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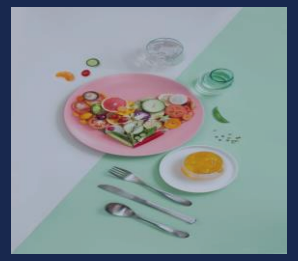
Addressing cancer anorexia-cachexia in older patients: Potential therapeutic strategies

Theocharis Ispoglou

Professor in Exercise and Nutrition Sciences



*Focus on Nutritional and Exercise Interventions for Enhanced Quality of Life

Objectives

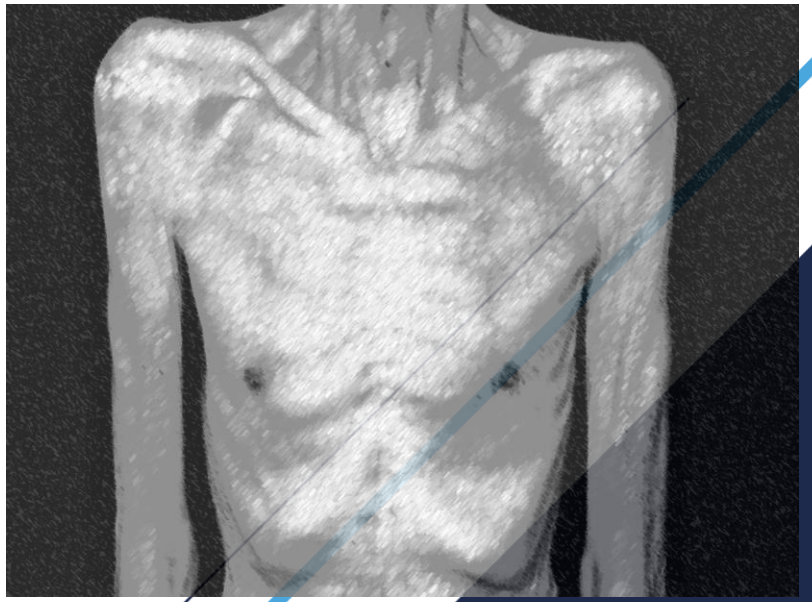
- ❑ Provide relevant **background** on cancer cachexia, cancer-anorexia cachexia, and sarcopenia.
- ❑ Discuss the **impact** of cancer anorexia-cachexia on muscle mass and quality of life in older adults.
- ❑ **Discuss nutritional** and **exercise** strategies for muscle preservation.
- ❑ Briefly outline psychosocial interventions, the importance of behavioural approaches, as well as some examples of pharmacological approaches.
- ❑ Highlight the importance of multidisciplinary teams (MDT) in collaborative management of cachexia in older cancer patients.

**Focus on practical, team-based approaches for patient-centred care*.

Cachexia (examples: cancer, cardiac, pulmonary)

- *Hippocrates described it as "the flesh is consumed and becomes water and ….the illness is fatal."* (Etymology from Greek words "kakos" (bad) and "hexis" (condition or appearance))

- **Definitions**
  - 2008: "*Cachexia is a complex metabolic syndrome associated with an underlying illness and characterized by loss of muscle with or without loss of fat mass;*" set diagnostic criteria were proposed.
  - 2011: "*a multifactorial syndrome defined by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that can be partially but not entirely reversed by conventional nutritional support;*" plus revised diagnostic criteria.
  - 2019: consensus report from the global clinical nutrition community



Mariean et al. (2023); Hariyanto and Kurniawan, (2020).

Despite variations in definition, cachexia follows three main stages

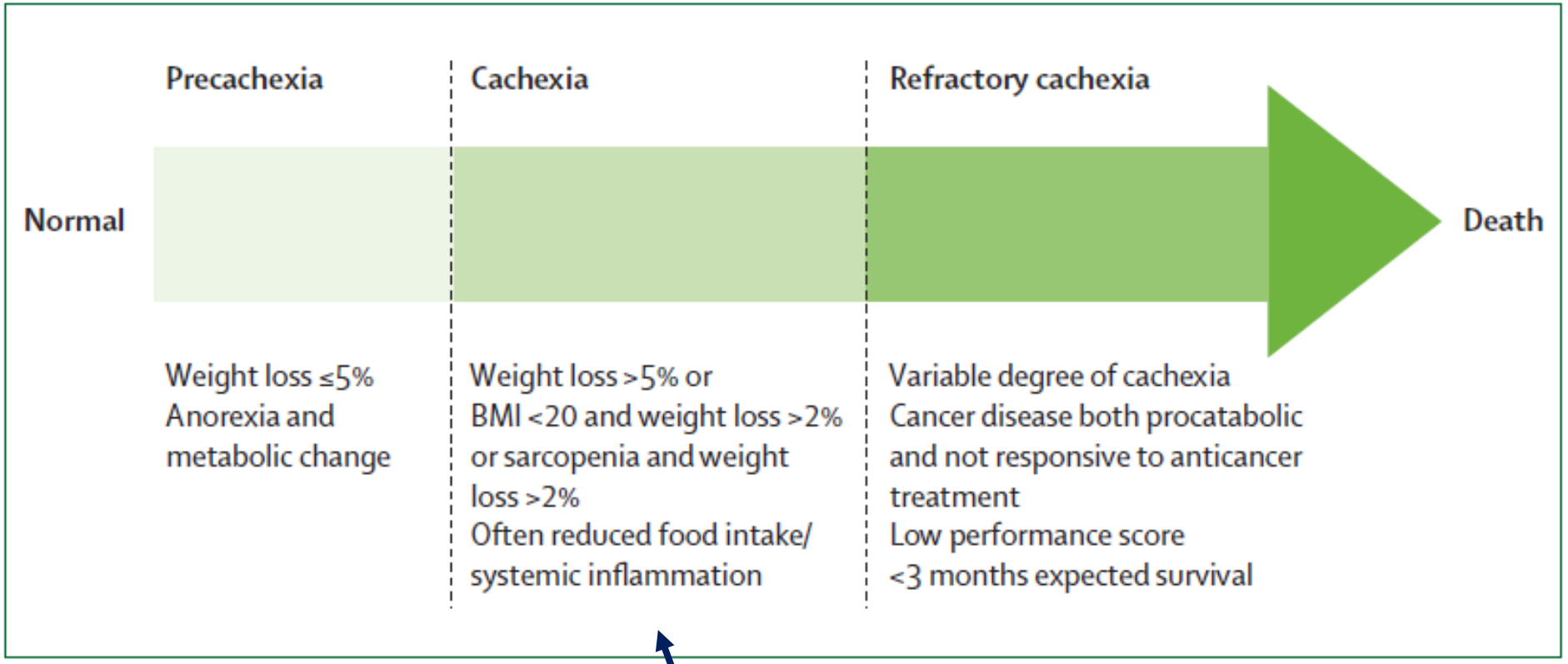


Figure 2: Stages of cancer cachexia

Revised 2011 criteria

>5% over the past 6 months; in previous definition was in the last 12 months or less

Fearon et al. (2011)

Cancer Cachexia (CC) vs. Cancer-Anorexia Cachexia (CACs)

- *Note: anorexia is a key component of the CC syndrome, characterised by **weight** loss, **muscle** mass reduction, and reduced appetite (**anorexia**).

- ***CC** and **CACs** are sometimes used interchangeably in literature.*

- **Session focus**: For this presentation, I'll refer to CC based on the official definition, though I will focus on addressing appetite loss in the context of CC.

Ispoglou et al. (2024); Rivas et al. (2023); Fearon et al. (2011)

Some challenges faced by older adults with cancer

- **High prevalence of CC**: up to 80% in advanced cancers.
- Impact on **quality of life (QoL)** and mortality: CC significantly lower QoL, with 20-30% of cancer-related mortality attributed to CC.
- **Older patients are greatly affected** due to the combined effects of ageing and cancer-related muscle wasting.
- In the USA, for example, 70% of cancer cases occur in those over 65.
- The combined effects of **ageing**, **sarcopenia**, and **cachexia** create unique challenges.
- **Older adults are more susceptible to muscle loss** than younger patients, making them more vulnerable to the effects of both CC and sarcopenia.

Ispoglou et al. (2024); Han et al. (2021); Hariyanto and Kurniawan, (2020);

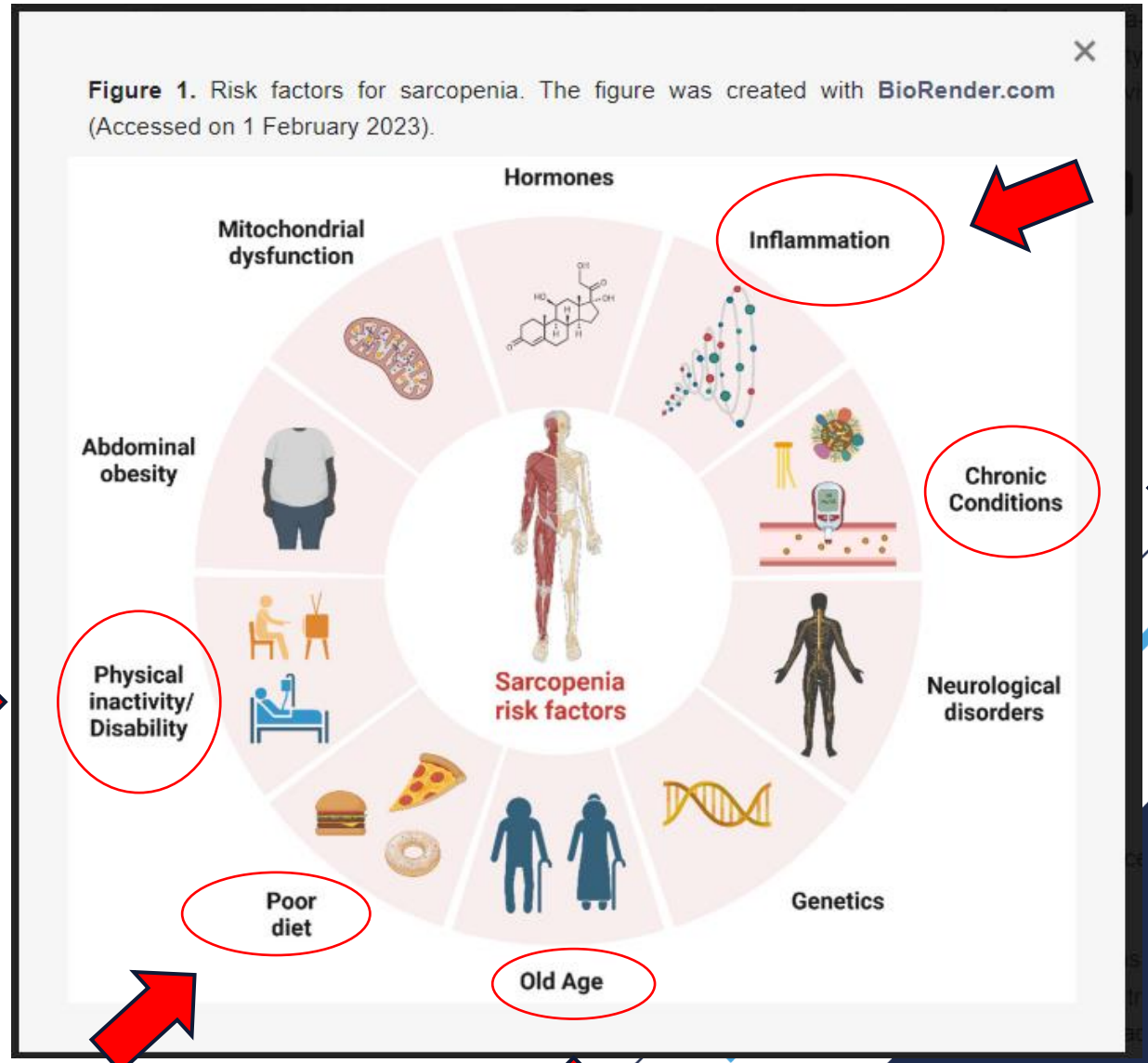
CC exacerbates sarcopenia by impairing appetite and nutrient intake, leading to further muscle deterioration in older adults.

Shared pathophysiology: CC and sarcopenia

❑**Sarcopenia**, characterised by reductions in muscle mass, strength, and function, adversely affects QoL, survival rates, and increases surgical complications and hospital stays in cancer patients.

❑CC and sarcopenia **share pathophysiological mechanisms**, particularly muscle wasting (with or without fat loss) both contributing to **lower QoL**. **Age-related anorexia**, **anabolic resistance** also contribute to sarcopenia.

❑Advanced cancers, **chemotherapy** side effects, and **hospitalisation** further exacerbate muscle loss, compounding challenges in increasing **protein and energy intakes** , and increasing infection risk.



Ispoglou et al. (2023)

**Let's examine next how sarcopenia is clinically defined and diagnosed.*

Ispoglou et al. (2024); Muscaritoli et al. (2017); Ali et al. (2014); Ney et al. (2009)

Sarcopenia: revised European consensus on definition and diagnosis

Alfonso J Cruz-Jentoft ✉, Gülistan Bahat, Jürgen Bauer, Yves Boirie, Olivier Bruyère, Tommy Cederholm, Cyrus Cooper, Francesco Landi, Yves Rolland, Avan Aihie Sayer ...
Show more

Age and Ageing, Volume 48, Issue 1, January 2019, Pages 16–31,

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.

1. Low muscle strength

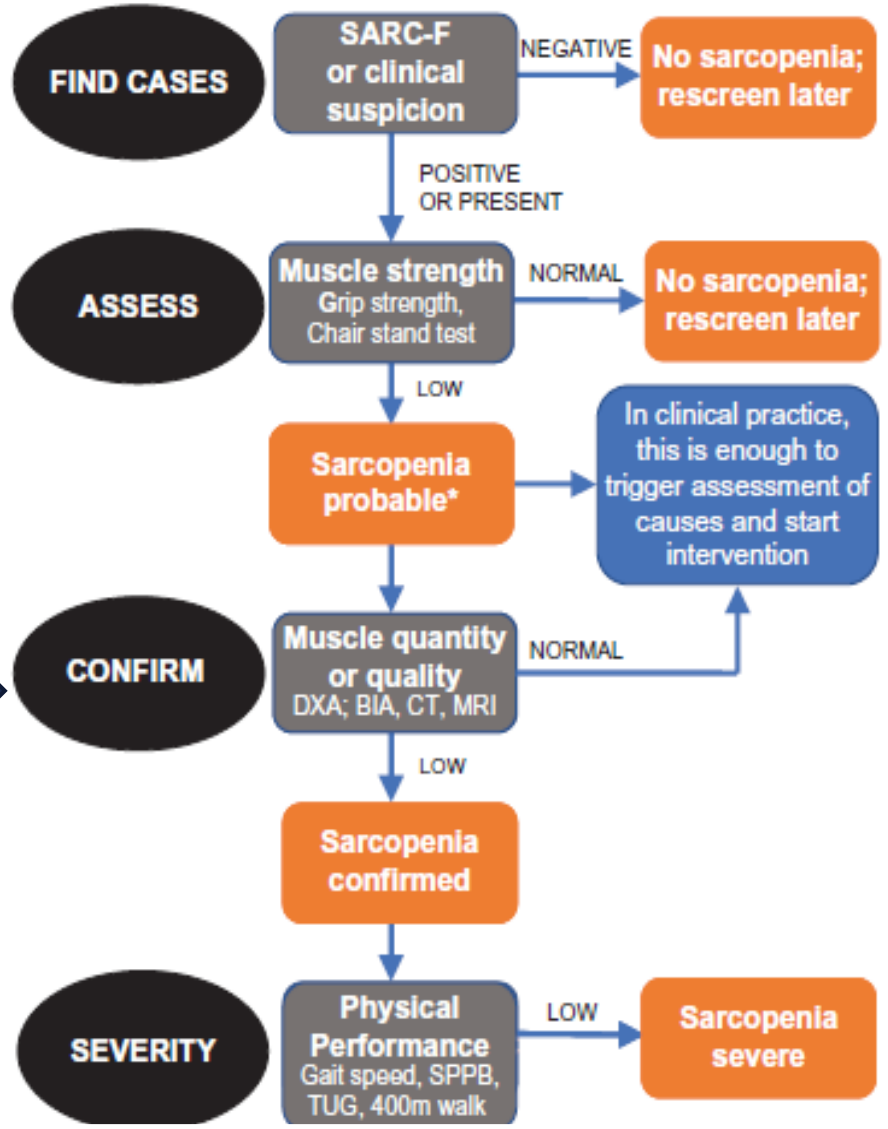
2. Low muscle quantity or quality

3. Low physical performance

Criterion 1: low muscle strength

Criterion 2: Muscle quantity or quality

Criterion 3: low physical performance



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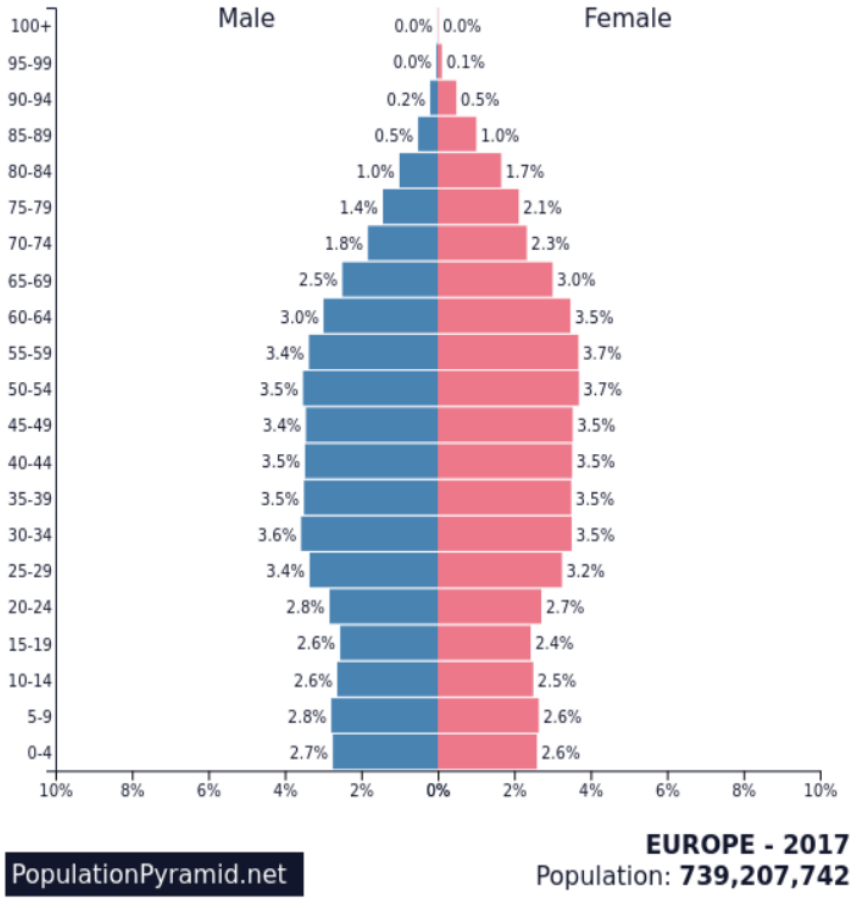
SARCOPENIA: A reduction in muscle mass, strength and function



Prevalence of Sarcopenia ~ 10%-40% in healthy older adults over 60

(Shafiee et al. 2017; Mayhew et al. 2018)

Table 2. Overall sarcopenia prevalence estimates.

Definition	Number of studies	Participants (*n*)	Forest plot	Prevalence estimate (%)	95% CI	Heterogeneity
EWGSOP/AWGS	83	58283		12.9	9.9, 15.9	93% ($P < 0.001$)
IWGS	12	10381		9.9	3.2, 16.6	52% ($P = 0.100$)
FNIH	16	6467		18.6	11.8, 25.5	75% ($P = 0.003$)
ALM/height	68	39135		30.4	20.4, 40.3	87% ($P < 0.001$)
ALM/weight	27	18985		40.4	19.5, 61.2	100% ($P < 0.001$)
ALM regression	6	16899		30.4	20.4, 40.3	87% ($P < 0.001$)
ALM/BMI	8	4984		24.2	18.3, 30.1	92% ($P < 0.001$)
Other	6	9243		18.0	7.3, 28.8	100% ($P < 0.001$)
			0% 40% 80%			

Mayhew et al. (2018)

- **In older adults with cancer, the prevalence and severity of sarcopenia may be even higher due to the combined effects of CC, which accelerates muscle deterioration.**

Acute sarcopenia in hospitalised patients: recent findings and implications

- Our recent systematic review and meta-analysis explores acute sarcopenia's rapid onset and muscle deterioration **during hospitalisation**.

- Although cancer patients were not included, the findings are crucial for understanding the enhanced risks in older adults who require hospitalisation, particularly when cachexia is also present.

- The study highlights the need for enhanced muscle assessments and prioritising muscle preservation strategies in high-risk populations.

Journal of Cachexia, Sarcopenia and Muscle

Acute sarcopenia: systematic review and meta-analysis on its incidence and muscle parameter shifts during hospitalisation

Open Access

DOI: 10.1002/jcsm.13662

Status: In Production

Aldrich et al. (2024)

Acute Sarcopenia

Rapid deterioration of muscle health *typically occurring as a result of an* ***illness or injury.***

Assessed using EWGSOP2 criteria involving assessments of **muscle strength, mass, quality and function**. However, **prevalence** and **specific changes** to these muscle parameters are **unknown during hospitalisation**.

Review Objectives:
to elucidate the prevalence of **acute sarcopenia** and examine **muscle parameter changes** during hospitalisation.

18% of hospitalised patients develop sarcopenia within ***4 to 44 days***

21754 records identified;
88 included in synthesis
(33 in meta-analyses (HGS, RFCSA, muscle function))

Muscle mass reduced significantly, in particular in the ***lower limbs*** (16.5% over 3 to 21 days), and was accompanied by ***reductions in muscle quality***

Handgrip strength (HGS) and ***muscle function*** remain stable

Conclusions and Future Recommendations

HGS and **muscle function** criteria are **not sensitive** enough for assessing sarcopenia in hospitalised populations

May lead to **underdiagnosis** and **insufficient care**, the prevalence of rapid sarcopenia development may be a lot higher than what this review has identified

Muscle mass and ***quality*** should be the ***primary determinants*** for assessing sarcopenia in hospitalised populations

Aldrich et al. (2024)

DOI: 10.1002/jcsm.13662

Multidisciplinary insights and solutions for cancer anorexia-cachexia

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Narrative Review

Addressing cancer anorexia-cachexia in older patients: Potential therapeutic strategies and molecular pathways

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Our recent publication brought together perspectives from various disciplines, including clinicians, academics, and researchers, to address the complex challenges of cancer anorexia-cachexia.

The role of exercise in CC management

- Exercise as a key strategy
  - **Crucial for preventing muscle loss**, a central challenge in both sarcopenia and cancer cachexia.

- Maintaining **muscle mass**
  - Essential for preserving **independence and QoL** in older adults during and after cancer treatment.
  - Increases **appetite and nutrient intak**e, which addresses muscle loss and nutritional needs in CC management.

- **Immune and metabolic benefits**
  - Supports immune function and energy metabolism.
  - Can potentially lower cancer progression risk.

- **Programmes for older adults**
  - Prehabilitation (pre-treatment) and rehabilitation (post-treatment) strategies can be adjusted to accommodate physical limitations, ensuring accessibility for older patients with physical limitations.

Giallauria et al. (2023); Johnson et al. (2021);Pin et al. (2018); Buffart et al. (2014)

Key benefits of exercise – highlights

❑ 3x more effective than drugs

- ❑ Exercise has been shown to be more effective than pharmacological treatments in reducing cancer-related fatigue (CRF). Findings of SR and metanalysis by Mustian et. al (2017) was that "*Clinicians should prescribe **exercise and/or psychological interventions as first-line treatments for cancer-related fatigue**.; Aerobic and anaerobic exercise interventions were equally effective for treating CRF in the same study.*

❑ Comprehensive impact on well-being

- ❑ Improves physical function, QoL, and mental health (e.g., reduces anxiety).
- ❑ Effective when integrated at all stages: pre-, peri-, and post-treatment offering universal benefits.
- ❑ Those with low baseline physical function are more likely to benefit with regards to fatigue and physical functioning. However, when it comes to strength and QoL patients receiving treatment benefit regardless of baseline values.

❑ Reduces symptom burden

- ❑ Fatigue, anorexia, and cachexia are the most prevalent symptom clusters that worsen QoL and exercise plays a crucial role in managing these.

Weyhe et al. (2022)

Fig. 1 Patient with the bed bicycle

Weyhe et al. (2022); Hong et al. (2020); Buffart et al. (2018); Mustian et al. (2017); Alesi et al (2014)

Nutritional strategies: protein and energy targets

❑Targets

- ❑ Energy: **25–30 kcal/kg/day** to maintain weight and meet energy needs.
- ❑ Protein: **1.2–2.0 g/kg/day** to help preserve muscle mass, especially for those at high sarcopenia risk.
- ❑ **Protein quality and distribution:** spread protein intake evenly throughout the day, aiming for 20–30g of high-quality protein per meal to optimise muscle protein synthesis.
- ❑ **Purpose**: Meeting these targets can counteract muscle loss, support daily function, and improve resilience to treatment.

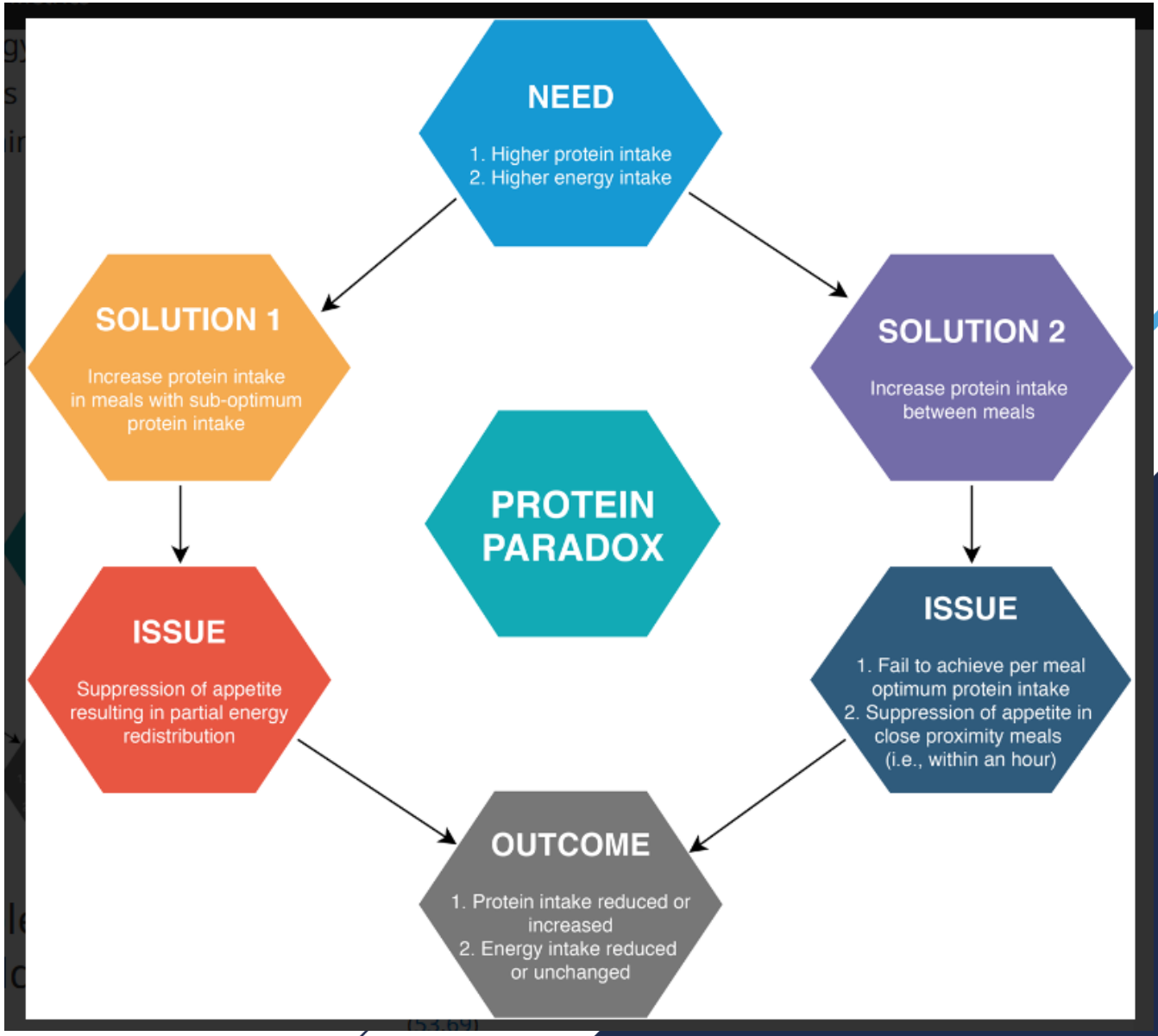
❑Challenges in nutritional intakes

- ❑ Older patients with CC often experience appetite loss and anorexia, compromising protein and calorie intake.
- ❑ **Strategy**: Use smaller, energy-dense meals to meet nutrient needs without suppressing appetite.

Yoon et al. (2023); Capitao et al. (2022); Ispoglou et al. (2021); Muscaritoli et al. (2021);Arends et al. (2021); Roeland et al. (2020); Talwar et al. (2016); Deutz et al. (2014)

Essential Amino Acids (EAAs)

- **Optimising protein intake with essential amino acids**
  - EAAs, particularly leucine, are essential for muscle maintenance and stimulate muscle protein synthesis without significantly affecting appetite.
  - **Supplementation**: EAA supplements may be of benefit in patients who have difficulty with whole proteins.



Nutrition Society Live 2020 was held virtually on 14–15 July 2020

Symposium five: Protein nutrition and ageing

The efficacy of essential amino acid supplementation for augmenting dietary protein intake in older adults: implications for skeletal muscle mass, strength and function

Theocharis Ispoglou[1]*, Oliver C. Witard[2], Lauren C. Duckworth[1] and Matthew J. Lees[1]
[1]*Carnegie School of Sport, Leeds Beckett University, Leeds LS6 3QS, UK*
[2]*School of Basic and Medical Biosciences, King's College London, London, UK*

Other Strategies

❑Probiotics and Omega-3 Fatty Acids

- ❑ **Probiotics**: Enhance gut health and nutrient absorption, potentially improving overall tolerance to nutritional interventions.
- ❑ **Omega-3 Fatty Acids**: These may help reduce inflammation and improve appetite. Regular intake could support nutritional goals in cachexia.

❑Enteral nutrition for severe cases

- ❑ For patients unable to achieve adequate intake orally**, enteral nutrition** may be necessary if intake remains below 50% for more than one week.
- ❑ Ensures that even patients with severe appetite and intake challenges receive essential nutrients.

❑Comprehensive multimodal approach

- ❑ Combining nutrition, exercise, and medical support offers a **holistic approach** to managing cachexia.
- ❑ Encourages collaboration between dietitians, physiotherapists, and clinicians, resultin I the development of a plan that addresses individual patient needs.

Yoon et al. (2023); Muscaritoli et al. (2021); Sim et al (2021); Sanchez-Lara et al. (2014); Zaid et al. (2012); Cerchietti (2007); Fearon et al. (2006)

Psychosocial Interventions

❑Addressing mental and social needs

- ❑ Counselling and support groups: Alleviate anxiety, depression, and isolation.
- ❑ Cognitive-Behavioural Therapy (CBT): Supports coping with body changes and cancer stress.
- ❑ Mindfulness techniques: Reduces anxiety, enhancing overall well-being.

❑Collaborative care approach

- ❑ **Interdisciplinary team**: Involves dietitians, physiotherapists, mental health professionals.
- ❑ **Family involvement**: Engages family to strengthen support networks.

❑Key benefits

- ❑ Improve QoL and adherence to treatment plans.

Hopkinson et al. (2021); Amano et al. (2019); Najafi et al. (2019); Portman et al. (2016); Michie et al. (2014)

Behavioural strategies for adherence in older adults

- *Behaviour modification approaches and **technology** for long-term adherence*
- ***Short term adherence (week one)** powerful predictor of long-term adherence*
- ***Client-centred** interventions*

A Narrative Review of Non-Pharmacological Strategies for Managing Sarcopenia in Older Adults with Cardiovascular and Metabolic Diseases

Theocharis Ispoglou *, Oliver Wilson, Deaglan McCullough, Luke Aldrich, Panagiotis Ferentinos, Gemma Lyall, Antonios Stavropoulos-Kalinoglou, Lauren Duckworth, Meghan A. Brown, Louise Sutton, Alexandra J. Potts, Victoria Archbold, Jackie Hargreaves and Jim McKenna

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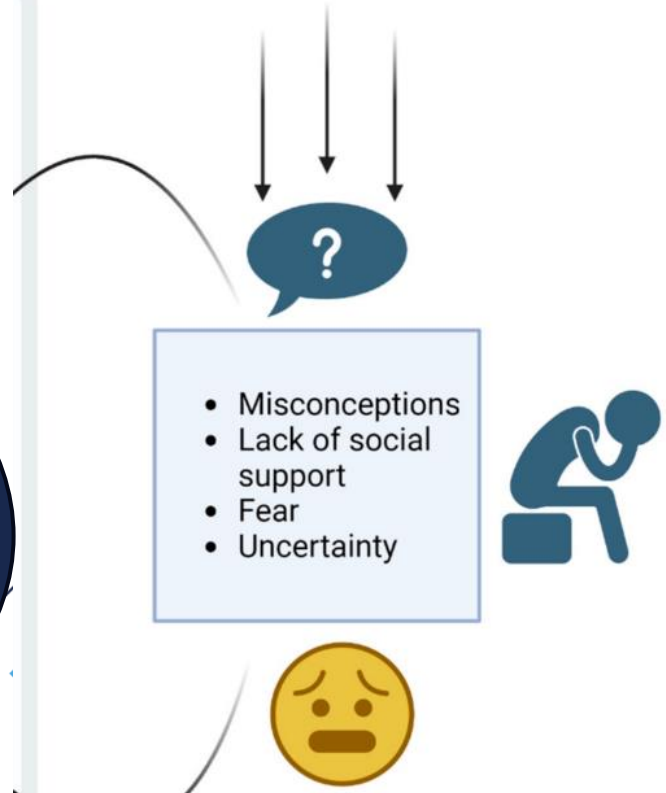
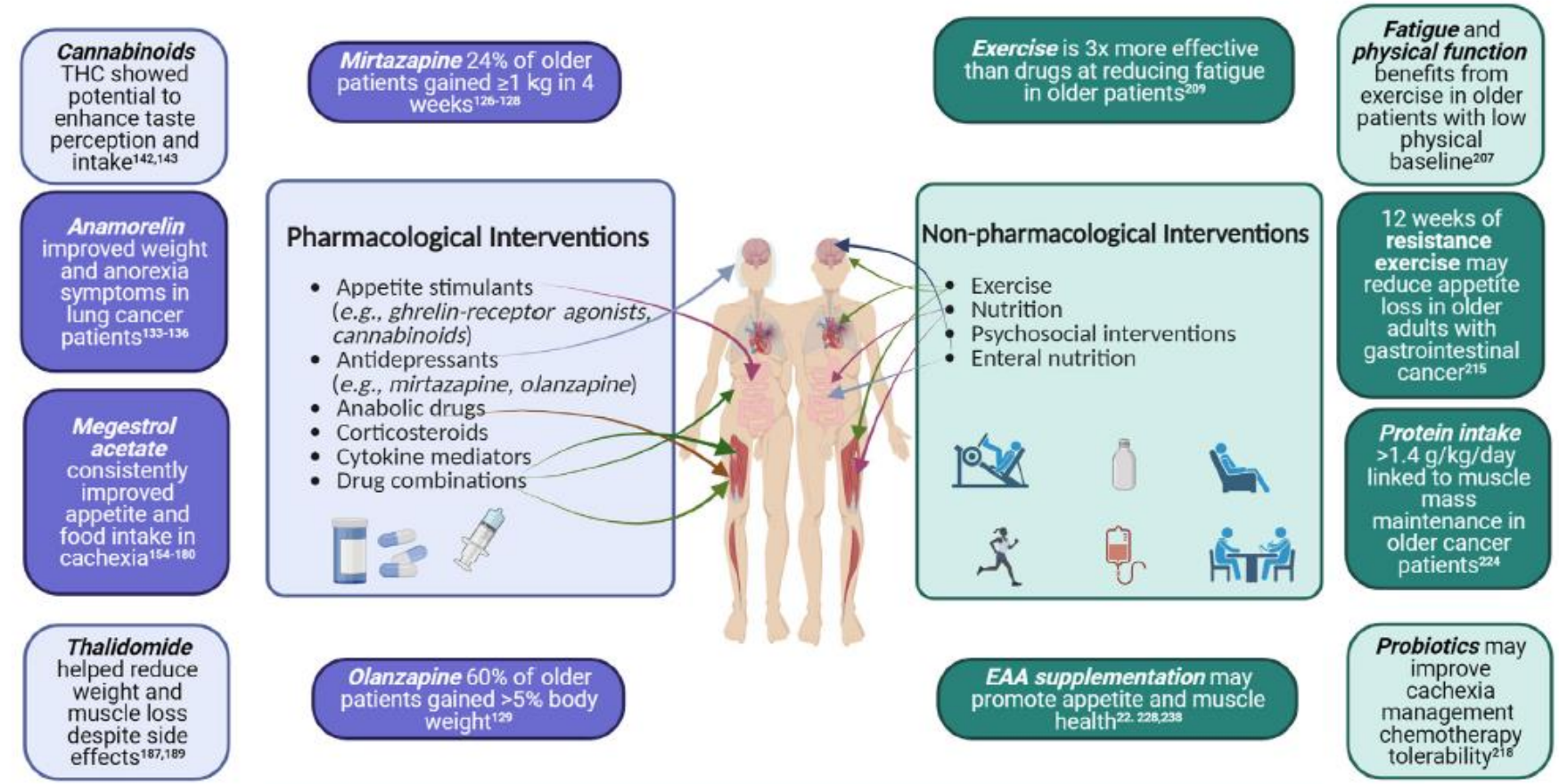
* Correspondence: t.ispoglou@leedsbeckett.ac.uk

To improve participation in health interventions for sarcopenia and related conditions, we must prioritise behaviour modification, technology, and individualisation. Early engagement is key to long-term commitment.

Challenges of Engaging in Interventions





Practical Considerations

1. Regularly check glucose levels for hyperglycaemia in older patients prescribed corticosteroids.
2. ***Closely monitor for drowsiness and potential polypharmacy interactions with mirtazapine.***
3. Tailor exercise programmes to individual capabilities and limitations of older CC patients.
4. ***Adjust nutritional plans to older cancer cachexia patients' altered taste and digestive function, ensuring high protein and caloric needs are met.***
5. Monitor for gastrointestinal side effects in older patients using anamorelin and other appetite stimulants.
6. ***Consider individual patient tolerance and potential interactions when using nutritional supplements, such as probiotics with other treatments.***

References cited in this figure are listed after those that have been cited in the text.

Fig. 3. Potential investigational, pharmacological, and non-pharmacological strategies for the treatment of CC.

Ispoglou et al (2024).

Key take away messages

- **Holistic management of cancer cachexia**
  - Effective management requires a multifaceted approach combining nutrition, exercise, and psychosocial support to address both physical and mental health challenges.

- **Nutritional strategies are vital**
  - Meeting protein and energy intake goals is essential for muscle preservation and resilience to treatment. Utilising essential amino acids (EAAs) and small, energy-dense meals can help overcome appetite loss. Regular nutritional assessment is essential to identify those at risk of malnutrition and ensure interventions are fit for purpose. Promote adherence through individualised approaches.

- **Exercise as core intervention**
  - Exercise is not only three times more effective than pharmacological interventions in reducing fatigue but also supports muscle mass, physical function, and overall quality of life. Personalising exercise programmes to individual needs maximises benefits and ensures long-term adherence.

Key take away messages

- **Psychosocial and behavioural support**
  - **Empowering patients**: Educating patients and addressing misconceptions about ageing and muscle health are essential for enhancing adherence. Psychosocial support, including counselling, family involvement, and behavioural strategies such as goal setting, self-monitoring, positive reinforcement, and habit formation, are all crucial for sustained adherence, and for enhancing the effectiveness of interventions.

- **Multidisciplinary collaboration**
  - **A team-based approach**: Engaging dietitians, physiotherapists, clinicians, and mental health professionals ensures that interventions are tailored to individual needs, optimising outcomes in older cancer patients. Collaborative care creates a **supportive environment** that enhances treatment success.

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