

Sarcopenia: criteri diagnostici e implicazioni scheletriche

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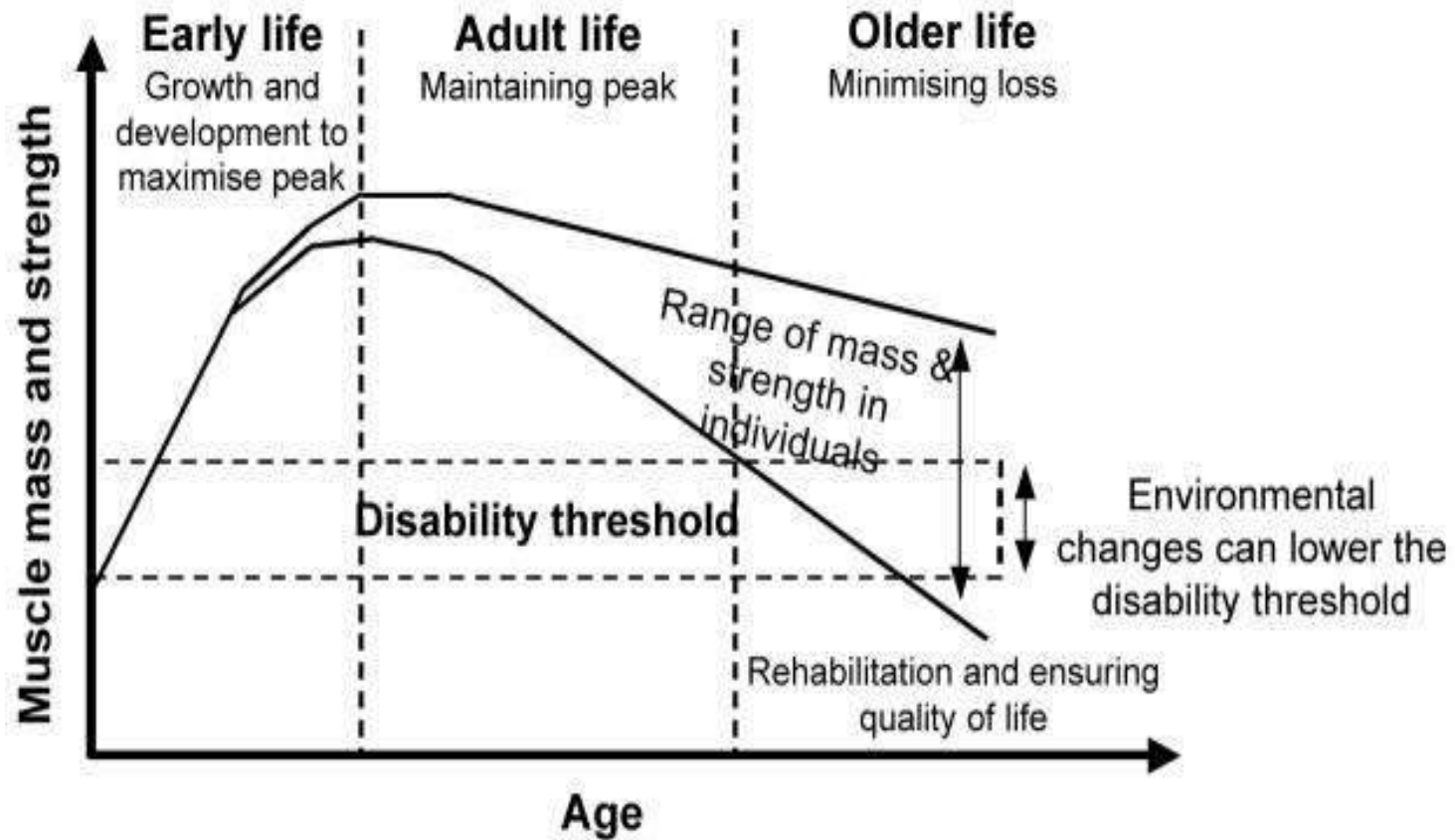
Siena, 09/10/2020

AGENDA

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

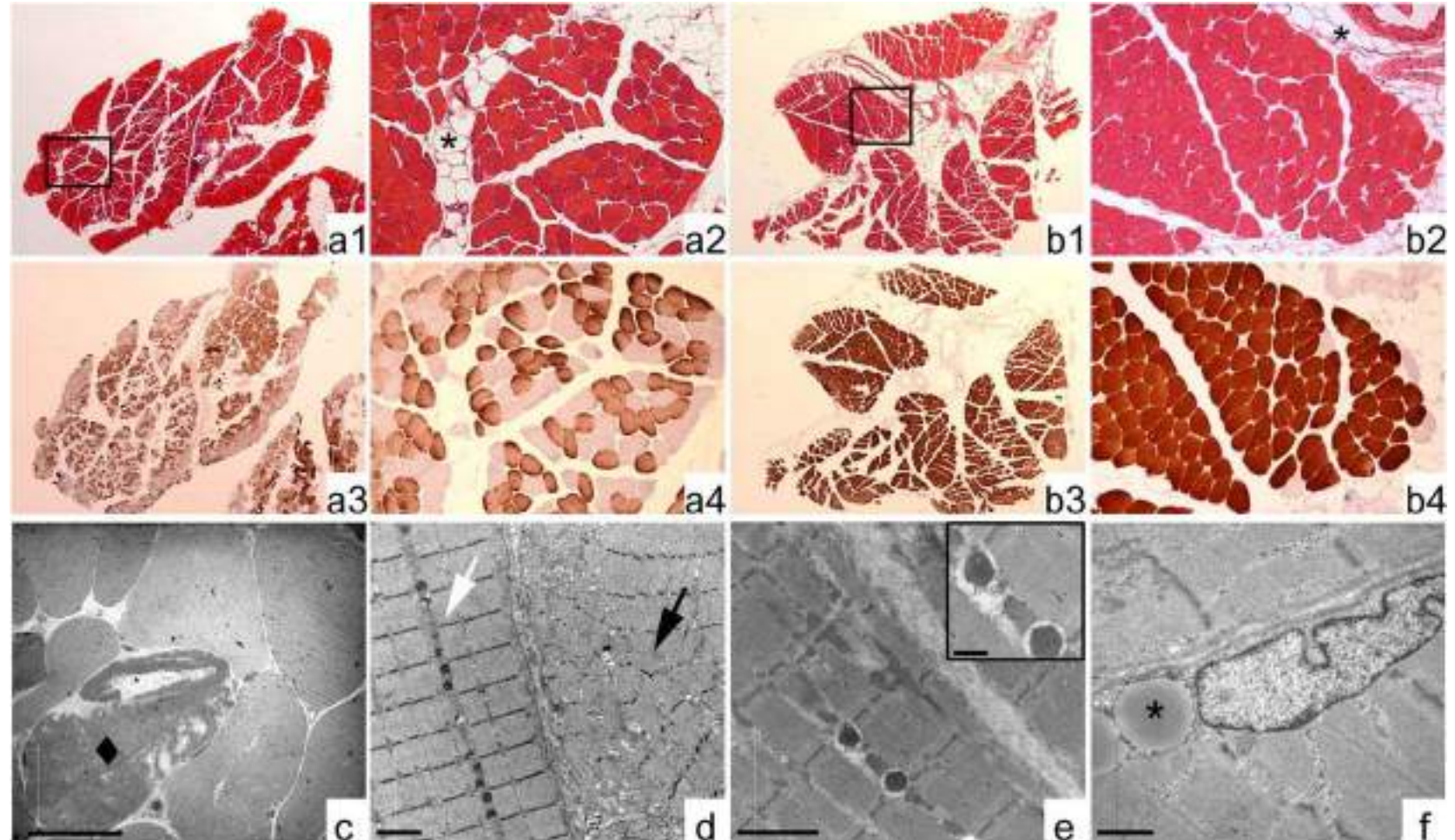
Sarcopenia

Disease or normal aging?

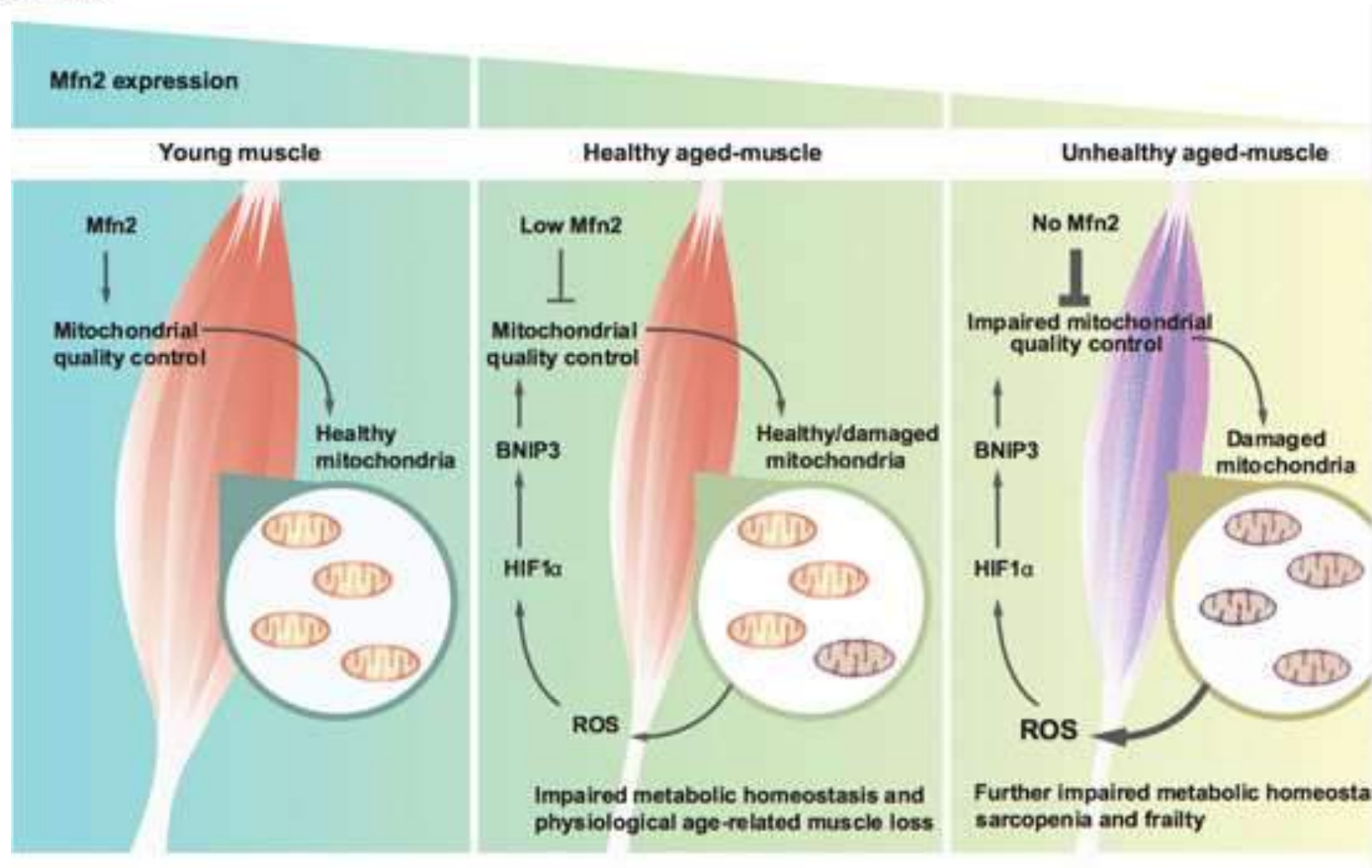


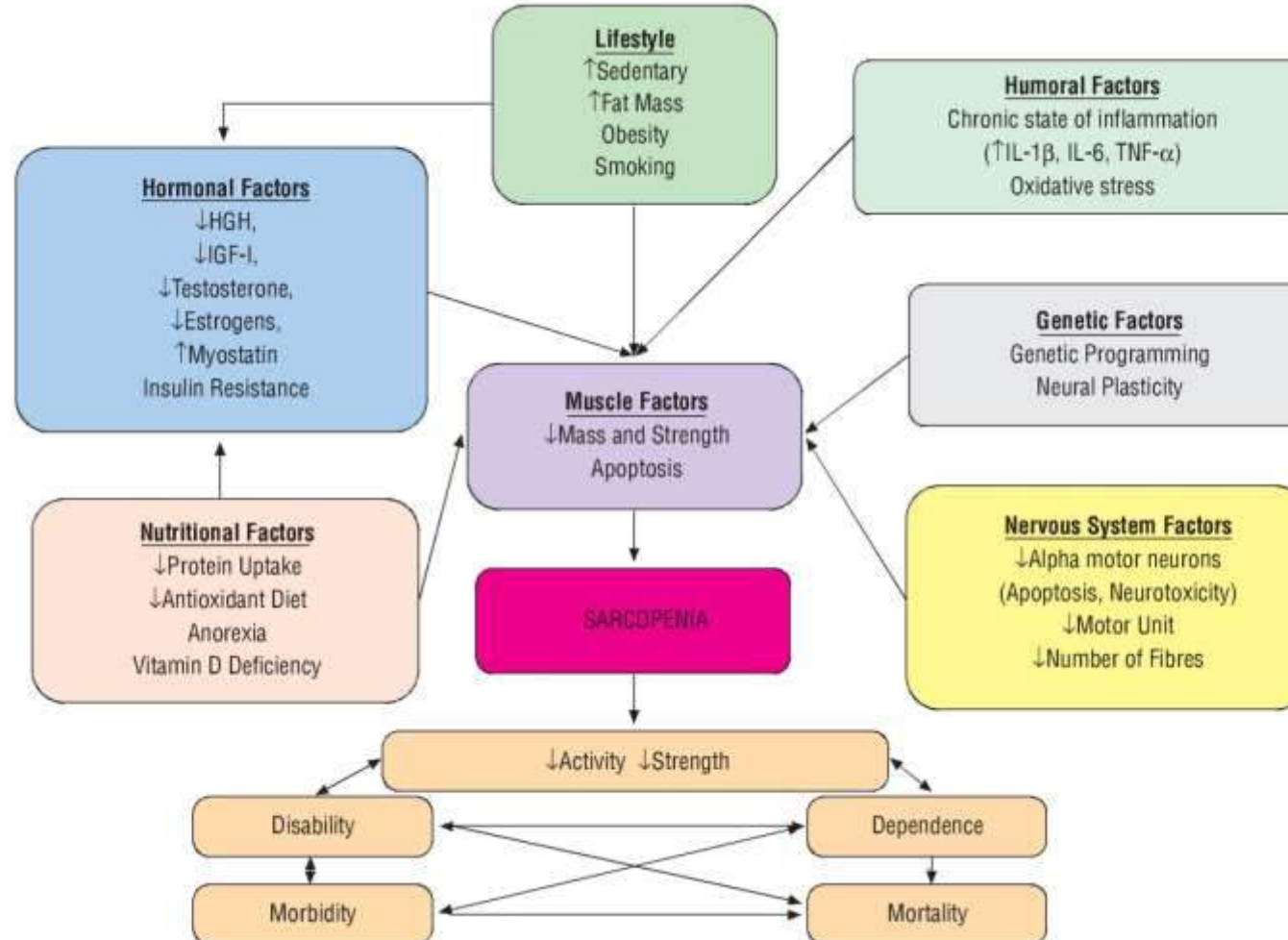
Sarcopenia

Changes in Muscle structure



Sarcopenic muscle function





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 ≤ 7.23 kg/m ²	Low lean mass
Newman	ND	ND	Residual of actual ALM–predicted ALM from equation	Low lean mass

2018 operational definition of sarcopenia

Low muscle strength

Low muscle quantity or quality

Low physical performance

- Probable sarcopenia is identified by Criterion 1.
- Diagnosis is confirmed by additional documentation of Criterion 2.
- If Criteria 1, 2 and 3 are all met, sarcopenia is considered severe.

Low muscle strength

2018 operational definition of sarcopenia
Low muscle strength
Low muscle quantity or quality
Low physical performance

Variable	Clinical practice	Research studies	Reference
Case finding	SARC-F questionnaire Ishii screening tool	SARC-F	Malmstrom <i>et al.</i> (2016)
			Ishii <i>et al.</i> (2014)
Skeletal muscle strength	Grip strength	Grip strength	Roberts <i>et al.</i> (2011)
	Chair stand test (chair rise test)	Chair stand test (5-times sit-to-stand)	American Academy of Orthotists & Prosthetists

SARC-F

Component	Question	Scoring
Strength	How much difficulty do you have in lifting and carrying 10 pounds?	None = 0 Some = 1 A lot or unable = 2
Assistance in walking	How much difficulty do you have walking across a room?	None = 0 Some = 1 A lot, use aids, or unable = 2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None = 0 Some = 1 A lot or unable without help = 2
Climb stairs	How much difficulty do you have climbing a flight of 10 stairs?	None = 0 Some = 1 A lot or unable = 2
Falls	How many times have you fallen in the past year?	None = 0 1–3 falls = 1 4 or more falls = 2

Low muscle quantity or quality

2018 operational definition of sarcopenia
Low muscle strength
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Low physical performance

Variable	Clinical practice	Research studies	Reference
Skeletal muscle mass or Skeletal muscle quality	Appendicular skeletal muscle mass (ASMM) by Dual-energy X-ray absorptiometry (DXA)*	ASMM by DXA	Schweitzer (2015) Mitsiopoulos (1998)
	Whole-body skeletal muscle mass (SMM) or ASMM predicted by Bioelectrical impedance analysis (BIA)*	Whole-body SMM or ASMM by Magnetic Resonance Imaging (MRI, total body protocol)	Shen (2004) Sergi (2017)
Skeletal muscle strength	Grip strength	Grip strength	Roberts <i>et al.</i> (2011)
	Chair stand test (chair rise test)	Chair stand test (5-times sit-to-stand)	American Academy of Orthotists & Prosthetists

Low physical performance

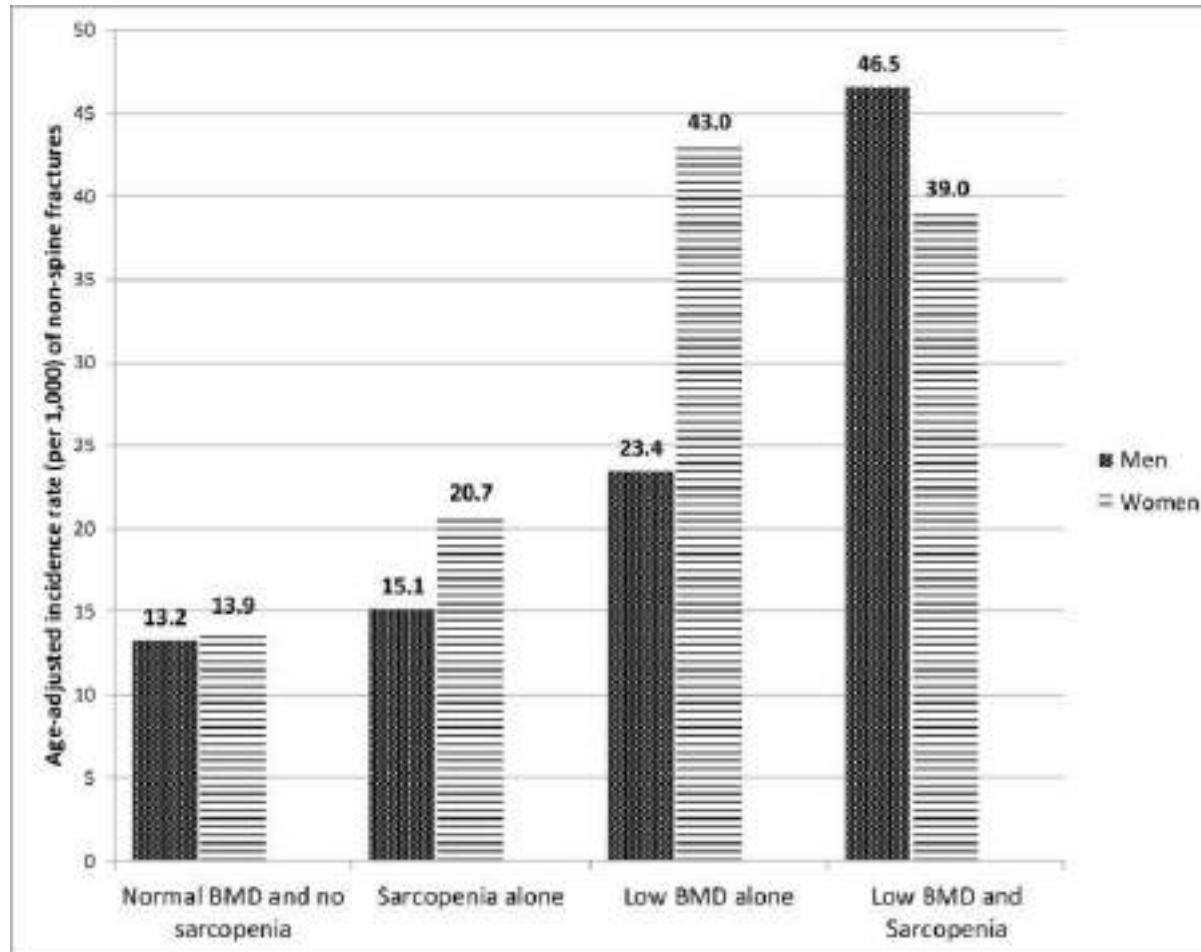
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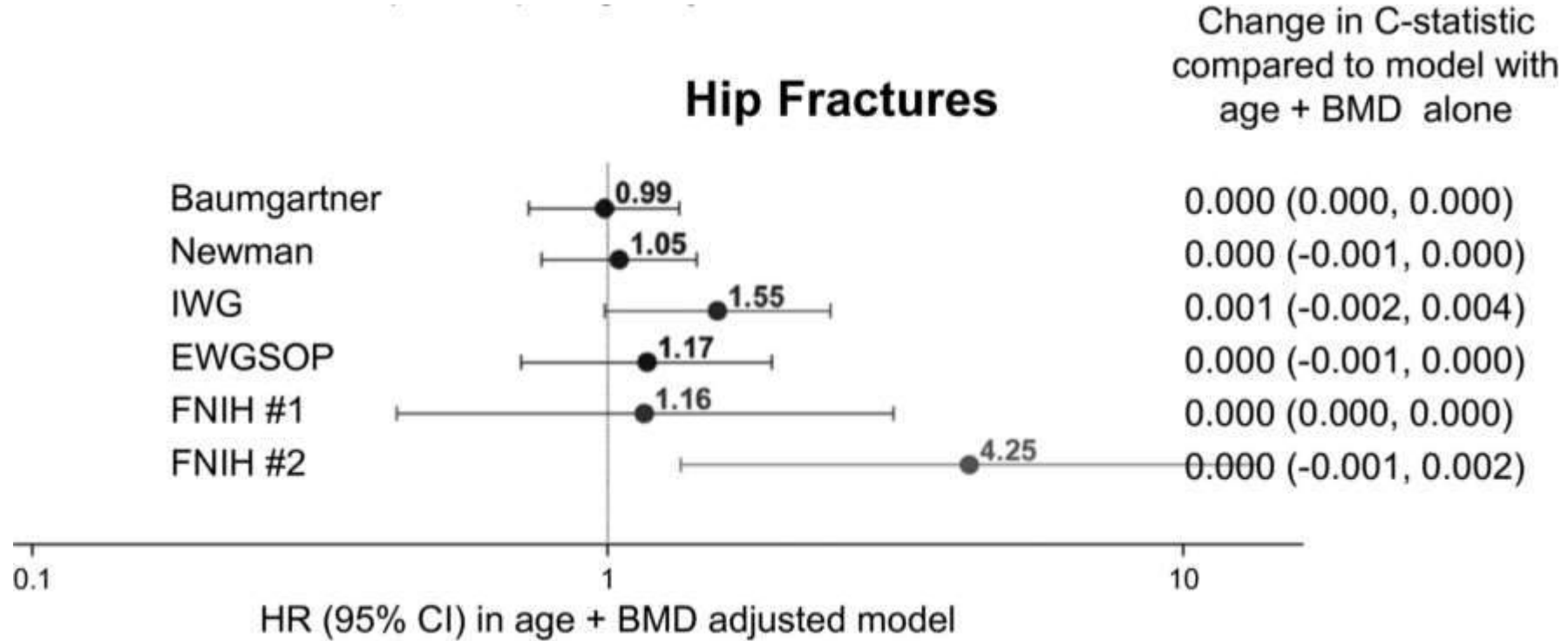
Variable	Clinical practice	Research studies	Reference
Physical performance	Gait speed	Gait speed	NIH Toolbox 4 Meter Walk Gait Speed Test
	Short physical performance battery (SPPB)	SPPB	Short Physical Performance Battery Protocol NIH Toolbox
	Timed-up-and-go test (TUG)	TUG	Mathias (1986)
	400-meter walk or long-distance corridor walk (400-m walk)	400-m walk	Newman (2006)

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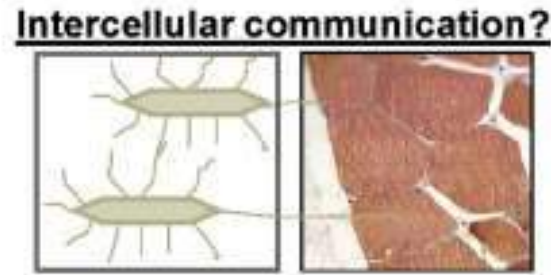
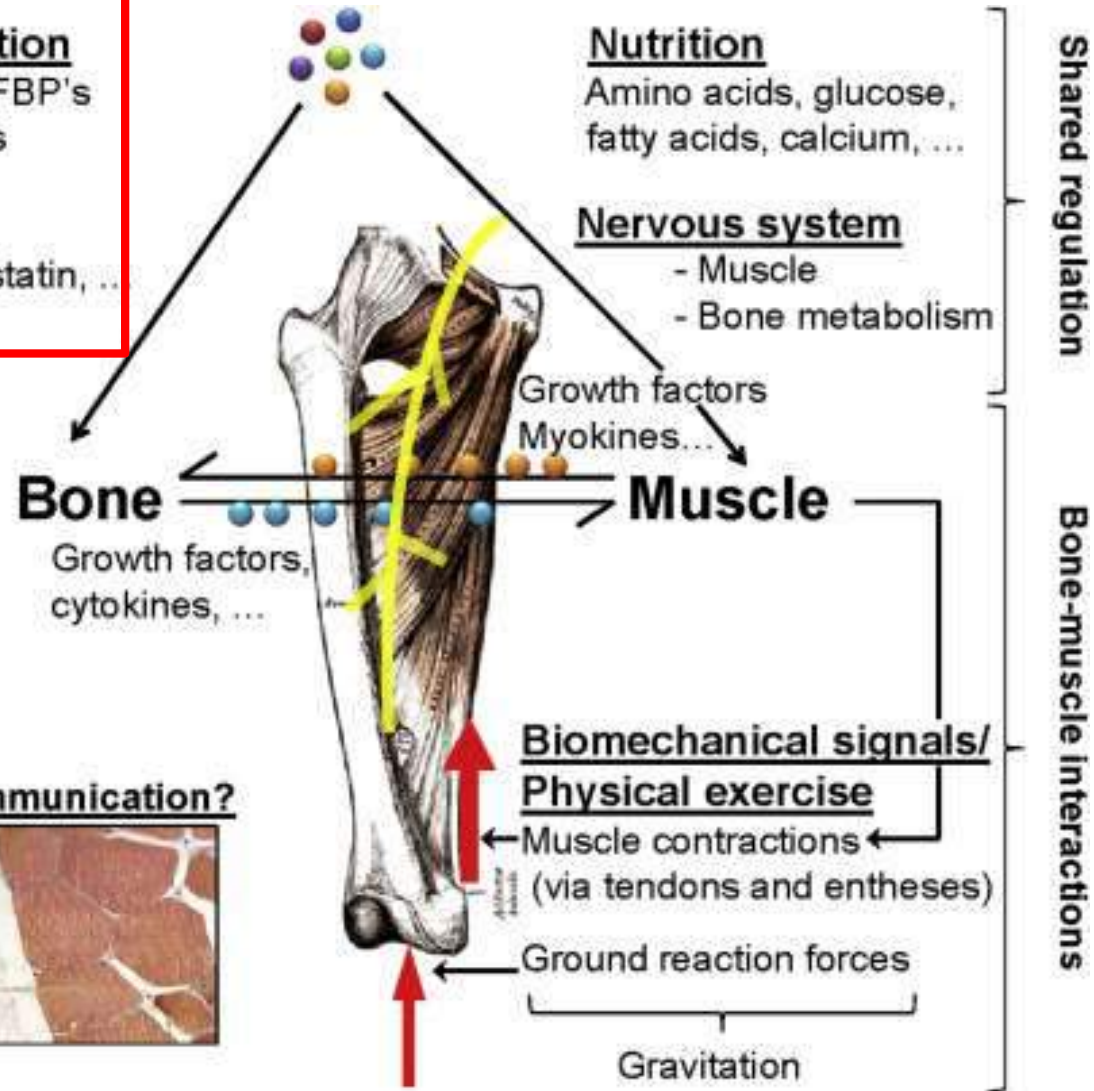
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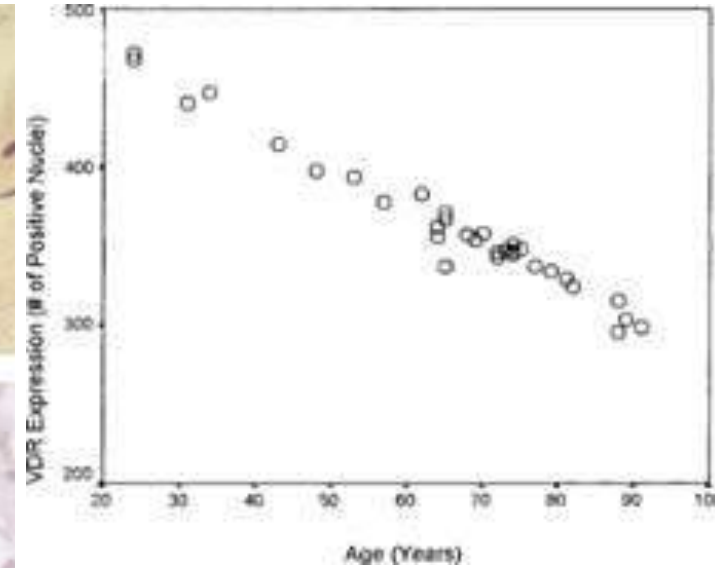
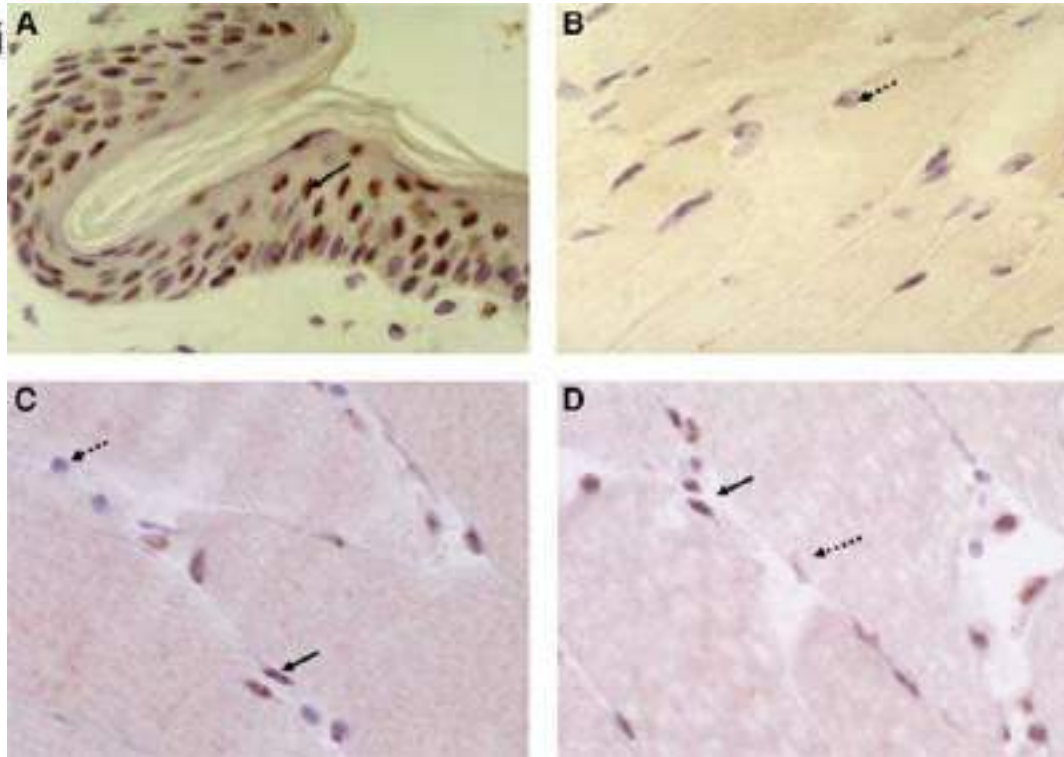
Sarcopenia and fractures





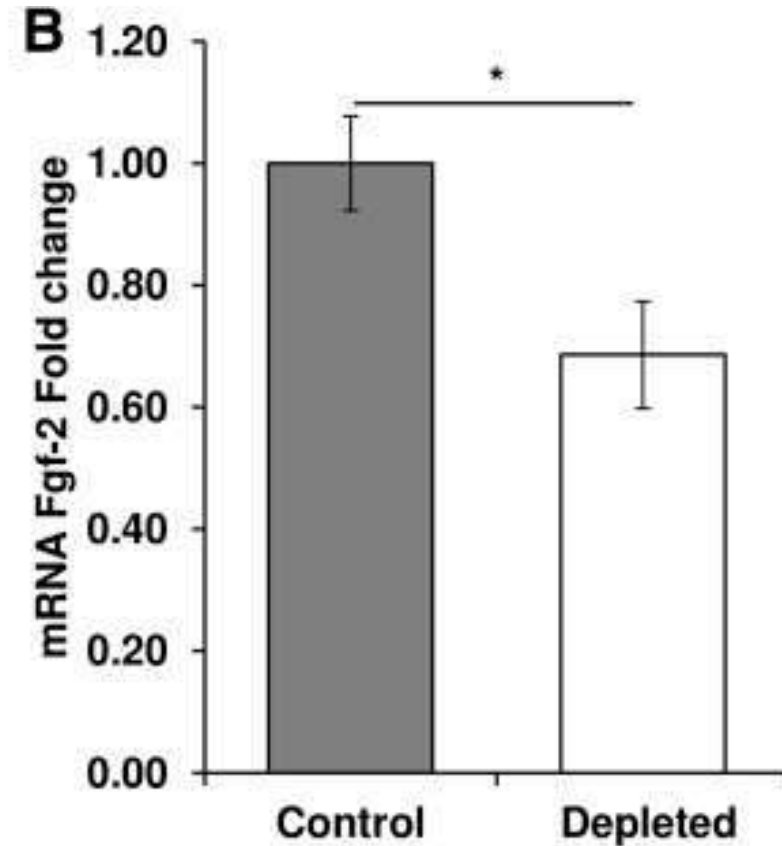
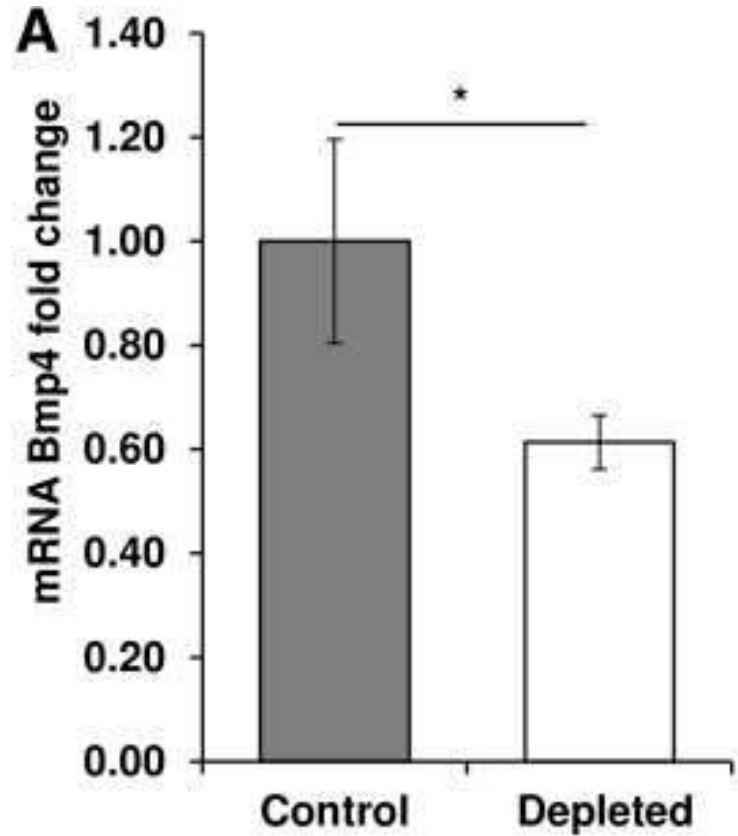
Endocrine regulation
 E.g. GH / IGF's / IGFBP's
 Glucocorticoids
 Sex steroids
Vitamin D
 Myostatin, follistatin, ...





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

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, ...

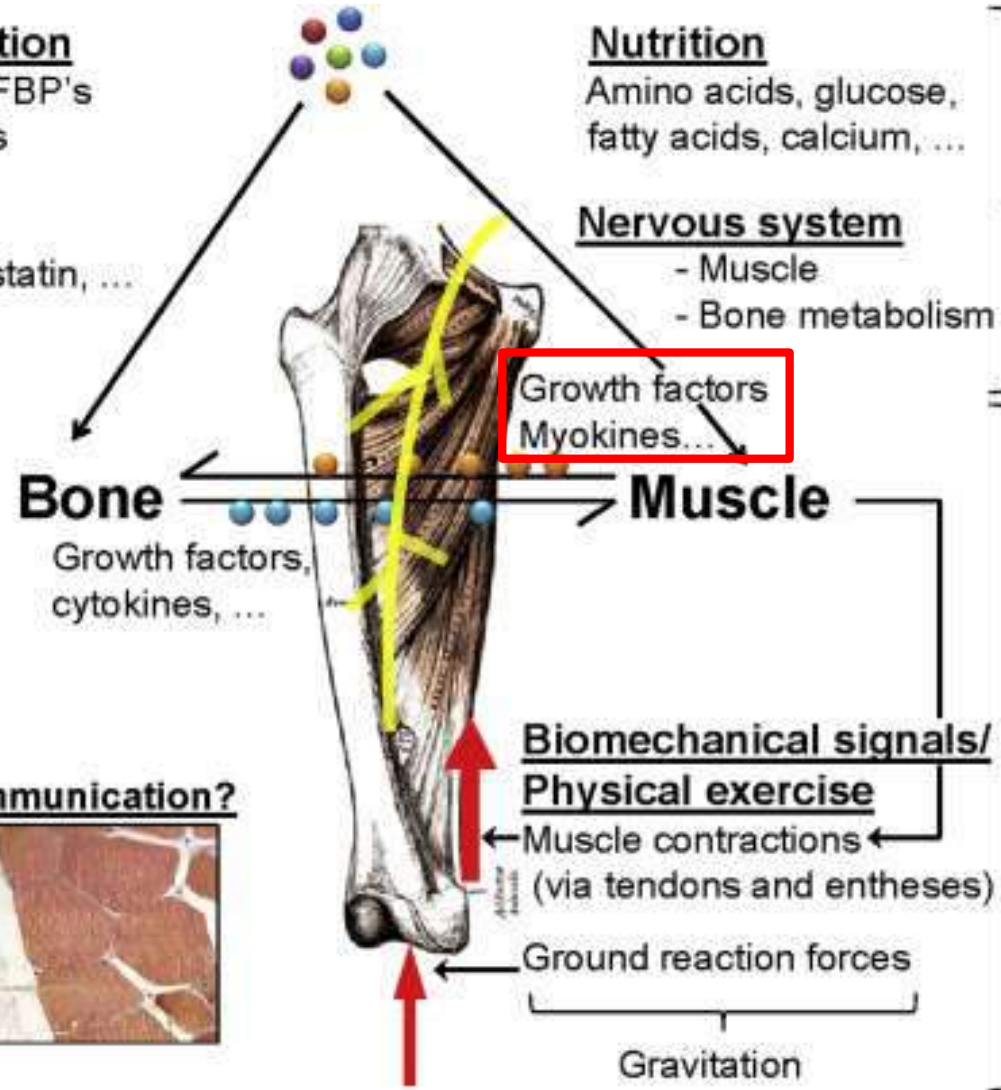
Nutrition

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

Nervous system

- Muscle
 - Bone metabolism

Shared regulation



Growth factors
 Myokines...

Bone

Muscle

Growth factors,
 cytokines, ...

**Biomechanical signals/
 Physical exercise**

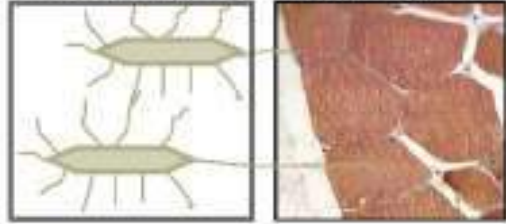
Muscle contractions
 (via tendons and entheses)

Ground reaction forces

Gravitation

Bone-muscle interactions

Intercellular communication?



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

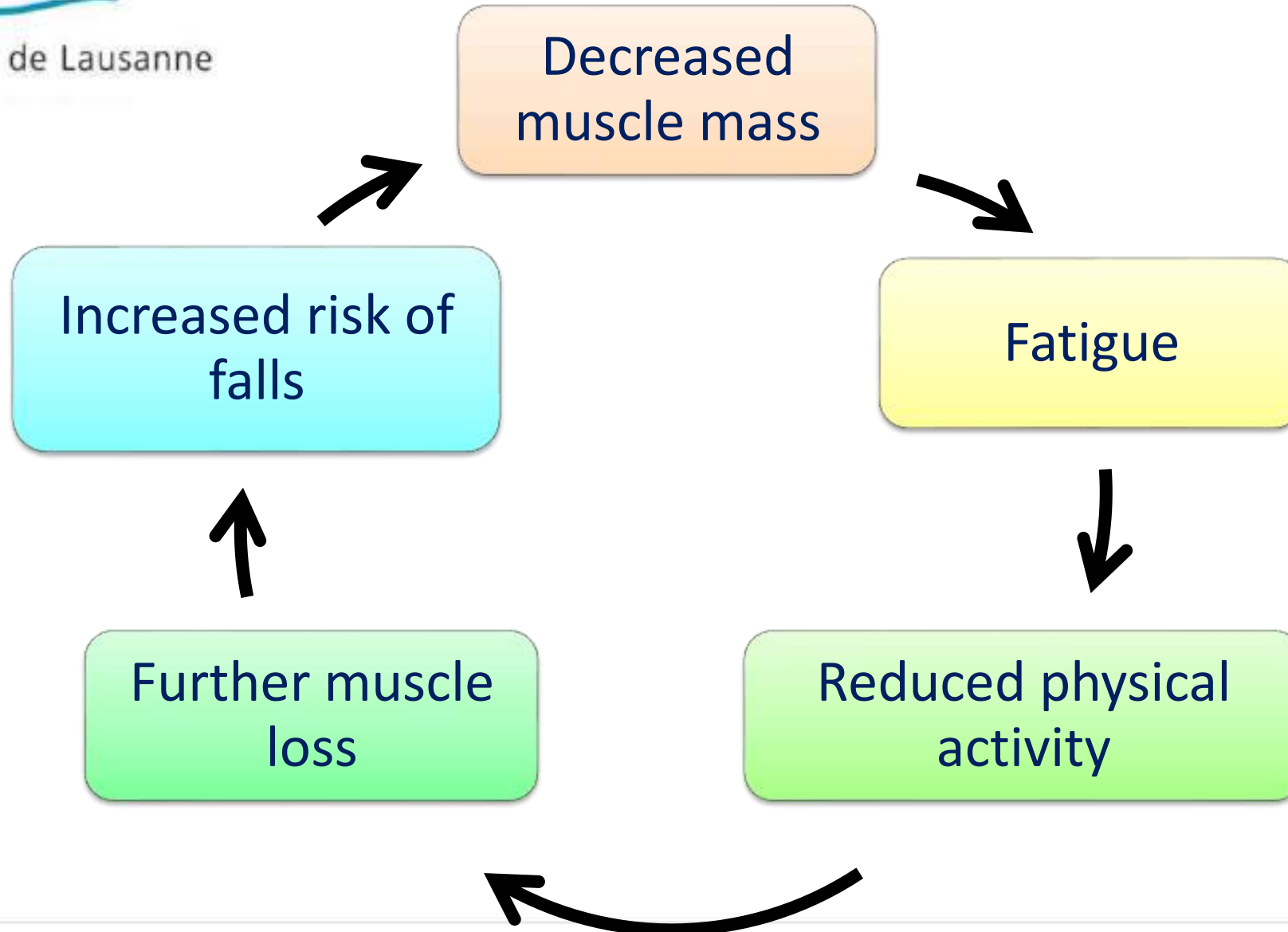
Matrix-related proteins	Ref.
Osteonectin	Chan et al., 2007, Henningesen et al., 2010
Matrix metalloproteinase 2 (MMP-2)	Chan et al., 2007, Henningesen et al., 2010
Cathepsins	Henningesen et al., 2010
Coagulation factors (tPA, uPA, TFPI, ...)	Henningesen et al., 2010



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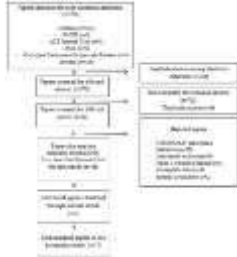
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Clinical effect of sarcopenia



Sarcopenia and disability

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

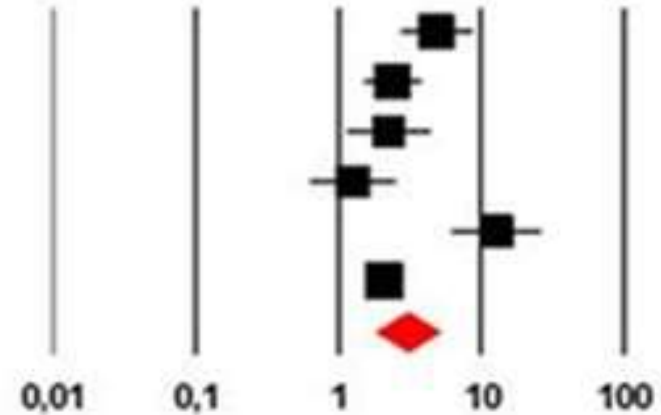


Study name

Statistics for each study

Odds ratio and 95% CI

Study name	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
Total	3,034	1,799	5,118	4,162	0,000



>17,000 participants

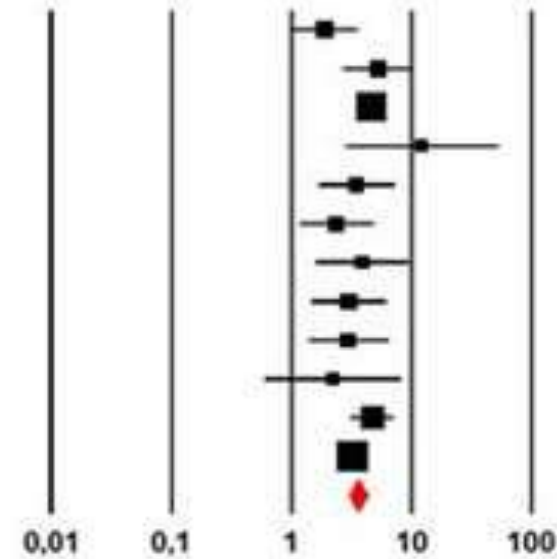
Sarcopenia and mortality

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Study name	Statistics for each study				
	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	2,984	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

Odds ratio and 95% CI



>17,000 participants

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