Sarcopenia
una definicion en evolucion

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Abbott
A Promise for Life

X Curso ALMA Cancun, Mexico, Julio 2011

NIA conference♪
Epidemiologic and Methodologic Problems in Determining ♪
the Nutritional Status of Older Persons♪

«No decline with age is more dramatic or potentially more functionally significant than the decline in lean body mass»

Sarcopenia

Greek 'sarx' or flesh + 'penia' or loss♪

«Clearly defining sarcopenia will allow investigators to appropriately classify patients and examine underlying pathogenic mechanisms and will allow funding agencies to appropriately target research funds to a taxonomically distinct syndrome»

Rosenberg IH. Summary Comments . Am J Clin Nutr 1989; J Nutr 1997

Correlation coefficients between leg extensor power and functional performance

N=26 nursing home residents aged >80 yrs♪

	r	p
Chair rising speed (s)	0.65	0.001
Stair-climbing speed (s)	0.81	0.001
Walking speed (km/hr)	0.80	0.001
Stair-climbing power (W)	0.88	0.001

Bassey et al Clin Sci 1992

Mass, density, strength, quality,…

«Computed tomography shows that after age 30 y, there is a decrease in cross-sectional areas of the thigh along with decreased muscle density associated with increased intramuscular fat.»

«…in very old persons muscle mass is an important but not the only determinant of functional status.»

«…cross-sectional as well as longitudinal data indicate that muscle strength declines by approximately 15% per decade in the sixth and seventh decade and about 30% thereafter.»

Symposium: Sarcopenia: Diagnosis and Mechanisms

Evans J Nutr 1997

What is sarcopenia?

«…age-related loss of skeletal muscle mass and strength»

Rosenberg J Nutr 1997

«…loss of skeletal mass, strength and quality…»

Dutta J Nutr 1997

«…sarcopenia should be related to loss of muscle mass … diagnosis should not rely on quantification of functional losses»

Evans J Nutr 1997

Symposium: Sarcopenia: Diagnosis and Mechanisms

Prevalence of sarcopenia

New Mexico Elder Health Study n=883 Hispanic/White men/women♪

	Male n=426	Female n=382
Age (yrs)	73.6±5.8	73.7±6.1
BMI (kg/m^2)	25.9±3.7	26.2±4.6
ASM (kg/m^2)	7.7±0.7	5.9±0.7
%<7.26 (kg/m^2)	13-57%	
%<5.45 (kg/m^2)		23-60%

Sarcopenia

Appendicular Skeletal Mass (kg/m^2) < 2SD below mean of young adults (18-40 yrs)

(Rosetta Study, Wang et al., Am J Physiol 1989)

Baumgartner et al Am J Epidemiol 1998

Sarcopenia* is associated with disability

New Mexico Elder Health Study n=883 Hispanic/White men/women♪

	OR (95% CI)	
	Male	Female
³ 3 disabilities	3.7 (1.4–10.0)	4.1(1.5-11.3)

Cross-sectional analyses adjusted for age, ethinicity, obesity, income, alcool, physical activity, smoking, co-morbidity

*Appendicular Skeletal Mass (kg/m^2) < 2SD below mean of young adults (18-40 yrs)

Baumgartner et al Am J Epidemiol 1998

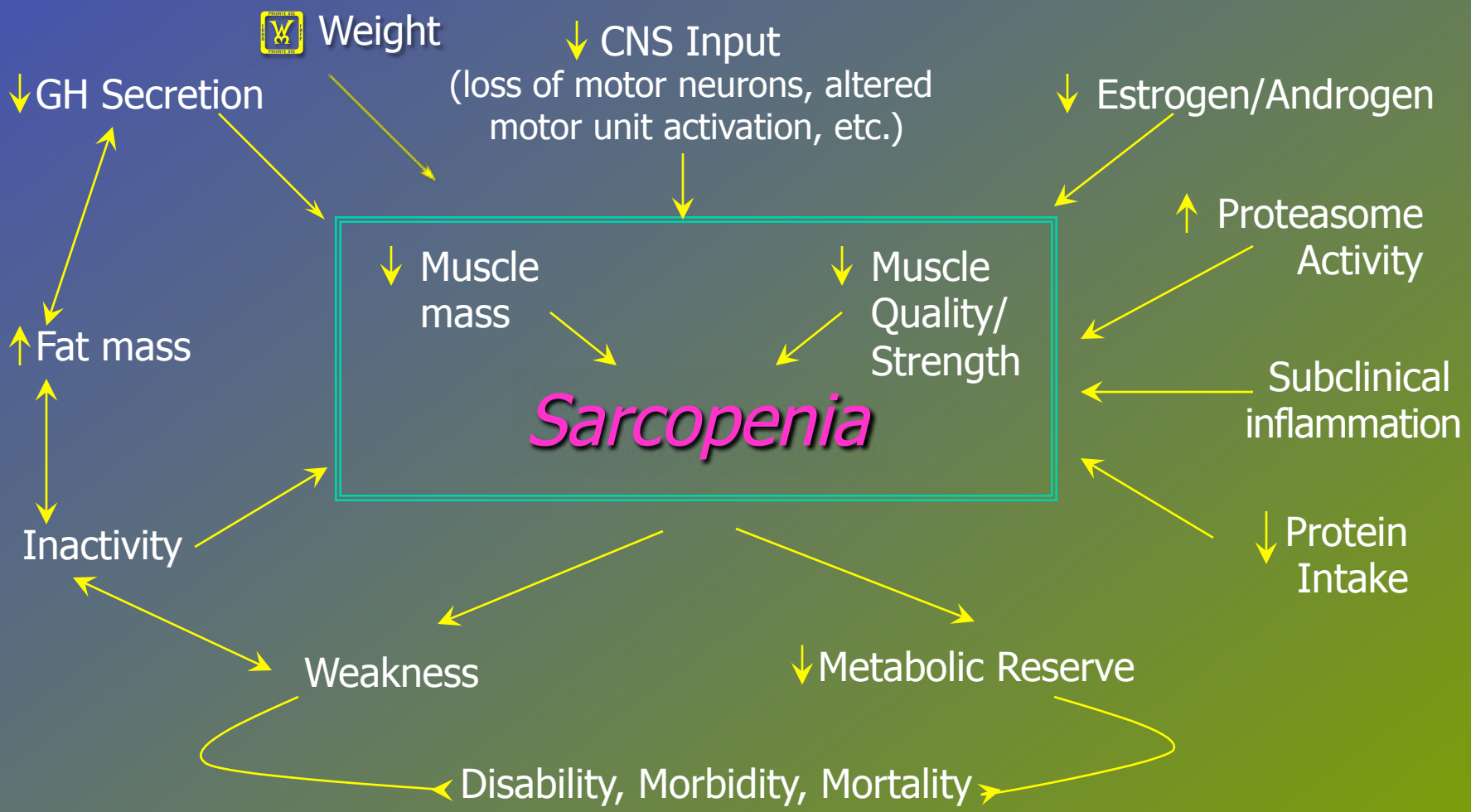
Lean Loss Syndromes

Wasting	Loss of all compartments Negative energy and protein balance
Cachexia	Loss of cell mass… weight or fat Intake near adequate or better Altered metabolism and cytokines
Sarcopenia	Age-associated loss of muscle Generalized withdrawal of anabolic stimuli and/or development of catabolic stimuli??

Roubenoff J Nutr Health Aging 2000

Potential contributors to the development of sarcopenia

Multifactorial Etiology



From Roubenoff J Gerontol 2000

Changes in Fat-Free Mass in Very Old Participants of Framingham Heart Study

FHS 22nd cycle (1992-1993), 232M & 326W, 2-yr follow-up♪

Mean FFM loss in M : -.75±2.1kg and W : -.58±1.52kg (BIA)

	Men		Women	
	₩ (SE)	P	₩ (SE)	P
Serum IGF-1, mg/dL	0.005 (.002)	.002		
Cellular IL-6, quartiles			- 0.14 (.06)	.024

Adjusted for age, baseline FFM index (kg/m^2) and % fat, weight change

Payette et al., JAGS 2003

Cross-sectional associations of elevated inflammatory cytokines (TNF₩, IL-6) with smaller muscle area (CT) & mass (DXA) & lower strength (leg & grip)
(Health ABC, Visser et al., 2002)

Inflammatory markers predict changes in muscle strength but not mass

Longitudinal Aging Study Amsterdam, n=986 men & women, ♪ mean age 74.6 yrs, 3-yr follow-up♪

Il-6 (pg/mL)	Grip strength change (SE)	P	P for trend
<1.7	ref.		
1.7-4.9	-6.37 (1.75)	<.001	<.001
>4.9	-8.15 (2.88)	.005	

Adjusted for age, sex, education, smoking, chronic disease, alcohol, physical activity, BMI, cognition, depression, anti-inflammatory drug use

No significant relationship observed for change in muscle mass (DXA)

Schaap et al 2006

Muscle mass or fat mass
Which one is important for outcome?

FHS 22nd cycle (1992-1993) 753 M & W aged 72 to 95 yrs ♪

«Low skeletal muscle mass (BIA) was not associated with self-reported physical disability but increased fat mass was strong contributor to impairment»

Visser et al J Gerontol 1998

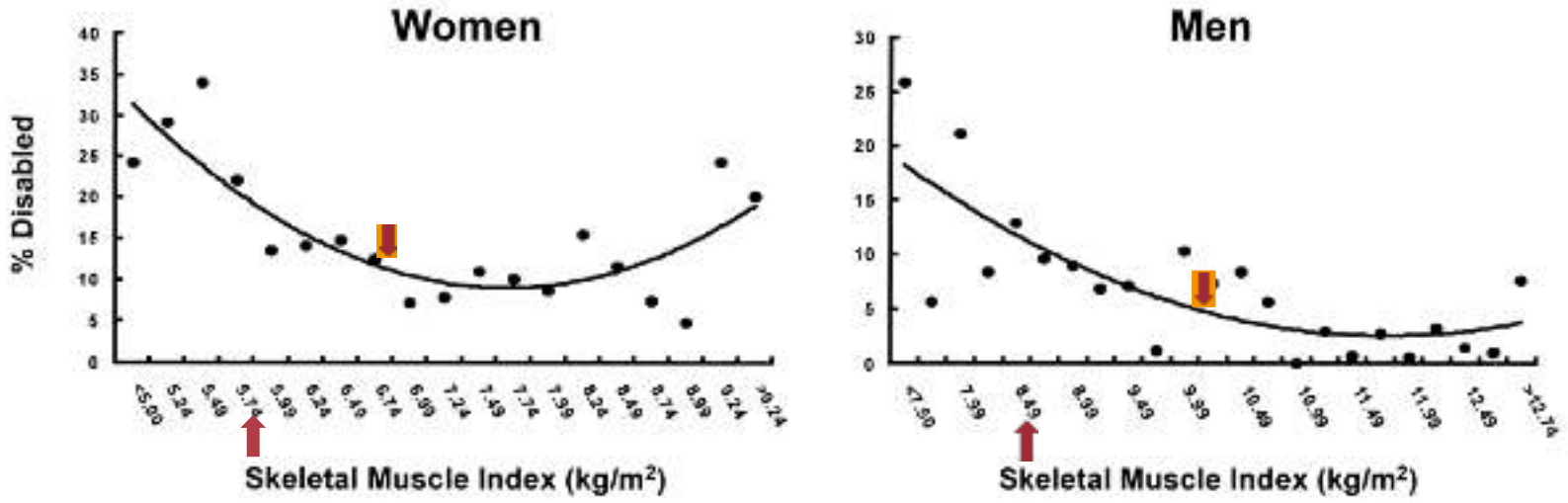
Cardiovascular Health Study 1843M 2504W 3-y follow-up♪

«Low fat-free mass (DXA) was not predictive of mobility-related disability. .. High body fatness is an independent predictor of mobility-related disability...» OR=2.7 (W); 3.08 (M)

Visser et al Am J Clin Nutr 1998

Skeletal Muscle Index and Physical Disability

NHANES III (1988-1994) n=4 449, ¥60 yrs ♪



Muscle mass (kg) (BIA)/height (m)²

OR: 3.3 W (5.75) ; 4.7 M (8.5)

adjusted for age, race, smoking status, alcohol intake, comorbidity, and body fat

Not replicated for incident disability (8yr) in CHS *(Jansen, JAGS 2006)*

* Rosow & Breslau, 1966; Katz et al. 1963

Janssen et al. Am J Epidemiol 2004

Alternative Definition of Sarcopenia* Predicts Incidence of Disability

Health ABC Study, n=2,976 men & women aged 70-79 yrs, 5-yr follow-up♪

Incident Lower Extremity Limitation	HR (95% CI)
Residuals method	
Men	0.91 (0.73 – 1.15)
Women	1.34 (1.11 – 1.61)
aLM/ht^2	
Men	0.76 (0.60 – 0.96)¶
Women	0.75 (0.60 – 0.93)¶

Adjusted for age, race, comorbidity, baseline low LEP, interim hospitalization

¶ NS after adjustment for fat mass

* Appendicular lean mass adjusted for height AND body fat mass (**residuals**)

Delmonico et al J Am Geriatr Soc 2007

Muscle Mass (DXA) or Muscle Strength (Nm*)

Cross-sectional analyses adjusted for race, study site, height

TABLE 2. Linear regression on lower-extremity performance in participants of the Health, Aging, and Body Composition Study, 1997–1998

	Men		Women	
	β(SE)	Stand.β	β(SE)	Stand.β
Body fat (kg)	0.059 (0.019)*	0.098	0.126 (0.032)**	0.149
Leg muscle strength (Nm)	–0.033 (0.004)**	–0.274	–0.088 (0.010)**	–0.259
Leg muscle mass (kg)	–0.064 (0.062)	–0.042	0.183 (0.138)	0.062

*$p < 0.05$, **$p < 0.001$.

NOTE: β = regression coefficient, SE = standard error, Stand.β = standardized regression coefficient; adjusted for race, study site, and body height. A higher lower-extremity performance score indicates poorer performance.

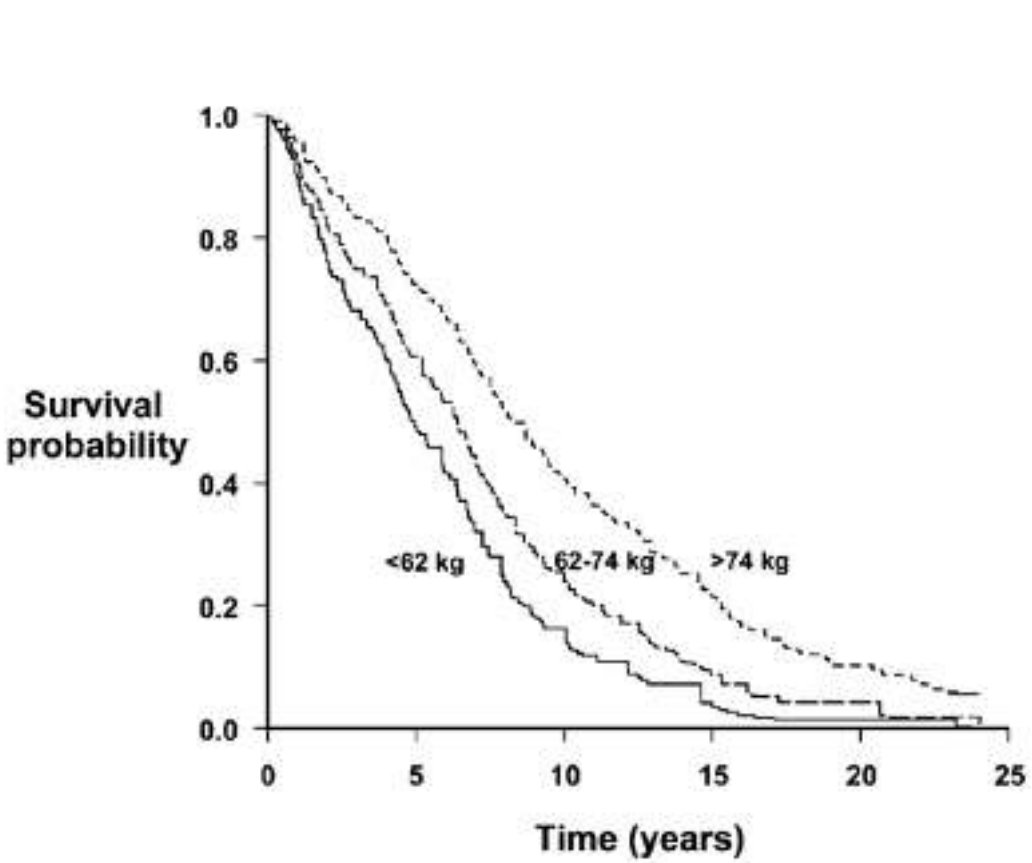
Lower-extremity Performance :Timed repeated chair stands

Leg Muscle Strength (Nm) : Maximal isokinetic torque

Visser et al., Ann NY Acad Sci 2000

Survival curves in for all-cause mortality in 452 men (≥65 yrs) according to grip strength

UK Department of Health & Social Security National Nutrition Survey, 24-yrs follow-up♪



Adjusted for all potential confounding factors, including body composition

Sayer & Cooper Rev Clin Gerontol 2007

Incident Mobility Limitations vs Quartiles of Muscle Parameters

Health ABC Study n=3075, aged 70–79 yrs, 2.5-yr follow-up♪

	Men HR (95% CI)	Women HR (95% CI)
Mid-thigh muscle area		
low	1.45 (0.92–2.27)	1.34 (0.95–1.88)
2	1.18 (0.79–1.77)	1.01 (0.74–1.38)
3	1.39 (0.96–2.02)	1.00 (0.75–1.32)
4 high	1.0	1.0
Mid-thigh muscle attenuation		
1 low*	**1.79 (1.22–2.65)**	**1.55 (1.10–2.17)**
2	1.38 (0.94–2.02)	**1.69 (1.23–2.34)**
3	1.06 (0.72–1.58)	1.33 (0.96–1.85)
4 high	1.0	1.0
Knee extensor strength		
1 low	**1.66 (1.10–2.51)**	**1.69 (1.22–2.35)**
2	1.34 (0.89–2.02)	**1.53 (1.11–2.10)**
3	1.23 (0.83–1.82)	1.08 (0.78–1.49)
4 high	1.0	1.0

Adjusted for age, race, study site, body height, total body fat mass, education, alcohol consumption, smoking status, physical activity, prevalent disease, self-rated health, depression, cognitive status, and the other variables in the table

*Lower muscle tissue attenuation indicates greater fat infiltration into the muscle.

Visser et al J Gerontol:MS 2005

Muscle Size & Quality → Mortality

Health ABC Study n=2292 men & women, aged 70–79 yrs♪

		HR (95% CI)
Size	CT leg muscle area (per 28.1 cm^2) *	1.16 (0.97–1.39)
	DXA leg lean (per 1.8 kg)	0.95 (0.76–1.20)
	DXA arm lean (per 0.9 kg)	0.99 (0.77–1.26)
Quality	Quad strength/CT area (per 0.2 units)	**1.24 (1.11–1.40)**
	Quad strength/DXA leg lean (per 3.4 units)	**1.34 (1.19–1.51)**
	Grip strength/DXA arm lean (per 2.5 units)	**1.23 (1.09–1.40)**

Adjusted additionally for age, race, height, smoking status, physical activity level, chronic conditions, education, log IL-6, and depression (CES-D)

** Standard deviation; **CT** subcutaneous and intermuscular fat, **DXA** total fat, leg lean mass, or arm lean mass*

Newman et al J Gerontol:MS 2006

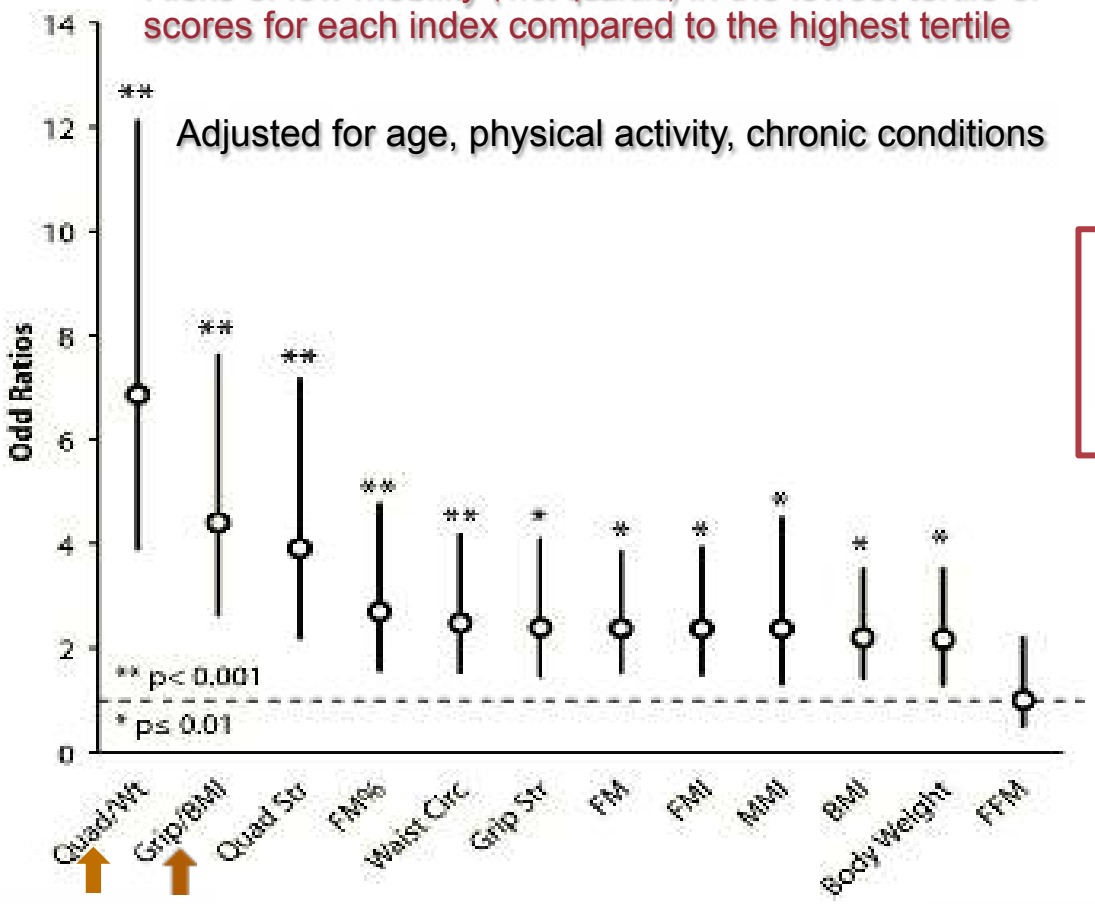
Muscle cross-sectional area NOT associated with ↑ mortality (InChianti Study)

Cesari et al J Gerontol MS 2009

Relative Strength and Mobility

NuAge Study, n=904 men & women, aged 68-82 yrs, cross-sectional

Risks of low mobility (1rst quartile) in the lowest tertile of scores for each index compared to the highest tertile

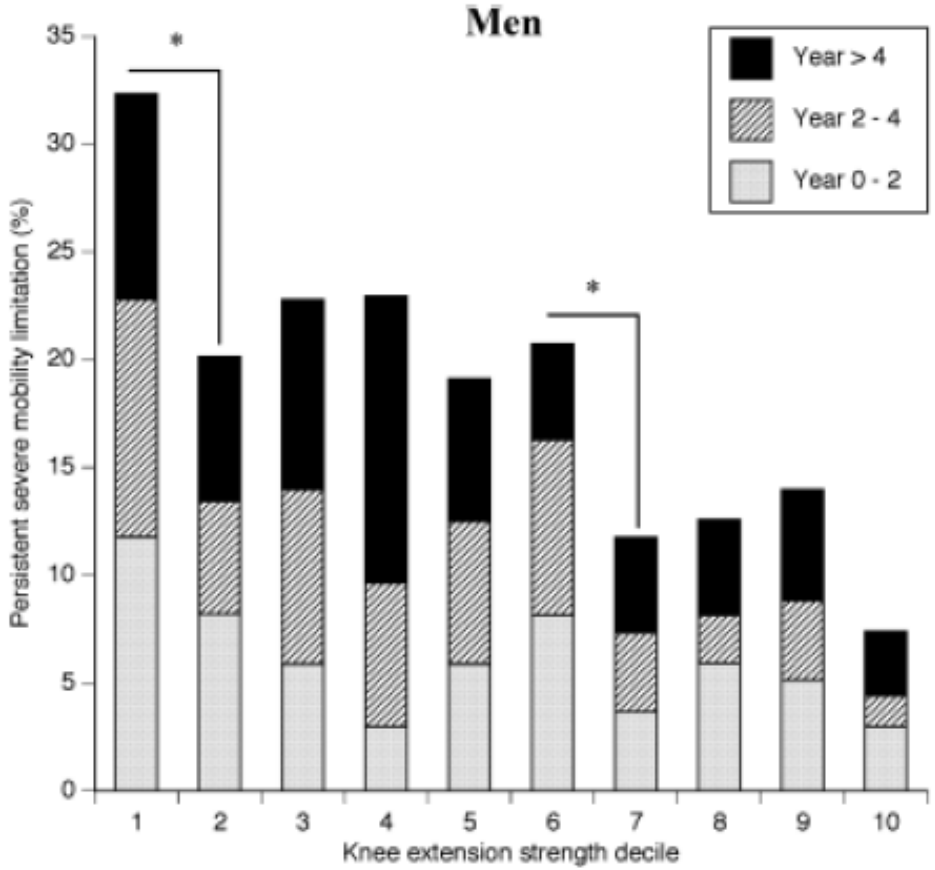


Mobility score
5 measures of lower extremity function

Choquette et al JNHA 2010

Accumulated rates of mobility limitation* by knee extension strength/body weight (Nm/kg)

Health ABC Study, 1,355M 1,429W, 73.6±2.85yrs, no mobility limitation, 5.9-yr follow-up (median)♪



* Perceived lot of difficulty or inability to walk one-quarter of a mile or climb 10 steps

Manini et al JAGS 2007

Sarcopenic Obesity

Sarcopenia: skeletal muscle mass ↓ 2 SD below mean of young population or <7.26 kg/m^2 M and <5.45 kg/m^2 W

+

Obesity: body fat percentage greater than median or >27% M and 38% W

New Mexico Aging Process Study, Baumgartner Ann N Y Acad Sci 2000

Sarcopenia: two lower quintiles of muscle mass (<9.12 kg/m^2 M and <6.53 kg/m^2 W)

+

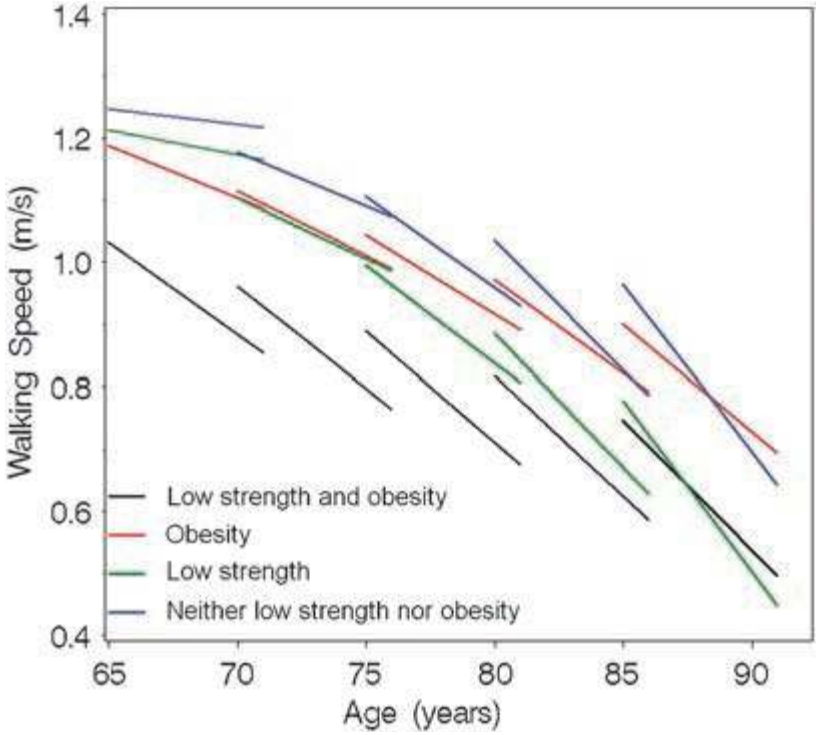
Obesity: two highest quintiles of fat mass (>37.16% M and >40.01% W)

NHANES III, Davidson et al JAGS 2002

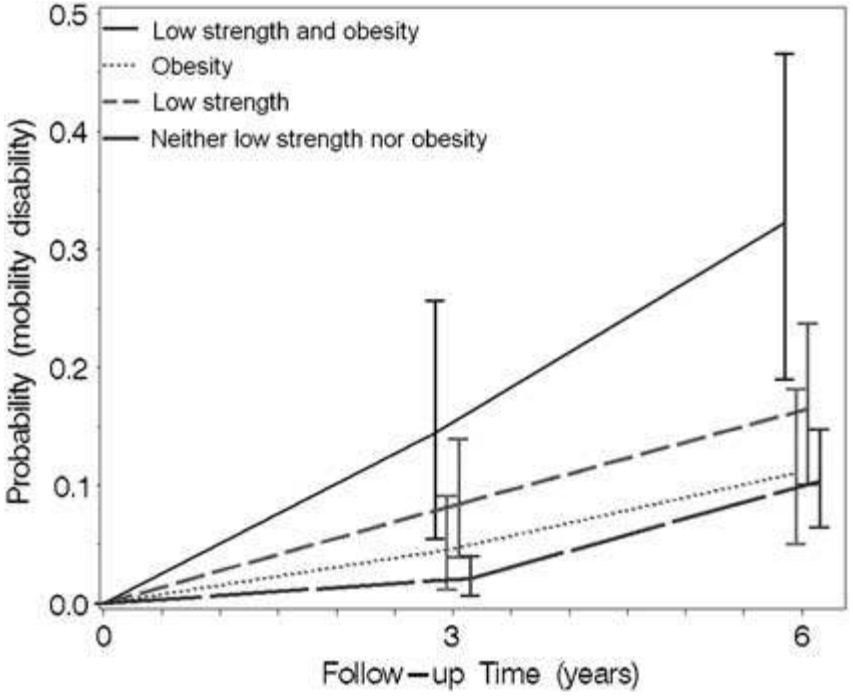
Sarcopenic Obesity & Mobility

InCHIANTI study, n=930 M & W 65+ yrs, 6-yr follow-up ♪

Lower sex-specific tertile of handgrip strength; BMI >30 kg/m^2



Longitudinal change in walking speed between ages 65–85 years according to the combination of low muscle strength and obesity.



Probability rate of a new mobility disability (95% CI) according to combination of low muscle strength and obesity among persons aged 65–85 years.

Stenholm et al Curr Opin Clin Nutr Metab Care 2008

Longitudinal changes in muscle mass, strength, quality and infiltration

Health ABC Study, n=1,678, aged 70-79yrs at baseline, 5-yr follow-up♪

- ✓ Loss of isokinetic leg muscle torque (MT) : M 16.1% ; W 13.4%
- ✓ Decreases in strength (MT) is 2-5 times greater than loss in muscle area in weight looser and weight stable → muscle quality
- ✓ Weight gain did not prevent loss of muscle strength (MT) despite ↑ muscle area
- ✓ Age-related increase in intermuscular fat in men & women independent of changes in weight (P<0.001)

Goodpaster et al J Gerontol 2006; Delmonico et al Am J Clin Nutr 2009

Some conclusions…

- ✓ Cross-sectional associations not always replicated in incident decline in physical function
- ✓ In addition to loss of muscle mass, definition of sarcopenia should include body height & fat
- ✓ Decrease in strength is more rapid than concomitant loss of muscle mass
- ✓ Definition based on muscle strength may be more relevant for functional outcomes
- ✓ Is sarcopenic obesity a useful concept?

Visser M, JNHA 2009

Sarcopenia ≠ Dynapenia

Sarcopenia

age-related muscle atrophy
AND
≠muscle strength / endurance

→ Same etiology & consequences

Dynapenia

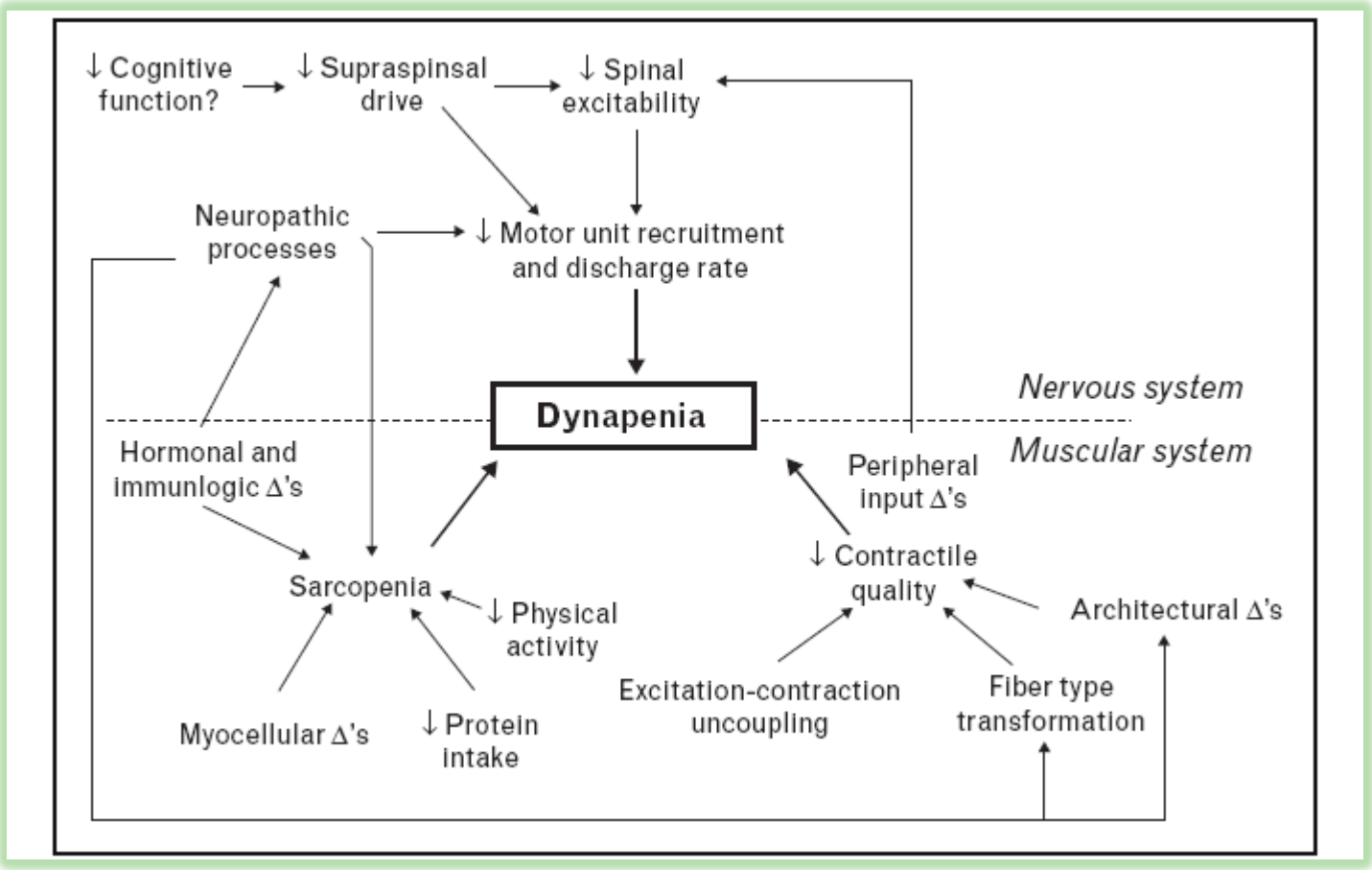
«poverty of strength»♪

«The age-related loss in muscle strength and function that partially results from muscle atrophy»

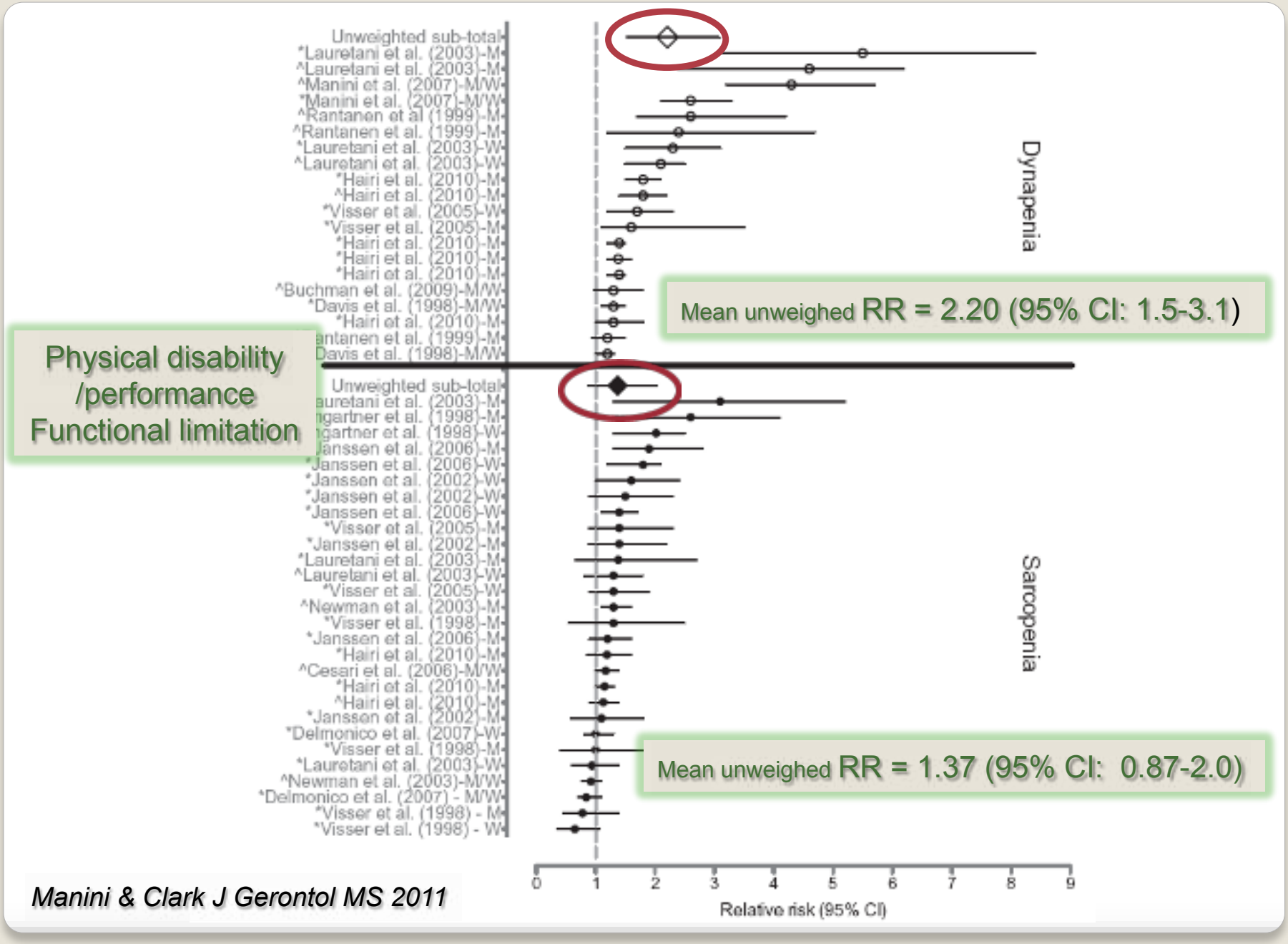
- Better understanding of determinants/mechanisms of age-related loss in muscle strength
- Designing of interventions to improve functional/physical capacity

Clark & Manini J Gerontol 2008

Proposed biologic mechanisms contributing to dynapenia



Clark & Manini Curr Opin Clin Nutr Metab Care 2010



Manini & Clark J Gerontol MS 2011

Sarcopenia
European Consensus on Definition and Diagnosis

Report of the European Working Group on Sarcopenia in Older People♪

What is sarcopenia ?

Criteria for the diagnosis of sarcopenia

Low muscle mass AND ⌈ low muscle strength
OR
low physical performance

Note : replacing sarcopenia by dynapenia might lead to confusion

Cruz-Jentoft et al Age Ageing 2010

Sarcopenia
European Consensus on Definition and Diagnosis

Report of the European Working Group on Sarcopenia in Older People♪

What is sarcopenia ?

Table 3. EWGSOP conceptual stages of sarcopenia

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

Cruz-Jentoft et al Age Ageing 2010

What parameters define sarcopenia?

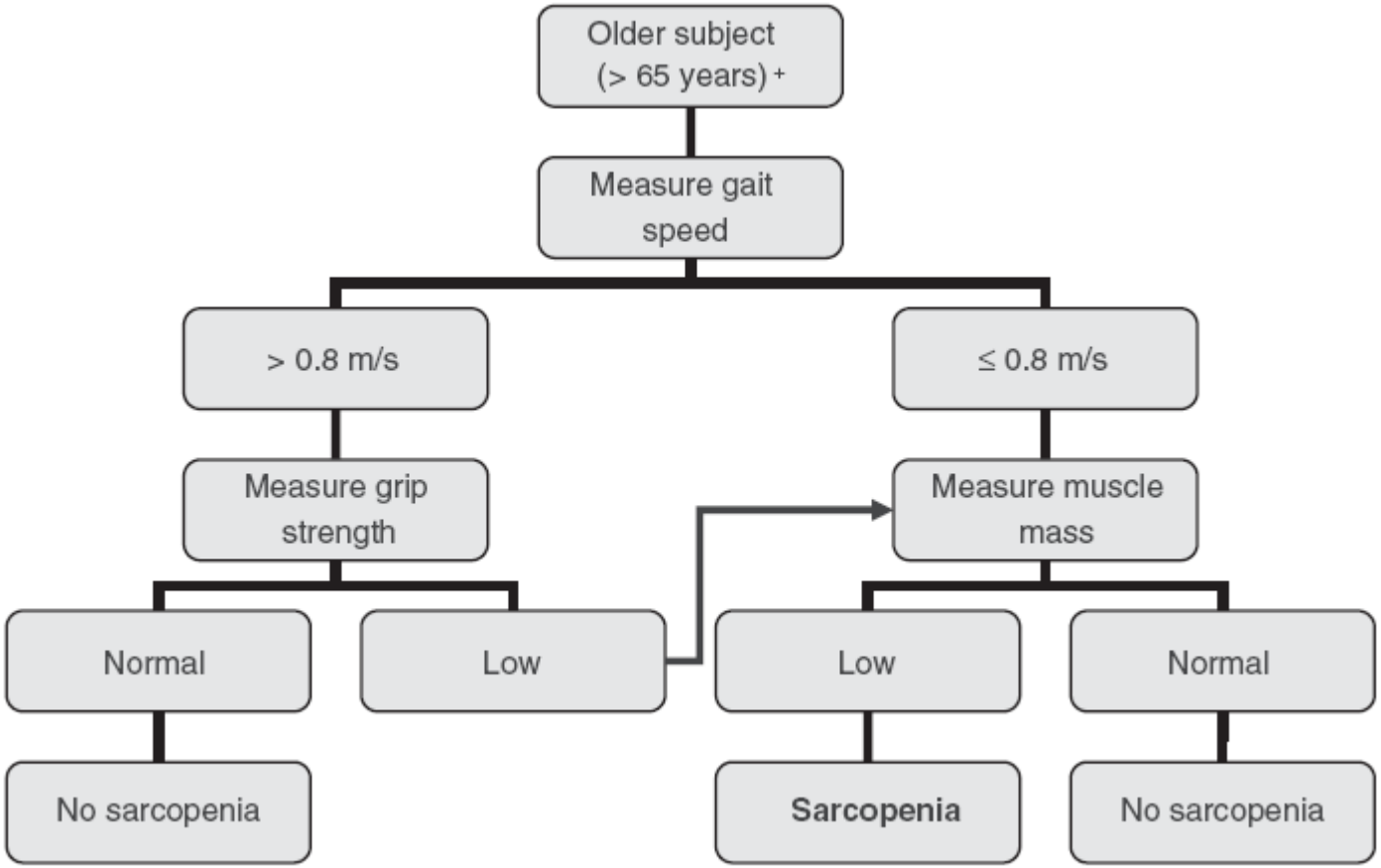
Report of the European Working Group on Sarcopenia in Older People♪

Variable	Research	Clinical practice
Muscle mass	CT MRI DXA BIA Body K/fat-free soft tissue	BIA DXA anthropometry
Muscle strength	Handgrip strength Knee flexion/extension Peak expiratory flow	Handgrip strength
Physical performance	Short Physical Performance Battery (SPPB) Usual gait speed Timed get-up-and-go test Stair climb power test	SPPB Usual gait speed Get-up-and-go test

Cruz-Jentoft et al Age Ageing 2010

Suggested Algorithm for sarcopenia case finding in older individuals

Report of the European Working Group on Sarcopenia♪



Cruz-Jentoft et al Age Ageing 2010

Sarcopenia
una definicion *todavía* en evolucion

- Epidemiology
- Etiology (vs disease)
- Relation to other geriatric syndromes (e.g. frailty)
- Lifestyle determinants (nutrition, physical activity)
- Consequences
- Targets for intervention

Need for well-designed research studies
«longitudinal & intervention»
High-quality measures & data

Gracias por su atencíon