755-763.

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Sarcopenia International Consensus Conference Definition: focus on mass

- Diagnosis consistent with 2 SD below the average **ASM/H²** using the reference sample of 35-year-old healthy individuals or
  - ≤ 7.23kg/m² for men
  - ≤ 5.67 kg/m² for women
- Gait speed < 0.8 meters per second

Fielding RA, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc*. 2011;12(4):249-256.

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Clinically, exclusively quantifying muscle mass had limited predictive value ….

By contrast, muscle strength and performance have a higher correlation to morbidity & mortality than muscle mass measurements…

Kara M, et al. Diagnosing sarcopenia: Functional perspectives and a new algorithm from the ISarcoPRM. *J Rehabil Med*. 2021;53(6):jrm00209. Published 2021 Jun 21

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Assessing muscle strength& performance includes:

- Mobility, gait speed, grip strength, dexterity (upper extremity functioning), ADL (activities of daily living including short distance walking, stair climbing, ability to stand from seated position); Short physical performance battery test (**SPPB**)
- **SPPB** = evaluation of balance, gait, strength, endurance by examining an individual's ability to stand with feet together in side-by-side, semi-tandem, and tandem positions, time to walk 8 feet and time to rise from a chair and return to seated position five times

Kara M, et al. 2021

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First: European Working Group on Sarcopenia in Older People (EWGSOP) Definition expanded & added sarcopenia stages

Diagnosis based on criterion 1 (quantifying mass) plus 2 or 3

Low muscle mass (1)
Low muscle strength (2)
Low physical performance (3)

stage	Muscle mass	Muscle strength	Muscle performance
Pre	↓		
Sarcopenia Severe	↓ Decreased-**all** parameters	↓ **OR**	↓

Cruz-Jentoft AJ, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*. 2010;39(4):412-423.; Burton LA, et al. Optimal management of sarcopenia. *Clin Interv Aging*. 2010;5:217-228. Review

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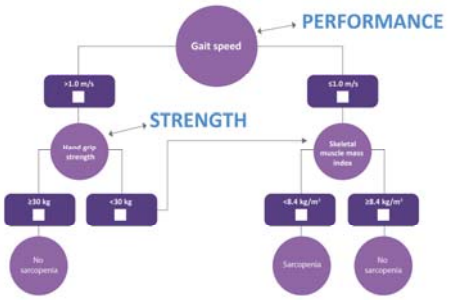
First: European Working Group on Sarcopenia in Older People (EWGSOP), 2010, Screening added strength & performance



Based on: Cruz-Jentoft AJ. (2010); Burton LA, et al. (2010)

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Evolving definition & diagnosis..10 years later

- Second: European Working Group on Sarcopenia in Older people (EWGSOP) goal: early intervention

Primary parameters of focus:

- ***Low Muscle Strength**
- **Low physical performance**

Most widely accepted method of screening

Cruz-Jentoft AJ, et al. Sarcopenia: revised European consensus on definition and diagnosis [published correction appears in Age Ageing. 2019 Jul 1;48(4):601]. *Age Ageing*. 2019;48(1):16-31; Cruz-Jentoft AJ. Diagnosing sarcopenia: turn your eyes back on patients. *Age Ageing*. 2021;50(6):1904-1905.

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Second: 2019 (EWGSOP): recommend clinically practical tool to screen for sarcopenia

- Screen using the SARC-F tool: none=0; some=1; a lot=2; score≥ 4=diagnosis
  - Includes: strength (can you lift 10 pounds)?
  - Do you need walking assistance?
  - Rise from chair 5 times-12 seconds?
  - Climb 10 stairs unassisted?
  - Any falls in past year?
  - SARC-F: sarcopenia, assess, refer, confirm, find

Köller M. Sarcopenia-a geriatric pandemic : A narrative review [published online ahead of print, 2022 Apr 13]. *Wien Med Wochenschr*. 2022

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Comparing 1st vs 2nd EWGSOP:

- Both include mass & strength as criteria, but **strength** is key in 2nd
- Specific cut-off values for various parameters not included or recommended in 1st
- 2nd: does not include performance parameters
- 2nd Regional normative population cut-offs are recommended

Wallengren,et al BMC Geriatr 21:600-612, 2021

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Sarcopenic obesity: Consensus statements

- European Soc. Parenteral & Enteral Nutrition (ESPEN) & Eur. Soc. Study Obesity (EASO):
- Defined: co-existence of sarcopenia & obesity
- Defined procedure for screening and diagnosis

Donini LM, et al. Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement [published online ahead of print, 2022 Feb 23]. *Obes Facts*. 2022;1-15

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ESPEN & EASO consensus:

- **Screening:**
- Recommend using WHO values for **BMI** or Waist circumference (with ethnicity specific cut-offs)
- AND
- Surrogate indicators of sarcopenia such as clinical symptoms, clinical suspicion, validated questionnaires (SARC-F)

Donini LM, et al. 2022

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ESPEN & EASO consensus:

- **Diagnosis**: 2 steps– include BOTH:
- Muscle strength assessed via
  - hand grip or
  - knee extension, or
  - functional assessments (SPPB)
- Altered body composition
  - DXA or BIA for ↓muscle mass and ↑ fat mass
    - BIA=bio-impedance analysis (electrical conductivity, fat has more impedance & resistance than muscle)

Donini LM, et al. 2022

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2: Identify the challenges related to prevention & management of sarcopenia, including sarcopenic obesity

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Challenges remain:

- Different definitions for sarcopenia & obesity
- Heterogeneity in diagnostic approaches
- Approximately 1/3 of published studies are using only the original definition (based on body composition)
- No agreement on how to assess mass, strength, performance
- No agreement on which cutoff points to use
- Weak agreement on which screening techniques to use

Editorial: Cruz-Jentoft AJ. Diagnosing sarcopenia: turn your eyes back on patients. *Age Ageing*. 2021;50(6):1904-1905.

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State of the art interventions

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State of the art: Prevention & management

1. Exercise & physical activity: Resistance training
2. Nutrition
3. Weight management: Sarcopenia & obesity

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Exercise as therapy can't be haphazard

- Refer to exercise specialist
  - ACSM: (acsm.org) American College Sports Medicine
- Most efficacy to ↑strength/mass with resistance training
- Individualized
  - Baseline fitness; medical status, hx exercise, nutritional status
- Dose (frequency)
- Degree of stimulus (duration & specificity)

Hurst C, et al. Resistance exercise as a treatment for sarcopenia: prescription and delivery. *Age Ageing*. 2022;51(2):afac003

31

No single type of exercise 'adequately addresses the need for therapeutic exercise for age related sarcopenia'

Camajani E, et al. Whey Protein, L-Leucine and Vitamin D Supplementation for Preserving Lean Mass during a Low-Calorie Diet in Sarcopenic Obese Women. *Nutrients*. 2022;14(9):1884

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Myth—it's too late to begin physical activity (PA)….

- Never too late - later life interventions to increase physical activity & resistance training will improve physiologic function, muscle function & mass
- ↑PA after sedentary will restore/reduce risk profile (contrasted to sedentary)
- Achieving a fraction of PA recommendations positively impacts life expectancy & quality of life

Patterson, 2010; Paffenbarger, 2000, Seals, 2016, Gleason, 2011

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Most effective method of modulating sarcopenia: Nutrition intervention with resistance training

"Despite progressive sarcopenia with senescence, skeletal muscle retains ability for anabolic adaption to resistance training with adequacy of kcal/protein"

Esmarck B, et al. Timing of postexercise protein intake is important for muscle hypertrophy with resistance training in elderly humans. *J Physiol*. 2001;535(Pt 1):301-311

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State of the art: Nutrition interventions

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A quick backgrounder on protein & aging….

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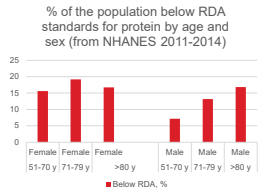
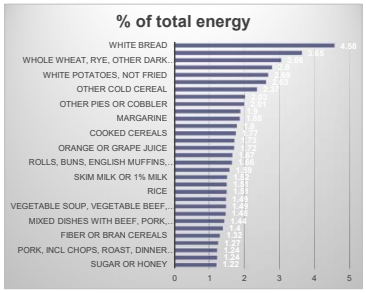
National Health & Examination Nutrition Survey (NHANES): Some older adults do not consume sufficient protein





Based on: J. Gerontology 56A:65, 2001; Gladys Block, et al; Berryman et al. (2018). *Am J Clin Nutr.*, 405-13.

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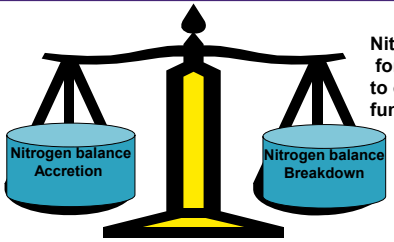
Adult protein recommendations based on nitrogen balance studies



Nitrogen equilibrium (balance) for the adult does not correlate to optimal physiologic or functional outcomes …….

Phillips SM, et al. Optimizing Adult Protein Intake During Catabolic Health Conditions [published correction appears in Adv Nutr. 2021 Mar 31;12(2):578]. *Adv Nutr*. 2020;11(4):S1058-S1069.

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Protein intake and muscle protein synthesis..

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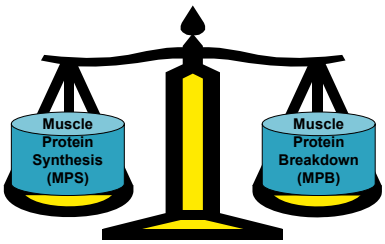
Maintaining body protein: balance between MPS & MPB



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Muscle protein synthesis (MPS), is determined by these protein factors:

- The *quality* of the protein (inclusion of all of the essential amino acids (EAA))
- The *quantity* of the protein (inclusion of all EAA at the amounts recommended- leucine)
- *Distribution* of the protein ingestion throughout the day
- Free amino acids or "intact" (in whole foods) results in equivalent MPS, (when quantity & quality factors met)

Phillips SM, et al. 20201; Weijzen, et al J Nutr 152:59, 2022

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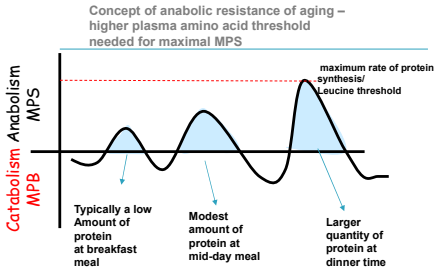
Typical meal protein distribution & muscle protein synthesis



Paddon-Jones D, et al. Dietary protein recommendations and the prevention of sarcopenia. *Curr Opin Clin Nutr Metab Care*. 2009;12(1):86-90.

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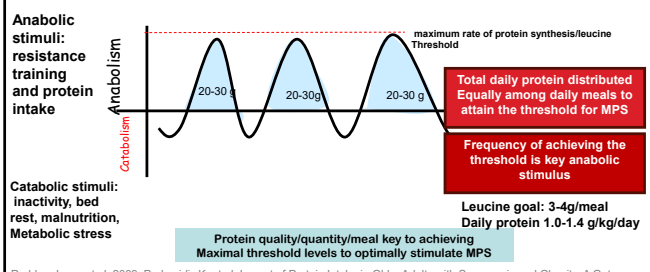
Daily protein distribution-optimal MPS



Paddon-Jones et al. 2009; Prokopidis K, et al. Impact of Protein Intake in Older Adults with Sarcopenia and Obesity: A Gut Microbiota Perspective. *Nutrients*. 2020;12(8):2285.

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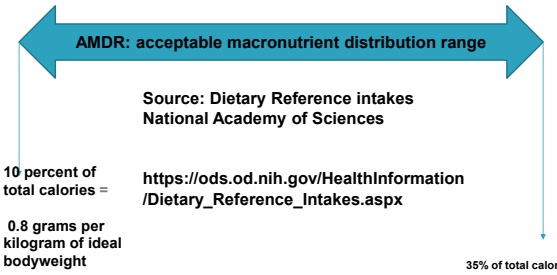
Current protein recommendations



Source: Dietary Reference intakes
National Academy of Sciences

https://ods.od.nih.gov/HealthInformation/Dietary_Reference_Intakes.aspx

10 percent of total calories =

0.8 grams per kilogram of ideal bodyweight

35% of total calories

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Protein in foods:

Food	Measure	Amount of Protein
Fruits		None or negligible
Cheese	1 ounce	8 grams
Yogurt	1 cup	14-20 grams
Milk	1 cup	8 grams
Grains	1 ounce	2-3 grams
Vegetables	1 ounce	~ 2 grams
Beef	1 ounce	7 grams
Fish	1 ounce	7-9 grams
Lentils/beans	1 cup cooked	18 grams
Tofu	3 ounces	8 grams

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Protein distribution throughout the day

20-30 grams	**2-egg omelet with 1 oz low-fat cheese and 1 oz lean meat wrapped in 1 medium whole grain tortilla + 1 cup of 100% juice**
20-30 grams	**2 slices of whole wheat toast with 2 tablespoons of peanut butter + 1 banana + 6 ounces Greek yogurt**
20-30 grams	**1 turkey and cheese sandwich (3 oz turkey/1 ou cheese) on 2 slices whole wheat bread + 1 cup milk**

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Nutrition recommendations for prevention & management of sarcopenia

- Synergistic, optimal effect on muscle protein synthesis with progressive resistance training and provision of sufficient, (not excessive), total daily kcal & protein
- Protein: quantity, quality, distribution
  - Specific sufficiency of leucine necessary, not branch chain amino acids
- Vitamin D status is correlated to sarcopenia
- Emerging evidence: inclusion of anti-inflammatory foods & adequacy of dietary fiber sources

Camajani, et al. 2022; Kumar V, et al. Human muscle protein synthesis and breakdown during and after exercise. *J Appl Physiol (1985)*. 2009;106(6):2026-2039; Kara M, et al. Diagnosing sarcopenia: Functional perspectives and a new algorithm from the ISarcoPRM. *J Rehabil Med*. 2021;53(6):jrm00209.

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Clarity in outcomes from interventions utilizing only increased protein

- Equivocal outcomes observed re: ↑ muscle mass and strength with no exercise components, only protein-based interventions
  - Why? Study length, lack of statistical power, protocol variations
- Clear data - consuming current protein recommended levels (.8g/kg body weight) does not abate sarcopenia

Phillips, et al 2020

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Nutrition meets metabolism = complex

- Known: protein needed for MPS, immune function, satiety, numerous metabolic functions
- Weight loss interventions need to be designed with attention to overall, sustainable metabolic health
- Not known: exact recommendation for % of protein AND carbohydrate (especially fiber rich sources)
- Diverse sources of protein to balance positive and negative metabolic benefits

Roh E, Choi KM. Health Consequences of Sarcopenic Obesity: A Narrative Review. *Front Endocrinol (Lausanne)*. 2020;11:332

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Vitamin D status and sarcopenia

- Vitamin D status and sarcopenia:
  - Aging results in: ↓intake, intestinal absorption, cutaneous synthesis; less sun exposure, ↓renal 1-hydroxylase; calcium intake issues with aging process
  - Supplementation at 800 IU vitamin D decreases bone loss, turnover, fracture rate
  - Dietary Recommended Intake: age adjusted: ≥ 70 is 20 mcg (800IU)
    - 1mcg=40IU

Jacques PF. The potential preventive effects of vitamins for cataract and age-related macular degeneration. *Int J Vitam Nutr Res*. 1999;69(3):198-205; Uchitomi R, et al. Vitamin D and Sarcopenia: Potential of Vitamin D Supplementation in Sarcopenia Prevention and Treatment. *Nutrients*. 2020;12(10):3189

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Vitamin D status and sarcopenia are correlated

- Vitamin D insufficiency, serum ≤ 30n/ml (75nM) and deficiency ≤ 20n/ml (50nM) positively correlated to sarcopenia and ↓ muscle function
- Systematic reviews with insufficient/deficient status observed ↑ increased muscle strength with supplementation 800-4,000 IU
- Interaction between D status & muscle function
  - Plasma < 30n/ml see " ostomalacic myopathy" clinical signs:
  - Change in gait, difficulty rising from chair, diffuse muscle pain in absence of specific pattern, pain upon extension, or flex of hip and knee AND muscle biopsy demonstrated atrophy of Type II fibers (recruited first for sudden movements)

Uchitomi, et al. 2020; Pfeifer M, et al. Vitamin D and muscle function. *Osteoporos Int*. 2002;13(3):187-194.

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Clinical pearl summary:

- Team approach to management is critical to success
- Adequate, not excessive, total kcal intake and protein provision (following guidelines explained herein), is critical
- Nutrition weight control protocols must also consider risk/benefit, attention to protein provision details and emerging data
- Screening tools should focus on validated tools such as SARC_F, and functional parameters: (strength, performance)
- Exercise protocols should be individualized and designed by exercise specialists

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For your reference:

- Quantifying skeletal muscle mass (SMM) must be adjusted for body size:
  - Weight– ASM/weight or
  - ASM/BMI
  - Height squared--ASM/height^2
- ASM: appendicular skeletal muscle mass

Cruz Jentoff, et al Age and Ageing 48:16-31,2019

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For your reference: summary of clinical assessment validated techniques, (next 2 slides)

- Screening: SARC-F tool
- Strength:
  - grip strength,
  - Chair sit to stand
- Mass:
  - appendicular skeletal muscle mass (ASMM) via DXA
  - or whole body skeletal muscle mass via BIA,
  - lumbar muscle, L-3, cross sectional area by CT or MRI;
  - ultrasound;
  - oral dose of labeled creatine
- Performance: gait speed; SPPB, rise from chair, 400 m walk

Cruz-Jentoff, et al Age and Ageing 48:16-31, 2019

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For your reference:

- Grip strength:
  - use calibrated, handheld dynamometer with interpretive data from reference population
  - or use isometric torque for lower limb strength (surrogate for arm/leg strength)
- Chair-sit to stand:
  - 5 times, no use of arms, in 30 seconds, (assesses strength and endurance)

Cruz Jentoft, et al Age and Ageing 48:16-31, 2019

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Thank you!

Type your questions in the Q&A panel

Make sure you select 'All Panelists'

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