

Understanding sarcopenia : causes, mechanisms and consequences

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Muscle wasting is a problem

«Take an old person suffering a process of physiological atrophy due to advanced age, of his/her muscular elements, for instance of the muscles of the legs, where it usually happens, causing total or partial paraplegia. Why not calling it wasting, degeneration with no reincorporation?»

Lozano E. Enfermedades en los viejos y crónicos. Madrid: G Juste, 1899.



Starting point

- Sarcopenia is a medical condition not yet broadly recognized by the international medical community. Discussions on definition, diagnostic methods and interventions are ongoing.
- Sarcopenia is in the process to receive an ICD-10 code and is most certainly under-diagnosed.

Sarcopenia: first steps



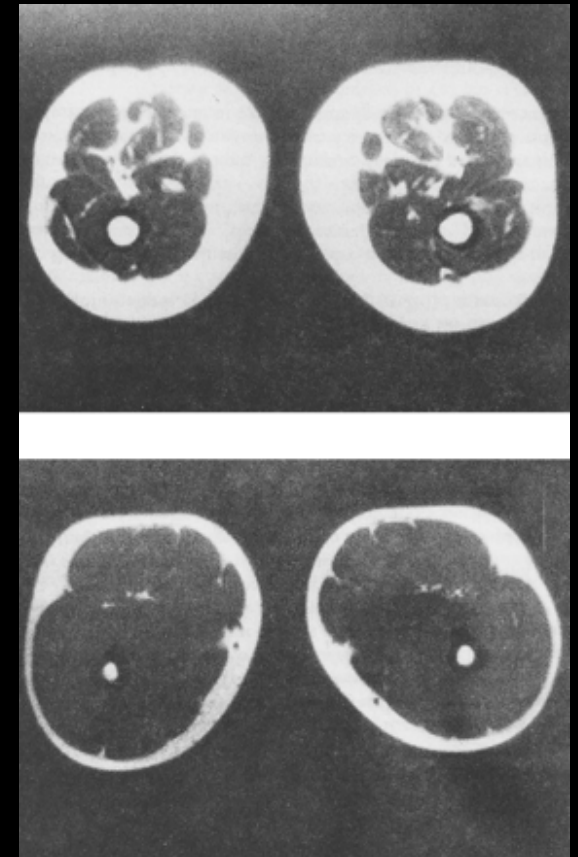
- “No decline with age is as dramatic or potentially more significant than the decline in lean body mass. In fact, there may be no single feature of age-related decline more striking than the decline in lean body mass in affecting ambulation, mobility, energy intake, overall nutrient intake and status, independence and breathing.
- I suggested that if this phenomenon were to be taken seriously, we had to give it a name. I proposed that the name for this phenomenon should be derived from the Greek.”

Sarcopenia: the concept



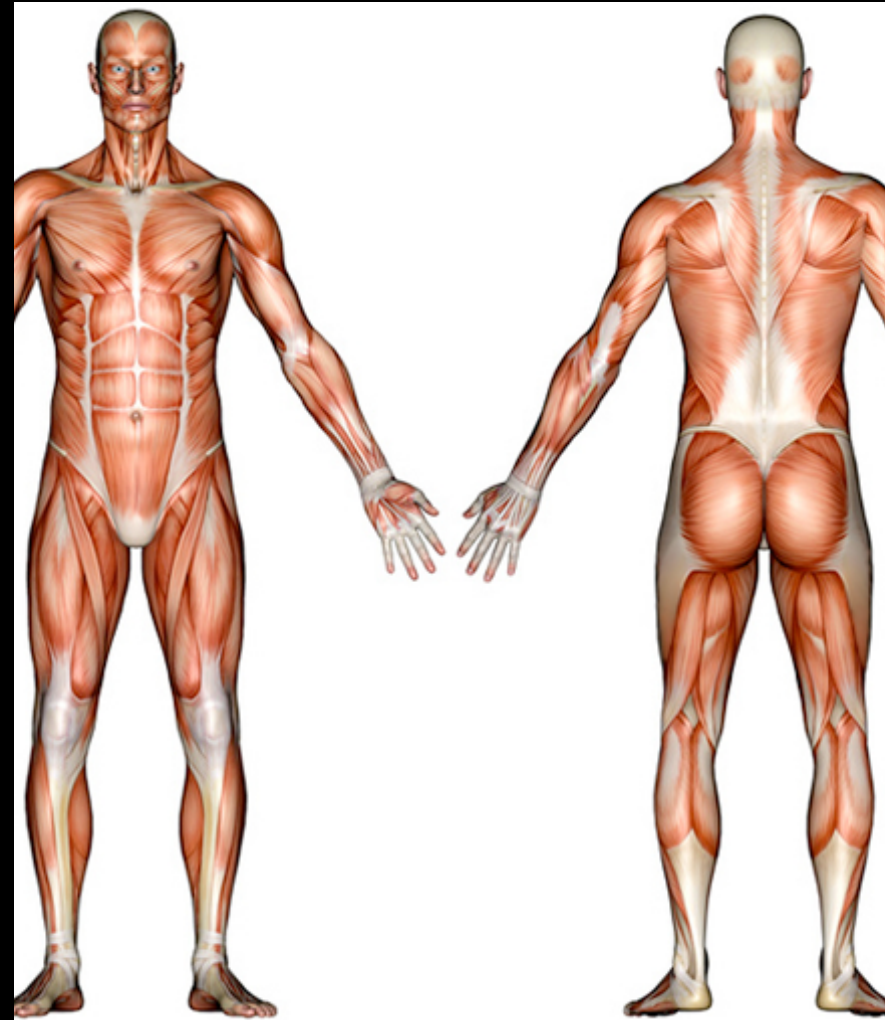
Sarcopenia is a threat in old age

- Linked with the geriatric evolving concept of “frailty”
- Related with weight loss, malnutrition and cachexia
- The main consequences are disability, dependence and death

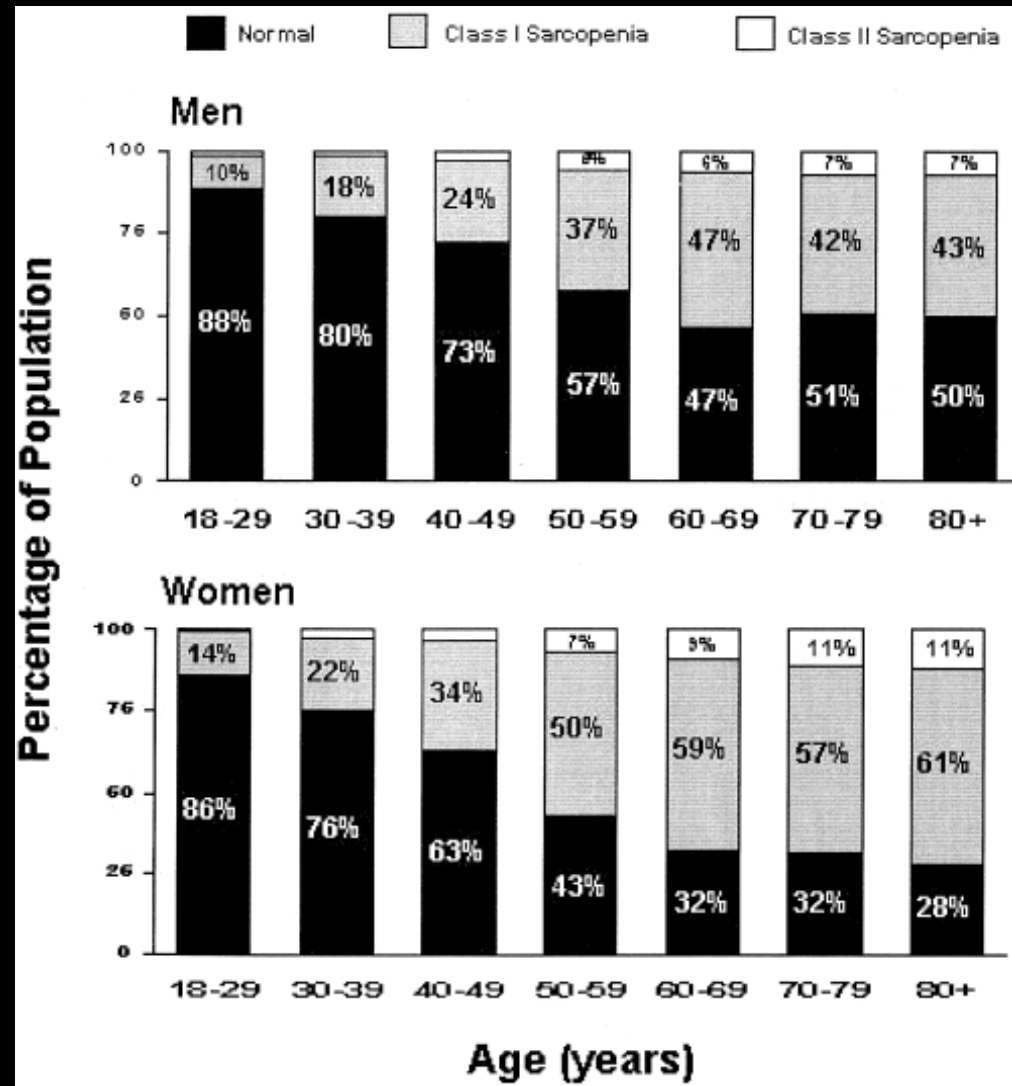


Human muscles

- 600 muscles in human body
- Skeletal muscles: 40-45% of total body mass
- 55% of skeletal muscle mass in lower limbs
- 50% of total body protein is in muscles



Low skeletal body mass and age



Janssen I et al. Low Relative Skeletal Muscle Mass (Sarcopenia) in Older Persons Is Associated with Functional Impairment and Physical Disability. J Am Geriatr Soc 2002



REPORT

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People

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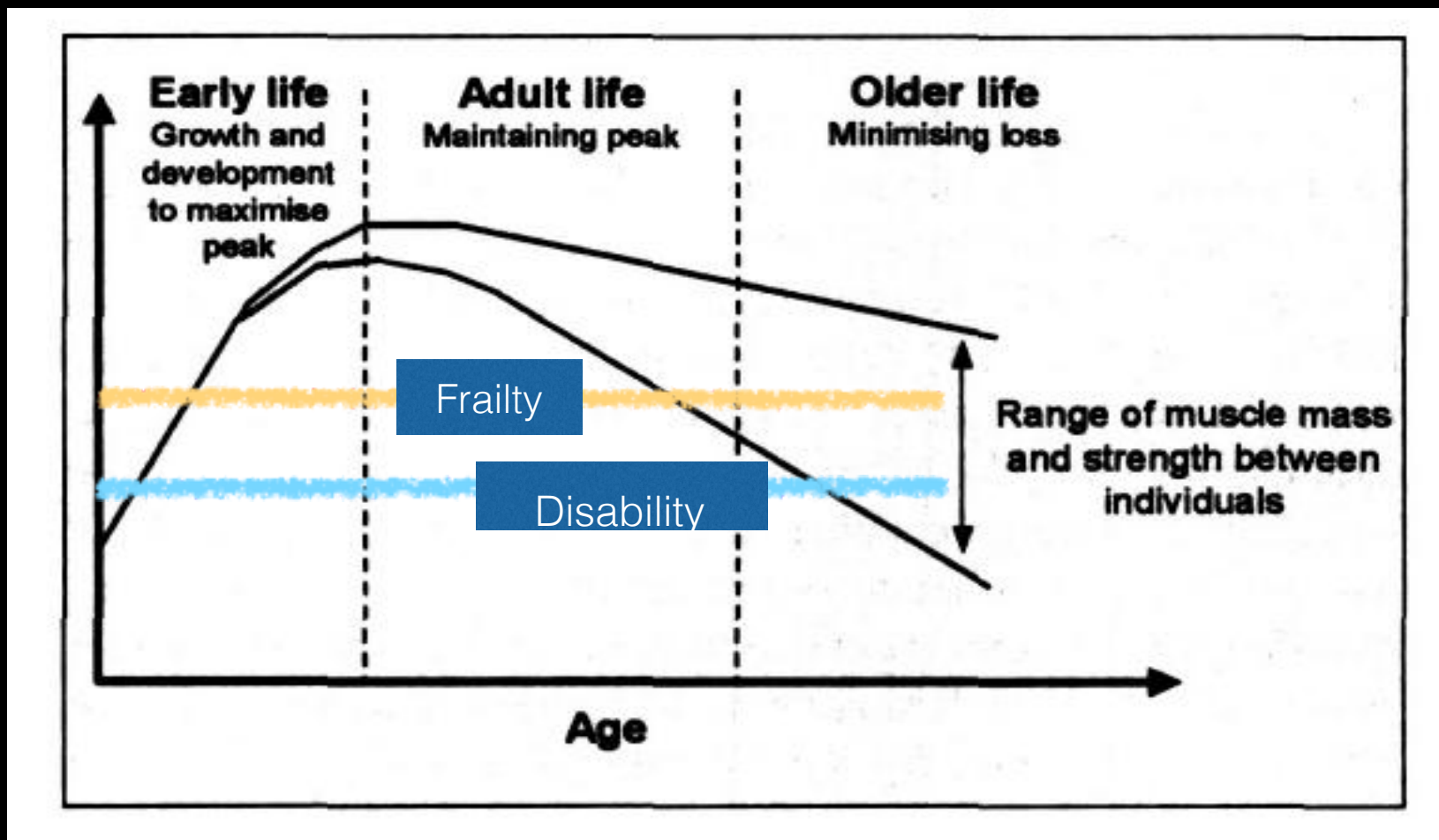
EWGSOP Definition of Sarcopenia

Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death.

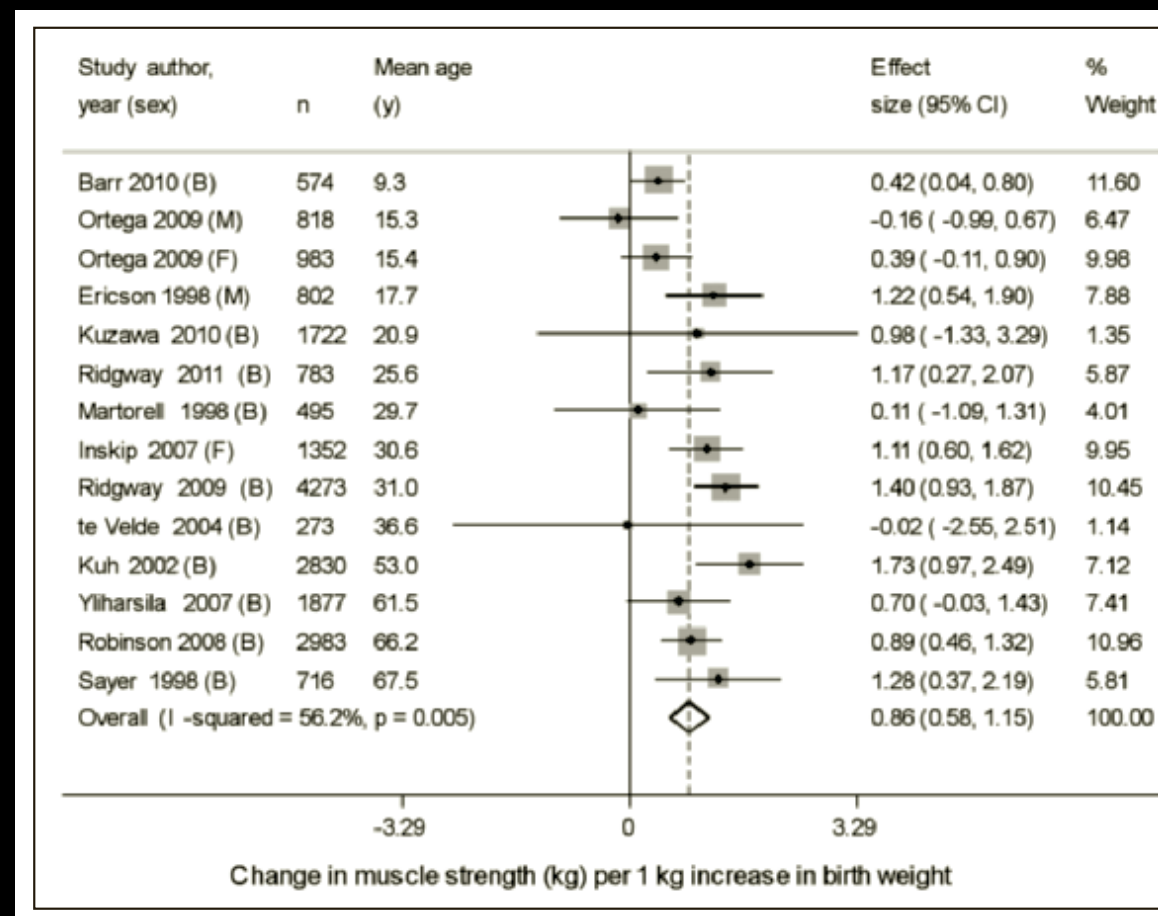
CRITERIA FOR THE DIAGNOSIS OF SARCOPENIA

progressive

A lifelong model of sarcopenia



Birth weight and muscle strength



Dodds R, et al. Birth weight and muscle strength: a systematic review and meta-analysis. *J Nutr Health Aging*. 2012;16(7):609-15.

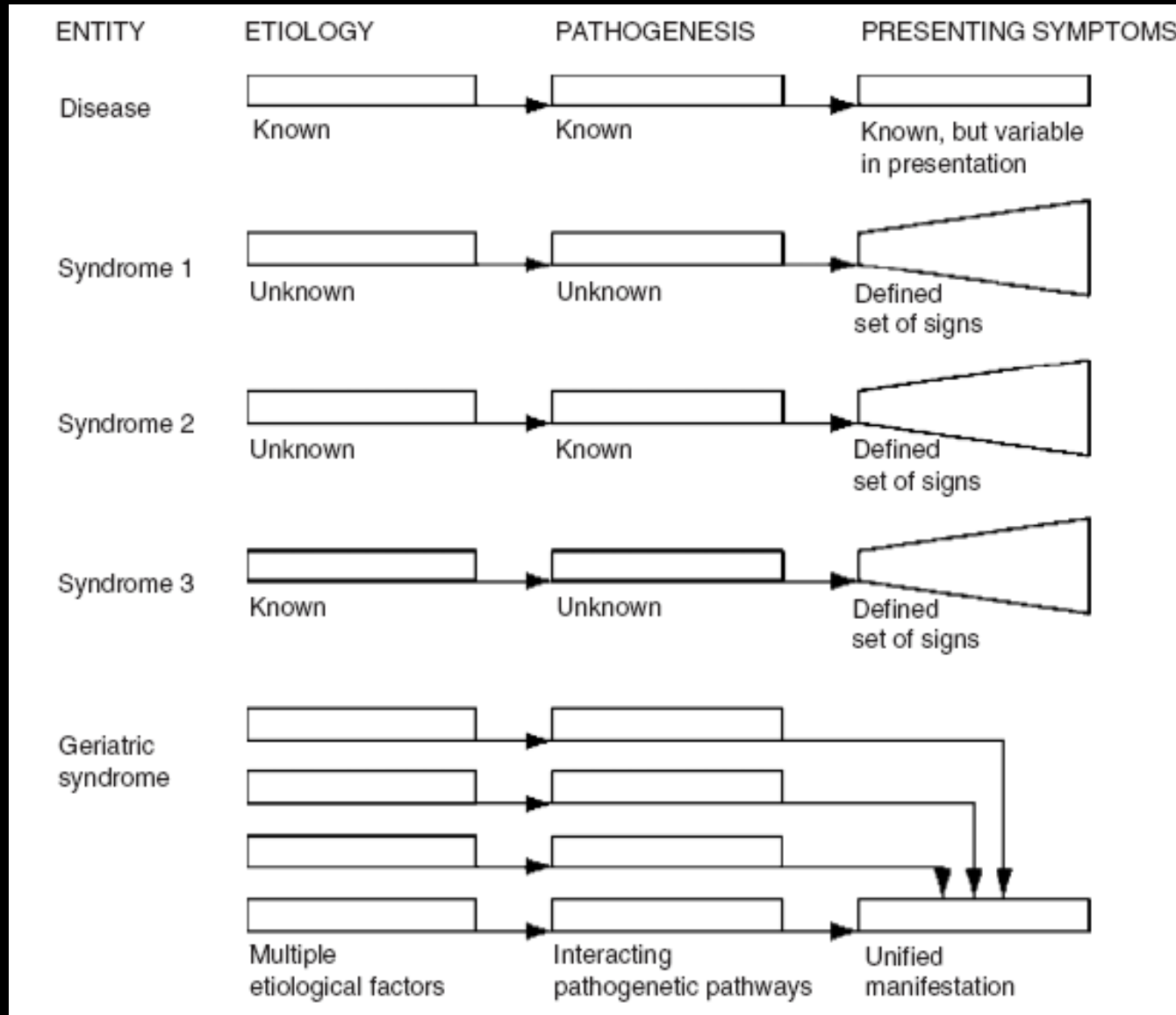
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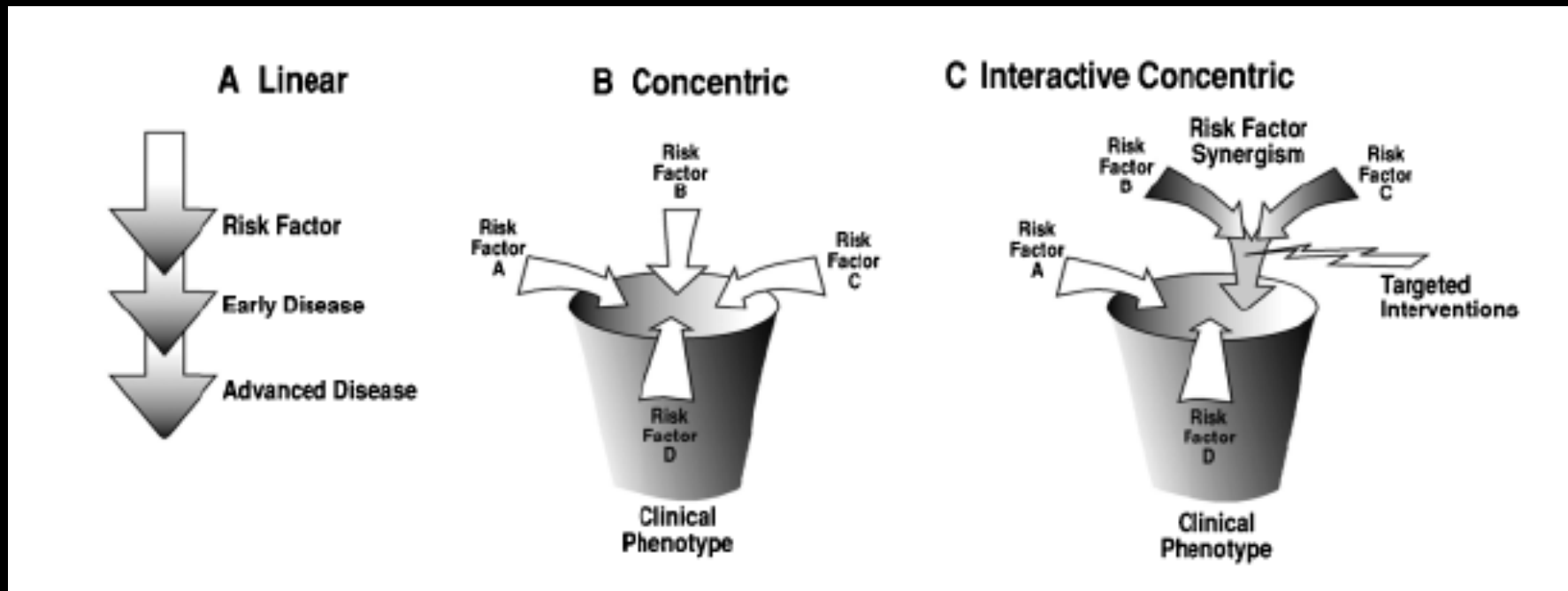
geriatric syndrome

The complexity of geriatric syndromes



- Hypothyroidism
- Chronic fatigue
- Cushing
- Marfan
- Delirium

Modeling geriatric syndromes



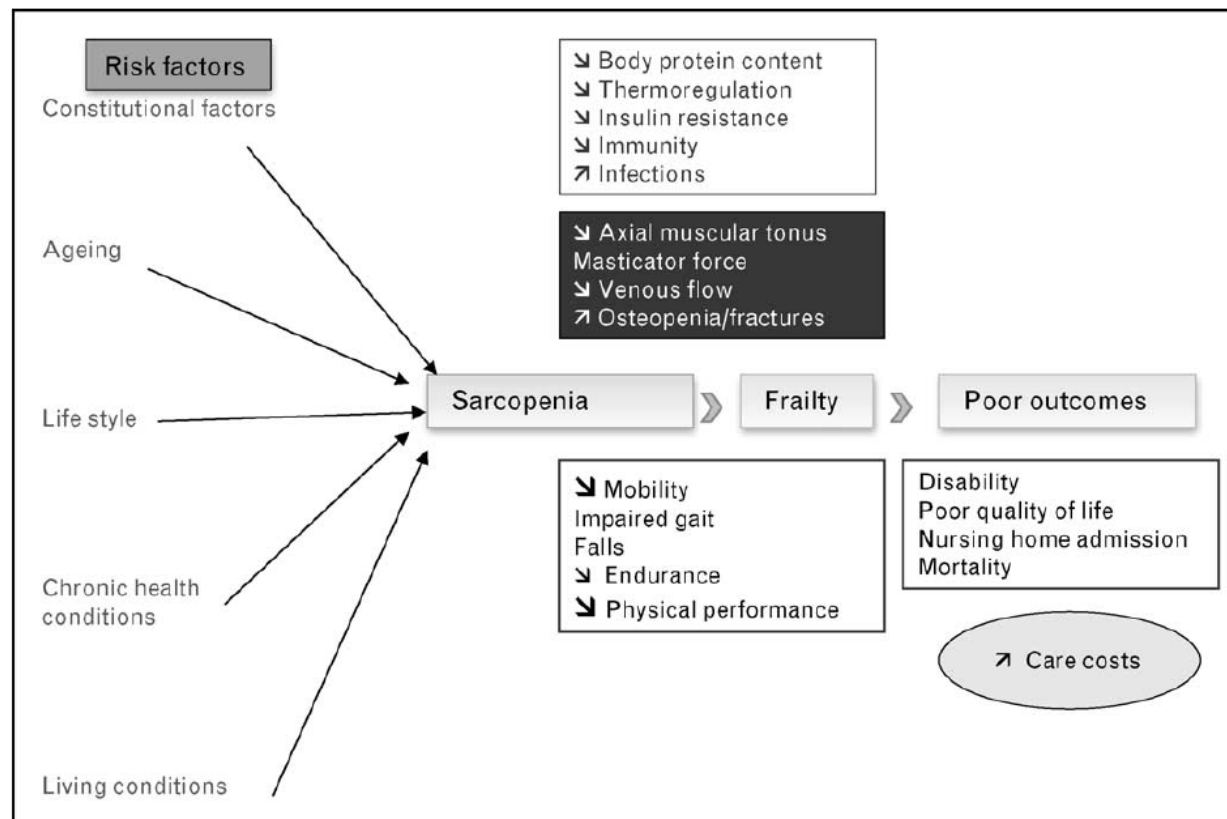
Congenital errors of metabolism

Cancer, ischemic heart disease

Geriatric syndromes

Sarcopenia is a geriatric syndrome

Figure 1 Sarcopenia is a geriatric syndrome



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adverse outcomes

Sarcopenia increases mortality

Table 2. Association between sarcopenia and all-cause mortality, after adjustment for various confounders (hazard ratios and 95% confidence intervals)

	Unadjusted	Model 1	Model 2	Model 3
	Hazard ratio (95% confidence interval)			
Sarcopenia	2.95 (1.44–6.04)	2.89 (1.40–5.96)	2.40 (1.07–5.42)	2.32 (1.01–5.43)
Age		1.15 (0.93–1.42)	1.08 (0.85–1.36)	1.12 (0.87–1.43)
Gender (female)		0.55 (0.29–1.03)	0.49 (0.25–0.99)	0.49 (0.23–1.04)
Education			0.87 (0.72–1.04)	0.87 (0.72–1.05)
ADL impairment			1.91 (1.29–2.83)	1.75 (1.20–2.56)
Body mass index			0.92 (0.86–0.99)	0.93 (0.86–1.01)
Hypertension				0.60 (0.26–1.35)
Congestive heart failure				6.71 (0.70–64.1)
COPD				1.46 (0.50–4.21)
Number of diseases				1.29 (0.92–1.80)
TNF- α				0.99 (0.85–1.15)

Model 1: adjusted for age, gender.

Model 2: adjusted for age, gender, education, ADL impairment, body mass index.

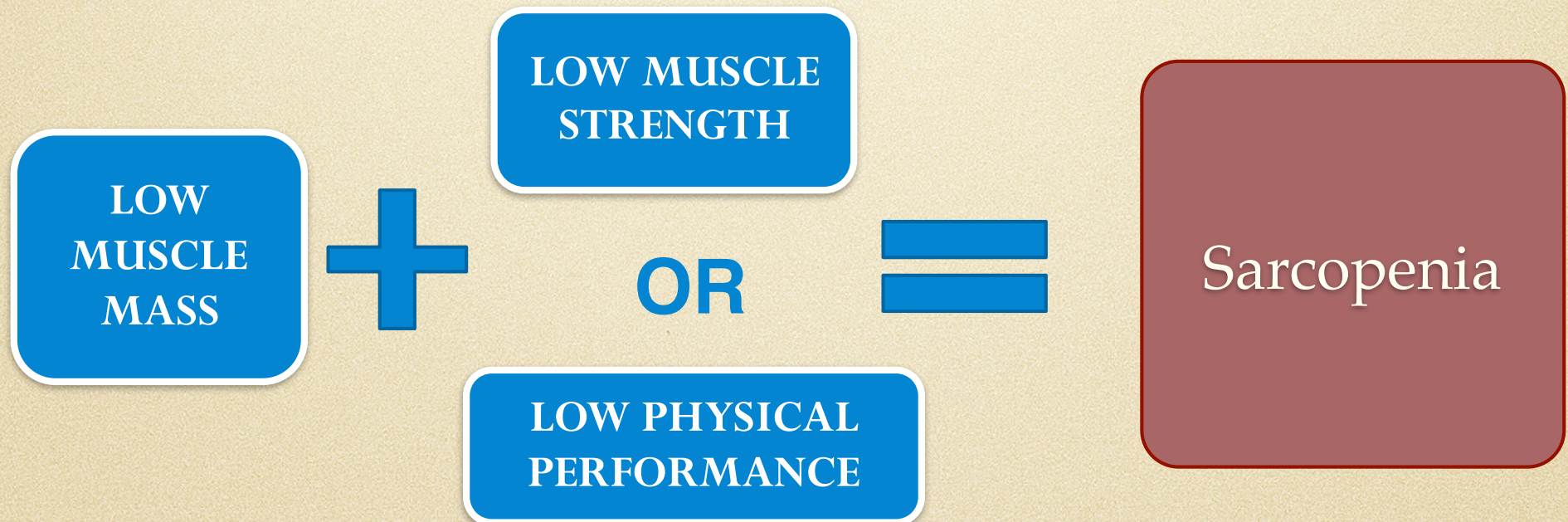
Model 3: adjusted for age, gender, education, ADL impairment, body mass index, hypertension, congestive heart failure, chronic obstructive pulmonary disease (COPD), number of diseases, TNF- α .

Age, education, ADL impairment, body mass index, number of diseases, TNF- α was treated as a continuous variable.

EWGSOP Definition of Sarcopenia

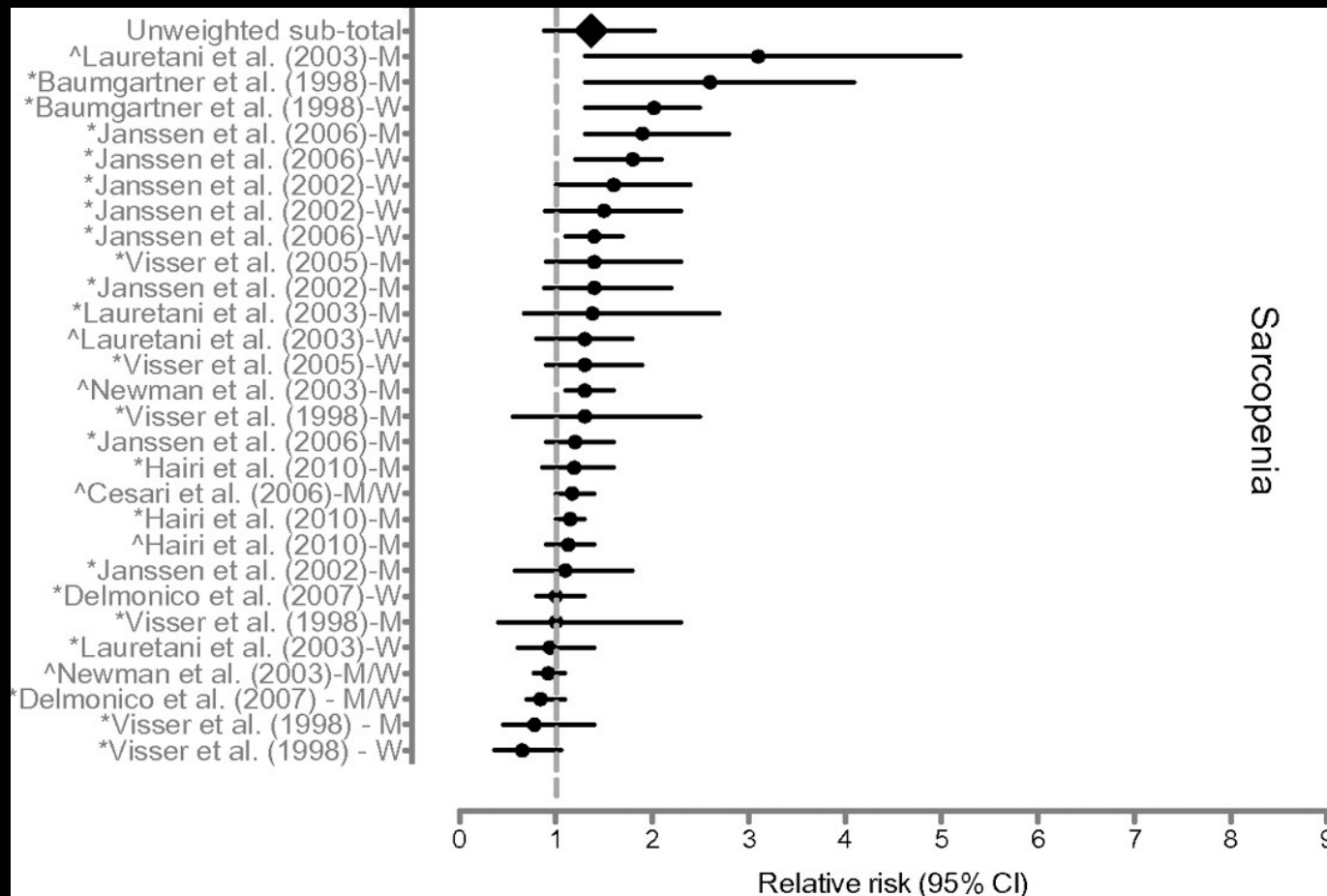
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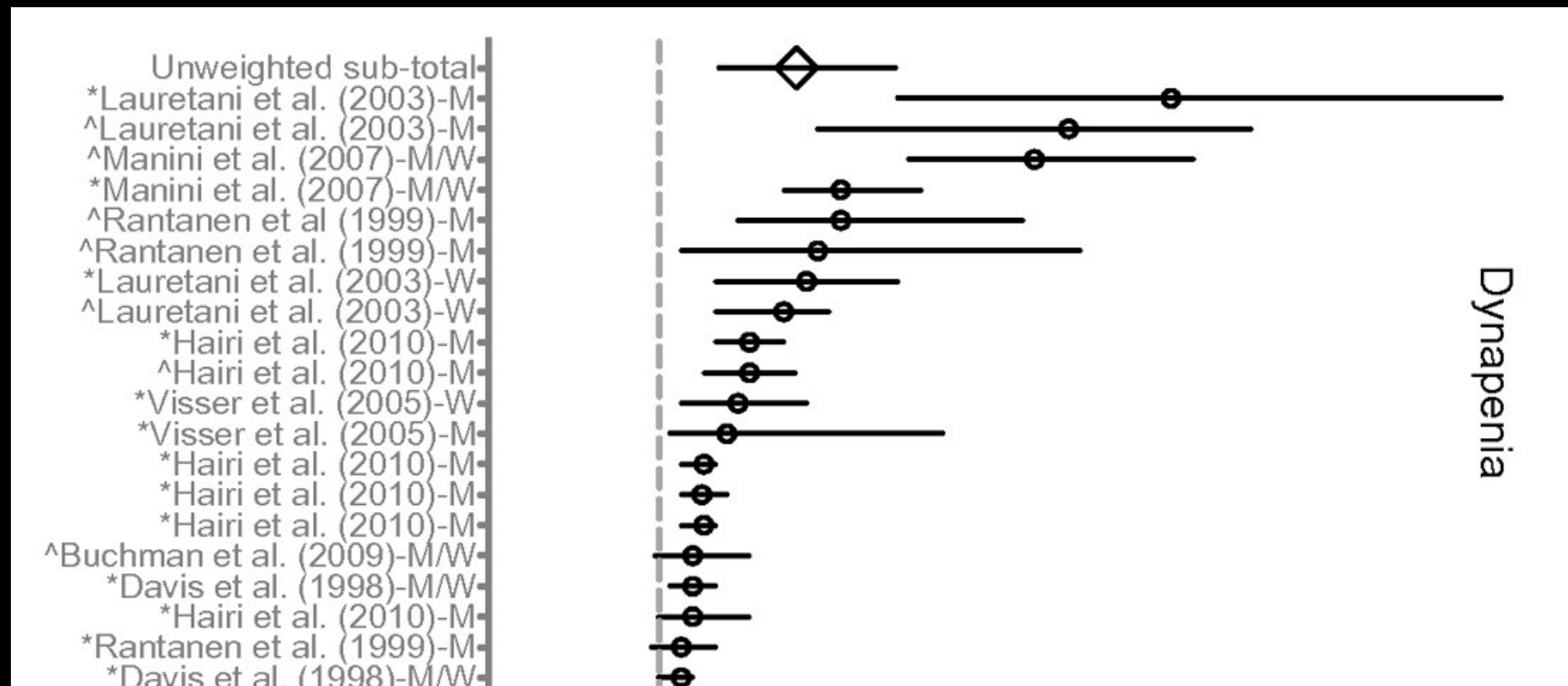


Cruz-Jentoft AJ et al. Sarcopenia: European consensus on definition and diagnosis. Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010

Risk of poor physical performance or physical disability in older adults with low muscle mass

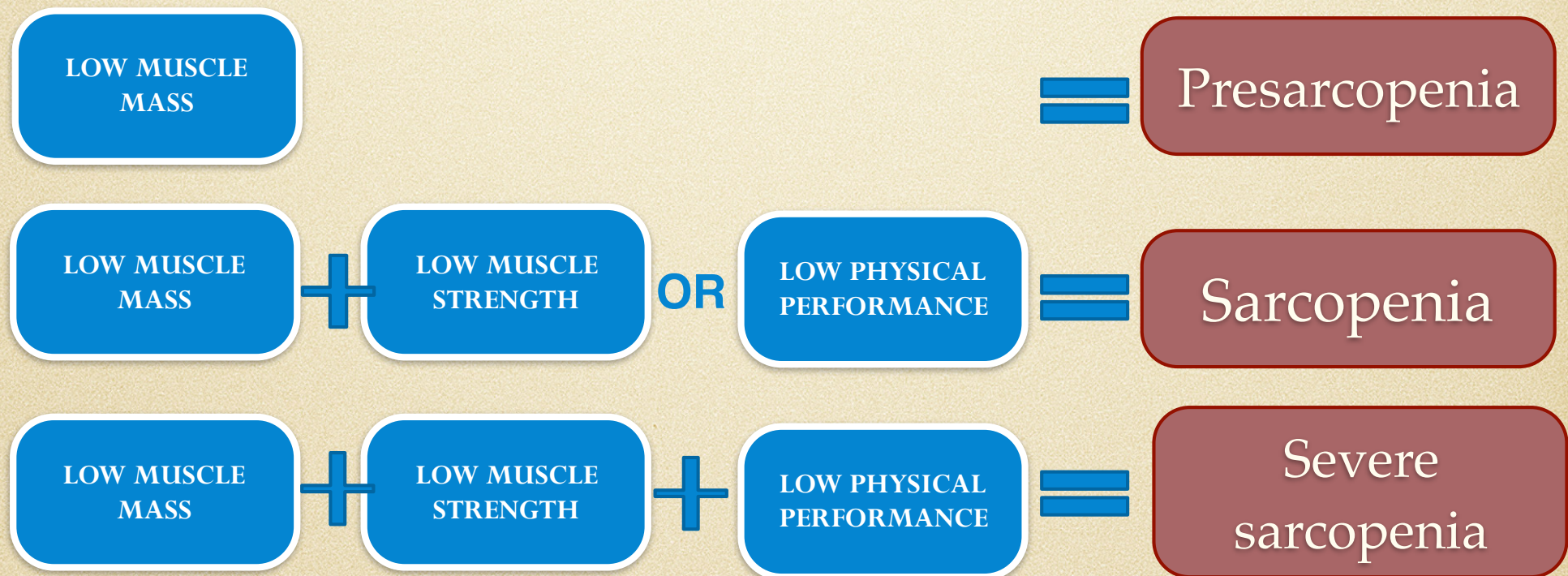


Risk of poor physical performance or physical disability in older adults with low muscle strength



EWGSOP Conceptual Stages of Sarcopenia

Sarcopenia staging, which reflects the severity of the condition, is a concept that can help guide clinical management of the condition.



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

EWGSOP

Secondary

Activity related

Bed rest
Sedentary lifestyle
Deconditioning

Disease related

Advanced organ failure
Inflammatory diseases
Malignancy
Endocrine diseases

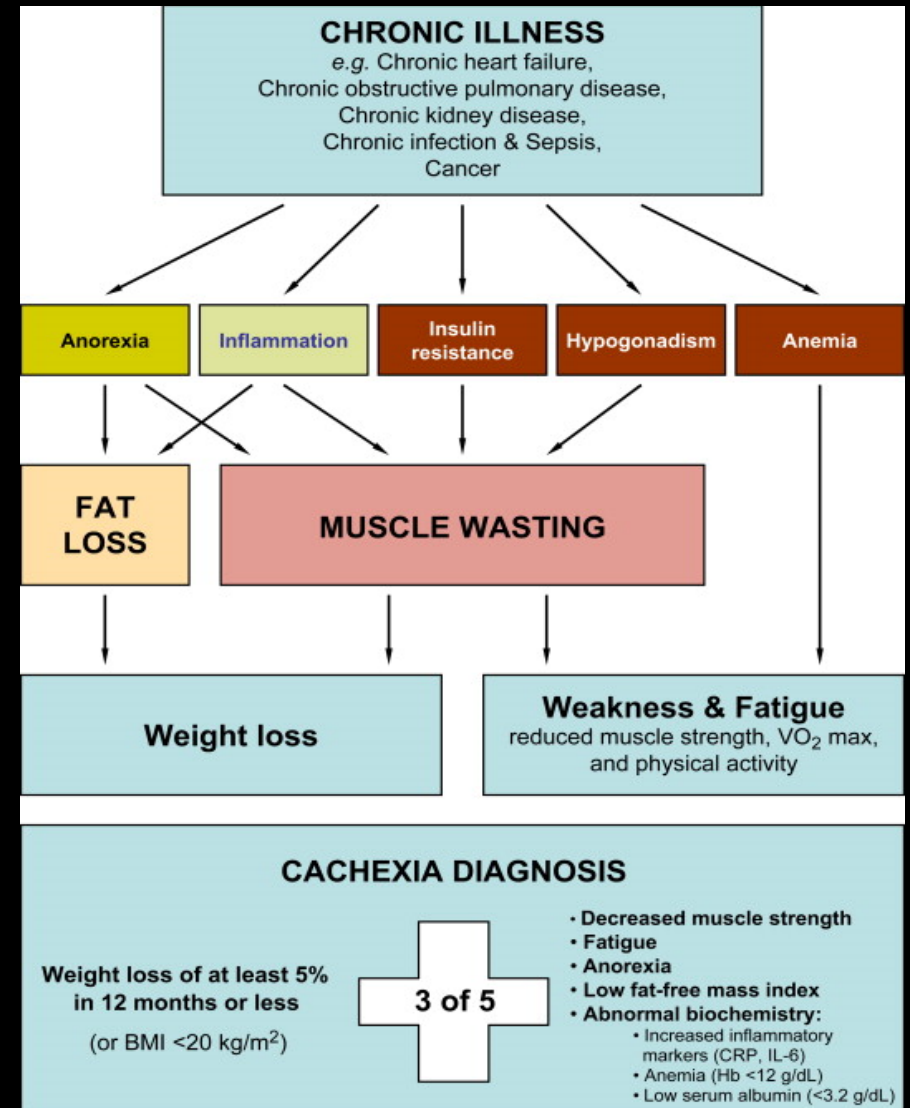
Nutrition related

Inadequate diet
Malabsorption
Gastrointestinal disorders
Drug induced anorexia

Primary
Age-related

Sarcopenia, cachexia, inflammation

- Systemic inflammation seems to be linked to muscle wasting
- Some degree of inflammation may be present in sarcopenia
- Inflammation is key in the pathogenesis of cachexia
 - CRP (>5.0 mg/l, IL-6 >4.0 pg/ml)
- Low muscle mass and strength are part of the definition of cachexia

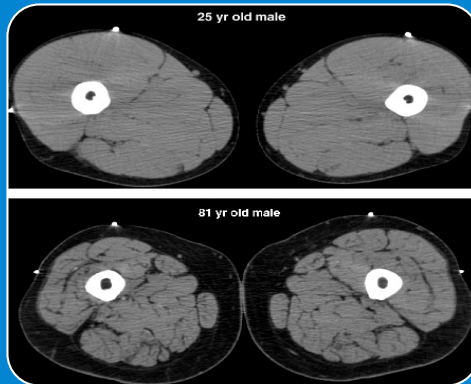


Evans WJ et al. Cachexia: A new definition. Clin Nutr 2008.

Muscaritoli M et al. Consensus definition of sarcopenia, cachexia and pre-cachexia. Clin Nutr 2010.

Rolland Y et al. Cachexia versus sarcopenia. Curr Opin Clin Nutr Met Care 2011.

Suggested measures to diagnose sarcopenia



MUSCLE MASS

BIA
DEXA

CT
MRI



MUSCLE STRENGTH

Handgrip strength

Knee flexion-extension
PEF



PHYSICAL PERFORMANCE

SPPB

Gait speed
Get up&Go
Stair climbing

Sarcopenia with limited mobility

Society for Sarcopenia, Cachexia and Wasting Disorders

Sarcopenia with limited mobility is defined as a person with muscle loss whose walking speed is equal to or less than 1 m/s or who walks less than 400 m during a 6 minute walk.

Muscle loss: lean appendicular mass (corrected for height squared) >2 SD below healthy persons between 20 to 30 years of age of the same ethnic group.

Limitation in mobility not clearly attributable to the direct effect of specific disease such as peripheral vascular disease, or central or peripheral nervous system disorders, dementia, or cachexia.

Sarcopenia and physical frailty

Shrinking: unintentional weight loss, sarcopenia

Weakness

Poor endurance, exhaustion

Slowness

Low activity

Positive for frailty phenotype: 3 or more criteria present

Intermediate or prefrail: 1 or 2 criteria present

Sarcopenia may be a more practical concept than physical frailty in the quest to reduce disability