SOCIETÀ ITALIANA
G.U.I.D.A.
PER LA GESTIONE UNIFICATA E INTERDISCIPLINARE
DEL DOLORE MUSCOLO-SCHELETRICO E DELL'ALGODISTROFIA

Sarcopenia e dolore

Stefania Maggi

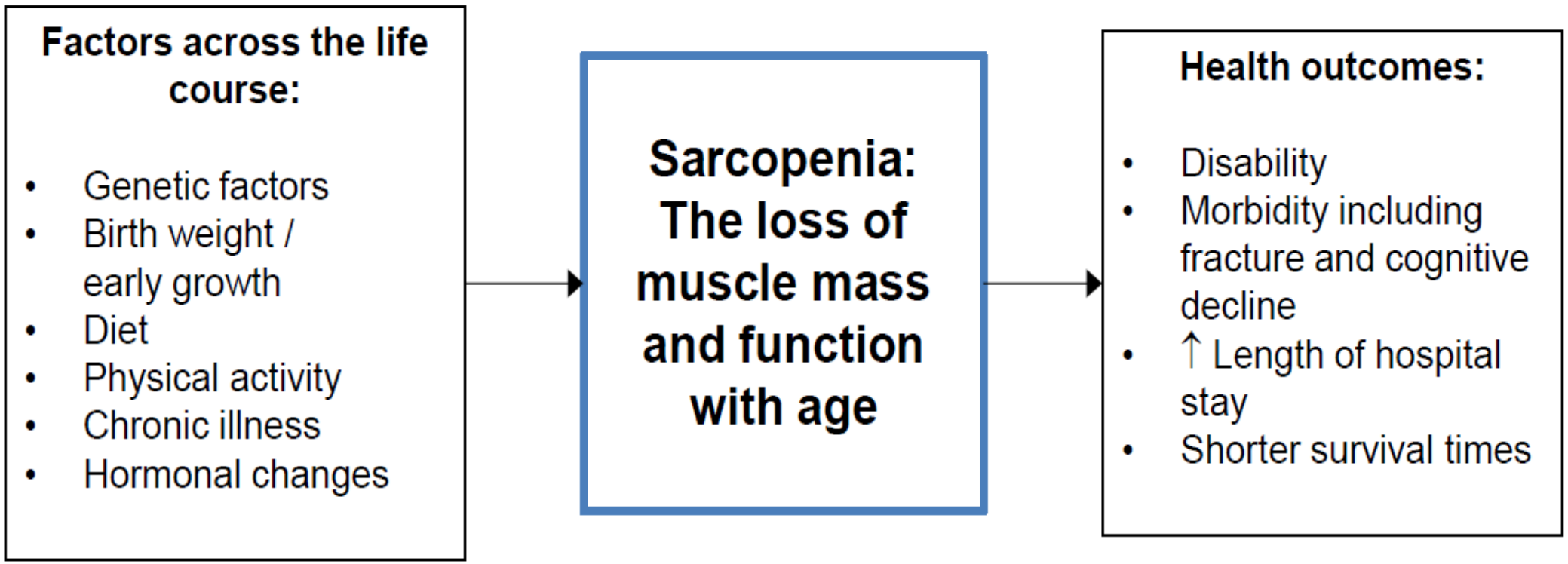
CNR Sezione Invecchiamento

Padova (Italy)

Consiglio Nazionale delle Ricerche

Sarcopenia: Primary and secondary causes

Figure 2. Sarcopenia: major health outcomes and risk factors



Dodds et al, J Clin. Dens, 2015

EWGSOP 2010 Working Definition of Sarcopenia

LOW MUSCLE MASS

+

LOW MUSCLE STRENGTH

AND

LOW PHYSICAL PERFORMANCE

=

PRE-SARCOPENIA

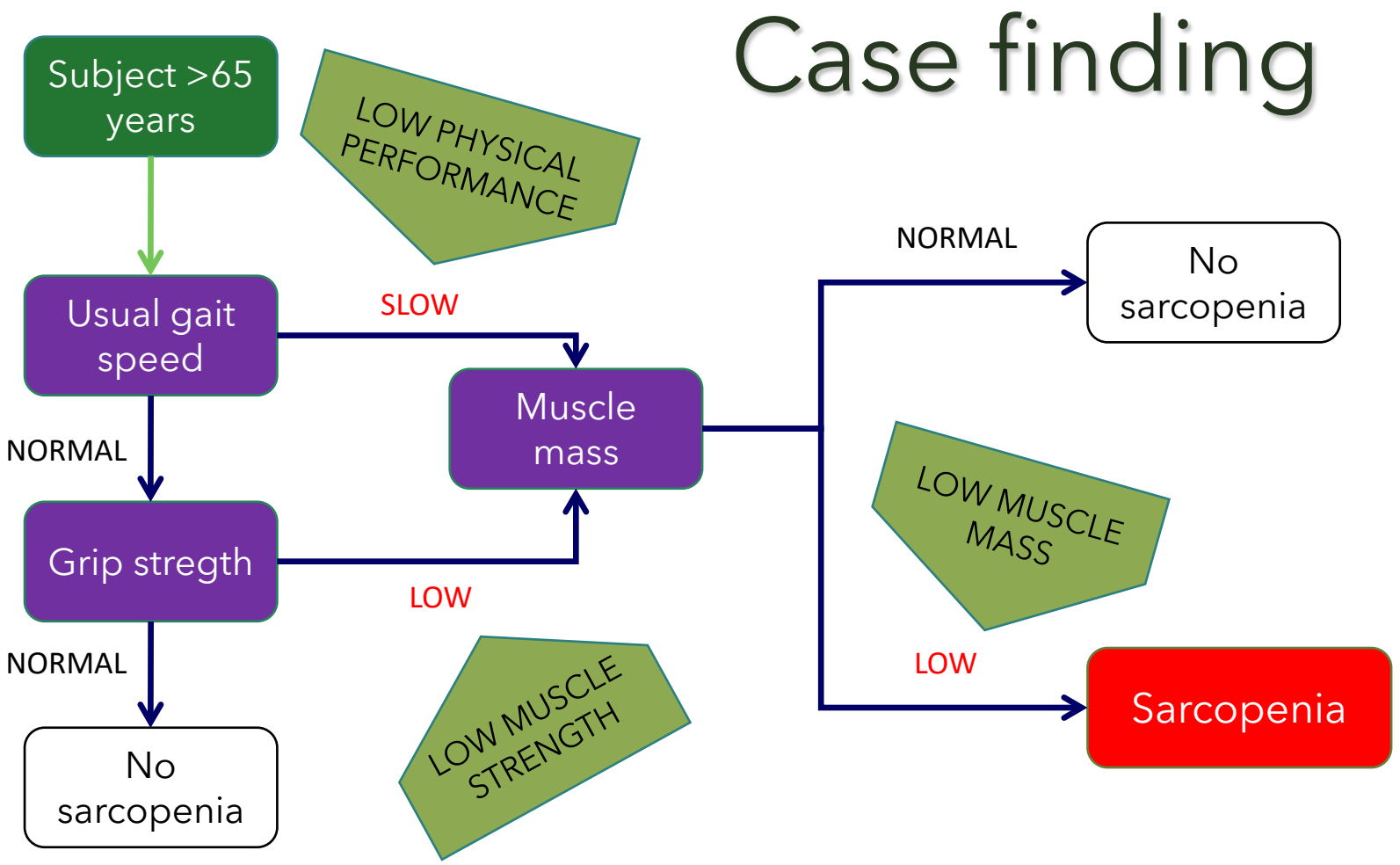
REPORT

Sarcopenia: European consensus on definition and diagnosis

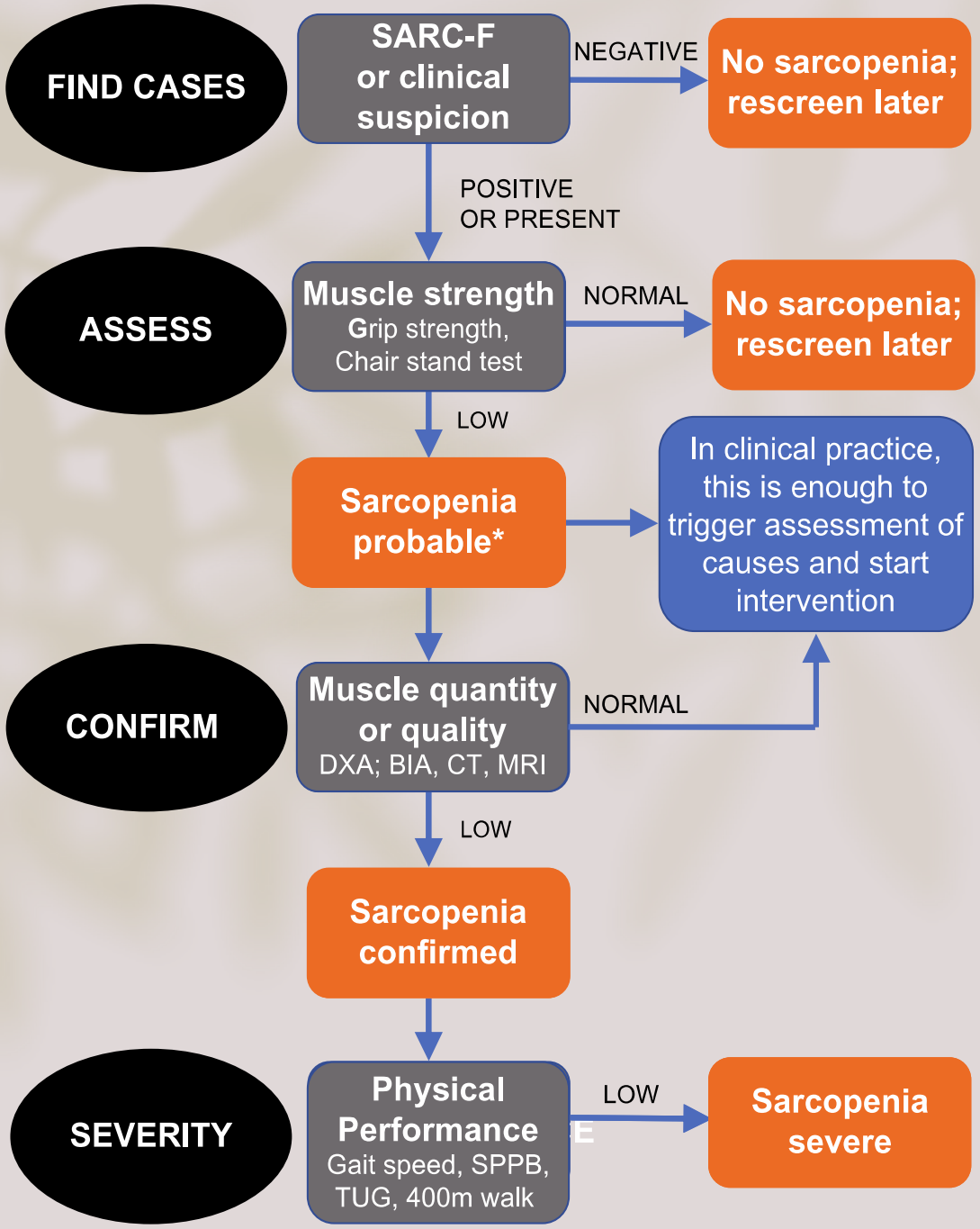
Report of the European Working Group on Sarcopenia in Older People

ALFONSO J. CRUZ-JENTOFT[1], JEAN PIERRE BAEYENS[2], JÜRGEN M. BAUER[3], YVES BOIRIE[4], TOMMY CEDERHOLM[5], FRANCESCO LANDI[6], FINBARR C. MARTIN[7], JEAN-PIERRE MICHEL[8], YVES ROLLAND[9], STÉPHANE M. SCHNEIDER[10], EVA TOPINKOVÁ[11], MAURITS VANDEWOUDE[12], MAURO ZAMBONI[13]

EWGSOP Working Definition of Sarcopenia

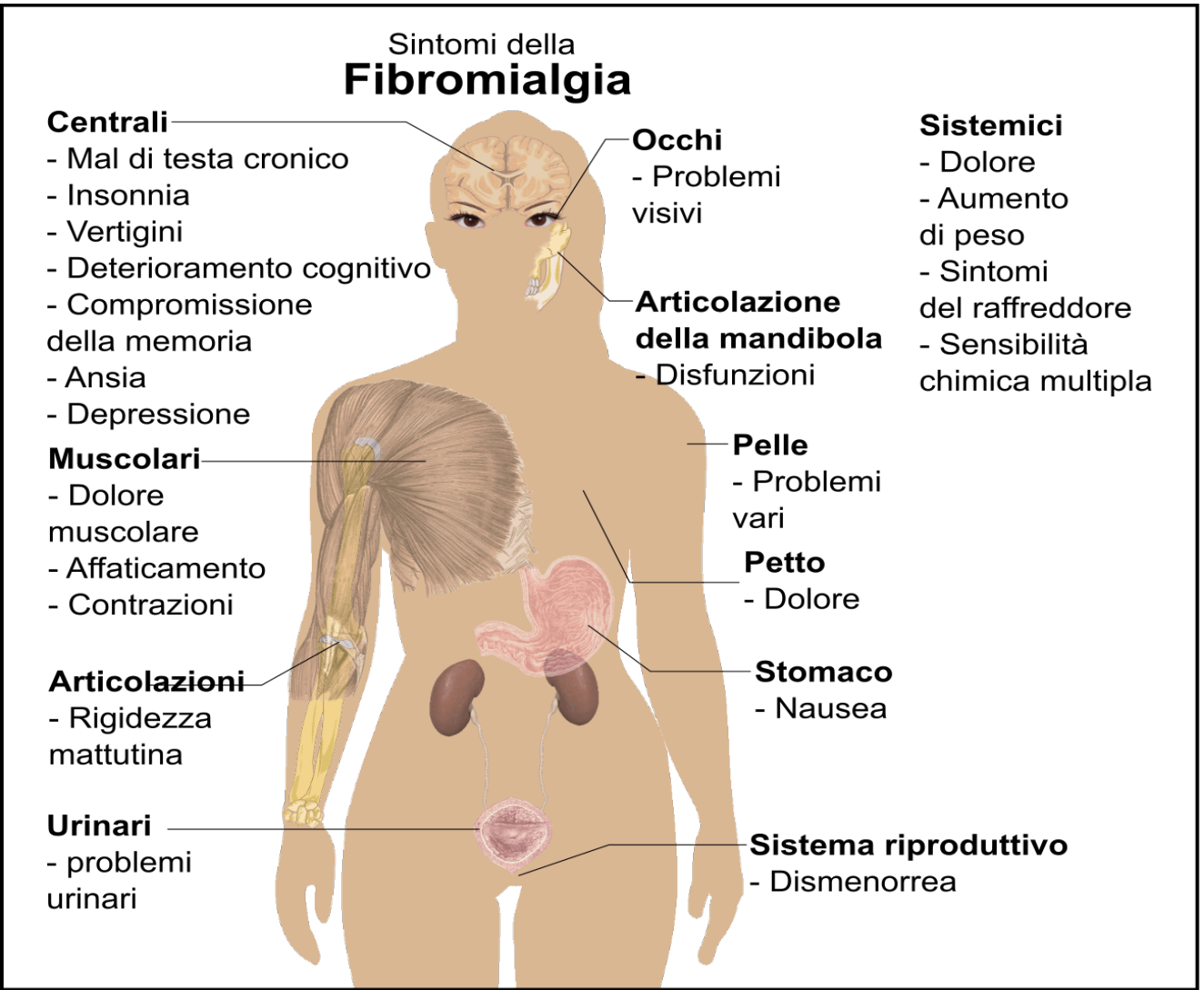


Cruz-Jentoft AJ et al. Sarcopenia: European consensus on definition and diagnosis. Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010



EWGSOP2 algorithm (Age Ageing 2019) for case-finding, making a diagnose and quantifying severity in practice. The steps of the pathway are represented as Find-Assess-Confi rm-Severity or F-A-C-S. *Consider other reasons for low muscle strength (e.g. depression, stroke, balance disorders, peripheral vascular disorders)

*Why is the definition important when focusing on pain and sarcopenia? The examples of **Fibromialgia***



According to the first definition, no patients with **fibromialgia** are sarcopenic, according to the second definition 1 out of 4 patients with fibromialgia are probably sarcopenic (*Kapuczinski, Rheumatol Int, 2021)*

Osteoporosis and Sarcopenia 5 (2019) 23–26

Contents lists available at ScienceDirect

Osteoporosis and Sarcopenia

journal homepage: http://www.elsevier.com/locate/afos

759 free-dwelling 65-79 older prts, 340 with lower limb pain

Original article

Sarcopenia and lower limb pain are additively related to motor function and a history of falls and fracture in community-dwelling elderly people

Kohei Maruya [a, *], Hiroaki Fujita [a], Tomoyuki Arai [a], Ryoma Asahi [b], Yasuhiro Morita [c], Hideaki Ishibashi [d]

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[b] Department of Physical Therapy, Faculty of Health Science, Japan University of Health Sciences, Saitama, Japan
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[d] Department of Orthopedic Surgery, Medical Corporation Aggregate Aiyukai Ina Hospital, Saitama, Japan

Table 1
The prevalence of pain in sarcopenia or nonsarcopenia groups.

Pain	Nonsarcopenia	Sarcopenia
Total	734 (96.7)	25 (3.3)
Pain (+)	325 (44.3)	15 (60.0)
Pain (−)	409 (55.7)	10 (40.0)

Values are presented as number (%).
P = 0.121, chi-square test.

Table 3
Comparison of motor functions and body compositions by presence of sarcopenia.

Variable	Lower limb pain		p-value
	With	Without	
BMI[a], kg/m^2	22.1 ± 0.3	21.1 ± 0.3	<0.001
%BF, %	26.3 ± 0.3	26.2 ± 0.4	ns
SMI, kg/m^2	6.75 ± 0.05	6.73 ± 0.05	ns
HGS, kg	25.5 ± 0.5	26.0 ± 0.5	ns
SLS, s	39.0 ± 3.9	44.4 ± 3.9	0.041
FRT, cm	35.3 ± 0.6	36.1 ± 0.6	ns
Normal WS, m/s	1.30 ± 0.02	1.35 ± 0.02	0.002
Maximum WS, m/s	1.77 ± 0.03	1.84 ± 0.03	<0.001
2-Step value, m/m	1.32 ± 0.02	1.37 ± 0.02	<0.001
KES, Nm/kg	1.55 ± 0.05	1.61 ± 0.05	ns
GLFS-25, point	10.5 ± 0.6	4.7 ± 0.6	<0.001

Values are presented as adjusted mean ± standard deviation.
BMI, body mass index; %BF, body fat percentage; SMI, skeletal muscle mass index; HGS, handgrip strength; SLS, single leg standing; FRT, functional reach test; WS, walking speed; KES, knee extension strength; GLFS-25, 25-question geriatric locomotive function scale; ns, no significance.
Covariance analysis adjusted by age, sex, BMI, and presence of sarcopenia.
[a] Adjusted by age, sex and presence of sarcopenia.

Chronic Pain and Risk of Injurious Falls in Community-Dwelling Older Adults

N=765, ≥ 70 years, 4 year follow-up

Table 2. Rate Ratio for Injurious Falls During the 4.3 y of Follow-up According to Pain Characteristics ($N = 765$)

Pain Characteristics	*n*	No. of Injurious Falls	No. of PYs	Rate of Injurious Falls (/100 PY)	Model 1[a]	Model 2[b]	Model 3[c]
					Adj. RR (95% CI)		
Pain severity							
No pain	163	134	437.4	30.6	1.0	1.0	1.0
Very mild pain	210	188	624.0	30.1	0.99 (0.73, 1.34)	0.95 (0.70, 1.28)	0.93 (0.69, 1.25)
Mild pain	200	198	551.9	35.9	1.18 (0.87, 1.60)	1.14 (0.84, 1.55)	1.05 (0.78, 1.43)
Moderate-to-severe pain	189	197	506.6	38.9*	1.34 (0.99, 1.82)	**1.47 (1.07, 2.03)**	1.24 (0.88, 1.74)
Pain interference							
1st tertile	288	212	793.0	26.7	1.0	1.0	1.0
2nd tertile	219	209	655.1	31.9	1.21 (0.93, 1.56)	1.13 (0.88, 1.46)	1.10 (0.85, 1.42)
3rd tertile	255	296	672.4	44.0**	**1.69 (1.32, 2.15)**	**1.80 (1.40, 2.31)**	**1.61 (1.23, 2.13)**
Pain site							
No pain	274	197	764.6	25.8	1.0	1.0	1.0
Single site pain	186	167	519.0	32.2	1.24 (0.94, 1.63)	1.19 (0.90, 1.57)	1.19 (0.91, 1.57)
Multisite pain	304	354	842.7	42.0**	**1.65 (1.30, 2.09)**	**1.68 (1.32, 2.14)**	**1.57 (1.22, 2.01)**

Notes: Adj. RR = adjusted rate ratio; CI = confidence interval; PY = person-years. The values in bold indicate statistically significant results ($p < .05$).

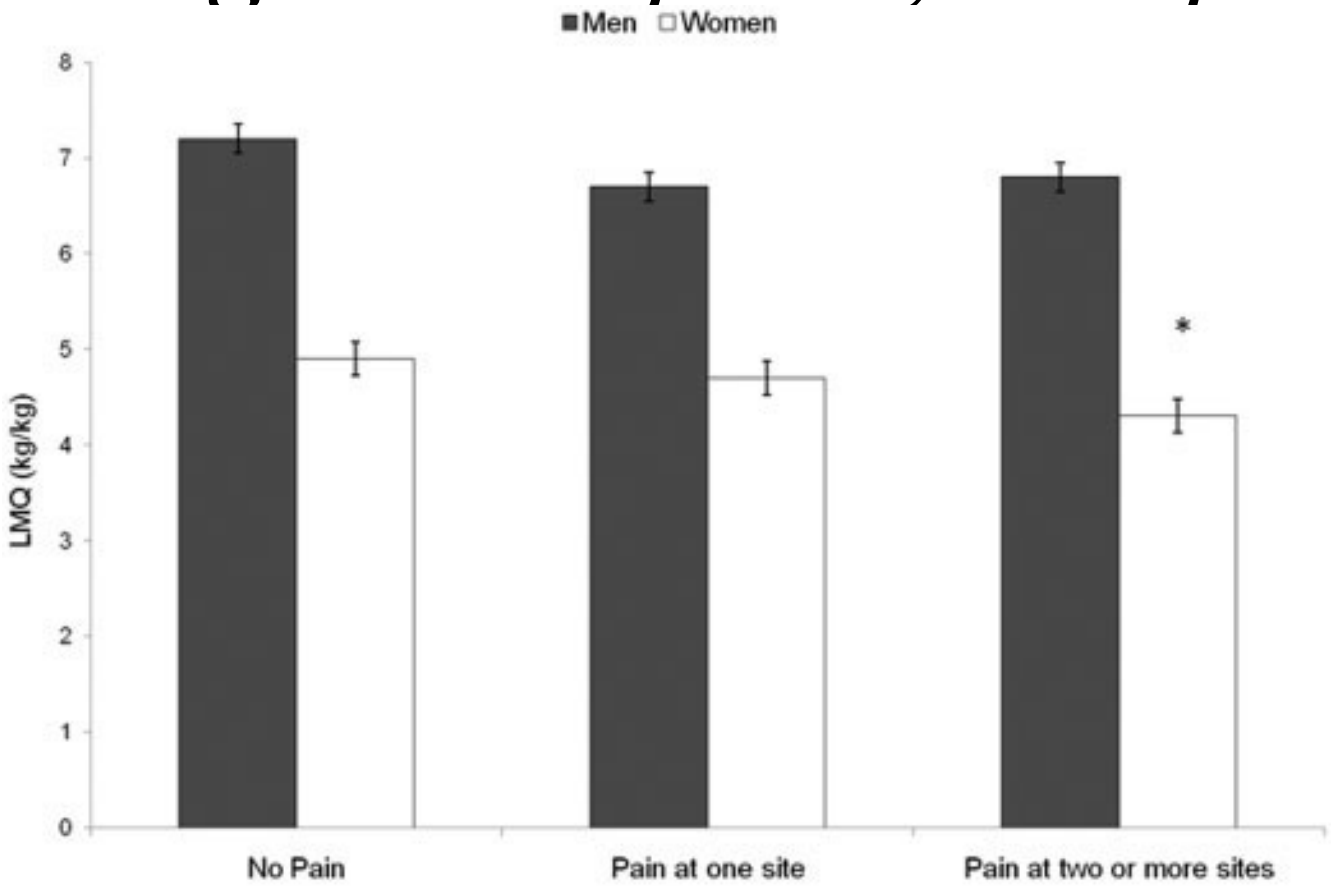
[a]Model 1 estimated unadjusted rate ratio from negative binomial models. [b]Model 2 was adjusted for age, gender, race, education, body mass index, peripheral neuropathy, peripheral arterial disease, heart disease, and vision impairment. [c]Model 3 was additionally adjusted for mobility difficulty, opioid analgesic use, and psychiatric medications use.

*Test for trend, p-value <.05, **p-value < .001.

Cai et al, J Gerontol 2021

Leg muscle quality and pain. TASOAC Study

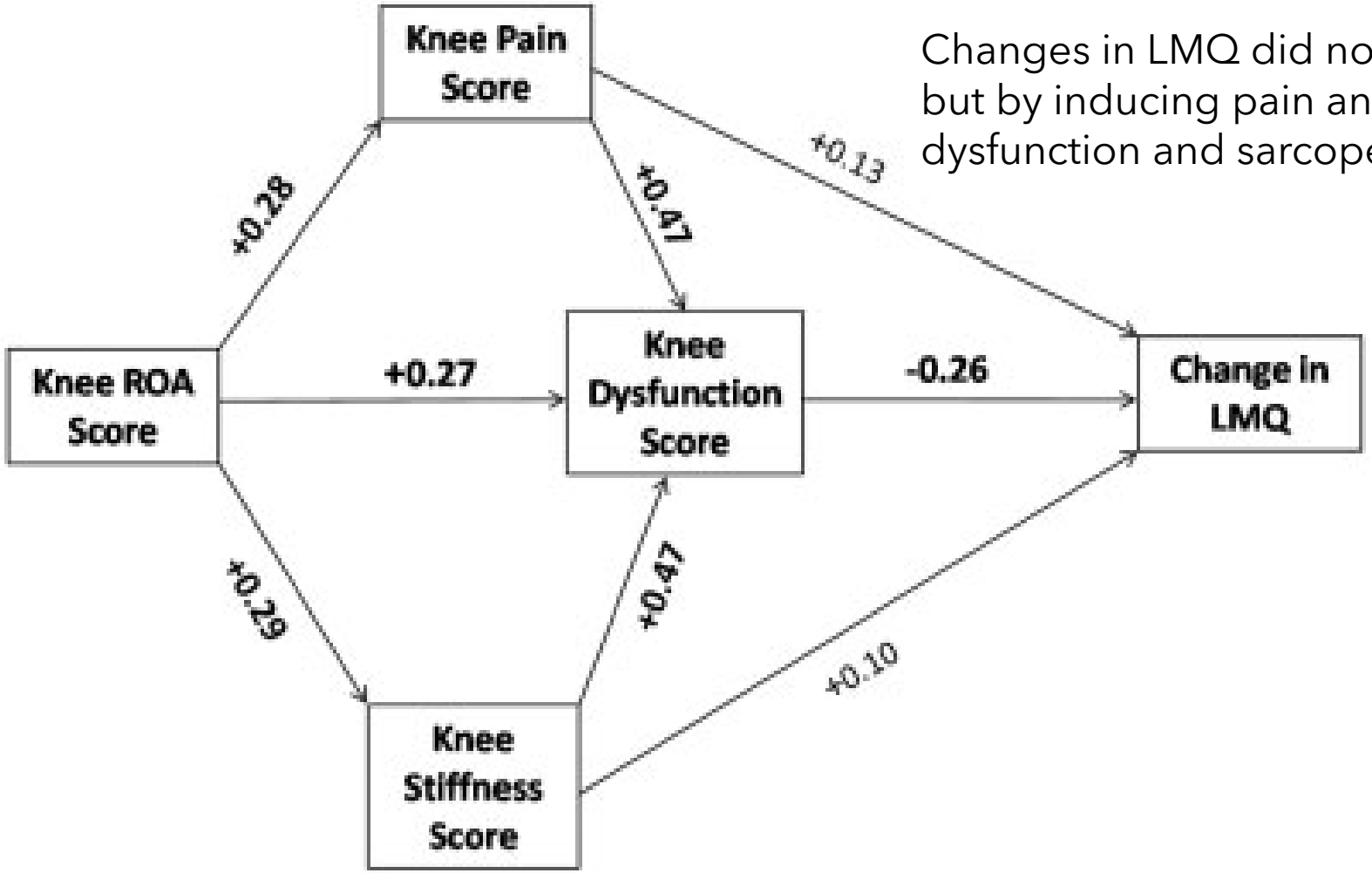
Prospective study, N=709



Greater declines in Lower extremity muscle quality (strength/mass) and greater increase on falls over 3 yr were observed in women, but not in men, who reported pain at baseline in more than one site.

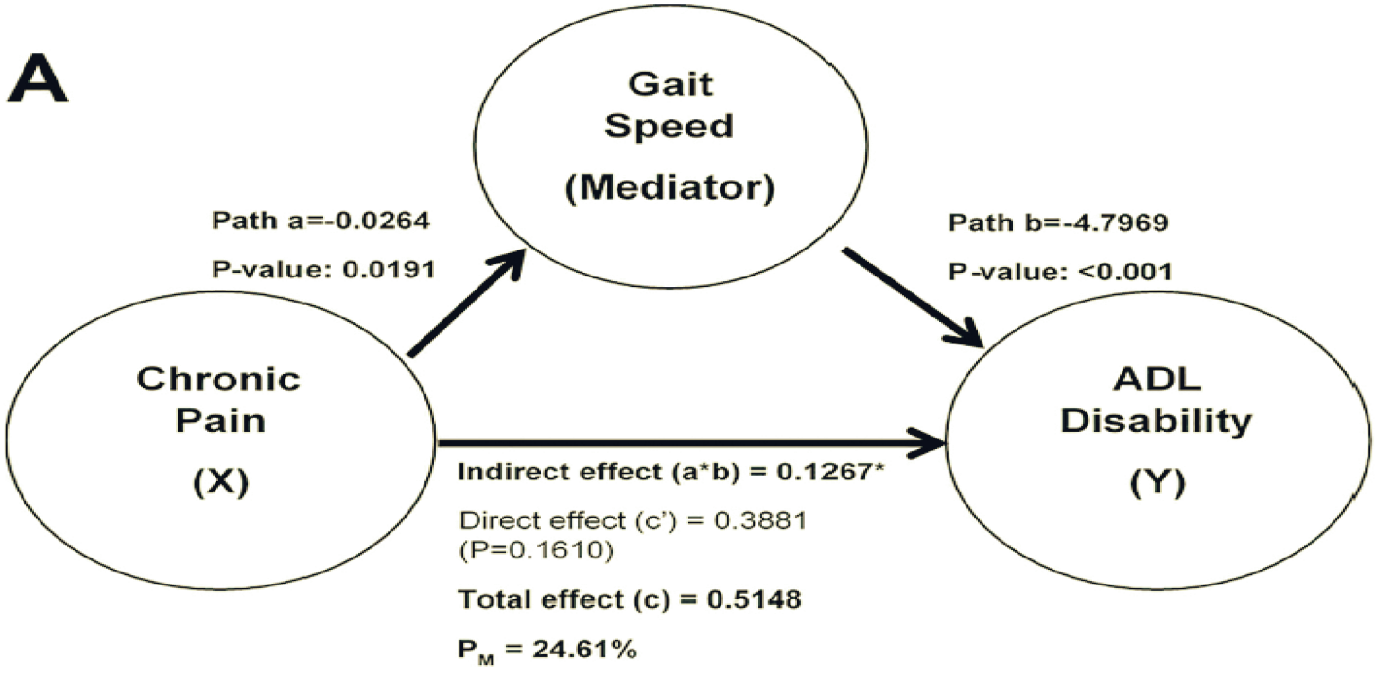
Scott, 2012

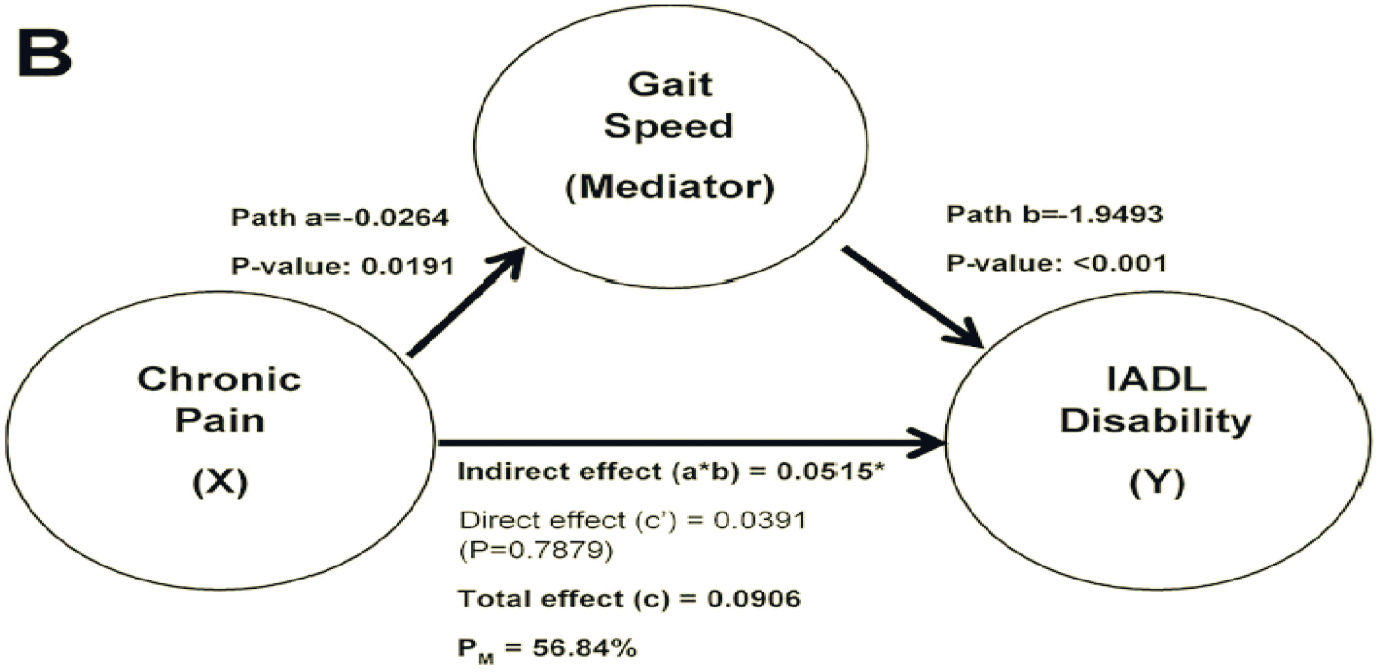
Link between ROA and Lower extremity Muscle function in older women. TASOAC Study



Changes in LMQ did not differ for ROA at baseline, but by inducing pain and stiffness that lead to dysfunction and sarcopenia

Scott, 2012





N=1452 community-dwelling men aged ≥ 70 followed for 5 yrs

Prevalence rate of pain=11%

Mediation analysis of the effect of Self-reported chronic pain on ADL and IADL disability and the mediating effect of gait speed (not ALM nor grip strength).

Chronic pain might lead to disability even before muscle mass loss: room for early interventions by treating pain

Scott, 2021

Sarcopenia as main cause of pain in OA. The Health ABC Study

Table 2. Odds ratios and 95% confidence intervals for the effect of baseline ALM or grip strength on the likelihood of incident clinically diagnosed, symptomatic knee OA or knee pain over the first 5 years of follow-up in the Health ABC Study, stratified by sex

	Men		Women	
	Knee OA Cohort (n = 1385)	Knee Pain Cohort (n = 1115)	Knee OA Cohort (n = 1394)	Knee Pain Cohort (n = 1067)
ALM,[a] kg	**0.68 (0.47-0.97)**[b]	0.93 (0.74-1.18)	1.12 (0.76-1.65)	0.76 (0.56-1.05)
Grip strength,[a] kg	1.00 (0.76-1.32)	**1.20 (1.01-1.42)**[b]	1.14 (0.83-1.55)	1.07 (0.84-1.37)
Low ALM (yes/no)[c]	**0.21 (0.05-0.87)**[b]	0.82 (0.52-1.28)	0.94 (0.59-1.50)	0.88 (0.63-1.22)
Low grip strength (yes/no)[c]	1.08 (0.45-2.60)	1.17 (0.68-2.02)	1.32 (0.73-2.38)	1.49 (0.92-2.41)

Abbreviation: ALM, appendicular lean mass; OA, osteoarthritis.
All models are adjusted for race, baseline age, baseline body mass index, walking per week, nonsteroidal anti-inflammatory drug use, oral glucocorticoid use, and prevalent comorbidities (malignancy, pulmonary disease, cardiac disease, cerebrovascular disease, and diabetes mellitus).
[a] Odds ratios are expressed per SD decrement in the predictor variable.
[b] Bold font indicates $P < 0.05$.
[c] Low ALM: men, <19.75 kg; women, <15.02 kg. Low grip strength: men, <26 kg; women, <16 kg (4).

Andrews, ACR, 2021

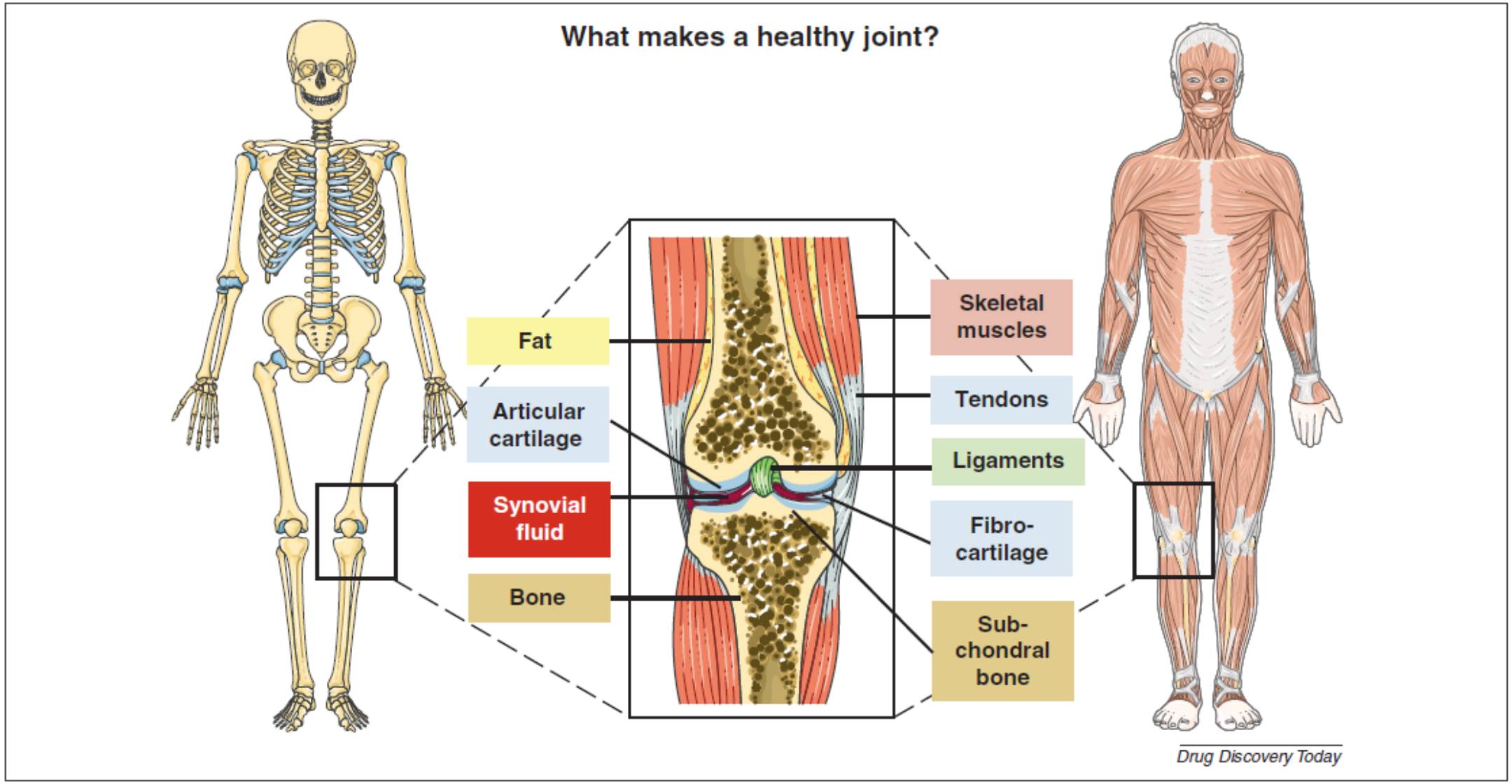


FIGURE 1

What makes a healthy joint? At the adult age, in healthy conditions, the skeleton (bones and cartilage) and skeletal muscles represent approximately 15–20% and 35–45% of the total body mass, respectively. The local joint environment includes tissues among which periarticular muscles, bones, cartilage, and their associated ligaments build an intricate and interrelated anatomical network.

De Ceunick et al, DDT, 2014

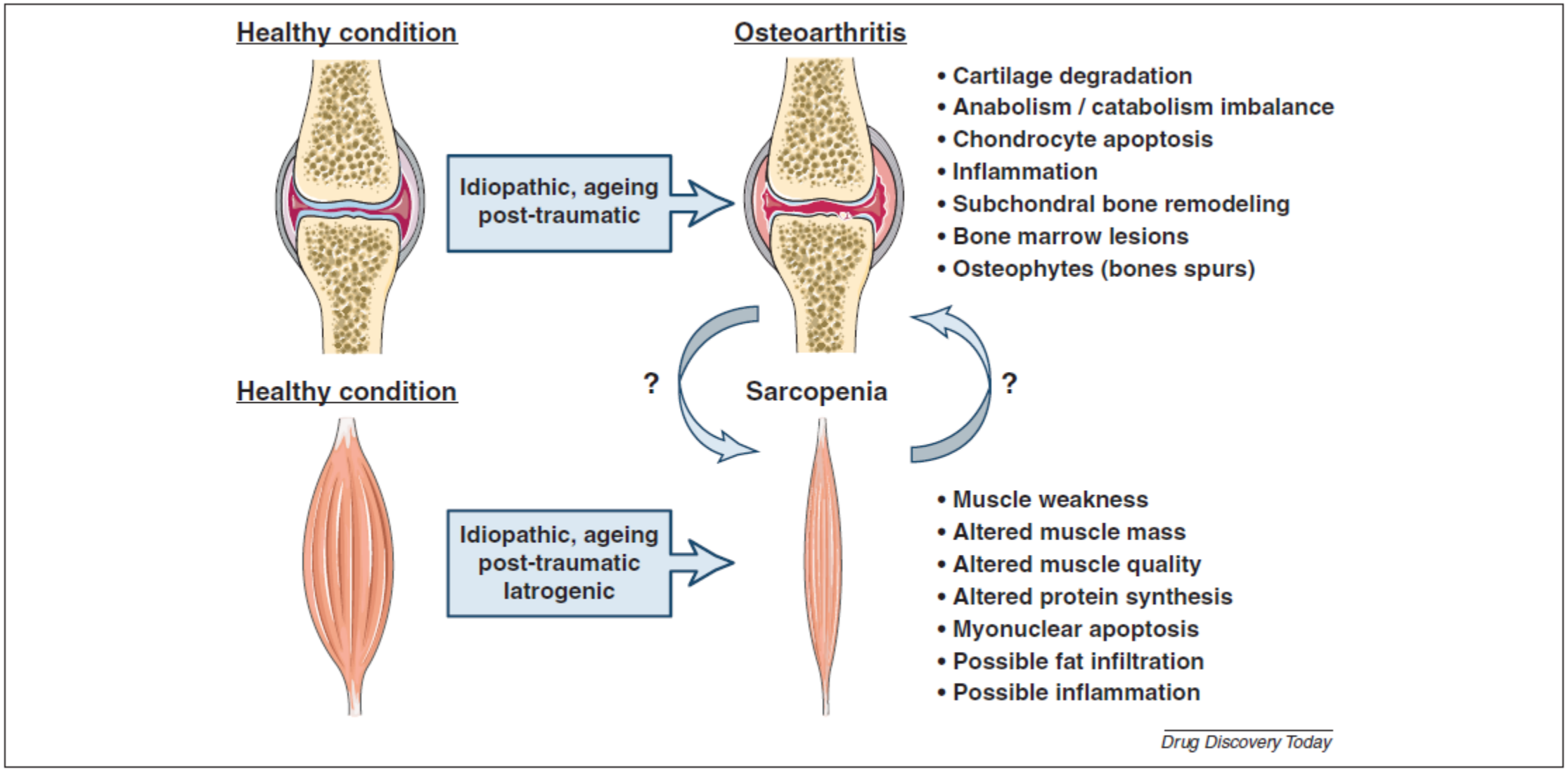


FIGURE 2

Main features of osteoarthritis and sarcopenia. Although still being a matter of debate, both conditions may be caught in a vicious circle where muscle weakness favours cartilage degradation, and *vice versa*.

De Ceunick et al, DDT, 2014

….. vicious cycle even worst with sarcopenic obesity

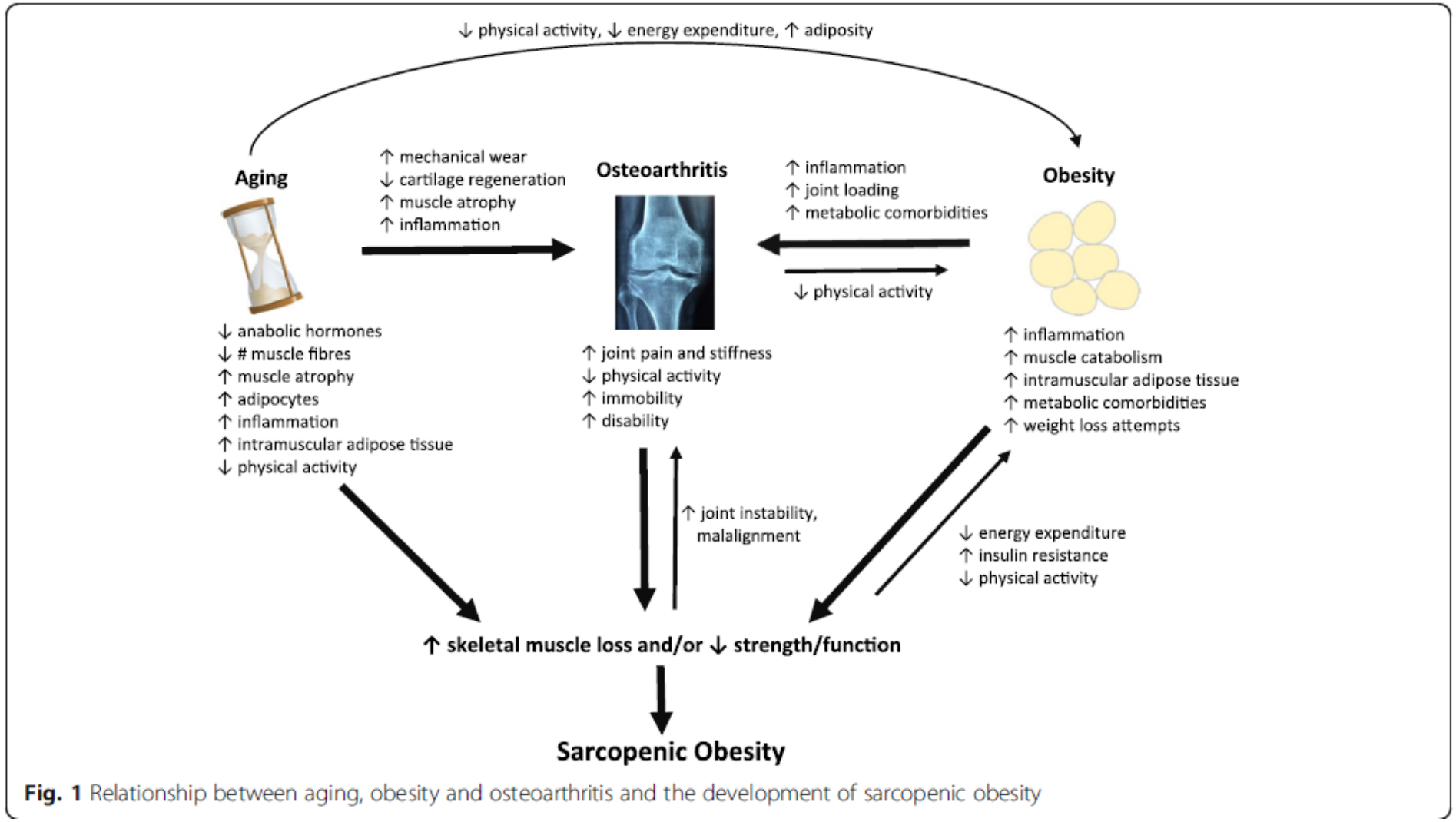


Fig. 1 Relationship between aging, obesity and osteoarthritis and the development of sarcopenic obesity

Godziuk, 2018

Sarcopenia and immunosenescence

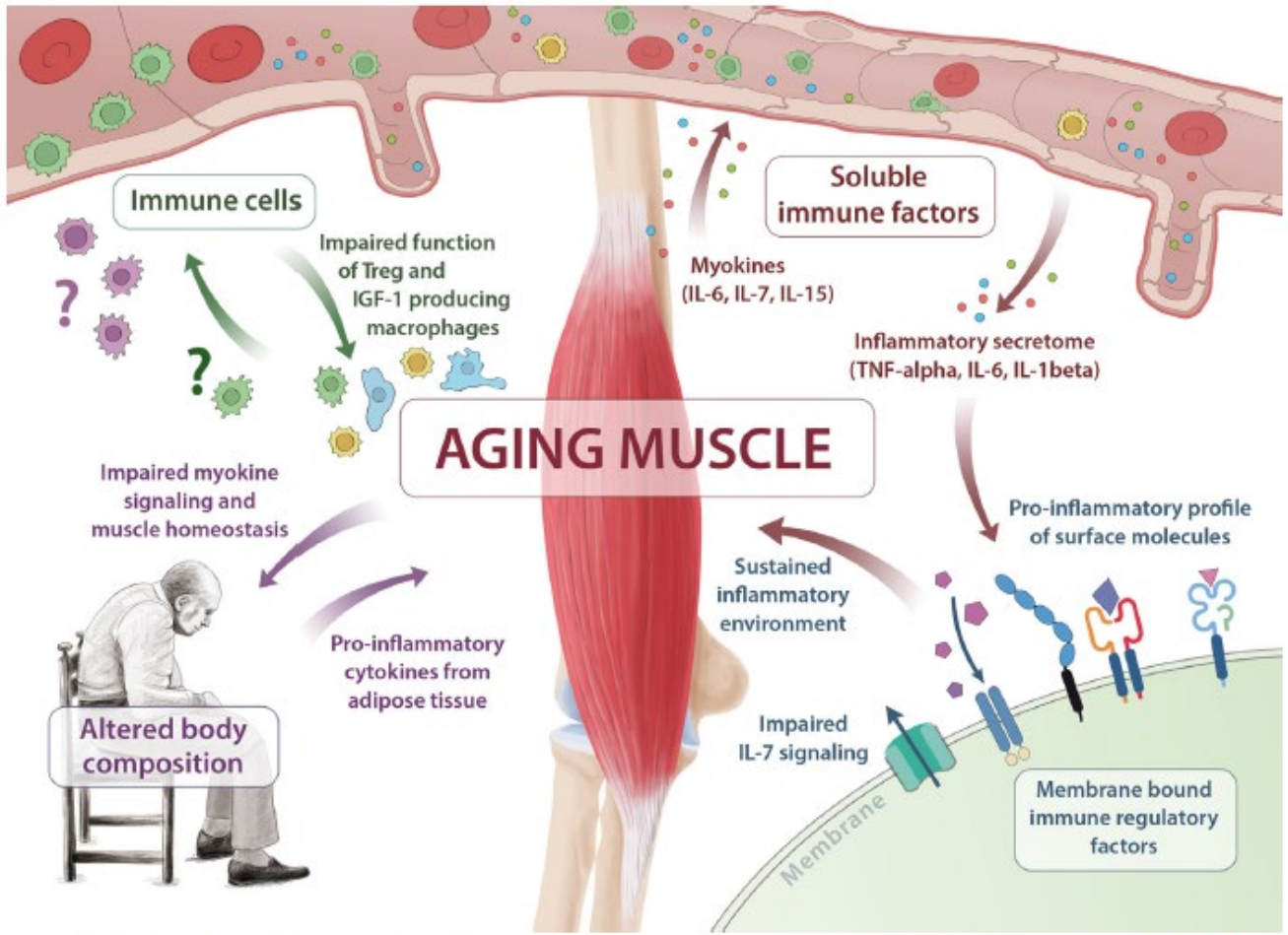


Fig. 1. Aging of skeletal muscle is central in the pathogenesis of immune senescence and sarcopenia. Multiple pathways are affected, including insufficient myokine signalling (IL-6, IL-7, IL-15), shifting of membrane bound immune regulatory factors towards a pro-inflammatory profile, impaired immune cell function and altered body composition.

Potential central role of the skeletal muscle in regulating the immune system function during age

Nelke, 2019

Sarcopenia and Inflammation

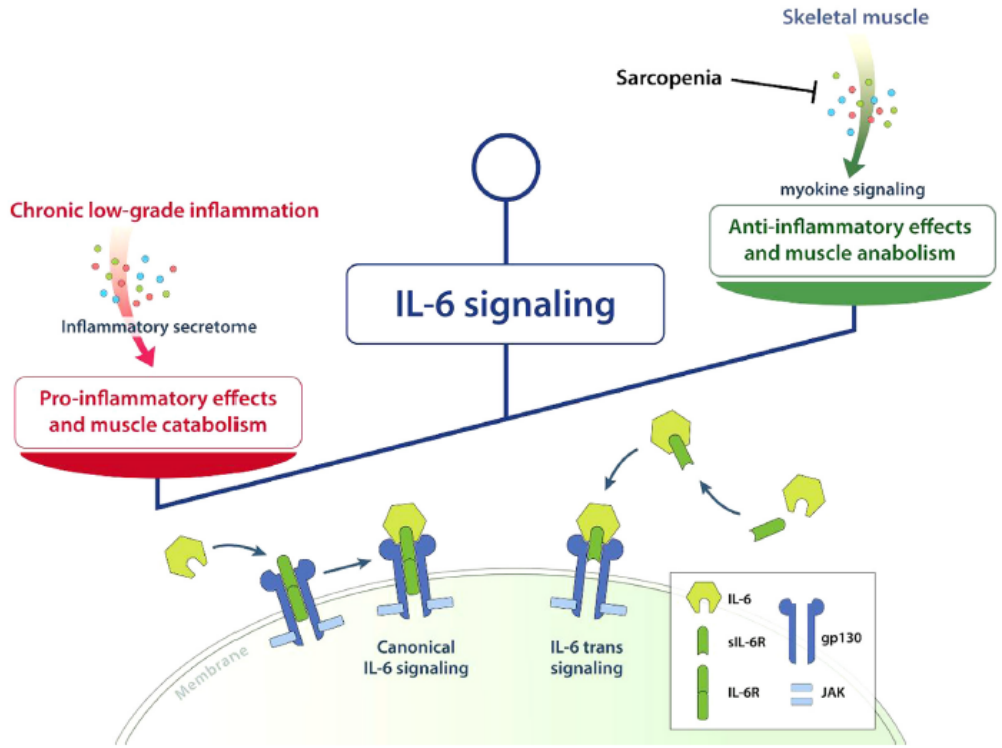


Fig. 2. Aging tips the scales of IL-6 signalling. Chronic exposure to IL-6 and the concomitant release of pro-inflammatory cytokines promote pro-inflammatory effects and muscle catabolism due to IL-6 signalling. The pulsatile release of IL-6 in response to exercise is impaired in sarcopenia resulting in reduced anti-inflammatory effects and impaired muscle anabolism mediated by IL-6. The biological effect of IL-6 is mediated both by canonical and by trans-signalling.

Nelke, 2019

Low-grade inflammation and sarcopenia: the role of exercise and nutrition

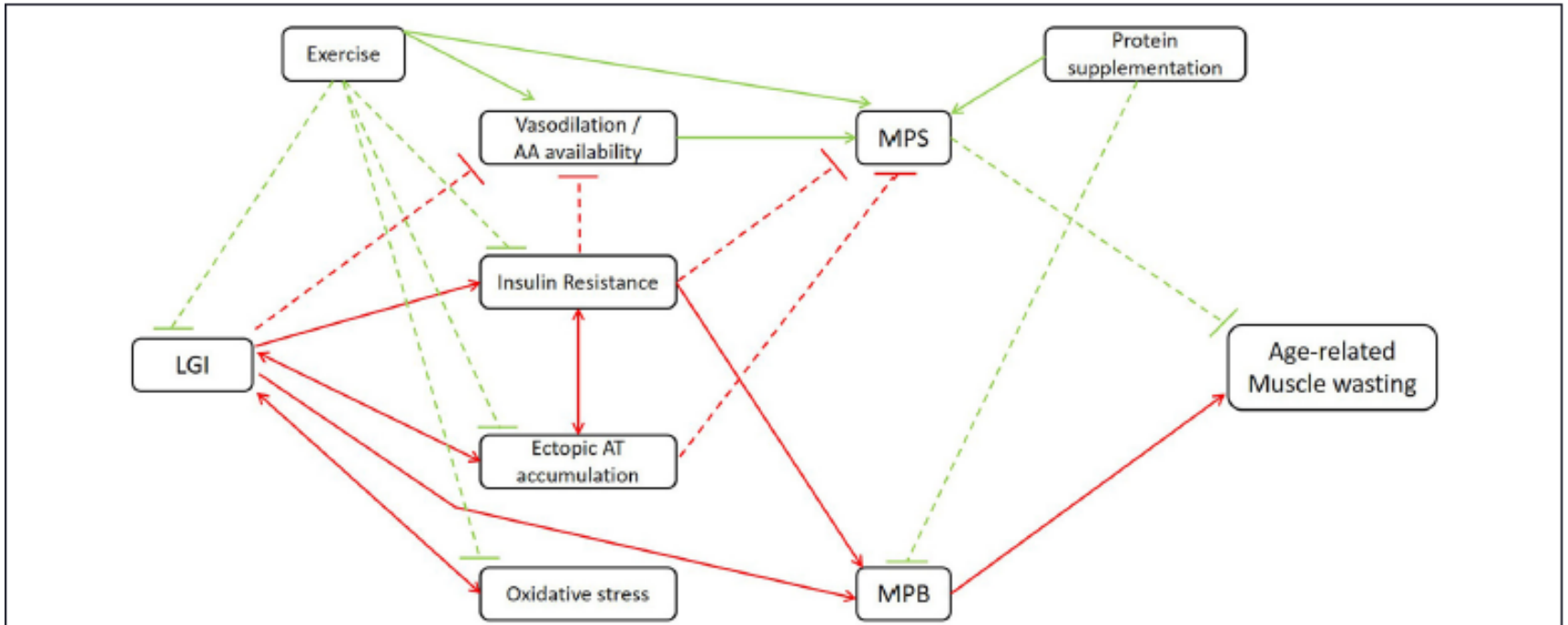
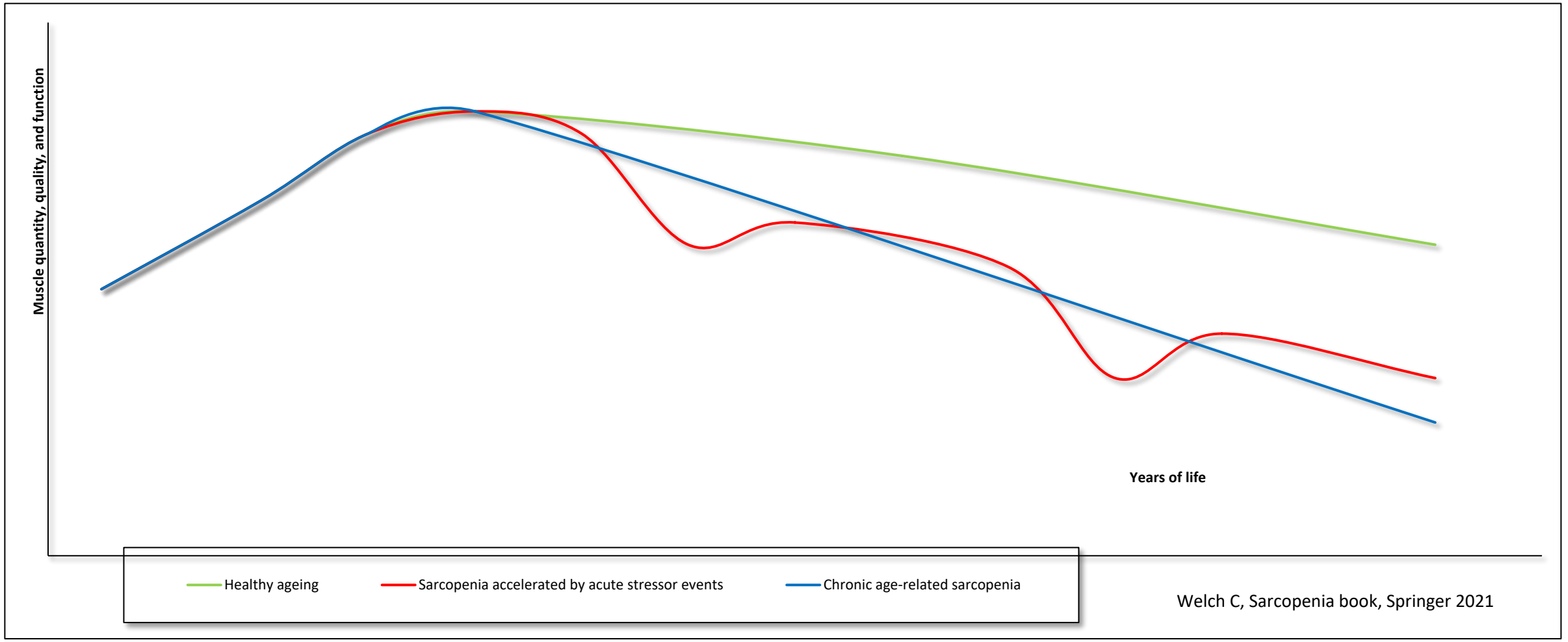


FIGURE 1 | Schematic illustration of the mechanisms through which LGI may indirectly affect age-related muscle wasting. LGI, low-grade inflammation; AA, amino acid; AT, adipose tissue; MPS, muscle protein synthesis, MPB, muscle protein breakdown. Red lines contribute to the induction of muscle wasting; green lines to the attenuation of muscle wasting. Dashed lines: inhibitory signaling; full lines: stimulatory signaling. Additional to the association between LGI and age-related muscle wasting, the beneficial effects of classic strategies such as exercise and protein supplementation are illustrated.

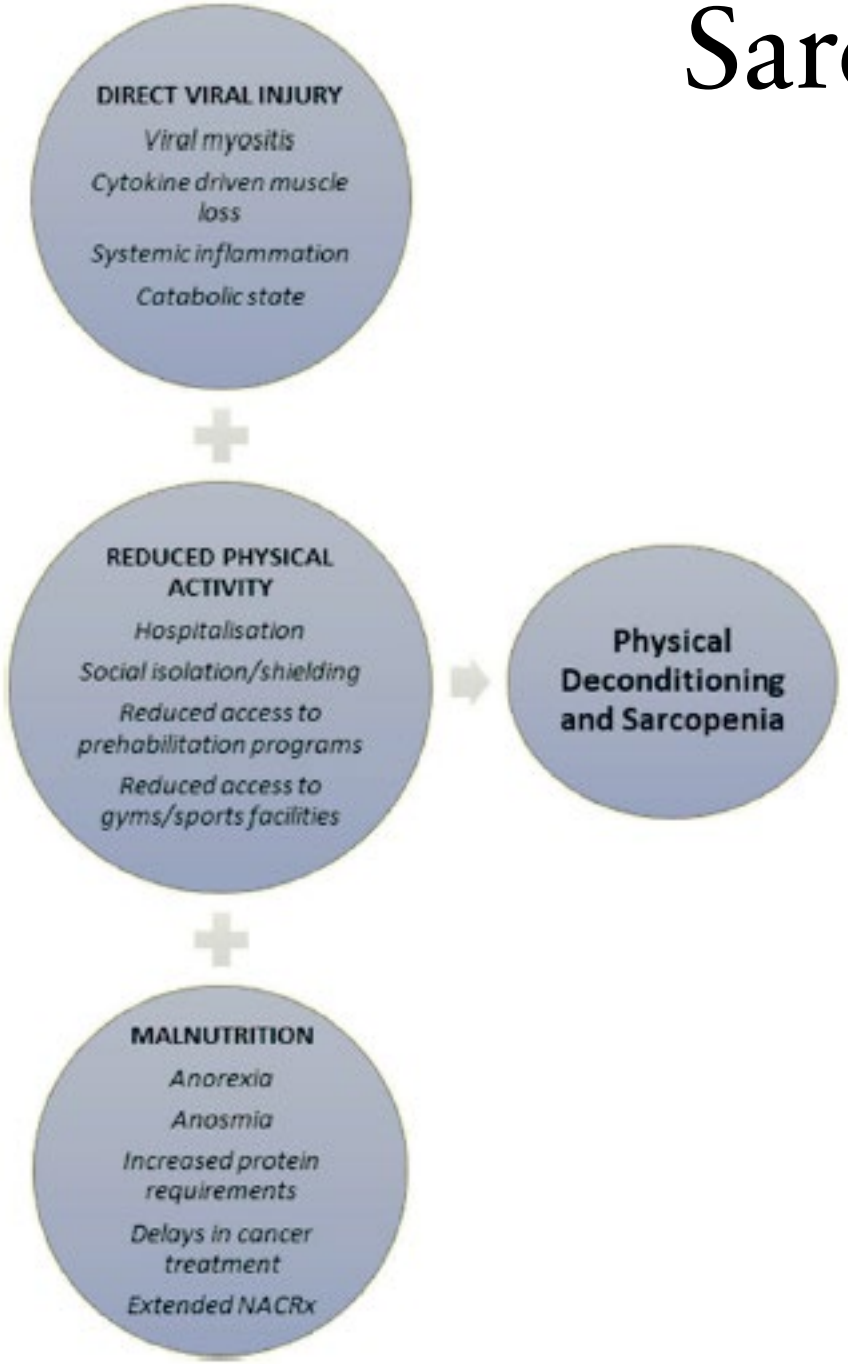
Dalle et al, 2017

Life-course approach to sarcopenia



Welch C, Sarcopenia book, Springer 2021

Sarcopenia and Covid-19



…but we also know that sarcopenia:

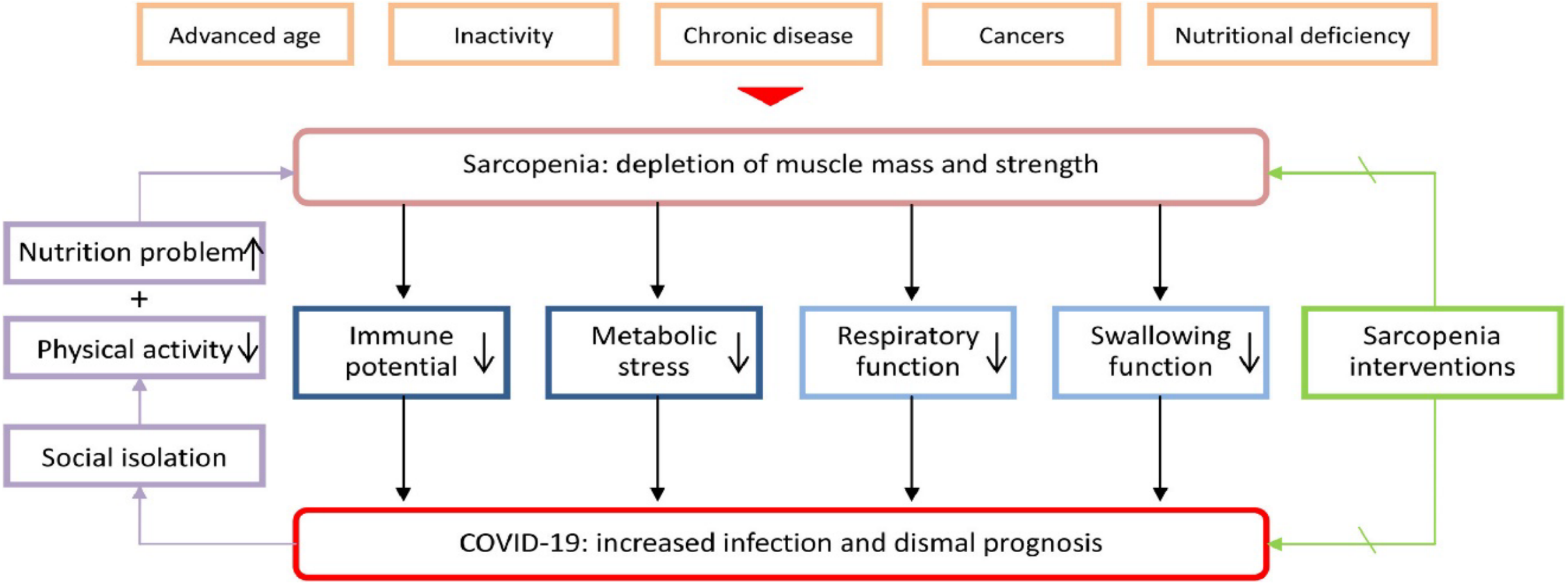
1. Predicts the risk for infections after surgery
2. Sarcopenic patients have a three-fold increase risk for nosocomial infections
3. In community-dwelling sarcopenia predicts the risk for community acquired pneumonia

therefore

A vicious cycle is established between sarcopenia and infectious diseases

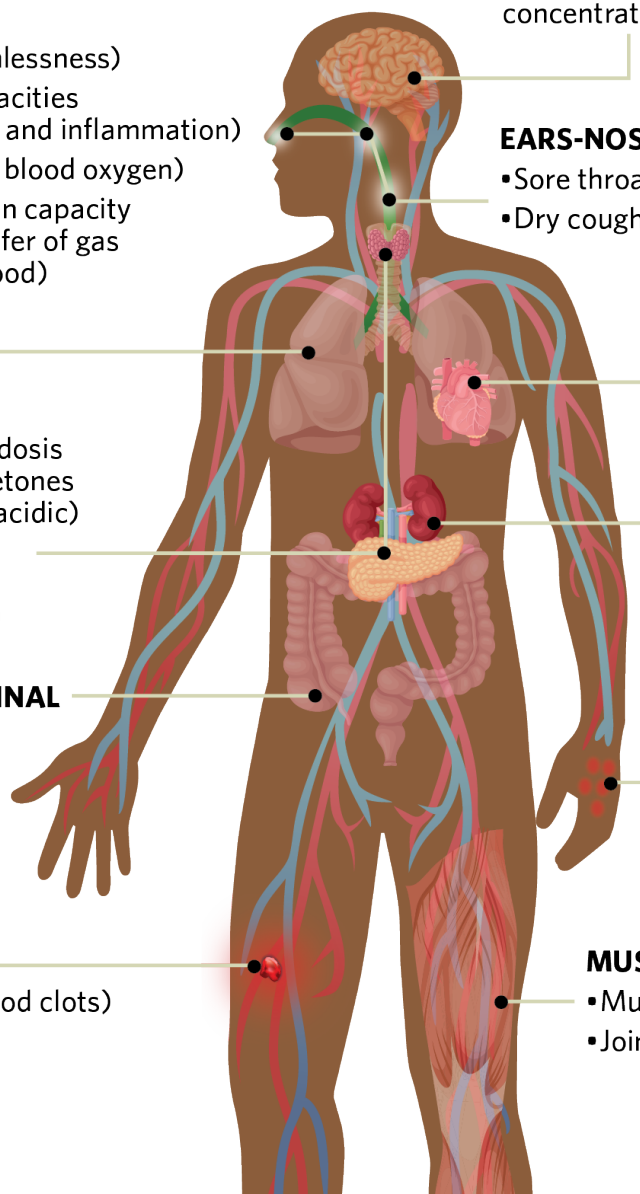
Casey et al, World J Surg Oncol, 2021

Vitamin D and Covid-19



Teshome et al. The Impact of Vitamin D Level on COVID-19 Infection: Systematic Review and Meta-Analysis. Front Public Health. 2021

Post-acute covid-19 syndrome



SYSTEMIC
- Fatigue
- Post-exertional malaise

NEUROPSYCHIATRIC
- Anxiety
- Depression
- Insomnia
- Brain fog (impaired attention, concentration, memory)

PULMONARY
- Dyspnea (breathlessness)
- Ground glass opacities (signs of fibrosis and inflammation)
- Hypoxemia (low blood oxygen)
- Reduced diffusion capacity (inefficient transfer of gas from lungs to blood)

EARS-NOSE-THROAT
- Sore throat
- Dry cough

CARDIOVASCULAR
- Nonspecific chest pain
- Myocarditis (inflammation of heart muscle)
- Palpitations
- High heart rate

ENDOCRINE
- Diabetic ketoacidosis (high levels of ketones make blood too acidic)
- Mild thyroiditis (inflammation of thyroid gland)

RENAL
- Acute kidney injury (sudden inability to filter)

GASTROINTESTINAL
- Diarrhea
- Loss of appetite

DERMATOLOGIC
- Alopecia (hair loss)
- Rashes

HEMATOLOGIC
- Thrombosis (blood clots)

MUSCULOSKELETAL
- Muscle ache
- Joint Pain

No one really knows how or why long-covid happens, who is more likely to get it, or how to treat it, but for sure muscle pain and joint pain are frequent and pathophysiologic mechanisms need to be explored

Nalbandian, A., Sehgal, K., Gupta, A. *et al.* Post-acute COVID-19 syndrome. *Nat Med* **27,** 601–615 (2021).

geriatrics

MDPI

Review

Evidence-Based Role of Nutrients and Antioxidants for Chronic Pain Management in Musculoskeletal Frailty and Sarcopenia in Aging

Simone Perna [1,*], Tariq A. Alalwan [1], Salwa Al-Thawadi [1], Massimo Negro [2], Mauro Parimbelli [2], Giuseppe Cerullo [3], Clara Gasparri [4], Fabio Guerriero [5,6], Vittoria Infantino [4], Mariaconcetta Diana [6], Giuseppe D'Antona [2,7] and Mariangela Rondanelli [7,8]

Conclusioni

- La **definizione di sarcopenia** è in continua evoluzione e questo influenza l'associazione o meno con altre patologie MS, quali la fibromialgia e il back pain
- Il **dolore cronico e la sarcopenia sono interconnessi** e portano a perdita della funzionalità e dell'autonomia, perdita che è comune a tutte le patologie muscoloscheletriche associate alla sarcopenia (quindi con effetto sinergico sulla perdita di funzionalità e su altri outcome negativi, quali cadute, fratture, peggior qualità di vita)
- Il trattamento del dolore nella sarcopenia deve tener conto dell'**eterogeneità delle cause e delle co-morbidità**
- Un trattamento multidimensionale, con **interventi nutrizionali e fisioterapici in supporto alla terapia farmacologica**, rappresenta l'approccio più adeguato per il management di questi pazienti, che hanno quadri clinici e prognostici molto eterogenei