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## Conference on ‘Micronutrient malnutrition across the life course, sarcopenia and frailty’

### Symposium three: Ageing, frailty, sarcopenia, osteoporosis and micronutrients

#### Nutritional concerns later in life

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In an ageing society, the preservation of health and function is becoming increasingly important. The present paper acknowledges that ageing is malleable and focuses on diets and key nutritional concerns later in life. It presents evidence for the importance of healthful dietary patterns and points towards specific nutritional concerns later in life and conveys three main messages: (1) considering health maintenance and malnutrition risk, both dietary quality in terms of healthful dietary patterns and dietary quantity are important later in life, (2) ageing-related changes in nutrient physiology and metabolism contribute to the risk of inadequacies or deficiencies for specific nutrients, e.g. vitamin D, vitamin B12 and protein and (3) that current food-based dietary guidelines propagate a shift into the direction of Mediterranean type of diets including more plant-based foods. Limited scientific evidence on nutritional requirements of older adults, along with envisaged shifts towards diets rich in plant foods, are challenges that need to be addressed in order to develop tailored nutritional recommendations and dietary guidance for older adults.

**Keywords: Nutrition: Diet: Vitamins: Health**

#### Ageing and nutrition

The world is facing an unprecedented increase in population ageing. In the Netherlands, the number of older adults over the age of 65 will have increased from 3.3 million at present to 4.8 million (from 19 to 25% of the population) by the year 2040<sup>(1)</sup>. Even though most people reach old age in reasonable good health, the consequences of the ageing process – defined as the gradual, lifelong accumulation of molecular and cellular damage – remain impending. Manifestations include chronic diseases (e.g. CVD, cancer) around middle age and *ageing-related pathologies* such as osteoporosis, dementia, sarcopenia and the consequences of anorexia of ageing. As these disabling, interlinked processes are decidedly malleable<sup>(2)</sup>, there is an urgent need for research into the prevention of ageing-related pathologies and their functional consequences.

Currently, the wider range of disciplines acknowledges that preventive strategies should incorporate modifiable lifestyle factors, including nutrition<sup>(3)</sup>. Hereby – regardless of age – healthful eating patterns are relevant, whereby specific nutritional concerns appear to be related to vitamin D, vitamin B12 and protein nutrition<sup>(4)</sup>. Due attention needs to be given to these concerns later in life, along with current shifts in dietary guidelines towards more plant-based, sustainable diets.

#### Dietary patterns, health and survival

By now, several systematic reviews of prospective studies demonstrated inverse associations between the level of adherence to dietary guidelines/patterns or recommendations and overall mortality. In an updated review including sixty-eight studies, diets that scored high on the

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healthy eating index, alternate healthful eating index and Dietary Approaches to Stop Hypertension score were associated with a 22% risk reduction of all-cause mortality<sup>(5)</sup>. Furthermore, twenty-nine prospective studies with 1 676 901 participants and 221 603 cases of all-cause mortality suggest an inverse association between adherence to a Mediterranean diet – characterised by a high intake of olive oil, fruit, vegetables and legumes, a moderate intake of fish and red wine during meals – and the risk of all-cause mortality (10% reduction for a 2-point increment in adherence to a Mediterranean diet), especially in Mediterranean regions (18% reduction)<sup>(6)</sup>.

Also, adherence to global dietary recommendations and the combination of Dietary Approaches to Stop Hypertension and Mediterranean diet (by the MIND diet) appeared to be beneficial: better adherence to the dietary recommendations for cancer prevention of the World Cancer Research Fund/American Institution for Cancer Research (WCRF/AICR) (by 1 point on a 0–4 scale) postponed the risk for colorectal cancer diagnosis by about 3 years<sup>(7)</sup>, adherence to the dietary guidelines of the WHO lowered CVD mortality by 13–15% in the South of Europe and the USA<sup>(8)</sup>, and higher adherence to the Mediterranean, Dietary Approaches to Stop Hypertension, or MIND diets was associated with less cognitive decline and a lower risk of Alzheimer's disease (AD), where the strongest associations were observed for the MIND diet<sup>(9)</sup>.

Stronger effects emerge when healthful, Mediterranean type of diets are combined with other healthful lifestyle practices including physical activity, moderate alcohol consumption or non-smoking, which jointly reduce the mortality rate by about two-thirds<sup>(10)</sup>. These combined lifestyle practices have found their way towards intervention studies, in which multidomain trials start to show benefits for, e.g. elderly populations at risk for cognitive decline and dementia<sup>(11)</sup>; improvement was 25, 83 and 150% better in the intervention group than it was in the control group, for overall cognition, executive function and processing speed, respectively.

Current food-based dietary guidelines build on such findings and also for older adults propagate a shift into the direction of Mediterranean type of diets including more plant-based foods<sup>(12)</sup>, whereby this guidance starts to include healthy vegetarian-style patterns<sup>(13)</sup> and recommendations on how to eat more sustainably at the population level<sup>(14)</sup>.

### Specific nutritional concerns in old age

Ageing comes with changes in nutrient physiology and metabolism<sup>(4)</sup>. Examples of these include the reduced capacity of the skin to produce vitamin D, malabsorption of food-bound vitamin B12 and reduced muscle protein synthetic response to protein intake, termed 'anabolic resistance'. Also for the loss of appetite due to the ageing process a physiological basis has been established, entitled 'the anorexia of ageing'<sup>(15)</sup>. Nutritional recommendations should account for these alterations, not only for reducing risk of diseases such as osteoporosis (vitamin D), megaloblastic anaemia

(vitamin B12), sarcopenia (protein) but also for the preservation of functional health and quality of life into old age. Because age-specific evidence to derive nutritional requirements for older adults is often lacking<sup>(16)</sup>, requirements of older adults are often considered the same as for the rest of the older populations for most nutrients<sup>(17)</sup>. Therefore, a recent critical review of a total of 190 papers was conducted in the UK to propose evidence-based nutritional recommendations for the 65+ population segment, particularly for most nutrients with important physiological functions in older adults. For some of these nutrients, an adequate supply is hard to achieve, even with an apparently adequate food intake, including vitamin D, vitamin B12 and protein.

### Vitamin D

Vitamin D is considered important for musculoskeletal health. In older adults, endogenous vitamin D production is lower, and sun exposure is more limited than it is in younger adults. An adequate supply is, therefore, key to meet the requirements for reducing risk fracture risk and/or sustaining adequate serum-25(OH) levels. According to a review of thirty-seven studies reporting the dietary intake of more than 28 000 community-dwelling older adults over the age of 65 in twenty different Western countries, the inadequacy of intake was most pronounced for vitamin D. Dietary intake of 84% of men and 91% of women was below the estimated average requirement of 10 µg daily<sup>(18)</sup>. Also, the prevalence of biochemical vitamin D deficiency is high worldwide<sup>(19)</sup>, including the older adults as a specific risk group<sup>(20)</sup>. SENECA – the European Study on Nutrition and the Elderly, a Concerted Action – reported levels of 25-hydroxyvitamin D below 30 nmol/l in 40% of its population<sup>(21)</sup>, at a time that the standard was well below the current reference values of 50 nmol/l in e.g. the Netherlands<sup>(22)</sup> and the USA<sup>(23)</sup>. Vitamin D intake, genes and sun exposure are considered important determinants of vitamin D status. Thus, as older people have lower dermal synthesis or do not come outside frequently, they are at high risk of poor vitamin D status. Yet, in an older population with poor supplement use sun exposure still appeared to be an important determinant of serum 25(OH)D, closely followed by genes, and vitamin D intake<sup>(24)</sup>. For the dietary supply of vitamin D, fats and oils (28%), meat (22%), eggs (7%) and dairy (7%) are the dominant sources in the Netherlands<sup>(25)</sup>. Concurrently, older adults in the UK are encouraged to consume vitamin-D rich foods such as oily fish, egg yolk and (fortified) diet. To this end, the recommendation to use a supplement of 10 µg daily is added to achieve the reference intake of 10 µg daily (15) in the UK. Assuming limited exposure to sunlight, other countries – including the Netherlands – propose to use a supplement of 20 µg daily as to reach their recommended level of intake of 20 µg daily<sup>(22)</sup>.

### Vitamin B12

Current recommendations on vitamin B12 intake are based on the amount needed for the maintenance of haematologic status and on the amount needed to



compensate for obligatory losses. Nevertheless, inadequacies might be associated with a wide variety of health concerns, including neurological impairments, osteoporosis and cognitive decline<sup>(26)</sup>.

As for vitamin D, vitamin B12 inadequacy is highly prevalent later in life, but the proportion varies widely between studies, with averages of 16% below the estimated average requirement (of 1.4 µg daily) in men and 19% in women<sup>(18)</sup>. The current prevalence of biochemical deficiency is uncertain due to the ongoing debate of markers and cut-points of deficiency<sup>(26)</sup>. Among the participants of the SENECA study, the prevalence amounted to 25%, with deficiency defined by a combination of plasma cobalamin concentrations <260 pmol/l and elevated methylmalonic acid levels (>0.32 µmol/l)<sup>(27)</sup>. A low intake and malabsorption of the vitamin from food are the major causes of poor vitamin B12 status. Dominant sources in the Dutch diet are dairy and meat, followed by fish and shellfish<sup>(28)</sup>. Notably, animal source foods are the only commonly consumed natural food sources of the vitamin<sup>(26)</sup>. Recommended intakes of vitamin B12 have been collated within the EURRECCA network of excellence, demonstrating a range of 1.5–3.0 µg daily (RDA's for adults and elderly<sup>(29)</sup>). In the UK, the proposed recommendation amounts to 2.4 µg daily, along with the food-based advice to consume foods fortified with vitamin B12, such as breakfast cereals or yeast extract or animal products including lean meat, fish, poultry, eggs and dairy<sup>(16)</sup>.

### Protein

A well-known consequence of ageing is the gradual loss of skeletal muscle mass, strength and function. This has been attributed to many factors, including the impaired ability of the ageing muscle to respond to the main stimuli for protein muscle synthesis, exercise and protein intake<sup>(30)</sup>. There is a growing body of evidence to indicate that higher (than recommended) protein intakes among older adults are beneficial for muscle health and function later in life. Examples of controlled intervention studies in older adults conclude that dietary protein supplementation (twice daily a 250-ml milk protein-supplemented beverage containing 15 g protein) enhances muscle mass<sup>(31)</sup> and strength gains during prolonged resistance-type exercise training in frail older subjects<sup>(32)</sup> and induces a shift in gene-expression levels of older adults towards levels observed in younger adults<sup>(33)</sup>; that additional protein (milk-based proteins, essential amino acids and leucine) might be required to allow muscle mass gain during exercise training in frail elderly people<sup>(34)</sup>, but that beyond recommended intake levels, it does not help to preserve lean body mass, strength or physical performance during prolonged energy intake restriction in overweight older adults<sup>(35)</sup>. Furthermore, foods fortified with protein are helpful in achieving target intakes per meal (20–25 g)<sup>(36)</sup> and preventing malnutrition<sup>(37,38)</sup>. Despite repeated calls that for optimising muscle health it should be recommended that older individuals consume ≥1.2 g protein/kg daily<sup>(39)</sup> or even higher<sup>(40,41)</sup> the debate on changing the

current protein recommendations beyond the RDA of 0.8 g/kg body mass<sup>(42)</sup> is still ongoing. Yet, Dorrington *et al.*<sup>(16)</sup> propose to change the current UK protein recommendation for adults ≥65 years (0.75 g/kg daily) to 1.2 g/kg daily acknowledging the likely benefits of particularly animal protein for muscle mass and function, and potentially for frailty and disability. The food-based dietary advice which comes with this recommendation is to have with each meal a portion of lean meat, poultry, fish, eggs, dairy or legumes<sup>(16)</sup>.

Such nutrient-dense foods become particularly important when dietary intakes decline to levels below requirements and the risk of malnutrition increases. Especially, elderly are at risk for developing poor nutritional status as ageing not only modulates protein metabolism<sup>(43)</sup> but also is associated with decreases in appetite and food intake<sup>(44)</sup>, which has been termed the physiological 'anorexia of ageing'<sup>(15)</sup>. Numerous risk factors for malnutrition, including the presence of illness, possibly exacerbate the risk for malnutrition<sup>(45)</sup>. According to a recent systematic review as many as 23% of European older adults are at high risk of malnutrition, ranging from 8.5% in community-dwelling older adults to 28.0% in the hospital setting<sup>(46)</sup>. For its effects on homeostatic reserve and resilience malnutrition relates to poor outcomes, e.g. increased rates of infections and increased length of hospital stay, as well as increased mortality<sup>(47)</sup>. Its treatment requires an individualised, multimodal comprehensive approach addressing modifiable causes of malnutrition<sup>(48)</sup>. Pooled analysis data of nine intervention studies with a total of 990 participants underlines the role of nutrition herein: protein and energy supplementation were effective at increasing energy intake (>1046 kJ daily) and body weight (>1 kg) among older adults at risk of malnutrition<sup>(49)</sup>.

### Additional considerations

Although tackling the specific nutritional concerns later in life appears most relevant for public health, there are several seemingly incompatible considerations.

- (1) To address the protein, vitamin B12 and vitamin D inadequacies most of the current evidence supports recommending increasing animal-based foods, as dominant sources of vitamin B12, vitamin D and high-quality proteins. However,
- (2) Biological research on the impact of protein nutrition on health and longevity of a variety of model organisms, primates and human subjects suggests that – at least until the age of 65 – low protein consumption confined to plant-derived sources is associated with healthy ageing<sup>(50)</sup>.
- (3) Furthermore, in dietary recommendations there is growing recognition of healthful plant-based diets in the prevention of chronic diseases as environmentally sustainable dietary options<sup>(51,52)</sup>.

In recently reviewing the literature for proposing evidence-based nutritional recommendations for older

adults, Dorrington *et al.*<sup>(16)</sup> signalled significant gaps in current nutritional research among older adults. For most nutrients, they uncovered a lack of age-specific evidence, particularly addressing dietary intake, which limited their ability to confidentially propose nutritional recommendations. For the proposed changes (protein, calcium, folate and vitamin B12) there was insufficient evidence to differentiate between men and women or between young-older (65–79 years) and old-older (over the age of 80). Thus, there is an urgent need to address the existing knowledge gaps by conducting high-quality research in older adults, in particular. Addressing these knowledge gaps requires an integrated approach acknowledging the challenging complexity of the ageing process in interaction with nutrient and food intake, dietary patterns and lifestyle factors in developing tailored dietary strategies that protect not only health and function in later life but also the environment.

### Key messages

- Considering health maintenance and malnutrition risk, both dietary quality in terms of healthful dietary patterns and dietary quantity are important later in life.
- Ageing-related changes in nutrient physiology and metabolism contribute to the risk of inadequacies or deficiencies for specific nutrients, e.g. vitamin D, vitamin B12 and protein. Current food-based dietary guidelines propagate a shift into the direction of Mediterranean type of diets, including more plant-based foods, moving away from the dominant dietary sources of vitamin D, vitamin B12 and protein.
- High-quality research in older adults requires an integrated approach acknowledging the challenging complexity of the ageing process in interaction with nutrient and food intake, dietary patterns and lifestyle factors in developing tailored dietary strategies that protect not only health and function in later life but also the environment.

### Conflict of Interest

None.

### Authorship

The authors had sole responsibility for all aspects of preparation of this paper.

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