# Age-Related Sarcopenia

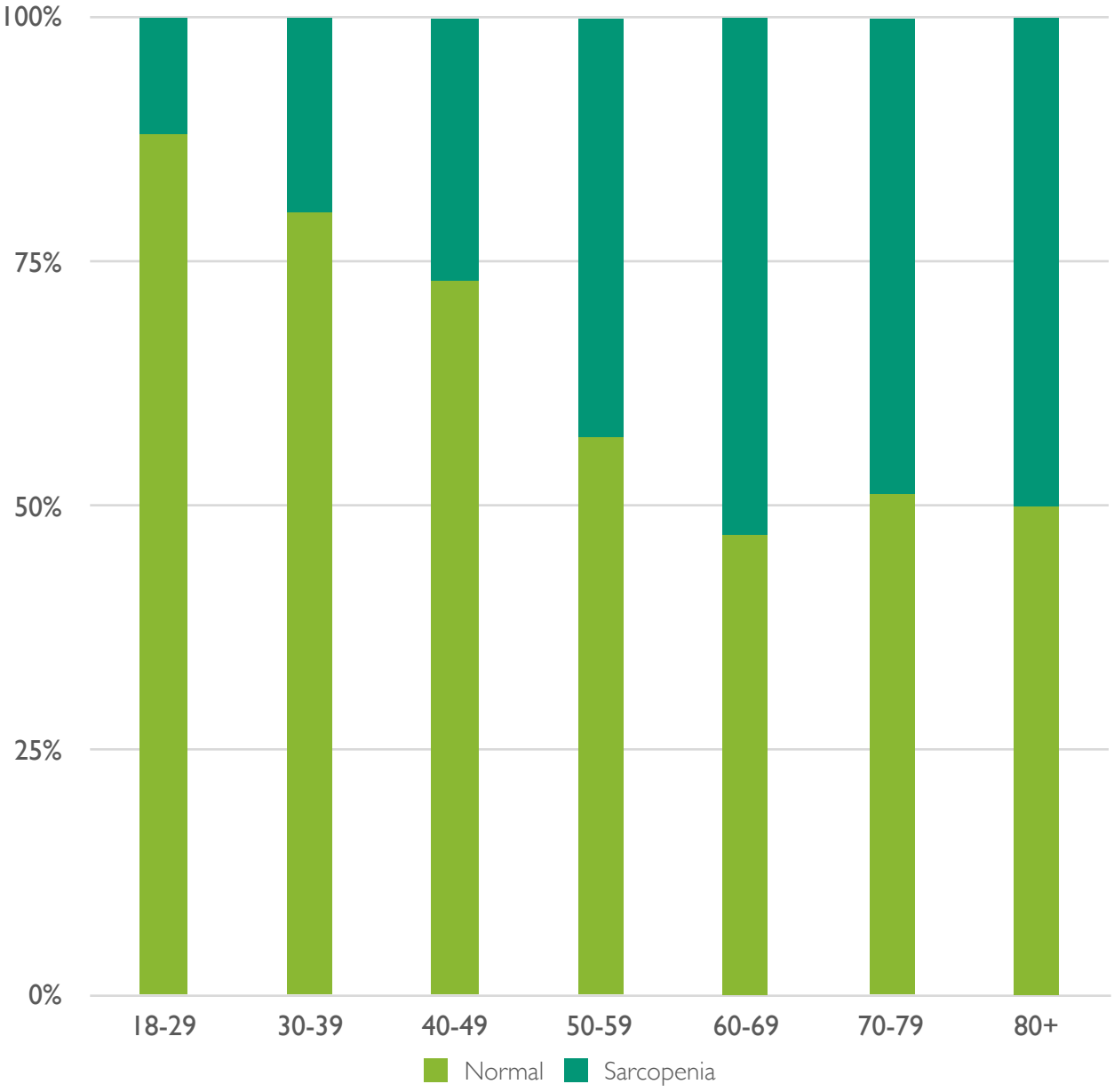
Michael Hull

**Sarcopenia**: a syndrome characterized by the progressive loss of muscle mass and function that can occur in the absence of an underlying illness.

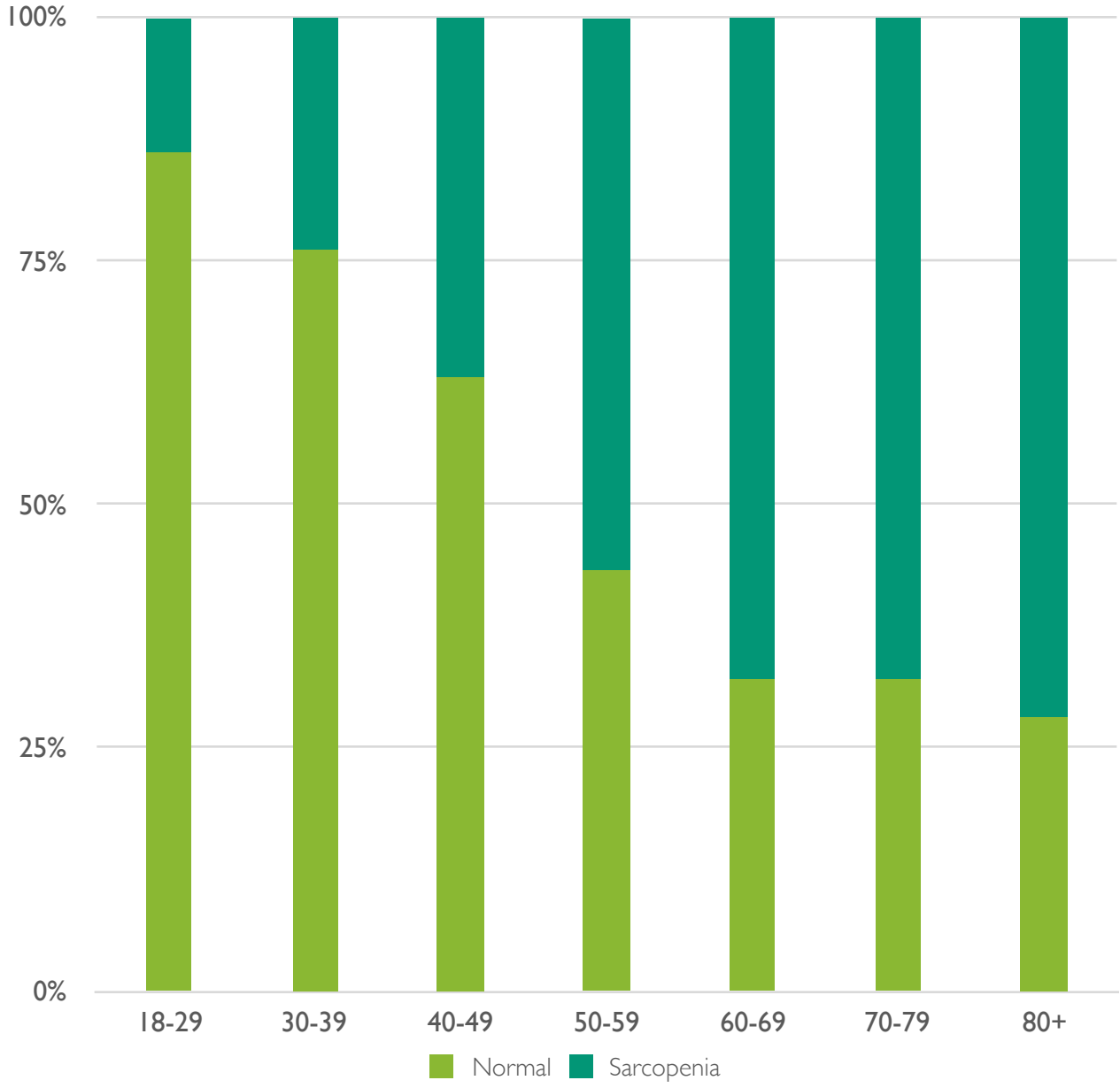


Keevil and Romero-Ortuno. Proc Nutr Soc. 2015 Nov;74(4):337-47. | Janssen. Clin Geriatr Med. 2011 Aug;27(3):355-63.

# PREVALENCE IN MEN




# PREVALENCE IN WOMEN






Janssen et al. J Am Geriatr Soc. 2002 May;50(5):889-96.

# Sarcopenia vs Frailty

## Sarcopenia

- Age-related skeletal muscle loss
- Poor muscle quality

## Commonalities

- Physical function impairment
- Weak muscle strength
- Slow gait speed
- Poor Balance

## Frailty

- Deficits accumulate
- Fatigue
- Weight loss
- Cognitive impairment



Cesari et al. Front Aging Neurosci. 2014; 6: 192.

# Sarcopenia Defined: It's Complicated

## IANA

International Academy on Nutrition and Aging

- Usual gait speed <1.0 m/s
- Low muscle mass: appendicular lean mass/height ≤7.23 kg/m$^2$ (men) and ≤5.67 kg/m$^2$ (women)

## EWGSOP

European working group on sarcopenia in older people

- Usual gait speed ≤0.8 m/s
- Grip strength <30 kg (men) or <20 kg (women)
- Low muscle mass: appendicular lean mass/height <7.23-.26 kg/m$^2$ (men) and <5.50-.67 kg/m$^2$ (women)

## AWGS

Asian working group for sarcopenia

- Usual gait speed ≤0.8 m/s
- Grip strength <26 kg (men) or <18 kg (women)
- Low muscle mass: appendicular lean mass/height <7.0 kg/m$^2$ (men) and <5.4 kg/m$^2$ (women)

## FNIH

Foundation for the National Institutes of Health: Sarcopenia

- Usual gait speed ≤0.8 m/s
- Grip strength <26 kg (men) or <16 kg (women)
- Low muscle mass: appendicular lean mass/BMI <0.789 kg/m$^2$ (men) and <0.512 kg/m$^2$ (women) as measured by DXA scan



Keevil and Romero-Ortuno. Proc Nutr Soc. 2015 Nov;74(4):337-47.

# Competing Definitions

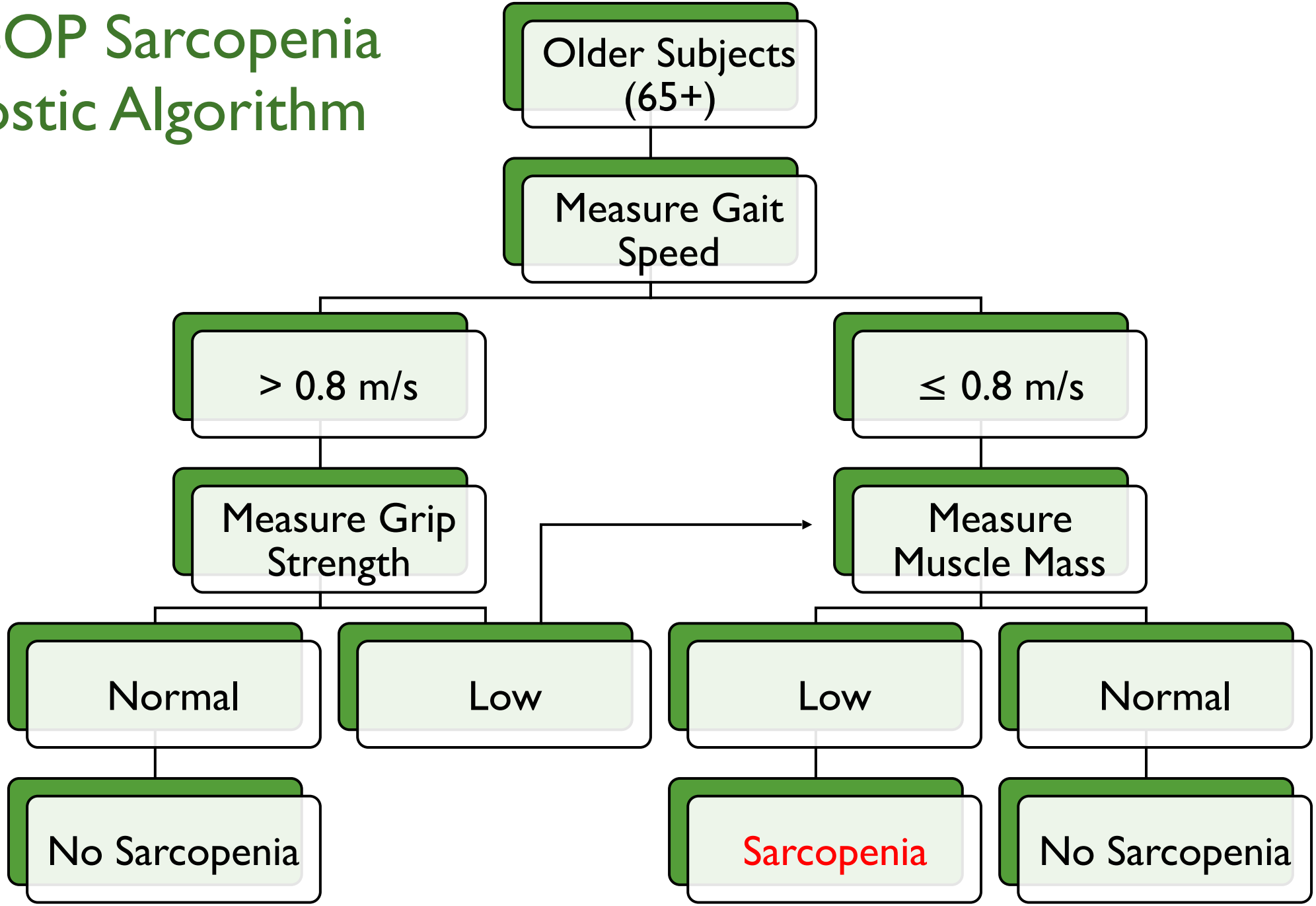
## COMMONALITIES

- A measure of muscle mass
- A measure of muscle function (strength + performance)

## DIFFERENCES

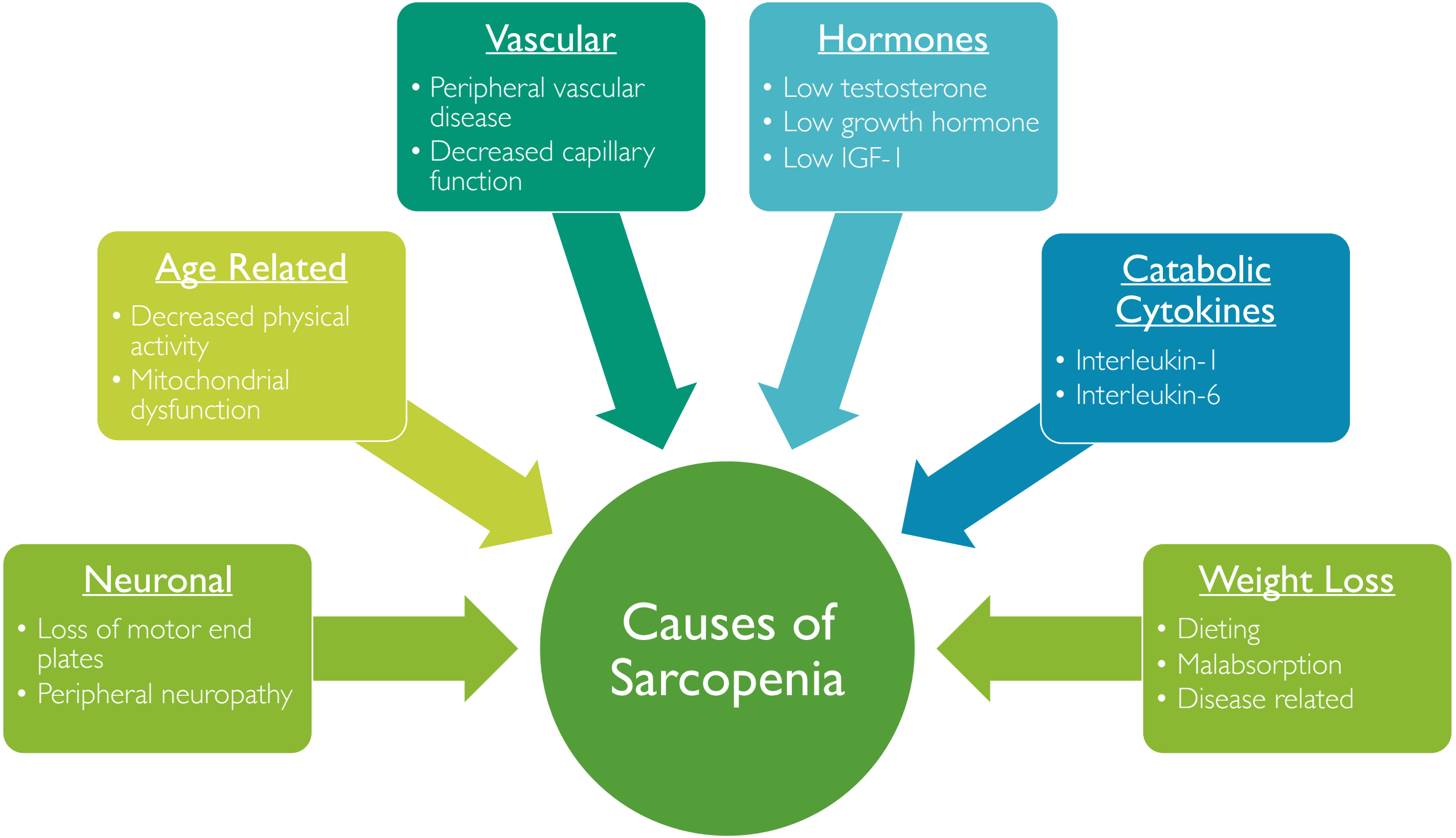
- Cutoff points
- Low muscle mass = 2-2.5 SD below population or risk threshold?

# EWGSOP Sarcopenia Diagnostic Algorithm






Cruz-Jentoft et al. Age Ageing. 2010 Jul;39(4):412-23.






Morley et al. J Cachexia Sarcopenia Muscle. 2014 Dec; 5(4): 253–259.

# MP Synthesis & Catabolism in Age-Related Sarcopenia

## Internal Processes

- Reductions of anabolic hormones
  - Testosterone, estrogens, growth hormone, IGF-1
- Apoptotic activities increase in myofibers (TNF-α)
- Pro-inflammatory cytokines increase
  - TNF-α, IL-6, IL-1
- Decline of mitochondrial function of muscle cells
- Decline in the number of α-motor neurons

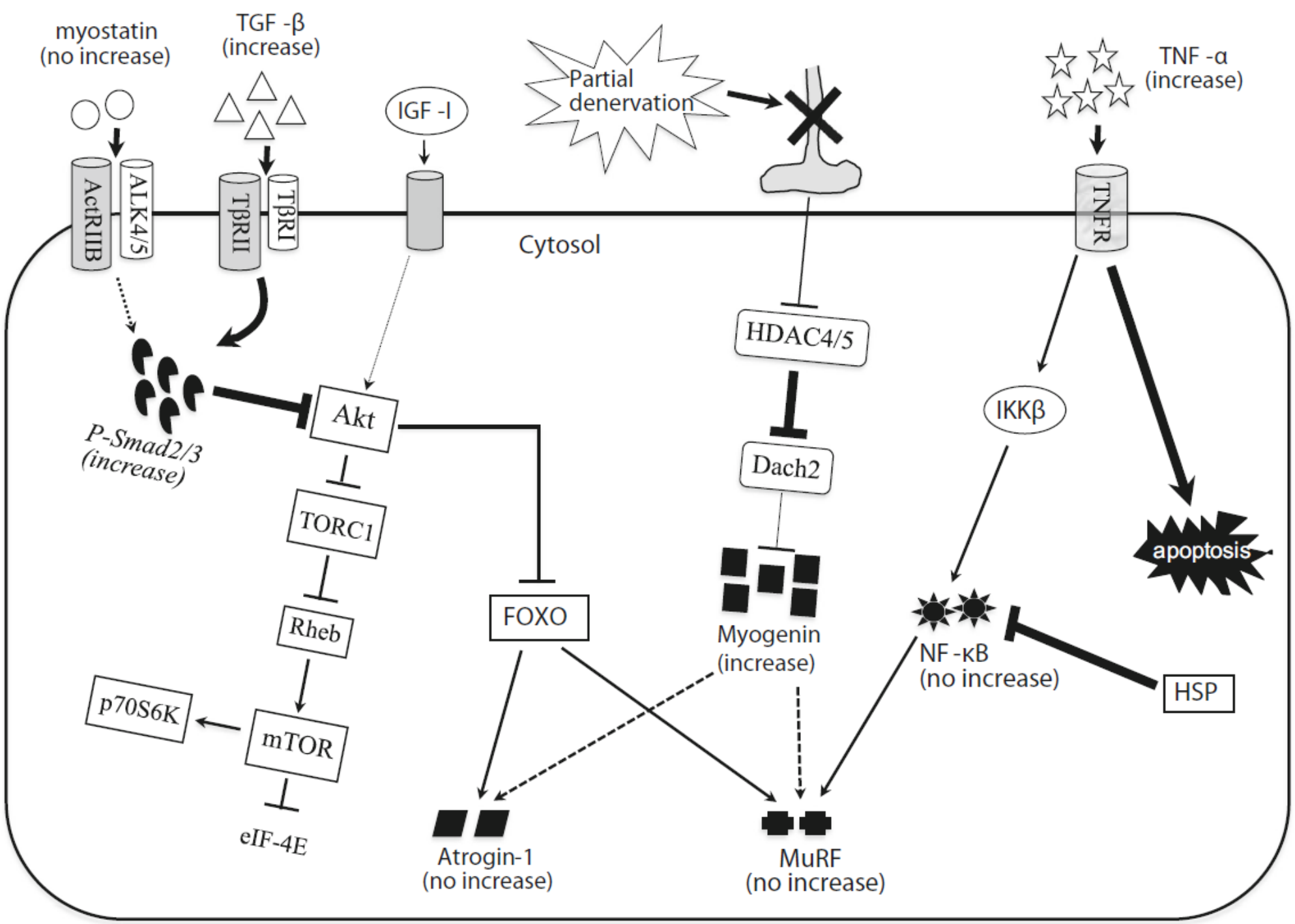
## External Processes

- Deficits in energy intake
- Deficits in protein intake
- Low vitamin D intake
  - Aids in recruitment of satellite cells (aka muscle repair)
- Decreased physical activity



Muscaritoli et al. Clin Nutr. 2010 Apr;29(2):154-9. | Joseph et al. Mol Aspects Med. 2005 Jun;26(3):181-201. | Owens et al. Am J Physiol Endocrinol Metab. 2015 Dec 15;309(12):E1019-31.

# Catabolic Pathway in Sarcopenic Muscle




Sakuma et al. Pflugers Arch. 2015 Feb;467(2):213-29.

# MP Synthesis & Catabolism in Age-Related Sarcopenia

- First-pass hepatic extraction of amino acids may be increased in the elderly. Less AA available for systemic circulation
  - Less leucine available to initiate MPS
  - A larger bolus of high-quality protein may be able to overcome this (40 vs 20 g)
- Elderly have reduced response of mTORC1 following volume matched resistance exercise compared to the young
  - Larger volumes of resistance exercise can increase mTORC1 response
- Suggestive evidence that elderly muscle is less sensitive to the anti-proteolytic effects of insulin
  - Insulin resistance may dampen the effect insulin can have on mTORC1
- Mitochondrial dysfunction
  - Contributes to insulin resistance
  - Can lead to accumulation of intramuscular fat, as energy cannot be used normally and will accumulate



Churchward-Venne et al. Biofactors. 2014 Mar-Apr;40(2):199-205. | Fry et al. Skelet Muscle. 2011 Mar 2;1(1):11. | Wilkes et al. Am J Clin Nutr. 2009 Nov;90(5):1343-50. | Volpi et al. Am J Physiol. 1999 Sep;277(3 Pt 1):E513-20. | Boirie et al. Am J Clin Nutr. 1997 Feb;65(2):489-95.

# Does the muscle protein synthetic response to exercise and amino acid-based nutrition diminish with advancing age? A systematic review

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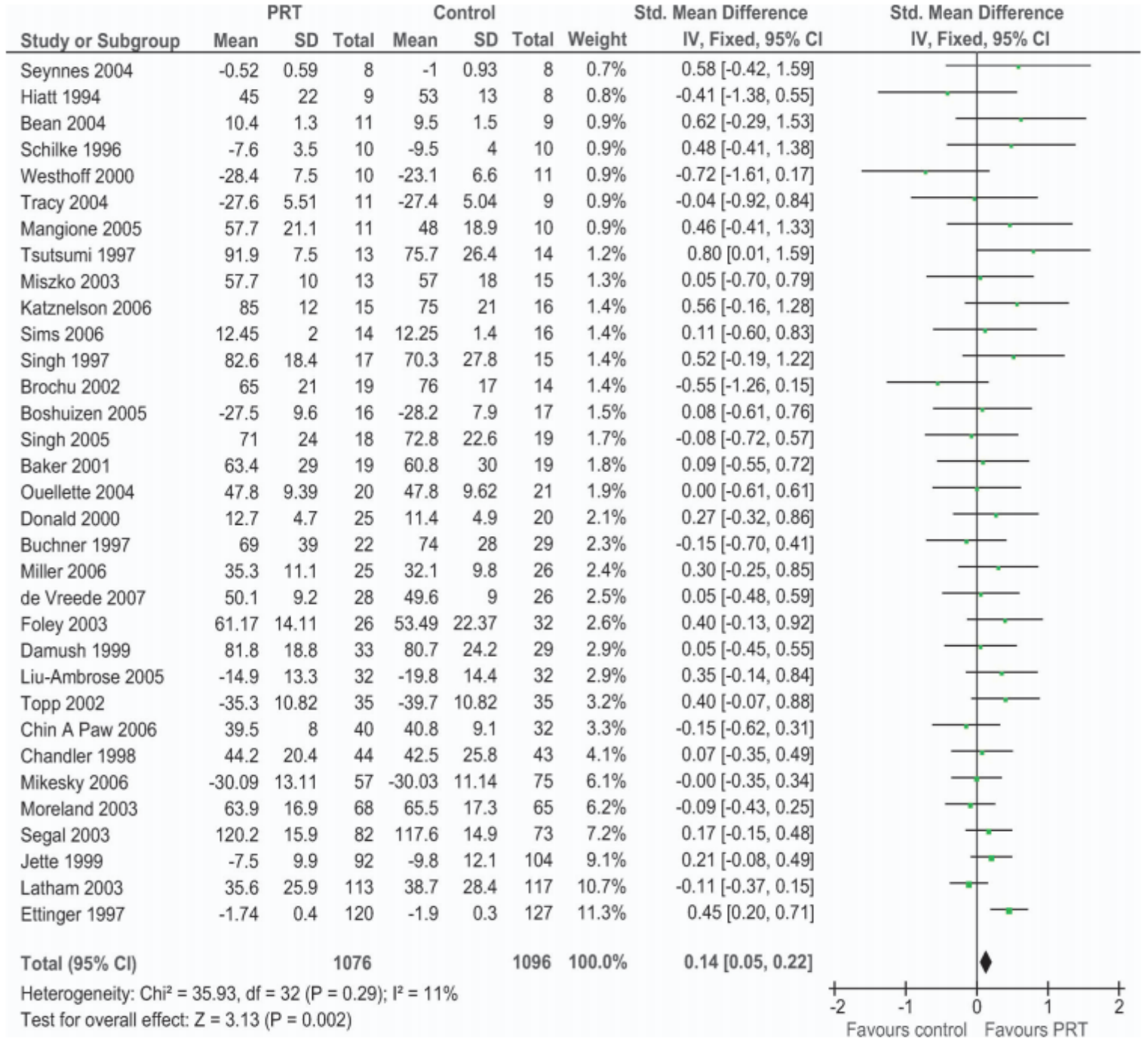
Submitted 2 June 2016; accepted in final form 16 August 2016

"Our results highlight that optimization of exercise and amino acid-based nutrition is sufficient to induce a comparable MPS response between young and older individuals. However, the **exercise volume completed and/or the amino acid/protein dose and leucine content must exceed a certain threshold to stimulate equivalent MPS rates in young and older adults**, below which age-related muscle anabolic resistance may become apparent."



Shad et al. Am J Physiol Endocrinol Metab. 2016 Nov 1;311(5):E803-E817.

# Effect of Progressive Resistance Training on Physical Disability in Older Adults



| Study or Subgroup | PRT Mean | PRT SD | PRT Total | Control Mean | Control SD | Control Total | Weight | Std. Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Seynnes 2004 | -0.52 | 0.59 | 8 | -1 | 0.93 | 8 | 0.7% | 0.58 [-0.42, 1.59] |
| Hiatt 1994 | 45 | 22 | 9 | 53 | 13 | 8 | 0.8% | -0.41 [-1.38, 0.55] |
| Bean 2004 | 10.4 | 1.3 | 11 | 9.5 | 1.5 | 9 | 0.9% | 0.62 [-0.29, 1.53] |
| Schilke 1996 | -7.6 | 3.5 | 10 | -9.5 | 4 | 10 | 0.9% | 0.48 [-0.41, 1.38] |
| Westhoff 2000 | -28.4 | 7.5 | 10 | -23.1 | 6.6 | 11 | 0.9% | -0.72 [-1.61, 0.17] |
| Tracy 2004 | -27.6 | 5.51 | 11 | -27.4 | 5.04 | 9 | 0.9% | -0.04 [-0.92, 0.84] |
| Mangione 2005 | 57.7 | 21.1 | 11 | 48 | 18.9 | 10 | 0.9% | 0.46 [-0.41, 1.33] |
| Tsutsumi 1997 | 91.9 | 7.5 | 13 | 75.7 | 26.4 | 14 | 1.2% | 0.80 [0.01, 1.59] |
| Miszko 2003 | 57.7 | 10 | 13 | 57 | 18 | 15 | 1.3% | 0.05 [-0.70, 0.79] |
| Katznelson 2006 | 85 | 12 | 15 | 75 | 21 | 16 | 1.4% | 0.56 [-0.16, 1.28] |
| Sims 2006 | 12.45 | 2 | 14 | 12.25 | 1.4 | 16 | 1.4% | 0.11 [-0.60, 0.83] |
| Singh 1997 | 82.6 | 18.4 | 17 | 70.3 | 27.8 | 15 | 1.4% | 0.52 [-0.19, 1.22] |
| Brochu 2002 | 65 | 21 | 19 | 76 | 17 | 14 | 1.4% | -0.55 [-1.26, 0.15] |
| Boshuizen 2005 | -27.5 | 9.6 | 16 | -28.2 | 7.9 | 17 | 1.5% | 0.08 [-0.61, 0.76] |
| Singh 2005 | 71 | 24 | 18 | 72.8 | 22.6 | 19 | 1.7% | -0.08 [-0.72, 0.57] |
| Baker 2001 | 63.4 | 29 | 19 | 60.8 | 30 | 19 | 1.8% | 0.09 [-0.55, 0.72] |
| Ouellette 2004 | 47.8 | 9.39 | 20 | 47.8 | 9.62 | 21 | 1.9% | 0.00 [-0.61, 0.61] |
| Donald 2000 | 12.7 | 4.7 | 25 | 11.4 | 4.9 | 20 | 2.1% | 0.27 [-0.32, 0.86] |
| Buchner 1997 | 69 | 39 | 22 | 74 | 28 | 29 | 2.3% | -0.15 [-0.70, 0.41] |
| Miller 2006 | 35.3 | 11.1 | 25 | 32.1 | 9.8 | 26 | 2.4% | 0.30 [-0.25, 0.85] |
| de Vreede 2007 | 50.1 | 9.2 | 28 | 49.6 | 9 | 26 | 2.5% | 0.05 [-0.48, 0.59] |
| Foley 2003 | 61.17 | 14.11 | 26 | 53.49 | 22.37 | 32 | 2.6% | 0.40 [-0.13, 0.92] |
| Damush 1999 | 81.8 | 18.8 | 33 | 80.7 | 24.2 | 29 | 2.9% | 0.05 [-0.45, 0.55] |
| Liu-Ambrose 2005 | -14.9 | 13.3 | 32 | -19.8 | 14.4 | 32 | 2.9% | 0.35 [-0.14, 0.84] |
| Topp 2002 | -35.3 | 10.82 | 35 | -39.7 | 10.82 | 35 | 3.2% | 0.40 [-0.07, 0.88] |
| Chin A Paw 2006 | 39.5 | 8 | 40 | 40.8 | 9.1 | 32 | 3.3% | -0.15 [-0.62, 0.31] |
| Chandler 1998 | 44.2 | 20.4 | 44 | 42.5 | 25.8 | 43 | 4.1% | 0.07 [-0.35, 0.49] |
| Mikesky 2006 | -30.09 | 13.11 | 57 | -30.03 | 11.14 | 75 | 6.1% | -0.00 [-0.35, 0.34] |
| Moreland 2003 | 63.9 | 16.9 | 68 | 65.5 | 17.3 | 65 | 6.2% | -0.09 [-0.43, 0.25] |
| Segal 2003 | 120.2 | 15.9 | 82 | 117.6 | 14.9 | 73 | 7.2% | 0.17 [-0.15, 0.48] |
| Jette 1999 | -7.5 | 9.9 | 92 | -9.8 | 12.1 | 104 | 9.1% | 0.21 [-0.08, 0.49] |
| Latham 2003 | 35.6 | 25.9 | 113 | 38.7 | 28.4 | 117 | 10.7% | -0.11 [-0.37, 0.15] |
| Ettinger 1997 | -1.74 | 0.4 | 120 | -1.9 | 0.3 | 127 | 11.3% | 0.45 [0.20, 0.71] |
| **Total (95% CI)** | | | **1076** | | | **1096** | **100.0%** | **0.14 [0.05, 0.22]** |

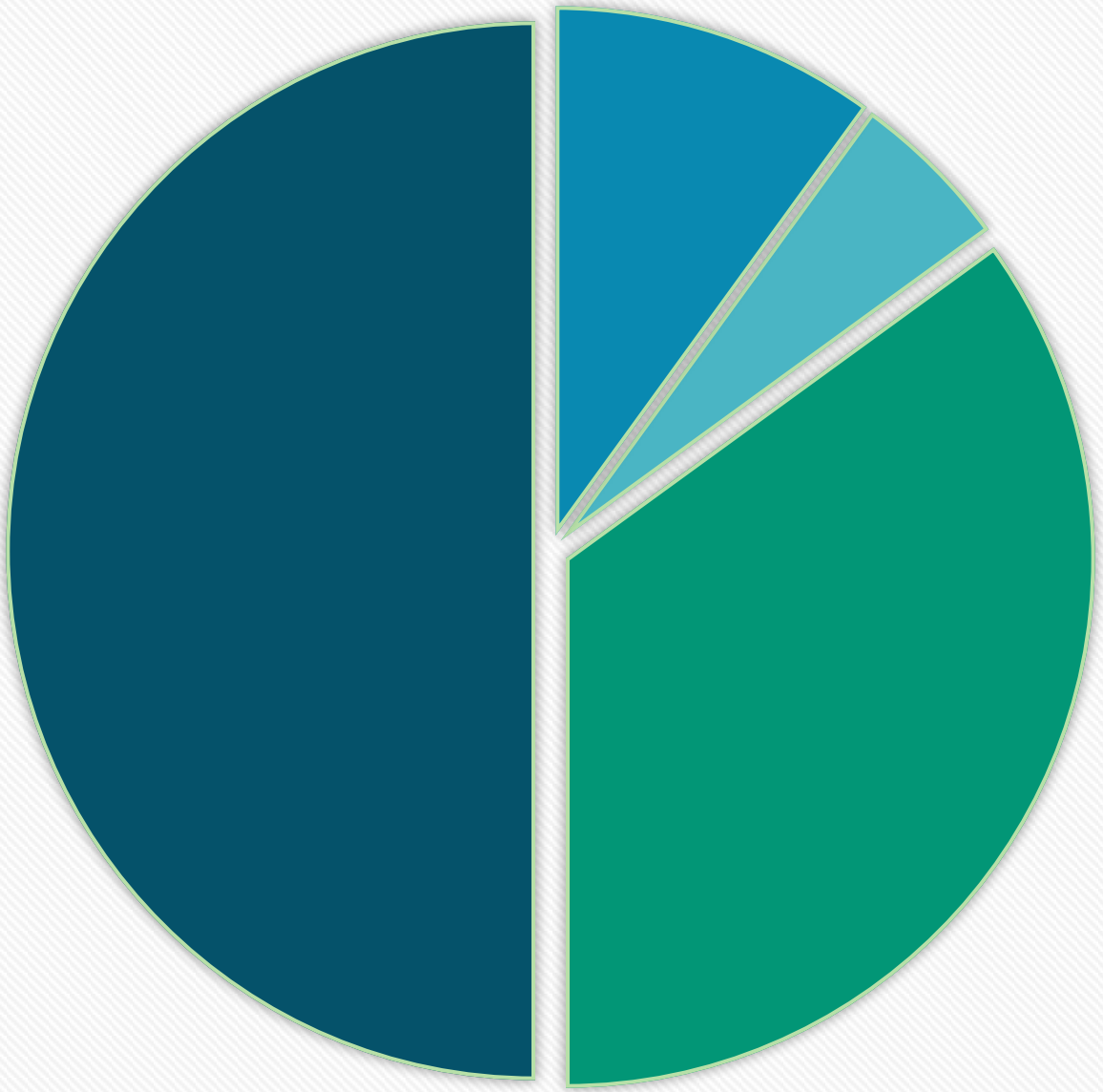
Heterogeneity: Chi² = 35.93, df = 32 (P = 0.29); I² = 11%
Test for overall effect: Z = 3.13 (P = 0.002)



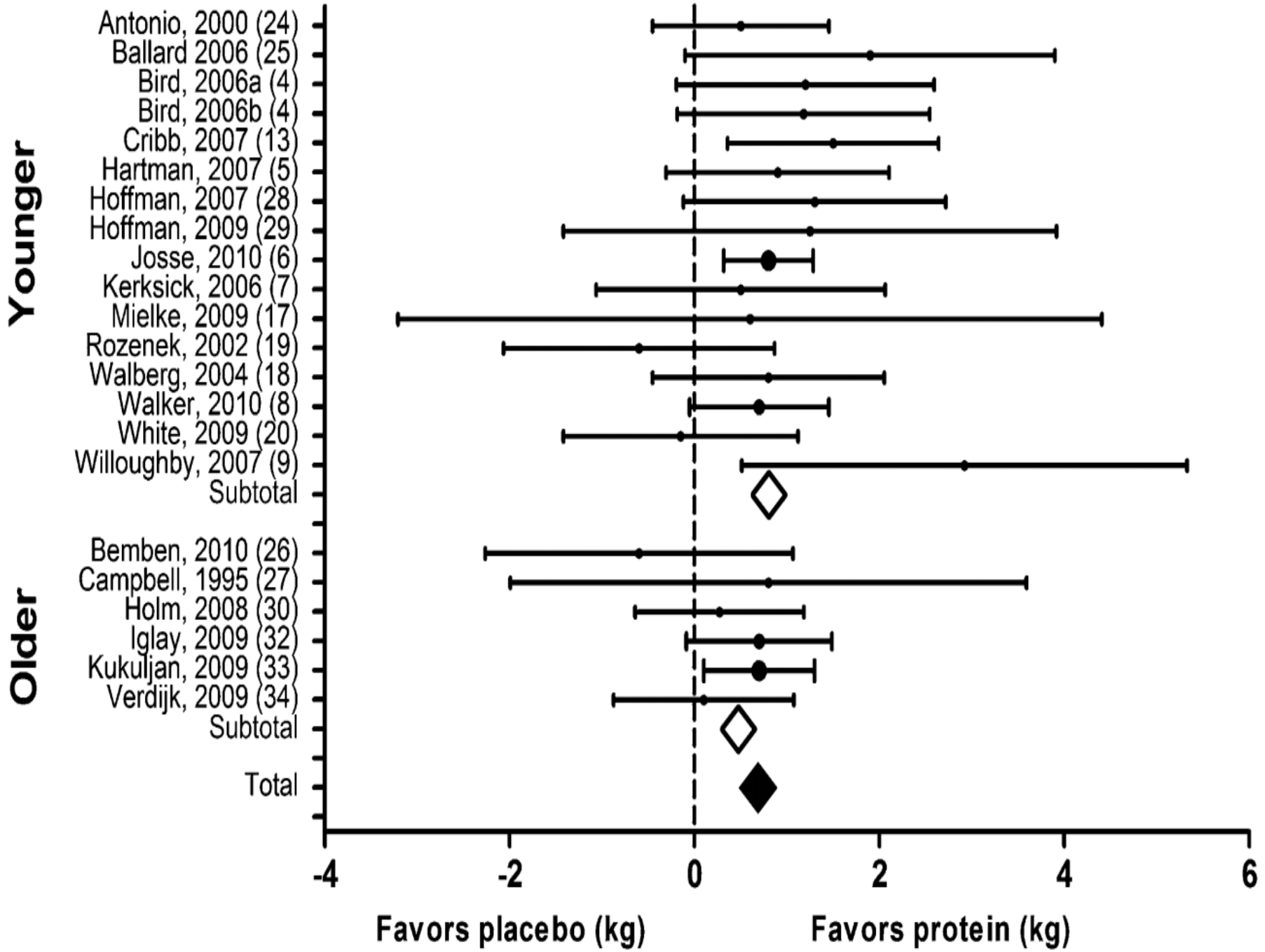


Liu and Latham. Disabil Rehabil. 2011;33(2):87-97.

# Exercise Engagement in US Adults 50-79



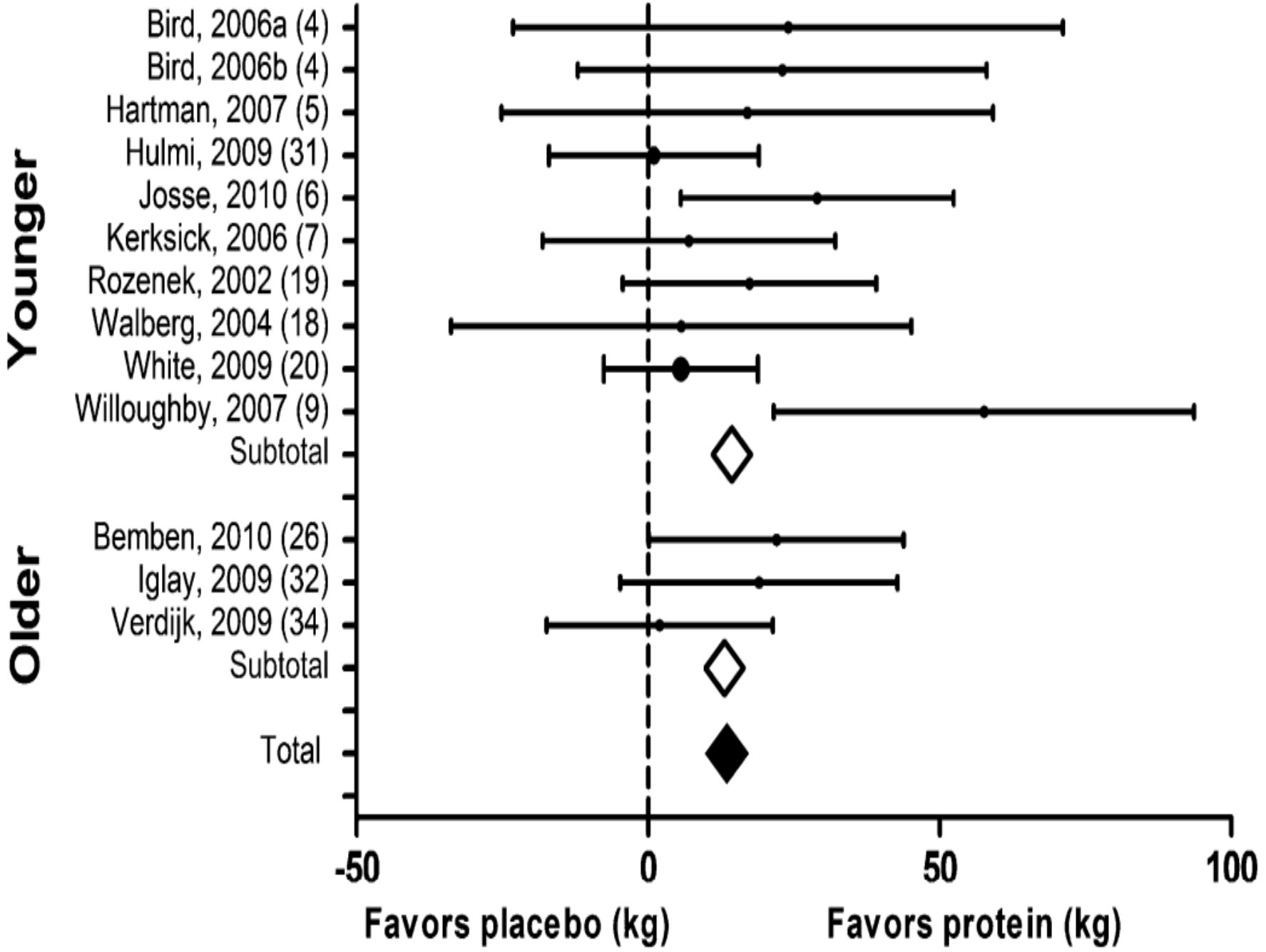
# Effect of Resistance Training and Protein Supplement on Lean Mass






Cermak et al. Am J Clin Nutr. 2012 Dec;96(6):1454-64.

# Effect of Resistance Training and Protein Supplement on 1RM Leg Press






Cermak et al. Am J Clin Nutr. 2012 Dec;96(6):1454-64.

## Exercise

-Resistance training

-Low-load blood flow restriction RT

-Aerobic activity can have some, but not a potent enough effect

## Diet

-Higher protein intake (1.2 g/kg)

-Evenly spaced protein intake is optimal

-Can be timed around exercise