Protein's Critical Role in Malnutrition and Frailty

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Malnutrition is recognised as a significant aetiological factor in the development of adverse health outcomes. It commonly contributes to impaired physical function[1] and poor outcomes, e.g. increased rates of infections and pressure ulcers, increased length of hospital stay, increased duration of convalescence after acute illness, as well as increased mortality.[2]

While there are many factors that contribute to the adverse mentioned health consequences, malnutrition has been identified as a key independent variable.[3, 4] Malnutrition has a growing economic burden. In the United Kingdom (UK), annually estimated costs of malnutrition are >£23 billion, with older adults (>65 years old) accounting for 52% of these costs.[5] It costs 3 times more to treat a patient with malnutrition than to treat similar patients without malnutrition (£7,408 vs. £2,155).[5, 6]

It is very easy to focus on the financial savings that can be made in the field of malnutrition. However, in some areas across the UK, this has led to the deprescribing of oral nutritional supplements (ONS), the substitution of ready-to-drink ONS with powdered alternatives, or, in some cases, the refusal to prescribe ONS when clinically indicated. The majority of the costs of malnutrition are as a result of complications of the condition and the direct costs of appropriate treatment are <2.5%.[5] This is not unlike other conditions, like diabetes, where associated costs of complications are very high, and the costs of appropriate treatment and diagnosis are lower.[7]

A 2022 survey conducted by British Association for Parenteral and Enteral Nutrition (BAPEN),[8] focusing on malnutrition and nutritional care in UK adults, indicated that 45% of individuals screened using the 'MUST' ('Malnutrition Universal Screening Tool') across various health and care environments were at risk of disease-related malnutrition. This represents an increase from previous years, with recorded risk percentages of 42% in 2019, 40% in 2020, and 39% in 2021. The survey also identified specific populations with higher malnutrition risk, including those with cancer (62%), gastrointestinal disorders (50%), respiratory illnesses (48%), frailty (45%), and neurological conditions (43%). Regarding care settings, the highest risk was observed in individuals living at home (56%) and residents of care homes (55%), while hospital patients showed a 44% risk.

There has been no global consensus on the definition of malnutrition until recently but the below is commonly used in literature across the UK: *Malnutrition is a state of nutrition in which a deficiency or excess (or imbalance) of energy, protein and other nutrients causes measurable adverse effects on tissue/body form (body shape, size and composition) and function and clinical outcome.*[9]

This lack of consensus makes malnutrition difficult to identify, diagnose and treat, while simultaneously making it difficult to conduct research that has generalisability.

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Diagnostic framework for malnutrition & sarcopenia

Recent efforts have standardised diagnostic criteria globally for both malnutrition and sarcopenia through the Global Leadership Initiative on Malnutrition (GLIM)[10] and the European Working Group on Sarcopenia in Older People (EWGSOP2)[11] initiatives, respectively. Both frameworks utilise a consistent three-step approach: screening, diagnostic confirmation, and severity grading. The GLIM defines malnutrition by combining phenotypic (weight loss, low body mass index [BMI], muscle mass) and aetiologic (reduced intake/assimilation, disease burden/inflammation) criteria, while EWGSOP2 defines sarcopenia by low muscle strength and mass. Both use muscle mass as a key diagnostic factor to promote study comparability. Severity is graded based on phenotypic features in GLIM and physical performance in EWGSOP2.

The 'MUST'[12] is a screening tool, whereas the GLIM is a diagnostic framework. Despite the GLIM being available, uptake in the UK has been low. Widespread use of the GLIM framework will ultimately contribute to more effective diagnosis and treatment of malnutrition.

The current landscape in the UK

The UK's population is growing and in 2022 19% of people in the UK were aged 65 or over (12.7 million), and by 2072 this could rise to 22.1 million people, or 27% of the population as per prediction.[13] It is this age group of older adults that are at increased risks of malnutrition and related complications as this population group have more complex healthcare needs, often involving multiple conditions. Malnutrition is estimated to impact 1 in 10 older adults in the community.[5]

Frailty also has no agreed definition, and the following is usually used in the UK: *"consequence of a decline in several physiological systems, which collectively results in a vulnerability to sudden health state changes triggered by relatively minor stressor events"*.[14]

Malnutrition and frailty have overlapping features and often co-exist;[15] people with malnutrition are four times more likely to have frailty,[15] and malnutrition is present in around 45% of people with frailty.[16] Frailty prevalence, like malnutrition and the number of older adults in the UK, has also been increasing (from 26.5% in 2006 to 38.9% in 2017).[17] While the average age of frailty onset was 69, frailty was already present in 10.8% of people aged 50-64 in 2006, which increased to 19.6% in 2017 for the same age group.[17] Frailty is present in around 25% of persons aged 85 years or older.[18] There are varying rates of frailty reported in research and, like research in malnutrition, the lack of consensus on defining frailty accounts for variances in reporting rates.

The role of protein & muscle in health

Protein is an essential macronutrient which plays a crucial role in maintaining human health. Beyond its basic function as a building block for tissues, protein significantly influences inflammation, energy production, and metabolic processes.

The physiology of protein metabolism is significantly altered in malnutrition and frailty and ageing.[19] The aetiology is multifactorial and is impacted by:

a. Reduced oral intake: decreased appetite, early satiety, dysphagia and social isolation can lead to inadequate protein intake, as well as disease states and medications, especially polypharmacy affecting appetite and nutrient absorption.[19, 20, 21]
b. Inflammation: chronic low-grade inflammation, which is common in frailty and chronic diseases, increases protein catabolism and reduces muscle protein synthesis, as well as inflammatory cytokines which promotes muscle breakdown, thus exacerbating muscle wasting.[19, 20, 21]
c. Impaired metabolism: age-related changes in metabolism that includes decreased anabolic response to protein intake, which also contributes to muscle loss and muscle wasting. Reduced physical activity further exacerbates muscle atrophy.[19, 20, 21]

As a result of these factors, older adults have a higher nutritional requirement for protein.

- Protein intake recommendations for older adults by the European Society for Clinical Nutrition and Metabolism (ESPEN)[22] are:
  - 1-1.2 g protein per kg for healthy older adults
  - 1.2-1.5 g protein per kg for older adults with acute or chronic illness
  - Up to 2.0 g per kg for older adults with severe illness, injury or malnutrition.

This is in sharp contrast to the UK recommendations[23] of 0.75 g of protein per kg per day, which were based on studies of young adults with the aim to prevent nutrient deficiencies. This approach is insufficient for older adults as it does not reflect the physiology of altered protein metabolism affected by ageing in order to support optimal health and well-being.

It is estimated that fewer than 50% of older adults meet current UK recommendations and fewer than 15% meet the higher ESPEN age-specific recommendation.[24]

Due to majority of older adults not meeting their daily protein requirements they are at increased risks of muscle loss and sarcopenia. Skeletal muscle serves as the principal protein reservoir within the body, playing a critical role in systemic protein metabolism.[25, 26] It functions as a dynamic pool of amino acids, enabling the maintenance of protein synthesis during periods of inadequate amino acid absorption from the gastrointestinal tract.[25, 26] If this reservoir of protein is not replenished then muscle atrophy is exacerbated. In the long term, depletion of muscle mass is incompatible with life.[25]

The importance of muscle mass and strength is well accepted for metabolism and for activities of daily life, but skeletal muscle plays a more multifaceted role in overall health. Beyond its mechanical contributions of movement, power and breathing, muscle tissue exerts significant influence on various physiological processes.[26] Specifically, it has been implicated in limiting osteoporosis, enhanced glucagon like peptide-1 (GLP-1) secretion, suppression of colon tumorigenesis, augmentation of lipolysis, increased muscular glucose uptake (thereby improving insulin sensitivity), increased thermogenesis, promotion of adipose tissue browning (allows fat to mirroring muscle activity), enhanced cognitive function, and increased adenosine triphosphate (ATP) production (energy production). Skeletal muscle is being appreciated for its role as an endocrine system.[27]

It is evident that malnutrition, frailty and sarcopenia are intertwined and have negative health consequences.

Managing malnutrition

Studies have shown that dietary counselling given with or without ONS is effective at increasing nutritional intake and weight.[28] Therefore, interventions based on a 'food first' approach are often used, but as the National Institute for Health and Care Excellence (NICE) guidelines[29] recommends, care is needed when using food fortification as this tends to supplement energy at the detriment of other nutrients.

The typical way to fortify the diet is using a combination of oil, cheese, butter, cream, full fat milk, skimmed milk powder and sugar. This is a simple way of increasing caloric content of diet and is estimated to increase the energy in foods/drinks eaten by 30% and with the exception of cheese/milk/and skimmed milk powder, the rest offer very little to no protein.

The protein requirement of an older person with chronic obstructive pulmonary disease (COPD) weighing 60 kg per day is 75-90 g (based on ESPEN guidelines).[22] **Table 1** shows what 75 g of protein a day would look like.

By taking into account early satiety, reduced appetite, dysphagia, social isolation, polypharmacy and financial costs, it is very hard to meet this requirement on a daily basis.

For people at risk of malnutrition, and who are unable to meet their protein requirement, an ONS would be of benefit. NICE[29] recommends that healthcare professionals should consider oral nutrition support to improve nutritional intake for people who can swallow safely and are malnourished or at risk of malnutrition, this echoes ESPEN recommendations.[22]

Patients recently discharged from hospitals with high rates of estimated malnutrition are at increased risk of failed discharge and readmission.[30, 31, 32]

The ESPEN guidelines[22] recommend that: *'After discharge from the hospital, older persons with malnutrition or at risk of malnutrition shall be offered ONS in order to improve dietary intake and body weight, and to lower the risk of functional decline.'*

There is much research documenting the benefits of ONS in the management of malnutrition,[33, 34] and while powder ONS are much more cost effective than ready to drink, they often don't provide adequate protein or micronutrients, are difficult to make, are large in volume, and people can struggle with compliance. Ultimately, the 'right' ONS is the one that the patient can comply with.

In summary

It is important to remember that malnutrition's impact extends far beyond statistics and economic considerations. Each individual affected is a person whose life is profoundly altered, often resulting in a diminished quality of life. Malnutrition can prematurely end lives, leaving voids in the lives of loved ones. Focusing solely on numbers obscures the very real human cost; the loss and suffering experienced by individuals and their families.

Table 1: Dietary sources of 75 g protein

2 eggs	12 g
Mini cheese (20 g)	5 g
Handful of almonds (30 g)	6 g
1 chicken breast	26 g
1 pint of milk	20 g
Yoghurt (single serving, 120 g)	4 g
½ bag of baby spinach	2 g

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