Non-pharmacological interventions as a means to promote healthy ageing

Dr Theocharis Ispoglou

Senior Lecturer in Sport and Exercise Physiology and Nutrition, PhD, MSc, PGCHE, ASCC, Senior HEA Fellow, Carnegie School of Sport.

t.ispoglou@leedsbeckett.ac.uk

@Theo_Ispoglou

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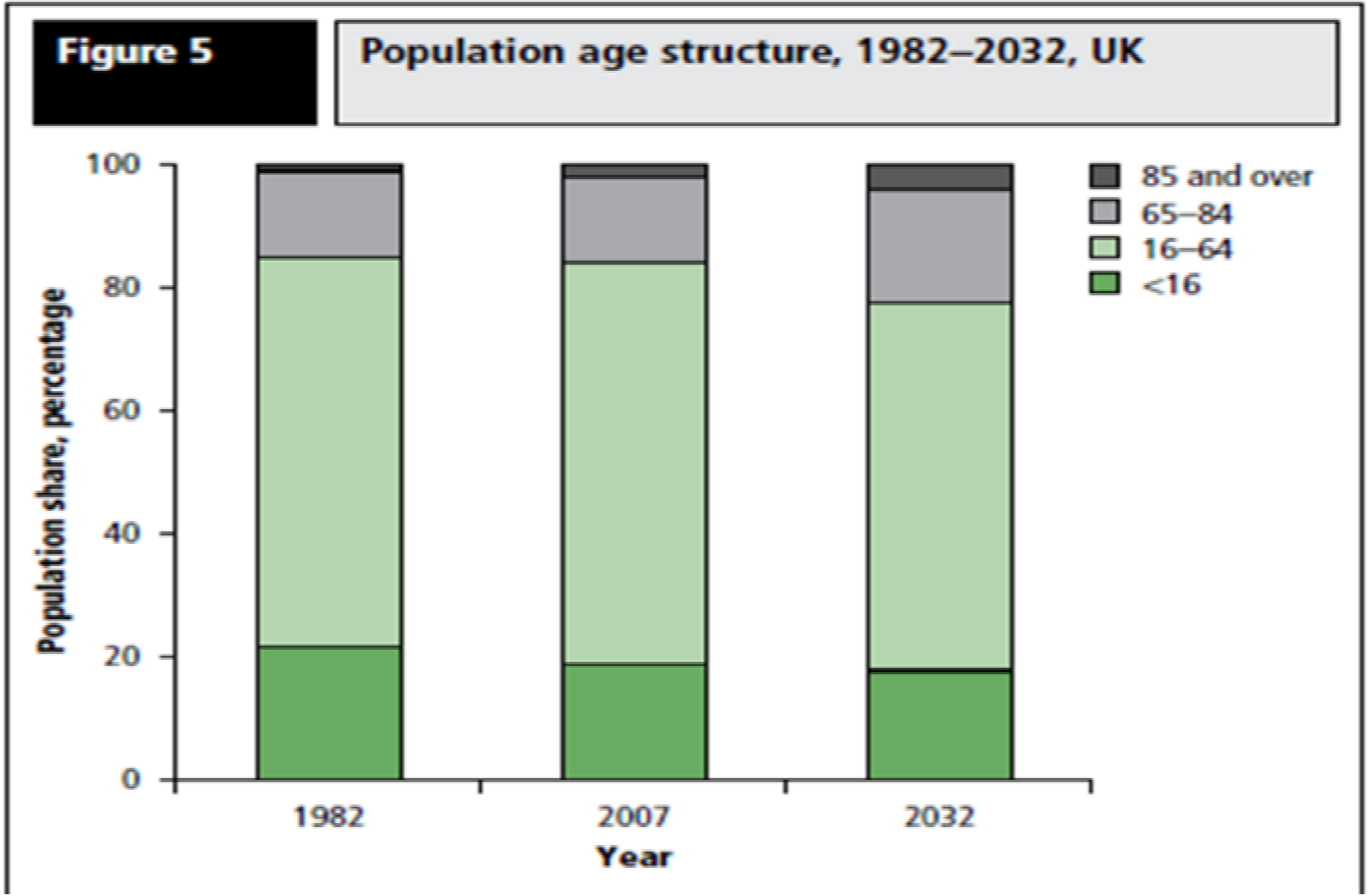
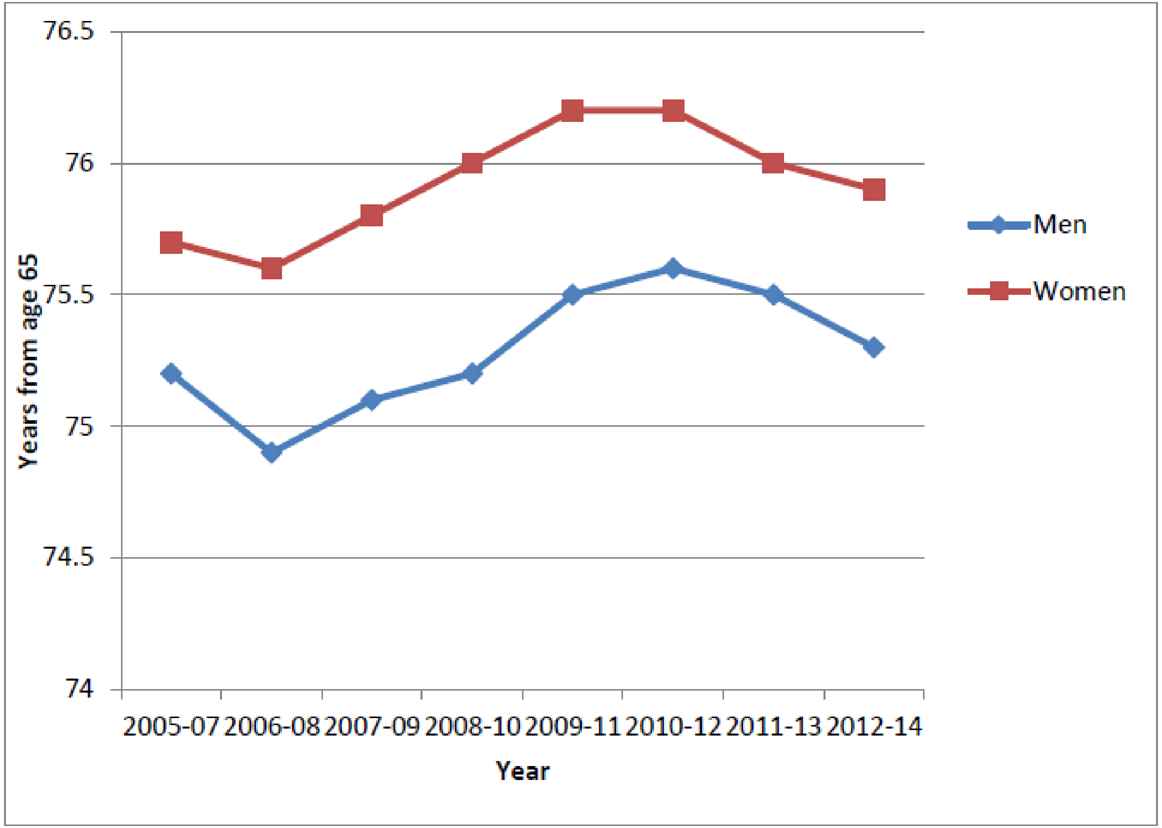


Demographics

Figure 4: Average disability free life expectancy at age 65 in England, 2005-07 to 2012-14



Alarming!

Source: Office for National Statistics (2016[5], 2012[6])[c]

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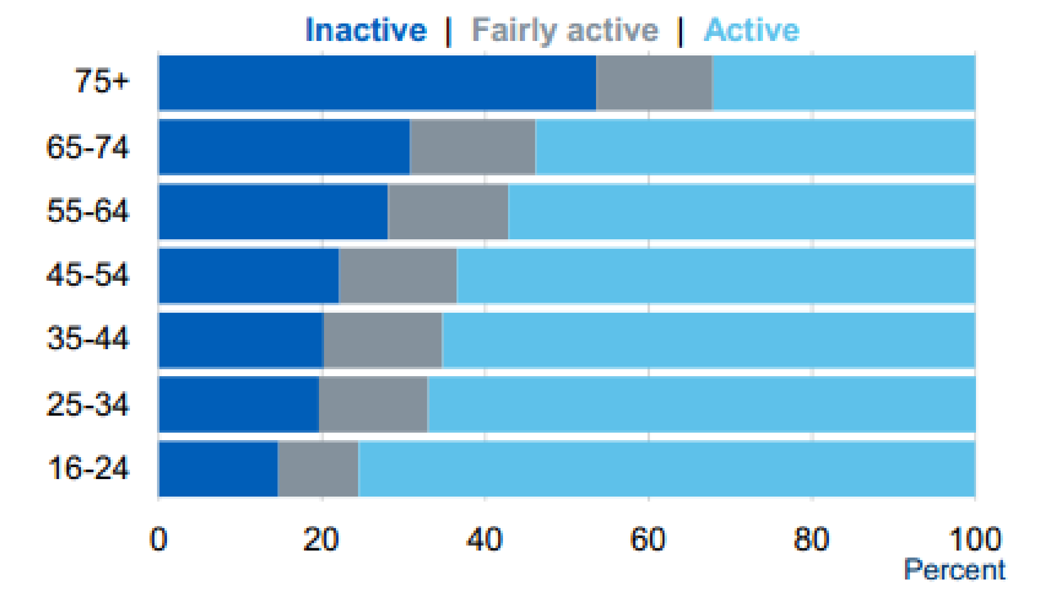
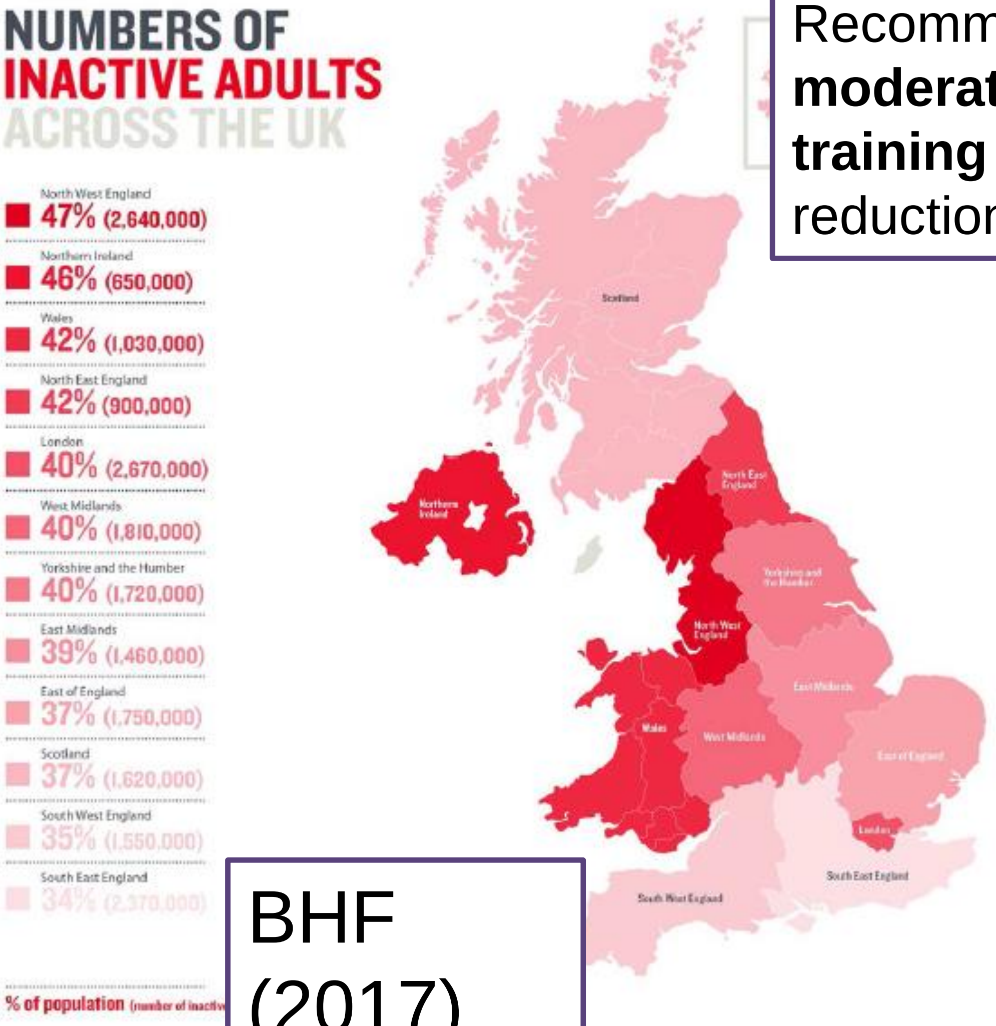
Age group

Inactivity levels increase with age. Those aged 16-24 were least likely to be inactive (15%) whilst those aged 75+ were most likely to be inactive (54%).



National Statistics (2017)

Recommendations: of at least **150 min of moderate intensity** activity and **resistance training** twice a week. Equally important reduction of sedentary behaviour



BHF (2017)

- In 1989, Rosenberg propose the term “sarcopenia” (poverty of flesh) to describe the age-related decline in muscle mass

- Widely accepted definition by Morley et al (2001)**:** **Sarcopenia** is the loss of **muscle mass and strength** that occurs with aging.

- ~1% of muscle mass loss per year from age of 40)

SARCOPENIA

René Koopman, and Luc J. C. van Loon (2009)

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Table 1. Criteria for the diagnosis of sarcopenia

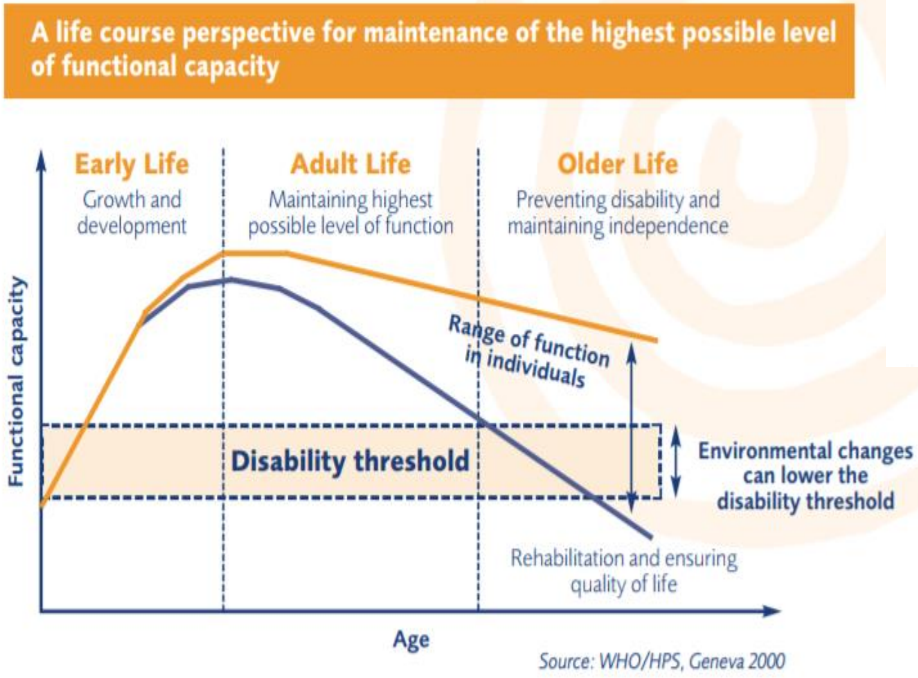
Diagnosis is based on documentation of criterion 1 plus (criterion 2 or criterion 3)
1. Low muscle mass
2. Low muscle strength
3. Low physical performance

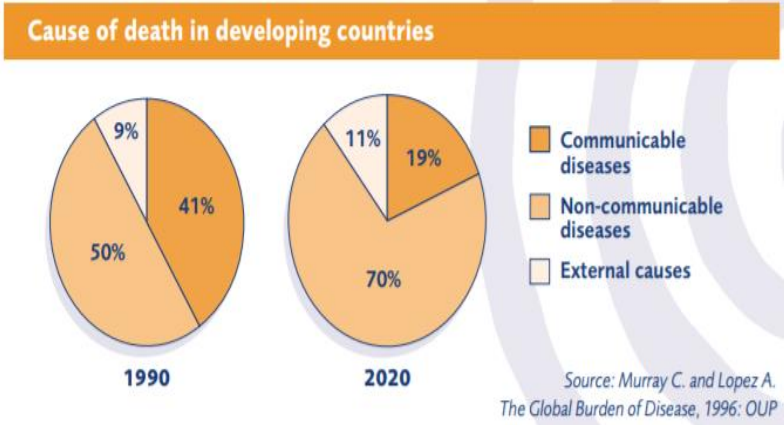
Table 3. EWGSOP conceptual stages of sarcopenia

Stage	Muscle mass	Muscle strength		Performance
Presarcopenia	↓			
Sarcopenia	↓	↓	Or	↓
Severe sarcopenia	↓	↓		↓

Diagnostic Criteria and stages of sarcopenia

Functional capacity and the life course





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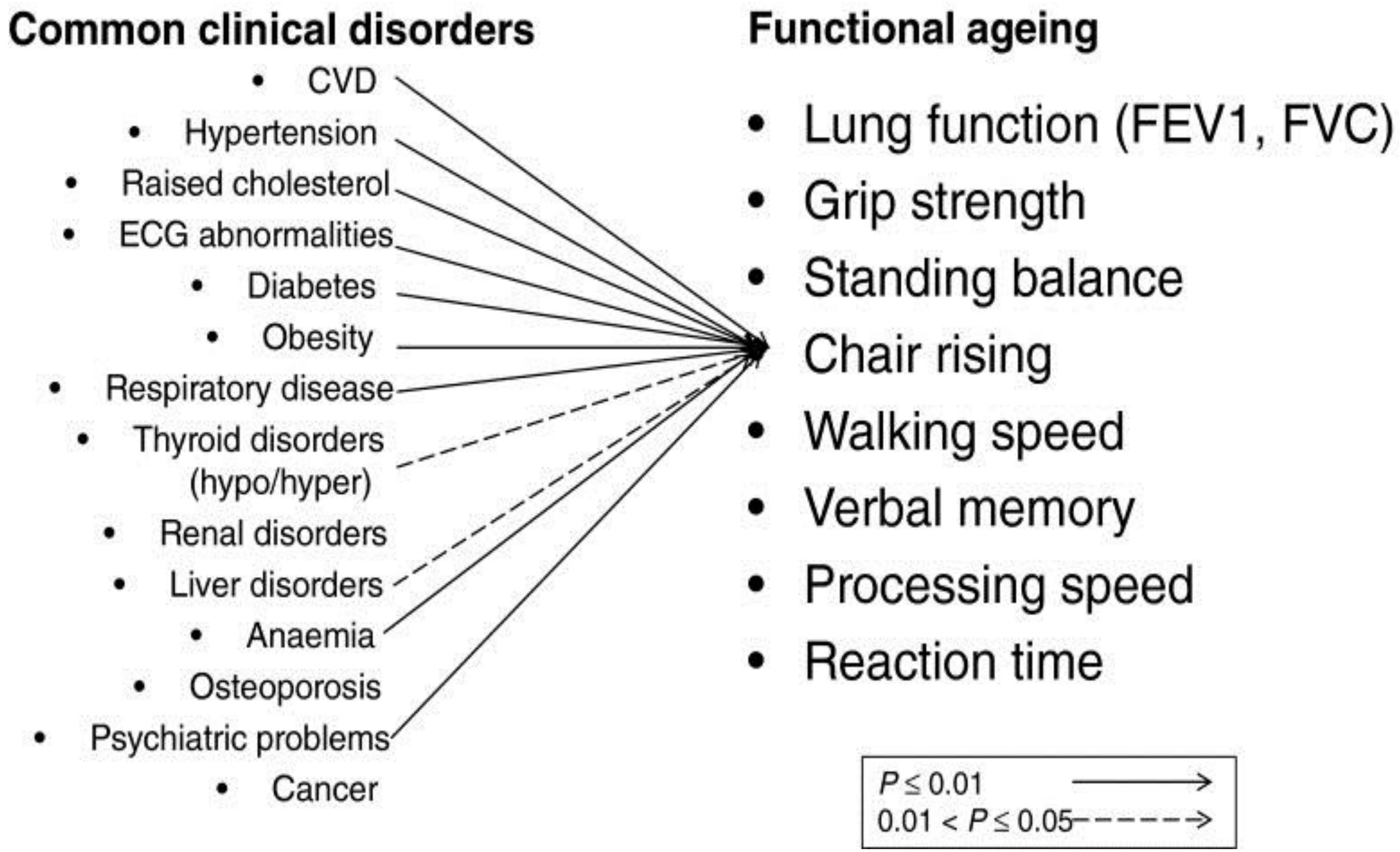
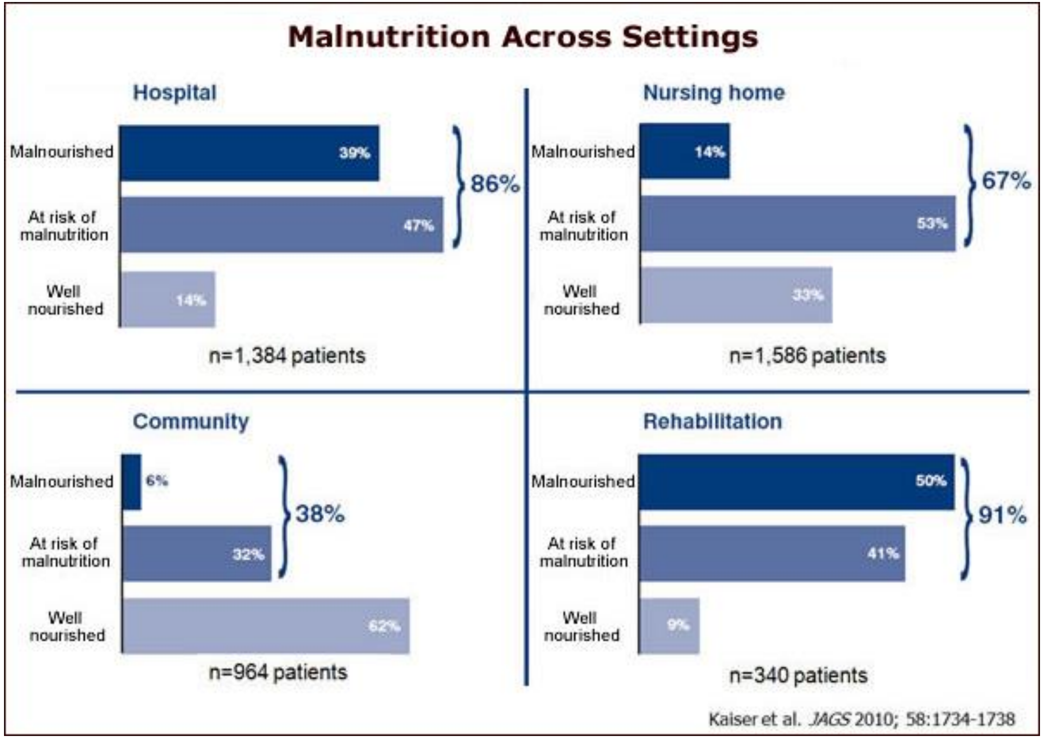
Functional decline and link with non-communicable diseases



Kuh et al (2014)

SARCOPENIA CATEGORIES BY CAUSE	
PRIMARY SARCOPENIA **AGE- RELATED**	No other cause evident except ageing
SECONDARY SARCOPENIA	
ACTIVITY- RELATED	Can result from bed rest, sedentary lifestyle, deconditioning or zero- gravity conditions
DISEASE- RELATED	Associated with advanced organ failure (heart, lung, liver, kidney, brain), inflammatory disease, malignancy or endocrine disease
NUTRITION- RELATED	Results from inadequate dietary intake of energy and/or protein, as with malabsorption, gastrointestinal disorders or use of medications that cause anorexia



“The total public expenditure on malnutrition in health and social care was estimated to be **£19.6 billion**, with **older adults accounting for 52% of the total. (2011-12)**

Elia (2015)

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Editorial

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Sarcopenia: An Emerging Giant Greater Than Osteoporosis

Sarcopenia is defined as the loss of skeletal muscle mass and strength with increased age, resulting in weakness, limited mobility, and increased susceptibility to injury. There are many reports on the clinical features, etiologies, pathomechanisms, clinical course, and prognosis of patients with sarcopenia. In particular, frailty, muscle wasting, and sarcopenia are common among older adults, and are chronic problems that threaten the healthy life expectancy of each country. Prevention, treatment, and rehabilitation of these conditions have become a major concern in health care today. For the clinical application of sarcopenia in medical

In particular, the cutoffs used for diagnosis are different according to regions and population. In order to expand clinical applications, achieving consensus on diagnostic criteria with standardized values obtained from diagnostic references at regional or national level should be a top priority.

Another important condition for clinical application is to designate a disease code in the International Classification of Diseases (ICD). There is a need to raise awareness of sarcopenia as a new disease. Since the National Institutes of Health publicized osteoporosis as a disease in 1984 and the U.S. Food and Drug Administration approved the use of osteopo-

❑ *Background*

- ❑ ***Key points***
  - ❑ *We are getting older and in UK, health span has been reduced since 2012*
  - ❑ *Physical activity levels decrease with ageing*
  - ❑ *Sarcopenia major public health challenge*
  - ❑ *Physical (in)activity and protein-energy malnutrition key contributing factors to sarcopenia*

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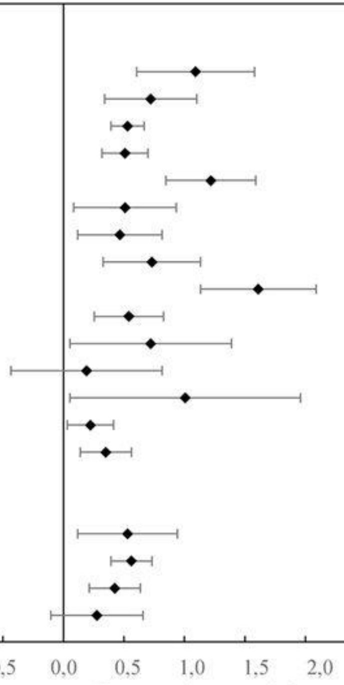
Effect of resistance training on functional capacity in chronic diseases.

Disease	Meta-analysis	AMSTAR score	Studies/ Comparisons (Participants)	Outcome	SMD (95% CI)
Objective measures of physical performance					
Cancer	Strasser et al, 2013[42]	8	9 (752)	Upper limb muscle strength	1·03 (0·57 to 1·49)*,†
			9 (719)	Lower limb muscle strength	0·68 (0·32 to 1·04)*,†
Cancer (breast)	Cheema et al, 2014b[37]	7	11 (1252)	Upper body muscular strength	0·50 (0·37 to 0·76)
			9 (1079)	Lower body muscular strength	0·48 (0·30 to 0·67)
Chronic kidney disease	Cheema et al, 2014a[36]	7	7 (249)	Strength	1·15 (0·80 to 1·49)
COPD	Liao et al, 2015[40]	2	5 (103)	Muscle strength, leg press	0·48 (0·08 to 0·87)
Intermittent claudication	Miranda et al, 2013[41]	3	3 (141)	Total walking distance	0·44 (0·11 to 0·78)
Rheumatoid arthritis	Baillet et al, 2012[34]	6	3 (148)	Isokinetic strength	0·69 (0·31 to 1·07)*
			5 (300)	Isometric strength	1·52 (1·07 to 1·98)*
			4 (126)	Grip strength	0·51 (0·24 to 0·78)*
			5 (275)	50 feet walking test	0·68 (0·05 to 1·32)*
Stroke	Saunders et al, 2016[30]	7	4 (104)	Maximal gait speed	0·18 (-0·41 to 0·76)
	Harris & Eng, 2010[38]	4	6 (306)	Grip strength	0·95 (0·05 to 1·85)
			11 (465)	Upper limb function	0·21 (0·03 to 0·39)*
	Ada et al, 2006[33]	4	14 (456)	Strength	0·33 (0·13 to 0·54)
Patient-reported measures of functional capacity					
Fibromyalgia	Busch et al, 2013[35]	9	3 (107)	SF-36 physical function scale	0·50 (0·11 to 0·89)
Osteoarthritis	Li et al, 2015b[39]	5	19 (2077)	Physical function	0·53 (0·37 to 0·70)
Rheumatoid arthritis	Baillet et al, 2012[34]	6	9 (404)	Disability (HAQ)	0·40 (0·20 to 0·60)
Stroke	Harris & Eng, 2010[38]	4	5 (210)	Activities of daily living	0·26 (-0·10 to 0·63)



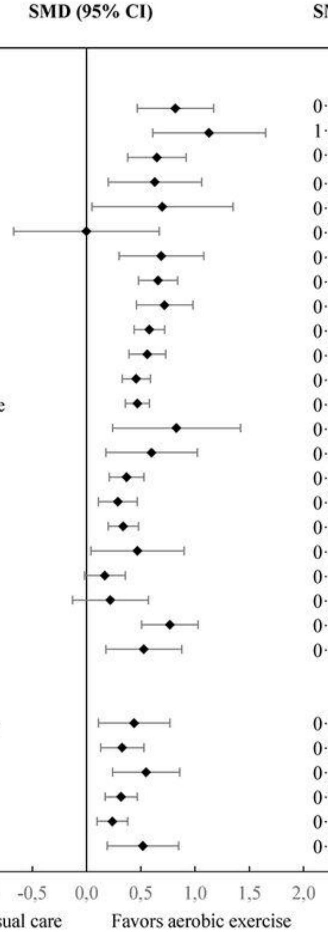
<0·5 SMD = small effect, 0·5-0·8 SMD = moderate effect, >0·8 SMD = large effect[15]
COPD = chronic obstructive pulmonary disease; HAQ = health assessment questionnaire
* SMD was calculated from data in the original RCTs using Review Manager 5·3
† The outcome may have positive publication bias

Pasanen et al. (2017)

BJSM

Effect of aerobic exercise on functional capacity in chronic diseases.

Disease	Meta-analysis	AMSTAR score	Studies/ Comparisons (Participants)	Outcome	SMD (95% CI)
Objective measures of physical performance					
Chronic Kidney Disease	Segura-Orti & Johansen 2010a[29]	6	5 (140)	Peak oxygen consumption	0·82 (0·47 to 1·18)
			4 (118)	Exercise test duration	1·13 (0·61 to 1·65)
Fibromyalgia	Häuser et al, 2010[24]	8	20 (339)	Physical fitness	0·65 (0·38 to 0·93)
	Bidonde et al, 2014[21]	11	4 (152)	Muscle strength	0·63 (0·20 to 1·05)
			3 (194)	6-minute walking distance	0·70 (0·05 to 1·36)
			3 (162)	Muscle endurance	0·00 (-0·67 to 0·67)
Heart failure	Ismail et al, 2013[25]	6	3 (114)	Peak oxygen cons. (high)	0·69 (0·30 to 1·07)*
			29 (3420)	Peak oxygen cons. (vig.)	0·66 (0·48 to 0·85)*
			20 (779)	Peak oxygen cons. (mod.)	0·72 (0·46 to 0·98)*
Peripheral arterial disease	Parmenter et al, 2015[28]	4	26 (823)	Peak oxygen consumption	0·58 (0·44 to 0·73)
			10 (635)	6-minute walking distance	0·56 (0·39 to 0·73)
			24 (1116)	Initial claudication distance	0·46 (0·33 to 0·58)
			28 (1365)	Absolute claudication distance	0·47 (0·36 to 0·58)
Stroke	Saunders et al,s 2016[30]	7	9 (425)	Peak oxygen consumption	0·83 (0·24 to 1·43)
			4 (221)	Maximum cycling work rate	0·60 (0·18 to 1·02)
			14 (631)	Maximal gait speed	0·37 (0·21 to 0·54)*
			10 (505)	Preferred gait speed	0·29 (0·11 to 0·47)
			15 (826)	6-minute walking distance	0·34 (0·20 to 0·48)
			3 (154)	Gait endurance	0·47 (0·04 to 0·90)
			7 (435)	Berg Balance scale	0·17 (-0·02 to 0·36)
			3 (131)	Timed up and go	0·22 (-0·13 to 0·56)
	Pang et al, 2013[27]	6	5 (236)	Peak workload	0·77 (0·51 to 1·04)
Type 2 diabetes	Boule et al, 2003[22]	4	7 (266)	Peak oxygen consumption	0·53 (0·18 to 0·88)
Patient-reported measures of functional capacity					
Fibromyalgia	Bidonde et al, 2014[21]	11	5 (285)	SF-36 physical function scale	0·44 (0·11 to 0·76)
Haematological malignancies	Bergenthal et al, 2014[20]	9	4 (422)	Physical function	0·33 (0·13 to 0·52)
Osteoarthritis (knee)	Juhl et al, 2014[26]	6	8 (474)	Self-reported disability	0·55 (0·24 to 0·87)*
Osteoarthritis (knee and hip)	Bartels et al, 2016[19]	9	12 (1059)	Physical function	0·32 (0·17 to 0·47)
Rheumatoid arthritis	Baillet et al, 2010[18]	6	9 (771)	Self-reported function	0·24 (0·10 to 0·38)*
Stroke	Saunders et al, 2016[30]	7	8 (462)	Disability	0·52 (0·19 to 0·84)

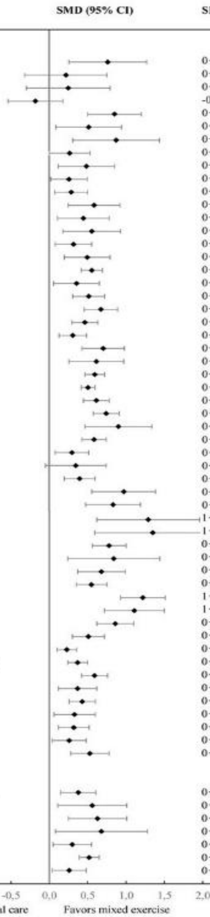


<0·5 SMD = small effect, 0·5-0·8 SMD = moderate effect, >0·8 SMD = large effect[15]
mod. = moderate intensity exercise; vig. = vigorous intensity exercise; high = high-intensity exercise
* The outcome may have positive publication bias

Pasanen et al. (2017)

Effect of combined endurance and RE on functional capacity in chronic diseases.

Disease	Meta-analysis	AMSTAR score	Studies/ Comparisons (Participants)	Outcome	SMD (95% CI)
Objective measures of physical performance					
Cancer	Dennett et al, 2016[49]	4	14 (1032)	Walking endurance	0·77 (0·26 to 1·28)
			4 (207)	Usual walking speed	0·22 (-0·32 to 0·77)
			5 (479)	Sit to stand	0·25 (-0·30 to 0·80)
			2 (120)	Stair climb	-0·18 (-0·54 to 0·18)
	Fong et al, 2012[51]	6	3 (140)	Peak power output	0·86 (0·51 to 1·20)
			5 (145)	Right handgrip strength	0·52 (0·09 to 0·94)
	Jones et al, 2011[60]	7	6 (571)	Peak oxygen consumption	0·88 (0·31 to 1·45)
Cancer (prostate)	Bourke et al, 2016[45]	4	3 (220)	Peak oxygen consumption	0·27 (0·00 to 0·54)
			6 (346)	Sub-maximal aerobic fitness	0·49 (0·12 to 0·85)
			4 (277)	Upper body strength	0·26 (0·02 to 0·51)
			6 (245)	Lower body strength	0·29 (0·07 to 0·50)
Cancer (colon)	Cramer et al, 2014[48]	9	3 (152)	Physical fitness	0·59 (0·25 to 0·93)
Cancer (non-small cell lung)	Cavalheri et al, 2013[46]	10	3 (139)	6-minute walking distance	0·45 (0·11 to 0·79)
Cancer (hematologic malignancy)	Persoon et al, 2013[67]	6	6 (312)	Lower extremity strength	0·56 (0·18 to 0·94)
			5 (263)	Upper extremity strength	0·32 (0·08 to 0·57)
Cancer (breast)	Kim et al, 2009[61]	4	3 (273)	12-minute walk time	0·50 (0·20 to 0·80)
Chronic kidney disease	Heiwe & Jacobson 2011[56]	9	24 (847)	Aerobic capacity	0·56 (0·42 to 0·70)
			7 (191)	Walking capacity	0·36 (0·06 to 0·65)
			9 (358)	Muscular strength	0·52 (0·31 to 0·73)
	Smart & Steele 2011[70]	2	8 (365)	Peak oxygen consumption	0·68 (0·46 to 0·89)
COPD	Lacasse et al, 2009[62]	8	16 (669)	6-minute walking distance	0·47 (0·30 to 0·65)
			13 (511)	Maximal exercise capacity	0·31 (0·13 to 0·48)
	Salman et al, 2003[69]	3	20 (979)	Walking test	0·71 (0·43 to 0·99)
			12 (723)	Shortness of breath	0·62 (0·26 to 0·91)
Coronary heart disease	Valkeinen et al, 2010[72]	4	18 (922)	Maximal oxygen uptake	0·60 (0·47 to 0·74)*
Cognitive impairment	Heyn et al, 2008[58]	3	31 (1938)	Endurance and strength	0·51 (0·42 to 0·60)
	Heyn et al, 2004[57]	3	18 (1059)	Cardiovascular fitness	0·62 (0·45 to 0·78)
			17 (979)	Strength	0·75 (0·58 to 0·93)
			4 (168)	Flexibility	0·91 (0·47 to 1·36)
			20 (1089)	Functional performance	0·59 (0·43 to 0·76)
Dementia	Potter et al, 2011[68]	6	4 (335)	Walking speed	0·30 (0·08 to 0·51)
Heart failure	Chen & Li, 2013[47]	7	3 (102)	Peak oxygen consumption	0·35 (-0·05 to 0·74)
			6 (425)	6-minute walking distance	0·40 (0·20 to 0·59)
	Hwang et al, 2009[59]	3	16 (734)	Peak oxygen consumption	0·98 (0·56 to 1·41)
	van Tol et al, 2006[73]	6	13 (511)	Anaerobic threshold	0·84 (0·48 to 1·20)
Intermitten claudication	Lane et al, 2014[63]	6	12 (577)	Maximal walking time	1·29 (0·62 to 1·96)
			10 (516)	Pain free walking time	1·35 (0·59 to 2·10)
			8 (371)	Pain free walking distance	0·78 (0·56 to 1·00)
			9 (480)	Maximum walking distance	0·84 (0·24 to 1·43)
Interstitial lung disease	Dowman et al, 2014[50]	10	5 (168)	6-minute walking distance	0·68 (0·37 to 1·00)
Multiple Sclerosis	Gunn et al, 2015[55]	3	15 (719)	Balance	0·55 (0·35 to 0·74)
Intermittent claudication	Watson et al, 2008[74]	7	7 (255)	Maximal walking time	1·22 (0·93 to 1·51)
			3 (150)	Pain-free walking time	1·11 (0·72 to 1·49)
			6 (322)	Pain-free walking distance	0·86 (0·62 to 1·10)
			6 (391)	Maximum walking distance	0·51 (0·30 to 0·73)
Osteoarthritis (hip and knee)	Waller et al, 2014[75]	5	15 (1295)	Physical function	0·23 (0·10 to 0·36)
Osteoarthritis (knee)	Tanaka et al, 2013a[71]	4	13 (1692)	Knee extensors muscle strength	0·37 (0·24 to 0·50)
			9 (1503)	Knee flexors muscle strength	0·59 (0·42 to 0·77)
Stroke	Saunders et al, 2016[30]	7	9 (639)	Preferred walking speed	0·37 (0·12 to 0·61)
			7 (561)	6-minute walking distance	0·43 (0·26 to 0·60)
			9 (596)	Balance	0·33 (0·06 to 0·60)
			4 (418)	Timed up and go	0·32 (0·12 to 0·51)
			7 (544)	Disability	0·26 (0·04 to 0·49)
	Marsden et al, 2013[66]	5	7 (253)	Peak oxygen consumption	0·53 (0·28 to 0·79)
Patient-reported measures of 1functional capacity					
Cancer	Persoon et al, 2013[67]	6	5 (294)	Physical functioning (HRQoL)	0·38 (0·15 to 0·61)
Chronic fatigue syndrome	Larun & Malterud, 2016[64]	9	5 (725)	SF-36 physical function	0·56 (0·11 to 1·02)
COPD	Liu et al, 2014[65]	7	3 (112)	SGRQ activity limitation	0·63 (0·25 to 1·02)
Dementia	Forbes et al, 2015[52]	9	6 (289)	Ability to perform ADLs	0·68 (0·08 to 1·27)
Osteoarthritis (hip)	Fransen et al, 2014[53]	8	9 (521)	Physical function	0·30 (0·05 to 0·54)
Osteoarthritis (knee)	Fransen et al, 2015[54]	7	44 (3913)	Physical function	0·52 (0·39 to 0·64)
Stroke	Saunders et al, 2016[30]	7	7 (544)	Combined disability scales	0·26 (0·04 to 0·49)



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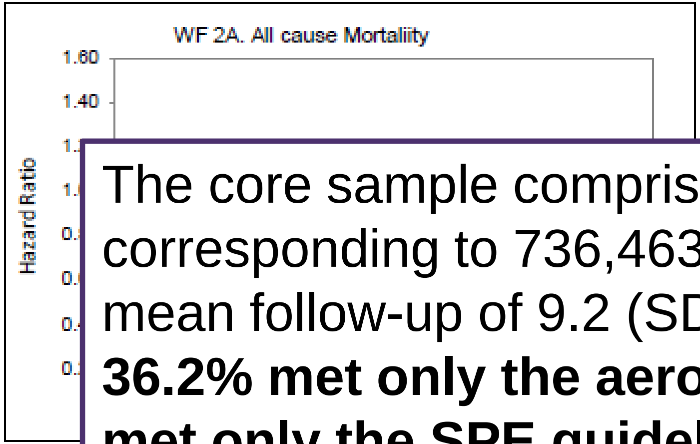
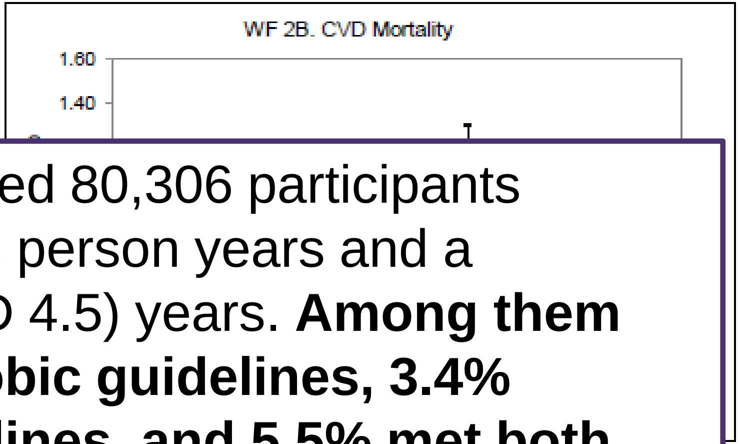
COPD = Chronic obstructive pulmonary disease; ADL = activities of daily living
* The outcome may have positive publication bias

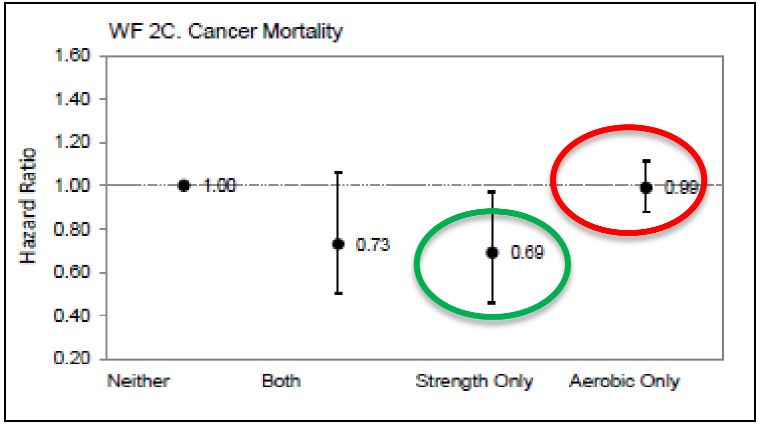
Pasanen et al. (2017)

BJSM



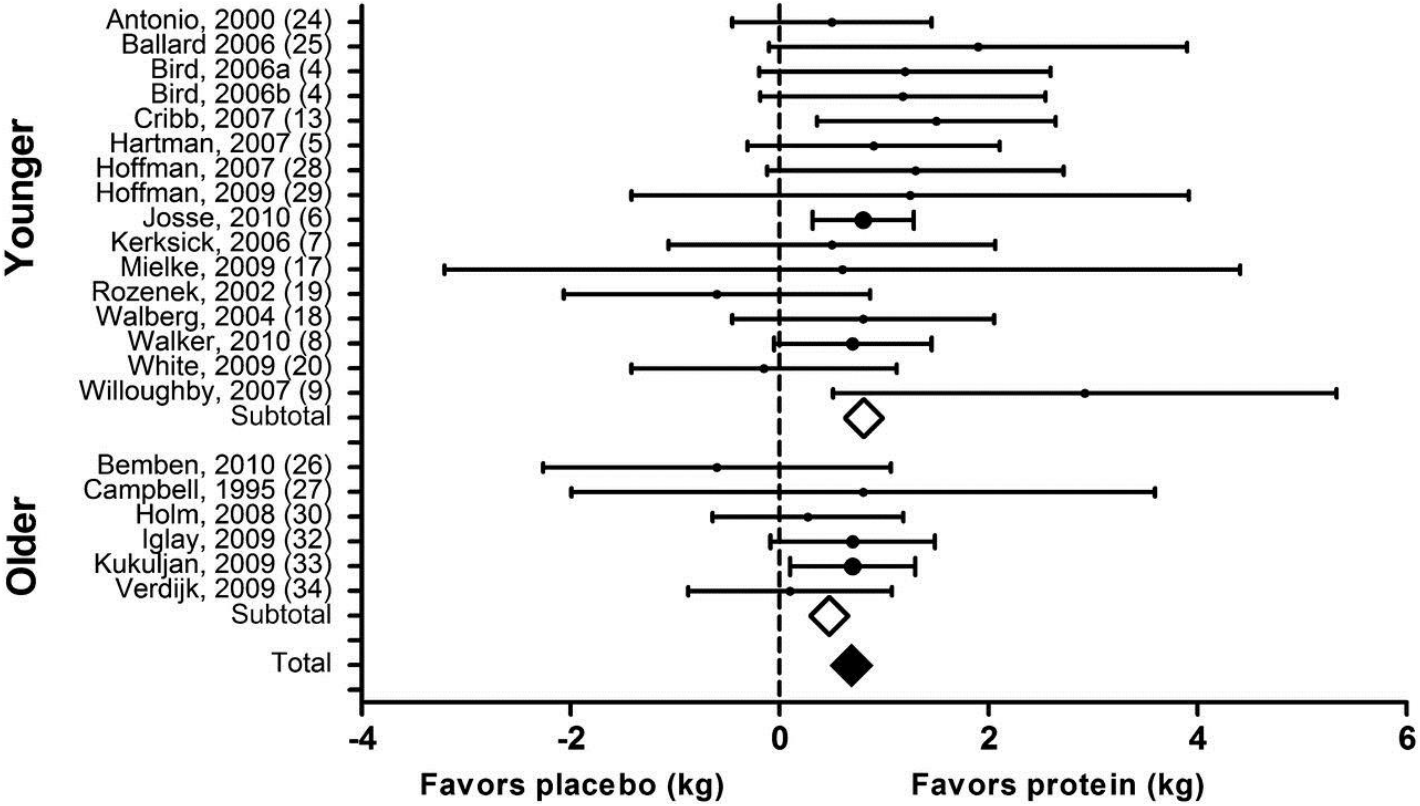


The core sample comprised 80,306 participants corresponding to 736,463 person years and a mean follow-up of 9.2 (SD 4.5) years. **Among them 36.2% met only the aerobic guidelines, 3.4% met only the SPE guidelines, and 5.5% met both.**



Fascinating data by Stamatakis et al. (2017) (Health Survey for England (HSE) and Scottish Health Survey (SHS) from 1994 – 2008.

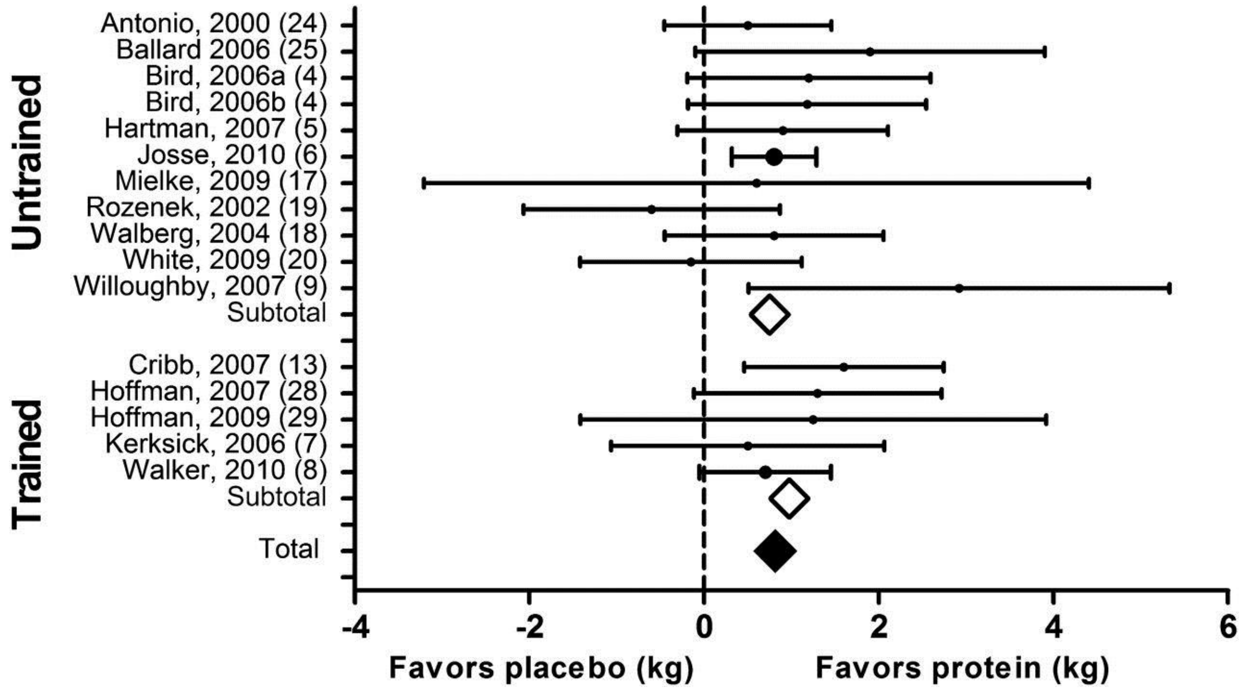
Does strength promoting exercise confer unique health benefits? A pooled analysis of eleven population cohorts with all-cause, cancer, and cardiovascular mortality endpoints.



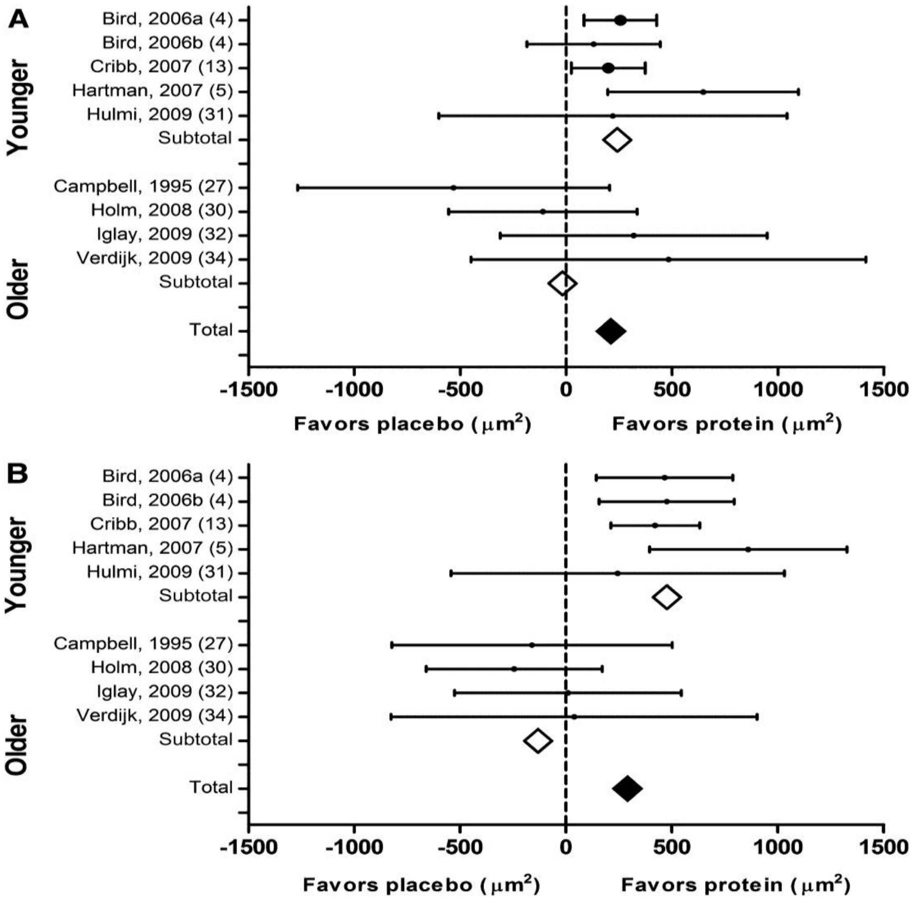
Resistance Exercise Plus Protein Supplementation

Cermak et al. (2012): Outcome-Fat Free Mass

Resistance Exercise Plus Protein Supplementation



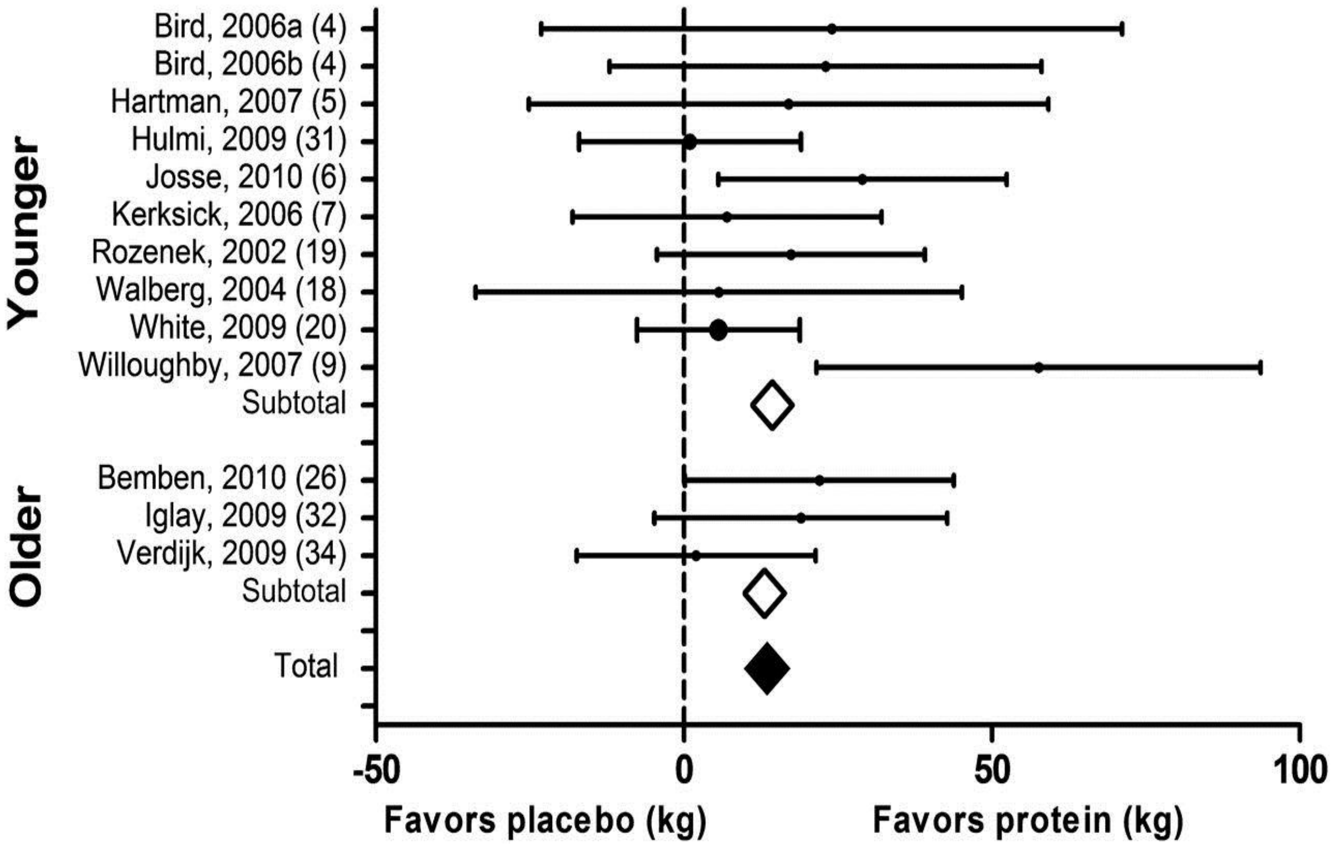
Cermak et al. (2012): Outcome-Fat Free Mass



Resistance Exercise Plus Protein Supplementation

Interestingly, no effect on Type II muscle fibres in Older

Cermak et al. (2012): Outcome-Type I (A) and Type II (B) muscle fibres



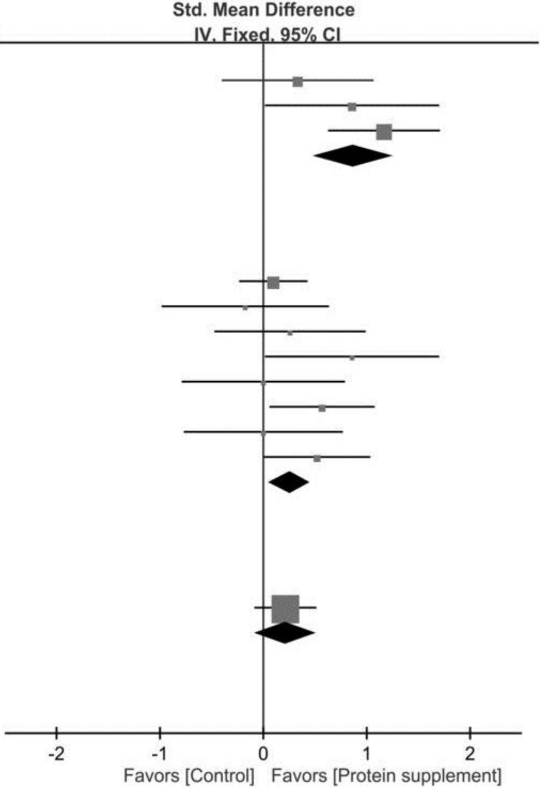
Resistance Exercise Plus Protein Supplementation

Cermak et al. (2012): Outcome-1RM Strength

Duration of training intervention important!

B

Study or Subgroup	Protein supplement Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
2.3.1 Appendicular lean mass, long (≥24wk)								
Leenders 2013 (25), men	0.5	0.6	15	0.2	1.1	14	27.8%	0.33 [-0.40, 1.07]
Leenders 2013 (25), women	0.8	0.9	12	0.2	0.32	12	21.1%	0.86 [0.01, 1.70]
Tieland 2012 (13)	0.9	0.96	31	-0.2	0.9	31	51.1%	1.17 [0.63, 1.71]
Subtotal (95% CI)			**58**			**57**	**100.0%**	**0.87 [0.48, 1.26]**
Heterogeneity: Chi² = 3.22, df = 2 (P = 0.20); I² = 38%								
Test for overall effect: Z = 4.41 (P < 0.0001)								
2.3.2 Appendicular lean mass, medium (≥12 wk, <24 wk)								
Arnarson 2013 (27)	0.6	1.2	75	0.5	0.8	66	36.7%	0.10 [-0.23, 0.43]
Gryson 2014 (33)	0.8	1.2	17	1	0.9	9	6.1%	-0.17 [-0.98, 0.63]
Leenders 2013 (25), men	0.5	0.8	15	0.2	1.4	14	7.5%	0.26 [-0.47, 0.99]
Leenders 2013 (25), women	0.8	0.9	12	0.2	0.32	12	5.7%	0.86 [0.01, 1.70]
Maltais 2016 (18)	0.4	0.18	16	0.4	0.28	10	6.4%	0.00 [-0.79, 0.79]
Tieland 2012 (13)	0.3	0.56	31	0	0.48	31	15.6%	0.57 [0.06, 1.08]
Verdijk 2009 (34)	1	0.3	13	1	0.8	13	6.8%	0.00 [-0.77, 0.77]
Verreijen 2015 (21)	0.4	1.2	30	-0.5	2.1	30	15.2%	0.52 [0.00, 1.03]
Subtotal (95% CI)			**209**			**185**	**100.0%**	**0.26 [0.06, 0.46]**
Heterogeneity: Chi² = 7.22, df = 7 (P = 0.41); I² = 3%								
Test for overall effect: Z = 2.54 (P = 0.01)								
2.3.3 Appendicular lean mass, short (<12wk)								
Björkman 2011 (29)	0.9	3.52	86	0.2	3	86	100.0%	0.21 [-0.09, 0.51]
Subtotal (95% CI)			**86**			**86**	**100.0%**	**0.21 [-0.09, 0.51]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.39 (P = 0.16)								



Chun-De Liao (2017): Outcome-Appendicular Lean Tissue Mass

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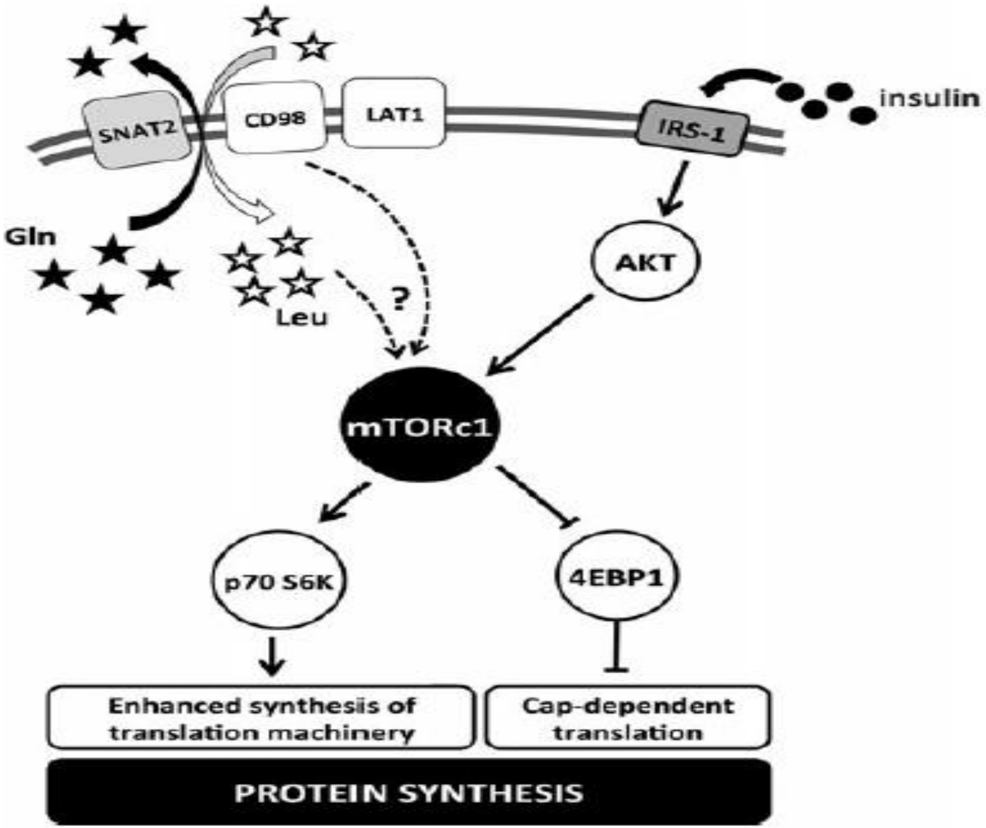
❑ *Exercise and Nutrition Modifiable Risk Factors*

- ❑ ***Key points***
  - ❑ *Good Evidence for the role of* ***Resistance exercise (RE) and Protein Supplementation*** *as a means to promote muscle and bone health and improve functional outcomes.*
  - ❑ *Physical activity (PA), aerobic and resistance exercise work! Resistance exercise even better with regards to mortality risk reduction!!*
  - ❑ *Resistance exercise + protein supplementation works even better*
  - ❑ *Avoid long periods of time sitting but if you do ensure you counteract by completing at ~70 min of moderate PA*
  - ❑ ***DO NOT*** *forget to complete RE at least twice weekly!*



"Muscle anabolic response to a given amount of protein may decline with age, a phenomenon that has been **termed anabolic resistance**"

Anabolic resistance (Murton, 2015)

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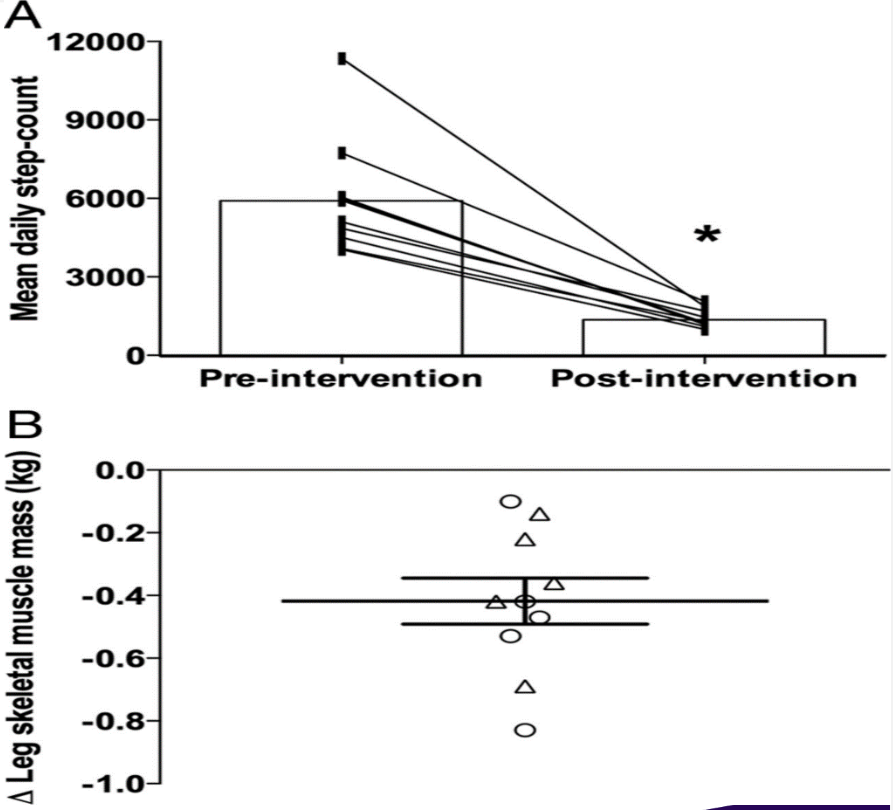
Reducing daily step-count by 76 % for 14 d, from **5900** to ~ **1400** steps daily, was shown to:

- ✓ reduce leg FFM by **3·9 %** and
- ✓ attenuate the rise in postprandial **MPS** rates by 26 %, independent of mTORc1 signalling.



Bed-rest and muscle disuse (Breen et al. 2013)

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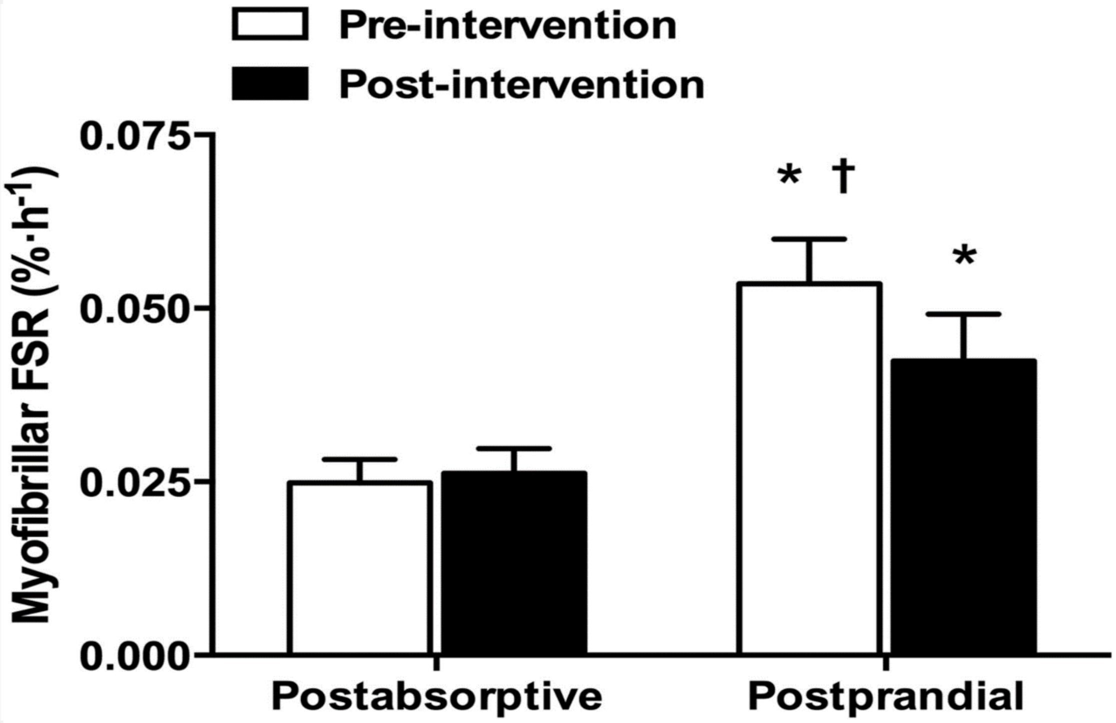


From: Two Weeks of Reduced Activity Decreases Leg Lean Mass and Induces “Anabolic Resistance” of Myofibrillar Protein Synthesis in Healthy Elderly

J Clin Endocrinol Metab. 2013;98(6):2604-2612. doi:10.1210/jc.2013-1502

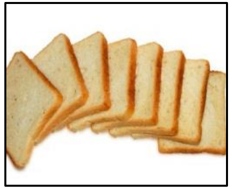
Protein Intake in Older Individuals

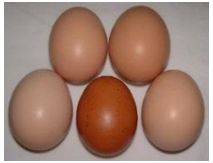
- Daily recommendations of **0.8** $g \cdot kg^{-1} \cdot Bm \cdot d^{-1}$ inadequate **is too low** to avoid sarcopenia

- Need for higher protein per meal-at least 30g or 0.4 $g \cdot kg^{-1} \cdot BM \cdot d^{-1}$ per meal

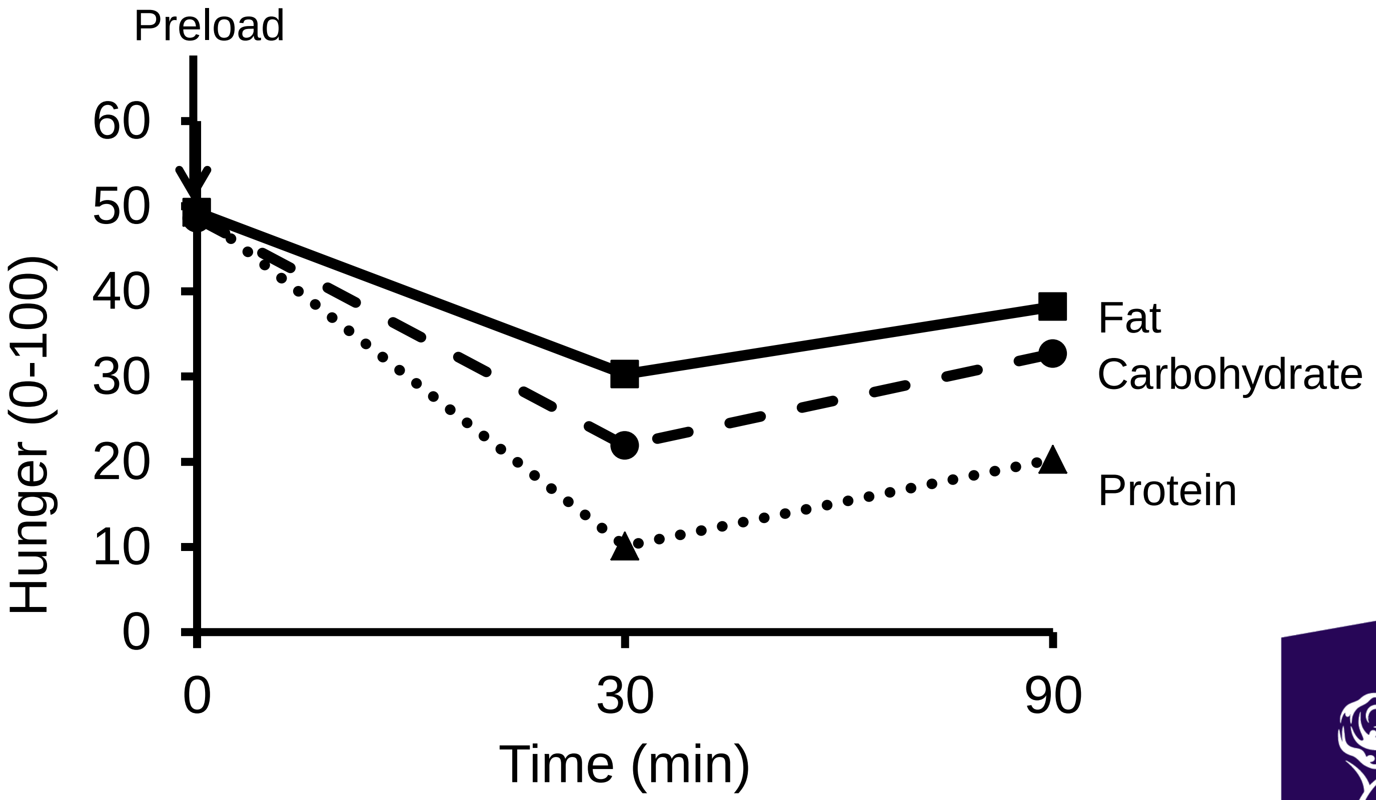
- **Challenge**: age-related anorexia and satiating effects of protein

This is what 30g protein looks like……





Protein is the most satiating macronutrient



Poppitt et al., 1998. *Physiol Behav* 64: 279-85.

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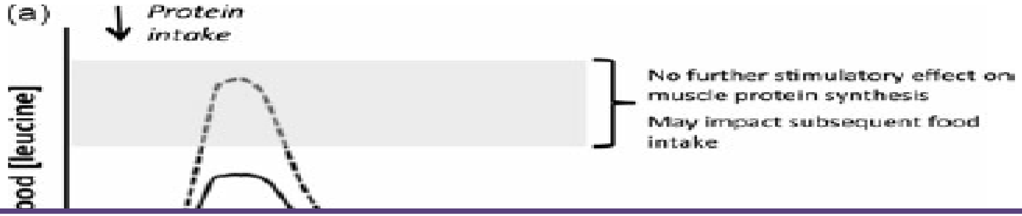


Older individuals **have a higher leucine threshold** and they would benefit from larger amounts of leucine either within a meal or as a protein/EAAs supplement (Katsanos et al., 2006, Bauer et al., 2015, Ispoglou et al., 2016, Phillips et al., 2016, Komar et al., 2015, Yang et al., 2012, Pennings et al., 2011, Verreijen et al., 2015).

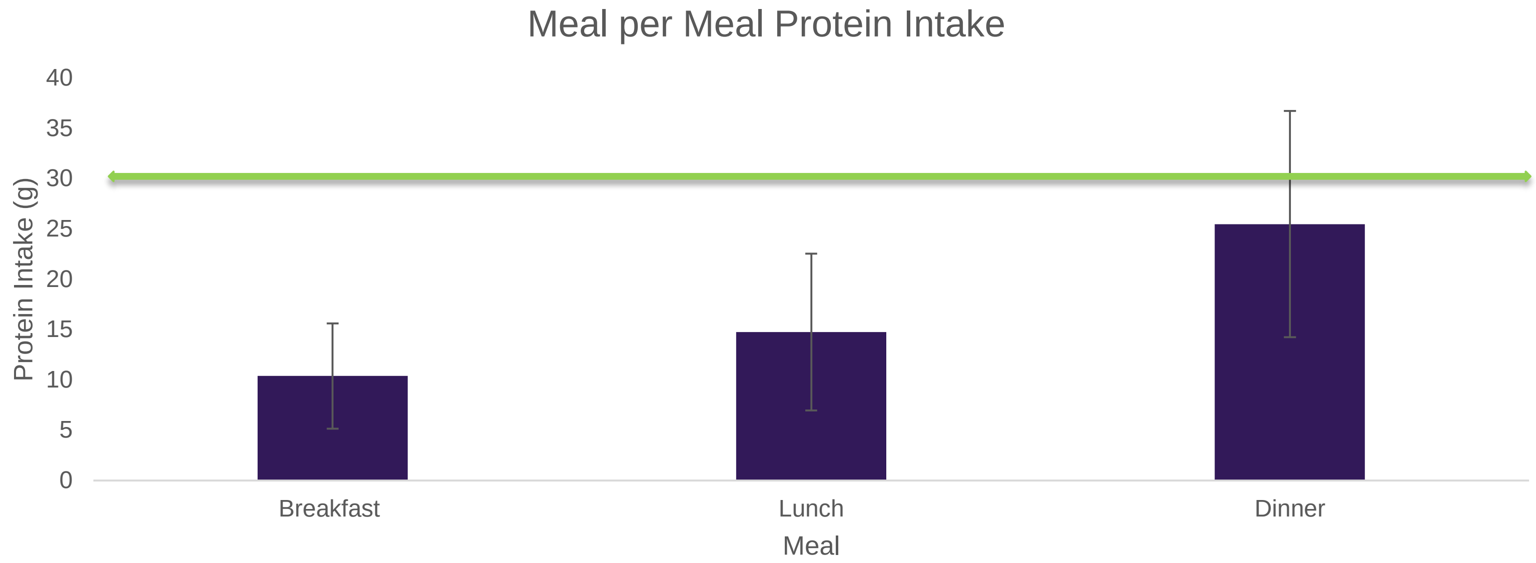
Total protein intake, **protein intake per meal**, or **leucine intake**

Table 2. Dietary protein intake of community-dwelling, frail and institutionalized elderly people distributed throughout the day.

Protein Intake	Breakfast			Morning Snack			Lunch			Afternoon Snack			Dinner			Evening Snack		
	CD	Frail	INST	CD	Frail	INST	CD	Frail	INST	CD	Frail	INST	CD	Frail	INST	CD	Frail	INST
Protein intake (g/day)	11 (7)	10 (7)	12 (7)	3 (4)	3 (4)	2 (3)	22 (13)	18 (10)	15 (8)	4 (6)	4 (6)	3 (4)	27 (13)	31 (15)	24 (12)	5 (6)	5 (7)	2 (4)
Protein intake (% of total protein intake)	16%	14%	21%	4%	5%	3%	31%	26%	25%	5%	5%	6%	38%	43%	41%	7%	7%	4%
Plant-based protein (g/day)	6 (4)	5 (3)	4 (2)	1 (2)	1 (2)	1 (2)	8 (4)	7 (4)	5 (3)	2 (2)	2 (3)	1 (1)	8 (5)	8 (4)	5 (3)	2 (3)	2 (3)	1 (1)
Animal protein (g/day)	5 (5)	5 (6)	8 (6)	1 (2)	2 (3)	1 (2)	14 (11)	11 (9)	10 (7)	2 (5)	2 (5)	2 (4)	19 (13)	23 (14)	19 (11)	3 (5)	3 (5)	1 (3)

Values are means ± SD; CD: Community-dwelling elderly; INST: Institutionalized elderly.

Tieland et al (2015)



Older people do eat enough protein per meal- especially at breakfast and lunch. Green line indicates recommendations (unpublished PhD data)

- Nutritional interventions can have a significant impact on reducing rates of sarcopenia with protein and essential amino-acids crucial in maintaining muscle.

- In older people, current **protein recommendations are considered far below** the actual requirements while those individuals **have higher leucine threshold**.

- **Therefore, specially formulated oral nutritional supplements may address energy and protein deficits**

- When considering the satiating effects of EAAs-based nutritional supplements enriched with leucine, no studies have examined the impact on appetite and concurrent mealtime intake nor the practical aspects of palatability

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European Journal of Clinical Nutrition advance online publication 17 June 2015; doi: 10.1038/ejcn.2015.91

Double-blind, placebo-controlled pilot trial of L-Leucine-enriched amino-acid mixtures on body composition and physical performance in men and women aged 65–75 years

OPEN

T Ispoglou[1], H White[1], T Preston[2], S McElhone, J McKenna[1] and K Hind[1]

[1]Carnegie Faculty, School of Sport, Leeds Beckett University, Leeds, UK
[2]Scottish Universities Environmental Research Centre, University of Glasgow, Glasgow, Scotland

Correspondence: Dr T Ispoglou, Carnegie Faculty, School of Sport, Leeds Beckett University, Headingley Campus, Fairfax Hall, Leeds LS6 3QS, UK. E-mail: t.ispoglou@leedsbeckett.ac.uk

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Ispoglou *et al. Nutrition Journal* (2017) 16:75
DOI 10.1186/s12937-017-0298-6

Nutrition Journal

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Novel essential amino acid supplements enriched with L-leucine facilitate increased protein and energy intakes in older women: a randomised controlled trial

Theocharis Ispoglou[1,3*], Kevin Deighton[1], Roderick FGJ King[1], Helen White[2] and Matthew Lees[1]

The journal of nutrition, health & aging
November 2017, Volume 21, Issue 9, pp 994–1001 | Cite as

The impact of dietary protein or amino acid supplementation on muscle mass and strength in elderly people: Individual participant data and meta-analysis of RCT's

Authors | Authors and affiliations

M. Tieland, R. Franssen, C. Dullemeijer, C. van Dronkelaar, H. Kyung Kim, T. Ispoglou, K. Zhu, R. L. Prince, L. J. C. van Loon, Lisette C. P. G. M. de Groot

Butterworth, M., Hind, K., Duckworth, L., Wilson, O. and ***Ispoglou****, T. Diet, functional performance and muscle quality of independent-living men and women aged 65-75 years. In: Joint Meeting of the American Physiological Society and The Physiological Society, July 29-31, 2016, Dublin.*

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Abstracts of the 38th ESPEN Congress, Copenhagen, Denmark, 17–20 September 2016

Nutrition and chronic diseases 2

MON-P108: The Impact of Essential Amino Acid Supplements Enriched with L-Leucine on Appetite and Energy Intake in Elderly Women

T. Ispoglou, K. Deighton, R. King, H. White, M. Lees
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Original Article

European Journal of Clinical Nutrition advance online publication 17 June 2015; doi: 10.1038/ejcn.2015.91

Double-blind, placebo-controlled pilot trial of L-Leucine-enriched amino-acid mixtures on body composition and physical performance in men and women aged 65–75 years

OPEN

T Ispoglou[1], H White[1], T Preston[2], S McElhone, J McKenna[1] and K Hind[1]

[1]Carnegie Faculty, School of Sport, Leeds Beckett University, Leeds, UK
[2]Scottish Universities Environmental Research Centre, University of Glasgow, Glasgow, Scotland

Correspondence: Dr T Ispoglou, Carnegie Faculty, School of Sport, Leeds Beckett University, Headingley Campus, Fairfax Hall, Leeds LS6 3QS, UK. E-mail: t.ispoglou@leedsbeckett.ac.uk

Received 30 July 2014; Revised 10 April 2015; Accepted 17 April 2015
Advance online publication 17 June 2015

Pilot study (Ispoglou et al. 2016)

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Table 1. Composition of essential amino-acid mixtures per 100 g

Amino acids	*Standard essential amino-acid mixture containing 20% leucine*	*Modified essential amino-acid mixture containing 40% leucine*
Histidine	10	5
Isoleucine	11	11
Leucine	20	40
Lysine	15	12
Methionine	3	2
Phenylalanine	15	7
Threonine	14	11
Valine	12	12

Protocol

Subjects received one of the following daily:

(A) Standard EAA mixture (20% leucine)
(B) Modified EAA mixture (40% leucine)
(C) Isocaloric placebo (lactose).

The supplementation period was 3 months and it was in accordance with EWGSOP recommendations. Primary outcomes were total lean mass and physical performance. Measurements were taken at baseline and immediately post intervention. A standardised health screening and a pre-exercise screening questionnaire, blood pressure, resting heart rate and oxygen saturation levels were taken at each time point.

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Leucine enriched modified EAAs mixture

Table 3. Assessment of body composition at baseline and at the end of the intervention period[a]

Body composition variables	Group A (n = 8)				Group B (n = 8)				Group C (n = 9)		
	Baseline	Week 12	%	ES	Baseline	Week 12	%	ES	Baseline	Week 12	%
Total LTM (kg)	44.8 ± 7.1	44.8 ± 7.2	0.2 ± 2.4	−0.4	45.5 ± 8.9	46.0 ± 9.1[b]	1.1 ± 1.1	0.2	42.6 ± 8.9	43.0 ± 9.3	0.8 ± 1.3
Total FM (kg)	27.8 ± 11.4	28.5 ± 11.2	4.3 ± 6.7	0.4	25.6 ± 6.2	25.7 ± 6.0	0.5 ± 2.6	−0.2	24.9 ± 9.9	25.1 ± 9.7	1.5 ± 6.3
Percentage BF (%)	36.0 ± 10.5	36.7 ± 9.7	3.3 ± 6.1	0.5	34.8 ± 6.6	34.7 ± 6.5	−0.4 ± 2.1	−0.2	35.2 ± 11.2	35.2 ± 11.0	0.4 ± 4.7
Total BMC (kg)	2.6 ± 0.5	2.6 ± 0.5	0.1 ± 1.4	−0.3	2.5 ± 0.6	2.5 ± 0.6	0.0 ± 1.0	−0.4	2.4 ± 0.5	2.4 ± 0.5	0.4 ± 1.0
Total BMD (g/cm^2)	1.1 ± 0.1	1.1 ± 0.1	0.2 ± 1.2	0.5	1.1 ± 0.2	1.1 ± 0.2	0.3 ± 1.6	0.5	1.1 ± 0.1	1.1 ± 0.1	−0.4 ± 1.1

Abbreviations: A, standard essential amino-acid mixture (containing 20% leucine); B, modified amino-acid mixture (containing 40% leucine); C, placebo; BMC, bone mineral content; BMD, bone mineral density; BF, body fat; ES, Effect Size; FM, fat mass; LTM, bone mineral-free lean tissue mass; %, mean percentage change from baseline to week 12. [a]All values are means ± standard deviations. [b]Denotes significantly different from baseline value ($P < 0.05$). ME = mean of the experimental group, MP = mean of the placebo group. ES Cohen's d = (ME-MP)/SD pooled).

- We have shown the **benefits** of supplementing diets of older people with EAAs enriched with leucine.

- One of the issues we faced was that participants managed only **75-85**% of prescribed dosage.

Follow-up study (Ispoglou et al. 2017)

Ispoglou *et al. Nutrition Journal* (2017) 16:75
DOI 10.1186/s12937-017-0298-6

Nutrition Journal

RESEARCH Open Access

Novel essential amino acid supplements enriched with L-leucine facilitate increased protein and energy intakes in older women: a randomised controlled trial

Theocharis Ispoglou[1,3*], Kevin Deighton[1], Roderick FGJ King[1], Helen White[2] and Matthew Lees[1]

- When considering the satiating effects of EAAs-based nutritional supplements enriched with leucine, no studies have examined the impact on appetite and concurrent mealtime intake nor the practical aspects of palatability

Development of prototypes (Bar and gel)



Nutritional information per 100 g:

-**BAR**: energy 1511 kJ, fat 8.2 g, carbohydrate 47.5 g, protein 25.4 g of which 15 g was EAAs, fibre 2.8 g, salt 0.2 g.


-**GEL**: energy 967 kJ, fat 0.0 g, carbohydrate 47.5 g, protein 15 g which was entirely due to the EAAs content, fibre 0.5 g, salt 0.2 g.

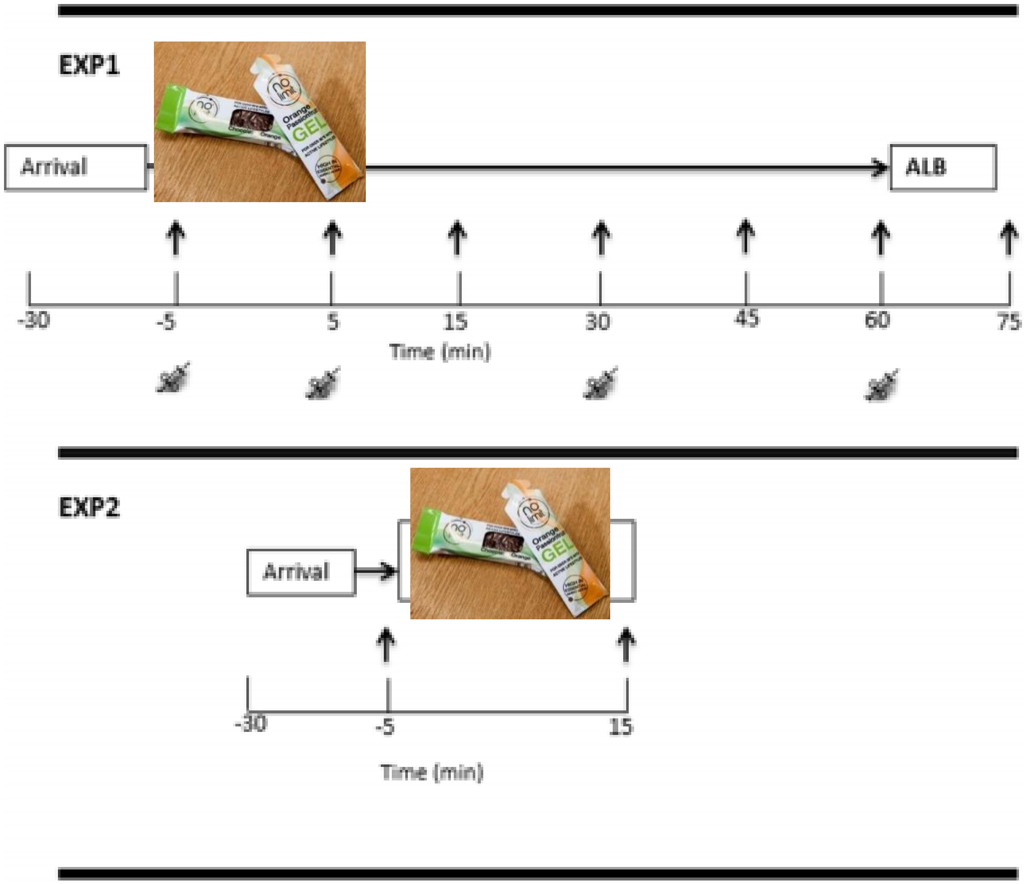

Fig. 1 A schematic representation of the design for experiment one (EXP1) and two (EXP2). The three conditions consisted of either a bar (BAR), gel (GEL), or nothing (CON). Black arrows = appetite rating assessment; syringe picture = blood samples. Ad libitum *breakfast* (ALB)

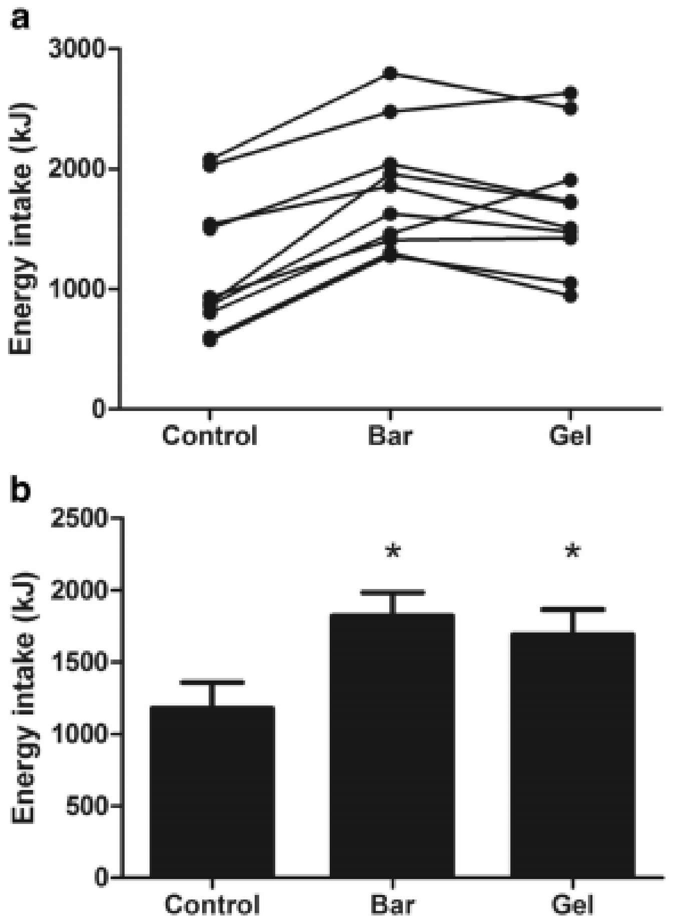

Fig. 2 Total energy intake in the control, bar and gel trials (experiment one). Data are displayed as individual responses (**a**) and mean (SEM) (**b**), *n* = 10

Our nutritional prototypes (GEL and BAR) are effective means to facilitate an increase in protein and energy intake when taken one hour before an ad lib breakfast meal. (Ispoglou et al. 2017)

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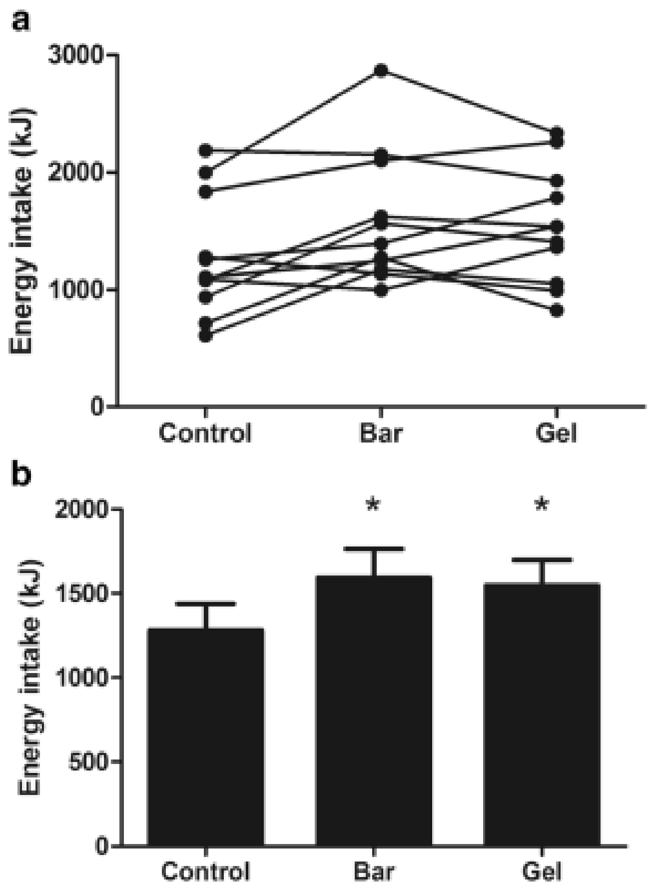

Fig. 5 Total energy intake in the control, bar and gel trials (experiment two). Data are displayed as individual responses (**a**) and mean (SEM) (**b**), *n* = *11*

Our nutritional prototypes (GEL and BAR) are effective means to facilitate an increase in protein and energy intake when taken alongside an ad lib breakfast meal. Ispoglou et al (2017)

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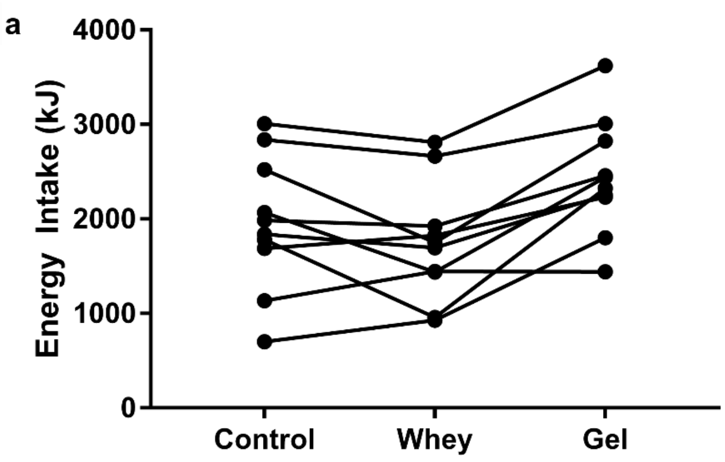
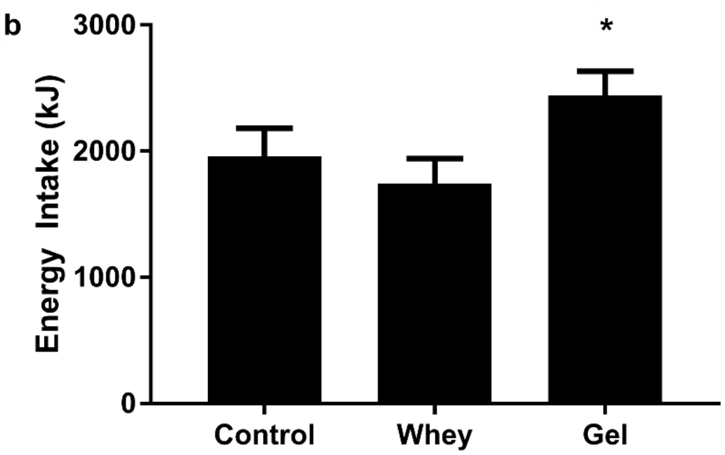


Our GEL is effective means to facilitate an increase in protein and energy intake when taken one hour before an ad lib breakfast meal.



PhD Project (Unpublished data-in process of publication)

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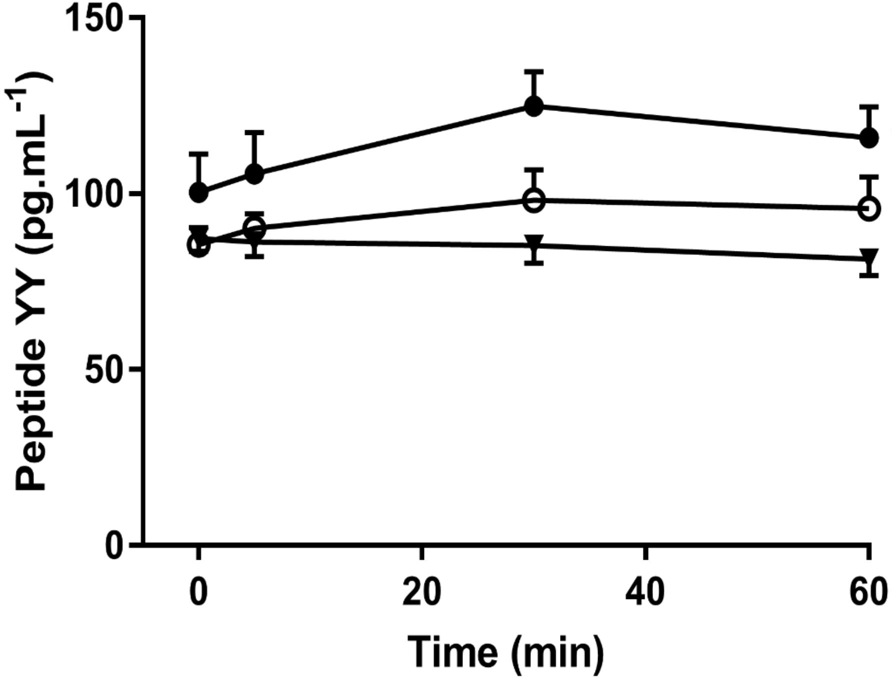
a



The current gold standard (whey protein) enhances satiety and as a result people eat less

PhD Project (Unpublished data-in process of publication)

❑ *Challenges in older people*

- ❑ ***Key Points***

  - ❑ ***Short term inactivity detrimental to muscle mass and function. Development of anabolic resistance***

  - ❑ ***Current protein recommendations inadequate. Need at least 1.2 g/kg/bm daily, more protein per meal, and more leucine!***

  - ❑ ***Age-related anorexia. Dietary protein and protein supplements enhance satiety***

  - ❑ ***Use of EAAs dietary supplements may be a necessity in certain groups***

Our current and future research is primarily focused on strengthening evidence base of non-pharmacological interventions on:

- **Health and wellbeing**: Prevention of sarcopenia in healthy older individuals contributing to retention of lean tissue mass, prevention of osteoporosis and enhanced functional capacity.

- **Clinical settings**: Treatment of sarcopenia in frail older individuals in chronic disease conditions such as respiratory, rheumatoid arthritis, diabetes, CHD and CF, liver and gastro-intestinal disease, where increased protein requirements may be a result of enhanced requirements or malabsorption.

Present and Future

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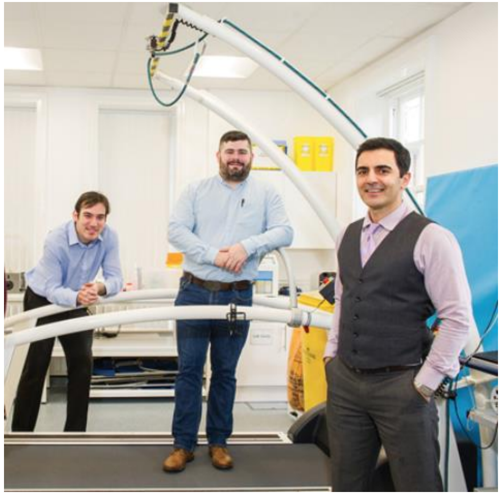

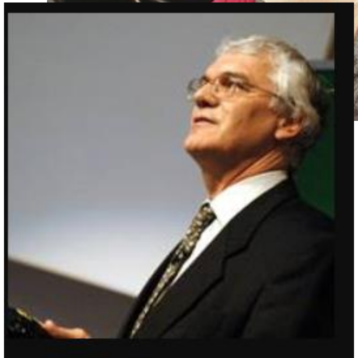

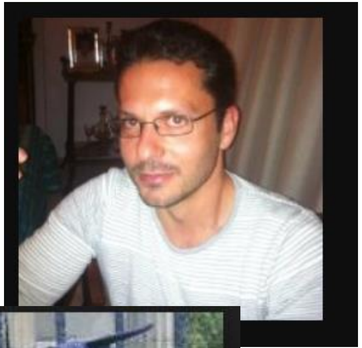

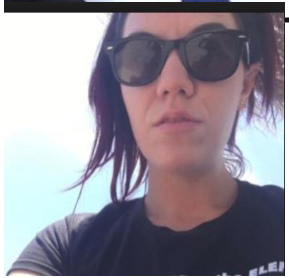

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Current Projects

1. **Dr Karen Hind and Dr Theocharis Ispoglou (Mid Career Prize)**: “Effects of Exercise and a Leucine and Vitamin D-enriched Essential Amino Acid Supplement on Bone Health in Older Women: a Randomised Controlled Trial”
2. **Matthew Butterworth (PhD):** “Exercise and nutritional based interventions to combat age-related sarcopenia”
3. **Kelsie Johnson (PhD):** “Exercise and Nutritonal interventions to improve appetite regulation, body composition and muscle function in older men and women”
4. **Matthew Lees (PhD)**: “The effect of age and physical (in)activity on the anabolic resistance to essential amino acids and exercise in elderly populations”
5. **Panos Ferentinos (PhD)**: “Acute and Chronic effects of different exercise modalities in ageing population: The role of endothelial progenitor cells on endothelial function”
6. **Linsey King (PhD)**: “Clinical trial to investigate the effectiveness of the nutritional prototypes we developed in clinical settings, Bronchiectasis patients”
7. **Chelsea Moore (PhD):** “Audit of Cardiac Rehab Programme in UK ; endothelial function, physical activity levels and dietary intakes”

Staff Webpage: http://www.leedsbeckett.ac.uk/staff/dr-theocharis-ispoglou/
LinkedIn: https://www.linkedin.com/in/theocharis-ispoglou-b7b71a2a/
Twitter: @Theo_Ispoglou