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# Understanding age-related changes: exploring the interplay of protein intake, physical activity and appetite in the ageing population

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Globally, we are currently facing a rapid demographic shift leading to an increase in the proportion of older adults within the population. This raises concerns about the potential increase in age-related diseases and their impact on our ability to provide adequate health and end-of-life care. To apply appropriate interventions, understanding the changes that happen with ageing becomes essential. Ageing is often accompanied by a decrease in appetite and physical activity, which may lead to malnutrition, resulting in decreased muscle mass, physical capabilities and independence. To preserve muscle mass, older adults are advised to increase protein intake and physical activity. However, protein's high satiating effect may cause reduced energy intake. Physical activity is also advised to maintain or enhance older adult's appetite. This review paper aims to discuss appetite-related changes that occur with ageing and their consequences. In particular, it will focus on investigating the relationship between protein intake and physical activity and their impact on appetite and energy intake in the ageing population. Recent studies suggest that physical activity might contribute to maintaining or enhancing appetite in older adults. Nevertheless, establishing a definitive consensus on the satiating effect of protein in ageing remains a work in progress, despite some promising results in the existing literature.

**Keywords:** Ageing: Protein: Physical activity: Appetite: Food intake: Older adults

### Ageing

Ageing is the lifelong process of getting older at the cellular, organ or whole-body level<sup>(1)</sup>. The ageing process is unique across all populations due to the differences in genetics, lifestyle and overall health<sup>(2)</sup>. While the UN has

agreed that individuals aged 60 years and above could be referred to as part of the older population<sup>(3)</sup>, most developed countries globally have adopted the definition of ‘elderly’ or ‘older person’ as the chronological age of 65 years<sup>(4)</sup>.

**Abbreviations:** NDNS, UK National Diet and Nutrition Survey; SACN, Scientific Advisory Committee on Nutrition; ESPEN, European Society for Clinical Nutrition and Metabolism; PYY, Peptide Tyrosine Tyrosine; GLP-1, Glucagon-Like Peptide-1; CCK, Cholecystokinin; EAR, Estimated Average Requirement.

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Over the last decades of the 20th century, significant advancements in society and technology, such as improved healthcare, better nutrition, public health initiatives and advancements in sanitation and hygiene, have resulted in increased life expectancy and longer lifespans<sup>(5)</sup>. The global population is experiencing an upward trend in the numbers of older people, and the majority of individuals today can expect a prolonged lifespan extending beyond their sixties<sup>(6)</sup>. The WHO estimates that one in six people globally will be aged 60 years or over by 2030, and this demographic is projected to double, reaching 2.1 billion by 2050, with the number of those 80 or older tripling to 426 million<sup>(6)</sup>.

The rapid growth of the ageing population has led to significant changes in the primary causes of morbidity and mortality over the past century; in particular, cases of dementia and cancer have escalated<sup>(7)</sup>. By 2030, the number of cancer cases is projected to reach 27 million, while the worldwide population affected by dementia/Alzheimer's disease is estimated to reach 115 million by 2050<sup>(8)</sup>. In addition, the incidence of falls, obesity, diabetes and CVD are also expected to continue to increase<sup>(9,10)</sup>. Consequently, with the continued growth of the older population, the healthcare system will encounter significant challenges presented by these diverse health conditions, leading to an increased need for resources and healthcare professionals. To reduce the pressure on the health system, promoting a healthy lifestyle is crucial<sup>(11)</sup>. Therefore, it is essential to understand the physiological and behavioural changes that occur as people age and to apply appropriate interventions. This review paper will commence by exploring age-related changes impacting nutritional status, including body composition, physical activity, nutritional requirements and appetite changes (anorexia of ageing), as well as the associated risk factors and consequences (Fig. 1). Subsequently, it will delve into the relationship between protein intake and physical activity and their impact on appetite and energy intake within the ageing population.

#### *Age-related changes in body composition*

Among the various physiological changes that accompany ageing, changes in body composition are particularly noticeable<sup>(12)</sup>. In general, with ageing, there is typically an increase in the percentage of body fat accompanied by a decrease in lean mass and bone density, independent of general and physiological fluctuations in weight and BMI<sup>(13,14)</sup>. Factors contributing to this shift include decreased physical activity and secretion of growth hormones and reduced sex hormones, as well as a diminished RMR<sup>(15)</sup>. This increase in fat mass is predominantly spread within the abdominal region, which is particularly associated with CVD and diabetes<sup>(16,17)</sup>. Reductions in fat-free mass occur due to skeletal muscle losses<sup>(15)</sup>, and a decline in muscle mass among older adults is directly associated with reduced muscle strength, diminished maximal aerobic capacity and decreased bone density<sup>(18)</sup>. However, these changes may not be immediately noticeable since muscle mass loss is often masked by an unchanged or even increasing BMI, due to increased

fat mass<sup>(19)</sup>. Reduced muscle mass can have significant consequences for older individuals, impacting various aspects of daily life. One notable consequence is a decrease in independence, affecting routine activities such as shopping and cooking<sup>(20)</sup>. Moreover, individuals with decreased muscle mass face an increased vulnerability to falls. Muscle strength plays a crucial role in maintaining balance and stability, and a decrease in muscle mass can contribute to a higher risk of falls<sup>(20)</sup>.

#### *Age-related changes in physical activity*

A sedentary lifestyle is becoming more common across all age groups<sup>(21)</sup>, and sedentary behaviour in ageing is a significant risk factor for chronic disease, morbidity and mortality. As individuals age, the frequency of engaging in high-intensity activities tends to decrease, while the reported incidence of immobility tends to rise<sup>(22)</sup>. In a comprehensive survey conducted in England, involving over 92 000 individuals (the Taking Part survey, 2011), exercise participation and desire to participate have been found to decrease throughout adulthood<sup>(23)</sup>. Since the majority of people aged 65 years and over spend an average of 10 h sitting each day, they are considered the most sedentary age group within the population<sup>(24)</sup>.

As per the guidelines provided by WHO<sup>(6)</sup> and UK Chief Medical Officers<sup>(25)</sup>, older adults are advised to do moderate-intensity aerobic physical activity for a minimum of 150 min per week or high-intensity aerobic physical activity for at least 75 min per week, or an equivalent combination of both intensities. In cases where older individuals are unable to meet the recommended levels of physical activity, the WHO advises them to be as physically active as their abilities and conditions allow<sup>(26)</sup>. Moreover, older adults in the UK are advised to participate in a combination of bone and muscle strengthening exercises, such as carrying heavy bags, going to the gym or participating in yoga, twice a week. Additionally, engaging in balanced activities like dancing, playing bowls or practising Tai Chi twice a week is also advised, as it can help reduce the risk of frailty and falls<sup>(25)</sup>. Despite these recommendations, the vast majority of older adults do not meet the minimum recommended activity levels for maintaining a healthy lifestyle<sup>(27)</sup>.

Understanding the physical activity behaviours of older adults is essential to develop interventions for promoting health and well-being, preventing chronic diseases and improving life quality<sup>(28)</sup>. As older adults experience progressive declines in physiological function, including slower walking speed and difficulties in standing up from a seated position and maintaining balance<sup>(29)</sup>, it becomes evident that addressing these aspects is essential. Research indicates that the great majority of older adults in their seventies had a lower physiological function compared with young adults, even without apparent difficulties in their daily activities<sup>(30)</sup>. These changes observed during the ageing process, both in physiological function and physical activity behaviours, may result from a wide variety of factors. One compelling factor contributing to these changes is that older adults commonly experience irreversible motor neurone and muscle fibre losses as part

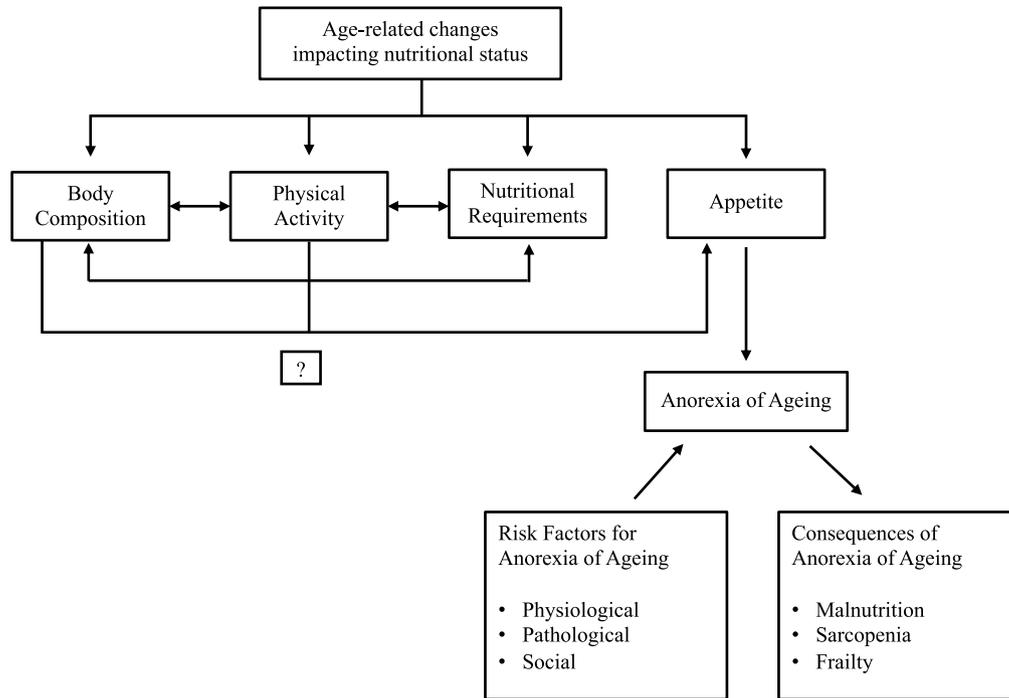


Fig. 1 Age-related changes impacting nutritional status.

of the natural ageing process<sup>(29,31)</sup>. Cross-sectional studies reveal that compared with younger adults, older adults have higher BMI, reduced muscle size and strength (particularly in the legs), lower bone mineral density and poorer performance in cognitive tests<sup>(32)</sup>. Furthermore, research on the relationship between muscle power and mobility in older adults suggests that the decline in mobility associated with ageing may be attributed to decreases in both muscle strength and power<sup>(33)</sup>. Beyond the natural decline in physical activity associated with ageing, it is also important to understand, from the older individuals' own perspective, the factors contributing to reduced activity levels with ageing. A study focused on sedentary or less active older individuals aimed to explore their motivations and barriers to physical activity<sup>(34)</sup>. The findings highlight that while interest in physical activity persists with age, misconceptions and incomplete perceptions prevent engagement<sup>(34)</sup>. This reveals the importance of activity counselling for this population.

#### Age-related changes in nutritional requirements

As people age, they often encounter challenges that make it more difficult to meet nutritional requirements effectively<sup>(35)</sup>. According to the UK National Diet and Nutrition Survey (NDNS) 2014–2016 data, free-living individuals aged 75 years and over do not meet estimated average requirements (EAR)<sup>(36)</sup>. However, maintaining a good nutritional status is crucial for older adults, as this will not only increase well-being but also reduce the risk of disease, enabling them to maintain an independent and high quality of life<sup>(37)</sup>.

Age-related decreases in physical activity and metabolic changes lead to a reduction in the energy needs of

older adults<sup>(38)</sup>. Although the energy requirement is lower due to changes in body composition and reduced physical activity in this population, it is important to note that the requirement for many nutrients remains relatively unchanged<sup>(39)</sup>. Therefore, older adults need a more nutrient-dense diet with lower energy<sup>(40)</sup>. Dietary recommendations for macronutrients for older adults in the UK are the same as for the rest of the population<sup>(41)</sup>. The Dietary Reference Values suggest that carbohydrates should contribute to 50 % of daily energy intake, while fat intake should not exceed 35 % of daily food intake for both males and females aged 65 years and over.

Adequate protein intake is one of the key nutritional factors for maintaining independence, predominantly by preventing muscle mass loss and strength (known as sarcopenia), frailty and associated comorbidities in later life<sup>(42,43)</sup>. In order to avoid progressive lean body mass loss, regardless of age, the Reference Nutrient Intake for protein for all adults in the UK is 0.75 g/kg/per d<sup>(44)</sup>. The Scientific Advisory Committee on Nutrition (SACN) 2021 report for older adults has also maintained this guideline<sup>(45)</sup>. This recommendation is the minimum amount of protein necessary to maintain nitrogen balance in the body, regardless of physical activity level. However, individuals with low physical activity levels experience decreased nitrogen retention rates, resulting in a relative increase in protein requirement compared with those who are more physically active, in order to preserve muscle tissue<sup>(46)</sup>. Therefore, it is important to evaluate protein requirements in older adults considering their reduced physical activity<sup>(47)</sup>. Furthermore, physiological changes that affect protein utilisation, including anabolic resistance (reduced response of muscle protein synthesis rates to anabolic stimuli like dietary protein and exercise), as well as insulin resistance,

impaired digestion and inflammation occurring in the body with ageing, should also be considered<sup>(48–50)</sup>. Considering all these factors, the European Society for Clinical Nutrition and Metabolism (ESPEN) and the PROT-AGE study group recommend increasing protein intake to 1–1.2 g/kg per d for healthy older individuals and to 1.2–1.5 g/kg per d for older individuals who are malnourished or at risk of malnutrition<sup>(41,48,51)</sup>. Additionally, nutritionally vulnerable adults in health and care settings in the UK are also recommended a higher intake of 1.2 g/kg body weight<sup>(52)</sup>.

#### *Age-related changes in appetite: anorexia of ageing*

Appetite is a complex regulatory system involving a multitude of physiological, psychological and environmental variables<sup>(53)</sup>, controlled by hormonal and neural factors that communicate between the gut and the brain<sup>(54)</sup>. With ageing, many people experience a decline in their appetite, and a number of studies have reported that there is a decrease in food intake in older adults<sup>(55,56)</sup>. A meta-analysis has shown that compared with younger adults, older adults are less hungry, are fuller and have a lower energy intake<sup>(57)</sup>. In 1988, this reduction in appetite due to age-related changes was first named as the ‘anorexia of ageing’ by John Morley<sup>(58)</sup>. The anorexia of ageing occurs in 15–30% of community-dwelling individuals aged 65 years and over<sup>(59,60)</sup>, and this rate is higher in women, residents in nursing homes and hospitals, with a prevalence of up to 85%<sup>(61)</sup>. Anorexia of ageing may be caused by physiological, pathological and social factors and can lead to dramatic consequences such as protein-energy malnutrition, sarcopenia, frailty, functional deterioration, morbidity and mortality<sup>(62)</sup>. Each of these risk factors and consequences will now be discussed.

#### *Physiological risk factors for anorexia of ageing*

Age-related nutritional status can be affected by several changes in physiological functions, including decreased lean body mass, increased cytokine activity, changed gastric distension, delayed gastric emptying, hormonal changes and deterioration of the sense of smell and taste<sup>(15)</sup>.

*Reduction in lean body mass.* As people age, there is a physiological decrease in energy needs and expenditures, leading to a reduction in energy intake. These changes may result from body composition changes, including decreased lean body mass and increased fat mass<sup>(63)</sup>. Over the last 20 years, cross-sectional research results strongly support the idea that muscle mass plays a vital role in influencing both energy intake and hunger<sup>(64)</sup>. In an initial study investigating the associations between body composition and objectively measured *ad libitum* food intake in adults (aged 19–67 years), a positive relationship was found between energy intake and fat-free mass<sup>(65)</sup>. Subsequent studies have further corroborated these findings, highlighting that fat-free mass exhibits a stronger association with self-selected meal size and energy intake compared with fat mass in young adults<sup>(64,66)</sup>. Additionally, research involving older adults also found a link between increases in muscle

mass and higher *ad libitum* energy intake, along with increased postprandial appetite<sup>(67)</sup>. Existing evidence suggests that the impact of fat-free mass on eating behaviours may be mediated through RMR<sup>(68,69)</sup>. Consequently, the loss of muscle mass is believed to contribute to a reduction in RMR and energy requirements, leading older adults to naturally consume less<sup>(35)</sup>.

*Increase in cytokine activities.* Cytokines, which are soluble peptide messengers synthesised by various cells including lymphocytes, neutrophils, macrophages and neuronal cells<sup>(70)</sup>, undergo changes in concentration as people age. The ageing process is associated with an increase in pro-inflammatory cytokines due to increased concentrations of glucocorticoids and catecholamines and decreased growth and sex hormone production<sup>(71)</sup>. These age-related changes result in increased cytokine levels, which in turn can contribute to delayed gastric emptying and reduced motility in the small intestine, leading to decreased food intake<sup>(72)</sup>.

*Changes in the gastrointestinal tract.* Another physiological factor that can impact nutritional status in older adults is the occurrence of age-related changes in the gastrointestinal tract, including impaired gastric motility and decreased gastric acid secretion<sup>(15)</sup>. Receptive relaxation impairment in the gastric fundus with ageing leads to rapid antral filling and distension, causing early satiation in older adults<sup>(73)</sup>. Research with younger adults has revealed that stomach distension produces a satiety effect, with fullness being related to total gastric volumes for both nutrient and non-nutrient meals<sup>(74)</sup>. The stomach’s mechanosensitivity is evident through experiments utilising intragastric balloon inflation in healthy volunteers, emphasising its role in generating sensations from the stomach<sup>(74,75)</sup>. It has also been proposed that the presence of a balloon not only directly inflates the proximal stomach but also promotes antral distension during food consumption, further increasing the feeling of fullness<sup>(76)</sup>. Studies involving younger adults indicate that delayed gastric emptying is also linked to an increased sense of satiety and fullness, resulting in decreased food intake<sup>(77,78)</sup>. This prompts the belief that the ageing process plays a role in a significant delay in gastric emptying, contributing to an increased sense of early satiety<sup>(79)</sup>. Nevertheless, the intricacies of this process in older adults are still not fully understood.

*Hormonal changes.* Peptide hormones, believed to be one of the main regulators of appetite, are released from the gastrointestinal tract in response to nutritional stimuli<sup>(80)</sup>. The initiation or cessation of food intake, along with the presence of food in the stomach or small bowel, prompts the secretion of hormones through mechanical and chemical stimuli from the gut<sup>(81)</sup>. These hormones can be categorised into satiety hormones (such as peptide tyrosine tyrosine (PYY), glucagon-like peptide-1 (GLP-1), cholecystikinin (CCK), leptin and insulin) and hunger hormones (ghrelin)<sup>(80)</sup>.

The alterations in these hormones with ageing are considered another physiological factor that may impact the nutritional status of older adults<sup>(82)</sup>. For example, increased concentration of circulating PYY, early production of PYY post-prandially or enhanced sensitivity to PYY with ageing may all result in increased feelings of fullness, subsequently leading to decreased food intake in older adults, and are believed to contribute to anorexia of ageing<sup>(83,84)</sup>. Additionally, some age-related changes in CCK have also been reported, including an increased number of CCK immunoreactive cells in the duodenum<sup>(85)</sup>, higher fasting plasma CCK levels<sup>(86)</sup> and a persistent elevation post-meal in older adults<sup>(84,87)</sup>, contributing to increased satiety and reduced food intake compared with younger adults<sup>(86)</sup>. Most, but not all, studies have also shown that there is a reduction in ghrelin concentration in older adults compared with younger adults<sup>(87,88)</sup>. A negative correlation has been found between ghrelin concentration and proportion of body fat<sup>(89)</sup>. Therefore, it has been suggested that the increase in body fat with ageing causes a decrease in fasting and postprandial ghrelin concentration, resulting in a decline in appetite in older adults<sup>(87,88)</sup>. Several studies, including a meta-analysis, have reported increased circulating leptin levels linked to adipose tissue accumulation in older individuals, both in fasted and postprandial states, contributing to a decrease in appetite and energy intake<sup>(84,90,91)</sup>. Moreover, ageing has been suggested to be associated with elevated blood insulin levels, decreased glucose tolerance and increased blood glucose levels<sup>(92)</sup>. A meta-analysis confirmed higher concentrations of circulating insulin in both fasted and postprandial states among older adults, correlating with a decrease in appetite and energy intake<sup>(84)</sup>.

*Sense of smell and taste changes.* Food-related odours have a role in the stimulation of appetite, and both senses of smell and taste have a significant role in making eating and drinking enjoyable<sup>(72,93)</sup>. However, sensory sensitivity to both taste and smell can decrease with age due to factors such as a reduction in the replenishment of taste and olfactory receptor cells<sup>(62,94)</sup>. Such changes in smell and taste perception can contribute to a decline in the perception of the hedonic properties of food in older adults<sup>(95)</sup>. Therefore, food can be perceived as less delicious, and this may result in changes in preference for the types and amounts of food consumed<sup>(96)</sup>.

#### *Pathological risk factors for anorexia of ageing*

Anorexia of ageing can be attributed to various pathological factors, including chronic diseases, depression, medications or poor dentition<sup>(15)</sup>. Among these factors, depression is commonly associated with inadequate food intake and nutritional deficiencies in older adults<sup>(97)</sup>. Older adults with depression are more likely to experience anorexia of ageing and malnutrition than those without depression<sup>(98)</sup>. Additionally, dementia, particularly Alzheimer's disease, is another pathological factor contributing to inadequate food intake<sup>(99)</sup>. Individuals with dementia have nearly twice the risk of anorexia compared with people without dementia<sup>(100)</sup>.

Many chronic diseases, including cardiac failure, chronic pulmonary obstructive disease, kidney failure, chronic liver disease, chronic constipation, cancer and Parkinson's disease, can contribute to a decrease in appetite<sup>(59,82)</sup>, which leads to anorexia of ageing<sup>(62)</sup>. Along with diseases, medications can also play an important role in reducing food intake in older adults<sup>(101)</sup>. A large number of prescribed drugs can cause side effects such as dry mouth, metallic taste, nausea, vomiting, constipation and diarrhoea, all of which can negatively affect food intake in older adults<sup>(102)</sup>.

Poor oral health is another pathological factor which contributes to decreased taste sense, and loss of appetite is frequently observed among older adults<sup>(103)</sup>. The weakening of teeth and dry mouth can cause older adults to limit their choice of food<sup>(104)</sup>. Chewing problems, resulting from poor dentition and inappropriate dentures, can further restrict the type and quantity of food consumed by older adults<sup>(59)</sup>. Additionally, swallowing problems (dysphagia), often associated with conditions such as stroke and other neurological diseases, can limit the amount and type of food intake<sup>(62)</sup>.

#### *Social risk factors for anorexia of ageing*

In addition to physiological and pathological factors, various social factors such as loneliness, widowhood, poverty and low education can affect eating behaviour in older adults<sup>(105)</sup>. Among these social factors, socioeconomic inequality emerges as an important contributor to reduced appetite and food intake in older adults<sup>(72)</sup>. In many countries, poverty plays a crucial role in reducing food diversity and often leads to inadequate dietary patterns among older adults<sup>(106)</sup>. Additionally, low education levels and common misconceptions about dietary restrictions can contribute to poor food choices in this population<sup>(62)</sup>.

Numerous studies have demonstrated that older adults who live alone have a higher nutritional risk compared with those who live with family members or others<sup>(105)</sup>. Widowhood, among the prevalent conditions faced by older adults, has been recognised as a significant factor influencing their food intake<sup>(107)</sup>. Studies indicate that widows and widowers are at a higher risk of nutritional issues compared with those who are married, partnered, divorced, separated or have never married<sup>(107)</sup>.

The shift from an independent living setting to a nursing home or hospital represents another social factor that notably influences the eating behaviour of older adults<sup>(55,108)</sup>. This alteration in the social environment has been linked to an increase in the prevalence of anorexia among older adults living in institutions, such as hospitals (26.7% men, 33.3% women), compared with those living independently (11.3% men, 3.3% women)<sup>(109)</sup>. Additionally, the nutrition intake of older adults can be adversely affected by difficulties in shopping and preparing food, particularly in the presence of illnesses and disabilities<sup>(104)</sup>. A study investigating the home food environment, and the shopping and meal preparation abilities of older adults, showed that individuals struggling with these activities were more likely to have difficulty consuming food, leading to inadequate food intake<sup>(110)</sup>.

### *Consequences of anorexia of ageing: malnutrition*

Anorexia of ageing is considered one of the main risk factors for malnutrition among older individuals<sup>(111)</sup>. Although there is no consensus on the definition of malnutrition<sup>(112)</sup>, according to ESPEN, it can be defined as ‘a state resulting from lack of uptake or intake of nutrition leading to altered body composition (decreased fat-free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease’<sup>(113)</sup>. Recent studies focusing on malnutrition in older adults, as indicated by a systematic review, emphasise the link between nutritional deficits and functional disorders<sup>(114)</sup>. Inadequate energy intake causes unintentional weight loss and loss of muscle mass and physical function<sup>(115)</sup>, contributing significantly to the development of sarcopenia and frailty<sup>(116)</sup>. This, in turn, aggravates nutritional problems and can worsen malnutrition<sup>(114)</sup>.

Malnutrition risk increases after the age of 65 years<sup>(117)</sup>, with higher prevalence observed in older adults ( $\geq 65$  years) compared with younger individuals according to the British Association of Parenteral and Enteral Nutrition’s (BAPEN) Nutrition Screening Survey in the UK (28% *v.* 21%)<sup>(118)</sup>. Data from the NDNS for the combined period of 2014/2015–2015/2016 showed that individuals aged 65 years and older had a mean daily energy intake below (65–74 years; males 17%, females 22%, 75+ years; males 18%, females 27%) the EAR and the total energy intake of women aged 75 years and older was significantly lower compared with previous years<sup>(36)</sup>. Recent NDNS datasets have shown similar findings<sup>(119)</sup>. This higher risk of malnutrition is not limited to older individuals experiencing weight loss; it also includes overweight and obese older adults, with a notable prevalence of 18% among the overweight and 29% among the obese<sup>(120)</sup>.

### *Consequences of anorexia of ageing: frailty*

While it has also been difficult to reach a consensus on the definition of frailty, it is considered a progressive age-related reduction in physiological systems, resulting in decreased internal capacity reserves, creating extreme weakness against stress factors and increasing the risk of negative health consequences<sup>(121)</sup>. The causes of frailty, a multidimensional condition influenced by genetic, psychological, physiological and environmental factors, are complex<sup>(122)</sup>. There is abundant evidence supporting the notion that the prevalence of frailty increases with advancing age<sup>(123,124)</sup>. According to a large European-based cross-sectional study, the estimated prevalence of frailty was found to be 4.1% among individuals aged 50–64 years, and this percentage increased to 17% in those aged 65 years and over<sup>(125)</sup>.

Frailty is a strong determinant of important adverse health consequences in older adults, and its adverse effects on health-related outcomes, including physical impairment, reduced muscle strength and impaired functional status, have been demonstrated across studies worldwide<sup>(121,126)</sup>. Additionally, many reviews consistently highlight the role of reduced food intake associated with anorexia of ageing in frailty development<sup>(127–129)</sup>. It

has also been linked to an increased risk of falls, prolonged hospital stays and higher mortality rates<sup>(130–132)</sup>.

### *Consequences of anorexia of ageing: sarcopenia*

Sarcopenia is an age-related loss of muscle and function<sup>(133)</sup>, despite no consensus on the definition<sup>(134)</sup>. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) developed a practical clinical definition of sarcopenia, and they defined it as a geriatric syndrome characterised by the presence of both low muscle mass and low muscle function, causing increased negative outcomes such as physical disability, poor life quality and increased mortality rates<sup>(135)</sup>. In 2018, the same group updated the definition, emphasising that muscle strength serves as a superior determinant compared with muscle mass in predicting the adverse outcomes associated with sarcopenia<sup>(136)</sup>.

Sarcopenia, while potentially observed at any age due to factors like inflammatory diseases, malnutrition, cachexia, disuse atrophy or endocrine disorders<sup>(137)</sup>, is primarily considered a disease of older adults<sup>(138)</sup>. Linked to various adverse health outcomes, sarcopenia is associated with falls, physical frailty, disability and mortality<sup>(133)</sup>. The estimated worldwide prevalence of sarcopenia among individuals aged 60 years and over was found to be 10% for both males and females<sup>(139)</sup>. Additionally, a recent systematic review of individuals aged 60 years or over showed that the prevalence of sarcopenia ranged widely between 17.7 and 73.3% in older adults living in nursing homes and between 22 and 87% in those living in assisted-living facilities<sup>(140)</sup>.

The pathophysiology of sarcopenia in older adults is complex, involving a number of internal and external factors that contribute to its development<sup>(137)</sup>. Internal factors include age-related declines in anabolic hormones such as testosterone and growth hormone, oxidative stress caused by free radicals accumulation and changes in the functioning of muscle cells<sup>(141)</sup>. Insufficient energy and particularly protein intake<sup>(137,142)</sup>, along with a sedentary lifestyle and decreased physical activity<sup>(143)</sup>, alcohol and tobacco use and long-term bed rest<sup>(144)</sup>, are external factors that contribute to the loss of muscle mass and function<sup>(137)</sup>.

Abundant evidence indicates that anorexia of ageing poses a significant risk for physical and mental disruption and is a major factor in the development of sarcopenia in older adults<sup>(145)</sup>. Inadequate food intake associated with anorexia causes a decrease in exercise capacity, muscle mass and strength<sup>(137)</sup>. Community studies highlight the prevalence of anorexia in free-living older adults (21%) and its independent association with sarcopenia<sup>(146)</sup>. In addition to inadequate energy and protein intake, another contributing factor to sarcopenia in older adults is overnutrition, which can lead to sarcopenic obesity and further accelerate the loss of muscle mass<sup>(147)</sup>. Increasing body fat due to ageing complicates the effects on skeletal muscle, reducing protein synthesis stimulation and contributing to muscle mass loss<sup>(148)</sup>. Furthermore, the secretion of adipocytokines, such as leptin, by increased adipose tissue can have a catabolic effect on muscle mass, ultimately reducing both muscle mass and strength<sup>(149)</sup>.

### *The impact of dietary protein on appetite and food intake in older adults*

Preserving muscle mass is crucial for older adults to maintain independence and overall health<sup>(150)</sup>. As highlighted above, dietary protein plays a crucial role in ageing, contributing to the preservation of muscle mass and the prevention of conditions such as sarcopenia, frailty, osteoporosis, impaired immune response and associated comorbidities later in life<sup>(42,43,151,152)</sup>. To achieve this, there is a growing emphasis on the importance of maintenance of appetite and increased protein intake for older adults<sup>(51)</sup>. Although older adults are advised to maintain or increase their protein intake to preserve their muscle mass<sup>(41,48,51)</sup>, it is worth noting that studies conducted on younger individuals have consistently demonstrated that protein is the most satiating macronutrient<sup>(153–156)</sup>. Considering that older adults often experience decreased appetite and food intake, the possibility of increasing protein intake may potentially exacerbate appetite suppression and result in further reductions in overall energy intake. Contrary to this concern, a recent meta-analysis highlighted a positive effect of protein supplementation on energy intake in older adults<sup>(157)</sup>. However, it is important to acknowledge that most of the included studies comparing protein and other nutrients were not isovolumetric and equienergetic. Consequently, the satiety effect of protein in ageing and its comparability to younger adults remain uncertain.

From this perspective, the authors of this review conducted a randomised controlled trial focused on examining changes in appetite and food intake in response to isoenergetic (~300 kcal) and isovolumetric (250 ml) preloads containing varying macronutrient compositions (high in protein (48 g v. 5 g), carbohydrate (71 g v. 20 g) and fat (26 g v. 2 g)) in both 20 younger and 20 older adults<sup>(158)</sup>. The findings of the study indicated that the consumption of preloads with different macronutrient content had no significant impact on subsequent energy intake and appetite in either younger or older adults<sup>(158)</sup>. In addition to the primary objective of this study, it has also aimed to investigate the effect of different macronutrients on the gastric emptying rate. The study's findings revealed that, in older adults, protein consumption resulted in a decrease in the ascension time, one of the parameters, representing a period of high <sup>13</sup>CO<sub>2</sub>-excretion rates. However, it was also observed that the latency phase, representing an initial delay in the excretion curve, accelerated, indicating that protein had no overall effect on the total gastric emptying half-time<sup>(158)</sup>. While this outcome contradicts some, but not all, of the previous studies on protein and appetite in young individuals, it is a promising result for the ageing population<sup>(153,155,156)</sup>. Notably, the findings suggest that increasing protein intake in older adults can be achieved without adversely affecting subsequent energy intake<sup>(158)</sup>. Contrary to the many studies in the literature, the lack of significant changes in appetite and food intake in young adults following protein consumption compared with other macronutrients may be attributed to alterations in appetite hormones. The macronutrient content of the

diet may influence the secretion of appetite hormones, potentially modulating appetite and energy intake<sup>(159)</sup>. For example, protein has been found to increase GLP-1 and PYY stimulation more so than carbohydrate or fat<sup>(160)</sup>. In contrast, another study within the authors' research group, exploring the effect of protein and physical activity on appetite and energy intake in older adults<sup>(161)</sup>, revealed different results<sup>(158)</sup>. This study showed that in a home environment, the consumption of a higher protein preload suppressed the subsequent energy intake and prolonged gastric emptying in older adults without having any effect on perceived appetite<sup>(161)</sup>. The fact that such a difference occurred between these two studies<sup>(158,161)</sup>, even though the protein amounts and preload volume and energies were equal, showed how important the environmental factor is in the measurement of appetite and energy intake studies and that this should also be taken into account in future studies.

### *The impact of physical activity on appetite and food intake in older adults*

Physical activity is widely encouraged as a health-promoting behaviour for the management of body composition and the prevention of overweight and obesity, among many other benefits for general health<sup>(162,163)</sup>. Physical activity is believed to have the potential to regulate appetite control by influencing the satiety signal system, additionally influencing food choices and macronutrient preferences by altering the hedonic response to foods in younger individuals<sup>(164)</sup>. Studies investigating the impact of physical activity on appetite and food intake are divided into two broad categories: those examining the acute responses to single bouts of exercise and those exploring the chronic responses to exercise training conducted over weeks or months<sup>(165)</sup>. Compared with a single bout of exercise, it is more difficult to examine whether physical activity or regular exercise training increases energy intake over the long term due to the difficulty of objectively measuring energy intake in free-living conditions<sup>(165)</sup>.

Evidence on the effect of physical activity on appetite and energy intake varies between different age groups. It is commonly believed that being more physically active results in increased energy intake and better appetite control, and some cross-sectional studies on younger adults have suggested significantly higher energy intake among physically active individuals compared with inactive groups<sup>(166–170)</sup>. Additionally, it has been indicated that young individuals who engage in habitual exercise tend to compensate better for energy deficits by increasing their energy intake. Notably, findings reveal that young men involved in regular physical activity (> 120 min/week) demonstrate better energy intake regulation compared with sedentary controls<sup>(171)</sup>. Similarly, in another study involving both older and younger adults, it was found that energy intake compensation was more accurate in active individuals compared with sedentary subjects. However, no age-specific interaction with physical activity was identified<sup>(172)</sup>. As a result, the extent to which this phenomenon applies to older adults remains



not fully understood. If older adults can compensate for the energy deficit by becoming more active and maintaining their energy balances, there may be potential for physical activity to play a role in preventing the 'anorexia of ageing'<sup>(173)</sup>. Therefore, the relationship between energy balance and appetite needs to be better understood in older adults. The current guidelines of organisations such as the National Health Service (NHS) and Age UK recommend increasing physical activity levels to increase appetite in older adults<sup>(24,174)</sup>. However, a systematic review has raised concerns regarding the limited evidence supporting the recommendation of increasing habitual physical activity as a means to improve appetite in older adults, without specific knowledge on the types and limits of physical activity to recommend<sup>(175)</sup>.

In the literature, conflicting results emerge regarding the impact of physical activity on appetite and energy intake in older adults. For example, in a cross-sectional study, habitual physical activity in older adults was linked to increased energy intake with no significant changes in appetite ratings<sup>(176)</sup>. Conversely, insights from a recent randomised controlled trial examining the effects of an acute resistance exercise bout on appetite and energy intake in healthy older adults revealed a slight decrease in perceived appetite, yet no subsequent impact on energy intake<sup>(177)</sup>. Adding to the complexity, a systematic review with meta-analysis proposed that exercise and physical activity might modulate resting hunger and satiety in older adults through reductions in fasting glucose and serum leptin levels<sup>(178)</sup>. To address the confusion in the existing literature, a cross-sectional study was conducted by the authors of this review examining the relationship between physical activity levels, appetite and energy intake in older adults<sup>(179)</sup>. While the findings did not reveal a difference in energy intake, the group with high physical activity levels demonstrated a higher desire to eat<sup>(179)</sup>. This aligns with existing literature, supporting the notion that higher physical activity levels are associated with higher desire to eat among older adults. This also provides strong support for previously unconfirmed recommendations advocating increased physical activity to maintain appetite in this population. Beyond assessing physical activity levels, participants in this study were also categorised into tertiles (low, medium, high) based on both activity and total energy expenditure. The findings revealed a trend towards increased energy intake in the high total energy expenditure group compared with the low group<sup>(179)</sup>. Additionally, significantly higher protein intake was observed in the high activity and total energy expenditure groups compared with the low groups, while the high physical activity group showed a significant increase in fibre intake compared with the low group<sup>(179)</sup>.

To strengthen this finding, the authors of this review also conducted a randomised intervention focusing on both protein intake and physical activity<sup>(161)</sup>. The effects of isoenergetic (~300 kcal) and isovolumetric (250 ml) preloads with varying protein levels (57% (~50 g) v. 17% (~13 g) energy as protein) on appetite, food intake and gastric emptying were compared in older adults with either high or low physical activity levels. Contrary to their cross-sectional study<sup>(179)</sup>, the results of their

intervention study revealed that having more physical activity exerted a suppressive effect on perceived appetite by delaying gastric emptying<sup>(161)</sup>. Interestingly, despite this influence on gastric emptying, being more physically active did not have a significant impact on subsequent energy intake<sup>(161)</sup>. Hence, it is crucial to note the complexity of appetite, involving hormones and the nervous system, as discussed earlier. Looking ahead, future studies should include the analysis of appetite hormones such as ghrelin, PYY and leptin, which play vital roles in satiety, incorporating blood samples for a more comprehensive understanding of the impact of protein intake and physical activity in older adults.

### Conclusion

This review paper discusses appetite-related changes with ageing and their consequences, with a specific focus on exploring the association of protein intake and physical activity with appetite and energy intake in the ageing population. As individuals age, preserving muscle mass becomes crucial, and both protein intake and physical activity play significant roles in this context. Recent studies indicate promising findings that physical activity may play a role in maintaining or increasing appetite among older adults. However, there is still no clear consensus regarding the satiating effect of protein in this population. Therefore, to deepen our understanding of the association of protein and physical activity with appetite, future research should incorporate more intervention studies that include examination of appetite-related hormones and investigations in natural settings.

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### Author contributions

DD drafted the manuscript, with LM and MEC providing intellectual contributions and revisions. All authors approved the final version of the manuscript.

### Conflicts of interest

There are no conflicts of interest.

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