

MALNUTRITION, SARCOPENIA AND FRAILITY: *IMPLICATIONS FOR DIAGNOSIS AND INTERVENTION*



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Disclosures

- Speaker: Baxter, Abbott, Fresenius Kabi
- Consultant: Baxter, Abbott, Fresenius Kabi, Nestle, Takeda
- Research Support: Baxter, Fresenius Kabi

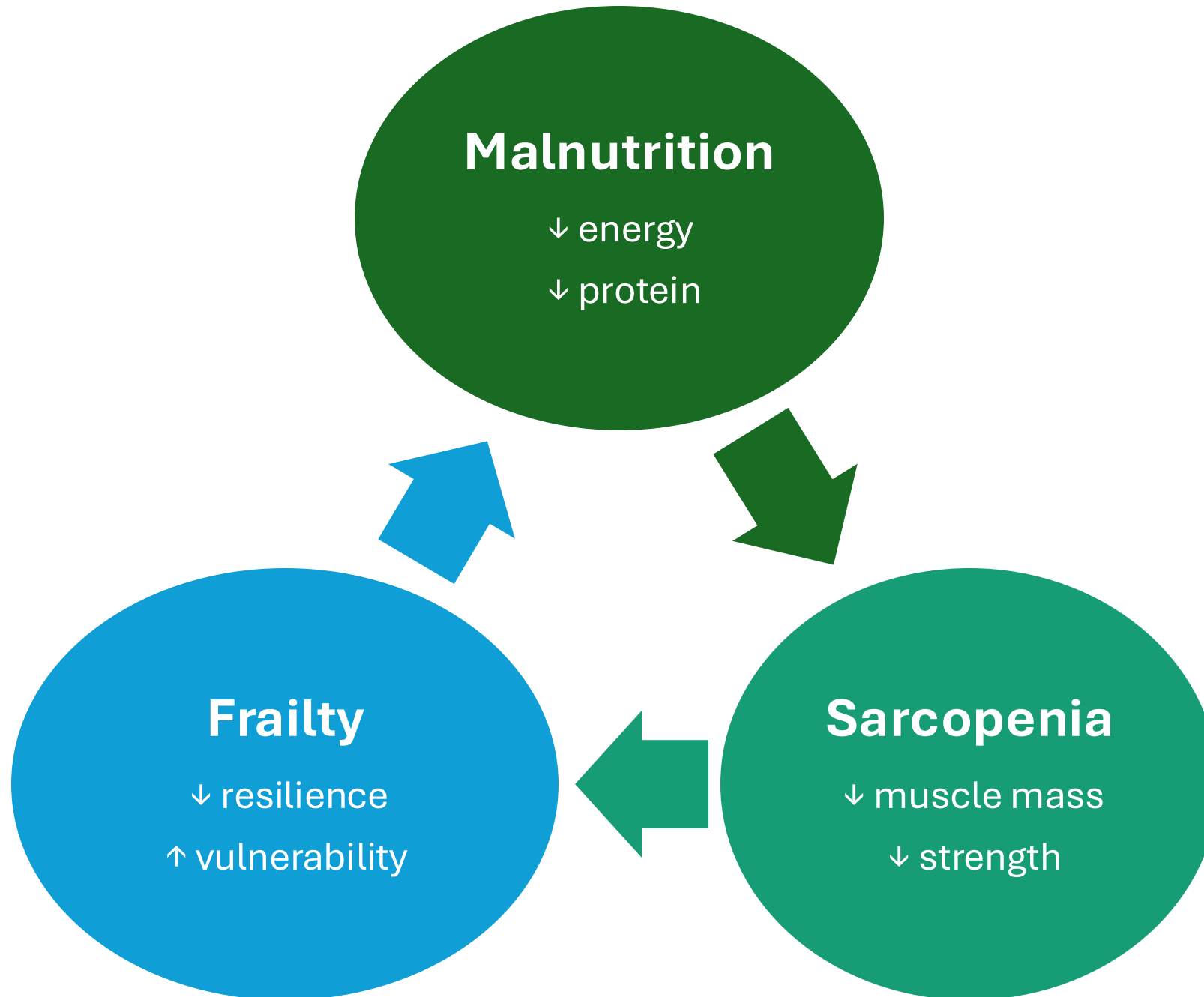
Objectives:

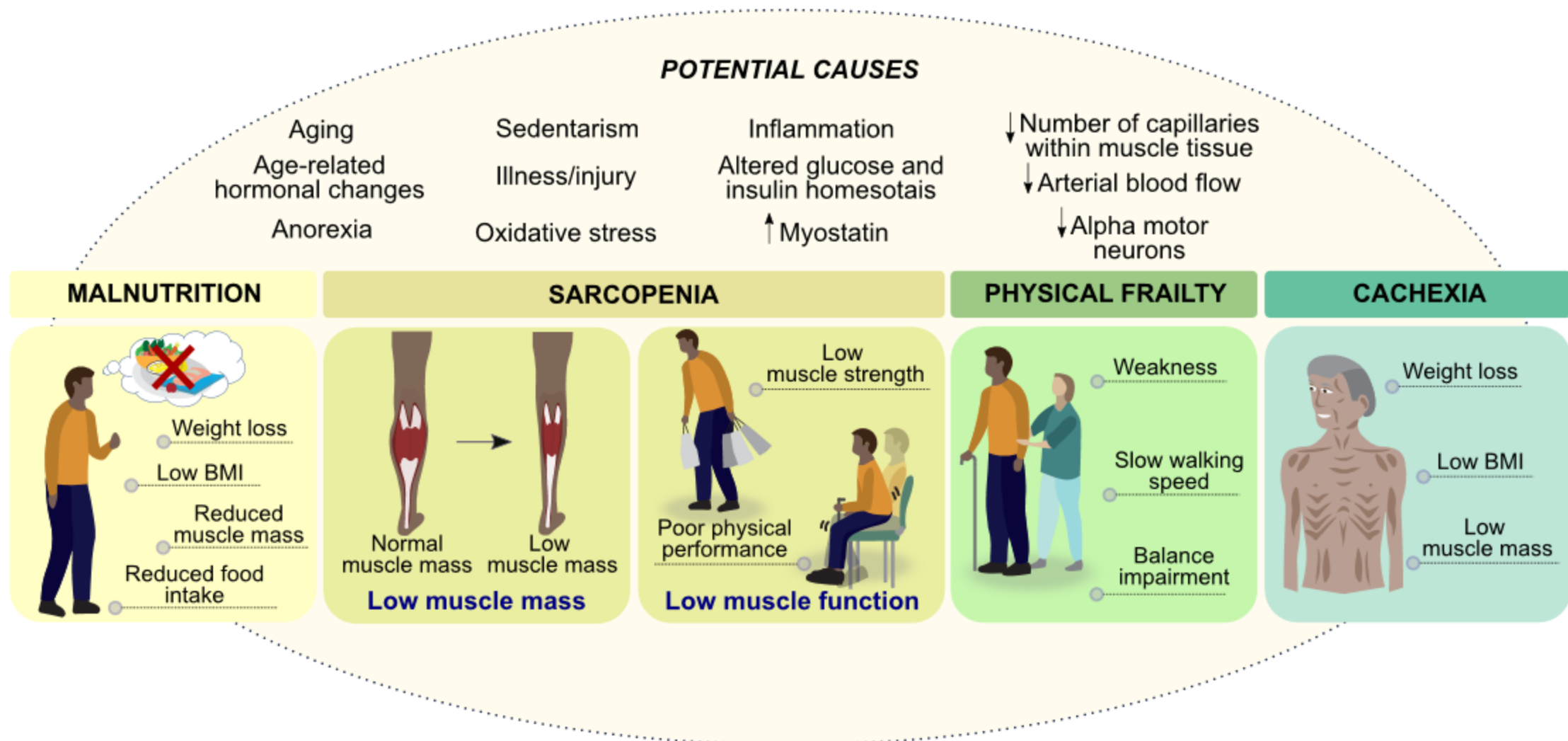
- Describe the features of Malnutrition, Sarcopenia and Frailty and overlap between these conditions
- Review the screening, assessment and diagnosis of Malnutrition, Sarcopenia and Frailty
- Highlight intervention opportunities to break the cycle

Starting at 10,000 ft

- **Malnutrition, Sarcopenia** and **Frailty** are interrelated conditions that form a synergistic triad which contributes to functional decline, morbidity and mortality
- Understanding the relationship between these conditions inform detection, prevention and treatment of these conditions
- The cycle of Malnutrition > Sarcopenia > Frailty can be broken through timely recognition and targeted action

Condition	Malnutrition	Sarcopenia	Frailty	Cachexia
Cause	Inadequate nutrient intake	Aging, inactivity, malnutrition	Accumulation of deficits	Coexisting disease such as cancer, advanced chronic illness
Key Deficit	Protein, Energy, N3 FAs micronutrients	Muscle mass and strength/function	Physiologic reserve	Weight loss, Muscle, adipose loss
Assessment	GLIM, MNA, SGA	EWGSOP2 Criteria, grip strength, DEXA, CT, US, GLIM	Fried Frailty Phenotype, Clinical Frail Scale, Frailty index	Include assessment of inflammation
Overlap	Can cause or result from sarcopenia or frailty	Often due to malnutrition, worsens frailty	May include elements of malnutrition and sarcopenia	Always associated with Malnutrition, sarcopenia and accompanied by frailty

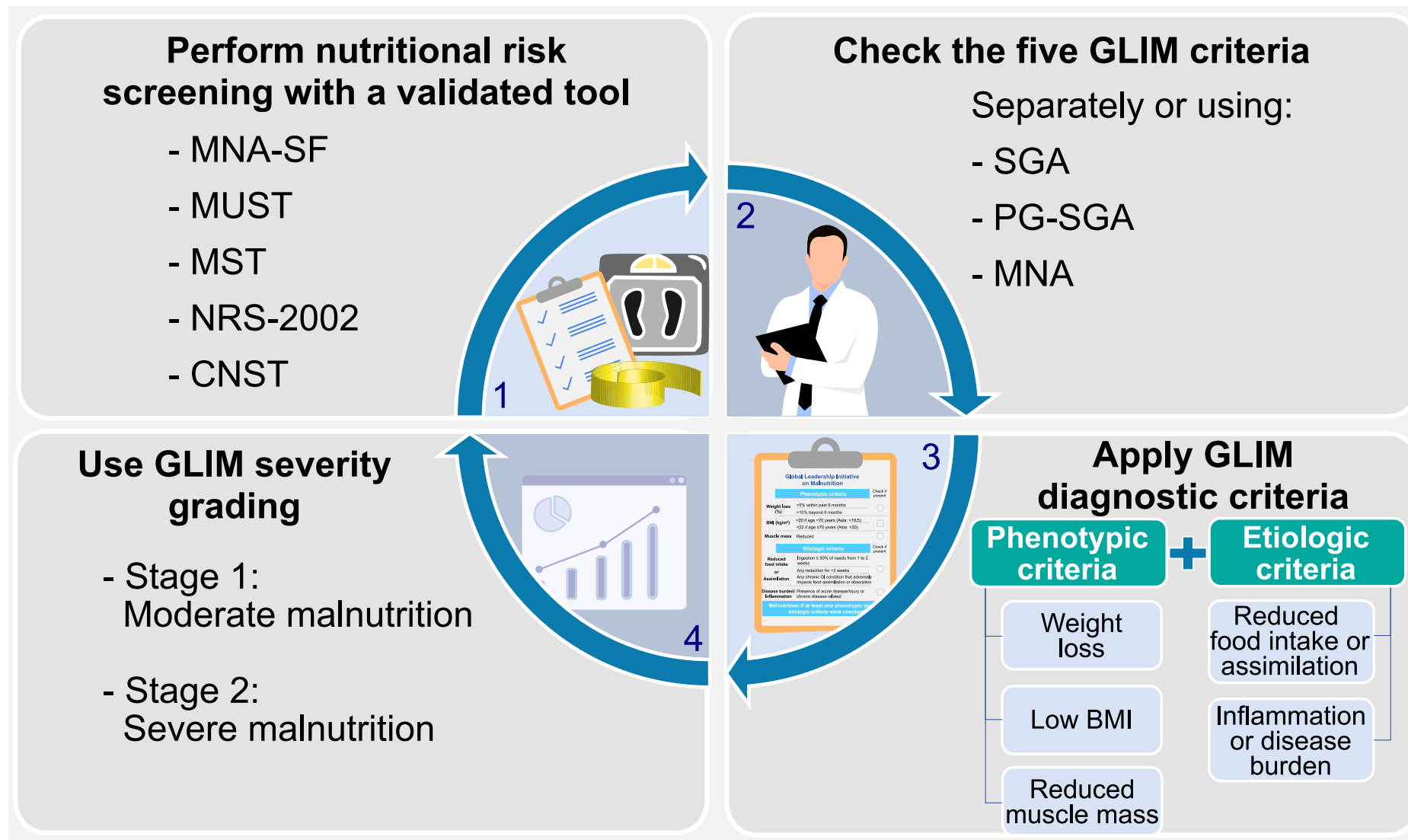


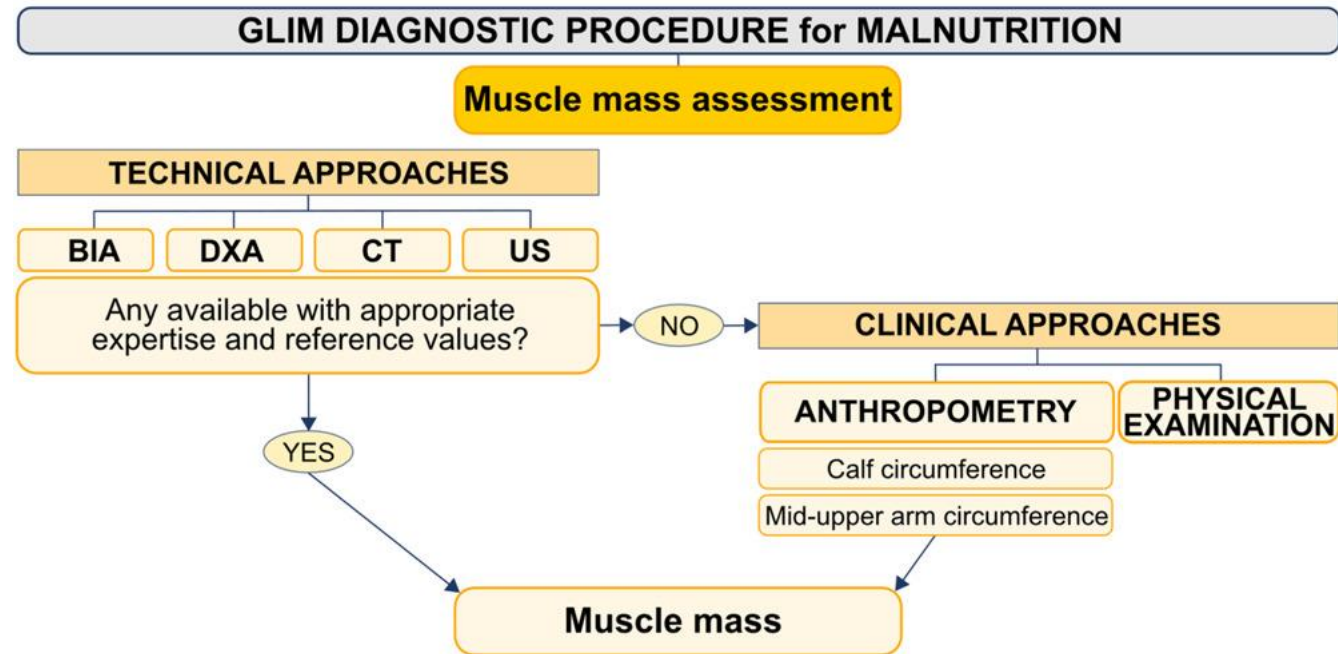


Malnutrition

- Malnutrition is the result of nutritional intake or absorption or digestion that is inadequate to support physiologic requirements
- Several factors can contribute to malnutrition including inadequate intake, physical and anatomic barriers, physiologic and psychological and socio-environmental causes
- Evidence based guidelines support the use of a variety of **screening** tools and strategies for diagnosis

GLIM approach to diagnosis of malnutrition





Malnutrition: Scaling Best Nutrition Care Practices

Keller H, Koechl JM, Laur C, et al. More-2-Eat implementation demonstrates that screening, assessment and treatment of malnourished patients can be spread and sustained in acute care; a multi-site, pretest post-test time series study. *Clin Nutr.* 2021;40(4):2100-2108.

Table 2. Percentage of screening, malnutrition and other nutrition diagnoses, advanced care and standardized care strategies by implementation period.

Practice	First Audit ^a	Mid-point ^a	Final Audit ^a	p-value
Sample size	N=541	N=533	N=484	
	%	%	%	
Screening & Assessment				
Screening completed at admission	50*	75 [†]	84 [‡]	<0.00
At risk for malnutrition ^b	25	30	31	0.275
SGA completed, of those screened at risk	71	69	71	0.645
SGA Mild/moderate malnutrition ^c	56	60	62	0.665
SGA Severe malnutrition	12	14	11	

More-2-Eat implementation demonstrates that screening, assessment and treatment of malnourished patients can be spread and sustained in acute care; a multi-site, pretest post-test time series study.

Clin Nutr. 2021;40(4):2100-2108.

Nutrition Treatment/Care

Any action taken	68*	66*	74 [†]	0.016
ONS as MedPass	7*	9*, [†]	13 [†]	0.007
ONS at other times/with meals	21	17	16	0.070
Nutrient dense diet	9	10	10	0.954
Liberalized diet	5	3	4	.481
Enteral nutrition	6	5	4	0.174
Parenteral nutrition	3	3	4	0.795
Medication change to address GI symptoms/pain	32*	40 [†]	47 [‡]	<0.001
Micronutrient supplementation	22*	35 [†]	42 [‡]	<0.001
Volunteer mealtime assistance	6*	10 [†]	16 [‡]	<0.001

Monitoring and Discharge

Food intake monitoring occurred	61*	70 [†]	73 [†]	<0.001
Body weight measured at admission	68*	59 [†]	68*	0.003
Body weight monitored post admission	32	34	30	0.506
Nutrition discharge plan initiated	14	13	12	0.660

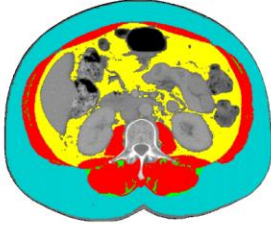
Is Malnutrition Screening Done?

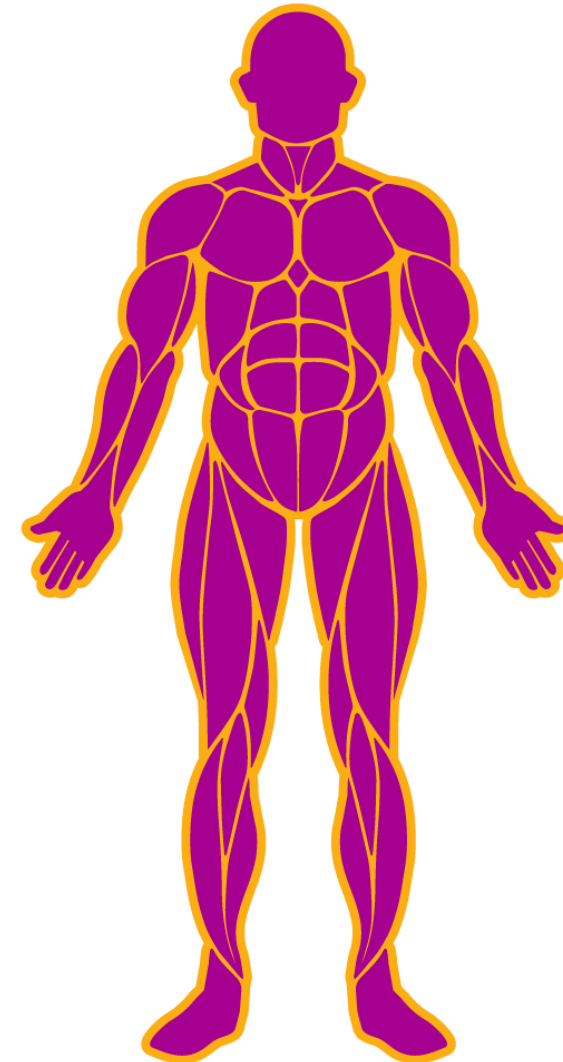
- Unlike frailty, **malnutrition screening *is* routinely done in many healthcare settings**, particularly:
 - **Hospitals**
 - **Long-term care facilities**
 - **Some primary-care and community programs**
- However, the **consistency and quality** of screening vary between regions and institutions
- Scale of screening requires a tailored, implementation science – based approach

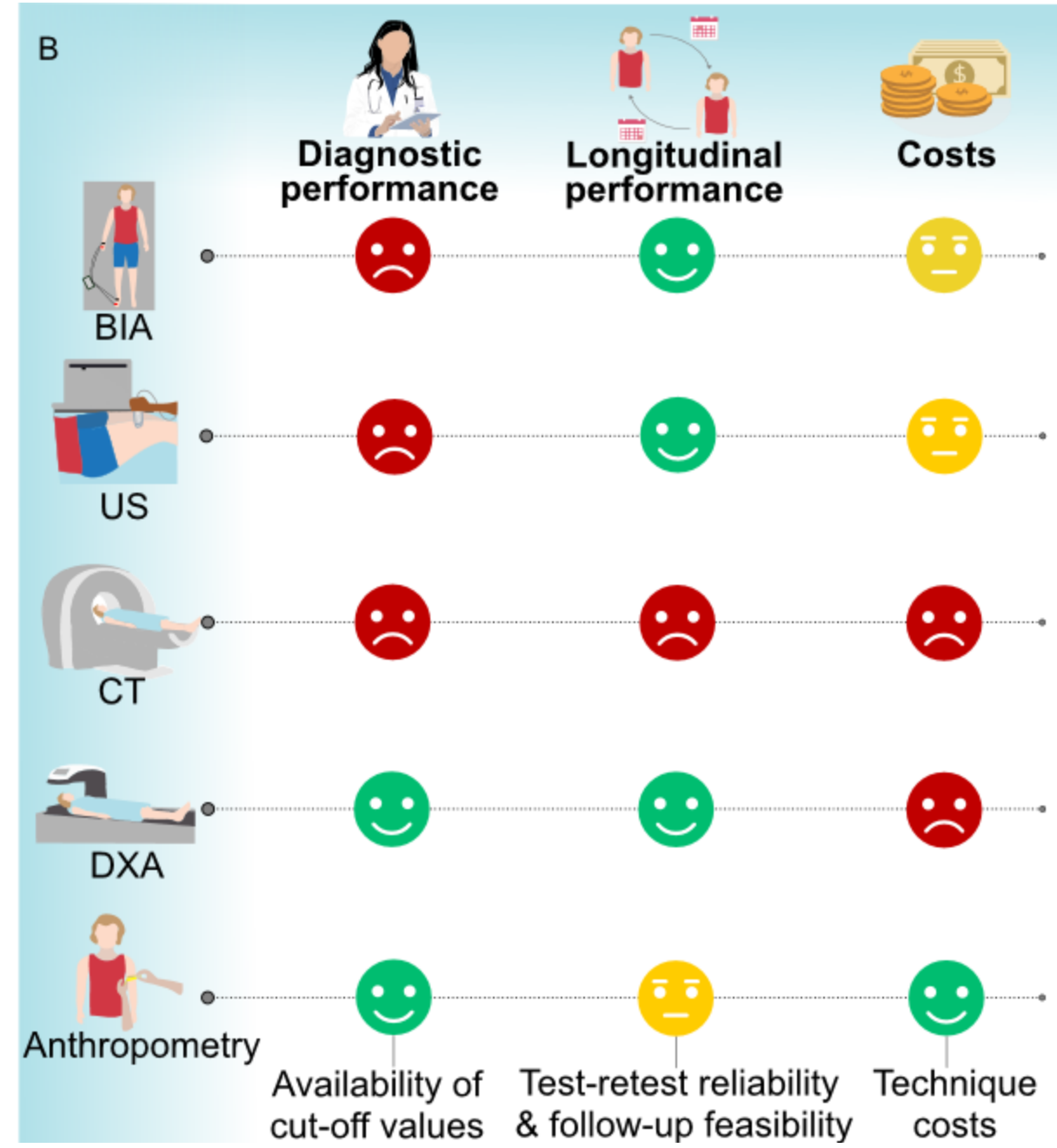
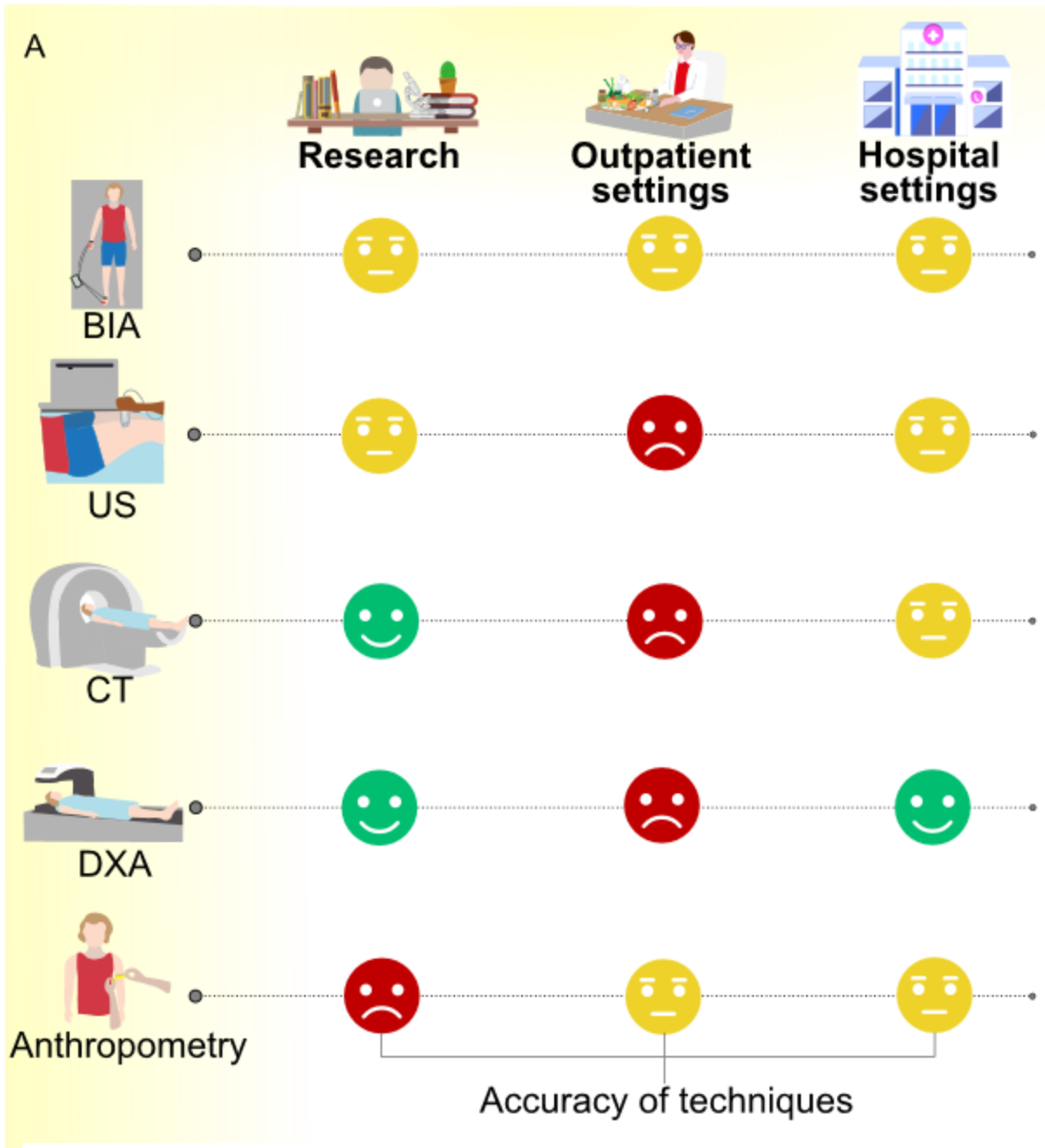
Sarcopenia

- Age-associated loss of skeletal muscle and function
- Life long process
- Complex multifactorial etiology
- Effects of inactivity (bedrest in particular) may mimic sarcopenia
- From 20 to 80 years there is a 30% reduction in muscle mass with decline in muscle fiber number and size

Assessing Lean Tissue: Sarcopenia

PROS	TECHNIQUE	CONS
Computed tomography		
- High resolution - Precise - Muscle “quality” measurement - Separate subcutaneous and visceral adipose tissues - Automated software available - Frequently available in cancer and other conditions		- Radiation exposure - Cost - Subject size limitations - Healthy cohort reference values are scarce
Dual-energy X-ray absorptiometry		
- Fast, non-invasive - Convenience and comfort, no pre-test protocol - Direct quantification of body composition - Values for bone density and mass - Safe for serial measurement - low radiation - Regional and whole-body measurements		- Height and weight restrictions - Requires licensed technician - Operator error - Cannot compare data from different manufacturers' machines - Not mobile - High cost to purchase and operate - Cannot specifically discern skeletal muscle mass and quality (like CT)
Bioelectrical impedance analysis		
- Safe - Potentially portable - Useful longitudinal observations - Variable instrument cost		- Measurement sensitive to subject conditions such as hydration and recent activity - Instrument predictions may be population specific
Ultrasound		
- Portable - Low/moderate cost - No radiation - Available in many hospitals - Useful for assessment of muscle changes - Utility in the intensive care unit		- Require trained personnel - Lack of protocols/cut-off values - Measurement sensitive to edema, subcutaneous adipose tissue thickness, probe angle, and tissue compression





Is Sarcopenia Routinely Screened for?

-  **Not routinely screened for** in most healthcare systems — but **recommended** in at-risk groups (especially older adults, people with chronic illness, or those who are malnourished or frail).
- Unlike malnutrition or frailty, sarcopenia screening is **not yet standard practice** outside of research, geriatrics, and rehabilitation settings.

Frailty

- A state of increased vulnerability resulting from age-associated declines in reserve and function across multiple physiological systems, such that the ability to cope with everyday or acute stressors is compromised Fried et al 2001
- Models:
 - Phenotypic (Fried)
 - Cumulative deficit model (Frailty Index) (Rockwood and Mitniski)
 - Clinical Frailty Score (CFS)

Frailty

Key Characteristics

- Reduced strength and endurance
- Slowed motor performance
- Unintentional weight loss
- Exhaustion or low energy
- Decreased physical activity
- Impaired balance and mobility
- Cognitive psychoses and decline

Causes and Contributing Factors

- Biological aging
- Chronic inflammation
- Hormonal dysregulation
- Sarcopenia (loss of muscle mass and strength)
- Nutritional deficiencies
- Comorbidities (e.g., cardiovascular disease, diabetes)
- Cognitive decline or depression

Models of Frailty

Feature	Fried Phenotypic Model (2001)	Cumulative Deficit Model (Rockwood & Mitnitski, 2007)
Core Concept	Frailty is a physical syndrome defined by observable signs and symptoms.	Frailty reflects the accumulation of health deficits across multiple systems.
Basis	Biological phenotype (observable characteristics).	Quantitative index (numerical calculation).
Criteria / Components	1. Unintentional weight loss 2. Weakness (grip strength) 3. Exhaustion 4. Slow walking speed 5. Low physical activity	Dozens of possible deficits (e.g., diseases, symptoms, disabilities, lab results). Each deficit scored as 0 (absent) or 1 (present).
Scoring	- 0 = Robust - 1–2 = Pre-frail - ≥3 = Frail	Frailty Index (FI) = (Number of deficits present) ÷ (Total number assessed).
Focus	Physical performance and sarcopenia.	Global health and biological aging.
Advantages	Easy to apply in clinical settings; simple and quick.	Captures full complexity of aging and comorbidity.
Limitations	May miss cognitive or psychosocial aspects.	Requires detailed data collection; less intuitive for quick screening.

Is Screening for Frailty Routinely Done?

-  **Recommended** by most geriatric and public health authorities.
-  **Implemented routinely** in only a few healthcare systems (notably the UK).
-  **Not yet universal** — often opportunistic rather than systematic.

screening is recommended, but **not yet universally routine** in most health systems.

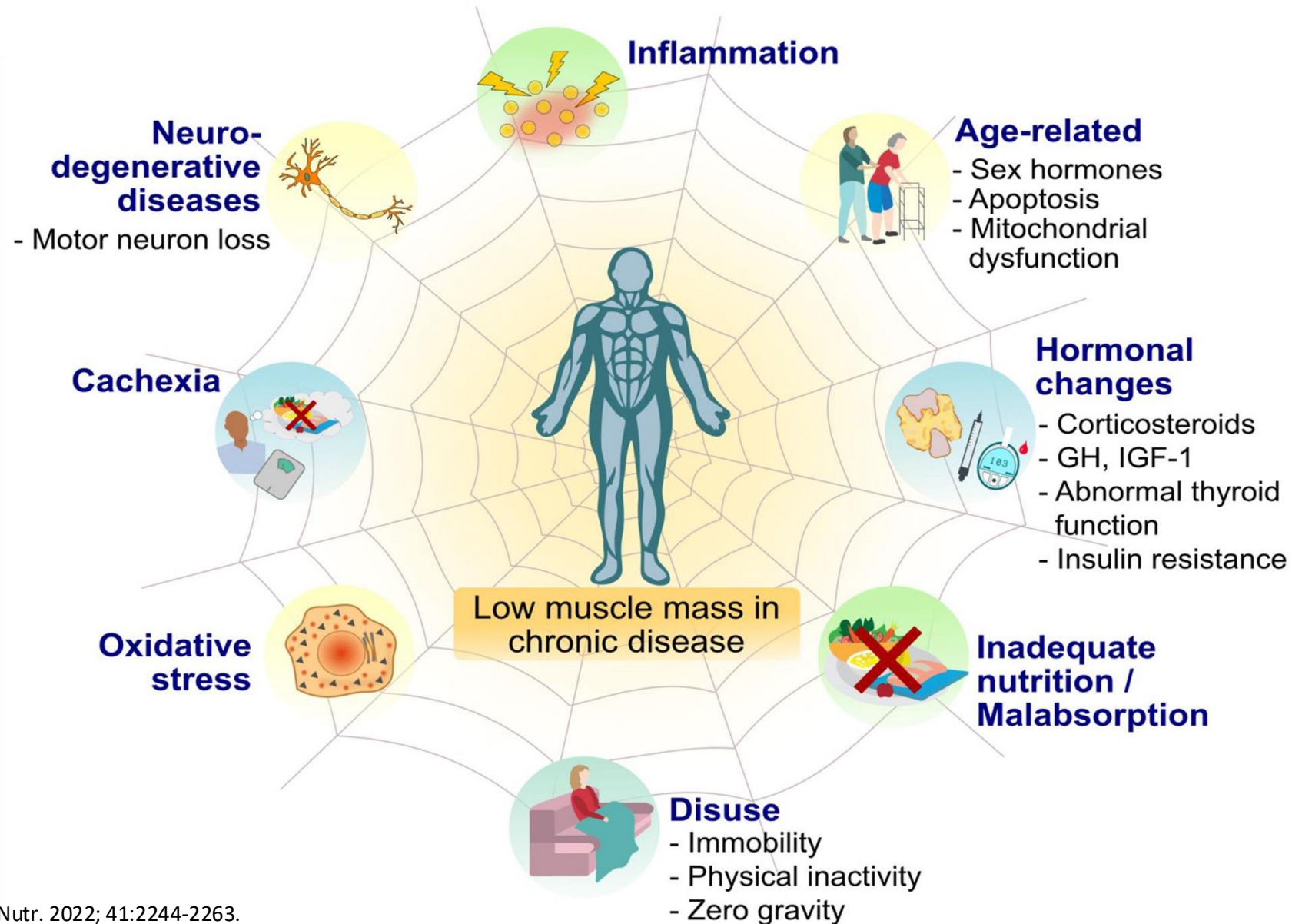
Many **guidelines** now encourage frailty assessment, especially for **older adults**, but **implementation varies** widely.

In practice, frailty screening tends to occur in **specific contexts** — e.g., before surgery, during hospital admissions, or in primary care for elderly or multimorbid patients.

Cachexia

- Cachexia is a metabolic condition that is always associated with underlying illness and inflammation,
- Characterized by loss of skeletal muscle and body weight
- Nutrition interventions have shown limited success in preserving fat but not muscle mass.
- Accelerated or exaggerated loss of skeletal muscle distinguishes cachexia from weight loss that is solely due to reduced energy intake
- TNF and interferon gamma reduce expression of myosin impacting protein degradation and synthesis
- Associated with reduction in circulating anabolic hormones
Testosterone, IGF1 sensitivity

SELECTED RISK FACTORS LEADING TO muscle wasting

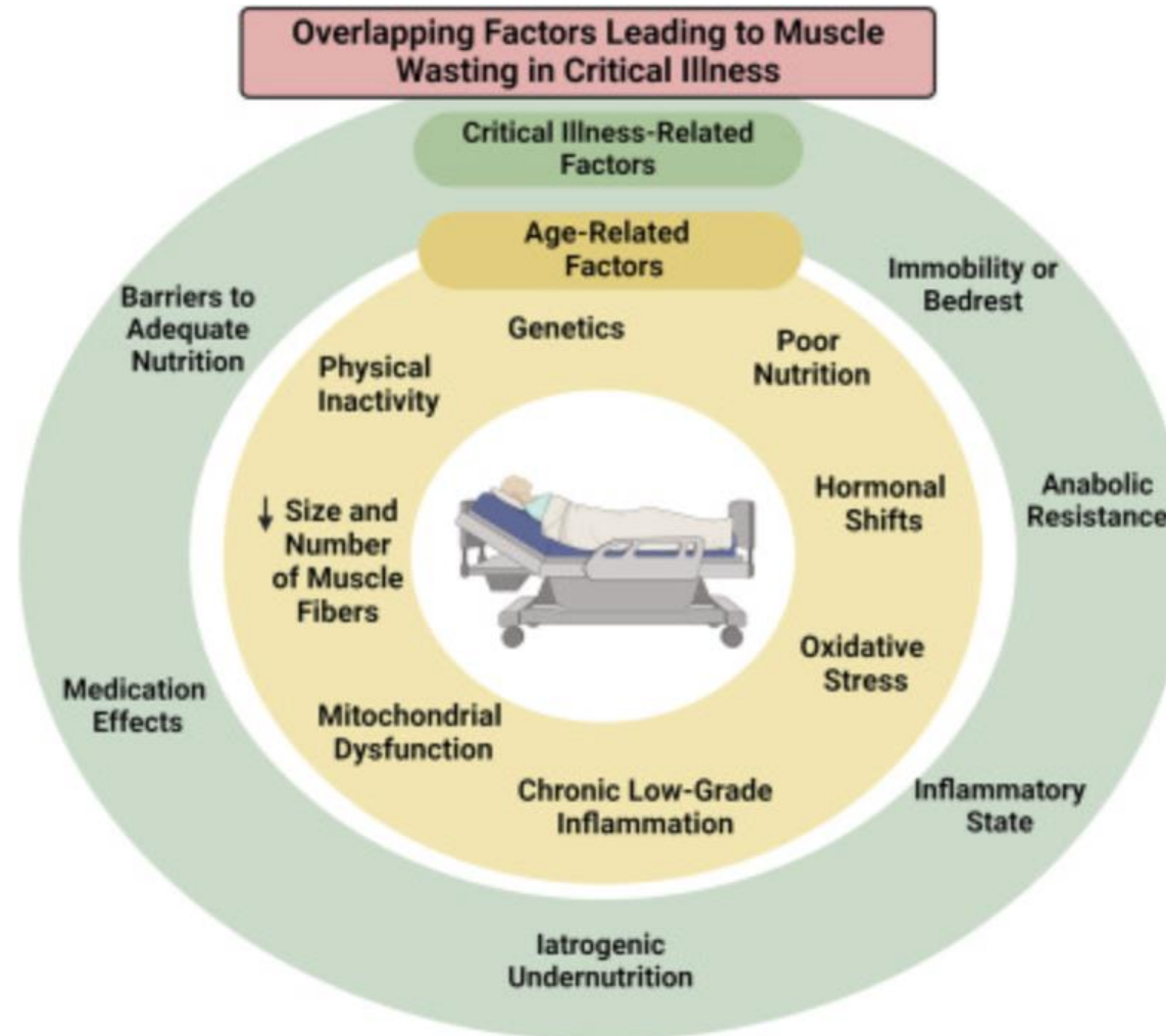


Clinical Implications of Malnutrition, Sarcopenia and Frailty

- Increased risk of falls
- Hospitalization and institutionalization
- Disability and dependence
- Poor hospital outcomes including increased length of stay, complications, readmissions
- Mortality

Skeletal Muscle – A critical organ for recovery

Matthew J. Lees, Carla M. Prado, Paul E. Wischmeyer, Stuart M. Phillips. Skeletal Muscle: A Critical Organ for Survival and Recovery in Critical Illness, Critical Care Clinics, 2025



Unravelling Complexity in Sarcopenia

Ceyhan AB, et al. Int J Molec Scie 2025;26,8527

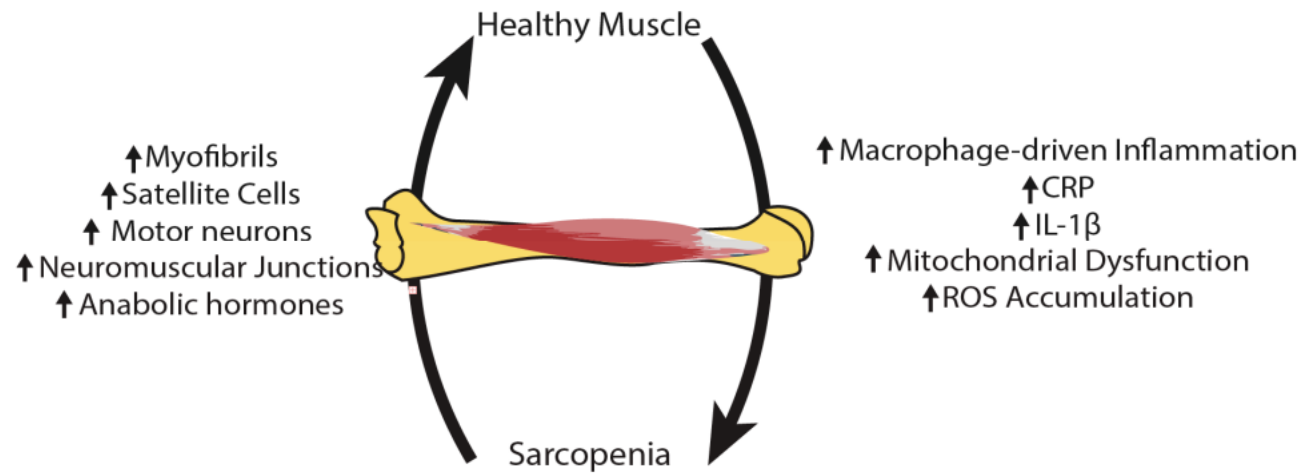
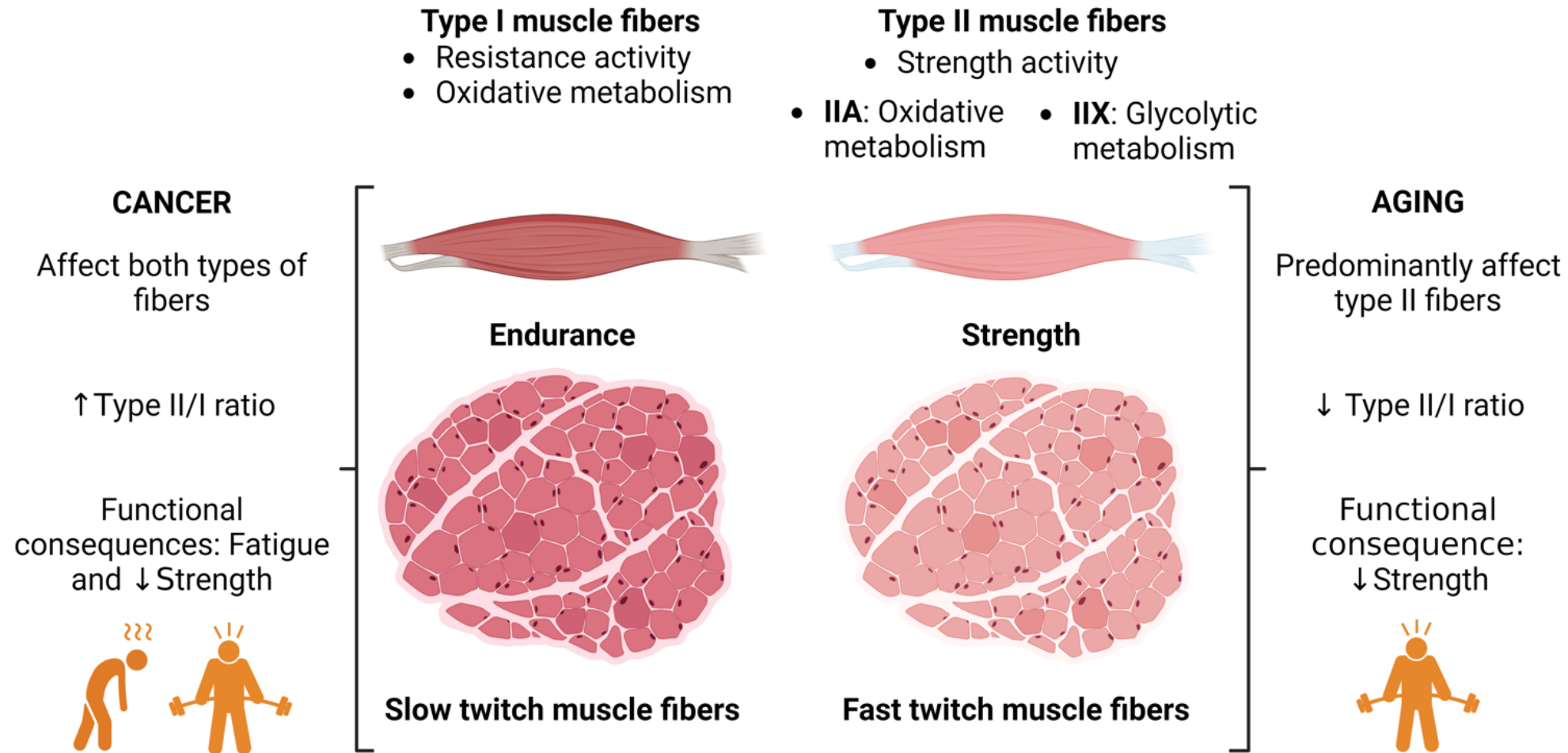
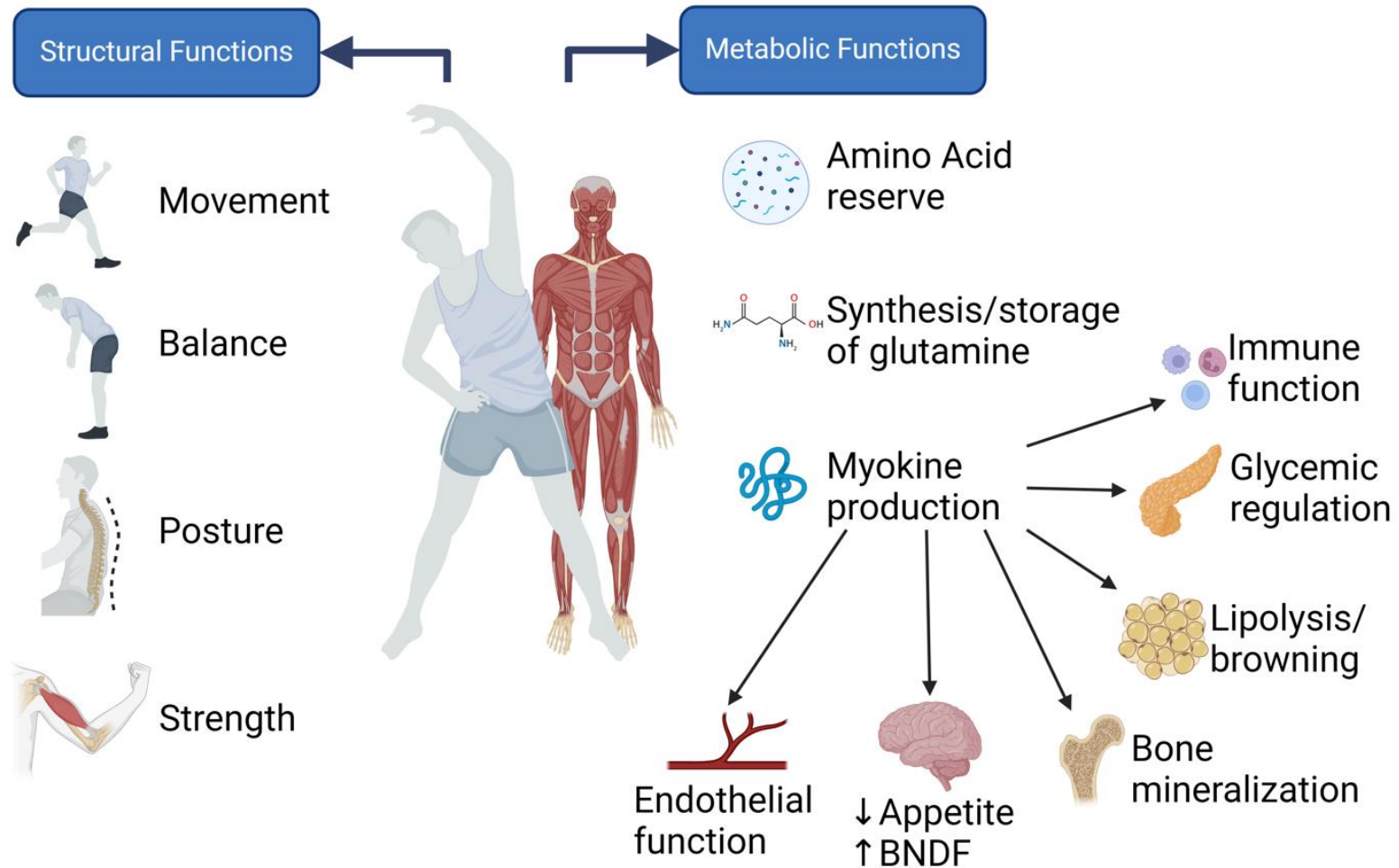


Figure 2. The pathophysiology of sarcopenia is complex and varied. As inflammation, mitochondrial dysfunction and reactive oxygen species (ROS) rise in sarcopenic muscles, there is a decline in the number of myofibrils, satellite cells, motor neurons, and neuromuscular junctions, along with anabolic hormones.

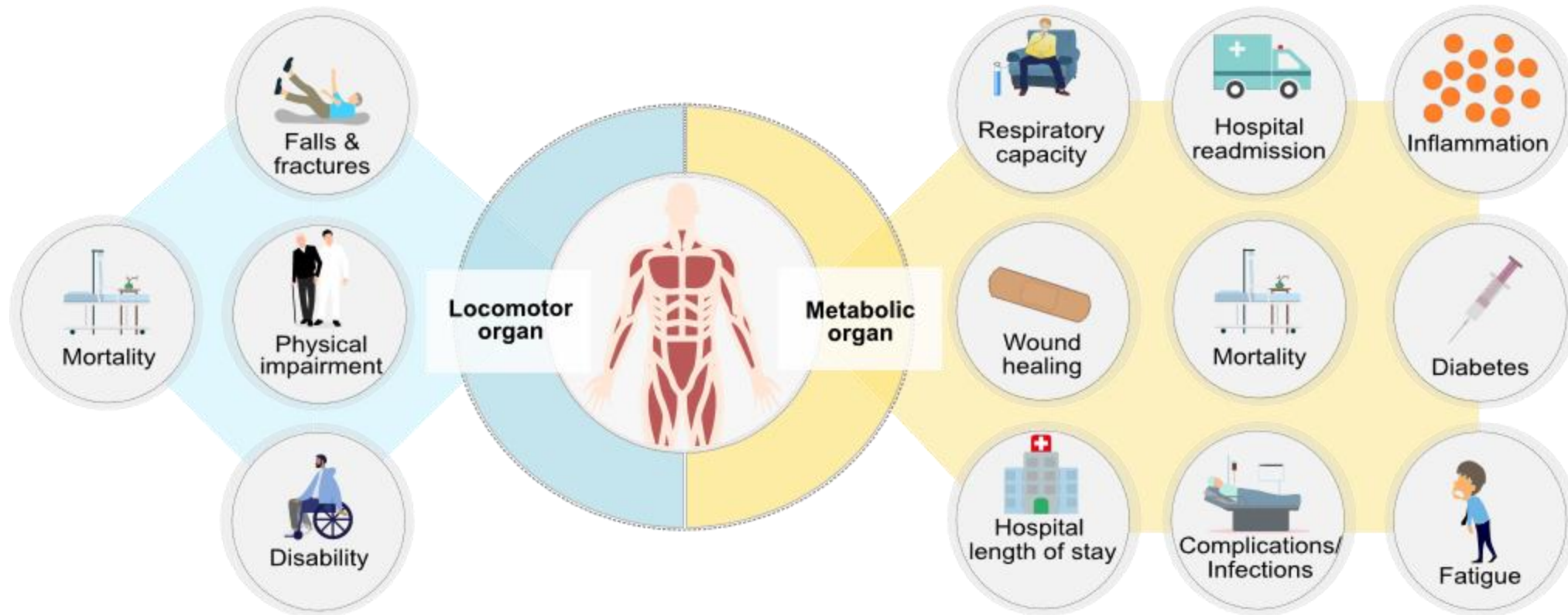
Muscle loss: one size does not fit all?



Muscle's Widely Recognized Yet Frequently Overlooked Roles



Clinical consequences of low muscle mass



Management and Prevention:

Malnutrition, Sarcopenia, Frailty

Break the cycle

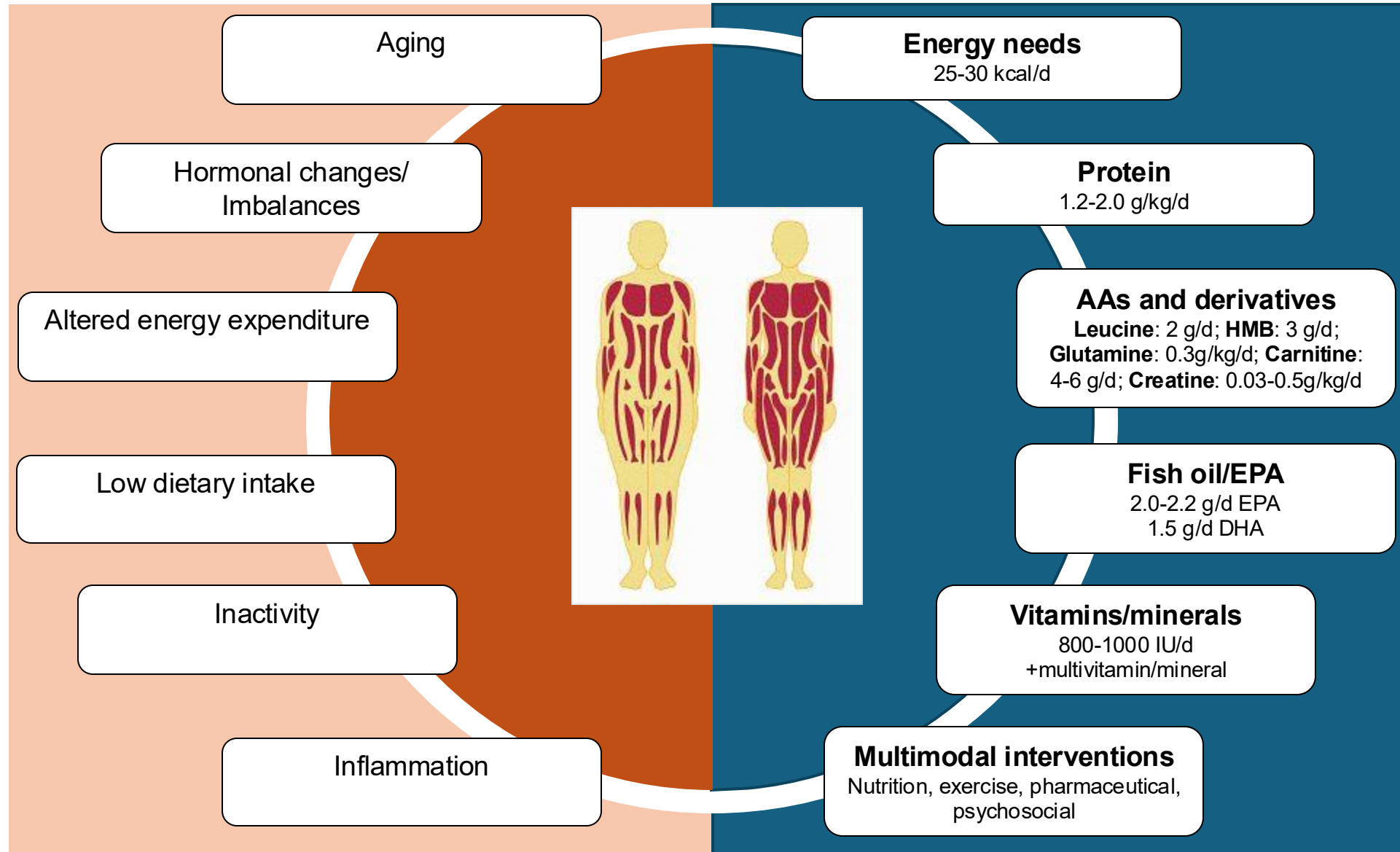
- Multidisciplinary approach – include medical, physical and psychosocial interventions (frailty)
- Start with Screening
- Exercise: resistance and balance training
- Nutrition: Adequate protein and vitamin D; pay attention to oral intake and psychosocial impacts on nutrient intake
- Medication review – minimize poly pharmacy
- Social Support and cognitive engagement

Meta-analysis
N= 68 studies
34 countries

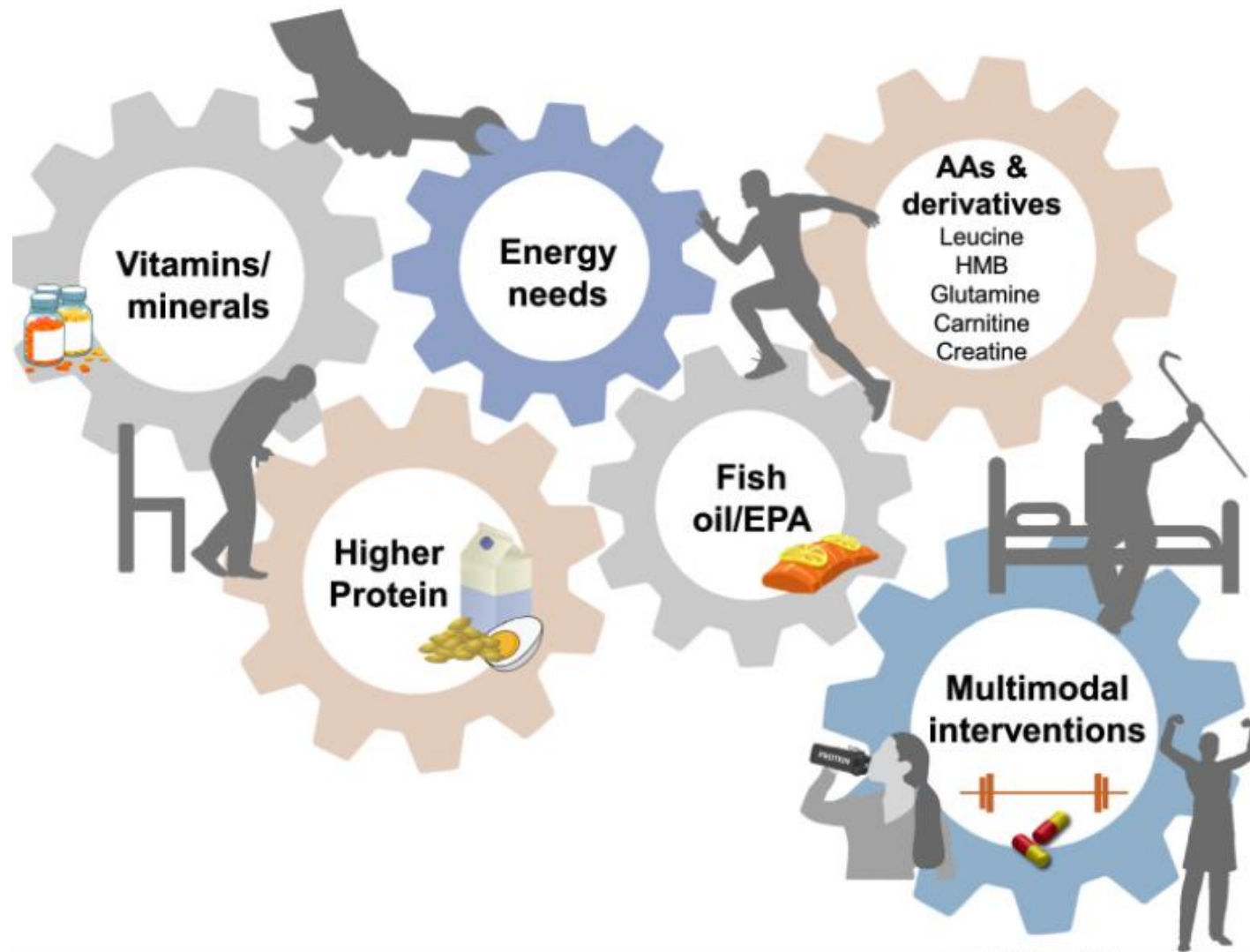
LOW MUSCLE MASS & MORTALITY - pooled hazard ratio

Study group	Overall (HR [95% CI]); I ²
Older adults	1.41 [1.30, 1.53]; 0%
Cancer	1.69 [1.56, 1.83]; 63%
Cardiovascular disease	1.85 [1.32, 2.59]; 30%
Hepatic disease	2.43 [1.72, 3.44]; 61%
Respiratory disease	2.82 [2.02, 3.94]; 0%
Renal disease	1.65 [1.38, 1.98]; 47%
Other diseases	2.09 [1.24, 3.51]; 85%
In general	1.74 [1.63, 1.85]; 63%

Breaking the Cycle



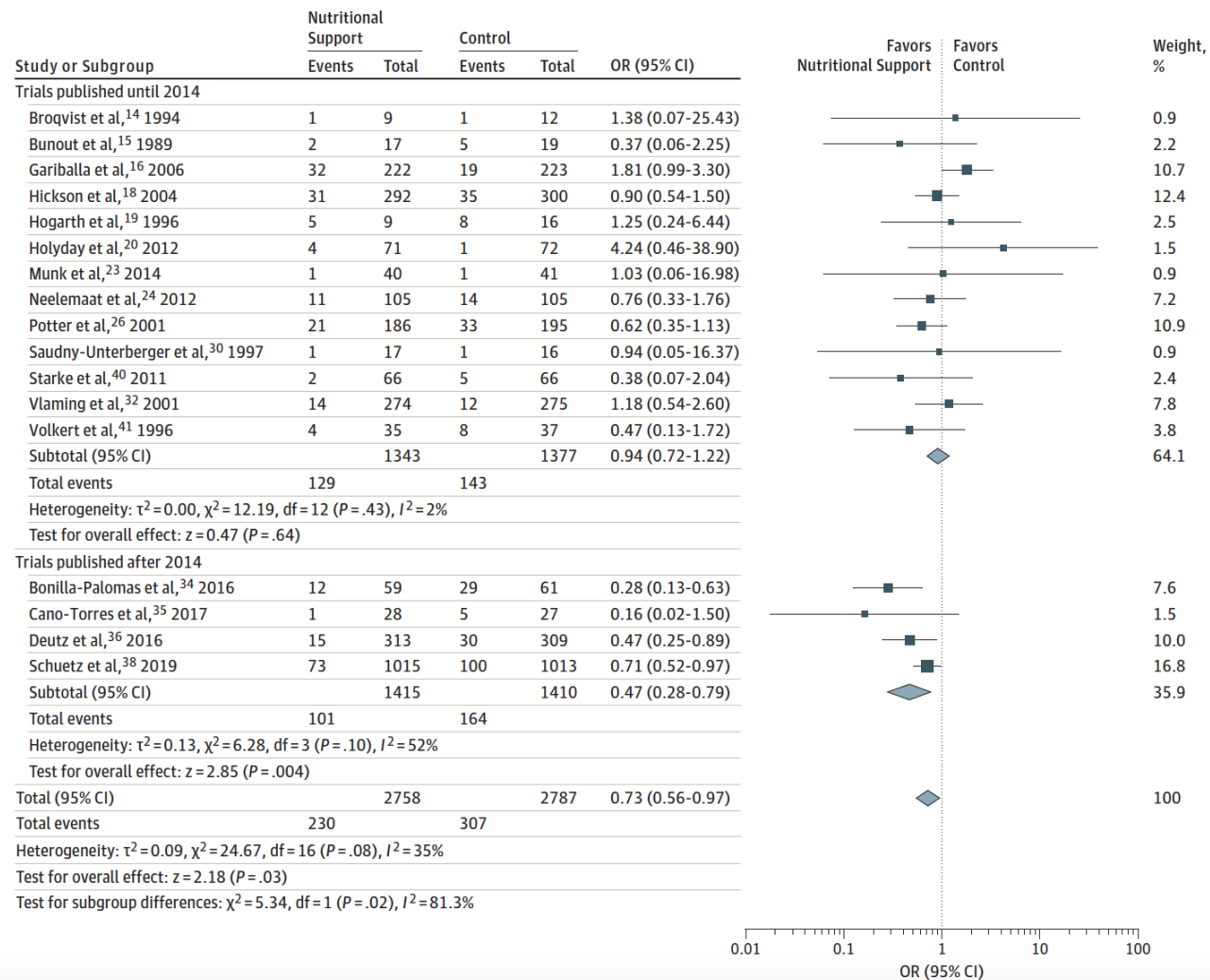
Nutrients & Ingredients under Consideration for the Treatment of low muscle mass



Association of Nutritional Support With Clinical Outcomes Among Medical Inpatients Who Are Malnourished or at Nutritional Risk

An Updated Systematic Review and Meta-analysis

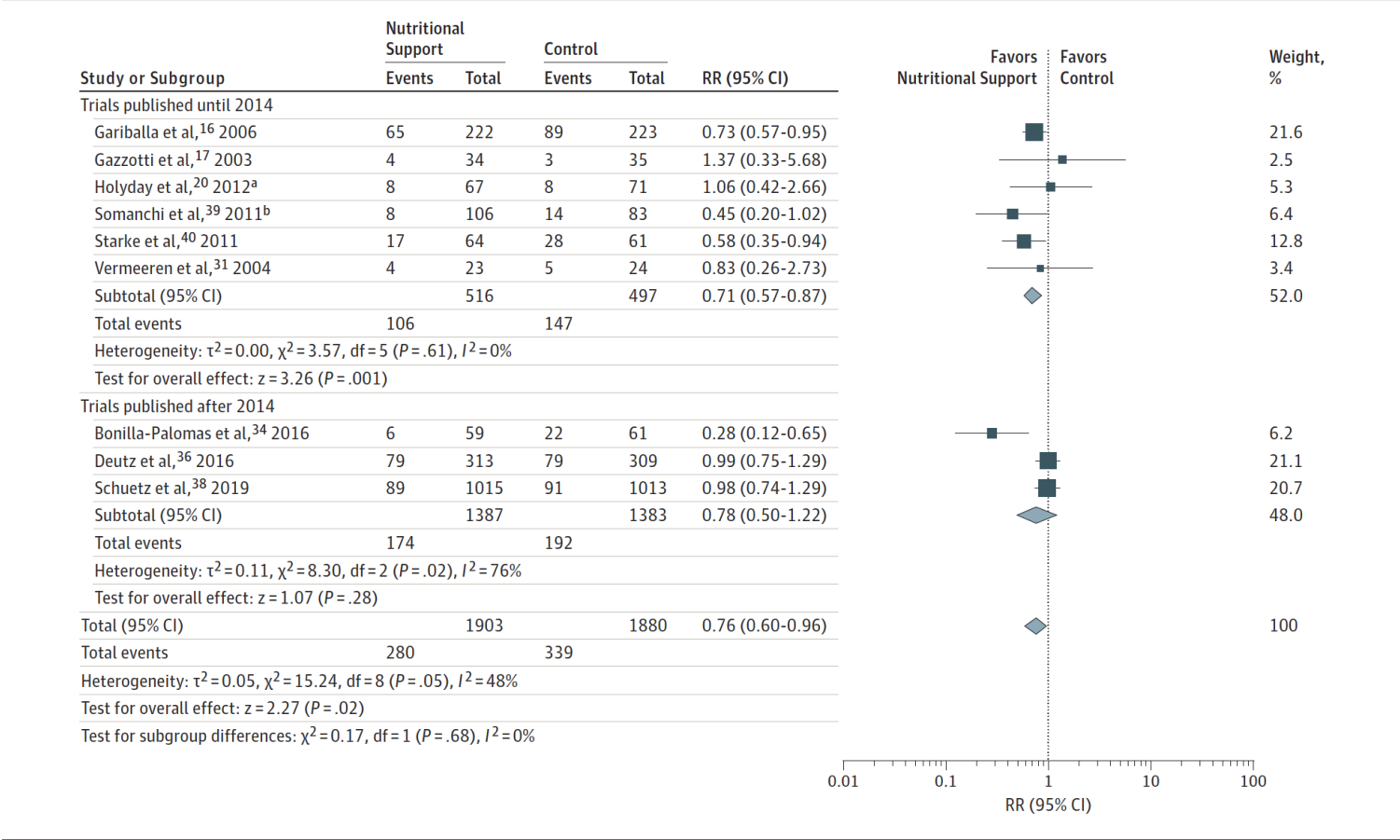
Figure 1. Forest Plot Comparing Nutritional Intervention vs Control for Mortality, Stratified by Publication Year



**Association of Nutritional Support With Clinical Outcomes
Among Medical Inpatients Who Are Malnourished
or at Nutritional Risk**
An Updated Systematic Review and Meta-analysis

Nutritional support was also
associated with a reduction in
nonelective hospital readmissions

Figure 2. Forest Plot Comparing Nutritional Intervention vs Control for Nonelective Hospital Readmissions, Stratified by Publication Year



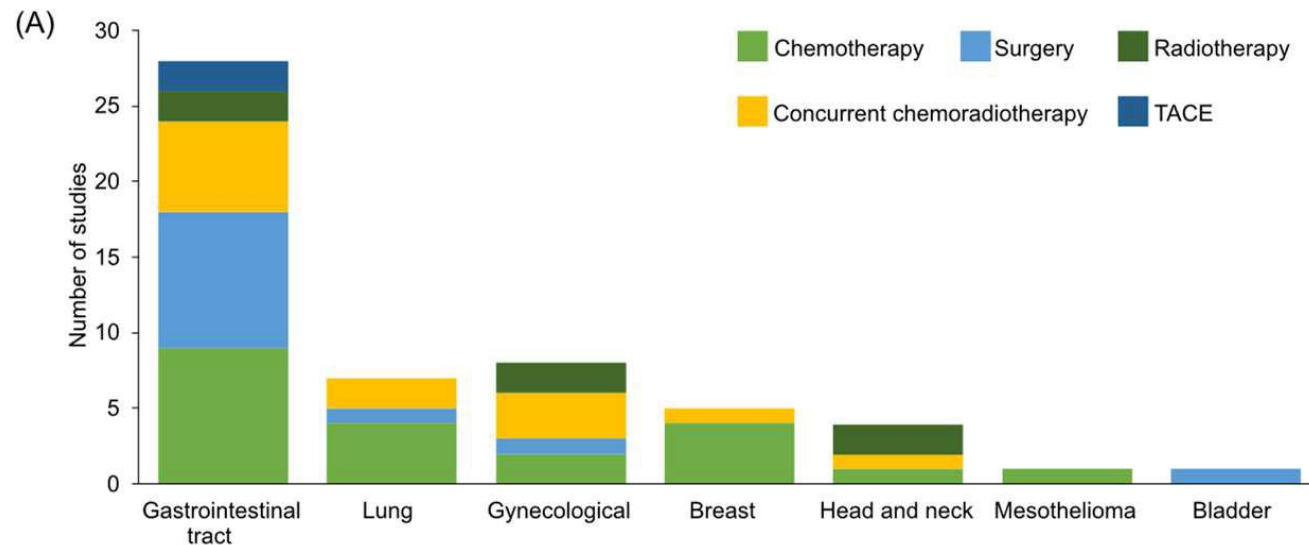
^a Mantel-Haenszel random effects model was used. Squares indicate mean values, with

^b Calculated and approximated from readmission frequency.

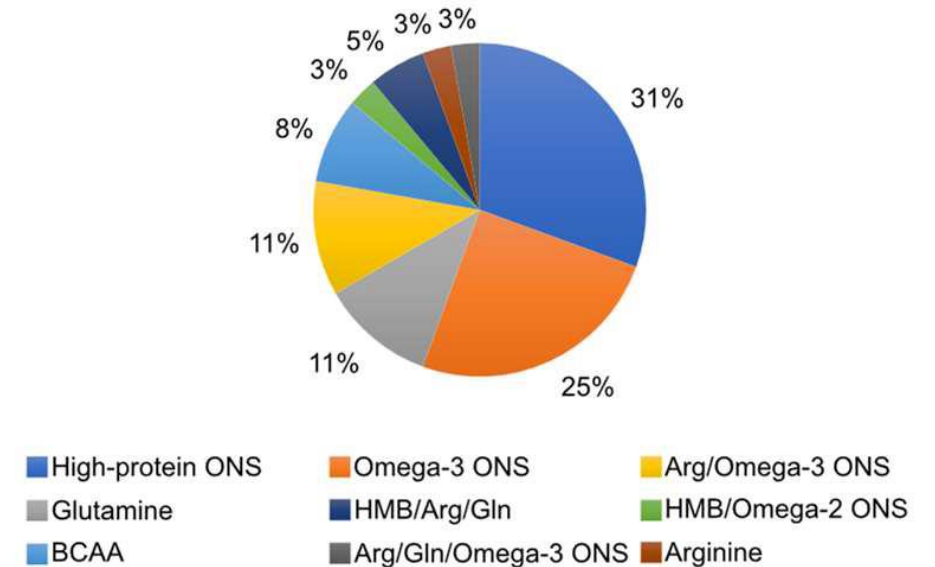
High-Protein Supplementation Beneficial for Patients on Cancer Treatment?

A Systematic Review and Meta-Analysis

- 35 studies; 3701 patients
- RCTs ≥ 10 g protein/serving



Percentage of studies by high-protein supplementation type



HMB: β -Hydroxy β -Methylbutyric Acid
 Arg: Arginine
 BCAA: Branched-Chain Amino Acid
 Gln: Glutamine

Muscle mass



2 of 2 (100%)

6 of 7 (86%)

1 of 1 (100%)

2 of 2 (100%)

11 of 13 (85%)

Muscle strength



1 of 1 (100%)

2 of 2 (100%)

2 of 2 (100%)

1 of 1 (100%)

6 of 6 (100%)

Performance



1 of 1 (100%)

1 of 1 (100%)

1 of 1 (100%)

3 of 3 (100%)

Hospitalization rate



2 of 2 (100%)

1 of 1 (100%)

1 of 2 (50%)

1 of 2 (50%)

1 of 1 (100%)

6 of 8 (75%)

Survival



1 of 3 (33%)

2 of 4 (50%)

1 of 1 (100%)

2 of 3 (67%)

1 of 1 (100%)

7 of 16 (44%)

Length of stay



1 of 3 (33%)

1 of 1 (100%)

2 of 3 (67%)

4 of 10 (40%)

Postoperative complications



2 of 2 (100%)

1 of 1 (100%)

1 of 3 (33%)

4 of 9 (44%)

Supplement type

High-protein ONS

Omega-3 ONS

HMB/Omega-3 ONS

HMB/Arg/Glutamine

BCAA

Glutamine

Arg/Omega-3

Arg/Gln/Omega-3 ONS

High-protein supplementation
(all supplements combined)

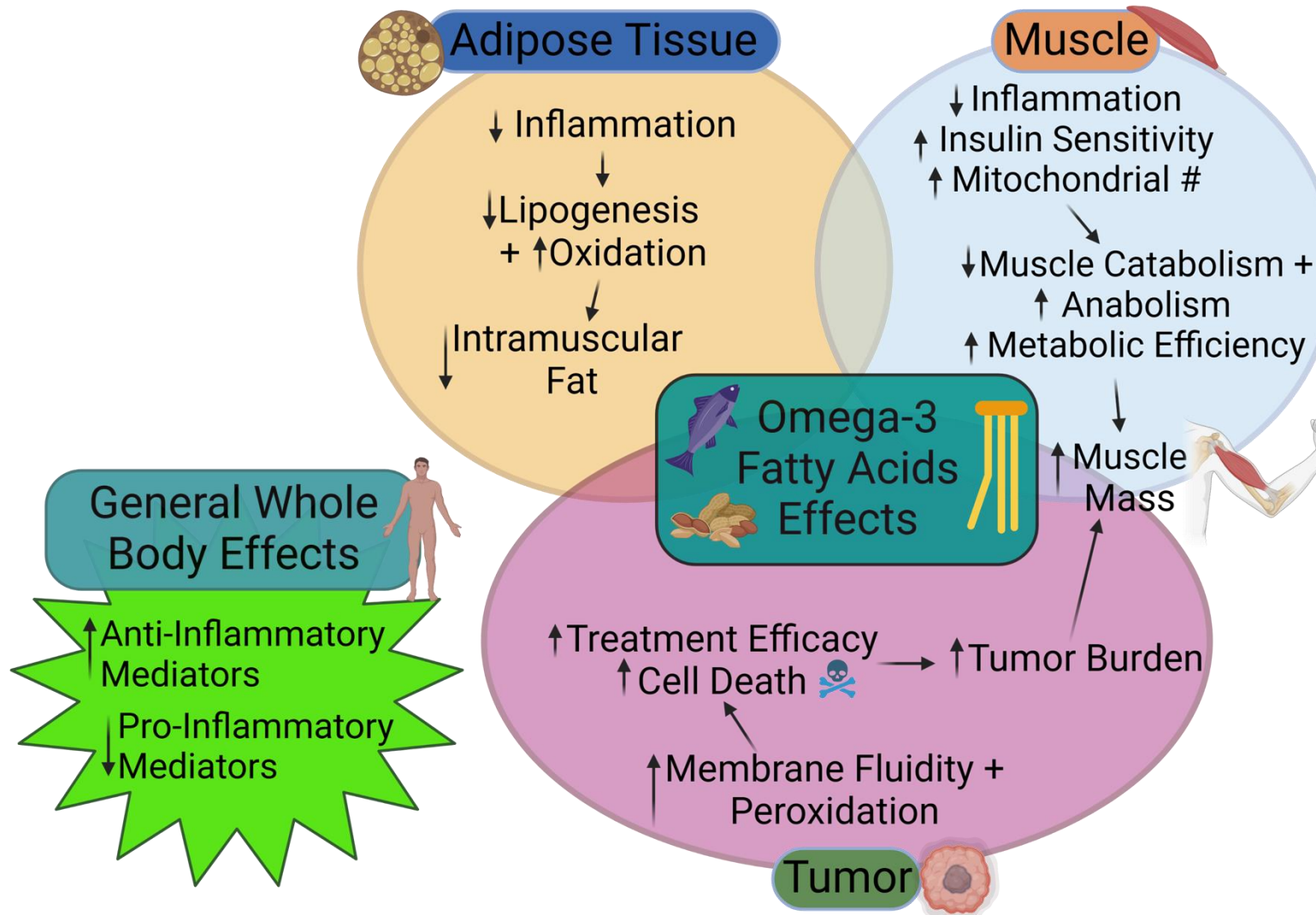
HMB: β -Hydroxy β -Methylbutyric Acid

Arg: Arginine

BCAA: Branched-Chain Amino Acid

Gln: Glutamine

ANTICATABOLIC EFFECT OF OMEGA 3 FA



HMB ANTICATABOLIC EFFECTS

ANABOLIC SIGNALLING PATHWAYS

↑ protein synthesis

mTOR system

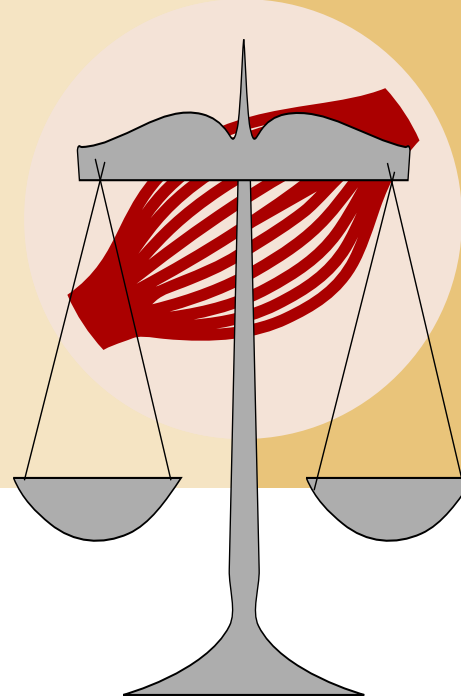
GH/IGF-1
axis

↓ protein degradation

Ubiquitin
proteasome

Autophagy-
lysosome

CATABOLIC SIGNALLING
PATHWAYS

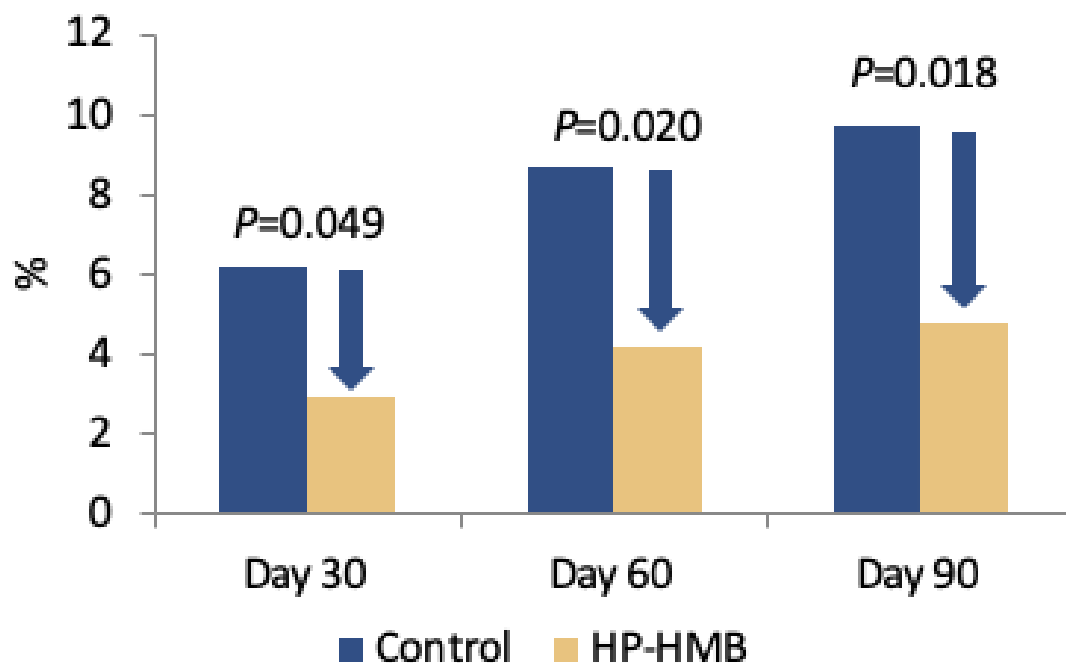


GH- Growth Hormone
IGF-1- Insulin-Like Growth Factor 1
mTOR- Mechanistic Target of Rapamycin

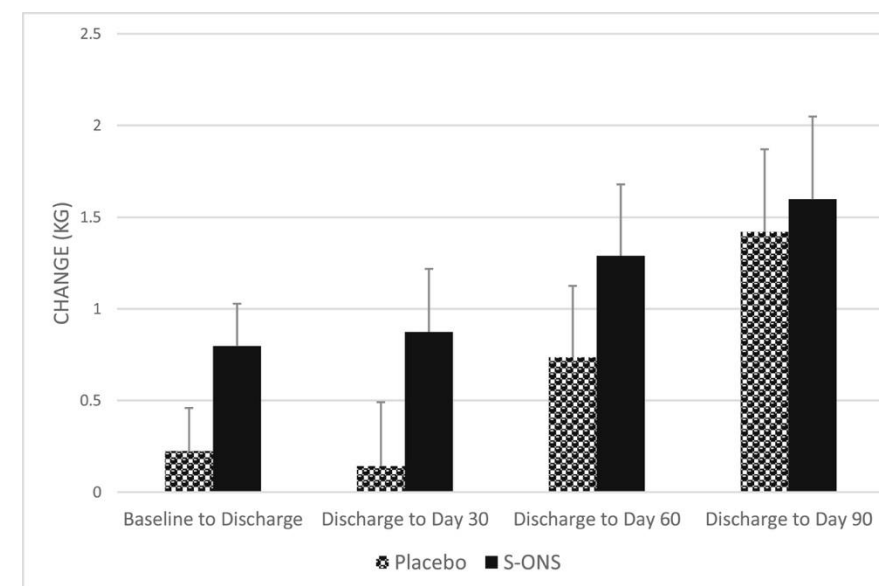
49% lower mortality rate in older malnourished patients with cardiac or pulmonary disease (90 days post-hospitalization, receiving ONS)

Increase in **handgrip strength** (23.3 ± 0.3 kg) compared to the control group (22.6 ± 0.3 kg), $p = 0.043$.

MORTALITY



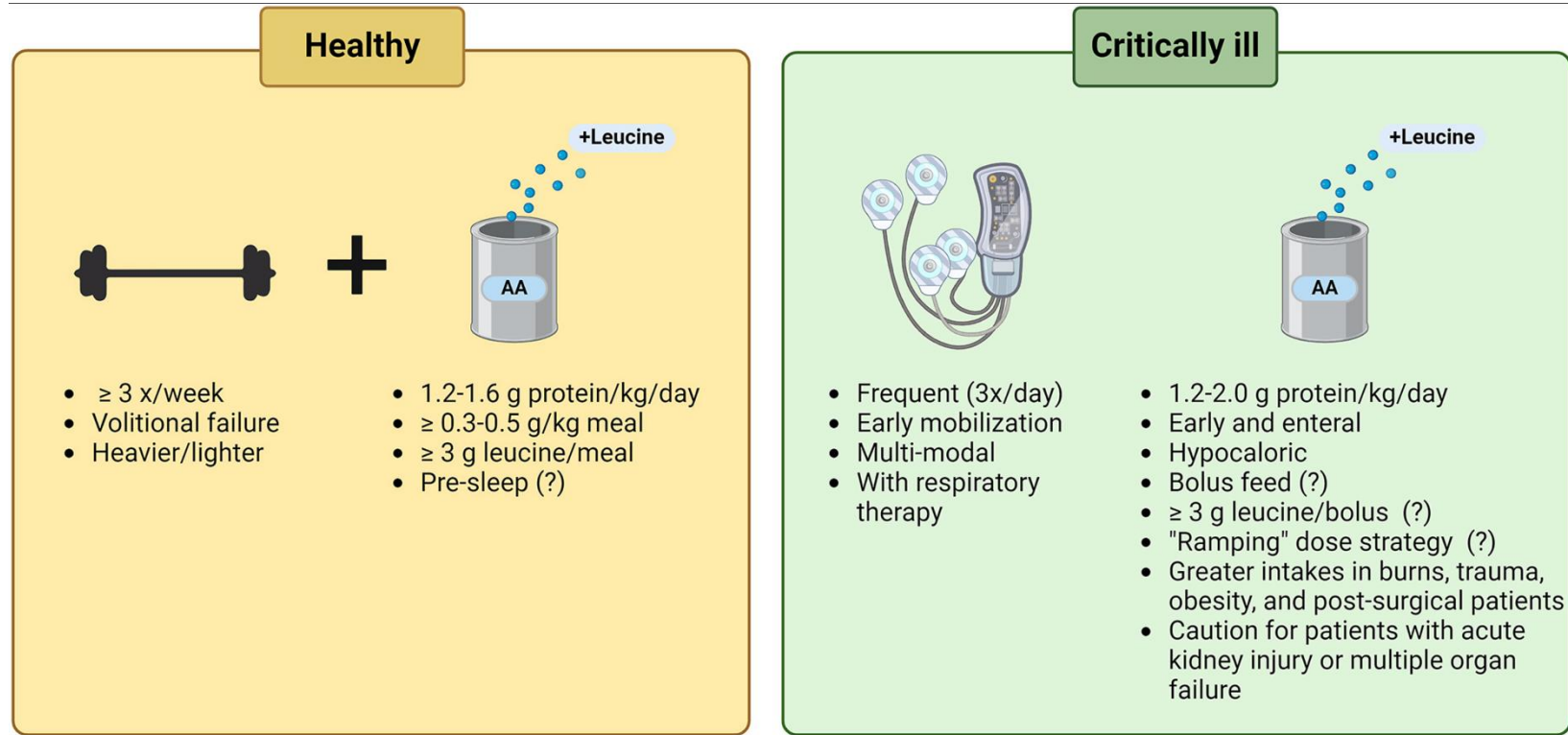
STRENGTH



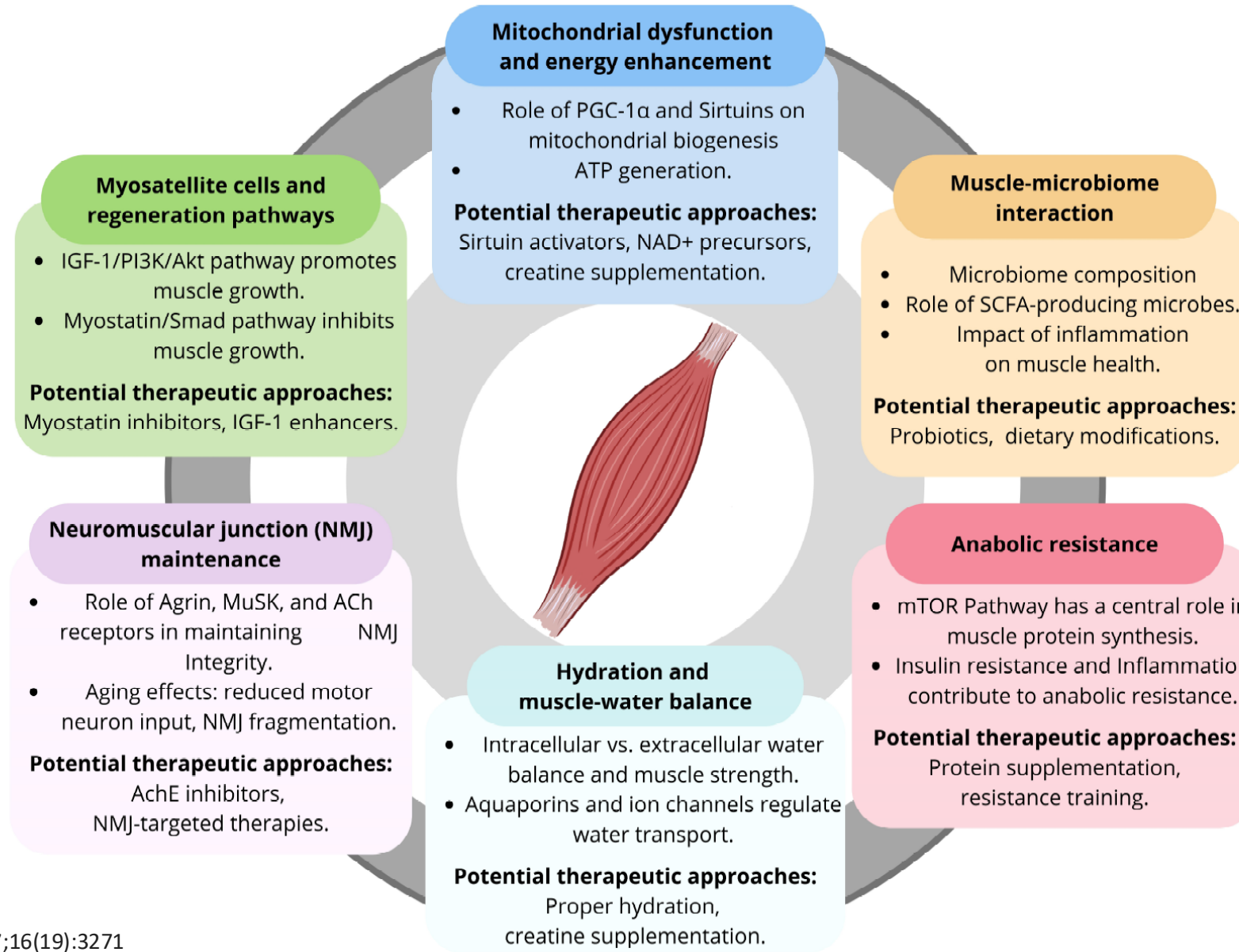
N=652

ONS: Oral Nutrition Support - high quality protein, HMB, Vit D

Unique Patient Populations may Require different interventions: ICU



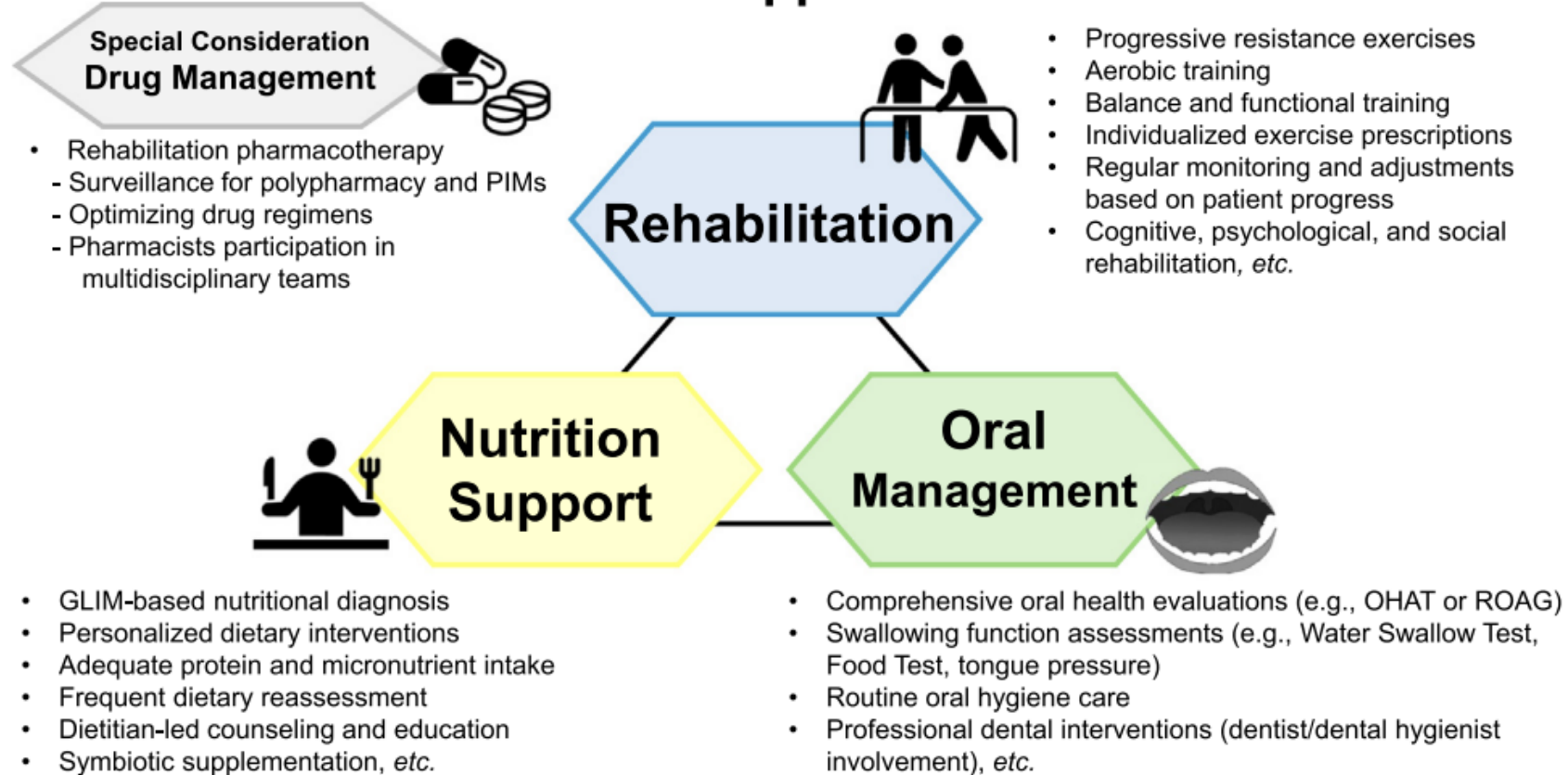
Emerging Targets and Treatments for muscle loss



Practicalities: Oral Dysfunction and Dysphagia

- Tooth loss, periodontal disease, salivary decline with aging and compromise mastication and swallowing heightening malnutrition and aspiration risk
- Further compromised with sarcopenia and frailty
- Japan has an “oral Hypofunction” insurance category; prompts early intervention and accountability

Triad Approach



Conceptual Framework of the Triad Approach: Rehabilitation, Nutrition Support, and Oral Management for Older Adults. The triad approach emphasizes coordination across three domains—rehabilitation, nutrition support, and oral management—to enhance functional status, nutritional health, and quality of life. Rehabilitation includes tailored exercise programs addressing physical aspects. Nutrition support ensures adequate protein-energy and micronutrient intake. Oral management involves comprehensive oral health assessments and interventions to maintain safe and effective nutritional intake. The effectiveness of this triad is supported by careful drug management, as polypharmacy can significantly impact all three components. Abbreviations: GLIM, Global Leadership Initiative on Malnutrition; OHAT, Oral Health Assessment Tool; PIMs, Potentially Inappropriate Medications; ROAG, Revised Oral Assessment Guide.

Malnutrition, Sarcopenia, Frailty

- Screening: All should be routinely assessed in high-risk populations (older adults, chronic disease, hospitalized patients)
- Early intervention can break the cycle
 - Nutrition support (eg. high protein diets, Supplements)
 - Resistance exercise, physical therapy
 - Treat underlying disease
 - Multidisciplinary management

Conclusions

- Malnutrition, Sarcopenia and Frailty co-locate
- Identification of risk with screening may allow opportunities to break the cycle
- Specific targeted nutrient interventions can have an impact on outcome
- Multimodal approaches are needed to address malnutrition, sarcopenia and frailty

Thanks ...

- Thanks to Carla Prado for sharing her slides, knowledge and skills