



APPROCCI INTERDISCIPLINARI IN REUMATOLOGIA
6a Edizione
GERIATRIA E MALATTIE REUMATICHE)



Sarcopenia

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S.C. GERIATRIA-MALATTIE METABOLICHE DELL'OSSO

Torino, 12 Ottobre 2018

CONFLICT OF INTEREST

Erre Kappa, Professional Dietetics, Bruno
Farmaceutici , Amgen, Eli Lilly, Alfa-Sigma, Co-
founder of NOVAICOS

AGENDA

- Sarcopenia: what are we talking about?
- Sarcopenia, falls and fractures
- Relationship between skeletal muscle and bone
- Sarcopenia a socio economic burden
- Conclusions

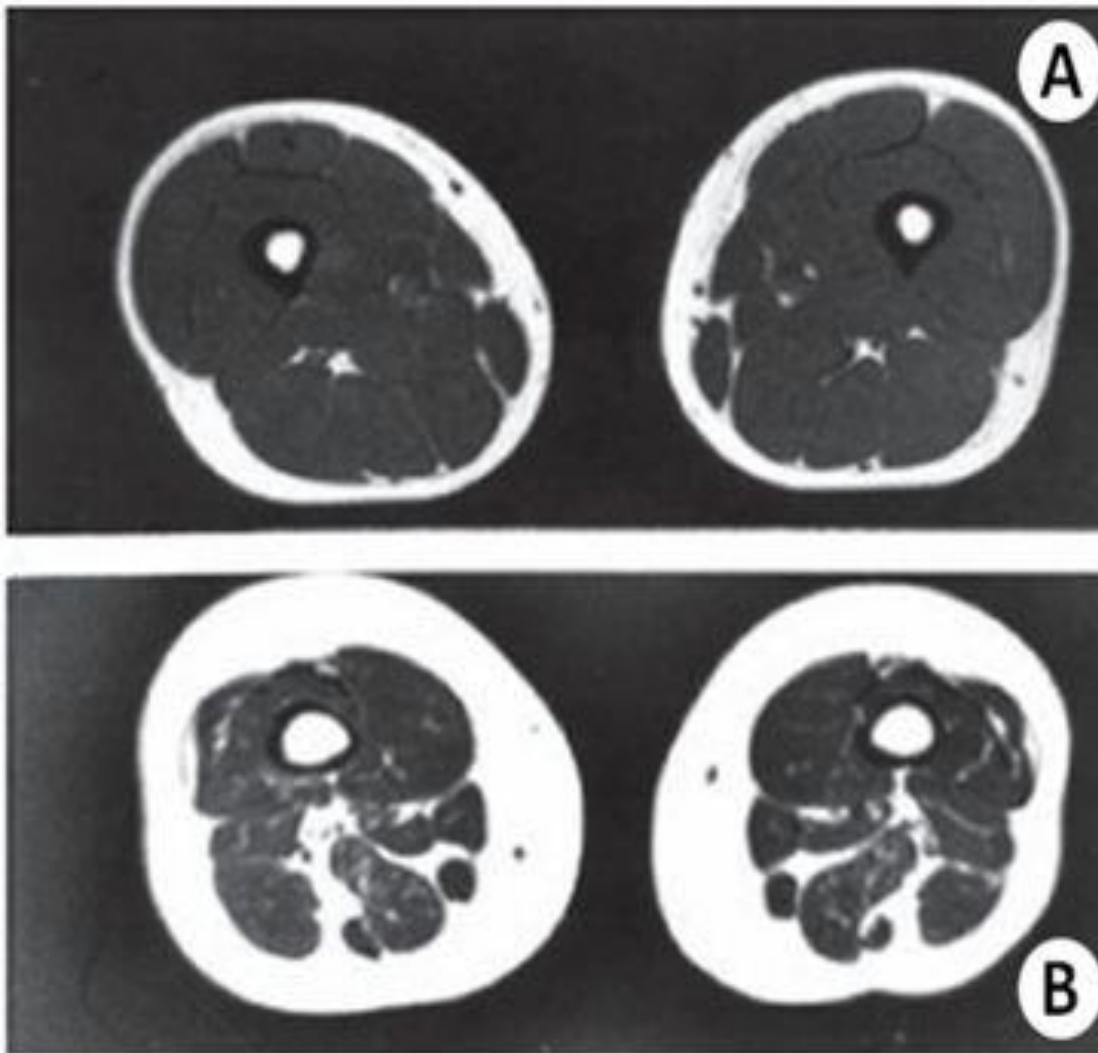
SARCOPENIA

Greek, 'lack of flesh', loss of muscle mass and strength with aging



SARCOPENIA

Altered muscle structure



Criteria for the diagnosis of sarcopenia



Criterion	Slowness	Weakness	Low lean mass	Summary definition
International Working Group	Gait speed <1.0 m/s	Not included	ALM/ht ² ≤7.23 kg/m ²	Sarcopenia: slowness and low lean mass
EWGSOP	Gait speed ≤0.8 m/s	Grip strength <30 kg	ALM/ht ² ≤7.23 kg/m ²	(1) Sarcopenia: low lean mass plus slowness or weakness
				(2) Severe sarcopenia: all three criteria

Criterion	Slowness	Weakness	Low lean mass	Summary definition
FNIH Sarcopenia Project primary definition	Gait speed ≤ 0.8 m/s	Grip strength < 26 kg	ALM/body mass index < 0.789	(1) Weakness and low lean mass
				(2) Slowness with weakness and low lean mass
Baumgartner	ND	ND	$ALM/ht^2 \leq 7.23$ kg/m ²	Low lean mass
Newman	ND	ND	Residual of actual ALM–predicted ALM from equation	Low lean mass

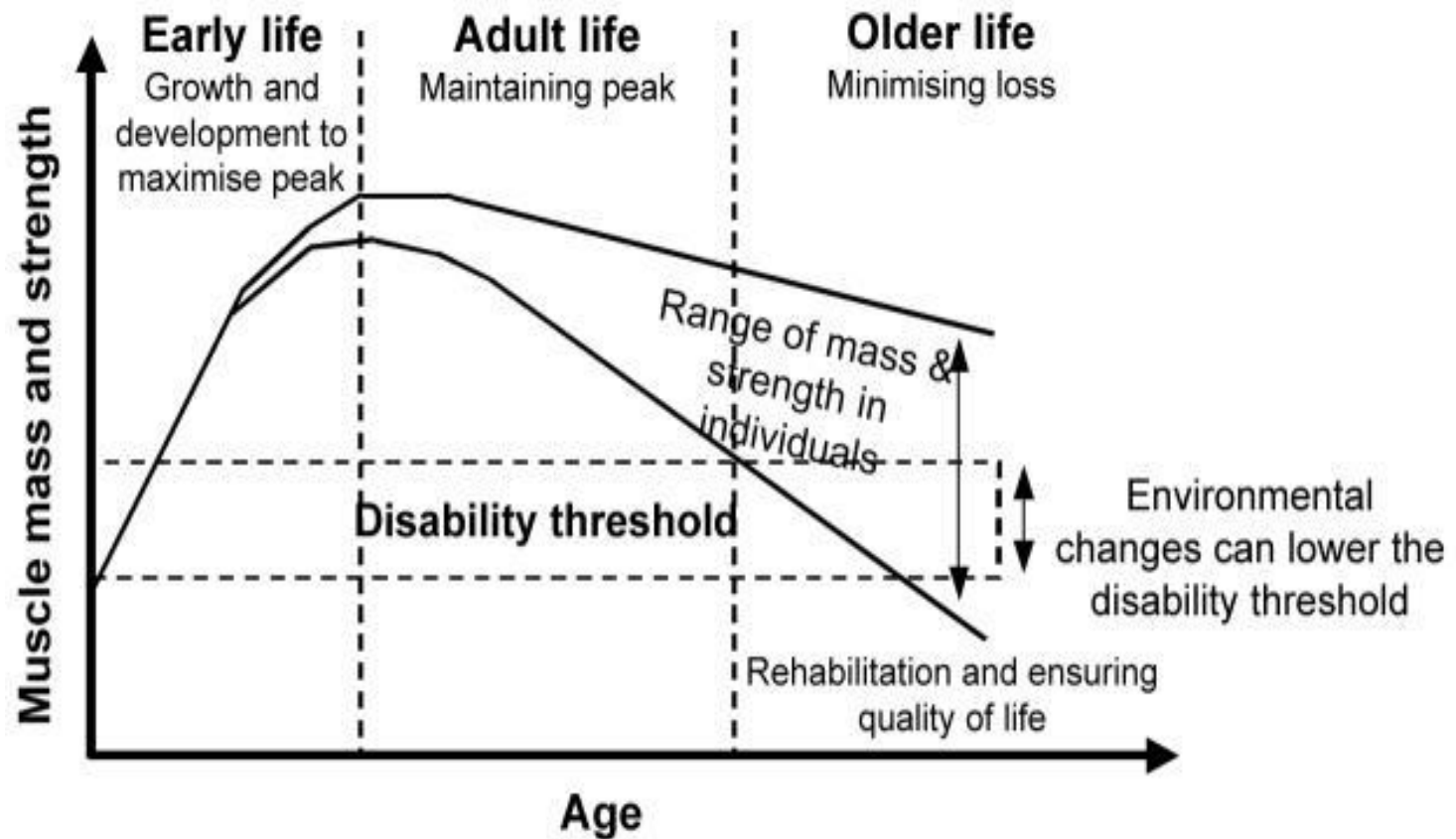
Sarcopenia

Disease or normal aging?

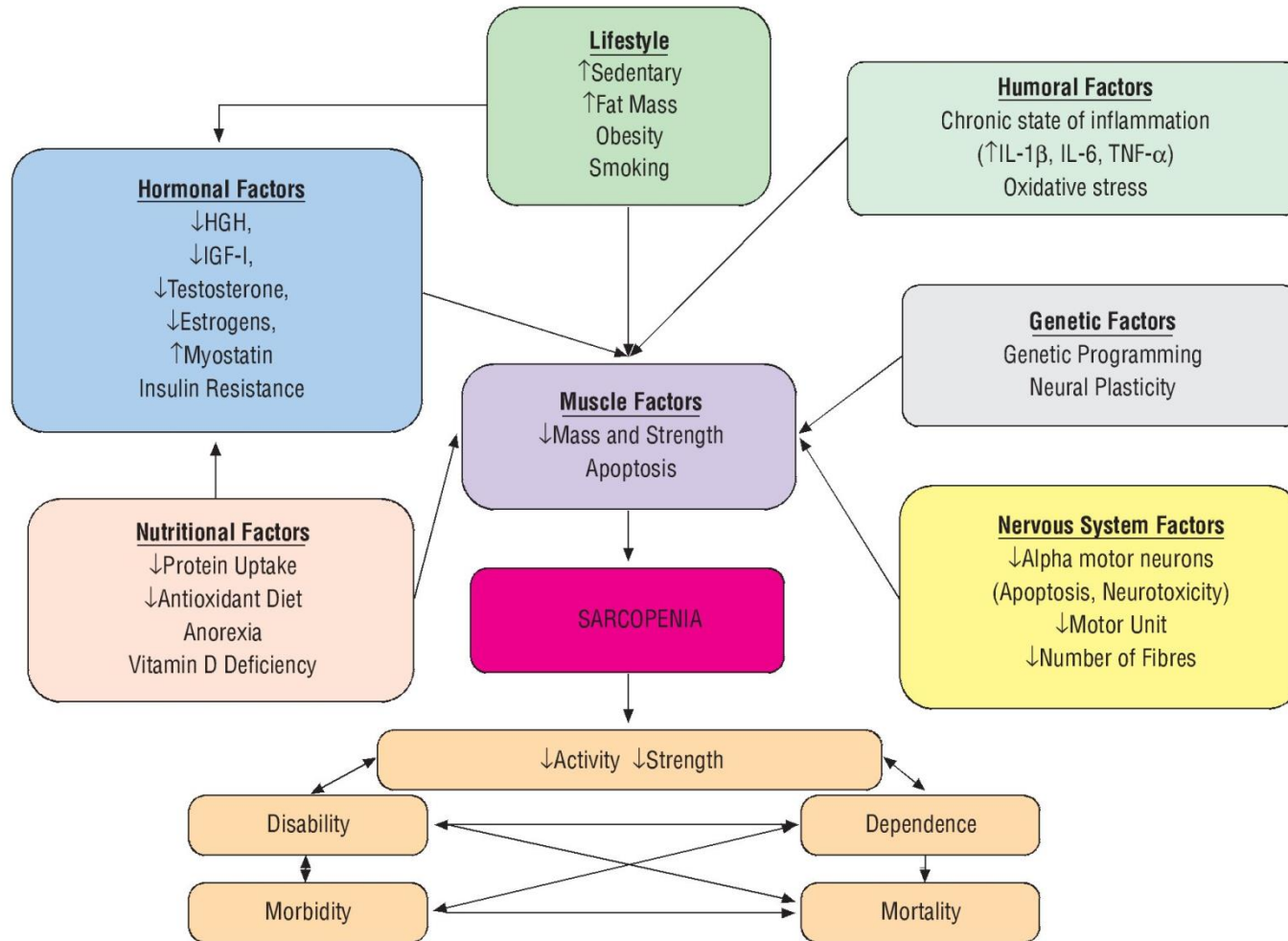


Sarcopenia

Disease or normal aging?

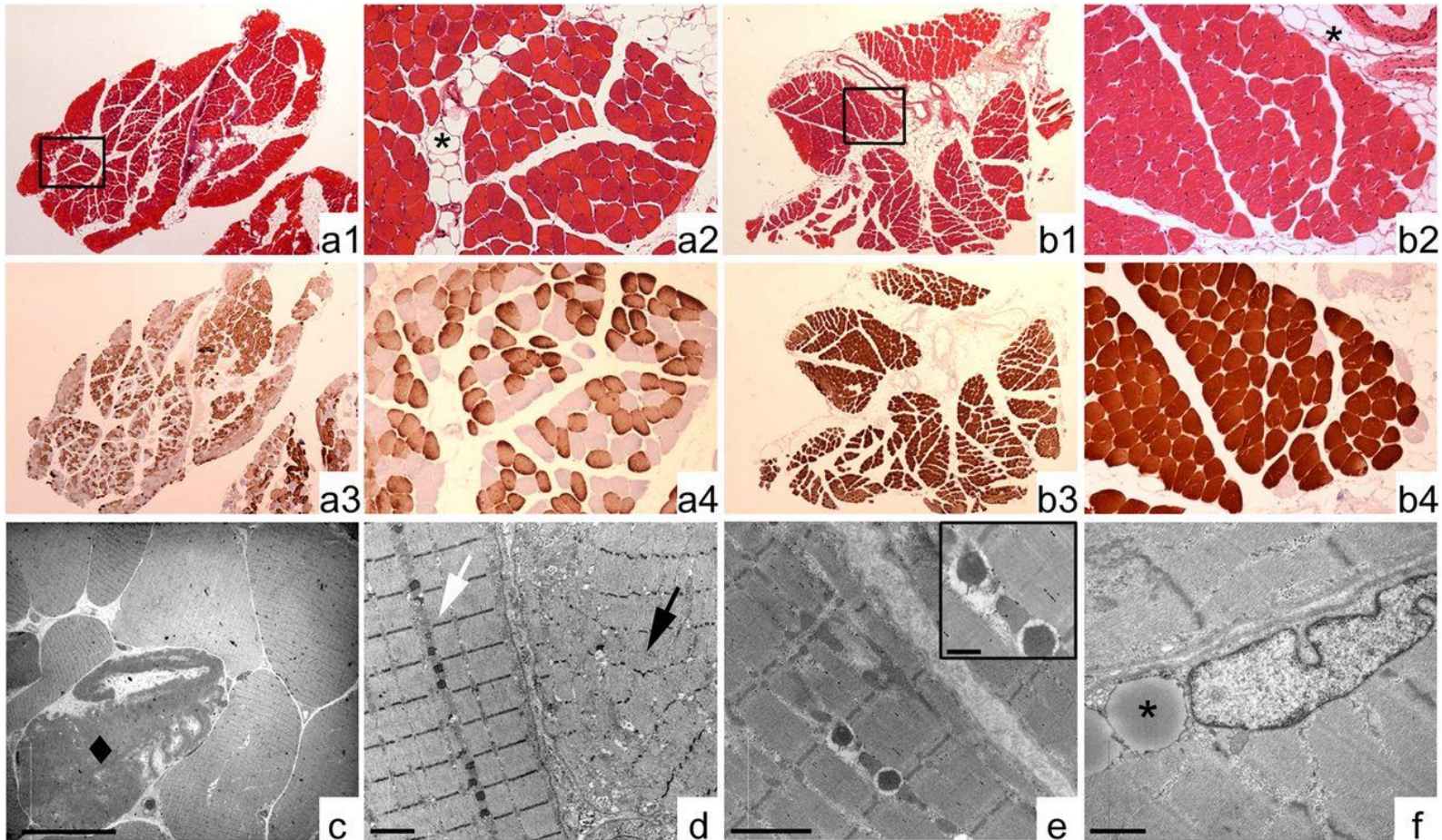


Ethiologic factors in sarcopenia

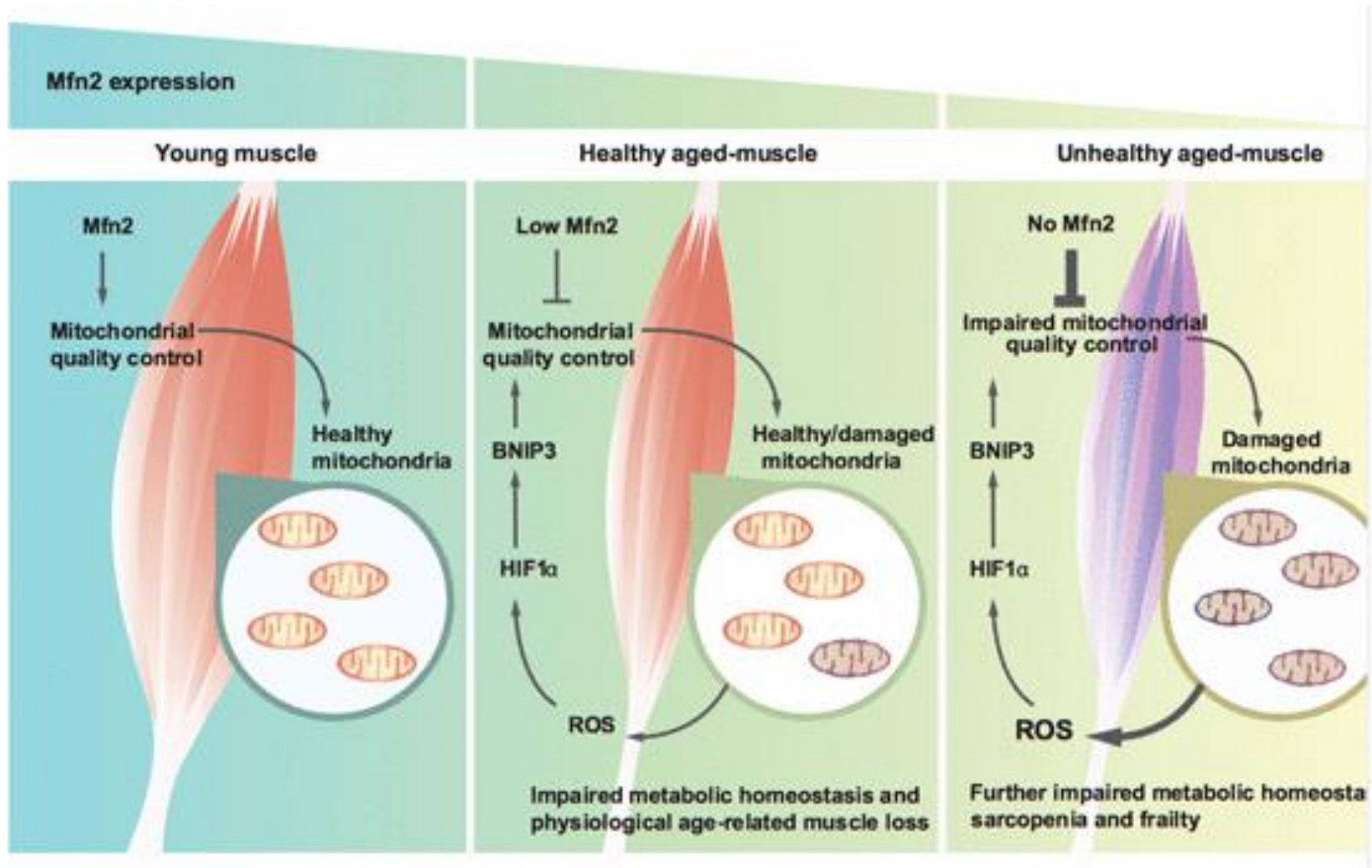


Sarcopenia

Changes in Muscle Anatomy



Sarcopenic muscle function



AGENDA

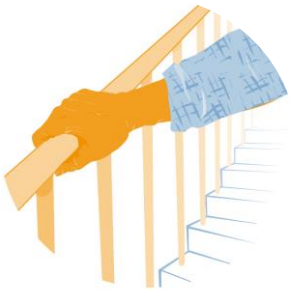
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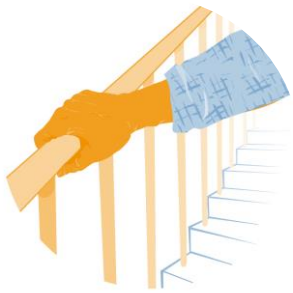
✓ Sarcopenia: what are we talking about?

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- Conclusions



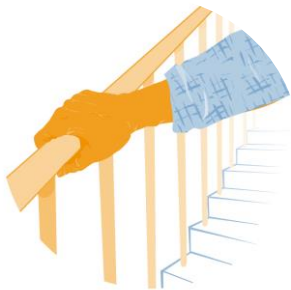
Falls

- Falls are a major cause of morbidity and mortality in elderly people
- Each year, about 20–35% of older adults suffer a fall worldwide

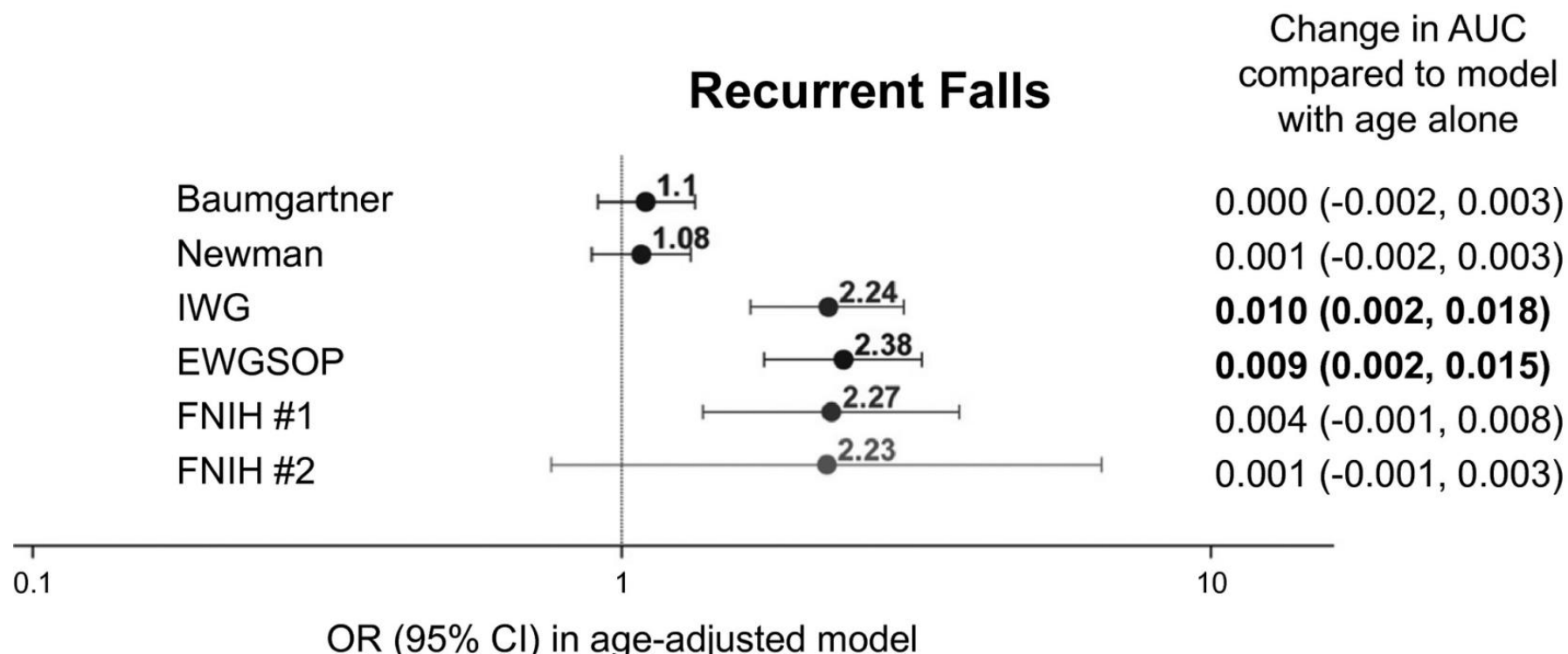


Sarcopenia and falls

	Unadjusted	Model 1	Model 2	Model 3
	Hazard ratio (95% confidence interval)			
Sarcopenia	3.45 (1.68–7)	3.25 (1.54–6.88)	2.55 (1.06–6.14)	3.23 (1.25–8.29)
Age	1.02 (0.93–1.13)	1.01 (0.92–1.10)	1.04 (0.94–1.14)	
Gender (female)	2.19 (0.98–6.53)	2.79 (1.00–7.76)	3.94 (1.97–9.99)	
Cognitive impairment (CPS)	1.22 (0.90–1.66)	1.21 (0.86–1.71)		
ADL impairment	1.01 (0.78–1.31)	0.94 (0.78–1.27)		

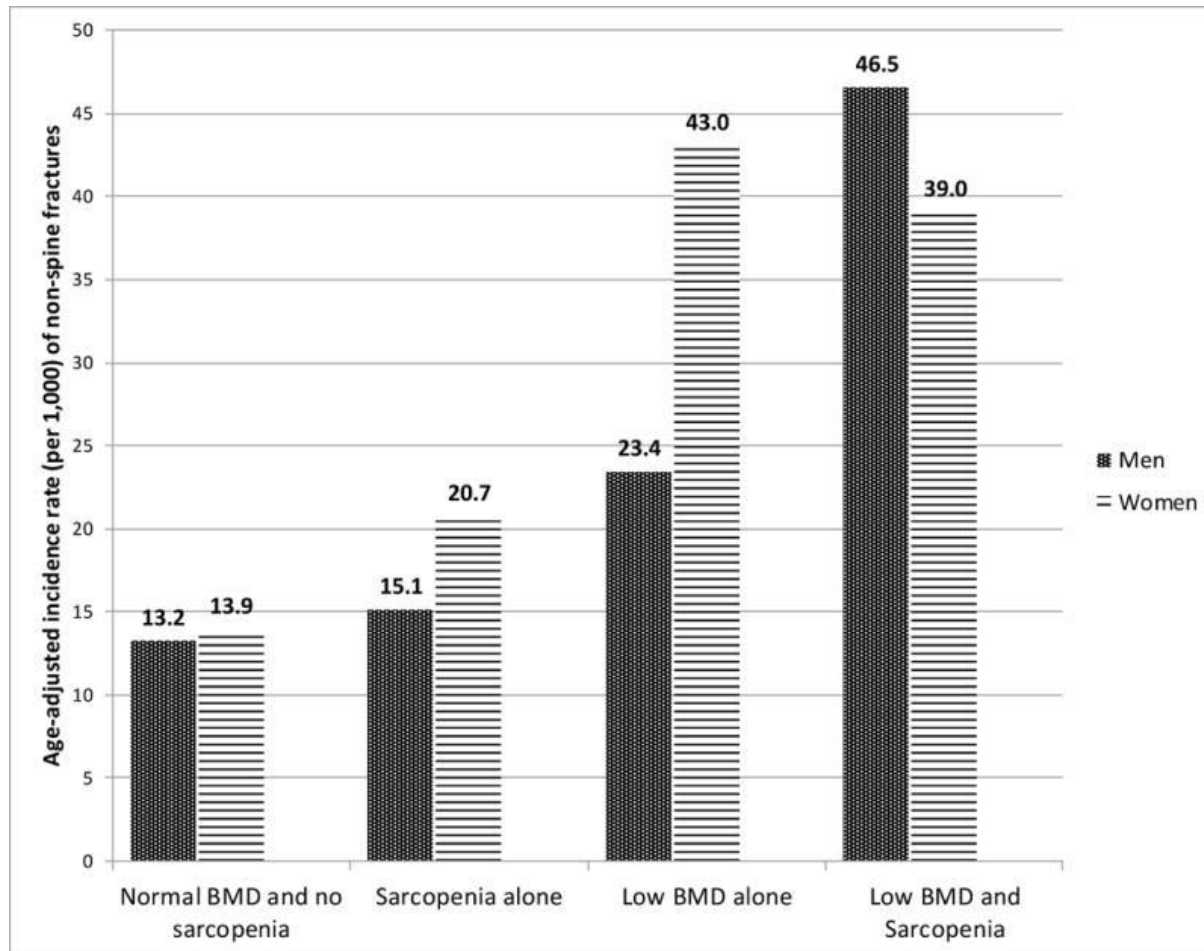


Sarcopenia and falls





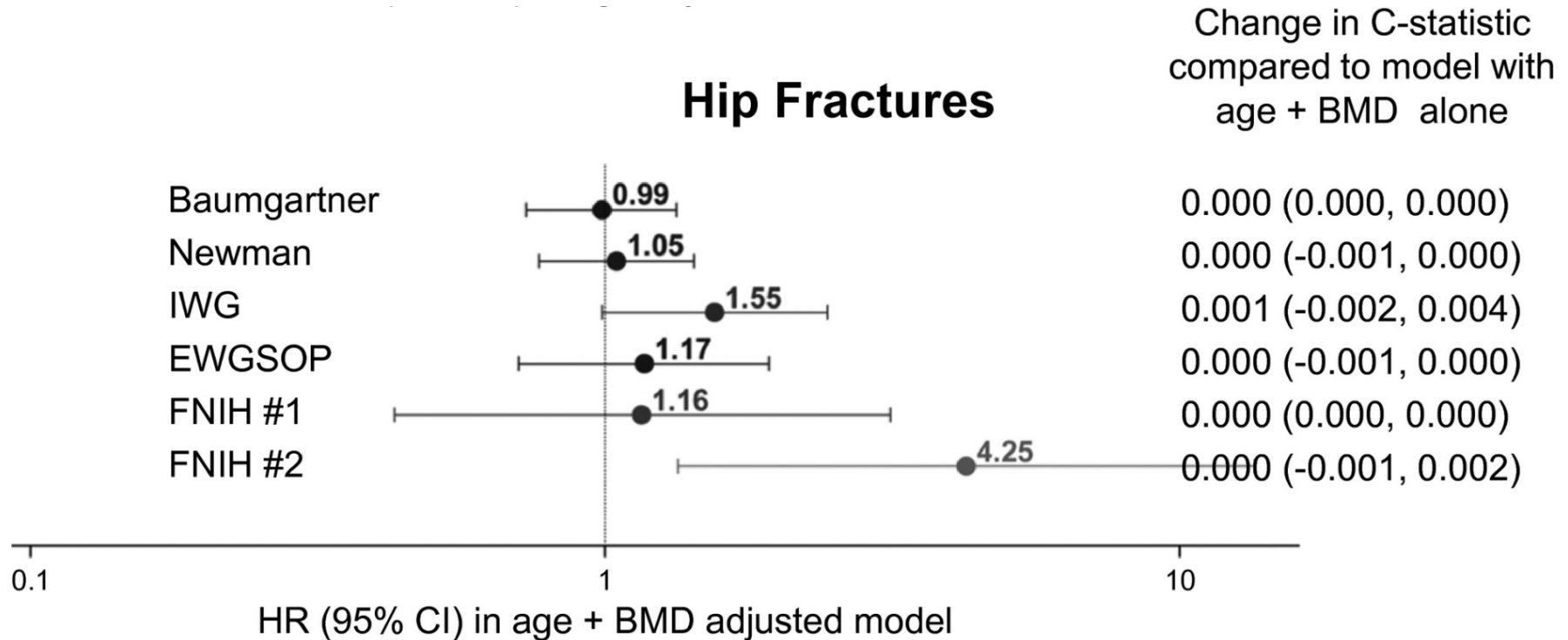
Sarcopenia and fractures





Sarcopenia and fractures

Hip Fractures



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Endocrine regulation

E.g. GH / IGF's / IGFBP's
Glucocorticoids
Sex steroids
Vitamin D
Myostatin, follistatin, ...

Nutrition

Amino acids, glucose,
fatty acids, calcium, ...

Nervous system

- Muscle
- Bone metabolism

Shared regulation

Bone

Growth factors,
cytokines, ...

Muscle

Growth factors
Myokines...

Bone-muscle interactions

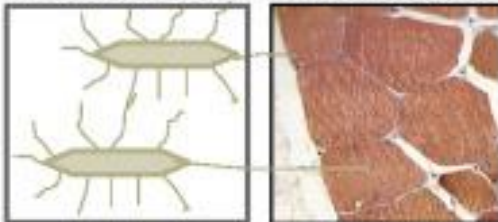
Biomechanical signals/ Physical exercise

Muscle contractions
(via tendons and entheses)

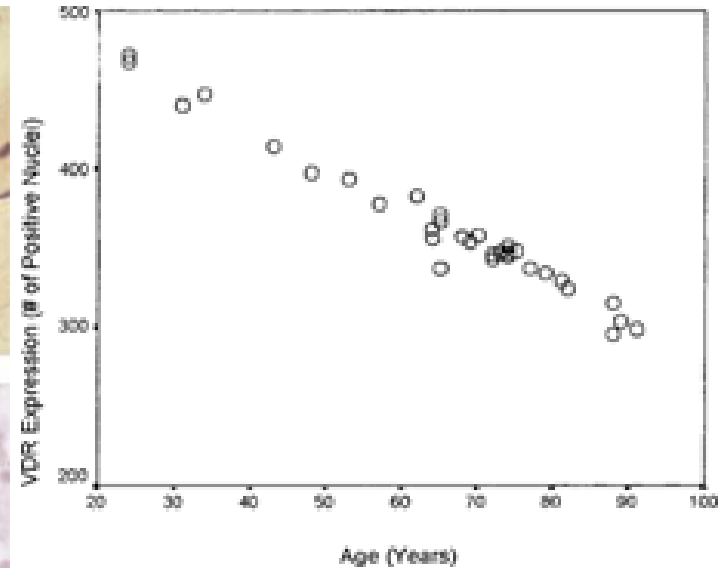
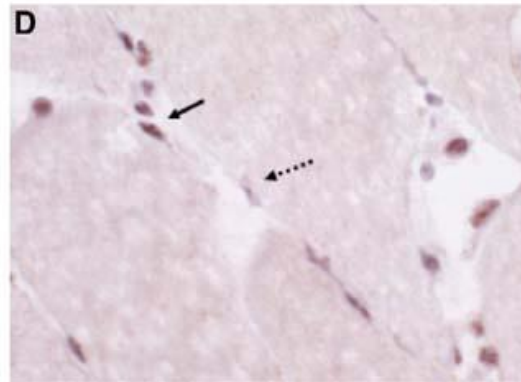
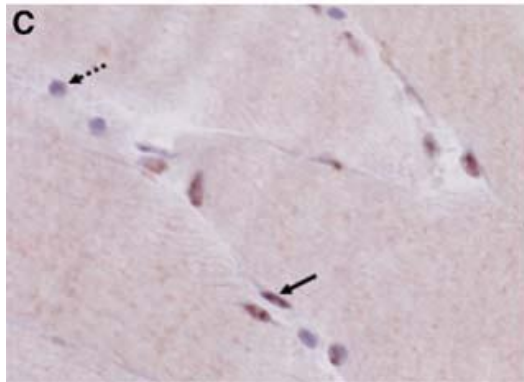
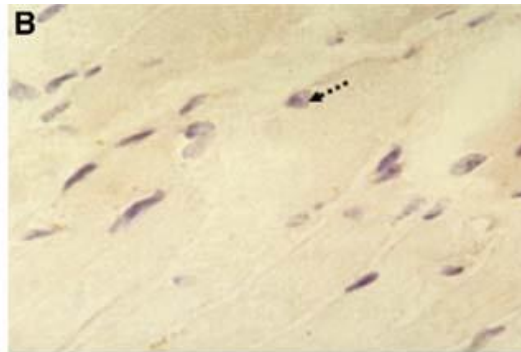
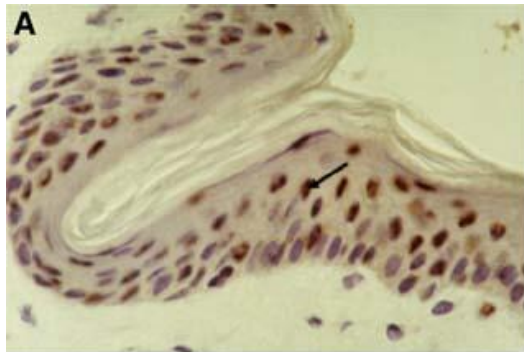
Ground reaction forces

Gravitation

Intercellular communication?

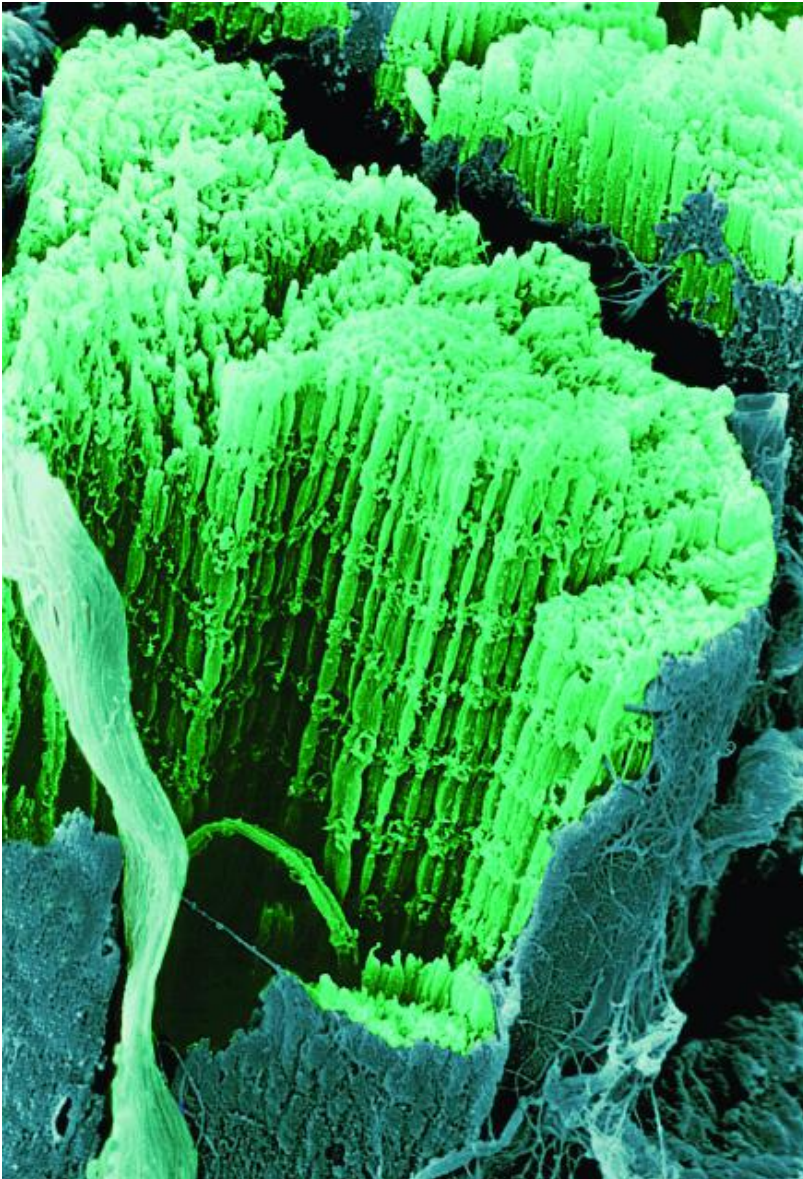


Human skeletal muscle expresses VDR

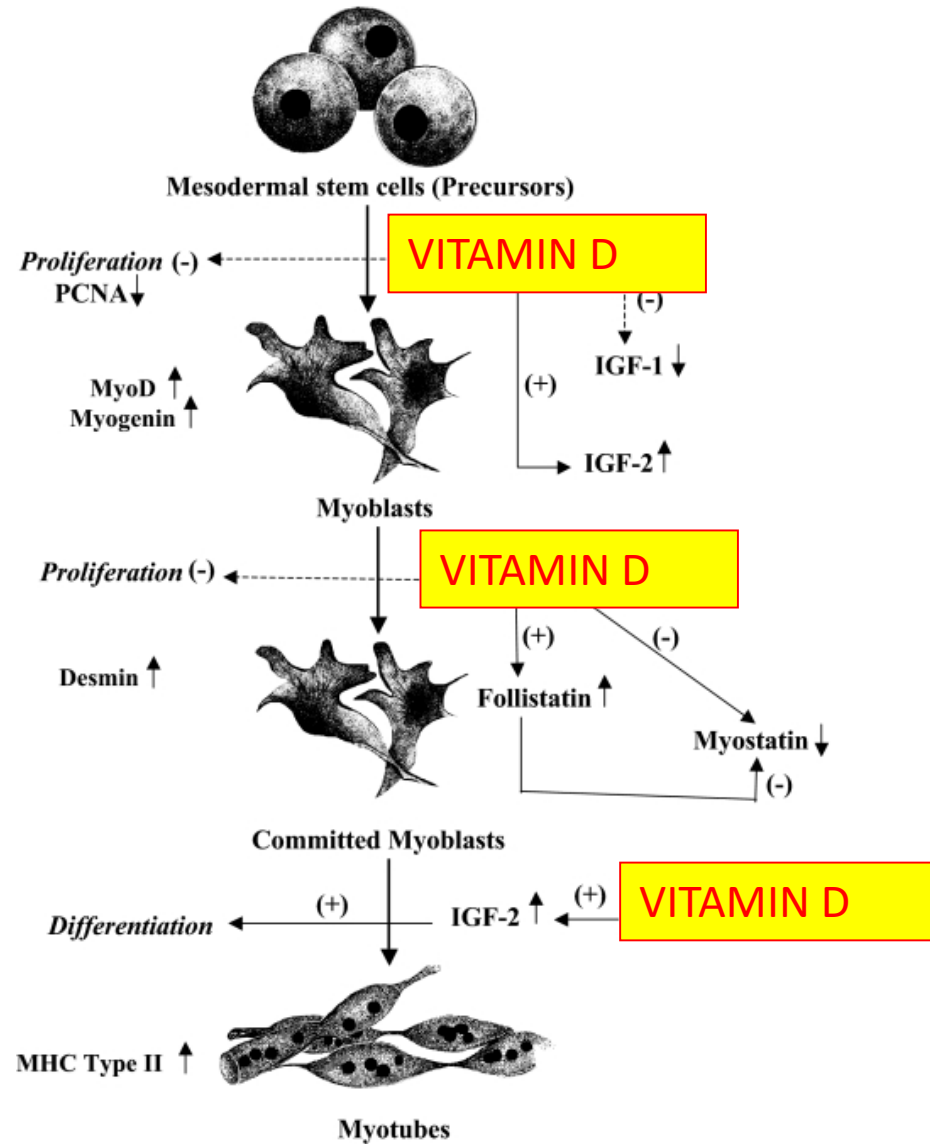


- Regulation of calcium transport
- Uptake of inorganic phosphate for production of energy-rich phosphate compounds
- Protein synthesis

Vitamin D and muscular development

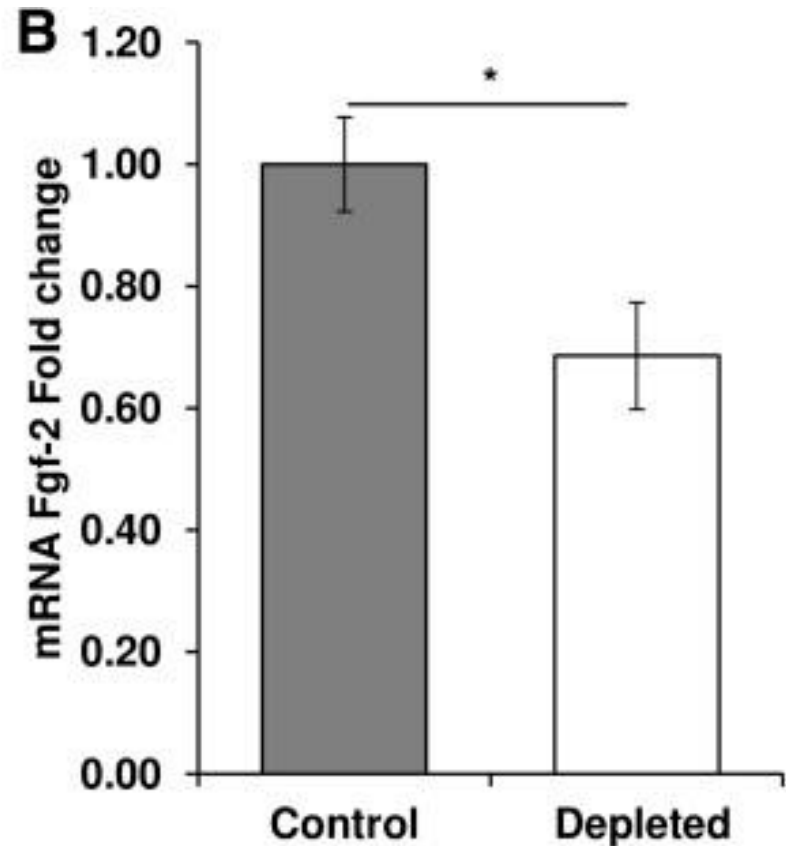
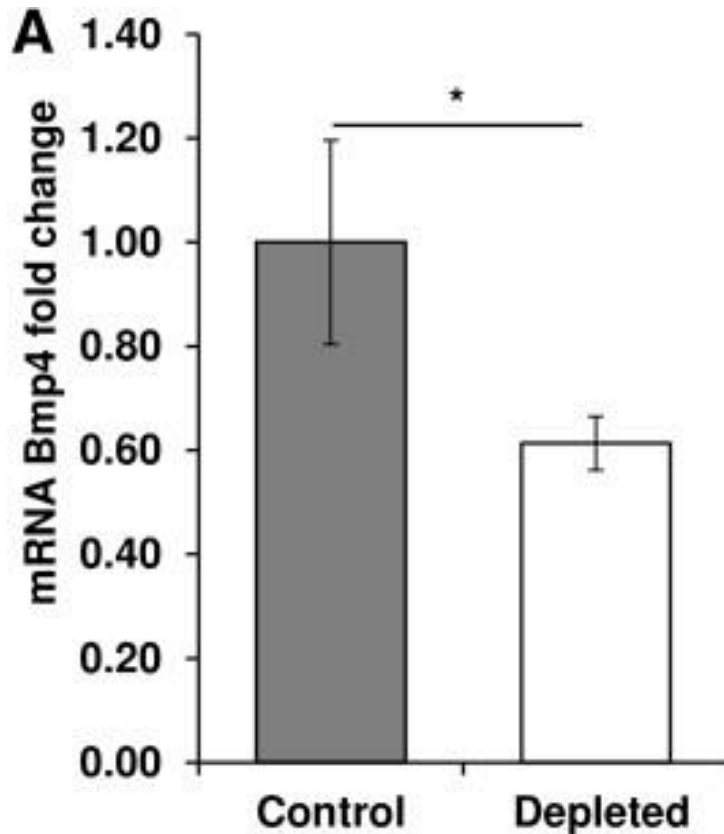


Venning G. BMJ 2005



Garcia LA et al. Endocrinology 2011

Vitamin D deficiency affects muscle protein synthesis in old rats



Endocrine regulation

E.g. GH / IGF's / IGFBP's
Glucocorticoids
Sex steroids
Vitamin D
Myostatin, follistatin, ...

Nutrition

Amino acids, glucose,
fatty acids, calcium, ...

Nervous system

- Muscle
- Bone metabolism

Shared regulation

Bone

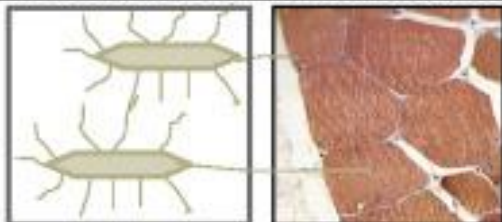
Growth factors,
cytokines, ...

Growth factors
Myokines...

Muscle

Bone-muscle interactions

Intercellular communication?



Biomechanical signals/ Physical exercise

Muscle contractions
(via tendons and entheses)

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Gravitation

Cytokines and chemokines (myokines)	Ref.
IL-6	Pedersen et al., 2003
IL-7	Haugen et al., 2010
IL-8	Onan et al., 2009
IL-15	Quinn et al., 2009
Leukemia inhibitory factor (LIF)	Walker et al., 2010
Ciliary neurotrophic factor (CNTF)	Johnson et al., 2014
RANKL	Juffer et al., 2014
Myostatin.	Laurent MR 2015
Semaphorins	Henningesen et al., 2010

Growth factors	Ref.
Insulin-like growth factor 1 (IGF-1)	Hamrick et al., 2010,
IGF-2	Henningesen et al.2010
Fibroblast growth factor 2 (FGF-2)	Hamrick et al., 2010
FGF-21	Henningesen et al2010
TGF- β	Henningesen et al2010
PDGF	Henningesen et al2010
Connective tissue growth factor	Henningesen et al2010
Bone morphogenetic protein 1 (BMP1)	Henningesen et al2010

Matrix-related proteins	Ref.
Osteonectin	Chan et al., 2007, Henningesen et al., 2010
Matrix metalloproteinase 2 (MMP-2)	Chan et al., 2007, Henningesen et al., 2010
Cathepsins	Henningesen et al., 2010
Coagulation factors (tPA, uPA, TFPI, ...)	Henningesen et al., 2010

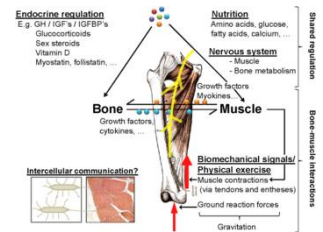
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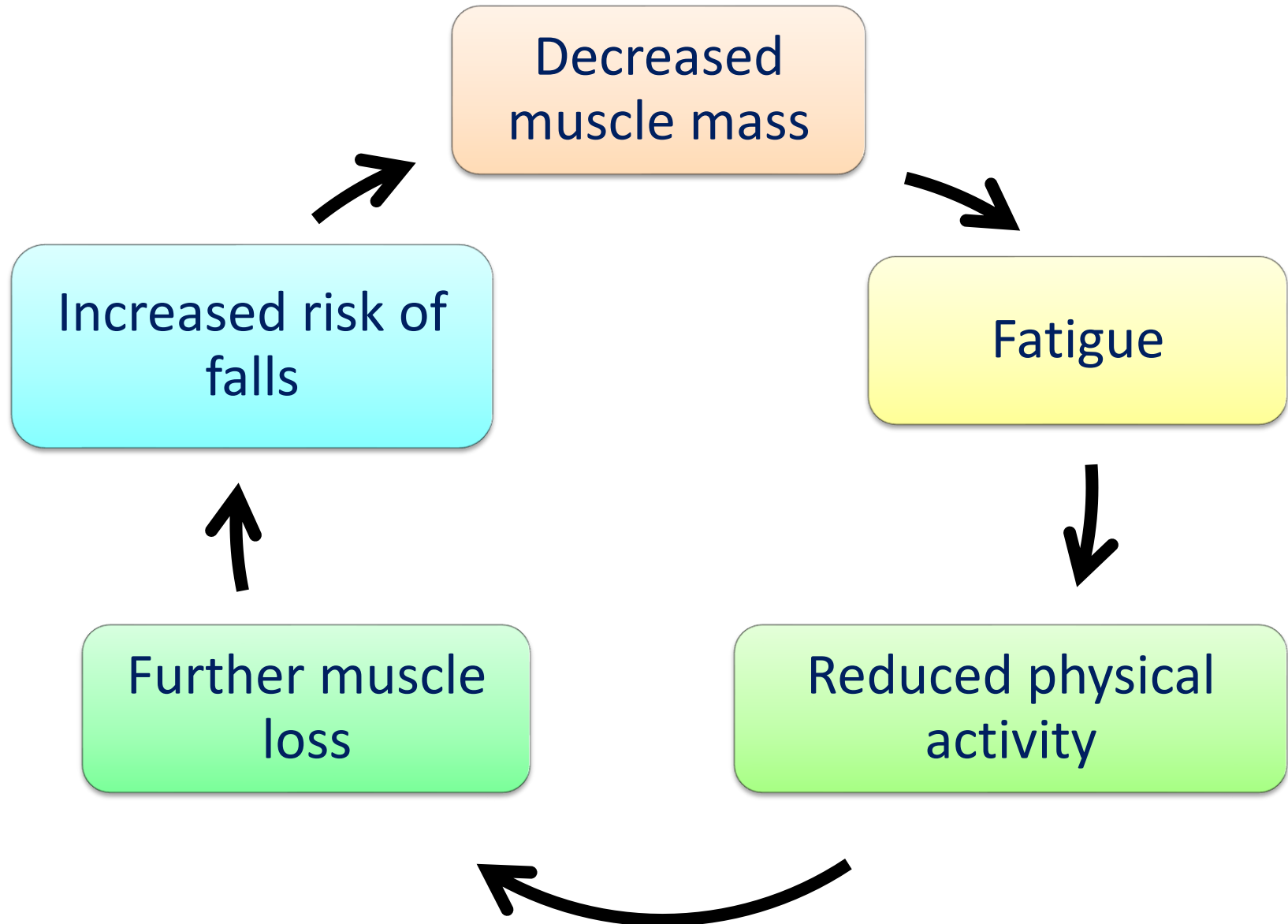


SARCOPENIA

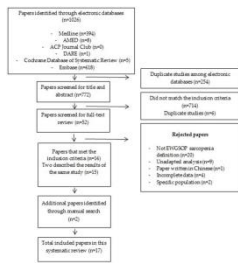
Greek, 'lack of flesh', loss of muscle mass and strength with aging



Clinical effect of sarcopenia



Sarcopenia and disability



Rejected papers

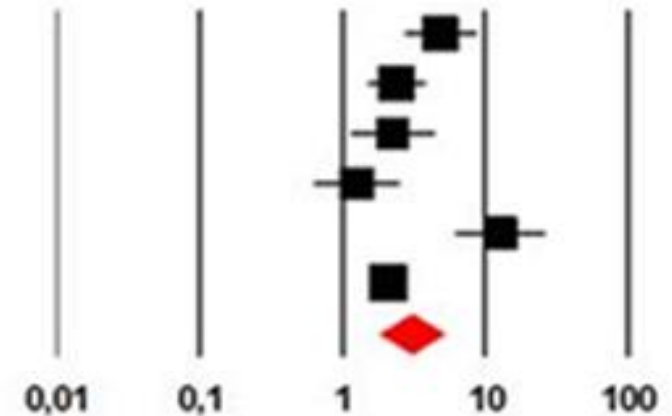
- Not EWGSOP sarcopenia definition (n=20)
- Unadapted analysis (n=9)
- Paper written in Chinese (n=1)
- Incomplete data (n=4)
- Specific population (n=2)

Study name

Statistics for each study

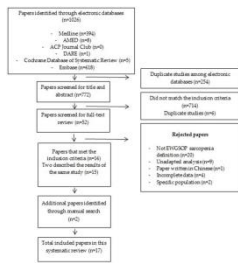
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Bianchi, 2015	4,890	2,677	8,931	5,164	0,000
Cawthon, 2015	2,420	1,495	3,917	3,597	0,000
Da Silva, 2014	2,260	1,124	4,545	2,287	0,022
Sanchez-Rodriguez, 2015	1,273	0,624	2,597	0,663	0,507
Tanimoto, 2013	12,820	6,059	27,125	6,671	0,000
Woo, 2015	2,100	1,591	2,772	5,239	0,000
	3,034	1,799	5,118	4,162	0,000

Odds ratio and 95% CI



>17,000 participants

Sarcopenia and mortality



Rejected papers

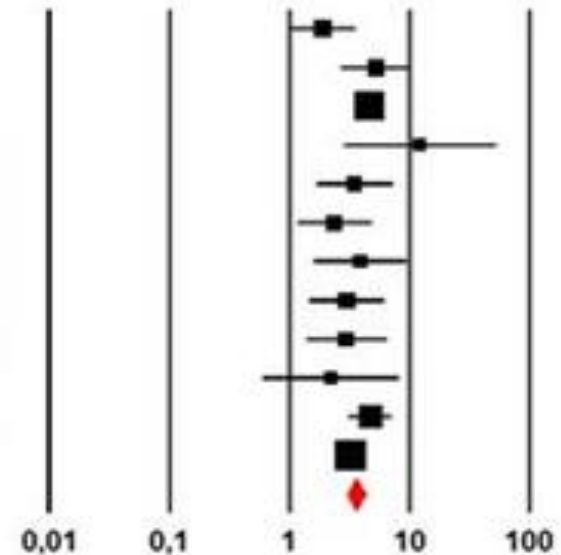
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Study name

Statistics for each study

Odds ratio and 95% CI

	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Arango-Lopera, 2013	1,866	0,978	3,561	1,892	0,059
Bianchi, 2015	5,239	2,705	10,145	4,911	0,000
Cawthon, 2015	4,580	3,501	5,992	11,101	0,000
Cerri, 2015	12,133	2,815	52,300	3,348	0,001
Da Silva, 2014	3,462	1,661	7,216	3,314	0,001
Kim, 2014	2,360	1,153	4,833	2,349	0,019
Landi, 2012	3,873	1,572	9,542	2,943	0,003
Landi, 2013	2,992	1,465	6,111	3,008	0,003
Saka, 2015	2,964	1,364	6,441	2,743	0,006
Sanchez-Rodriguez, 2014	2,199	0,600	8,055	1,189	0,234
Vetrano, 2014	4,716	3,109	7,153	7,295	0,000
Woo, 2015	3,190	2,542	4,003	10,013	0,000
	3,596	2,957	4,373	12,821	0,000



>17,000 participants

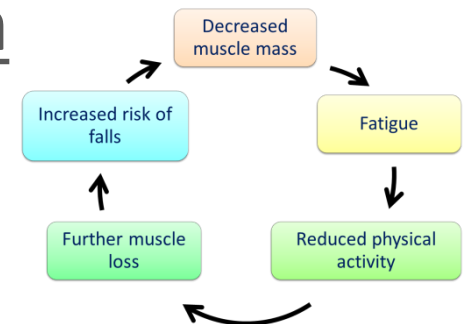
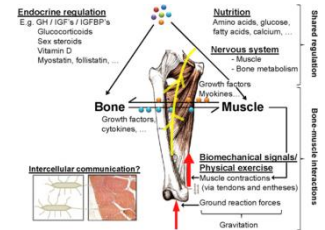
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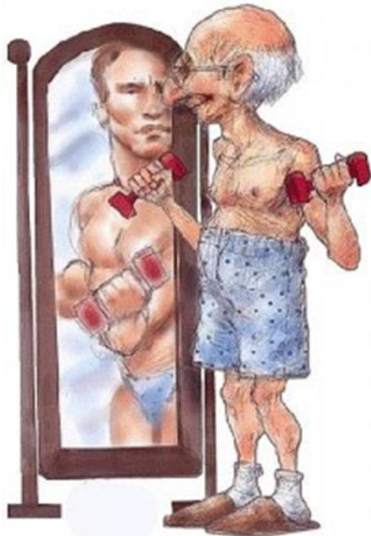
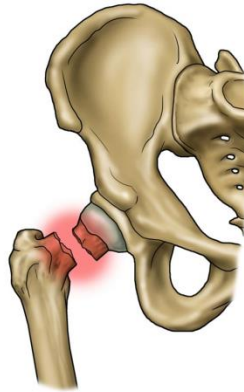
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GRAZIE