



# **SACN statement on nutrition and older adults living in the community**

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# 1 Introduction

## Background

- 1.1 The Committee on Medical Aspects of Food and Nutrition Policy (COMA) published a report on the Nutrition of Elderly People in 1992 (Department of Health, 1992). Subsequent reports and position statements published by the Scientific Advisory Committee on Nutrition (SACN) have updated recommendations for older adults.
- 1.2 The purpose of this position statement is to provide an overview of the currently available evidence on nutrition in older adults and its impact on healthy ageing.
- 1.3 This is a position statement rather than a full risk assessment. It is not intended to be a comprehensive review of the evidence base. It provides an overview of current evidence up to February 2019.
- 1.4 This position statement evaluates systematic reviews and meta-analyses examining the relationship between nutrition and healthy ageing in adults aged 65 years and over living in the community.
- 1.5 It does not consider:
  - the treatment or management of conditions or evidence relating to older adults who are frail, malnourished and/or living in residential care or nursing homes
  - evidence where COMA or SACN has already published relevant conclusions and/or recommendations for this age group.
- 1.6 Healthy ageing is defined as “the process of developing and maintaining the functional ability that enables wellbeing in older age” (WHO, 2015). Functional ability refers to “the health-related attributes that enable people to be and to do what they have reason to value; it is made up of the intrinsic capacity of the individual, relevant environmental characteristics and the interactions between the individual and these characteristics” (WHO, 2015).

## Terms of reference

1.7 In July 2018, SACN convened a working group to consider the evidence in this area. The terms of reference were:

- to review current evidence on the role of nutrition in community-dwelling older adults and its impact on healthy ageing. This will include consideration of:
  - key nutritional issues relevant to age-related health, including age-related changes in cognition, physical and metabolic function
  - current dietary intake and patterns compared to current UK government advice
  - evidence according to chronological age: 65 to 74 years, 75 years and above.
- to draw conclusions on the state of the evidence in relation to existing advice and make recommendations where possible.

## 2 Background

### Demographics

- 2.1 In 2018 there were nearly 12 million people aged 65 years and over in the UK, of whom 45% were men and 55% women. This age group is predominantly white (95%) and married (59%) with a quarter widowed (ONS, 2019d). 1.6 million were aged 85 years and over (ONS, 2019a).
- 2.2 The number and proportion of older adults is increasing (ONS, 2018; ONS, 2019b; ONS, 2019c). In 1998, around 1 in 6 people (15.9%) were 65 years and over; this increased to 1 in 5 people (18.3%) in 2018 and is projected to reach around 1 in 4 people (24.2%) by 2038 (ONS, 2019b).
- 2.3 Improvements in living standards, medical advances and public health initiatives have all contributed to people living longer (ONS, 2018). In the period 2014 to 2016, men in England aged 65 lived a further 18.8 years and women of the same age lived an additional 21.1 years (PHE, 2018). However, life expectancy is not matched by healthy life expectancy and this is more marked in disadvantaged communities. People living in the most deprived areas spend 20 fewer years in good health compared to those living in the least deprived areas of the country (PHE & CAB, 2019).

### Factors that impact on people as they age

- 2.4 Biologically, ageing is associated with the gradual accumulation of molecular and cellular damage. Over time, this damage leads to a gradual decrease in physiological reserves and a decline in capacity of the individual (WHO, 2015). The rate of these biological changes varies between individuals, for example, some 70 year old adults may be physically healthy, whereas others may be frail or require significant support to meet their basic living needs (WHO, 2015).
- 2.5 Ageing is a life-long process and how an individual ages can be modified by a vast number of external influences throughout life (WHO, 2015). These include, but are not limited to:
  - lifestyle – diet, smoking, physical activity, alcohol, stress
  - economic factors – income, employment
  - health and social care systems
  - physical environment including living conditions
  - social environment
  - cultural and personal factors.

Many of these factors (although outside SACN's remit) may impact on food choice, eating habits and dietary intake.

- 2.6 The risk of many diseases and chronic conditions increases with age, in particular cardiovascular disease (CVD), neurological diseases (such as Alzheimer's disease and other dementias), diabetes, sensory disorders and musculoskeletal conditions (particularly lower back and neck pain). More than half of people aged over 65 years have at least 2 chronic health conditions (Kingston et al, 2018). Many chronic conditions may be prevented or delayed by lifestyle behaviours including healthier eating, physical activity and maintaining a healthy weight (WHO, 2015).
- 2.7 Globally, it is estimated that older adults take an average of 2 to 9 medications per day (Dagli & Sharma, 2014). Polypharmacy (the routine use of several medications at the same time by a patient), is common among older people with multimorbidity (NICE, 2019). Polypharmacy can have many effects, including an increased risk of hypofunction of the salivary gland. This is associated with a large variety of symptoms including oral dryness, dental erosion and oropharyngeal impairment which may lead to disturbances in chewing, swallowing and perception of taste, flavour and texture (Pedersen et al, 2018).
- 2.8 Social factors, such as isolation and loneliness, are associated with decreases in health status and quality of life and may also impact on dietary intake in older adults (WHO, 2015). Three point eight million people in the UK over the age of 65 live alone, 58% of whom are over 75 (around 2.2 million individuals) (ONS, 2017). Other factors, such as a bereavement may also impact on eating behaviour (Johnson, 2002; Rosenbloom & Whittington, 1993).

## **Nutrition, health and changes with ageing**

- 2.9 Nutrition, age-related physiological changes and health are often interconnected. In some cases, age-related physiological changes can impact on nutritional intake and status; in others nutritional intake and status can impact on how people age.

### **Appetite**

- 2.10 Although many older adults are in positive energy balance and are living with overweight or obesity, poor appetite is commonly reported and can contribute to weight loss, nutritional deficiencies and risk of adverse health outcomes (Cox et al, 2020). There are many reasons why changes in appetite may occur with advancing age, including changes to the physiology of the body, changes in psychological functioning, changes in social circumstances, acute illness, chronic diseases and use of medication (Cox et al, 2020) (see also paragraphs also 2.12, 2.21, 2.23 and 2.32).

### **Smell and taste**

- 2.11 Sense of smell and taste may decline with age, contributing toward reduced appetite and risk of malnutrition in some older individuals (Mathieu et al, 2019;

WHO, 2015). However, it is uncertain whether these changes are major influences on the eating behaviours and intakes of the general population of community living older adults (Kershaw & Mattes, 2018; Sergi et al, 2017).

- 2.12 Olfactory functions (that form the sense of smell) can deteriorate with age due to the progressive reduction of olfactory receptors and fibres in the olfactory bulbs, as well as increased occurrences of receptor cell death. Over time, the physiology of the taste cell membranes may also change, and the functions of receptors and ion channels are affected. Medications can also impact taste sensitivity and can affect taste acuity (Schiffman & Graham, 2000).
- 2.13 When senses are hampered, it may be harder to detect and recognise particular food flavours and tastes, such as salty and sweet. It has been suggested that these changes may contribute to older adults adding extra salt and sugar to food and beverages to enhance flavour, as well as altering the quantity, quality and variety of food consumed. Such sensory losses could also lead to the overall eating experience becoming less enjoyable and reduced motivation to eat. However, evidence that sensory changes drive significantly different food choices or additions of salt or sugar to foods by older adults is equivocal (see also paragraphs 4.28, 4.29 and 4.36).

### **Oral health**

- 2.14 Poor oral health can affect the general health and wellbeing of older adults through its influence on nutrition (WHO, 2015). Dental status, number of teeth, bite force and chewing problems may all be associated with the variety of food and nutrient intake, including fibre and vegetables, in older adults (Kiesswetter et al, 2018). For example, older adults may avoid foods that are hard to chew, such as some fruit, nuts and vegetables, well-cooked meat and some bread, therefore decreasing their intake of fibre and some micronutrients (Mann et al, 2013). Consistent with this finding, older adults who are well-nourished have been reported to have a significantly higher number of pairs of teeth or 'functional teeth units' in comparison to individuals with malnutrition or who are at risk of malnutrition (Toniazzo et al, 2018).
- 2.15 There have also been very significant changes in the oral health of the population over the last 50 years with many more older people retaining some natural teeth rather than relying on dentures for function (Steele et al, 2012). In 1968, close to 90% of people aged 75 and over had no teeth. Data from the most recent national dental survey in 2009 showed that this had reduced to 30%, with a continued trend for reduction since. The changes in oral health status are not distributed evenly within the population, with a greater proportion of women and people from less affluent socio-economic groups with edentulism (having no teeth) compared with men or the more affluent. Edentulism is much more common in Scotland and the North of England than it is in the South (Steele et al, 2012).



## Hydration

- 2.16 Evidence suggests that older adults may be vulnerable to dehydration; for example data from a prospective cohort study (PCS) conducted in a UK hospital showed that a third of older adults admitted to hospital as an emergency were dehydrated (El-Sharkawy et al, 2015).
- 2.17 Older adults are at a greater risk of dehydration due to reduced fluid intake and increased fluid loss (WHO, 2002). Reduced fluid intake may be caused by older adults feeling less thirst in response to water deprivation and other factors such as delirium, dementia, diuretic use, swallowing problems, laxative abuse, incontinence and problems with dexterity and mobility (WHO, 2002). An increase in fluid loss is common in older adults due to a reduction in renal concentrating capacity in response to dehydration and decreases in plasma renin activity and aldosterone secretion (Begg, 2017). This causes older adults to be less able to concentrate urine and to have higher minimum urine output (WHO, 2002).
- 2.18 All adults are advised to drink 6 to 8 glasses of fluid per day. However, there is not a universal consensus on the best test for detecting dehydration, and therefore dehydration may be missed in older adults (Hooper, 2014).
- 2.19 Cross-sectional data have shown that dehydration is associated with chronic health problems in older adults such as falls, fractures, confusion, pressure ulcers, poor wound healing, constipation, urinary tract infections, heat stress, infections, kidney stones, renal failure, stroke and myocardial infarction (Hooper, 2014).

## Gastrointestinal health

- 2.20 Functional decline of the ageing gastrointestinal tract (GIT) can have negative impacts on the digestion and absorption of foods, leading to poor nutrient bioavailability and subsequent malnutrition (Rémond et al, 2015).
- 2.21 Appetite is influenced by gut hormones, which are released in response to nutritional stimuli (Cox et al, 2020). The release of specific gut hormones, e.g. cholecystikinin, decreases with age, possibly influencing feelings of hunger and satiety, and impacting on appetite control. There are also physiological changes during ageing that result in increases in gastric emptying time and colonic transit time. Reduced rates of gastric emptying accentuate the feeling of fullness during meals and satiety is reached at lower levels of food intake (Shimamoto et al, 2002).
- 2.22 The development of atrophic gastritis increases with age and is associated with low or absent production of hydrochloric acid in the stomach and other digestive organs (hypo- or achlorhydria). Rates of hypochlorhydria and achlorhydria increase from around 24% in people aged 60 to 69 years to 37% in those over 80 years (Feldman et al, 1998; Feldman et al, 1996). Duodenal absorption of the B complex vitamins is pH dependent, so absorption is reduced in people with reduced gastric

acidity. Pernicious anaemia is a condition, in which reduced production of the protein intrinsic factor, required for vitamin B12 absorption in the stomach, results in vitamin B12 deficiency. The prevalence of B12 deficiency in the UK population aged 65 and over is around 5% (though higher in the 75+ age group) compared to 3% in adults aged 19 to 64 years (Clarke et al, 2004; Roberts et al, 2018) (see paragraphs 4.50 to 4.51).

- 2.23 Changes in the colon can also affect appetite and the desire to eat. The decline in colonic neurons leads to the reduction of neural transmitters in the colon, affecting its peristaltic and propulsive activities and increasing bowel transit time. This can result in constipation, a condition commonly observed in older adults, where the abdominal discomfort may affect appetite (Pilgrim et al, 2015). Constipation is more common in women and in older adults (Cullen & O'Donoghue, 2007; Higgins & Johanson, 2004). Reported prevalence rates vary widely, at least partly because criteria for diagnosis differ (SACN, 2015). Randomised controlled trials (RCTs) show a beneficial effect of increasing dietary fibre intake in terms of decreasing constipation, decreasing intestinal transit times and increasing faecal mass (SACN, 2015).

### **Anthropometry**

- 2.24 The prevalence of overweight and obesity is high in older adults. Data from the Health Survey for England (HSE) show that 75% and 71% of adults aged 65 to 74 years and aged 75 years and over respectively are living with overweight or obesity (HSE, 2018). This compares with 63% of the adult population as a whole (aged 16 years and older). Around 1% of adults aged 65 years and over were reported to be underweight, compared to 2% in the adult population as a whole (HSE, 2018).
- 2.25 Assessment of BMI measurement can be more difficult in older adults, as it does not necessarily reflect body composition changes (an increase in fat mass and decrease in muscle mass) and the natural loss of weight and height that occurs with advancing age (Butler et al, 2017) (see section on sarcopenia, paragraphs 2.51 to 2.57).
- 2.26 As for younger adults, obesity is an important risk factor for some health conditions in older adults (see sections on CVD and diabetes, paragraphs 2.28 to 2.31).

### **Energy requirements**

- 2.27 Changes in body composition in older age can lead to a reduction in basal metabolic rate. However, age-related changes in lifestyle and activity are variable. In the UK, the estimated average requirement (EAR) of energy for older adults is set at a lower level than for younger adults, with different estimates for less and more active adults (SACN, 2012). Energy requirements can also be influenced by health status and mobility (SACN, 2012).

## **Cardiovascular health**

- 2.28 CVD is generally categorised into 3 types: coronary heart disease (CHD) (including myocardial infarction), cerebrovascular disease (including stroke) and peripheral vascular disease. CVD is a lifelong process, with risk increasing with age (NHS, 2018). Data from 2017 showed that the prevalence of CHD increased from 3% of adults aged 45 to 54 years to 16% of adults aged 75 years and over, and the prevalence of stroke increased from 2% of adults aged 45 to 54 years to 9% of adults aged 75 years and over (HSE, 2018).
- 2.29 Poor cardiovascular health can cause heart attacks, strokes, heart failure, chronic kidney disease, peripheral arterial disease and the onset of vascular dementia. Furthermore, it disproportionately affects people from the most disadvantaged communities (PHE & CAB, 2019).
- 2.30 The underlying pathology of CVD is atherosclerosis, which may develop over many years and is usually advanced by the time symptoms occur (WHO, 2007). The rate of progression of atherosclerosis is influenced by diet, physical activity, obesity, smoking, elevated blood pressure (hypertension), abnormal blood lipids (dyslipidaemia) and elevated blood glucose (diabetes). Continuing exposure to these risk factors leads to progression of atherosclerosis, resulting in unstable atherosclerotic plaques, narrowing of blood vessels and obstruction of blood flow to vital organs, such as the heart and the brain (SACN, 2019).

## **Type 2 diabetes**

- 2.31 The prevalence of diabetes increases with age. In England, it is estimated that approximately 2% of 16 to 44 years olds have diabetes. This increases to around 9.0% of 45 to 54 year olds, 17% of 65 to 74 years year olds and 24% of adults age 75 years and over (PHE, 2016). There are many potential physiological and lifestyle factors that contribute to the increased prevalence of type 2 diabetes with advancing age. These may include age related changes to liver and pancreatic function, leading to changes in insulin action and secretion and hormonal dysregulation (Bradley and Hsueh, 2016). Type 2 diabetes also has a strong association with obesity, and body weight control is a key factor in the prevention of progression from impaired glycaemic control to type 2 diabetes (Pi-Sunyer et al, 2007). A considerable body of research has indicated that diabetes is a strong independent risk factor for CVD (Sarwar et al, 2010). Often, CVD and type 2 diabetes co-exist as they share common modifiable risk factors, such as obesity, and in particular elevated central adiposity.

## **Endocrine function**

- 2.32 Age-related changes to the endocrine system impact on function, through reduced responsiveness of tissues as well as reduced hormone secretions (Chahal & Drake, 2007). These changes include reduced levels of oestrogen (menopause),

testosterone (andropause), growth hormone/insulin-like growth factor-I axis (somatopause), hypothalamic–pituitary–thyroid axis, hypothalamic–pituitary–cortisol axis and dehydroepiandrosterone and its sulphate (adrenopause) (Chahal & Drake, 2007). Endocrine factors affected by ageing also include hormones involved in the control of appetite and feeding, such as ghrelin, cholecystokinin, and leptin (van den Beld et al, 2018).

## **Eye health**

- 2.33 Good vision is essential to maintain quality of life and functional independence, such as the ability to shop and prepare meals (Brown & Barrett, 2011). In the UK, it is estimated that 14% of adults aged over 65 years, 35% of adults aged over 75 years and 50% of adults aged over 90 years have sight loss which affects their day to day living (Age UK, 2018). The major causes of severe loss of vision and blindness in older adults include ocular complications of diabetes mellitus, glaucoma, age-related cataracts and age-related macular degeneration (AMD) (Pelletier et al, 2016).
- 2.34 AMD is the most common cause of loss of sight in older adults in the UK. The prevalence of visual loss caused by AMD increases exponentially from the age of 70 years of age, with 3.5% of the population having visual impairment caused by AMD beyond the age of 75 years (Owen et al, 2003). A recent Cochrane review concluded that individuals with AMD may have some delayed progression of the disease with multivitamin, antioxidant vitamin and mineral supplementation but noted that a systematic review of the evidence of harms of vitamin supplementation is required (Evans & Lawrenson, 2017).

## **Immune health**

- 2.35 Immune function, particularly T-cell activity, declines with age (WHO, 2015). This decline is reflected in an increased susceptibility to infectious diseases, poorer response to vaccination and an increased risk of cancer, autoimmune and other chronic diseases (Castelo-Branco & Soveral, 2014). Nutrition may impact on immune function changes with age, and immune response and host defence against infection (Pae et al, 2012).
- 2.36 Previous SACN risk assessments and position statements (notably the SACN reports on vitamin D and iron and position statements on selenium and trans fats) have explored immune function related outcomes (SACN, 2007; SACN, 2011; SACN, 2013; SACN, 2016).
- 2.37 While the evidence gathered for this position statement was completed before the outbreak of COVID-19, SACN has recently published a summary of a scoping exercise on nutrition and immune function in relation to COVID-19 (SACN, 2020a). Although this summary was not specific to older adults, SACN noted the complexity of this area of research and agreed to keep the topic under review. This

would include any high quality research on specific population groups, including older adults.

### **Skin health**

- 2.38 As humans age, the skin undergoes a series of structural and functional changes, leaving it vulnerable to damage such as tears and ulcers (Todd, 2019). There is evidence that age-related changes to the epidermis and dermis, such as changes to the dermoepidermal junction, lead to a change in the skin's integrity, increasing susceptibility to damage. When injury or damage does occur to the skin, the wound healing is slower (Bonifant & Holloway, 2019).

### **Cognitive health**

- 2.39 Cognitive function varies greatly from person to person and becomes increasingly heterogeneous with increasing age (WHO, 2015). It is closely related to years of education and strongly influenced by many factors including socioeconomic status, lifestyle, the presence of chronic disease and the use of medication. While some cognitive functions show little apparent decline with age (for example the capacity to concentrate), declines in other cognitive functions are common in older adults, such as memory, speed of processing and the capacity to tackle complex tasks (WHO, 2015).
- 2.40 In its position statement on Diet, Cognitive Impairment and Dementias (SACN, 2018) , SACN concluded that adherence to a Mediterranean dietary pattern is associated with a reduced risk of mild cognitive impairment and dementias, including Alzheimer's disease. However, most of the evidence was observational (only one RCT was identified) and potentially subject to residual confounding and reverse causality. Further evidence is required to establish whether this association signifies a protective effect of a Mediterranean dietary pattern, or of specific dietary components of such a pattern. There was no evidence of protective effects for any of the individual nutrients thought to account for the health benefits of a Mediterranean dietary pattern (SACN, 2018).
- 2.41 SACN also concluded that there was:
- insufficient evidence to draw any conclusions on the association between 'healthy' dietary patterns, other than Mediterranean diets, and risk of cognitive impairment
  - insufficient evidence to draw any conclusions on the association between individual nutrients (B vitamins, vitamins C and E and omega-3 fatty acids) and risk of cognitive decline or cognitive impairment
  - insufficient evidence to draw any conclusions on the association between polyphenols (including flavonoids) and cognition. For caffeine, the evidence provided by the reviewed literature is limited and indicates that there is no

association between caffeine intake and cognition over the longer term (SACN, 2018).

- 2.42 As SACN published its position statement on Diet, Cognitive Impairment and Dementias in 2018, it was agreed not to consider nutrition and cognition in this position statement.

### **Physical activity**

- 2.43 Physical activity has numerous benefits during the life-course (WHO, 2015) and regular physical activity can contribute to key determinants of healthy ageing, such as good physical and cognitive function (DHSC, 2019). In the UK, the Chief Medical Officer's Physical Activity guidelines recommend that older adults should participate in daily physical activity, aiming for at least 150 minutes/week of moderate physical activity or 75 minutes/week of vigorous activity, or an equivalent combination of the 2. It is also recommended that older adults should maintain or improve their physical function by undertaking activities aimed at improving or maintain muscle strength, balance and flexibility on at least 2 days a week (DHSC, 2019).
- 2.44 In 2016, 57% of men and 54% of women aged 65 to 74 years and 36% of men and 25% of women aged 75 years and over met the guidelines for aerobic activity in England. This compares with 71% of men and 63% of men in the 19 to 64 years group (HSE, 2016).

### **Musculoskeletal health**

- 2.45 Measures of musculoskeletal health include bone health, fracture/osteoporosis risk, sarcopenia, mobility and frailty.

#### **Bone health**

- 2.46 Bone mass and density tend to fall with age, particularly among postmenopausal women. This can lead to the development of osteoporosis, greatly increasing the risk of vertebral and hip fracture, which has serious implications for disability, reduced quality of life and mortality (WHO, 2015).
- 2.47 Vitamin D and calcium are well known for their important roles in bone health. Calcium is an essential architectural component of bones and teeth. Vitamin D plays a role in calcium absorption and maintaining serum calcium and phosphorus homeostasis. When vitamin D status is low, calcium absorption is disturbed.
- 2.48 In its report of the evidence on Vitamin D and Health SACN drew a number of conclusions in relation to older adults (SACN, 2016):
- efficiency of cutaneous vitamin D synthesis may be lower in older adults, but the evidence is limited (see also paragraph 3.8)

- vitamin D supplementation has beneficial effects on bone health indices in adults age 50 years and over
- on balance, for adults age 50 years and over, the evidence suggests that vitamin D supplementation does not reduce fracture risk, however the evidence was mixed, and interpretation of the data may be dependent on baseline vitamin D status – i.e. in vitamin D replete subjects, vitamin D supplementation may not be effective
- vitamin D supplementation improves muscle strength and function in adults age 50 years and over, with mean baseline serum 25(OH)D concentrations across a range of values. However, again the evidence was mixed.
- evidence suggests vitamin D supplementation reduces fall risk in community-dwelling adults age 50 years and over with mean baseline serum 25(OH)D concentrations across a range of values. Again, the evidence was mixed.

2.49 As SACN recently reviewed the evidence on vitamin D and musculoskeletal health (SACN, 2016) only systematic reviews and meta-analyses published after the search periods covered in the vitamin D and Health report were considered in this position statement.

2.50 In 2003, the Expert Group on Vitamins and Minerals (EVM) set a Guidance Level for retinol intake of 1500µg/day for adults, based on evidence that intakes above this level may increase the risk of bone fracture. Following a request by the Food Standards Agency (FSA) to reassess dietary advice to consumers on foods and supplements containing retinol, in its 2005 Review of Dietary Advice on Vitamin A, SACN made the following recommendations at that time:

- there is currently insufficient evidence on the association between bone health and retinol intakes above 1500µg/day to justify a change in dietary advice to all consumers regarding consumption of foods or supplements containing retinol (see also paragraph 3.9)
- as a precaution, however, it may be advisable for regular consumers of liver (once/week or more) not to increase liver intakes or take supplements containing retinol (including those containing fish liver oil)
- it may also be advisable for population subgroups at increased risk of osteoporosis, such as postmenopausal women and older people, not to consume more than 1500µg/day of retinol. This could be achieved by limiting intakes of liver and limiting intakes of supplements containing retinol (including those containing fish liver oil).

## **Sarcopenia**

2.51 Sarcopenia is a muscle disease (muscle failure) rooted in adverse muscle changes that accrue across a lifetime. It is associated with increased likelihood of adverse outcomes including falls, fractures, physical disability and mortality (Cruz-Jentoft et al, 2019).

- 2.52 Sarcopenia is common among adults of older age but can also occur earlier in life. The progressive loss of muscle mass and strength is associated with age (or immobility at any age); muscle mass and strength increase with growth in children and young adults, are maintained in midlife and then decrease with ageing. The rate of muscle loss is affected by genetics and lifestyle factors, such as the level of physical activity of the individual (Cruz-Jentoft et al, 2019). The mechanisms for the development of sarcopenia are not clear but it appears that ageing results in an imbalance between muscle protein anabolic and catabolic pathways, leading to an overall loss of skeletal muscle (Cruz-Jentoft & Sayer, 2019). The abnormal response of muscle to previously well-established anabolic stimuli is known as anabolic resistance and may be a key factor in the development and progression of sarcopenia. Factors such as age, obesity, inflammation, and lipotoxicity contribute to this anabolic resistance (Haran et al, 2012).
- 2.53 The European Working Group on Sarcopenia in Older People has concluded that probable sarcopenia is identified by low muscle strength and diagnosis confirmed with the detection of low muscle quantity and quality. Sarcopenia is considered severe if low muscle strength, low muscle quantity and quality and poor physical performance are all identified (Cruz-Jentoft et al, 2019).
- 2.54 Sarcopenia is largely attributable to ageing and is known as ‘primary sarcopenia’ when no other cause is evident. Sarcopenia can also occur secondary to chronic conditions that result in lower levels of exercise, immobility or disability or due to a systemic disease which increases in systemic inflammatory processes, known as ‘secondary sarcopenia’ (Cruz-Jentoft et al, 2019).
- 2.55 A higher amount of moderate-vigorous physical activity may contribute to counteracting the development of sarcopenia (Mijnarends et al, 2016). It is also important to maximise muscle mass and strength in children and young adults, maintain this in middle age and minimise losses in older age to help prevent or delay sarcopenia (Cruz-Jentoft et al, 2019).
- 2.56 It is suggested that sarcopenia may also develop due to an inadequate intake of energy or protein, which may be caused by a number of factors, including anorexia, malabsorption or a limited access or ability to eat ‘healthy’ foods (Cruz-Jentoft et al, 2019).
- 2.57 Higher muscle mass is found in older adults living with obesity, since about 25% of body weight is muscle, and it takes more physical strength for a person living with obesity to move. However, in the longer term, obesity may exacerbate sarcopenia by increasing the infiltration of fat into muscle, reducing physical function and increasing the risk of mortality (Cruz-Jentoft et al, 2019). Prevalence of sarcopenic obesity, namely obesity in combination with sarcopenia, is also increasing in adults aged 65 and over (Batsis & Villareal, 2018).



## **Osteoarthritis and joint health**

- 2.58 Osteoarthritis, a degenerative joint disease, is a major cause of joint pain in older adults, leading to disability and impacting on an individual's quality of life (Rahmati et al, 2017). It is characterised by chronic and progressive degeneration of the articular cartilage in the joints and abnormal bone remodelling (Rahmati et al, 2017). During the ageing process the articular cartilage undergoes structural, molecular, cellular and mechanical changes, therefore leading the tissues to be more vulnerable to degeneration (WHO, 2015). The fluid decreases around the joint as the cartilage erodes, leading the joint to become more rigid and fragile, resulting in joint pain (WHO, 2015).

## **Mobility**

- 2.59 Mobility refers to a person's ability to move independently and safely. The most common risk factors for mobility impairment are older age, low physical activity, obesity, strength or balance impairment, and chronic diseases such as diabetes or arthritis (Brown & Flood, 2013). Physical inactivity, either due to a sedentary lifestyle or resulting from disease related immobility or disability (as mentioned above) can also contribute to the development of sarcopenia (Cruz-Jentoft et al, 2019).
- 2.60 Limitations in movement, mobility and other physical impairments such as arthritis are likely to affect accessibility of food shopping and meal preparation, subsequently impacting on food consumption. Difficulties in food preparation can include the weight, packaging and opening mechanisms of food containers and the ability to physically prepare and cook food. Other physical challenges for older adults can include cutting food, standing for long periods, carrying and pouring food and liquid without causing injury or spilling, as well as cooking and being able to use the oven safely (PHE, 2017).

## **Frailty**

- 2.61 Frailty is more common in older age. It has been defined as “ a state of increased vulnerability to poor resolution of homeostasis following a stress” and results in people being less able to adapt to stress factors such as acute illness, injury or changes in their environment, personal or social circumstances (Clegg et al, 2013). Such changes are more likely to result in adverse health outcomes and loss of independence (NHS & Skills for Health, 2018). It is estimated that around 50% of people over the age of 65 are living with some degree of frailty: 35 to 37% mild, 12 to 16% moderate, and 3 to 4% severe (Clegg et al, 2013).
- 2.62 Frailty is closely associated with malnutrition; individuals who are frail are at increased risk of malnutrition and vice versa (Wei et al, 2018).

## **UK dietary advice for older adults**

- 2.63 Policy and advice on diet in the UK is now largely devolved. In England, the issue is under the remit of the Department of Health and Social Care and Public Health England (PHE); relevant guidance is also available from the National Institute for Health and Care Excellence (NICE). In Scotland, the issue is under the remit of the Scottish Government and Food Standards Scotland. In Wales policy and advice on diet is the responsibility of the Welsh Government, with the support of Public Health Wales. In Northern Ireland, guidance is provided by the Department of Health, Public Health Agency and Food Standards Agency in Northern Ireland.

## **3 Current UK government dietary recommendations**

### **Energy and macronutrients**

- 3.1 Dietary Reference Values (DRVs) for energy, macronutrients and salt for older adults aged 65 years and over are set out in Table 1.
- 3.2 For protein, DRVs were set as Reference Nutrient Intakes (RNI) for males and females in the age groups 19 to 50 years and over 50 years while DRVs for other macronutrients (fat, carbohydrates and fibre) and salt were set for adults aged 19 years and over as a single group. No specific macronutrient recommendations were made for adults aged 65 years and over. The DRVs for total fat, fatty acids, total carbohydrates and free sugars (all expressed as a percentage of energy intake), protein (per kg body weight), and for fibre and salt (expressed as absolute quantities), in adults aged over 50 years are identical to those for younger adults aged 19 to 50 years. For energy, Estimated Average Requirements (EARs) were set for males and females in ten-year age bands, including 65 to 74 years and 75 years and over.
- 3.3 As a comparison, some non-UK recommendations for energy and macronutrients are set out in Annex 1.

**Table 1 – UK Government dietary recommendations for energy and macronutrients and salt for older adults in the UK**

Dietary Reference Value		65 to 74 years		75 years and over	
		Men	Women	Men	Women
Energy <sup>1</sup>	EAR (MJ/day)	9.8	8.0	9.6	7.7
	EAR (kcal/day)	2342	1912	2294	1840
Protein <sup>2</sup>	RNI g/kg body weight/day	0.75			
	RNI g/day	53.3	46.5	53.3	46.5
Total fat <sup>3</sup>	DRV % total energy	Reduce to about 35% of dietary energy			
Saturated fats <sup>4</sup>	DRV % total energy	Reduce to no more than about 10% of dietary energy			
Cis monounsaturated fats <sup>3</sup>	% total energy	No specific recommendations <sup>8</sup>			
Cis polyunsaturated fats n-6 PUFA <sup>3</sup>	DRV % total energy	No further increase in average intakes and the proportion of the population consuming in excess of about 10% of energy should not increase. Provide at least 1% of total energy Increase from 0.2g/day to 0.45g/day <sup>9</sup> Provide at least 0.2% of total energy			
Linoleic acid <sup>2</sup>					
Long chain n-3 PUFA <sup>5</sup>					
Alpha linolenic acid <sup>3</sup>					
Trans fats <sup>3</sup>	DRV % total dietary energy	Provide no more than about 2% of dietary energy			
Carbohydrates <sup>6</sup>	DRV % total energy	Approximately 50% of total dietary energy			
Free sugars <sup>6</sup>	DRV % total energy	Should not exceed 5% of total dietary energy			
Dietary fibre <sup>6</sup>	DRV g/day	30g/day <sup>10</sup>			
Salt <sup>7</sup>	Recommended maximum g/day	Should not exceed 6g/day			

<sup>1</sup> From: SACN Dietary Reference Values for Energy 2011.

<sup>2</sup> From: COMA Dietary Reference Values for Food Energy and Nutrients for the United Kingdom (1991)

<sup>3</sup> From COMA Nutritional aspects of cardiovascular disease (1994) recommendations

<sup>4</sup> From: SACN Saturated Fats and Health. 2019.

<sup>5</sup> From: SACN Advice on Fish Consumption: benefits & risks (2004). SACN endorsed the population recommendation to eat at least two portions of fish per week, of which one should be oily. Two portions of fish per week, one white and only oily, contain approximately 0.45g/day long chain n-3 PUFA.

<sup>6</sup> From: SACN Carbohydrates and Health (2015).

<sup>7</sup> From: SACN Salt and Health (2003) recommendations for the adult population.

<sup>8</sup> Based on COMA 1994; COMA Dietary Reference Values for Food Energy and Nutrients for the United Kingdom (1991) recommended that cis-MUFA (principally oleic acid) should continue to provide on average 12% of dietary energy for population.

<sup>9</sup> To note that COMA Nutritional Aspects of Cardiovascular disease (1994) recommended 'an increase in the population average consumption of long chain n-3 PUFA from about 0.1g/day to about 0.2g/day (1.5g/week)'.

<sup>10</sup> DRV for adults aged 19 years and over.

## Micronutrients

- 3.4 RNIs and Lower Reference Nutrient Intakes (LRNI) for vitamins and minerals are set out in Table 2. The DRVs for all vitamins are the same for older age groups (65 to 74 years, 75 years and over) as for younger adults (19 to 64 years). The DRVs for thiamin and niacin are defined in relation to energy intake (per 1000kcal) and the DRVs for vitamin B6 are defined per gram of protein intake so when calculated as absolute values the DRVs for these vitamins are lower in the 65 to 74 years and 75 years and over age groups than in younger adults (19 to 64 years).
- 3.5 The DRVs for minerals are the same for older age groups (65 to 74 years, 75 years and over) as for younger adults (19 to 64 years). The only exception is a lower iron RNI (and LRNI) for women aged 50 years and over of 8.7mg/d (4.7mg/d LRNI) compared with 14.8mg/d (8.0 mg/d LRNI) for women aged up to 50 years.
- 3.6 SACN (2016) recommended that blood 25-hydroxyvitamin D (25(OH)D) concentration should not fall below 25nmol/L at any time of the year and set a RNI of 10 micrograms µg/day (400IU/day) of vitamin D for the general UK population (including older adults). This is the amount needed for the majority of the population to maintain a 25(OH)D concentration of 25nmol/L when sunshine exposure is minimal. The RNI applies throughout the year, as a precautionary measure, to cover population groups in the UK identified to be at risk of having vitamin D blood concentrations below 25nmol/L. It also covers unidentified individuals in the population with minimal sunshine exposure who would be at risk of vitamin D blood concentrations below 25nmol/L in the summer.
- 3.7 UK government accepted SACN's conclusions and recommendations, but recognised that in spring and summer, most of the UK population would get enough vitamin D through sunlight exposure and a healthy, balanced diet, while during autumn and winter dietary sources of vitamin D would be required. UK government advice on vitamin D is:
- in spring and summer, the majority of the population get enough vitamin D through sunlight on the skin and a healthy, balanced diet. During autumn and winter everyone will need to rely on dietary sources of vitamin D. Since it is difficult for people to meet the 10µg/day recommendation from consuming foods naturally containing or fortified with vitamin D, they should consider taking a daily supplement (10µg) in autumn and winter.
  - people whose skin has little or no exposure to the sun, such as those who are frail or housebound; are in an institution such as a care home so are not often outdoors; and those who usually wear clothes that cover up most of their skin when outdoors, should take a daily supplement containing 10µg vitamin D throughout the year

- people from minority ethnic groups with dark skin, such as those of African, African-Caribbean or South Asian origin, might not get enough vitamin D from sunlight – so they should consider taking a daily supplement containing 10µg of vitamin D throughout the year.

**Table 2 – Reference Nutrient Intakes and Lower Reference Nutrient Intakes for vitamins and minerals for older adults<sup>1</sup>**

Dietary Reference Value		65 to 74 years				75+ years			
		Men		Women		Men		Women	
		RNI	LRNI	RNI	LRNI	RNI	LRNI	RNI	LRNI
Vitamin A	µg/day	700	300	600	250	700	300	600	250
Thiamin	mg/1000kcal	0.4	0.23	0.4	0.23	0.4	0.23	0.4	0.23
	mg/day	0.9	0.5	0.8	0.4	0.9	0.5	0.7	0.4
Riboflavin	mg/day	1.3	0.8	1.1	0.8	1.3	0.8	1.1	0.8
Niacin equivalent	mg/1000kcal	6.6	4.4	6.6	4.4	6.6	4.4	6.6	4.4
	mg/day	15.5	10.3	12.6	8.4	15.1	10.1	12.1	8.1
Vitamin B6	µg/g protein	15	11	15	11	15	11	15	11
	mg/day	1.0	0.9	0.8	0.7	1.0	0.8	0.7	0.6
Vitamin B12	µg/day	1.5	1.0	1.5	1.0	1.5	1.0	1.5	1.0
Folate	µg/day	200	100	200	100	200	100	200	100
Vitamin C	mg/day	40	10	40	10	40	10	40	10
Vitamin D <sup>2</sup>	µg/day	10	n/a	10	n/a	10	n/a	10	n/a
Iron	mg/day	8.7	4.7	8.7	4.7	8.7	4.7	8.7	4.7
Calcium	mg/day	700	400	700	400	700	400	700	400
Magnesium	mg/day	300	190	270	150	300	190	270	150
Potassium	mg/day	3500	2000	3500	2000	3500	2000	3500	2000
Zinc	mg/day	9.5	5.5	7.0	4.0	9.5	5.5	7.0	4.0
Copper	mg/day	1.2	n/a	1.2	n/a	1.2	n/a	1.2	n/a
Iodine	µg/day	140	70	140	70	140	70	140	70
Selenium	µg/day	75	40	60	40	75	40	60	40
Phosphorus	mg/day	550	n/a	550	n/a	550	n/a	550	n/a
Chloride	mg/day	2500	n/a	2500	n/a	2500	n/a	2500	n/a
Sodium	mg/day	1600	575	1600	575	1600	575	1600	575

n/a: No LRNI has been set for this micronutrient

<sup>1</sup> COMA Dietary Reference Values for food energy and nutrients for the UK (1991). COMA set DRVs for micronutrients for men and women aged 19 to 50 years and 50 years and over.

<sup>2</sup> SACN Vitamin D and health (2016)

- 3.8 There is some evidence that ageing skin may have a lower capacity to produce vitamin D, due to less availability of the precursor molecule. One study found that people aged 77 to 82 years had half the capacity to produce vitamin D compared with those aged 8 to 18 years (MacLaughlin & Holick, 1985). Another study of individuals exposed to ultraviolet B radiation found a decrease in precursor molecule calcifediol (25(OH)D) production with increasing participant age (Datta et al, 2016). However, age, in combination with genetics, height and skin pigmentation only explained 15% of overall variation in 25(OH)D production, suggesting that age itself may not be a large contributor to 25(OH)D status. The oldest person in the study was 62 years and effects may be theoretically stronger in older individuals.
- 3.9 In its Review of Dietary Advice on Vitamin A, SACN recommended that it may be advisable for population sub-groups at increased risk of osteoporosis such as postmenopausal women and older people not to consume retinol at intakes greater than 1500µg/day due to evidence of high retinol intakes being associated with increased risk of bone fracture. This could be achieved by limiting intakes of liver, either by consuming smaller portions or eating liver less often and limiting intakes of supplements containing retinol (including those containing fish liver oil such as cod liver oil) (SACN, 2005).
- 3.10 As a comparison, some non-UK recommendations for micronutrient intakes are set out in Annex 1.

## Food-based recommendations

3.11 Table 3 shows food-based recommendations for adults in the UK.

**Table 3 – UK Government food-based recommendations for adults**

Food	Recommendation
Fruit and vegetables	At least 5 portions per day (equivalent to 400g) for those aged 11 years and over
Red and processed meat <sup>1</sup>	For adults, average intakes of red and processed meat should not exceed 70g per day
Oily fish <sup>2</sup>	At least 1 portion per week for adults (140g)
Liver <sup>3</sup>	Regular consumers of liver (once/week or more) not to increase liver intakes or take supplements containing retinol (including those containing fish liver oils such as cod liver oil). Population subgroups at increased risk of osteoporosis, such as postmenopausal women and older people, not to consume more than 1500µg/day of retinol. This could be achieved by limiting intakes of liver and limiting intakes of supplements containing retinol (including those containing fish liver oil).

<sup>1</sup> Includes beef, lamb, pork, sausages, burgers and kebabs, offal, processed red meat and other red meat

<sup>2</sup> Includes anchovies, carp, trout, mackerel, herring, jack fish, pilchards, salmon (including canned), sardines, sprats, swordfish and whitebait. Excludes tuna.

<sup>3</sup> Also see paragraph 3.9.



## 4 Dietary intakes and nutritional status

- 4.1 Annex 2 presents energy and nutrient intakes, and consumption of fruit and vegetables, red and processed meat and oily fish for older adults aged 65 to 74 years (71 men and 110 women) and 75 years and over (70 men and 84 women) (split by sex) based on data from the National Diet and Nutrition Survey (NDNS) years 7 and 8 (2014/15 to 2015/16). Intakes and consumption for the 19 to 64 years age group are also presented for comparison.
- 4.2 Annex 2 also presents, for the first time, energy and nutrient intakes and consumption of fruit and vegetables, red and processed meat, and oily fish for older adults aged 80 years and over. This is based on data for 134 men and 201 women from NDNS years 1 to 8 (2008/09 to 2015/16), as numbers in this age group were not large enough to present intakes based on years 7 and 8 only.
- 4.3 When interpreting data for adults aged 80 years and over alongside other age groups, it should be noted that some individuals in the 75 years and over age group for NDNS years 7 and 8 will also be in the 80 years and over age group for years 1 to 8. As the estimates for the 80 years and over age group are based on data collected over eight years, they cannot be directly compared with estimates for the 65 to 74 years and 75 years and over age groups or used to assess changes in diet with age. Furthermore, the impact of any changes over time need to be considered. A time trend analysis of NDNS data published in 2019 showed no significant trends over time in energy or macronutrient intakes for people aged 65 years and over. Intakes of some micronutrients (vitamin A, folate, iron and zinc) however, showed a downward trend over time (Bates et al, 2019).
- 4.4 The dietary data collection method used in the NDNS was a 4-day diary. Participants were asked to keep a detailed diary of all foods and drinks consumed for 4 consecutive days. Quantities consumed were estimated using a combination of household measures and photographs with portion sizes. The survey was designed to represent all days of the week equally. Although the NDNS sample is designed to be representative of the population in each age group, it is possible that the sample of older adults may underrepresent people who have long term health conditions which make it more difficult to take part in a survey (such as poor sight or memory problems).
- 4.5 Annex 2 also presents Body Mass Index (BMI) based on interviewer-measured heights and weights for 64 men and 97 women aged 65 to 74 years and 50 men and 64 women aged 75 years and over, based on data from NDNS years 7 and 8 (2014/15 to 2015/16). BMI data are also presented for older adults aged 80 years and over, based on data for 95 men and 158 women aged 80 years and over collected in years 1 to 8 (2008/09 to 15/16). It should be noted that these numbers are small and are lower than for the dietary data as it was not possible to obtain height and weight measurements from all participants.

- 4.6 Annex 2 presents, for the first time, blood indicators of nutritional status based on NDNS years 1 to 8 (2008/09 to 2015/16) for adults aged 65 to 74 years and 75 years and over. Data for the 19 to 64 years age group, based on NDNS years 7 and 8 (2014/15 to 2015/16), are also presented for comparison. Time trend analysis of the 65 years and over age group found little evidence of trends over time in blood analytes (Bates et al 2019). Blood samples were obtained from 55% of the 65 to 74 years age group and 39% of the 75 years and over age group who completed diet diaries in NDNS years 7 and 8. Sample numbers were insufficient to present separate data for adults aged 80 years over.
- 4.7 Urinary iodine concentrations are presented based on NDNS years 7 and 8 (2014/15 to 2015/16). Spot urine samples were obtained from 83% of the 65 to 74 years age group and 73% of the 75 years and over age group who completed diet diaries in years 7 and 8. Salt intakes are based on 24-hour urinary sodium collected in NDNS years 1 to 4 (2008/09 to 2011/12) for adults aged 65 years and over. Twenty-four-hour urine samples for sodium analysis were obtained for 58% of adults aged 65 years and over who completed a diary in years 1 to 4. Salt intakes for adults aged 19 to 64 years from the 2018/19 urinary sodium survey are presented for comparison.
- 4.8 Where differences between groups are highlighted, these are observed differences and have not been statistically tested.

## **Self-reported health and conditions limiting day-to-day activities**

- 4.9 As part of the face-to-face interview, NDNS participants were asked to self-assess their general health and report any long-term health conditions which limit their day-to-day activities. This data is presented in Table 1. Seventy-three percent of older adults aged 65 to 74 years and 57% of those aged 75 years and over reported good or very good health. These percentages are slightly lower than for younger adults (19 to 64 years), 79% of whom reported good or very good health. The proportions of men and women reporting good or very good health were similar in each age group. Five percent of the 65 to 74 years age group and 7% of the 75 years and over age group self-reported their health as bad or very bad.
- 4.10 Fifty-six percent of the 65 to 74 years age group and 69% of the 75 years and over age group reported that they had a physical or mental condition or illness lasting more than 12 months. This compares with 32% of younger adults (19 to 64 years). This apparent discrepancy with the proportions reporting good or very good health may be explained by older adults assessing their health in relation to their expectations for their age.
- 4.11 About half of the 65 to 74 years age group and 57% of the 75 years and over age group who reported a condition said that their mobility was affected and a fifth of

the 65 to 74 years age group and 29% of the 75 years and over age group said that their stamina/breathing was affected. About half of those aged 65 to 74 years and 70% of those aged 75 years and over who reported a health condition said that it affected their ability to carry out day to day activities such as shopping or food preparation.

- 4.12 A substantial proportion of the NDNS sample of older adults reported that their day-to-day activities were limited by one or more long term conditions or illnesses. This suggests that the sample is not atypical of the general population of this age and does not suggest that it is a self-selected group representing the healthiest section of the older adult population. However, it is still possible that the sample could underrepresent people who have specific long-term health conditions which make it more difficult to take part in a survey (such as poor sight and memory problems). Around 20% of those aged 75 years and over reported a condition that limited or prevented them from food preparation, generally due to problems standing or walking, problems using their hands or getting tired easily.

## **Body mass index**

- 4.13 BMI for the NDNS sample (years 7 and 8, 2014/15 to 15/16) and the percentages who were underweight, a healthy weight, or living with overweight or obesity are set out in Annex 2 Table 2. It should be noted that the numbers in each age group are small (64 men and 97 women aged 65 to 74 years and 50 men and 64 women aged 75 years and over). Mean BMI in the 65 to 74 years age group was higher than in the 75 years and over age group in both men (29.0 and 26.8kg/m<sup>2</sup> respectively) and women (28.0 and 26.8kg/m<sup>2</sup> respectively). Mean BMI in the 19 to 64 years age group was 27.6kg/m<sup>2</sup> for men and 27.0kg/m<sup>2</sup> for women, lower than for men and women in the 65 to 74 years age group (29.0 and 28.0kg/m<sup>2</sup>). Mean BMI was higher in men (29.0kg/m<sup>2</sup>) than in women (28.0kg/m<sup>2</sup>) in the 65 to 74 years age group but was the same for men and women aged 75 years and over (26.8kg/m<sup>2</sup>).
- 4.14 In the 65 to 74 years age group 87% of men and 68% of women were living with overweight or obesity; 36% of men and 30% of women were living with obesity, 12% of men and 29% of women were a healthy weight and less than 1% of men and 3% of women were underweight.
- 4.15 In the 75 years and over age group 69% of men and 58% of women were living with overweight or obesity; 23% of men and 23% of women were living with obesity. 24% of men and 39% of women were a healthy weight and 7% of men and 3% of women were underweight.
- 4.16 The percentage of people in the 19 to 64 years age group living with overweight or obesity (69% of men and 57% of women) was lower than in the 65 to 74 years age group but similar to the 75 years and over age group. Conversely, the percentage

in the 19 to 64 years age group who were a healthy weight (36%) was higher than in the 65 to 74 age group (21%) but similar to those aged 75 years and over (33%).

- 4.17 BMI data are also presented for older adults aged 80 years and over, based on NDNS data for 95 men and 158 women collected in years 1 to 8 (2008/09 to 15/16). As data for this age group was collected over a longer time period it cannot be directly compared with data for the 75 years and over age group. Mean BMIs for men and women in the 80 years and over age group and the percentages living with overweight or obesity or who were underweight were similar to those aged 75 years and over.
- 4.18 The BMI profile of the NDNS sample was similar to that of the HSE 2018 sample, in which 79% of men and 70% of women in the 65 to 74 year age group and 75% of men and 67% of women aged 75 years and over were living with overweight or obesity.

## **Energy and macronutrient intakes**

- 4.19 Energy and macronutrient intakes are set out in Annex 2 Table 3. The energy intake data indicate a decline with age in reported energy intake as a percentage of EAR.

### **Energy**

- 4.20 Mean energy intakes in the age group 65 to 74 years were 1940kcal/day (8.16MJ/day) (EAR 2342kcal/day (9.8MJ/day)) and 1483kcal/day (6.24MJ/day) (EAR 1912kcal/day (8.0MJ/day)) for men and women respectively. In the age group 75 years and over, mean energy intakes were 1824kcal/day (7.67MJ/day) (EAR 2294kcal/day (9.6MJ/day)) and 1344kcal/day (5.66MJ/day) (EAR 1840kcal/day (7.7MJ/d)) for men and women respectively. Underreporting of food consumption in NDNS, as in all dietary surveys, is well documented and is likely to be the cause of at least some of the shortfalls between reported energy intakes and the EARs. The most recent NDNS doubly labelled water (DLW) sub-study carried out in 2013/14 to 14/15, found that reported energy intake in adults aged 65 years and over was on average 28% lower than total energy expenditure measured by the DLW technique (Bates et al 2019).
- 4.21 Mean energy intakes were lower in the older age group (75 years and over) than in the 65 to 74 years group, both in absolute terms and in relation to the EAR and were also lower in the 65 to 74 years age group than in the 19 to 64 years age group. For women in the age group 19 to 64 years, reported mean energy intakes were 82% of the EAR; while this reduced to 78% and 74% of the EAR for women aged 65 to 74 years and 75 years and over respectively. For men in the age group 19 to 64 years, reported mean energy intakes were 84% of the EAR, compared with 83% and 80% for men in the two older age groups. The difference between

reported energy intakes (means) and EARs was slightly larger for women than men.

## **Protein**

- 4.22 Mean protein intakes for both sexes and all age groups exceeded the RNI expressed as grams per day (53.3g/day males; 46.5g/day females; for age 50 years and over) and as per kg body weight (0.75g protein per kg body weight). Twenty-seven percent of the 65 to 74 years age group and 33% of the 75 years and over age group had protein intakes below the RNI per kg body weight. Protein intakes are also presented as a percentage of total energy intake.
- 4.23 Mean protein intakes, expressed as grams per day and percentage total energy intake, were lower in the 75 years and over age group than in the 65 to 74 years age group (79.5g/day (16.6% of total energy) for men and 64.0g/day (17.8% of total energy) for women in the 65 to 74 years age group, and 70.9g/day (15.7% of total energy) for men and 56.3g/day (17.1% of total energy) for women aged 75 years and over. Compared with the 19 to 64 years age group (87.4g/day; 17.0% total energy for men; 66.6g/day; 16.7% total energy for women), mean protein intake in adults aged 65 to 74 years was slightly lower as a percentage of energy for men but higher for women.
- 4.24 Mean intakes of protein in grams expressed per kg body weight were slightly higher for men but slightly lower for women in the 75 years and over age group compared to the 65 to 74 years age group (0.93g/kg for both men and women in the 65 to 74 years age group and 0.96 and 0.89g/kg for men and women, respectively, aged 75 years and over). These intakes were lower than for adults aged 19 to 64 years (1.04 and 0.97g/kg for men and women respectively).
- 4.25 Mean protein intakes expressed as a percentage of energy intake were higher for women than for men in the 65 to 74 years and 75 years and over age groups. When expressed per kg body weight, men aged 75 years and over had a higher protein intake than did women. This difference was not seen in the 65 to 74 years age group.

## **Carbohydrate**

- 4.26 Mean total carbohydrate intakes as a percentage of energy were slightly below the recommendation of at least 50% of total energy for all age/sex groups. Mean total carbohydrate intakes as a percentage of energy for the 75 years and over age group were higher than the 65 to 74 years age group for women (46.5% and 45.8% total energy respectively) and were similar in men (45.8% and 46.0% of total energy respectively). Compared with younger adults (19 to 64 years) men aged 65 to 74 had a higher and women slightly lower mean % energy from carbohydrates. In the 75 years and over age group women had a higher mean

percentage energy from carbohydrates than did men but this difference was not seen in the 65 to 74 years age group.

### **Free sugars**

- 4.27 Mean intakes of free sugars in all age/sex groups were at least double the recommended maximum intake of 5% of total dietary energy. Mean intake of free sugars as a percentage of total energy was higher in the 75 years and over age group than the 65 to 74 years age group for men (12.5% and 11.8% energy respectively), but not for women (10.4% energy in each age group). However, the percentage meeting the DRV of no more than 5% energy from free sugars was higher for men but lower for women in the 75 years and over group compared to the 65 to 74 years age group (12% and 11% of men and women in the 75 years and over age group compared with 7% and 20% of men and women in the 65 to 74 years age group). Within the 65 to 74 years and 75 years and over age groups, mean free sugars intakes were higher for men than for women.
- 4.28 Compared with the 19 to 64 years age group, mean free sugars intakes were higher for men but lower for women in the 65 to 74 years age group and the percentage meeting the DRV of no more than 5% energy from free sugars was lower for men and higher for women.

### **Dietary fibre**

- 4.29 The recommended fibre intake (30 grams per day (g/d)) was met by only 9% and 6% of men and women, respectively, in the 65 to 74 years age group and 10% and 2% of men and women, respectively, in the 75 years and over age group. These percentages were similar to younger adults (13% of men and 4% of women aged 19 to 64 years). Mean intakes of fibre were lower in the 75 years and over age group than in the 65 to 74 years age group for both men and women: 19.5 and 17.4g/d for men and women aged 65 to 74 years and 18.3 and 15.1g/d for men and women aged 75 years and over. Mean intakes of fibre in younger adults (19 to 64 years) were slightly higher than the 65 to 74 years age group for men (20.7 g/d and 19.5g/d) but the same for women (17.4g/d). Mean gram fibre intakes were lower for women than for men and a lower proportion of women than men met the recommendation. In the 80 years and over age group, no women met the recommendation.

### **Total fat**

- 4.30 Mean total fat intakes were within the recommended maximum 33% of total energy in men aged 65 to 74 years (31.8%), slightly above in women aged 65 to 74 years (33.4%) and exceeded the maximum in both men and women aged 75 years and over (35.2% and 35.1%, respectively). Mean intakes were higher in the 75 years and over group than in the 65 to 74 years age group. Compared with the 19 to 64

years age group, total fat intakes in the 65 to 74 years age group were slightly lower, particularly for men. In the 65 to 74 years age group mean total fat intake was higher for women than for men. This difference was not seen for older age groups.

### **Saturated fats**

- 4.31 Mean intakes of saturated fat exceeded the recommended maximum of 10% of total energy in both age groups, as for adults aged 19 to 64 years. Mean intakes as a percentage of total energy were higher in the 75 years and over age group than in the 65 to 74 years age group for both men (14.0% and 11.9%, respectively) and women (14.6% and 13.0%, respectively). Compared with the 19 to 64 years age group, mean saturated fat intake in the 65 to 74 years age group was higher for women but similar for men. Mean intakes for women were higher than for men in the 65 to 74 years age group and slightly higher in the older age groups.

### **Cis monounsaturated fats**

- 4.32 In the age group 65 to 74 years the mean intake of cis monounsaturated fatty acids was 11.6% of total energy. For those aged 75 years and over mean intake was very similar at 12.1% of total energy. There were no clear differences between the 65 to 74 years and 75 years and over age groups or between men and women except that mean percentage of energy from cis monounsaturated fat for men aged 75 years and over was lower than for women (11.7 and 12.5% total energy, respectively). Compared with the 19 to 64 years age group, mean intakes of cis monounsaturated fat were slightly lower in the 65 to 74 years age group.

### **Cis polyunsaturated fats**

- 4.33 In the age group 65 to 74 years the mean intake of cis n-3 PUFAs and cis n-6 PUFAs were 1.1% and 4.4% of total energy, respectively. For those aged 75 years and over mean intakes were very similar at 1.0% and 4.5% total energy, respectively. There were no clear differences between the 65 to 74 years and 75 years and over age groups or between men and women.

### **Salt**

- 4.34 Mean salt intakes in older adults exceeded the recommended maximum intake of 6g/day. In the age group 65 years and over, mean salt intake based on 24-hour urinary sodium excretion (2008/09 to 2011/12), was 7.6g/d, slightly lower than more recent data for the 19 to 64 years age group (8.4g/d 2018/19). Thirty-eight percent of older adults and 31% of the 19 to 64 years age group met the recommended maximum intake of  $\leq 6$ g/d. It should be noted that the data for the 19 to 64 years age group were collected 8 years later than data for the 65 years and over age group. Trend analysis of the 19 to 64 years age group showed that there

had been no change in salt intake since 2008/09. Mean salt intakes based on data from the 4-day diary, which largely excludes discretionary salt use, showed a similar pattern but, as expected, were lower than intakes based on urinary sodium. Mean intakes in the 75 years and over age group were similar to those in the 65 to 74 years age group while mean intakes in the 65 to 74 years age group were lower than in the 19 to 64 years age group. Men had higher gram salt intakes than did women in all age groups.

### **Energy and macronutrient intakes in people aged 80 years and over**

- 4.35 Energy and macronutrient intakes are also presented for older adults aged 80 years and over, based on NDNS data for 134 men and 201 women collected over 8 years (2008/09 to 15/16). As data for this age group was collected over a longer time period it cannot be directly compared with data for the 75 years and over age group.
- 4.36 Mean intakes in the 80 years and over age group were generally very similar to those in the 75 years and over age group, although some small differences were seen for protein, free sugars and fibre intakes. Mean protein intakes as a percentage of energy were slightly higher in the 80 years and over age group than for those aged 75 years and over for men but slightly lower for women. Mean protein intakes per kg body weight were similar to the 75 years and over age group for men and slightly higher for women. Mean free sugars intake in the 80 years and over age group was slightly lower for men but higher for women than in the 75 years and over age group. Mean fibre intakes in the 80 years and over age group were similar to those aged 75 years and over for men and slightly higher for women.

### **Summary**

- 4.37 In summary, older adults exceed maximum recommendations for intakes of saturated fat, free sugars and salt and fail to meet recommendations for fibre. Reported energy intakes were below the EAR (although it is likely that this is at least partly attributable to underreporting). Energy intakes were lower in the 65 to 74 years than in the 19 to 64 years age group and were also lower in those aged 75 years and over compared to those aged 65 to 74 years. Over three quarters of the 65 to 74 years age group were living with overweight or obesity, a higher proportion than in the 19 to 64 years age group. Over 60% of the 75 years and over age group were living with overweight or obesity. Two percent of the 65 to 74 years age group and 5% of the 75 years and over age group were underweight.
- 4.38 Mean protein intakes met the RNI of 0.75g protein per kg body weight in all age groups although 27% of the 65 to 74 years age group and 33% of the 75 years and over age group had intakes below the RNI. Mean intakes as a percentage of energy were lower in the 75 years and over age group than in the 65 to 74 years age group, and intakes per kg body weight were lower in older age groups than in



the 19 to 64 years age groups. Saturated fat intakes as a percentage of energy were higher in older adults than in the 19 to 64 years age group and higher in the 75 years and over age group than in those aged 65 to 74 years.

- 4.39 Free sugars intakes were more than double the recommended maximum of 5% total energy and, for men but not women, were higher in the 75 years and over than the 65 to 74 years age group and higher for men in the 65 to 74 years age group than in younger men (19 to 64 years). Fibre intakes were lower in those aged 75 years and over than in the 65 to 74 years age group and men but not women in the 65 to 74 years age group had lower mean fibre intake than the 19 to 64 years age group. Salt intakes were slightly lower in the 65 to 74 years age group than in the 19 to 64 years age group but there was little difference between the 65 to 74 and the 75 years and over age groups.
- 4.40 Women in both age groups had a higher percentage of energy from protein and saturated fat and a lower percentage of energy from free sugars than did men. Fibre and salt intakes were lower in women than in men, and for fibre intakes the differences were more marked in the 75 years and over age group.
- 4.41 Mean intakes in the 80 years and over age group were generally very similar to those in the 75 years and over age group, although some small differences were seen for protein, free sugars and fibre intakes.

## **Micronutrient intakes and status**

- 4.42 Micronutrient intakes from food sources are set out in Annex 2 Table 4, and blood analytes indicating micronutrient status in Annex 2 Table 5.

### **Vitamin A**

- 4.43 Mean intakes of vitamin A from food sources were above the RNI for both sexes in the age groups 65 to 74 years (139%) and 75 years and over (168%). Seven percent of the 65 to 74 years age group and 5% of men and 10% of women aged 75 years and over had intakes below the LRNI. Mean vitamin A intakes were higher in the 75 years and over age group than in the 65 to 74 years age group for men but not for women. Compared with the 19 to 64 years age group, a lower proportion of the 65 to 74 years age group had intakes below the LRNI. Mean intake was higher in men than in women in the 75 years and over age group but not in the younger age group.
- 4.44 Seven percent of men and women in the 65 to 74 years age group and 11% of men and 7% of women in the 75 years and over age group had retinol intakes from food and supplements above 1500µg/day, the upper guidance level for adults.
- 4.45 No participants aged 65 to 74 years or 75 years and over had plasma retinol concentrations below 0.35µmol/l, the threshold indicating severe deficiency. Less

than 1% had concentrations between 0.35 to 0.70µmol/l, the range indicating mild deficiency. This was similar to the 19 to 64 years age group.

### **Thiamin, niacin and vitamin B6**

- 4.46 Mean intakes of thiamin (vitamin B1), niacin (B3) and vitamin B6 for those aged 65 to 74 years and 75 years and over were substantially above the RNIs (180% and 176%, respectively for thiamin; 237% and 209% for niacin and 188% and 174% for vitamin B6). Six percent of women aged 75 years and over had thiamin intakes below the LRNI compared with 0% of the 65 to 74 years age group; no more than 1% any age/sex group had intakes of niacin below the LRNI and the figure was less than 0.5% for vitamin B6. Compared with the 19 to 64 years age group, intakes of thiamin, niacin and vitamin B6 in older adults were similar and there were few differences between men and women.
- 4.47 Vitamin B6 status is assessed by plasma pyridoxal-5-phosphate (PLP). NDNS data is presented in Annex 2, Table 5. However, there is no accepted threshold for PLP concentration indicating low B6 status in the UK. There is no NDNS data available on blood indicators of status for thiamin or niacin.

### **Riboflavin**

- 4.48 Mean intakes of riboflavin (vitamin B2) from food sources were above the RNI for both sexes in the age groups 65 to 74 years (137%) and 75 years and over (130%). A higher percentage of women aged 75 years and over had riboflavin intakes below the LRNI (13%) than did women aged 65 to 74 years (7%), while in younger women (19 to 64 years), 14% were below the LRNI. In all adult age groups, a higher proportion of women than men had intakes below the LRNI.
- 4.49 The assessment of riboflavin status using the erythrocyte glutathione reductase activation coefficient (EGRAC) showed the percentage of the population with an EGRAC above 1.3 (indicating low status) to be lower for those aged 65 to 74 years (41% men and 45% women) and 75 years and over (39% men and 36% women) than in younger adults (19 to 64 years 47% men, 61% women). There is uncertainty about the interpretation of the EGRAC thresholds for riboflavin status.

### **Vitamin B12**

- 4.50 Mean intakes of vitamin B12 were above the RNI in both age groups (368% and 367%, respectively) and the percentage below the LRNI was 2% and 3% of men in the 65 to 74 years and 75 years and over age groups, respectively, and less than 0.5% of women. There was little difference in intakes compared to the RNI or LRNI by age group or between men and women.
- 4.51 Mean serum vitamin B12 concentrations for those aged 65 to 74 years and 75 years and over were 280 and 261 pmol/L respectively, with 5% and 8%

respectively, having serum concentrations below 150pmol/L, the lower threshold of the normal range. In the assessment of vitamin B12 status through holotranscobalamin, the mean concentration for those aged 65 to 74 years and 75 years and over were 87 and 77 pmol/L, with 3% and 5% of each age group having holotranscobalamin concentrations below the 32 pmol/L suggested threshold for biochemical B12 deficiency. These concentrations were slightly higher than in the 19 to 64 years age group. The NDNS sample may have included individuals being treated for vitamin B12 deficiency by supplements or injections. Such individuals would not have been excluded from the results.

## **Folate**

- 4.52 Mean folate intakes met the RNI in men and in women aged 65 to 74 years and almost met the RNI in women aged 75 years and over. Men and women in the 65 to 74 years age group had a mean intake of 139% (men) and 109% (women) of the RNI, while 0% (men) and 3% (women) had intakes below the LRNI. The equivalent figures for the age group 75 years and over were 119% (men) and 97% (women) of the RNI, while 3% (men) and 8% (women) had intakes below the LRNI. The 75 years and over age group had lower folate intakes in relation to the DRVs than did the 65 to 74 years age group but there was little difference between the 65 to 74 years and the 19 to 64 years age groups. Women, particularly in the 75 years and over group, tended to have lower folate intakes in relation to the RNI and LRNI than did men.
- 4.53 Red blood cell folate concentrations in older adults were generally similar to those for younger adults (19 to 64 years) and the percentages below thresholds for serum folate were lower in older adults than in the 19 to 64 years age group. Red blood cell folate concentrations were below the clinical threshold for risk of anaemia (305nmol/L) in 6% of the 65 to 74 years age group and 6% of the 75 years and over age group. For serum folate 4% of the 65 to 74 years age group and 3% of the 75 years and over age group were below the clinical threshold for folate deficiency of 7nmol/L, while 23% of the 65 to 74 years age group, and 25% of the 75 years and over group were below the 13nmol/L clinical threshold for possible deficiency. The proportions of men and women below the thresholds were similar.

## **Vitamin C**

- 4.54 Mean vitamin C intakes were 204% of the RNI in the 65 to 74 years age group and 175% of the RNI in the 75 years and over age group. Zero percent of the 65 to 74 years age group and 3% of the 75 years and over age group had vitamin C intakes below the LRNI. Intakes in the 19 to 64 years age group were similar to the 65 to 74 years age group.

## **Vitamin D**

- 4.55 Mean vitamin D intakes, including and excluding supplements, were below the RNI in all age/sex groups. Mean intakes from food sources were lower in the 75 years and over than in the 65 to 74 years age groups for both men and women (35% and 28% of the RNI for those aged 65 to 74 years, and 75 years and over, respectively), and were higher in men than in women. Thirty-one percent of adults aged 65 to 74 years and 28% of adults aged 75 years and over consumed a dietary supplement containing vitamin D during the 4-day diary period. Mean intakes including supplements were also lower in the 75 years and over group than in the 65 to 74 years group (53% and 60% of the RNI, respectively) but were higher in women than in men in both age groups. Compared with younger adults (19 to 64 years), mean intakes in the 65 to 74 years age group were higher, both including and excluding supplements.
- 4.56 Mean and median 25(OH)D concentrations were 47.7nmol/l for the 65 to 74 years age group and 43.3nmol/l in the 75 years and over age group, above the threshold indicating low status (25nmol/l) in both age/sex groups. Fifteen percent of those aged 65 to 74 years and 27% of those aged 75 years and over had 25(OH)D concentrations below 25 nmol/L, indicating low status. The proportions of younger adults with low vitamin D status were similar to the 65 to 74 years age group. A higher proportion of women (29%) than men (24%) in the 75 years and over age group had low vitamin D status but this difference was not seen in the 65 to 74 years age group.

## **Vitamin E**

- 4.57 The median vitamin E intakes in those aged 65 to 74 years was 8.2mg/day and for those aged 75 years and over was 7.6mg/day, meeting the safe intake set by COMA (4mg/day for men and 3mg/day for women).

## **Iron**

- 4.58 Mean iron intakes met the RNI in the 65 to 74 years age group (126% (men) and 102% (women)) and in men aged 75 years and over (117%) but mean intake in women aged 75 years and over was below the RNI (89%). Mean intakes for those aged 75 years and over were lower than in those aged 65 to 74 years and were lower in women than in men. Intakes were below the LRNI in a higher percentage of women aged 75 years and over (12%) than aged 65 to 74 years (8%). Women aged 65 to 74 years had a higher iron intake as a percentage of the RNI than younger women (19 to 64 years) (102% and 76% of RNI, respectively) and a lower percentage below the LRNI (8% and 27%, respectively).
- 4.59 Four percent of the 65 to 74 years age group and 5% of those aged 75 years and over had plasma ferritin concentrations below the threshold for low iron status. Two percent of men and 1% of women aged 65 to 74 years, and 1% of men and 5% of

women aged 75 years and over were below the threshold for both haemoglobin and plasma ferritin.

### **Calcium**

- 4.60 Mean calcium intakes met the RNI in the 65 to 74 years age group (127% (men) and 109% (women) of the RNI) and in men aged 75 years and over (126%) and were close to the RNI in women aged 75 years and over (99%). Intakes were below the LRNI in 11% of women aged 65 to 74 years and 10% of women aged 75 years and over. Mean intakes were slightly lower for women in the 75 years and over age group than in women aged 65 to 74 years. Intakes in the 19 to 64 years age group were similar to those in the 65 to 74 years age group. Calcium intakes in women in relation to the DRVs were lower than in men in both older age groups. There is no agreed biomarker for calcium.

### **Magnesium**

- 4.61 For magnesium, mean intake was close to the RNI in men aged 65 to 74 years (95%) but below the RNI in women aged 65 to 74 years (85%), and in both men and women in the 75 years and over age group (82% and 76% of RNI, respectively). Mean magnesium intakes were lower in those aged 75 years and over than in those aged 65 to 74 years. A higher proportion of the 75 years and over group had intakes below the LRNI (22% of men and 27% of women) than the 65 to 74 years age group (6% of men and 11% of women). Compared with the 19 to 64 years age group, intakes in the 65 to 74 years age groups were similar. Women had lower intakes of magnesium than men in relation to the DRVs in all older age groups. There is no agreed biomarker for magnesium.

### **Potassium**

- 4.62 Mean potassium intakes were below the RNI in men and women in both older age groups. Mean intakes were lower in the 75 years and over age group (81% of the RNI (men) and 64% (women)) than in the 65 to 74 years age group (91% of the RNI (men) and 77% (women)). Intakes were below the LRNI in 16% (men) and 34% (women) aged 75 years and over compared with 4% of men and 22% of women aged 65 to 74 years. Compared with the 19 to 64 years age group, intakes in the 65 to 74 years age group were similar. Women had lower intakes of potassium than men in relation to the DRVs in all older age groups. There is no agreed biomarker for potassium.

### **Iodine**

- 4.63 Mean intakes of iodine met the RNI in men in both age groups (131% and 136% of the RNI, respectively) and in women aged 65 to 74 years (112%) and was close to the RNI for women aged 75 years and over (96%). Mean intakes were lower for

women in the 75 years and over age group compared to the 65 to 74 years age group but not for men. Intakes were below the LRNI in 6% of women aged 65 to 74 years and 9% of women aged 75 years and over. Compared with the 19 to 64 years age group, iodine intakes in the 65 to 74 years age group was slightly higher and lower proportions were below the LRNI. Women had slightly lower intakes of iodine than men in relation to the DRVs in all older age groups.

- 4.64 In the age groups 65 to 74 years and 75 years and over, urinary iodine concentrations met the World Health Organization (WHO) criteria for adequate iodine intake (median concentrations between 100 and 199 µg/l and less than 20% of samples were below the threshold of 50 µg/L) indicating iodine sufficiency in the population.

### **Selenium**

- 4.65 For selenium, mean intakes were below the RNI for men and women in both age groups. Those aged 75 years and over (60% of the RNI (men) and 58% (women)) had slightly lower intakes than in the 65 to 74 years age group (72% of the RNI (men) and 68% (women)). Intakes were below the LRNI in 34% of men and 57% of women aged 65 to 74 years, and 39% of men and 76% of women aged 75 years and over. Selenium intakes in the 65 to 74 years age group were slightly lower than in the 19 to 64 years age group and intakes in women were lower than in men. Plasma selenium is measured in NDNS but there is no agreed threshold for low status.

### **Zinc**

- 4.66 Mean zinc intakes were close to meeting or met the RNI for men and women in both older age groups. Mean intakes for those aged 75 years and over (91% of the RNI (men) and 94% (women)) were slightly lower than in the 65 to 74 years age group (95% of the RNI (men) and 108% (women)). For those aged 65 to 74 years, intakes were below the LRNI in 5% of men and 3% of women, compared with 8% of men and 12% of women in those aged 75 years and over. There was little difference between the 65 to 74 years and 19 to 64 years age group or between men and women. Plasma zinc is measured in NDNS but there is no agreed threshold for low status.

### **Supplements**

- 4.67 Inclusion of dietary supplements increased mean intakes of some micronutrients, for example vitamin D, riboflavin and folate for men and women, iron and calcium for women, but had little or no impact on the percentages below the LRNI.

## **Micronutrient intakes in people aged 80 years and over**

- 4.68 Micronutrient intakes are also presented for older adults aged 80 years and over, based on NDNS data for 134 men and 201 women collected over 8 years (2008/09 to 15/16). As data for this age group were collected over a longer time period it cannot be directly compared with data for the 75 years and over age group. Mean intakes in the 80 years and over age group were generally very similar to those in the 75 years and over age group, although some differences were seen for vitamin A, vitamin D and iodine intakes. Mean vitamin A intakes in the 80 years and over age group were higher than in the 75 years and over age group for both men and women. Mean vitamin D intakes including supplements in the 80 years and over age group were similar to those in the 75 years and over age group in men but lower in women. Mean iodine intakes in women aged 80 years and over were slightly higher than in the 75 years and over age group and met the RNI.

### **Summary**

- 4.69 In summary, mean intakes of all vitamins were above RNIs in all age/sex groups for older adults except vitamin D (28 to 35% of RNI in all age groups), and folate (97% of RNI for women aged 75 years and over). However, there was evidence of low intakes (below LRNI) for vitamin A, riboflavin and folate in women aged 75 years and over (10% below the LRNI for vitamin A, 13% for riboflavin and 8% for folate).
- 4.70 There was evidence of poor status for vitamin D and folate and to a lesser extent for vitamin B12 and iron. Use of vitamin D supplements was low; less than a third of each age group took a vitamin D supplement during the survey period. Fifteen percent of those aged 65 to 74 years and 27% of those aged 75 years and over had 25(OH)D concentrations below 25 nmol/L, indicating low status. Red blood cell folate concentrations were below the clinical threshold for risk of anaemia (305nmol/L) in 6% of each age group; for serum folate the proportions below the threshold for deficiency were slightly lower but about a quarter of each age group were below the clinical threshold for possible deficiency.
- 4.71 Mean mineral intakes below the RNI were seen for magnesium, potassium and selenium for men and women in both age groups. Mean intakes for women aged 75 years and over were below the RNI for iron and just below the RNI for calcium. Both men and women aged 75 years and over had mean intakes just below the RNI for zinc (and men 65 to 74 years) and women aged 75 years and over had mean intakes just below the RNI for iodine. Smaller percentages of men, mainly in the 75 years and over age group and women in both age groups had intakes below the LRNI for iron, calcium, iodine and zinc.
- 4.72 Overall the 75 years and over age group tend to have lower micronutrient intakes as a percentage of the RNI and a higher percentage below the LRNI than did the 65 to 74 years age group. Compared with the 19 to 64 years age group

micronutrient intakes in the 65 to 74 years age group were similar. Women, and especially women in the 75 years and over age group, tended to have lower intakes of micronutrients compared to the DRVs than did men. There was evidence of poor status for vitamin D, and folate and to a lesser extent for iron and vitamin B12. With the exception of vitamin D, for which those aged 75 years and over showed poorer status than the younger age groups, the proportions with poor status were similar to the 19 to 64 years age group.

- 4.73 Mean intakes in the 80 years and over age group were generally similar to those in the 75 years and over age group, although some small differences were seen for vitamin A, vitamin D and iodine intakes. There was little evidence of lower intakes in the 80 years and over age group based on the available data.

## **Consumption of selected foods**

- 4.74 Consumption data for selected foods for which there is a dietary recommendation are presented in Annex 2 Table 6. Mean consumption of fruit and vegetables was below the 5-A-Day recommendation for men and women in both age groups, at 4.3 portions per day for both men and women aged 65 to 74 years and 3.8 and 3.2 portions per day for men and women, respectively, aged 75 years and over. Thirty-two percent of the 65 to 74 years age group and 19% of the 75 years and over age group achieved 5-A-Day. Fruit and vegetable consumption in the 65 to 74 years age group was very similar to that for younger adults (19 to 64 years) but consumption in the 75 years and over age group was lower than in the 65 to 74 years age group.
- 4.75 Mean consumption of red and processed meat exceeded the maximum recommendation of 70 g/day for men aged 65 to 74 years (73 g/day) but mean consumption for men aged 75 years and over and women in both age groups were within the recommendation. Mean consumption in the 65 to 74 years age group was very similar to younger adults (19 to 64 years).
- 4.76 Oily fish consumption was below the recommended one portion a week (equivalent to about 20g per day) in men and women in both age groups. Mean consumption in the 65 to 74 years age group was 15g/day (equivalent to 105g/week – less than a typical portion of around 140g) compared to 8g/day in the 19 to 64 years age group. Mean consumption in the 75 years and over age group was 10g/day.
- 4.77 Consumption data are also presented for older adults aged 80 years and over, based on NDNS data for 134 men and 201 women collected over 8 years (2008/09 to 15/16). As data for this age group was collected over a longer time period it cannot be directly compared with data for the 75 years and over age group. Mean consumption of fruit and vegetables, and red and processed meat was slightly higher in the 80 years and over age group than in the 75 years and over age group.



## **Energy and nutrient intakes by oral health status**

- 4.78 Annex 2, tables 7, 8 and 9 present energy, macronutrient and micronutrient intakes by measures of oral health status: self-reported presence of own (natural) teeth, use of dentures and reported difficulty chewing, based on NDNS data for years 1 to 8 (2008/09 to 2015/16).
- 4.79 Nineteen percent of the 65 to 74 years age group (59 men and 90 women) and 37% of those aged 75 and over (80 men and 146 women) reported having none of their own teeth (edentulous). Energy, protein, fibre and micronutrient intakes were generally slightly lower in the edentulous group while intakes of free sugars, fat and saturated fat were slightly higher in some age groups. These findings were comparable with those from other surveys (Finch et al, 1998; Kiesswetter et al, 2018) . The percentages below the LRNI for some vitamins and minerals were also slightly higher in the edentulous group. For example, for riboflavin, 16% of men aged 75 years and over with none of their own teeth had intakes below the LRNI compared with 1% of men with some or all of their own teeth. It should be noted that the sample sizes for the edentulous group were small (Annex 2, Table 7a and 7b).
- 4.80 Just under half (47%) of those aged 65 to 74 years (139 men and 234 women) and 52% of the 75 years and over age group (254 men and 246 women) reported that they used a denture. However, no information was collected on the type of denture used. There were few observed differences between the nutrient intakes of older adults who used a denture and those who did not, although mean fibre intakes were consistently lower and mean free sugars intakes higher in the denture using group (Annex 2, Table 8a and 8b).
- 4.81 Nineteen percent of those aged 65 to 74 years (49 men and 81 women) and 28% of those aged 75 years and over (59 men and 72 women) reported that they had a little difficulty chewing. The numbers reporting that they had a 'fair amount or a great amount' of difficulty chewing were too small for analysis (27 in the 65 to 74 years age group, and 43 in the 75 years and over age group). There were no observed differences in nutrient intakes between those who reported having a little difficulty chewing and those who did not (Annex 2, Table 9a and 9b).

## **Trends in nutrient intakes over time and with income**

- 4.82 The NDNS year 1 to 9 report included a time trend analysis and an income trend analysis for nutrient intakes, consumption of selected foods and blood status markers in men and women aged 65 years and over. The time trends in this age group are generally similar to the time trends observed in other age groups. There was a significant reduction in folate intake and red blood cell folate concentrations over time in the 65 years and over age group, in common with trends seen in all age groups.

- 4.83 Intakes of some nutrients (particularly micronutrients) and blood status markers increased with income in those aged 65 years and over. It should be noted that income may not be the best measure of socioeconomic status in older adults (Grundy & Holt, 2001).

## **Dietary intakes and nutritional status in people aged 85 and over**

- 4.84 There is no upper age limit for participation in NDNS. The survey includes people aged 85 years and over, although the numbers of participants in this age range are very low and the likelihood of individuals being unable to take part due to cognitive, sight, mobility or other health problems is higher than in younger age groups.
- 4.85 This statement presents energy and nutrient intakes and food consumption for older adults aged 80 years and over for the first time, based on data from NDNS years 1 to 8 (2008/09 to 2015/16). Numbers were insufficient to present separate data for adults aged over 85 years. However, a comparison was made between nutrient intakes of people aged 85 years and over in NDNS (based on years 1 to 8 data 2008/09 to 2015/16) and people aged 85 years and over in the Newcastle 85+ study, based on data collected from 793 participants in 2006/07 (Mendonca et al, 2016a; Mendonca et al, 2016b). No statistical comparison was undertaken, and it should be noted that there were only 50 men and 97 women in this age range in NDNS.
- 4.86 Table 10 (Annex 2) shows median intakes from NDNS (years 1 to 8) compared with median intakes from the Newcastle 85+ study. Median intakes of energy and macronutrients were lower in the NDNS 85 years and over age group than in the Newcastle 85+ study, particularly for men. For example, median energy intake for men was 1628kcal/day in NDNS and 1848kcal/day for the Newcastle 85+ study. The median percentage of energy from fat was higher for men but lower for women in NDNS than in the Newcastle 85+ study. The median percentage of energy from protein was similar for men but higher for women in NDNS compared with the Newcastle 85+ study. Reported intakes of some vitamins were higher in NDNS than the Newcastle 85+ study, notably vitamin B12 and vitamin D. The dietary assessment method used in the Newcastle 85+ study was the multiple pass 24-hour recall on two non-consecutive days, while the NDNS used a diary over 4 consecutive days. It is possible that these differences may be due to differences between surveys in the data collection methodologies and sample size.
- 4.87 Granic et al (2018) summarised recent epidemiological evidence from several studies of ageing that have investigated diet and nutritional status in very old adults (age not consistently defined across studies). They report the latest findings from the UK Newcastle 85+ Study, and the Life and Living in Advanced Age: A Cohort

Study in New Zealand (LiLACS NZ), the two on-going specialised cohorts involving the very old, with emphasis on the diet–physical functioning relationship.

- 4.88 Granic et al (2018) conclude that ‘dietary assessment in very old adults is challenging because of the higher prevalence of cognitive and physical impairment and reliance on proxy reporting in this age group’. However, the Newcastle 85+ Study and the LiLACS NZ Study have successfully collected nutritional data on representative population samples. The authors conclude from these studies that very old adults have high risks of macronutrient malnutrition (such as low protein intake) and micronutrient deficiencies (such as vitamin D, calcium and magnesium). Carbohydrates were the main source of energy, and cereals/cereal products and bread were the main contributors to intakes of energy and most macronutrients, folate and iron. Meats and milk were the major dietary sources of protein and also of vitamin B12.
- 4.89 In summary the limited sample numbers available from NDNS and concerns about the representativeness of the sample mean that it is difficult to draw firm conclusions about the nutrient intake and status of adults over 85 years in the UK.

## Overall Summary

- 4.90 Overall, the NDNS data on diet, nutrient intakes and blood analytes for people aged 65 to 74 years and 75 years and over in the UK indicate that older adults in the UK exceed maximum recommendations for saturated fat, free sugars and salt and fail to meet recommendations for fruit and vegetables, fibre and oily fish. There is also evidence of low intakes of some micronutrients, particularly in the 75 years and over age group and in women. These findings are similar to those in younger adults (19 to 64 years) for both macro and micronutrients.
- 4.91 Mean energy intakes were lower in the 75 years and over than in the 65 to 74 years age group and lower in the 65 to 74 years than in the 19 to 64 year age group. Mean intakes were below EARs in all age/sex groups; the shortfall is likely to be at least partly due to underreporting. A high proportion of older adults were living with overweight or obesity: over three quarters of the 65 to 74 years age group and over 60% of the 75 years and over age group. Mean protein intakes met the RNI for men and women in both age groups though were lower in the 65 to 74 years age group than in younger adults and lowest in the 75 years and over age group. Saturated fat intakes were higher in older adults than in the 19 to 64 years age group and were the highest in the 75 years and over age group for both men and women. Mean intakes of free sugars were more than double the maximum recommendation of 5% energy for both the 19 to 64 years and 75 years and over age groups. For men, but not women, mean free sugars intake was the highest in the 75 years and over age group. Fruit and vegetable consumption and fibre intakes were lower in those aged 75 years and over than in the 65 to 74 years age group but intakes in the 65 to 74 years and 19 to 64 years age groups were similar.

- 4.92 There is some evidence of low micronutrient intakes, particularly in women and older age groups but these were also seen in younger adults (19 to 64 years). Low intakes of vitamin D were common to all adult age groups. Overall the 75 years and over age group tended to have lower micronutrient intakes as a percentage of the RNI and a higher percentage below the LRNI than did the 65 to 74 years age group, particularly for women. Intakes below the LRNI for riboflavin, folate, iron, calcium and zinc were seen in women aged 75 years and over but also in women aged 19 to 64 years. Compared with the 19 to 64 years age group, micronutrient intakes in the 65 to 74 years age group were similar or slightly higher. There was some evidence of low micronutrient status for vitamin D and folate and to a lesser extent for iron and vitamin B12. This was also common to the 19 to 64 years age group. For vitamin D the proportions with low status were highest in the 75 years and over age group but for iron and folate there was little difference between the age groups.
- 4.93 In some respects, the diets of the 65 to 74 years age group were similar to and, for some foods and nutrients, better than the 19 to 64 years age group, particularly for women. For the 75 years and over age group there was evidence of a decline in energy, protein and micronutrient intakes particularly in women, although protein intakes remained above the RNI and micronutrient intakes were similar to women in the 19 to 64 years age group.
- 4.94 There were few differences between intakes in the 80 years and over age group and the 75 years and over age group and no evidence of poorer diets in the 80 years and over age group. However, data on this age group was available only for energy and nutrient intakes and consumption of selected foods and was collected over a longer time period than was the data for younger age groups.
- 4.95 Although the NDNS sample is designed to be representative of the population in each age group, it is possible that the sample may underrepresent those who have long term health conditions which make it more difficult to take part in a survey.

## 5 Methods

### Eligibility criteria and literature search

- 5.1 PHE's Knowledge and Library Services team conducted an online database search for systematic reviews and meta-analyses examining the relationship between nutrition and healthy ageing in older adults.
- 5.2 In keeping with SACN's Framework for the Evaluation of Evidence (SACN, 2020b), this position statement is based primarily on evidence provided by systematic reviews and meta-analyses of RCTs and PCS. While systematic reviews considering case-control studies or cross-sectional studies alongside RCTs and PCS were not excluded from this statement, the results are given less priority compared with those considering only RCTs and/or PCS.
- 5.3 Additional eligibility criteria included English language publications, published in peer-reviewed scientific or medical journals between 1990 and 9 November 2018. No geographical restriction was applied. The search started from 1990 to reflect publication of the COMA dietary reference values (DRVs) report in 1991 (Department of Health, 1991) and the COMA report on the Nutrition of Elderly People (Department of Health, 1992).
- 5.4 Additional inclusion criteria were:
  - studies in older adults aged 65 years and over (or mean age of  $\geq 60$  years) including relevant sub-group analyses
  - studies in community dwelling populations
  - studies which focused on largely healthy groups of adults. However, studies in mixed populations including adults living with common health conditions such as obesity, type 2 diabetes, CVD, hypertension or osteoporosis were also included.
- 5.5 There was particular interest in age-related changes in cognitive, physical and metabolic function in relation to the following outcomes:
  - mortality
  - musculoskeletal health (including bone and joint health and sarcopenia)
  - cardiovascular health (including circulation)
  - cancer
  - immune function
  - oral health
  - weight change
  - quality of life
  - eye health
  - skin and wound healing.

5.6 The following were excluded:

- publications which considered mostly evidence from studies conducted in hospitals, residential care or nursing homes
- publications which solely focused on populations with pre-existing conditions and/or on the treatment or management of conditions, as, in general, SACN provides advice for the general population and does not make recommendations related to clinical management
- evidence where SACN has already published relevant conclusions and/or recommendations for these age groups. In particular, additional evidence was not sought on cognitive impairment and dementias (SACN position statement published in 2018). Evidence on vitamin D was only considered if published after the search periods covered in the 2016 SACN report on Vitamin D and Health. The relevant conclusions and/or recommendations from these publications have been included in this statement as appropriate.
- systematic reviews and meta-analyses including only case-control or cross-sectional studies; non-systematic reviews; published abstracts; grey literature such as dissertations, foreign language publications; conference proceedings, magazine articles, books/book chapters, opinion pieces, information from websites, reports and other non-peer reviewed articles.

5.7 The bibliographic databases Embase, MEDLINE, Cochrane Library, and Food Science Technology Abstracts were searched using the search terms outlined in Annex 3. SACN also invited interested parties to highlight relevant evidence which satisfied the inclusion criteria for the report. A call for evidence, was published on the SACN website, which was open from 9 January 2019 to 5 February 2019. The reference lists of all included publications (identified through the online database search or highlighted by interested parties, up to February 2019) were hand-searched for additional publications meeting the inclusion criteria. Reference lists of relevant reviews by international organisations were also considered.

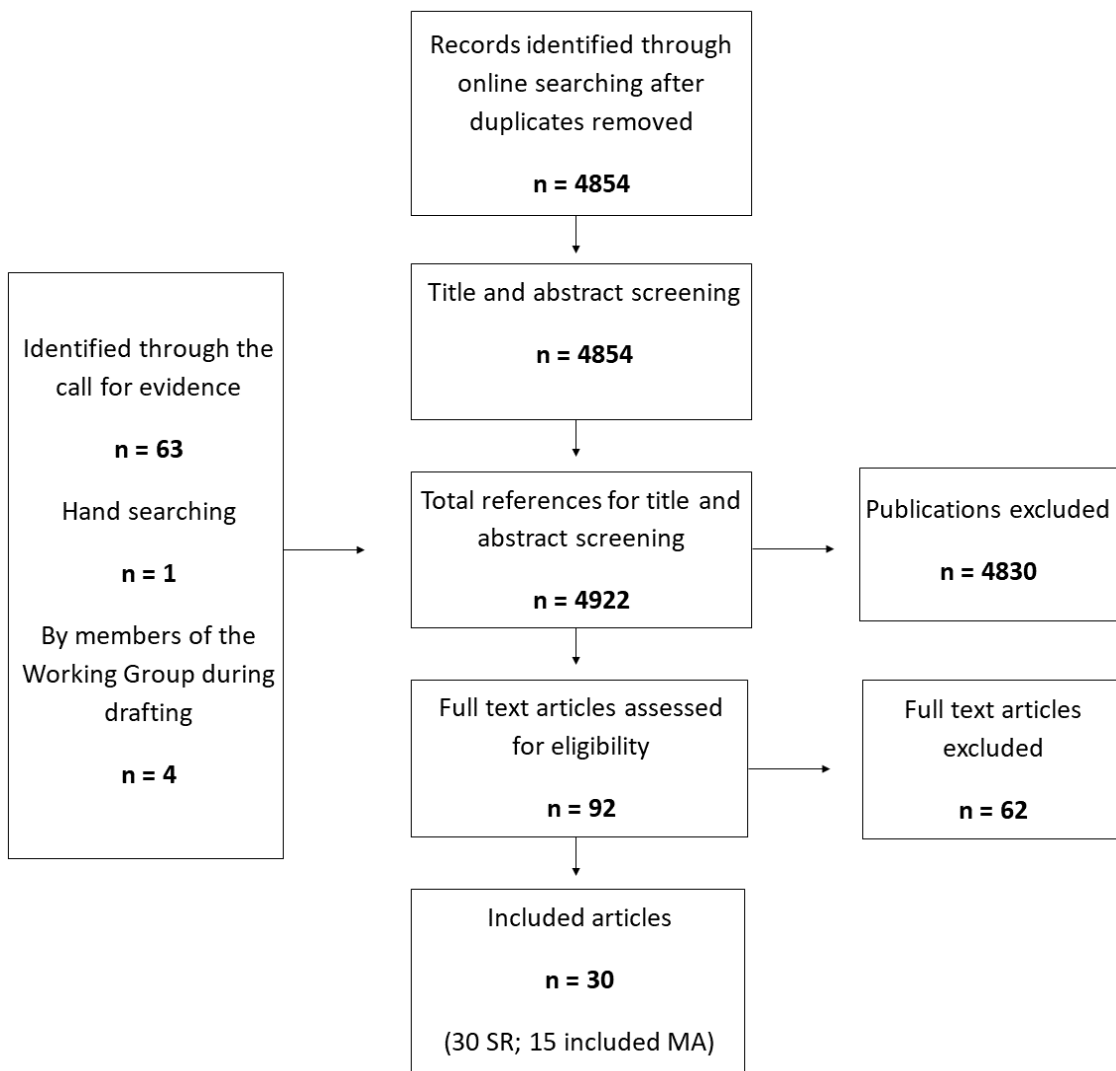
## **Selection of studies**

5.8 After removing duplicates, the titles and abstracts of the identified publications were screened for eligibility. Of the identified publications, 10% were screened by 2 reviewers, with 95% agreement. Publications were rejected on initial screen if the reviewers could determine from the title and abstract that they did not meet the inclusion criteria. Differences between reviewers were resolved by discussion with a third reviewer if necessary.

5.9 The full texts of potentially eligible publications were obtained and 100% of the publications were screened by 2 reviewers, with an agreement of 95%. Differences between reviewers were resolved by discussion with a third reviewer if necessary.

Where uncertainty remained, advice from the Older Adults Working Group was sought on which publications should be included.

5.10 After the duplicates were removed, 4854 references were identified through the online database search. An additional 68 references were identified: through the call for evidence (63), through hand-searching (1) and by members of the Older Adults Working Group (4). A total of 4922 references were screened for eligibility based on their title and abstract, resulting in the exclusion of 4830 references. The remaining 92 references were screened by full text, resulting in the exclusion of a further 62 references. The 30 references that passed the full-text screen were deemed eligible for inclusion as evidence in this position statement. Of the 30 eligible systematic reviews, 15 included meta-analysis. A full list of included studies by outcome is in Annex 4.1 and a list of publications excluded after consideration of the full text of the article is in Annex 4.2.



**Figure 2.1. Flow diagram showing the number of publications assessed for eligibility and included in the report.**

- 5.11 An additional web search was undertaken on PubMed to identify reviews that provide evidence on older adults in black, Asian and minority ethnic groups. The only 2 eligible publications that were identified had already been identified through the literature search. Both of these systematic reviews considered ethnicity as a factor in their analysis (Feng et al, 2017; Mello et al, 2014).

## **Data extraction and reporting of study results**

- 5.12 Relevant data from each of the included systematic reviews and meta-analyses were extracted into tables (see Annex 4.3). Extracted data included the name of the first author, year of publication, research question, selection criteria, statistical analysis, assessment of study quality, total number of participants, mean duration of study, demographics and results. Data on location, dietary assessment methods used and the study design of the primary evidence, as reported in the systematic reviews and meta-analyses, were also extracted into the table.
- 5.13 Where available, all relevant statistical findings (for example, effect sizes, confidence intervals, significance level and heterogeneity) for the included systematic reviews were extracted (Annex 4.3). If the systematic review did not include meta-analysis, primary study findings were reported by outcome. In chapter 6 (Results), statistical findings were only reported for meta-analyses, PCS and RCTs if they were statistically significant. If primary studies were of a cross-sectional or case-control design, chapter 6 (Results) only reported whether the findings were statistically significant without stating any values. If it was unclear if a cohort was prospective in nature, it has been reported as a cohort.
- 5.14 To help identify the individual primary studies included in each of the eligible systematic reviews and meta-analyses, the first author and year of publication of the primary studies were tabulated (see Annex 4.4).
- 5.15 Vitamin D intakes are expressed in International Units (IU) or in micrograms ( $\mu\text{g}$ ). In this position statement the unit of measurement used to express intake is  $\mu\text{g}$ ; the corresponding amount in IUs is also provided.

## **Methods for reviewing evidence**

- 5.16 SACN considered systematic reviews and meta-analyses that met the inclusion criteria. The statement was initially drafted by the secretariat. This provided the basis for the working group's discussions, with the final text, conclusions and research recommendations discussed and agreed with the SACN main committee.



## Evaluation of the quality of identified evidence

- 5.17 The quality of included systematic reviews and meta-analyses was assessed by:
- the SACN Framework for the Evaluation of Evidence (SACN, 2020b)
  - the AMSTAR 2 tool.

The criteria considered were:

### Systematic reviews and meta-analyses

- scope and aims
- search dates (publication dates of studies included in the reviews or meta-analyses)
- inclusion and exclusion criteria
- number of primary studies and total number of participants and number of events
- conduct and reporting of pre-specified outcomes consistent with registered protocol.

### Primary studies considered within systematic reviews and meta-analyses

- whether the primary studies were RCTs, PCS, case-control studies or cross-sectional studies
- exposure/intervention duration and follow-up
- components of the diet that were considered or manipulated in the case of trials
- populations considered and relevant characteristics (for example, presence of disease, smoking habits, physical activity levels, changes in relevant risk factors)
- quality of the dietary assessment methods and outcome assessment methods.

### Interpretation of results and their analysis

- appropriateness of statistical methods used
- whether and which confounding factors were taken into account (where relevant)
- consistency of the effect/association
- heterogeneity – an  $I^2$  statistic of 0-25% was considered to represent low heterogeneity, 26% to 75% was considered to represent medium heterogeneity and >75% was considered to represent high heterogeneity. While a high  $I^2$  statistic reflects uncertainty regarding the value of the pooled estimate, it does not necessarily reflect uncertainty regarding the direction of the effect/association (which may be consistent across studies).

- direction and size of effect, and statistical significance
- results of sub-group and sensitivity analyses.

5.18 In keeping with the SACN Framework for the Evaluation of Evidence (SACN, 2020b), the word '*effect*' was used to describe the evidence from RCTs and the word '*association*' was used when referring to evidence from PCS. An effect/association was deemed to be statistically significant using the  $p < 0.05$  criterion.

### **AMSTAR assessment**

- 5.19 For each eligible systematic review, the methodological quality was assessed using AMSTAR 2, a Measurement Tool to Assess Systematic Reviews (Shea et al, 2017). Each AMSTAR 2 assessment consists of 16 items. Of the 30 publications assessed with AMSTAR 2, 4 publications were assessed by 2 reviewers in duplicate to check the level of agreement and reconcile any differences.
- 5.20 The AMSTAR 2 tool has been used to assess the quality of each systematic review included in this position statement and to help aid discussion but not to draw conclusions. A summary of the AMSTAR 2 assessment is in Annex 4.5.

### **Grading of evidence**

- 5.21 SACN did not grade the evidence considered, as a full risk assessment was not undertaken.

### **Limitations of the evidence**

- 5.22 A number of limitations were identified in the evidence included in this position statement and also in the older adults evidence base in general. These are briefly summarised below.

#### **Specific to this position statement**

- Some systematic reviews and/or meta-analyses included small numbers of RCTs and/ or PCS, which were often of short duration and included a small number of participants.
- The definition of healthy ageing varied between publications. Some reviews excluded primary studies that considered participants with existing chronic conditions while others included them.
- The age range of participants varied between studies, making the comparison of results difficult. For example, some studies included adults older than 50 years, while other included adults from age 60, or 65 years.

- Some of the systematic reviews and/or meta-analyses included a number of studies conducted in hospital settings or institutions.
- Dietary assessment methods differed between studies making comparisons difficult.
- Some of the systematic reviews included case-control and cross-sectional studies alongside prospective studies and did not always present results for these separately.
- Studies often did not take into account mediating factors that are common in older age, such as swallowing or poor dentition.
- In protein supplementation studies, the type and source of protein differed between studies and some studies did not provide information on the type and source.
- In dietary pattern studies, the definition and assessment of a Mediterranean dietary pattern differed between studies.

### **Older adults evidence base in general**

- Older adults are a heterogenous group and chronological age is a poor indicator of an older adult's health status, which may differ widely. Some older adults are healthy and active while others have multiple conditions, diseases or disabilities.
- There can be significant differences between the youngest old and oldest old in terms of their physiological ability to respond to ill health (for example infections or chronic disease).
- Community-dwelling older adults are heterogenous in terms of the support they receive with some living independently and others receiving support from professional or family-member carers.
- Dietary assessment in some older people may pose a number of challenges and ethical considerations. This may be particularly the case for the oldest old. Challenges may include, for example, limits in participant's cognitive and/or physical ability, the high burden imposed on study participants, possible indirect reporting of food intakes by a carer or spouse, and/or limited participation in food shopping or preparation.
- Intervention studies in older adults tend to consider specific nutrients rather than broader dietary interventions.
- Observational studies are potentially subject to confounding and reverse causality.
- There was a lack of evidence on black, Asian and minority ethnic groups.
- There was a lack of evidence in older adults aged 65 years and over for all outcomes, though in particular in relation to major health outcomes, such as CVD and cancers.

## 6 Results

- 6.1 Thirty systematic reviews, of which 15 included a meta-analysis, were identified and included in the position statement. Fourteen systematic reviews included only RCTs, 12 systematic reviews included PCS and cross-sectional studies, 2 systematic reviews included RCTs, PCS and cross-sectional studies, 1 systematic review included RCTs, PCS and case-control studies and 1 systematic review included PCS, cross-sectional studies and case control studies. Only systematic reviews and meta-analyses identified by the end of February 2019 were considered. The characteristics of the included systematic reviews are summarised in Annex 4.
- 6.2 The methodological quality of systematic reviews (using the AMSTAR 2 tool) is summarised in Annex 4.5. One systematic review was assigned a high confidence rating and 12 systematic reviews a moderate confidence rating. The remaining 17 systematic reviews were assigned a low confidence rating (10 low and 7 critically low). The AMSTAR 2 tool was used to assess the quality of each included systematic review and to aid discussion; it was not used to draw conclusions.
- 6.3 Outcomes reported included:
- mortality
  - musculoskeletal health (including frailty, sarcopenia [muscle mass, muscle strength, physical performance], bone health)
  - cardiovascular health (including circulation)
  - cancer
  - immune function
  - oral health
  - weight change
  - quality of life.
- 6.4 The majority of included systematic reviews (26 out of 30 systematic reviews) focused on measures of musculoskeletal health, with only a small number of systematic reviews considering the other health outcomes. A list of all systematic reviews for each outcome is in Annex 4.1.
- 6.5 A table of exposures and outcomes considered by systematic reviews can be found in Annex 4.6. For each outcome, the direction of effect or association (and number of studies included) from the individual systematic reviews and meta-analyses has been tabulated in Annex 4.7. The tables were used to summarise the evidence and aid discussion but not to grade the evidence.
- 6.6 No systematic reviews or meta-analyses were identified on oral health, gastrointestinal tract health, eye health, hydration, skin and wound health or appetite and energy requirements.

- 6.7 The majority of included systematic reviews focused on primary studies of participants living in the community. Systematic reviews have been highlighted that included studies conducted in care homes or hospitals or among participants with pre-existing conditions.
- 6.8 Included primary studies were conducted worldwide, including in Europe, North and South America, Australia, Japan, Hong Kong and South Korea.
- 6.9 The definition of older adults varied between publications. The majority included participants with a mean age between 65 to 85 years; few primary studies included participants older than 85 years. No systematic reviews were identified that met the inclusion criteria that focused on nutrition in adults aged 85 years and over.
- 6.10 The duration of intervention or follow-up time in the primary studies varied, however, the majority were of short duration (in some cases only a few days or a couple of weeks).
- 6.11 The systematic reviews that explored the association between a Mediterranean dietary pattern and health outcomes included studies that used a variety of different indexes or scores to assess participants' adherence to a Mediterranean dietary pattern. The Mediterranean diet score (MeDi score) (Trichopoulou et al, 2003; Trichopoulou et al, 1995) is commonly used by studies to assess participants' adherence to a Mediterranean dietary pattern. While variations of the MeDi score are in use, the most commonly assessed components used to calculate the MeDi score are: higher intakes of vegetables, fruit, legumes, cereals and fish; higher ratio of mono- to saturated fatty acid intake; lower intake of dairy products and meat; and a regular but moderate alcohol intake. While there is no single Mediterranean diet, the dietary components that are characteristic of a Mediterranean dietary pattern broadly align with current UK healthy eating recommendations as depicted in the Eatwell Guide (SACN, 2018).
- 6.12 A key limitation of the use of the MeDi score is that because the population median intake is used to produce the MeDi scores, the score of individual study subjects is relative to a specific population. Therefore, a subject assigned a high score in one study population may be assigned a lower score if the same subject is placed within another study population, or vice versa. This limitation is of particular relevance when comparing the results of studies whose populations differ widely in their dietary intakes. More information about the assessment of a Mediterranean dietary pattern can be found in the SACN Statement on Diet, Cognitive Impairment and Dementias (SACN, 2018).
- 6.13 The following sections include commentaries on the evidence from systematic reviews that have been identified for each reported outcome. Where relevant, sub-sections have been included for different types of nutritional intervention or for dietary patterns. Systematic reviews with meta-analyses of RCTs and PCS are presented before systematic reviews without meta-analyses or with case control or cross-sectional studies, and more recent evidence is presented first.

## **Mortality**

- 6.14 Three systematic reviews were identified, 2 with meta-analyses (Milne et al, 2006; Winter et al, 2014) and 1 without meta-analysis (Tyrovolas & Panagiotakos, 2010). One systematic review with meta-analysis considered the relationship between protein and energy supplementation and mortality in RCTs (Milne et al, 2006) and the other systematic review with meta-analysis considered the relationship between BMI and mortality in PCS (Winter et al, 2014). The systematic review without meta-analysis considered associations between dietary patterns and mortality in PCS (Tyrovolas & Panagiotakos, 2010).

### **Body mass index (BMI)**

Winter et al (2014)

- 6.15 A systematic review with meta-analyses identified 32 PCS (197,940 participants, 72,469 deaths) considering the association between BMI and all-cause mortality in community dwelling older adults over 65 years (Winter et al, 2014). The average duration of follow-up was 12 years.
- 6.16 The association between BMI and all-cause mortality was reported to be U-shaped ( $p$  for non-linearity 0.001). Lower risks of mortality were observed between approximately a BMI of 25.0 to 30.0kg/m<sup>2</sup>, with the lowest risk of mortality observed between 27.0 and 27.9kg/m<sup>2</sup> (HR 0.90, 95% CI 0.88 to 0.92) compared to the reference BMI of 23.0 to 23.9kg/m<sup>2</sup>. Compared to the same reference BMI, individuals with a BMI of 19.0 to 19.9kg/m<sup>2</sup> had a 28% greater mortality risk (HR 1.28, 95% CI 1.24 to 1.32), with further increases in mortality risks being observed for lower BMIs. Individuals with a BMI of 35.0 to 35.9kg/m<sup>2</sup> had a 21% greater mortality risk (HR 1.21, 95% CI 1.10 to 1.33), with further increases in mortality risks being observed for higher BMIs. Similar results were observed in sub-analyses of PCS that used only measured BMIs (rather than self-reported BMIs), studies that made no adjustment for intermediary factors (for example, hypertension, diabetes or hyperlipidaemia), studies which excluded early deaths, and studies in populations with no pre-existing disease.
- 6.17 The authors reported that there was an increased risk of mortality in older adults at the lower end of the recommended BMI range for adults. Mortality risk also began to rise for BMIs over 33.0kg/m<sup>2</sup>. A number of confounders were adjusted for in the studies, including, age, sex, marital status, education, smoking status, employment status and pre-existing diseases.

## **Protein and energy supplementation**

Milne et al (2006)

- 6.18 A systematic review with meta-analyses identified 21 RCTs investigating protein and energy supplementation and different clinical and nutritional outcomes including mortality in adults over 65 years of age (Milne et al, 2006). The review included study populations based in a range of settings, but results were grouped post hoc for analysis by setting and only meta-analyses of community living participants have been included in this position statement. The duration of the trials ranged from 6 weeks to 3 months. Trials aimed to provide between 175kcal and 1000kcal additional energy and between 10g and 36g additional protein every day, most supplements included vitamins and minerals.
- 6.19 Based on a meta-analysis of 8 RCTs (596 participants), there was no evidence for a reduction in mortality from protein and energy supplementation for people living at home, regardless of nutritional status. There was also no effect of supplementation in participants 'undernourished' at baseline (4 RCTs; 357 participants) or in participants 'nourished' at baseline (4 RCTs; 261 participants) on mortality.
- 6.20 The authors noted that the trials included in the meta-analyses were generally of poor quality, with considerable heterogeneity between studies in the type of intervention.

## **Dietary patterns**

Tyrovolas & Panagiotakos (2010)

- 6.21 A systematic review without meta-analysis included 2 PCS (of the 9 included studies), which focused on the relationship between diet 'quality' or MeDi score and mortality in adults over 65 years of age living in the community (Tyrovolas & Panagiotakos, 2010).
- 6.22 There was no association between diet quality and risk of mortality in older adults (1 PCS, 1281 participants, 70 to 75 years, 10-year follow-up). A higher MeDi score was associated with a 23% lower risk of mortality (no statistics reported; 1 PCS, 2339 participants, 70 to 90 years, 10-year follow-up).
- 6.23 The authors stated that they graded the included evidence on factors including confounding. However, no further details were provided and so the extent of the adjustments for confounding is unclear.

## **Mortality summary**

- 6.24 There was evidence from 1 systematic review with meta-analysis of observational studies of an association between a BMI <25kg/m<sup>2</sup> or BMI >30kg/m<sup>2</sup> and a greater risk of mortality in older adults living in the community, with optimal BMI between

approximately 25.0 and 30.0kg/m<sup>2</sup>. One systematic review with meta-analysis of RCTs indicated that protein and energy supplements had no effect on reducing mortality or morbidity in older adults living in the community regardless of nutritional status, however the authors noted that the considered RCTs were generally of poor quality. The evidence on the association between dietary patterns and mortality was mixed and only based on a small number of observational studies.

## Musculoskeletal health

- 6.25 Twenty-six systematic reviews, 13 with meta-analyses, 1 with network meta-analysis and 12 without meta-analyses were identified that considered the relationship between BMI, dietary patterns or specific nutrients (mostly protein supplementation) and different aspects of musculoskeletal health. These included frailty, sarcopenia, risk of falls, fractures, mobility, bone mineral density (BMD) and bone mineral content (BMC) (Antoniak & Greig, 2017; Beaudart et al, 2018; Bloom et al, 2018; Coelho-Junior et al, 2018a; Coelho-Junior et al, 2018b; Cruz-Jentoft et al, 2014; Dedeyne et al, 2017; Dewansingh et al, 2018; Eglseer et al, 2016; Feng et al, 2017; Giné-Garriga et al, 2015; Lorenzo-Lopez et al, 2017; Mello et al, 2014; Milne et al, 2006; Nowson et al, 2018; Pedersen & Cederholm, 2014; Roman-Vinas & Serra-Majem, 2018; Rosendahl-Riise et al, 2017; Silva et al, 2018; Stanaway et al, 2017; Ten Haaf et al, 2018; Tieland et al, 2017; Trevisan et al, 2018; Tricco et al, 2017; Wu & Pang, 2017; Xu et al, 2015).
- 6.26 There was limited cross over in study inclusion across the 26 included systematic reviews. Thirteen systematic reviews contained only 1 or 2 of the same primary studies and 13 systematic reviews included 3 or more of the same primary studies.
- 6.27 Sarcopenia, which is an outcome explored in many of the included systematic reviews, is identified by low muscle strength, low muscle quantity and quality and poor physical performance (Cruz-Jentoft et al, 2019). Systematic reviews considering the evidence on sarcopenia generally included several sarcopenia-related outcomes and a range of methods/tools for identifying sarcopenia. Measurements of muscle strength included grip strength, chair stand test (chair rise test), leg press rate and knee extension rate. Appendicular skeletal muscle mass can be measured by dual-energy x-ray (DXA), magnetic resonance imaging (MRI) or predicted by bioelectrical impedance analysis (BIA). Whole body skeletal muscle mass can be predicted by BIA. Lumbar muscle cross-sectional area and mid-thigh muscle cross-sectional area can be measured by computerised tomography (CT) or MRI (Cruz-Jentoft et al, 2014). Physical performance was most commonly assessed by gait speed, short physical performance battery (SPPB), timed up and go test or 400 metre walk tests. Studies used different measures, which are not interchangeable, making it difficult to compare results.



## **Body mass index (BMI)**

- 6.28 Three systematic reviews, 1 with meta-analysis (Trevisan et al, 2018) and 2 without meta-analyses (Eglseer et al, 2016; Mello et al, 2014) were identified that considered the relationship between measures of nutritional status (including BMI) and measures of musculoskeletal health.

Trevisan et al (2018)

- 6.29 A systematic review with meta-analysis of 36 PCS (144,934 participants, follow-up 1 month to 11 years) evaluated the association between BMI and risk of falls (Trevisan et al, 2018). The mean age of the community dwelling participants ranged from over 64 to 90 years.
- 6.30 The association between BMI and risk of falls was reported to be U-shaped (p for non-linearity 0.003). The lowest risk of falls was observed between approximately a BMI of 26.0 and 28.0kg/m<sup>2</sup>. The pooled relative risk for risk of falls was 1.09 (95% CI 1.04 to 1.15; 36 PCS, 144,934 participants) for a BMI of 17.0kg/m<sup>2</sup> compared to the reference BMI of 23.5kg/m<sup>2</sup>. No association was found for BMI and risk of recurrent falls (23 PCS, 120,185 participants, follow-up 6 months to 6 years).
- 6.31 Of the 36 studies included in the review, 22 adjusted for confounders including age, sex and previous falls. The remaining 14 studies did not adjust for confounding.

Eglseer et al (2016)

- 6.32 A systematic review without meta-analysis looked at the relationship between nutritional status (measured by low BMI, unfavourable nutritional screening results, decreased laboratory parameters or anorexia) and components of sarcopenia, such as muscle strength, muscle mass and physical performance in adults aged over 60 years (Eglseer et al, 2016). Thirty-three observational studies (mainly cross-sectional studies) were identified, with 28 of the included studies in community-dwelling populations. Eighteen studies specifically looked at anthropometric parameters (BMI and waist circumference) and measures of muscle strength, muscle mass and physical performance, which are considered below.
- 6.33 Twelve out of 18 studies reported that a higher BMI (no BMI values reported) was associated with greater muscle strength, higher muscle mass or improved physical performance, whereas the other 6 studies reported that a higher BMI (no BMI values reported) was associated with lower measures of muscle strength, muscle mass and physical performance. Seven studies that assessed sarcopenia using the EWGSOP tool (European Working Group on Sarcopenia in Older People) observed that a lower BMI (no BMI values reported) was associated with a greater risk of sarcopenia.

- 6.34 No effect sizes, details on confounding or adjustments were provided in the systematic review. The authors concluded that despite methodological differences within the studies examined, sarcopenia may be present in older adults with low anthropometric parameters, such as low BMI.
- (Mello et al, 2014)
- 6.35 A systematic review without meta-analysis of 35 studies (8 cohorts, 27 cross-sectional studies, 77 to 40,657 participants, follow-up not reported) investigated factors associated with frailty in community dwelling adults over 65 years of age (Mello et al, 2014). Fourteen studies (3 cohorts, 11 cross-sectional studies, >65 years) assessed the relationship between BMI and frailty.
- 6.36 Nine studies (3 cohorts, 6 cross-sectional studies) observed a significant positive or negative association between BMI and frailty. Three studies observed an increased risk of frailty with a higher BMI (1 cohort, 2 cross-sectional studies) compared to 1 cohort that observed a reduced risk. Two studies observed an increased risk of frailty in overweight participants (1 cohort, 1 cross-sectional study) compared to 1 cross-sectional study that observed a reduced risk. There was an increased risk of frailty with obesity in 3 studies (1 cohort, 2 cross-sectional study) of which 1 cross-sectional study showed a positive association for women only. Three studies also observed an increased risk of frailty in non-obese participants (1 cross-sectional study) and underweight participants (1 cohort, 1 cross-sectional study). No statistics or participant numbers were reported. Five cross-sectional studies reported no association between BMI and frailty.
- 6.37 The systematic review reported that 16 out of the 35 included studies did not adjust for confounding. No further information was provided.

## **Protein**

- 6.38 Fourteen systematic reviews, 8 with meta-analyses (Beaudart et al, 2018; Coelho-Junior et al, 2018a; Coelho-Junior et al, 2018b; Dewansingh et al, 2018; Milne et al, 2006; Ten Haaf et al, 2018; Tieland et al, 2017; Xu et al, 2015) and 6 without meta-analyses (Cruz-Jentoft et al, 2014; Dedeyne et al, 2017; Eglseer et al, 2016; Lorenzo-Lopez et al, 2017; Nowson et al, 2018; Pedersen & Cederholm, 2014) were identified that considered the relationship between protein supplements or dietary protein intake and measures of musculoskeletal health.

## **Protein supplements**

Beaudart et al (2018)

- 6.39 A systematic review with meta-analysis investigated the relationship between protein supplementation and muscle strength, muscle mass and physical performance in adults aged over 60 years (Beaudart et al, 2018). The meta-analysis included 23 RCTs (sample sizes ranged from 14 to 280 participants,

mean age ranged from 64 to 83 years, mean intervention duration ranged from 5 days to 2 years). Four of these RCTs included participants in residential care settings and 2 RCTs based in the community included participants diagnosed as frail.

- 6.40 There was no significant effect of protein supplementation (3 RCTs, 310 participants), essential amino acids (EAA) supplementation (3 RCTs, 187 participants), or dehydroepiandrosterone (DHEA) supplementation (3 RCTs, number of participants not stated) on muscle strength measured by handgrip strength. Six RCTs measured the effect of creatine supplementation on muscle strength assessed by multiple measures. Four RCTs reported no effect while 2 RCTs reported significant effects (numbers of participants and statistics not stated).
- 6.41 There was no significant effect of protein supplementation (2 RCTs, 179 participants), EAA supplementation (4 RCTs, 81 participants) or DHEA supplementation (4 RCTs) on muscle mass (total lean body mass, appendicular lean mass or leg lean mass) measured by DXA or bioimpedance spectroscopy. There was no significant effect of protein supplementation (2 RCTs, number of participants not stated), creatine supplementation (1 RCTs, number of participants not stated) or  $\beta$ -hydroxy  $\beta$ -methylbutyrate (HMB) supplementation (2 RCTs, number of participants not stated) on physical performance measured by SPPB or timed up and go test. The results were mixed for the effect of EAA supplementation on physical performance measured by foot up and go, chair stand or 6-minute walk (4 RCTs, number of participants and statistics not stated).
- 6.42 The authors reported heterogeneity in protein supplementation interventions, population groups and duration of studies. Using the GRADE system, the evidence was judged by the authors to be low or very low quality, due to limitations in study design, inconsistency in results and because studies compared frail with healthy participants. Some meta-analyses only included 2 RCTs.

Dewansingh et al (2018)

- 6.43 A systematic review with meta-analysis assessed the effectiveness of dairy components (protein [7.4 to 45g/day] and amino acids [leucine 2.5g/day] on nutritional status (body weight and body mass) and physical fitness (body composition, muscle strength, and physical performance) in adults aged 55 years and over (Dewansingh et al, 2018). Thirty-six RCTs were identified and 10 RCTs were included in the meta-analyses for lean body mass and leg strength. Mean age of the participants ranged from 71 to 86 years and the duration of the trials ranged from 10 days to 6 months. All RCTs included in the meta-analyses for lean body mass and leg strength were based in the community. All RCTs included healthy participants, except 1 RCT which included participants with type 2 diabetes.

- 6.44 Two meta-analyses explored the effect of protein supplementation alone, or in combination with exercise, on musculoskeletal health. Protein supplementation had no significant effect on lean body mass, measured by DXA (8 RCTs, 474 participants) or on leg strength (6 RCTs, 417 participants). There was no effect of protein supplements in combination with exercise, compared to exercise alone, on lean body mass in a subgroup analysis (4 RCTs, 303 participants).
- 6.45 A limitation of the systematic review cited by the authors was the inclusion of trials with resistance-type exercise training in both the nutritional intervention and the control groups. Therefore, it is not possible to isolate the effect of the nutritional interventions.

Ten Haaf et al (2018)

- 6.46 A systematic review with meta-analysis of 11 RCTs (768 participants, age range 57 to 74 years) considered the relationship between protein supplementation and muscle strength, muscle mass and physical performance and 18 RCTs (914 participants, age range from 56 to 85 years) considered the relationship between protein supplementation combined with resistance exercise training (RET) and muscle strength, muscle mass and physical performance in non-frail, community dwelling older adults. The duration of the interventions ranged from 9 to 109 weeks (Ten Haaf et al, 2018).
- 6.47 There was no significant effect of protein supplementation on handgrip strength (7 RCTs, 479 participants), lower extremity muscle strength (3 RCTs, 380 participants), lean body mass measured by DXA in most studies (11 RCTs, 718 participants), or physical performance measured by gait speed (7 RCTs, 487 participants) and chair-rise ability (7 RCTs, 588 participants).
- 6.48 There was no significant effect of protein supplementation during RET compared to RET alone on upper body muscle strength (10 RCTs, 613 participants), lower extremity muscle strength (16 RCTs, 981 participants), lean body mass measured by DXA, hydrostatic weighting, Bod Pod or hydro densitometry, or physical performance measured by gait speed (8 RCTs, 840 participants) and chair-rise ability (7 RCTs, 685 participants).
- 6.49 The authors noted that a limitation of the systematic review was that protein intakes differed between the RCTs, including type of protein, amount and timing. Mean dietary protein intake was also higher than the recommendation (0.8g/kg/day) which could be sufficient to counteract age-related anabolic resistance.

Tieland et al (2017)

- 6.50 A systematic review with meta-analysis of 8 RCTs (557 participants, mean age 75 years, duration of intervention ranged from 84 to 730 days) reviewed the relationship between protein or amino acid supplementation and muscle strength

and muscle mass (Tieland et al, 2017). Of the 8 RCTs, 4 included healthy participants and 4 included participants with diabetes, sarcopenia or frailty.

- 6.51 There was no significant effect of protein supplementation on handgrip strength (6 RCTs, 471 participants), leg press strength (3 RCTs, 151 participants), leg extension strength (4 RCTs, 165 participants) or lean body mass, measured by DXA or BIA (8 RCTs, 557 participants).
- 6.52 The authors noted limitations in the systematic review including the variation in the source and amount of protein supplementation between studies; the different reporting of dietary intake of participants; and the considerable variation in the duration of studies.

Xu et al (2015)

- 6.53 A systematic review with meta-analysis evaluated the effectiveness of leucine supplementation on muscle protein synthesis, lean body mass and leg lean mass accretion (Xu et al, 2015). Nine RCTs were identified, with 6 RCTs included in the meta-analyses (8 to 57 participants, mean age ranged from 67 to 75 years, duration of intervention ranged from 10 days to 6 months). Four of the 6 RCTs included participants with conditions ranging from polymyalgia rheumatica, diabetes and cancer; 2 RCTs included only healthy participants.
- 6.54 Muscle protein fractional synthetic rate significantly increased with leucine supplementation using both the fixed-effects model (standard difference in mean changes 1.04, 95% CI 0.56 to 1.52;  $p < 0.001$ ; 4 RCTs; 79 participants) and random-effects model (standard difference in mean changes 1.08, 95% CI 0.50 to 1.67;  $p < 0.001$ ; 4 RCTs, 79 participants). There was no significant difference in lean body mass (4 RCTs, 121 participants) or leg lean mass (3 RCTs, 107 participants) with leucine supplementation. A sensitivity analysis demonstrated that no one study influenced the findings.
- 6.55 The authors report that limitations of the meta-analysis included differences in the amount and duration of the dose of leucine administered.

Milne et al (2006)

- 6.56 A systematic review with meta-analysis identified 21 RCTs that considered the relationship between protein and energy supplementation and a range of outcomes in adults over 65 years (Milne et al, 2006). The meta-analysis of mid-arm muscle circumference for adults living in the community included 6 RCTs (343 participants). Study populations were based in the community, hospital and institutions, but results were grouped post hoc for analysis by setting and only the meta-analysis of community living participants has been included in this position statement. In 81% of the trials based in community settings the duration was 8 weeks or more. Trials aimed to provide between 175kcal and 1000kcal additional

energy and between 10g and 36g additional protein every day, most supplements included vitamins and minerals.

- 6.57 Protein and energy supplements had no significant effect on mid-arm muscle circumference (6 RCTs, 343 participants).
- 6.58 The authors noted that the RCTs included in the meta-analysis were generally considered to be of poor quality.

Dedeyne et al (2017)

- 6.59 A systematic review without meta-analysis investigated the effect of multi-domain interventions compared to mono-domain interventions on frailty status and score, cognition, muscle mass, strength and power, functional and social outcomes in frail or pre-frail older adults (12 RCTs, 31 to 246 participants, mean age ranged from 71 to 79 years, intervention duration 3 to 6 months) (Dedeyne et al, 2017). The systematic review included interventions targeting two or more domains (physical exercise, nutritional, pharmacological, psychological, or social interventions), only the impact of nutrition intervention has been presented.
- 6.60 In 1 RCT (246 participants; mean age 70 years; intervention duration 6 months) protein with vitamin and mineral supplements had a significant effect on frailty status (OR=2.98, 95% CI 1.10 to 8.07;  $p<0.01$ ), frailty score (mean change -0.63, 95% CI -0.92 to -0.34;  $p<0.05$ ) and improvement in physical activity at the end of the intervention ( $p<0.01$ ) and at 6 months follow-up ( $p<0.01$ ). In 1 RCT (52 participants; mean age 79 years, intervention duration 3 months) there was a significant improvement in leg press rate ( $p<0.05$ ) and knee extension rate ( $p<0.01$ ) with exercise therapy combined with protein supplementation compared to exercise alone.
- 6.61 A further RCT (62 participants; mean age 78 years, intervention duration 24 weeks) reported a significant improvement in appendicular muscle mass ( $p<0.001$ ) and total muscle mass ( $p<0.01$ ) measured by DXA with exercise therapy with vitamin and mineral supplementation and protein supplementation, compared to exercise therapy alone. In another RCT (96 participants; mean age 83 years; intervention duration 9 months) in the exercise therapy plus nutritional advice group, the score step test (dynamic balance measure) significantly improved (mean change -1.1, 95% CI -3.2 to 1) compared to the exercise therapy only group (mean change 3.2, 95% CI 0.9 to 5.5;  $p>0.05$ ). In 1 RCT the exercise plus protein supplementation group significantly improved their function reach test rate (dynamic balance measure) compared to the exercise therapy only group ( $p>0.05$ ) (1 RCT, 52 participants, mean age 79 years, intervention duration 3 months).
- 6.62 The authors noted that there was heterogeneity in terms of study type, outcome measures, duration and participants. Their overall conclusions were that multi-domain interventions demonstrated a greater impact than mono-domain interventions or usual care for frailty, physical functioning, muscle mass or muscle

strength. Moreover, physical activity seemed to play a key role in the multi-domain intervention with some incremental benefits observed with additional interventions.

#### Cruz-Jentoft et al (2014)

- 6.63 A systematic review without meta-analysis investigated the relationship between nutrition supplementation and measures of muscle strength, muscle mass and physical performance (Cruz-Jentoft et al, 2014). The systematic review identified 12 RCTs (14 to 155 participants) of which 11 RCTs included participants living in the community and 1 RCT included participants living in an institution. The mean age of the participants in the 12 RCTs ranged from 65 to 81 years.
- 6.64 There was no effect of protein supplementation alone (1 RCT, 65 participants, intervention duration 24 weeks) or EAA supplementation (2 RCTs, 169 participants, intervention duration 3 months) on muscle mass (measured by DXA) or function (muscle mass measured by hand grip strength, knee extensor, leg extension, bicep curl or tricep curl; physical performance measured by SPPB or max walking speed). The authors reported that 'some effects' were seen with HMB supplementation on muscle mass and function, but sample sizes were low (no statistics provided; 4 RCTS, numbers of participants ranged from 19 to 98, intervention duration 8 to 24 weeks). Four RCTs considered protein supplements in combination with exercise, with 1 RCT reporting an increase in muscle mass and 3 RCTs reporting no effect (no statistics provided).
- 6.65 The authors concluded that no consistent effect of protein supplementation on muscle mass and function was found in the systematic review and noted the low number of studies identified and heterogeneity in study designs.

#### Nowson et al (2018)

- 6.66 A systematic review without meta-analysis investigated the relationship between dietary factors and functional factors that influence quality of life, including measures of musculoskeletal health such as falls, fractures, frailty, muscle strength (leg-extension strength test, quadriceps strength, peak power for knee extensors and hand grip strength) and muscle mass (measured by DXA) in community dwelling older adults in 19 studies (9 RCTs, 6 PCS, 4 cross-sectional studies) (Nowson et al, 2018).
- 6.67 There was no effect of protein supplements on muscle strength and muscle mass measured by DXA or risk of falls and fracture (1 RCT, 101 participants, over 65 years, 1 year follow-up).
- 6.68 Seven RCTs investigated the relationship between protein intake (from protein supplements, milk protein drink or dietary protein) combined with resistance training (614 participants; intervention duration 4 to 18 months). There was some evidence from 3 RCTs that higher protein intakes combined with resistance

exercise improved muscle strength and muscle mass (no statistics provided), however there was no effect reported in the other 4 RCTs.

- 6.69 The authors noted that the quality ratings of some of the studies were low.

### **Dietary protein**

Pedersen & Cederholm (2014)

- 6.70 A systematic review without meta-analysis of 17 studies (3 RCTs, 13 PCS, 1 case-control study) considered the relationship between dietary protein intake and health effects in healthy older adults (12 to 2006 participants) (Pedersen & Cederholm, 2014).
- 6.71 Three studies (1 RCT, 2 PCS) found a significant positive association between total dietary protein intake and muscle mass, measured by DXA; the RCT showed that low protein intake (0.45g/kg of body weight) resulted in a decrease in muscle mass from 17.0 to 14.7kg (1 RCT, 12 participants, age 66 to 79 years, duration not reported); one PCS reported that the highest quintile of protein intake (19% energy from protein) showed 40% lower loss of total lean mass and non-bone appendicular lean mass compared to the lowest quintile (11% energy from protein) (1 PCS, 2066 participants, age 70 to 79 years, follow-up not reported); the other PCS found that the top tertile of protein intake (1.6g/kg of body weight) had 5% higher lean mass and appendicular lean mass compared to the lowest tertile (0.84g/kg of body weight) (1 PCS, 862 participants, mean age 75 years, 5 years follow-up).
- 6.72 There was a significant positive effect of increased total dietary protein intake on BMC in 2 studies (1 RCT, 32 participants, mean age 65 [low protein group] and 72 years [high protein group], no duration and statistics reported; 1 PCS, 862 female participants, mean age 75 years, 5 years follow-up, highest tertile of protein intake had 5% higher whole-body BMC compared to lowest tertile) and a significant association between total dietary protein intake and hip BMD (1 PCS, 1077 female participants, mean age 75 years, follow-up not reported,  $p < 0.05$  for the highest compared to the lowest tertile). Significant positive associations were observed between a higher animal protein intake (women only) and vegetable protein intake (men and women) and hip BMD (1 PCS, 572 participants, mean age 71 years, 4 years follow-up, no statistics reported).
- 6.73 In 1 RCT a higher total dietary protein intake resulted in a significantly lower total body bone loss ( $p = 0.046$ ) and femoral neck bone loss ( $p = 0.001$ ) measured by BMD (within the intervention group of combined calcium and vitamin D supplement) compared to placebo (342 participants, age  $\geq 65$  years, 3 years follow-up). Out of 4 studies (4 PCS), 1 PCS observed a significant inverse association between a higher total protein (at femur  $p = 0.02$ , at spine  $p = 0.02$ , 615 participants, age 68 to 91 years, 4 years follow-up) and animal protein intake (no



statistics reported) and a lower bone loss. Another PCS also observed a significant association of bone loss with animal protein (no statistics reported, 742 female participants, >65 years, follow-up 3.6 years), while the other 2 PCS observed no association between protein intake and bone loss (1 PCS, 572 participants, age 55 to 92 years, 4 years follow-up; 1 PCS, 92 female participants, age 55 to 92 years, 3 years follow-up).

- 6.74 Two PCS considered fracture risk with 1 PCS observing a significant inverse association for total protein intake when comparing the upper 3 quartiles to the lowest quartile (1 PCS, 946 participants,  $\geq 65$  years, no follow-up reported, HR 0.63, 95% CI 0.41 to 0.97). The other PCS, which used the ratio of animal/vegetable protein, found a significant positive association, but became non-significant when adjusted for BMD (1 PCS, 1035 participants,  $\geq 65$  years, no follow-up reported, no statistics reported). A significant inverse association for total/animal/vegetable protein was observed in a case-control study for the participants aged 50 to 69 years, but not for the participants aged 70 to 89 years.
- 6.75 There was no significant association between total, animal or vegetable protein and risk of falls (1 PCS, 807 participants, mean age 75 years, 12 months follow-up, no statistics reported).
- 6.76 The PCS were adjusted for confounders, including common confounders such as age, sex and BMI and some also included confounders specific to the study populations such as hospital visits. The authors noted that a key limitation of the review was the potential underreporting of protein intakes in the Food Frequency Questionnaires (FFQs) used to evaluate protein intake in the PCS.

Coelho-Junior et al (2018a)

- 6.77 A systematic review with meta-analysis considered the association between relative dietary protein intake and physical function (4 PCS, 2 cross-sectional studies, 1 case-control study, 8654 participants, no follow-up reported) in community dwelling older adults (mean age ranged from 68 to 83 years) (Coelho-Junior et al, 2018a). Studies were allocated to 4 groups according to protein intake, categorised as low ( $<0.8\text{g/kg/day}$ ), middle ( $0.8\text{--}0.99\text{g/kg/day}$ ), high ( $\geq 1.0\text{g/kg/day}$ ) or very high ( $\geq 1.2\text{g/kg/day}$ ).
- 6.78 There was a significant improvement in lower limb muscle functioning (muscle strength and physical performance) measured by either knee extensor strength or SPPB or walking speed with very high compared to low protein intakes (standard mean difference (SMD) 0.18 units not stated, 95% CI 0.01 to 0.35;  $p=0.04$ ;  $I^2 = 74\%$ ; 2 PCS, 1 cross-sectional study, 3225 participants, no follow-up reported). There was no significant difference in upper-limb strength, as measured by isometric handgrip strength (2 PCS, 1 cross-sectional study, 5315 participants, no follow-up reported) or lower-limb strength (2 PCS, 1 cross-sectional study, 842 participants, no follow-up reported) when the high protein group was compared to the low protein group. There was a small significant improvement in walking speed

when high protein intake was compared to low protein intake (SMD=0.06 metres/second, 95% CI 0.02 to 0.11,  $p=0.003$ ,  $I^2=89\%$ ; 2 PCS, 4243 participants, no follow-up reported). When middle protein intake versus high protein intake was compared, there was no significant difference in measurements of upper limb and lower-limb muscle strength (1 PCS, 1 cross-sectional study, 1 case control study, 653 participants, no follow-up reported) or mobility (1 PCS, 1 cross-sectional study, 1 case control study, 653 participants, no follow-up reported). There was no significant difference with handgrip strength or chair rise ability.

- 6.79 Nine out of 10 included studies were adjusted for variables including age, sex, BMI, education, socioeconomic status, smoking status, alcohol consumption, chronic disease status and cognitive function. The authors concluded that participants with a very high or high protein intake had greater mobility and better lower-limb physical functioning than participants with relatively low protein intake (as defined above). Study limitations cited included the lack of comparison between the low and middle protein intake groups (due to a lack of data) and the use of mean protein intake to develop categories.

#### Coelho-Junior et al (2018b)

- 6.80 A systematic review with meta-analysis considered the relationship between dietary protein intake and frailty in community dwelling adults over 60 years (Coelho-Junior et al, 2018b). Ten studies (3 PCS, 7 cross-sectional studies) were identified, of which 4 cross-sectional studies were included in 2 meta-analyses (9091 participants). Two separate meta-analyses were conducted because 2 of the included studies used the same database.
- 6.81 There was a significant association between a higher dietary protein intake and a lower risk of frailty for both meta-analyses (OR 0.67, 95% CI 0.56 to 0.82;  $p<0.0001$ ; OR 0.66, 95% CI 0.54 to 0.80;  $p<0.0001$ ; 3 cross-sectional studies, 9091 participants, mean age ranged from 73.2 to 75.6 years).
- 6.82 No detail on confounding or adjustments were provided in the systematic review. The authors concluded that their findings suggest low consumption of protein is associated with greater frailty prevalence in older adults. The authors reported a number of limitations including that the findings from meta-analyses were based on cross-sectional studies only and that each study included in the meta-analyses classified protein intake levels differently.

#### Nowson et al (2018)

- 6.83 A systematic review without meta-analysis investigated the relationship between dietary factors and functional factors that influence quality of life, including measures of musculoskeletal health such as falls, fractures, frailty, muscle strength (leg-extension strength test, quadriceps strength, peak power for knee extensors and hand grip strength) and muscle mass (measured by DXA) in community

dwelling older adults in 19 studies (9 RCTs, 6 PCS, 4 cross-sectional studies) (Nowson et al, 2018).

- 6.84 Four observational studies (1 PCS, 3 cross-sectional studies) were identified that considered the relationship between dietary protein intake and measures of musculoskeletal health. The PCS (24,417 participants, >65 years, 3.9 years follow-up) found a 20% higher protein intake to be significantly associated with a 35% lower risk for frailty (no p-value reported). The 3 cross-sectional studies (4255 participants, >65 years) showed an association between higher dietary protein intake and reduced frailty prevalence.
- 6.85 The authors stated that 'a few' included studies did not adjust for confounders but no specific information was provided. Review limitations cited in the paper were that the quality ratings of some of the studies was low.

Lorenzo-Lopez et al (2017)

- 6.86 A systematic review without meta-analysis evaluated nutritional status (micro- and macronutrients, dietary patterns, malnutrition) and frailty in community dwelling older adults (Lorenzo-Lopez et al, 2017). The systematic review identified 19 studies (5 PCS, 14 cross-sectional studies, 21,033 participants, mean age 74.5 years, no follow-up reported).
- 6.87 Five studies looked at the association between dietary protein intake and frailty (5 cross-sectional studies, including 1 cross-sectional analysis of baseline data from a PCS). There was no association between dietary protein intake and frailty in two of the studies (6119 participants, mean age 75 years and 83 years), whereas the other 3 cross-sectional studies reported an association between a higher dietary protein intake and a lower risk of frailty (4255 participants, mean age range 74.1 to 75.6 years).
- 6.88 The authors noted that several associations were strongest after adjusting for age, socio-economic status, smoking status and BMI but did not provide any more specific information such as which or how many studies adjusted for confounding. A number of limitations were identified by authors, for example, most of the primary studies included in the review were cross-sectional and there was no analysis of other mediating factors such as swallowing or poor dentition. There was also large heterogeneity in outcome measurements.

Eglseer et al (2016)

- 6.89 A systematic review without meta-analysis looked at the relationship between nutritional status and sarcopenia in adults aged over 60 years (Eglseer et al, 2016). Thirty-three observational studies (mainly cross-sectional studies) were identified, of which 28 were in community-dwelling populations.
- 6.90 Six studies (2 PCS, 4 cross-sectional studies) were identified that considered dietary protein intake and sarcopenia. Two cross-sectional studies reported that

individuals with lower dietary protein intakes were more likely to have sarcopenia, whilst the other 4 studies (including 2 large PCS and 2 cross-sectional studies) found no association between dietary protein intakes and sarcopenia.

- 6.91 No statistics, details on confounding or adjustment were provided in the systematic review. The authors noted that few significant correlations between nutritional intake and sarcopenia were observed due to limitations with recording dietary intake in older adults.

### **Vitamin D supplementation**

- 6.92 As SACN published its report on Vitamin D and Health in 2016, only systematic reviews published after the search periods covered in the Vitamin D and Health report were included.
- 6.93 Four systematic reviews with meta-analyses of RCTs were included, that considered the relationship between vitamin D supplementation and measures of musculoskeletal health (Antoniak & Greig, 2017; Rosendahl-Riise et al, 2017; Tricco et al, 2017; Wu & Pang, 2017).
- 6.94 There was some overlap between the RCTs included in the systematic reviews identified in this position statement with those included in the SACN 2016 Vitamin D and Health report. There was no overlap in Antoniak & Greig (2017), 5 out of the 15 RCTs included in (Rosendahl-Riise et al, 2017) overlapped with the SACN 2016 report, 9 out of the 26 RCTs included in Wu & Pang (2017) overlapped with the SACN 2016 report and 8 out of the 41 RCTs included in (Tricco et al, 2017) overlapped with the SACN 2016 report.

#### **Antoniak & Greig (2017)**

- 6.95 A systematic review with meta-analysis evaluated the effectiveness of combined RET and vitamin D<sub>3</sub> supplementation on musculoskeletal health in community dwelling older adults aged ≥65 years (Antoniak & Greig, 2017). Seven RCTs were identified, of which 3 RCTs had relevant interventions of RET and vitamin D<sub>3</sub> supplements (doses ranging from 10µg (400IU) to 48µg (1920 IU)). Baseline 25-hydroxyvitamin D levels were >30nmol/L.
- 6.96 Vitamin D<sub>3</sub> supplementation in combination with exercise significantly improved muscle strength (lower limb) compared to exercise alone (SMD=0.98, 95% CI 0.73 to 1.24; p<0.001, I<sup>2</sup> = 70%; 3 RCTs, 266 participants, mean age ranged from 67 to 77 years, intervention duration ranged from 16 weeks to 2 years). There was no significant effect of vitamin D<sub>3</sub> supplementation on timed 'up and go' test, femoral neck BMD or spine BMD (2 RCTs, 249 participants, mean age ranged from 67 to 77 years, intervention duration ranged from 16 weeks to 2 years). Calcium supplementation was included in 2 of the 3 RCTs in both intervention and control groups.

- 6.97 The authors concluded that there was some support for the additive effect of vitamin D<sub>3</sub> supplementation when combined with RET for the improvement of muscle strength in older adults but no evidence of benefit of vitamin D<sub>3</sub> supplementation alone.
- 6.98 A number of limitations were identified by the authors including the limited number of studies included in the meta-analyses; potential skewing of the meta-analyses due to the high weighting of a particular study with a large number of participants; 2 smaller studies not accounting for confounding factors; and none of the RCTs reporting inclusion/ exclusion criterion for vitamin D status, although at baseline serum vitamin D was not significantly different between the groups.

Rosendahl-Riise et al (2017)

- 6.99 A systematic review with meta-analysis of 15 RCTs considered the effect of vitamin D supplementation with or without calcium on measurements of muscle strength and mobility (mean age ranged from 61.5 to 81 years) (Rosendahl-Riise et al, 2017). All study participants lived in the community and were generally in good health. Acute diseases but not a history of chronic disease, was an exclusion criterium. The duration of the interventions ranged from 4 months to 20 months. Doses of vitamin D included 10µg (400IU) to 100µg (4000IU) vitamin D<sub>3</sub>/day (7 RCTs); bolus oral vitamin D<sub>3</sub> 210µg (8400IU) /week (1 RCT); bolus oral vitamin D<sub>3</sub> 3750µg (150,000IU) every 3 months (1 RCT); bolus D<sub>2</sub> injection 15,000µg (600,000IU) (1 RCT); 1,25-dihydroxyvitamin D<sub>3</sub> 0.25µg (10IU) /day to 0.5µg (20IU) /day (2 RCTs); 25-hydroxyvitamin D<sub>3</sub> 20µg (800IU) /day or 140µg (5600IU) /week (1 RCT); alfacalcidol 500µg (20,000IU) /day (1 RCT). Mean baseline 25-hydroxyvitamin D concentration ranged from 25 to 82nmol/L.
- 6.100 There was no effect of vitamin D supplementation with or without calcium on muscle strength, measured by hand grip strength (7 RCTs, 1406 participants, mean age 61.5 years; follow-up 24 weeks to 12 months). The authors noted a small significant improvement in mobility with vitamin D alone (mean difference (MD) 0.31s, 95% CI -0.51 to -0.10; no p value reported; 5 RCTs, 1260 participants, mean age 61.5 years, follow-up 10 weeks to 20 months). In a sensitivity analysis, there was a significant effect of vitamin D supplements on hand grip strength when the 3 RCTs that included participants deficient in vitamin D were removed (MD 0.40kg, 95% CI 0.37 to 0.43; 4 RCTs, 930 participants).
- 6.101 The authors noted that study limitations included the small number of studies included in the meta-analyses due to heterogeneity of measurements used, variation in study populations and co-morbidities. However, according to the authors, heterogeneity was eliminated when the 3 RCTs of vitamin D deficient participants were removed from the meta-analysis. There were considerable differences in the amount and frequency of vitamin D doses across the RCTs.

Wu & Pang (2017)

- 6.102 A systematic review with meta-analysis of 26 RCTs considered the effect of vitamin D supplementation given either alone or in combination with calcium on the risk of falls (32,686 participants, mean age ranged from 67 to 92 years) (Wu & Pang, 2017). The duration of the interventions ranged from 1 month to 60 months and included healthy participants and participants in hospital. Vitamin D doses ranged from 5µg (200IU) to 27.5µg (1100IU)/day or 7500µg (300,000IU) once in 36 months to 2500 µg (100,000IU)/4 weeks in the longer-term dosage interventions. Baseline 25-hydroxyvitamin D not reported.
- 6.103 There was no significant effect of vitamin D<sub>2</sub> supplementation alone (6 RCTs, 13,545 participants, mean age ranged from 67 to 92 years) or vitamin D<sub>3</sub> supplementation alone (6 RCTs, 8199 participants, mean age ranged from 67 to 92 years) on the risk of falls (suffering at least 1 fall). Vitamin D combined with calcium supplementation significantly decreased the risk of falls (suffering at least 1 fall) (OR 0.87, 95% CI 0.80 to 0.94, p=0.0004; I<sup>2</sup>=46%; 14 RCTs, 13,585 participants, mean age ranged from 67 to 92 years). The authors concluded that calcium plus vitamin D supplementation combined is statistically significantly associated with a reduction in fall risks across various populations.
- 6.104 It was not clear from the review how many of the participants were healthy and living in the community. The authors noted that publication bias likely affected the results.

Tricco et al (2017)

- 6.105 A systematic review with meta-analysis of 283 RCTs (159,910 participants) and network meta-analysis of 54 RCTs (41,596 participants) assessed the potential effectiveness of a range of interventions (nutritional and non-nutritional), including vitamin D, for preventing injurious falls (Tricco et al, 2017). The mean age of participants was 78 years. The settings and health status of the participants varied; 142 RCTs were based on participants living at home, 75 RCTs were based in a clinic setting, 72 RCTs were based in the community and 51 RCTs were based in a hospital, with some RCTs conducted in multiple settings. The primary outcome was injurious falls and fall-related hospitalisations and secondary outcomes were rate of falls, number of fallers and number of fractures. Vitamin D doses and baseline 25-hydroxyvitamin D concentration were not reported.
- 6.106 There was no significant effect of vitamin D supplementation alone on number of fallers (7 RCTs, 17,966 participants, mean age 78 years, intervention duration not reported). There was no significant effect of vitamin D alone on fractures (6 RCTs, 21,018 participants, mean age 78 years, intervention duration not reported) or hip fractures (4 RCTs, 18,099 participants, mean age 78 years, intervention duration not reported). There was a significant effect of calcium plus vitamin D compared with calcium only on number of fallers (OR 0.73, 95% CI 0.58 to 0.9; no p value stated; 5 RCTs, 1389 participants, mean age 78 years, intervention duration not

reported). There was no significant effect of calcium plus vitamin D vs calcium alone on fractures (6 RCTs, 6462 participants, mean age 78 years, intervention duration not reported) or hip fractures (3 RCTs, 2918 participants, mean age 78 years, intervention duration not reported).

- 6.107 A network meta-analysis was also conducted on large numbers of RCTs, which reported significant effects of calcium plus vitamin D compared with calcium alone on number of fallers (OR 0.69, 95% CI 0.49 to 0.98; no p value stated; 78 treatments, 158 RCTs, 107,300 participants, mean age 78 years, intervention duration not reported).
- 6.108 The authors noted that as there was a large number of comparisons in the network meta-analysis, multiplicity may have elevated the rate of false positives in the statistically significant results. The meta-analyses combined RCTs from different settings, therefore it is unclear if the meta-analyses focus only on participants living in the community.

### **Other nutritional/dietary supplements**

- 6.109 Three systematic reviews without meta-analyses (Cruz-Jentoft et al, 2014; Lorenzo-Lopez et al, 2017; Stanaway et al, 2017) were identified that considered other nutritional/ dietary supplements and measures of musculoskeletal health. Two systematic reviews included RCTs and 1 systematic review included PCS and cross-sectional studies.

#### **Cruz-Jentoft et al (2014)**

- 6.110 A systematic review without meta-analysis investigated the relationship between nutrition supplementation and measures of muscle strength, muscle mass and physical performance (Cruz-Jentoft et al, 2014). The systematic review identified 12 RCTs (14 to 155 participants) of which 11 RCTs included participants living in the community and 1 RCT included participants living in an institution. The mean age of the participants ranged from 65 to 81 years.
- 6.111 One study was identified, which explored the effect of fatty acid supplementation in combination with exercise. There was no effect of  $\alpha$ -linolenic acid supplementation in combination with RET on muscle strength (leg press, chest press) or muscle mass (DXA) (1 RCT, 51 participants, intervention duration 12 weeks).

#### **Lorenzo-Lopez et al (2017)**

- 6.112 A systematic review without meta-analysis evaluated nutritional status (micro- and macronutrients, dietary patterns, malnutrition) and frailty in community dwelling older adults (Lorenzo-Lopez et al, 2017). The systematic review identified 19 studies (5 PCS, 14 cross-sectional studies, 21,033 participants, mean age 74.5 years, no follow-up reported).

- 6.113 Seven studies looked at the association between micronutrient intake and frailty (2 PCS, 5 cross-sectional studies). One PCS reported that women in the lowest quartile of serum carotenoids and  $\alpha$ -tocopherol had a significant increased risk of becoming frail over a 3 year period (Q1 versus Q2-Q3-Q4 HR 1.30, 95% CI 1.01 to 1.92; and HR 1.39, 95% CI 1.02 to 1.89, respectively; no p values reported; 1 PCS, 766 participants, mean age 78.2 years, no follow-up reported). Similarly, the results of 4 cross-sectional studies showed that a lower intake of micronutrients was associated with frailty (4 cross-sectional studies, 4377 participants, mean age 74.5 years). Two studies (1 PCS and 1 cross-sectional study) observed that a higher dietary antioxidant capacity was associated with a lower risk of frailty. The PCS observed that dietary resveratrol exposure was negatively associated with frailty risk over 3 years of follow-up (OR 0.17, 95% CI 0.05 to 0.63; no p value reported; 1 PCS, 769 participants, mean age 72.7 years), but not after 6 and 9 years of follow-up.
- 6.114 The authors mentioned that several associations were strongest after adjusting for age, socio-economic status, smoking status and BMI but did not provide any more specific information such as which or how many individual studies adjusted for confounding. The authors noted that most primary studies were cross-sectional and no analysis of other mediating factors including swallowing and poor dentition was undertaken. There was also heterogeneity in outcome measurements.

#### Stanaway et al (2017)

- 6.115 A systematic review without meta-analysis of 11 RCTs investigated the relationship between dietary nitrate supplementation and a number of health outcomes including physiological performance (175 participants, age ranged from 59.2 to 74.7 years) (Stanaway et al, 2017). Five RCTs were with healthy participants and 7 RCTs were with participants diagnosed with diabetes, peripheral arterial disease (PAD), chronic obstructive pulmonary disease (COPD) or with risk factors for CVD. Most RCTs used inorganic nitrate in the form of beetroot juice as the intervention, with the supplementation period varying from acute (2 to 4 hours before testing) to chronic (14 days).
- 6.116 Five studies investigated the effect of dietary nitrate supplementation on physiological performance, 2 of which were in healthy populations. These 2 studies provided conflicting results.
- 6.117 The authors noted that the RCTs had small sample sizes and there was variance between study designs.

#### **Diet quality and patterns**

- 6.118 Seven systematic reviews, 2 with meta-analyses (Giné-Garriga et al, 2015; Silva et al, 2018) and 5 without meta-analyses (Bloom et al, 2018; Feng et al, 2017; Lorenzo-Lopez et al, 2017; Nowson et al, 2018; Roman-Vinas & Serra-Majem,



2018) considered the relationship between dietary patterns and measures of musculoskeletal health. One systematic review included RCTs, PCS and cross-sectional studies (Giné-Garriga et al, 2015) and the other 5 systematic reviews included PCS and cross-sectional studies.

#### Silva et al (2018)

- 6.119 A systematic review with meta-analysis reviewed the association between a Mediterranean dietary pattern and musculoskeletal function including sarcopenia and frailty (Silva et al, 2018). Eleven studies were identified in total (8 PCS, 3 cross-sectional; 16,999 participants). All studies were based in the community and the mean age range of participants was 68 to 84 years.
- 6.120 The highest adherence to a Mediterranean dietary pattern compared with the lowest adherence to a Mediterranean dietary pattern was associated with reduced risk of frailty (OR 0.42, 95% CI 0.28 to 0.65;  $I^2=24.9\%$ ; no p value reported; 4 PCS, 5789 participants, mean age 68 to 82 years, follow-up not reported) and a reduced risk of functional disability (OR 0.75, 95% CI 0.61 to 0.93;  $I^2=0\%$ ; no p value reported; 3 PCS, 3493 participants, mean age 68 to 76 years, follow-up not reported). No association was found between adherence to a Mediterranean dietary pattern and sarcopenia for the 1 PCS included (2948 participants, mean age 74 years, follow-up not reported).
- 6.121 All included studies addressed confounding, including variables age, sex, BMI, energy intake, educational level, chronic diseases/ co-morbidities, depression, alcohol, smoking status and physical activity. Limitations reported by the authors included pooled ORs in the meta-analyses being generated from adjusted measures provided by authors and inability to perform sensitivity analysis to investigate sources of heterogeneity due to small number of studies identified.

#### Giné-Garriga et al (2015)

- 6.122 A systematic review with meta-analysis investigated the relationship between combined exercise and dietary interventions (diet modification rather than designed for weight loss (minority of included studies had overweight populations)) or diet interventions alone and improvements in physical function (gait speed, balance and functional capacity) (Giné-Garriga et al, 2015). The systematic review identified 7 studies (4 RCTs, 2 PCS, 1 cross-sectional study, >65 years) in community dwelling older adults. The diet interventions consisted of either a balanced diet with energy deficit of 500kcal to 750kcal plus behavioural therapy, personalised diet counselling and group session education and an increase in fruit and vegetable intake from <2 to 5 portions per day. Two studies included nutritional supplements plus dietary modification.
- 6.123 There was no effect of dietary change alone on gait speed (3 RCTs, 1 PCS, 2407 participants, >65 years) or balance measures (2 RCTs, 102 participants, mean age 80.5 years, intervention duration 3 to 6 months). A combination of diet plus

exercise had a significant effect on gait speed (95% CI 0.06 to 0.21,  $I^2= 0\%$ , 2 RCTs, 103 participants) but not on balance measures. A meta-analysis could not be performed for functional capacity. One RCT (80 participants, mean age 71 years, intervention duration not reported) reported no effect of a diet rich in fruit and vegetables on lower extremity physical function measures (chair-stand test) and 1 cross-sectional study observed that women who consumed more dairy were less likely to perform a slower timed up and go test. The authors concluded that it was not possible to confirm from the studies identified whether combined diet and physical activity interventions improved physical function outcomes more than exercise interventions alone.

- 6.124 No detail on confounding or adjustments were provided in the systematic review. The authors noted heterogeneity in both diet and exercise interventions.

Bloom et al (2018)

- 6.125 A systematic review without meta-analysis examined the association between diet quality (assessed using different methods) and individual components of sarcopenia in older adults (Bloom et al, 2018). Twenty-one studies were set in the community (11 PCS, 10 cross-sectional; ranging from 171 to 3957 participants, over 65 years).
- 6.126 Ten studies considered 'healthier' diets and muscle strength (6 PCS, 4 cross-sectional studies, 156 to 1872 participants, mean age 69 to 78 years, follow-up not reported). Of the 6 PCS, 5 showed no association between a 'healthier' diet and different measures of muscle strength and 1 showed a 'healthier' diet to be associated with a reduced risk of declining grip strength (OR 0.43, 95% CI = 0.19 to 0.99, 781 participants, 4 years follow-up). Of the 4 cross-sectional studies, 2 showed no association (496 participants, mean age range 83 to 86 years) and 2 showed positive associations for 'healthier' diets and muscle strength (4375 participants, mean age range 66 to 70 years). (Bloom et al, 2018) considered the evidence on 'healthier' diets and muscle strength to be limited.
- 6.127 Four studies (1 PCS, 3 cross-sectional studies) considered 'healthier' diets and muscle mass. The PCS showed no association of Dietary Variety Score (DVS) and muscle mass (542 participants, mean age 72 years; follow-up not stated). Of the 3 cross-sectional studies (171 to 1509 participants, age >65 years [1 study], mean age 68 years [2 studies]), 1 showed a positive association of 'healthier' diets and muscle mass; 1 showed a positive association in women, but not in men; and 1 showed no association for the Healthy Eating Index and a weak negative association for the Healthy Diet Indicator in women only. Overall the 4 studies were considered to provide weak evidence by the authors.
- 6.128 Thirteen studies (7 PCS, 6 cross-sectional studies, 690 to 5350 participants, mean age 51 to 75 years, follow-up ranged from 3 to 16 years) looked at physical performance, measured by a large variety of measures. Ten studies (6 PCS, 4 cross-sectional studies) found a significant association between a 'healthier' diet

and better physical performance. Five studies (3 PCS, 2 cross-sectional studies) found greater adherence to a Mediterranean dietary pattern was associated with improved walking speed outcomes (1 PCS, improved rapid 20m walking speed,  $p=0.012$ , 1201 participants, mean age 75 years, 8 years follow-up; 1 PCS: reduced risk of low walking speed, OR = 0.48, 95% CI 0.27, 0.86, 690 participants, mean age 73 years, 6 years follow-up; 1 PCS: reduced risk of low walking speed, OR = 0.53, 95% CI 0.35, 0.79, 1815 participants, mean age 69 years, 3.5 years follow-up).

- 6.129 One PCS found that the highest category of DVS, compared to the lowest category, was associated with a reduced risk for decline in usual gait speed (OR = 0.43, 95% CI 0.19, 0.99, 772 participants, mean age 72 years, 4 years follow-up). Three studies (1 PCS, 2 cross-sectional studies) reported improved lower body performance measured by SPPB was associated with a greater adherence to a Mediterranean dietary pattern (1 PCS, mobility disability [SPPB=9 points] HR = 0.71, 95% CI 0.51, 0.98,  $p=0.04$ , 705 participants, mean age 74 years, 3 years follow-up; 1 cross-sectional study, 304 participants, mean age 86 years), and the Healthy Diet Indicator (1 cross-sectional study, 171 participants, mean age 68 years).
- 6.130 One PCS (1072 participants, mean age 61 years, 10 years follow-up) examined the Nordic Diet Score (NDS) and found that the overall Senior Fitness Test score was 0.55 (95% CI 0.22, 0.88) points higher per 1 unit increase in NDS. Results for women in the highest NDS quartile were 17%, 16% and 20% higher in the walk, arm curl test and chair stand tests respectively compared to women in the lowest NDS quartile (all  $p$ -values  $<0.01$ ). Four studies found no significant association between 'healthier' diet and physical performance (1 PCS, 1872 participants, mean age 69 years, 3.5 years follow-up; 2 cross-sectional studies, 628 and 2132 participants, mean age 68 and 70 years).
- 6.131 One PCS reported a high vegetable/fruit pattern was associated with lower likelihood of sarcopenia in older men (data driven factor analysis of FFQ): adjusted OR = 0.60, 95% CI = 0.36 to 0.99,  $p$  for trend = 0.034; Diet Quality Index-International (DQI-I) adjusted OR = 0.50, 95% CI = 0.31 to 0.81,  $p$  for trend = 0.004; 3957 participants, mean age 72 years, 4 years follow-up), but found no associations in women. One cross-sectional study showed greater adherence to a Mediterranean dietary pattern to be associated with a lower risk for sarcopenia.
- 6.132 The authors graded the included evidence using a quality assessment tool. Studies ranged from medium to low risk of unadjusted/residual confounding. Some studies used adjusted statistical models and some did not. In general, the authors concluded that there was a small body of evidence, mainly consisting of cross-sectional studies, for a relationship between a 'healthier' diet and better muscle mass outcomes however the evidence was weak. The authors also concluded that there is some evidence from observational studies that 'healthier' diets are associated with benefits in physical performance.

Lorenzo-Lopez et al (2017)

- 6.133 A systematic review without meta-analysis evaluated nutritional status (micro- and macronutrients, dietary patterns, malnutrition) and frailty in community dwelling older adults (Lorenzo-Lopez et al, 2017). The systematic review identified 19 studies in total (5 PCS, 14 cross-sectional studies, 21,033 participants, mean age 74.5 years).
- 6.134 In 1 PCS, the risk of being frail significantly decreased with the higher score of the 'snacks-drinks milk products' in a sex-age adjusted model over a 4-year follow-up (adjusted OR 0.58, 95% CI 0.36 to 0.91; no p value reported; 1 PCS, 2724 participants, mean age 71.8 years) and with a better diet quality in sex-age-adjusted models over a 4-year follow-up (adjusted OR 0.59, 95% CI 0.42 to 0.85; no p value reported; 1 PCS, 2724 participants, mean age 71.8 years). There was no association between a MeDi score, 'vegetables-fruits' pattern, or 'meat-fish' pattern with incident frailty. One PCS found better diet quality to be inversely associated with frailty status (OR 0.18, 95% CI 0.03 to 0.97; no p value reported; 1 PCS, 5295 participants, mean age 75 years). A cross-sectional study found a 'healthier' diet to be significantly associated with a lower risk of being frail (192 participants, mean age 83 years).
- 6.135 The authors mentioned that several associations were strongest after adjusting for age, socio-economic status, smoking status and BMI but did not provide any more specific information such as which or how many individual studies adjusted for confounding. A number of limitations were identified by authors, for example, most of the primary studies included in the review were cross-sectional and there was no analysis of other mediating factors such as swallowing or poor dentition. There was also large heterogeneity in outcome measurements.

Nowson et al (2018)

- 6.136 A systematic review without meta-analysis considered the relationship between dietary factors and frailty in community dwelling older adults (Nowson et al, 2018). The systematic review identified 3 studies (2 PCS, 1 cross-sectional study).
- 6.137 Of the 3 identified studies, 1 PCS showed a 4-point increase in the MeDi score to be associated with a 70% lower risk for developing frailty (no further statistics reported, 690 participants, age > 65 years, 6.0-year follow-up). A further PCS showed a 3-point increase in the MeDi score to be associated with a 41% lower risk for developing frailty (no further statistics reported, 1872 participants, age > 65 years, 3.5-year follow-up). A small cross-sectional study (192 participants) also found a higher MeDi score to be associated with a lower risk of developing frailty.
- 6.138 The authors stated that 'a few' included studies did not adjust for confounders but no specific information was provided. Review limitations cited in the paper were that most of the evidence in the paper was from observational studies, which are subject to confounding, and that the quality ratings of some of the studies was low.

Feng et al (2017)

- 6.139 A systematic review without meta-analysis considered dietary factors associated with the risk of frailty in community dwelling over 60 years old (Feng et al, 2017). Six studies were identified, which looked at dietary patterns.
- 6.140 There was a significant association between a higher “Diet Quality Index score” ( $p < 0.05$ ; 1 PCS, 2724 participants,  $\geq 65$  years, 3.9 years follow-up), higher fruit/vegetable consumption ( $p < 0.01$ , 1 PCS, 2198 participants,  $\geq 60$  years, 3.5 years follow-up) and a higher measure of dietary resveratrol (polyphenol) exposure ( $p < 0.05$ , 1 PCS, 322 participants,  $\geq 65$  years, 9 years follow-up) and risk of frailty. Two PCS found a significant association between a MeDi score and a lower risk of frailty ( $p < 0.05$ ; 2 PCS; 2505 participants) whereas another 2 PCS found no association between a MeDi score and risk of frailty (2 PCS, 4539 participants,  $\geq 60$  years, 3.5 to 3.9 years follow-up).
- 6.141 One PCS observed a significant association between protein consumption (including total proteins, animal proteins and higher monounsaturated fatty acids) and a lower risk of frailty (1 PCS, 1822 participants,  $\geq 60$ y, follow-up 3.5 years). A significant association was found between low-fat milk and yoghurt intake and a lower risk of frailty ( $p < 0.05$ ; 1 PCS, 1871 participants,  $\geq 60$  years, 3 years follow-up). There was no significant association between a ‘vegetables-fruits’ pattern or ‘meat-fish’ pattern and risk of frailty (1 PCS, 2724 participants,  $\geq 65$  years, 3.9 years follow-up) or between consumption of vegetable-based protein, saturated fatty acids,  $\alpha$ -linolenic acid, linoleic acid, carbohydrates, simple sugars, polysaccharides or long-chain omega-3 fatty acids and risk of frailty (1 PCS, 1822 participants,  $\geq 60$  years, 3.5 years follow-up). There was no significant association between whole milk, whole-fat yogurt, low-fat yogurt, cheese or yoghurt and risk of frailty (1 PCS, 1871 participants,  $\geq 60$  years, 3 years follow-up).
- 6.142 The authors note that associations were only reported from fully adjusted models. A key limitation of the review is that all studies included were prospective cohort studies, which may be at risk of confounding.

Roman-Vinas & Serra-Majem (2018)

- 6.143 A narrative review with a systematic search identified 2 PCS (total number of participants unclear) and 4 cross-sectional studies (5073 participants) that considered the relationship between a Mediterranean dietary pattern and healthy ageing measured by physical function (for example, frailty, grip strength, walking speed, muscle strength, ability to conduct daily living tasks) in community dwelling adults over 65 years (Roman-Vinas & Serra-Majem, 2018).
- 6.144 Two studies considered a dataset from the same PCS at slightly different follow-up times (1911 participants, mean age 68 years, 3 years follow-up; and 1630 participants, mean age 68 years, 3.5 years follow-up). Both studies reported a significant association for physical function and the Mediterranean Diet Adherence

Screeener (beta coefficient = 1.34, 95% CI 0.21 to 2.47; and OR = 0.61, 95% CI 0.45 to 0.81 respectively), but not for the MeDi score. One of the 2 studies also analysed a dataset from a second PCS (2376 participants, mean age 70 years, 2 years follow-up), finding no association between a non-validated Mediterranean dietary pattern index and physical function. The 4 cross-sectional studies (5073 participants, mean age 71.2 to 86.3 years) considered 13 different measures of physical function and found a significant association of a Mediterranean dietary pattern with 9 of the 13 considered measures of physical function.

- 6.145 The authors noted that some of the included studies were adjusted for confounding, but no further detail was provided. The authors noted that the studies were not always comparable as outcomes measured different variables and the Mediterranean dietary pattern was evaluated differently. This was not a systematic review, however, a systematic search was undertaken.

## **Musculoskeletal health summary**

### Body mass index (BMI)

- 6.146 Three systematic reviews included evidence from PCS and cross-sectional studies on the association between BMI and musculoskeletal health. Evidence from 1 systematic review with meta-analysis of PCS observed the lowest risk of at least 1 fall in participants with a BMI between 24.5 and 30.0kg/m<sup>2</sup>. In the 2 systematic reviews without meta-analyses, 1 systematic review observed an association between a higher BMI and a higher muscle strength, muscle mass and improved physical performance, whereas evidence on BMI and frailty from the other systematic review was unclear. Most studies in the 2 systematic reviews without meta-analyses were cross-sectional and BMI data were not provided in the first review.
- 6.147 In summary, it was not possible to draw conclusions on the association between BMI and musculoskeletal health as evidence from systematic reviews reported on different musculoskeletal health outcomes and most evidence was from cross-sectional studies.

### Protein

#### Protein supplements

- 6.148 Nine systematic reviews considered the relationship between protein supplements and musculoskeletal health outcomes and 1 systematic review considered the relationship between dietary protein intake, including protein supplements, and musculoskeletal health outcomes.
- 6.149 Overall the evidence from 6 systematic reviews with meta-analyses of RCTs reported no significant effect of protein or amino acid supplements on musculoskeletal health in older adults, including measures of upper and lower

muscle strength, muscle mass and physical performance. The evidence from systematic reviews without meta-analyses of RCTs was unclear.

- 6.150 Evidence from 2 systematic reviews with meta-analyses of RCTs reported no additional benefit of protein supplements in combination with exercise on muscle strength or muscle mass compared to exercise alone. One systematic review without meta-analysis of RCTs included evidence from 1 RCT which suggested that protein supplements in combination with exercise had a positive effect on muscle strength and muscle mass, however, overall the evidence was unclear.
- 6.151 In summary, evidence from systematic reviews with meta-analyses of RCTs suggests no significant effect of protein supplements on measures of musculoskeletal health in older adults. Although there was considerable heterogeneity in interventions, population groups and outcome measures.

#### Dietary protein

- 6.152 Five systematic reviews considered the relationship between dietary protein intake and musculoskeletal health outcomes and 1 systematic review considered the relationship between dietary protein intake, including protein supplements and musculoskeletal health outcomes.
- 6.153 Evidence from 2 systematic reviews with meta-analyses of observational studies, considering higher dietary protein intakes and muscle strength and physical performance, was unclear and based on a small number of observational studies with no or small effects. Two systematic reviews, 1 with meta-analysis, observed an association between low dietary protein intakes and a higher prevalence of frailty, however, this was based on cross-sectional studies. Evidence from 3 systematic reviews without meta-analyses, looking at a range of different musculoskeletal health measures, was unclear and based largely on cross-sectional studies.
- 6.154 Evidence on the association between dietary protein intake and musculoskeletal health from observational studies was unclear.

#### Vitamin D supplementation

- 6.155 In its report of the evidence on Vitamin D and Health in 2016, SACN made a number of conclusions in relation to adults  $\geq 50$  years for bone health, fracture risk, muscle strength and function and falls. Since the publication of this review, 4 systematic reviews with meta-analyses were identified and included in this position statement. There was some overlap between RCTs in the systematic reviews included in this position statement and RCTs in the systematic reviews included in the 2016 SACN report (see paragraphs 6.94). A comparison follows of the evidence identified in the 2016 SACN report and the more recent systematic reviews included in this position statement.

- Bone health – the 2016 SACN report found evidence for a small beneficial effect of vitamin D supplementation on femoral neck BMD based on 1 meta-analysis but no effect on BMD in either the spine or hip BMD. The current position statement found no evidence for an effect of vitamin D supplementation on either femoral neck BMD or spine BMD, but this was based on meta-analyses of a small number of RCTs.
- Fracture risk – the 2016 SACN report found mixed evidence for vitamin D supplementation and fracture prevention but on balance, vitamin D supplements had no beneficial effect on fracture risk. The current position statement identified 1 systematic review with meta-analysis, which reported no effect of vitamin D alone, or in combination with calcium, on fracture risk.
- Muscle strength and function – the 2016 SACN report found evidence for a beneficial effect of vitamin D on muscle strength from 3 systematic reviews with meta-analyses. The current position statement reported mixed results from 1 systematic review with meta-analysis, which were based on different measurements (hand grip versus lower limb) and a small number of studies.
- Falls – the 2016 SACN report found evidence for vitamin D supplementation reducing fall risk was mixed but, overall, was suggestive of a beneficial effect. Out of 5 meta-analyses, 4 reported a beneficial effect of vitamin D on risk of falls; in 1 meta-analysis the effect was only seen when vitamin D was combined with calcium. In the current position statement, 1 systematic review with meta-analysis found a significant reduction in the risk of and 1 systematic review with meta-analysis found a significant reduction in the number of fallers but in both cases, only when vitamin D supplementation was combined with calcium.

6.156 SACN published its report on Vitamin D and Health in 2016. The 4 systematic reviews with meta-analyses identified in the current position statement, and not included in the previous SACN analysis, do not provide enough evidence to change the conclusions of the 2016 SACN report.

#### Other nutritional/ dietary supplements

6.157 There was not enough evidence on the relationship between other nutritional and or dietary supplements in older adults to draw conclusions.

#### Diet quality and patterns

6.158 Evidence on the benefits of compliance with a 'healthy' diet or a Mediterranean dietary pattern and measures of musculoskeletal health was largely from systematic reviews of observational studies. Evidence from 1 systematic review with meta-analysis of RCTs and PCS reported no effect between dietary interventions and the control groups on gait speed, balance measures and lower extremity physical function measures in older adults. Evidence from 1 systematic review with meta-analysis of PCS observed an association between adherence to a Mediterranean dietary pattern and a reduced risk of frailty and functional



disability. There was some evidence from 5 systematic reviews without meta-analyses of observational studies that a better diet quality, a 'healthy' diet or adherence to a Mediterranean dietary pattern was associated with a lower risk of being frail and better muscle strength, muscle mass and physical performance outcomes in older adults, however, the majority of the evidence was from cross-sectional studies.

6.159 In summary, evidence on dietary patterns, including a Mediterranean dietary pattern, and musculoskeletal outcomes was too mixed to draw conclusions.

## Cardiovascular health

6.160 Four systematic reviews without meta-analyses were identified that considered the relationship between dietary patterns and/ or specific nutrients and cardiovascular health in older adults. Two systematic reviews looked at a Mediterranean dietary pattern and cardiovascular health (Nowson et al, 2018; Tyrovolas & Panagiotakos, 2010) and 2 looked at supplement intake and cardiovascular health (Ruxton et al, 2016; Stanaway et al, 2017). Three systematic reviews included either RCTs alone and or RCTs and PCS (Nowson et al, 2018; Ruxton et al, 2016; Stanaway et al, 2017) and 1 systematic review included cross-sectional studies (Tyrovolas & Panagiotakos, 2010).

### Mediterranean dietary pattern

Nowson et al (2018)

6.161 A systematic review without meta-analysis identified 1 RCT and 3 PCS which considered the relationship between a Mediterranean dietary pattern and non-fatal cardiovascular events (including ischaemic heart disease and stroke) in community dwelling older adults (Nowson et al, 2018).

6.162 The RCT (7447 participants, >65 years, 4.8 years follow-up) reported a 28% (0.72, 95% CI 0.54 to 0.96; no p value reported) and 30% (0.70, 95% CI 0.54 to 0.92; no p value stated) reduced risk of cardiovascular events for participants following a Mediterranean dietary pattern supplemented with 30g/day mixed nuts or 4 tablespoons/day olive oil, respectively. One PCS reported that a five-point increase in a modified MeDi score (Elderly Dietary Index) was associated with a 34% reduced risk of coronary heart disease (CHD) events (no further statistics reported; 1 PCS, 3328 participants, follow-up 11.3 years), whilst 2 other PCS reported no association.

6.163 The RCT was assessed by the authors as having a low risk of bias; in contrast the authors noted that the evidence from the PCS was subject to confounding.

Tyrovolas & Panagiotakos (2010)

6.164 A systematic review without meta-analysis identified 2 cross-sectional studies investigating the relationship between a Mediterranean dietary pattern and CVD risk (Tyrovolas & Panagiotakos, 2010).

6.165 One cross-sectional study (1190 participants, mean age 76 years for men and 74 years for women) observed a high fish intake was associated with a reduction in cardiovascular risk factors (systolic blood pressure  $p=0.026$ ; fasting glucose  $p<0.001$ ; serum total cholesterol  $p=0.012$ ; triglycerides  $p=0.024$ ) and a reduction in 100g per week of fish was associated with 19% increase in cardiovascular risk factors (hypertension, hypercholesterolemia, diabetes or obesity). There was also an association between cereal intake and reduced risk of hypercholesterolemia

(OR 0.716; p=0.001), reduced risk of diabetes (OR 0.75; p=0.009) and reduced risk of obesity (OR 0.67; p=0.001). There was no association between dairy and fruit and vegetable consumption on cardiovascular health risk factors. The other cross-sectional study (785 participants, age not stated) observed greater adherence to a Mediterranean dietary pattern was associated with lower CVD risk.

- 6.166 Only cross-sectional studies were identified in this review for CVD risk, which are at high risk of confounding.

### **Other nutritional/dietary supplements**

Stanaway et al (2017)

- 6.167 A systematic review without meta-analysis examined the relationship between nitrate supplementation and cardiovascular health outcomes in older adults (Stanaway et al, 2017).
- 6.168 Ten RCTs (175 participants, age ranged from 59.2 to 74.7 years) were identified that looked at blood pressure and nitrate supplementation. Four RCTs were with healthy participants and 6 RCTs were with mixed or participants diagnosed with diabetes, peripheral arterial disease, chronic obstructive pulmonary disease or risk factors for CVD. Most RCTs used inorganic nitrate in the form of beetroot juice as the intervention, with the supplementation period varying from acute (2 to 4 hours before testing) to chronic (14 days). The effect of nitrate on systolic and diastolic blood pressure and endothelial function was inconsistent (no statistics provided).
- 6.169 No detail on confounding or adjustments were provided in the systematic review. The authors noted that the RCTs had a small sample size and there was variance between study designs.

Ruxton et al (2016)

- 6.170 A systematic review without meta-analysis identified 1 RCT that considered the effect of phylloquinone on coronary artery calcification (Ruxton et al, 2016). There was insufficient evidence for SACN to comment on the results.

### **Cardiovascular health summary**

- 6.171 Four systematic reviews without meta-analyses of either RCTs alone, RCTs and PCS or cross-sectional studies alone were identified that considered the relationship between dietary patterns and/ or specific nutrients and cardiovascular health. A systematic review without meta-analysis provided strong evidence from 1 RCT that compliance with a Mediterranean dietary pattern reduced the risk of CVD in older adults; evidence from PCS was mixed.
- 6.172 No systematic reviews were identified which looked specifically at the relationship between dietary fats and cardiovascular health outcomes in older adults. This aligns with the SACN review on Saturated Fats and Health, which concluded that

there was limited evidence on saturated fats and health in older adults and that this evidence did not provide a basis for changing existing recommendations for this age group (SACN, 2019).

## Cancers

Tyrovolas & Panagiotakas (2010)

- 6.173 One systematic review of PCS without meta-analysis considered the relationship between dietary habits and the risk of cancer and cancer mortality (Tyrovolas & Panagiotakas, 2010). The systematic review included 2 relevant PCS in community living older adults (EPIC elderly study, Europe, 99,744 participants; over 65 years; 10 years follow-up; Healthy Ageing: a Longitudinal Study in Europe (HALE), Europe, 2339 participants, 70 to 90 years, 10 years follow-up).
- 6.174 The EPIC Elderly Study observed that specific dietary factors were associated with a lower risk of different cancers and in particular, reported a reduced risk of colorectal cancer with a high fibre intake (top compared to bottom quintile) (adjusted RR=0.58, 95% CI 0.41 to 0.85); nut and seed intake in women (colon cancer, no statistics provided) and elevated fish intake (>80g/day versus <10g/day) (HR=0.69, 95% CI 0.54 to 0.88,  $p < 0.001$ ; 99,744 participants). A high intake of red or processed meat (highest >160g/day versus lowest <20g/day) was associated with increased colorectal cancer risk (HR 1.35, 95% CI 0.96 to 1.88,  $p=0.03$ ; 99744 participants). Fruit was associated with a protective effect on lung cancer risk (highest quintile compared to lowest quintile) (after adjustment HR 0.60, 95% CI 0.46 to 0.78,  $p=0.0099$ ; 99,744 participants) but no association was reported for vegetables. There was no association between fruit and vegetable intake and prostate cancer (1104 incident cases).
- 6.175 For the HALE PCS, the authors reported that adherence to a Mediterranean dietary pattern “was associated with a lower likelihood of having cancer” and that “60% of deaths due to cancer were attributed to an unhealthy lifestyle”.
- 6.176 The authors stated that they graded the included evidence on factors including confounding. However, no further details were provided and so the extent of confounding is unclear. The authors noted that geographical differences in the genetic risk for cancer may have over- or under-estimated the results in previous studies.

### Cancers summary

- 6.177 Only 1 systematic review of PCS was identified which considered the relationship between dietary factors and cancers in older adults.
- 6.178 In summary, the findings of this 1 systematic review broadly reflects the wider evidence base for the general adult population, that ‘healthier’ dietary patterns may reduce the risk for some cancers.

## **Immune health**

Ruxton et al (2016)

- 6.179 One systematic review without meta-analysis considered the relationship between dietary intake of fatty acids and various micronutrients and healthy ageing markers in 5 RCTs (1114 participants, >60 years) (Ruxton et al, 2016).
- 6.180 Based on very limited data the systematic review suggests there may be some effects of fatty acids or micronutrients on some aspects of immune health, but not others. No detail on confounding or adjustments were provided in the systematic review.

### **Immune health summary**

- 6.181 Only 1 systematic review of RCTs was identified that investigated immune health. Due to the variety of interventions and components of immune function included it was not possible to draw conclusions.

## Weight change

6.182 Two systematic reviews with meta-analyses (Dewansingh et al, 2018; Milne et al, 2006) of RCTs were identified that considered the relationship between energy and macronutrient intake and weight change in older adults.

(Dewansingh et al, 2018)

6.183 A systematic review with meta-analysis of 8 RCTs (418 participants, mean age ranged from 71 to 86 years) considered the relationship between protein and amino acid supplementation and body weight in older adults (Dewansingh et al, 2018). The majority of the RCTs were based in the community except 1 RCT of 103 participants in a nursing home.

6.184 Protein or amino acid supplementation was reported to significantly increase body weight (MD 1.13kg; 95% CI 0.59 to 1.67;  $p < 0.0001$ ;  $I^2 = 0\%$ ; 8 RCTs, 418 participants, mean age 71 to 86 years, intervention duration 10 days to 6 months). There was also a significant increase in body weight when the meta-analysis was limited to the RCTs that used a mixture of amino acids (MD 2.16kg; 95% CI 0.93 to 3.38;  $p = 0.0006$ ;  $I^2 = 0\%$ ; 5 RCTs, 330 participants, mean age 71 to 86 years, intervention duration 10 days to 6 months), the RCTs with a duration greater than 6 months (MD 2.09kg; 95% CI 0.88 to 3.29;  $p = 0.0007$ ;  $I^2 = 0\%$ ; 5 RCTs, 264 participants, mean age 71 to 86 years) and the RCTs that supplemented more than 20g/day of protein intake (MD 1.55kg; 95% CI 0.75 to 2.35;  $p = 0.0001$ ;  $I^2 = 0\%$ ; 5 RCTs, 330 participants, mean age 71 to 86 years, intervention duration 10 days to 6 months). There was also a significant increase in body weight with protein supplementation in combination with exercise compared to a control (MD 0.78kg; 95% CI 0.06 to 1.51;  $p = 0.03$ ;  $I^2 = 0\%$ ; 4 RCTs, 179 participants).

6.185 No information was included in the systematic review about the baseline weight status of study participants, specifically whether they fell into the under- or overweight or obese categories. Only one study specified that participants were healthy; in the other studies the health status was either not reported (3 RCTs) or participants were frail or prefrail (2 RCTs), had type 2 diabetes (1 RCT) or were mobility limited (1 RCT).

(Milne et al, 2006)

6.186 A systematic review with meta-analysis of 16 RCTs (1070 participants,  $>65$  years) considering the relationship between protein supplementation and body weight in older adults living in the community (Milne et al, 2006). Most RCTs aimed to provide between 175kcal (732KJ) and 1000kcal (4.2MJ) of energy and between 10g and 36g of protein daily.

6.187 There was a significant increase in weight with protein supplementation (pooled weighted MD for percentage weight change = 2.2%, 95% CI 1.70 to 2.76;  $p < 0.001$ ;  $I^2 = 14\%$ ; 16 RCTs, 1070 participants,  $>65$  years, intervention duration  $>8$  weeks).

The authors note that many of the included RCTs were of short duration and of poor quality.

- 6.188 The authors noted that the studies included in the systematic review were generally of poor quality. In addition, information on the baseline health and nutritional status of the study participants varied. Of the 16 studies included, only one specified that participants were healthy; in the other studies the health status was either not stated (9 RCTs) or participants had different health conditions (6 RCTs). Additionally, 8 of the 16 studies were undertaken with study participants with undernutrition.

### **Weight change summary**

- 6.189 There was evidence from 2 systematic reviews with meta-analyses of RCTs that protein supplements may increase body weight in healthy, pre-frail and malnourished older adults.
- 6.190 Many of the included trials were short term and reporting of participant weight and health status at baseline was limited.



## Quality of life

6.191 Two systematic reviews without meta-analyses were identified that considered the relationship between dietary patterns and micronutrient intake and quality of life in older adults (Govindaraju et al, 2018; Ruxton et al, 2016). One systematic review included RCTs (Ruxton et al, 2016) and the other included PCS and cross-sectional studies (Govindaraju et al, 2018).

Govindaraju et al (2018)

6.192 A systematic review without meta-analysis considered the association between dietary patterns and self-reported quality of life or self-rated health status (5 PCS, 8119 participants; 7 cross-sectional studies, 15,962 participants, mean age <60 years) (Govindaraju et al, 2018).

6.193 The evidence from PCS was inconsistent on measures of quality of life and different dietary patterns. Four studies (2 PCS, 2 cross-sectional studies) found a significant association between a Mediterranean dietary pattern (measured by variety of tools) and quality of life; 1 PCS found that those in the middle and highest tertiles of adherence to a Mediterranean dietary pattern had a higher Physical Component Score (quality of life assessment) compared to the lowest tertile (1<sup>st</sup> vs 3<sup>rd</sup> tertile: beta coefficient = 1.34, 95% CI 0.21 to 2.47, 1911 participants, mean age 60 years, follow-up not reported); the other PCS (2457 participants, mean age 60 years, follow-up not reported) found that those in the top quartile of adherence to a Mediterranean dietary pattern had a higher score for “energy” (OR = 1.53, 95% CI 1.11 to 2.10) and general health (OR = 1.52, 95% CI 1.11 to 2.08, adjusted for smoking and physical activity) compared to the lowest quartile.

6.194 Two studies (2 PCS) reported a significant association between adherence to dietary guidelines and different measures of quality of life (1 PCS, Health related quality of life OR = 1.56, 95% CI 1.22 to 1.99; bodily pain OR = 1.29, 95% CI 1.01 to 1.63; general health OR = 1.72, 95% CI 1.36 to 2.19; “energy” OR = 1.51, 95% CI 1.19 to 1.92; emotional wellbeing OR = 1.36, 95% CI 1.08 to 1.72; Physical Component Score OR = 1.46, 95% CI 1.15 to 1.86, 2457 participants, mean age 60 years, follow-up not reported; 1 PCS, 895 participants, mean age 67 years, 5 years follow-up, no statistics reported). One of the 2 studies above (1 PCS) also measured diet quality with a “Recommended Food Score”, which was associated with a significantly better health-related quality of life (OR = 1.41, 95% CI 1.13 to 1.82), general health (OR = 1.41, 95% CI 1.12 to 1.78), “energy” (OR = 1.55, 95% CI 1.22 to 1.96) and emotional wellbeing (OR = 1.41, 95% CI 1.12 to 1.77, 2457 participants, mean age 60 years, follow-up not reported).

6.195 Two studies did not find any significant association between ‘healthier’ dietary pattern and quality of life measures (2 PCS, 480 and 2376 participants, mean age

60 and 73 years). Five cross-sectional studies showed that better diet quality was associated with a variety of quality of life measures.

- 6.196 The majority of the studies scored 'strong' for addressing confounders. Key limitations of this review were that included studies were all observational, which are subject to confounding, and they used multiple measures of quality of life, making it difficult to compare studies.

Ruxton et al (2016)

- 6.197 A systematic review without meta-analysis identified 1 RCT (182 participants, >60 years) that reported a significant increase in self-reported energy levels ( $p=0.022$ ) (especially for women) and enhanced mood ( $p=0.027$ ) following a daily multivitamin supplement for 16 weeks (Ruxton et al, 2016). However, this was based on only 1 RCT.

### **Quality of life summary**

- 6.198 There was not enough evidence investigating quality of life and dietary intake to draw conclusions, with most of the evidence coming from observational studies.

# 7 Overall summary and conclusions

## Overall summary

- 7.1 In July 2018, SACN convened a working group to consider the evidence on nutrition and older adults. The terms of reference were:
- to review current evidence on the role of nutrition in community-dwelling older adults and its impact on healthy ageing. This will include consideration of:
    - key nutritional issues relevant to age-related health, including age-related changes in cognition, physical and metabolic function
    - current dietary intake and patterns compared to current UK government advice
    - evidence according to chronological age: 65 to 74 years, 75 years and above
  - to draw conclusions on the state of the evidence in relation to existing advice and make recommendations where possible.

## Background

- 7.2 The UK population has changed in recent decades and there is an increasing proportion and number of older adults. Currently 1 in 5 people are aged 65 years and over; life expectancy at age 65 years is 18.6 years for males and 21 years for females. Ageing is a life-long process and how people age can be modified by a range of influences throughout life, including diet.
- 7.3 A broad range of cultural, environmental and social factors can impact on health and dietary intake in older adulthood. The risk of many diseases and chronic conditions increases with age and more than half of UK adults aged over 65 years have at least two chronic health conditions that may affect day to day living. Other age-related changes in physical and metabolic function may also affect dietary intake.
- 7.4 Nutrition, age-related physiological changes and health are often interconnected. In some cases, age-related physiological changes, advancing illness and medication use can impact on nutritional intake and status. In other cases, nutritional intake and status can affect how people age and their health status in relation to a wide range of functions and conditions, including appetite, oral health, hydration, gastrointestinal health, cardiovascular health, type 2 diabetes, endocrine function, eye health, immune health, skin health, cognitive health and musculoskeletal health.

## **Dietary intakes and BMI**

- 7.5 Overall the NDNS data on diet, nutrient intakes and blood analytes for people aged 65 to 74 years and 75 years and over indicate that, similar to all UK adults, older adults exceed maximum recommendations for intakes of saturated fat, free sugars and salt and fail to meet recommendations for fruit and vegetables, fibre and oily fish.
- 7.6 The NDNS shows that energy intakes decline with age. Mean energy intakes were below EARs in both age/sex groups although evidence from doubly labelled water studies suggests that this was likely to be at least partly due to underreporting. NDNS data on BMI show that 87% of men and 68% of women in the 65 to 74 years age group were living with overweight or obesity, a higher percentage than for younger adults (19 to 64 years). In the 75 years and over age group, 69% of men and 58% of women were living with overweight or obesity, similar to the 19 to 64 years age group. The prevalence of underweight was low: 7% and 3% of men and women, respectively, in the 75 years and over age group and less than 1% of men and 3% of women in the 65 to 74 years age group were underweight. It should be noted that these percentages are based on small numbers of participants. The high prevalence of overweight and obesity in older adults suggests that energy intakes are generally likely to be adequate in this age group. Mean protein intakes met the RNI in all age/sex groups although they also showed a decline with age. Intakes of saturated fat and, for men, free sugars were higher in those aged 75 years and over.
- 7.7 There was some evidence of low micronutrient intakes, particularly in women and the 75 years and over age group; this was also seen in younger women (19 to 64 years). There was also evidence of poor status for vitamin D (particularly in those aged 75 years and over) and folate, and to a lesser extent for iron and vitamin B12, which was also seen in younger adults.
- 7.8 The diets of the 65 to 74 years age group are in some respects similar to, and for some foods and nutrients, better than the 19 to 64 years age group, particularly for women. However, for the 75 years and over age group there was evidence of a decline in energy, protein and micronutrient intakes particularly in women although protein intakes met the RNI. Based on the available data for the 80 years and over age group (pooled over 8 years), there was no evidence of poorer diets in this age group compared with the 75 years and over age group. However, data on this age group was available only for energy and nutrient intakes and consumption of selected foods and was collected over a longer time period than the data for younger age groups.
- 7.9 Although the NDNS sample is designed to be representative of the population in each age group, it is possible that the sample may underrepresent those who have long term health conditions which make it more difficult to take part in a survey.

## Methods

- 7.10 A search of key online databases (Embase, MEDLINE, Cochrane Library, and Food Science Technology Abstracts) was conducted in November 2018 to identify relevant English language articles published between 1990 and 9 November 2018, using an agreed list of search terms focusing on nutrition and healthy ageing.
- 7.11 This position statement considers evidence, primarily from systematic reviews and meta-analyses of Randomised Controlled Trials (RCTs) and Prospective Cohort Studies (PCS), examining the relationship between nutrition and healthy ageing in community-dwelling older adults aged 65 years and over. There was particular interest in age-related changes in cognitive, physical and metabolic function in relation to the following outcomes:
- mortality
  - musculoskeletal health (including bone and joint health and sarcopenia)
  - cardiovascular health (including circulation)
  - cancer
  - immune health
  - oral health
  - weight change
  - quality of life
  - eye health
  - skin and wound healing.
- 7.12 A number of important limitations were identified in the evidence included in this position statement and in the older adults evidence base in general.
- 7.13 Limitation specific to the position statement included: small number of RCTs and/or PCS included in the systematic reviews; the RCTs were of short duration and often included a small number of participants; different definitions of healthy ageing between studies; different age ranges of participants; some individual studies in the systematic reviews conducted in hospital settings rather than in the community; use of different dietary assessment methods; inclusion of cross-sectional and case-control studies with results not consistently presented separately; and studies failed to account for mediating factors that are common in older age, such as difficulty with swallowing or poor dentition.
- 7.14 Limitations of the older adults evidence base in general include: the diversity of the age group with chronological age being a poor indicator of an older adult's health status; and dietary assessment in some older people posing a number of challenges and ethical considerations, which may be particularly the case for the oldest old. Challenges may include, for example, limits in participants' cognitive and/or physical abilities, the high burden imposed on study participants, possible indirect reporting of food intakes by a carer or spouse, and limited participation in food shopping or preparation.

## Results

- 7.15 Thirty eligible systematic reviews, of which 15 included a meta-analysis, were identified and included in this position statement. Fourteen systematic reviews included only RCTs, 12 systematic reviews included PCS and cross-sectional studies, 2 systematic reviews included RCTs, PCS and cross-sectional studies, 1 systematic review included RCTs, PCS and case-control studies and 1 systematic review included PCS, cross-sectional studies and case-control studies.
- 7.16 The AMSTAR 2 tool was used to assess the methodological quality of each included systematic review (see Annex 4.5) and to help aid discussion but it was not used to draw conclusions on the evidence.
- 7.17 Much of the available evidence was considered to be of poor quality and where meta-analyses had been carried out, in some cases only a small number of RCTs or PCSs were included. For some outcomes there were a limited number of systematic reviews in adults over 65 years. Many of the systematic reviews considering observational evidence included PCS and cross-sectional studies, as well as case-control studies in 2 systematic reviews, all of which are subject to confounding and reverse causality.
- 7.18 The majority of the available literature on older adults considers musculoskeletal health outcomes. No evidence that met the inclusion criteria was identified on oral health, gastrointestinal tract health, eye health, hydration or skin and wound health.
- 7.19 There is a paucity of evidence on the relationships between diet, health and functioning in adults aged 85 years and over who are at increased risk of multimorbidity, disability, frailty and malnutrition. There is also little available evidence on any potential adverse health effects associated with nutrient deficiencies in this age group.
- 7.20 There was insufficient evidence to draw any conclusions in older adults in black, Asian and minority ethnic groups, as most of the systematic reviews or meta-analyses did not consider ethnicity.

## Mortality

- 7.21 There was evidence from 1 systematic review with meta-analyses of observational studies of an association between a BMI  $<25\text{kg/m}^2$  or BMI  $>30\text{kg/m}^2$  and a greater risk of mortality in older adults living in the community, with optimal BMI between approximately 25 and  $30\text{kg/m}^2$ . One systematic review with meta-analysis of RCTs indicated that protein and energy supplements had no effect on reducing mortality or morbidity in older adults living in the community regardless of nutritional status, however the authors noted that the RCTs considered were generally of poor quality. The evidence on the association between dietary patterns and mortality was mixed and only based on a small number of observational studies.

## **Musculoskeletal health**

### **Body mass index (BMI)**

- 7.22 Three systematic reviews included evidence from PCS and cross-sectional studies on the association between BMI and musculoskeletal health. Evidence from 1 systematic review with meta-analysis of PCS observed the lowest risk of at least 1 fall in participants with a BMI between 24.5 and 30.0kg/m<sup>2</sup>. In the 2 systematic reviews without meta-analyses, 1 systematic review observed an association between a higher BMI and a higher muscle strength, muscle mass and improved physical performance, whereas the evidence on BMI and frailty from the other systematic review was unclear. Most studies in the 2 systematic reviews without meta-analyses were cross-sectional and BMI figures were not provided in the first review.
- 7.23 In summary, it was not possible to draw conclusions on the association between BMI and musculoskeletal health as evidence from systematic reviews reported on different musculoskeletal health outcomes and most evidence was from cross-sectional studies.

### **Protein**

#### **Protein supplements**

- 7.24 Nine systematic reviews considered the relationship between protein supplements and musculoskeletal health outcomes and 1 systematic review considered the relationship between dietary protein intake, including protein supplements, and musculoskeletal health outcomes.
- 7.25 Overall the evidence from 6 systematic reviews with meta-analyses of RCTs reported no significant effect of protein or amino acid supplements on musculoskeletal health in older adults, including measures of upper and lower muscle strength, muscle mass and physical performance. The evidence from systematic reviews without meta-analyses of RCTs was unclear.
- 7.26 Evidence from 2 systematic reviews with meta-analyses of RCTs reported no additional benefit of protein supplements in combination with exercise on muscle strength or muscle mass compared with exercise alone. One systematic review without meta-analysis of RCTs included evidence from 1 RCT which suggested that protein supplements in combination with exercise had a positive effect on muscle strength and muscle mass, however, overall the evidence was unclear.
- 7.27 In summary, evidence from meta-analyses of RCTs suggests no significant effect of protein supplements on measures of musculoskeletal health in older adults, although there was considerable heterogeneity in interventions, population groups and outcome measures.

## Dietary protein

- 7.28 Five systematic reviews considered the relationship between dietary protein intake and musculoskeletal health outcomes and 1 systematic review considered the relationship between dietary protein intake, including protein supplements, and musculoskeletal health outcomes.
- 7.29 Evidence from 2 systematic reviews with meta-analyses of observational studies, which considered higher dietary protein intakes, muscle strength and physical performance, was unclear and based on a small number of observational studies reporting no or small effects. Two systematic reviews, 1 with meta-analysis, observed an association between low dietary protein intakes and a higher prevalence of frailty, however, these were based on cross-sectional studies. Evidence from 3 systematic reviews without meta-analyses, looking at a range of different musculoskeletal health measures, was unclear and based largely on cross-sectional studies.
- 7.30 Evidence on the association between dietary protein intake and musculoskeletal health from observational studies was unclear.

## Vitamin D

- 7.31 In its report of the evidence on Vitamin D and Health in 2016, SACN reached a number of conclusions in relation to bone health, fracture risk, muscle strength and function, and falls in adults  $\geq 50$  years. Since the publication of this review, 4 systematic reviews with meta-analyses were identified and included in this position statement. Overall, there was some overlap between RCTs in the systematic reviews included in this position statement and RCTs in the systematic reviews included in the 2016 SACN report. A comparison follows of the evidence identified in the 2016 SACN report and the more recent systematic reviews included in this position statement.
- Bone health: the 2016 SACN report found evidence for a small beneficial effect of vitamin D supplementation on femoral neck BMD based on 1 meta-analysis but no effect on BMD in either the spine or hip BMD. The current position statement found no evidence for an effect of vitamin D supplementation on either femoral neck BMD or spine BMD based on meta-analyses of a small number of RCTs.
  - Fracture risk: the 2016 SACN report found mixed evidence for vitamin D supplementation and fracture prevention but on balance, vitamin D supplements had no beneficial effect on fracture risk. The current position statement identified 1 systematic review with meta-analyses which reported no effect of vitamin D alone, or in combination with calcium, on fracture risk.



- Muscle strength and function: the 2016 SACN report found evidence for a beneficial effect of vitamin D on muscle strength from 3 systematic reviews with meta-analyses. The current position statement reported mixed results from 1 systematic review with meta-analysis, which were based on different measurements (hand grip versus lower limb) and a small number of studies.
- Falls: the 2016 SACN report found evidence for vitamin D supplementation reducing fall risk was mixed but, overall, was suggestive of a beneficial effect. Out of 5 meta-analyses, 4 reported a beneficial effect of vitamin D on risk of falls; in 1 meta-analysis the effect was only seen when vitamin D was combined with calcium. In the current position statement, 1 systematic review with meta-analyses found a significant reduction in the risk of falls and 1 systematic review with meta-analysis found a significant reduction in the number of fallers but in both cases, only when vitamin D supplementation was combined with calcium.

7.32 Overall, the 4 vitamin D systematic reviews with meta-analyses identified in the current position statement, and not included in the previous SACN analysis, do not provide enough evidence to change the conclusions of the 2016 SACN report on Vitamin D and Health.

#### Other nutritional/ dietary supplements

7.33 There was not enough evidence on the relationship between other nutritional and/or dietary supplements in older adults to draw conclusions.

#### Diet quality and patterns

7.34 Evidence on the benefits of compliance with a 'healthy' diet or a Mediterranean dietary pattern and measures of musculoskeletal health was largely from systematic reviews of observational studies. Evidence from 1 systematic review with meta-analyses of mostly RCTs reported no effect between dietary interventions and the control groups on gait speed, balance measures and lower extremity physical function measures in older adults. Evidence from 1 systematic review with meta-analysis of PCS observed an association between adherence to a Mediterranean dietary pattern and a reduced risk of frailty and functional disability. There was some evidence from 5 systematic reviews without meta-analyses of observational studies that a better diet quality, a 'healthy' diet or adherence to a Mediterranean dietary pattern was associated with a lower risk of being frail and better muscle strength, muscle mass and physical performance outcomes in older adults. However, the majority of the evidence was from cross-sectional studies.

7.35 In summary, evidence on dietary patterns, including a Mediterranean dietary pattern, and musculoskeletal outcomes was too mixed to draw conclusions.

## **Cardiovascular health**

- 7.36 Four systematic reviews without meta-analyses of either RCTs alone, RCTs and PCS, or cross-sectional studies alone were identified that considered the relationship between dietary patterns and/or specific nutrients and cardiovascular health. A systematic review without meta-analyses provided strong evidence from 1 RCT that compliance with a Mediterranean dietary pattern reduced the risk of CVD in older adults; evidence from PCS was mixed.
- 7.37 No systematic reviews were identified which looked specifically at the relationship between dietary fats and cardiovascular health outcomes in older adults. This aligns with the SACN review on Saturated Fats and Health, which concluded that there was limited evidence on saturated fats and health in older adults and that the evidence did not provide a basis for changing existing recommendations for this age group (SACN, 2019).

## **Cancers**

- 7.38 Only 1 systematic review of PCS was identified which considered the relationship between dietary factors and cancers in older adults. In summary, the findings of this 1 systematic review broadly reflect the wider evidence base for the general adult population, that 'healthier' dietary patterns may reduce the risk for some cancers.

## **Immune health**

- 7.39 Only 1 systematic review of RCTs was identified that investigated immune health. Due to the variety of interventions and components of immune function included it was not possible to draw conclusions.

## **Weight change**

- 7.40 There was evidence from 2 systematic reviews with meta-analyses of RCTs that protein supplements may increase body weight in healthy, pre-frail and malnourished older adults.
- 7.41 Many of the included trials were short term and reporting of participant weight and health status at baseline was limited.

## **Quality of life**

- 7.42 There was not enough evidence investigating quality of life and dietary intake to draw conclusions, with most of the evidence derived from observational studies.

## **Oral health**

- 7.43 No systematic reviews or meta-analyses were identified that investigated the impact of diet on oral health in relation to healthy ageing.
- 7.44 SACN's Carbohydrates and Health report (2015) considered evidence on the role of carbohydrates in cardio-metabolic, colorectal and oral health and made recommendations for free sugars (and fibre) for the whole population (including older adults). The report identified a lack of evidence in adults; evidence on the association between carbohydrates and oral health was only identified in children and adolescents.
- 7.45 Cross-sectional data from the NDNS showed that intakes of energy, protein, fibre and micronutrients were generally slightly lower in older adults with no natural teeth, while intakes of free sugars, fat and saturated fat were slightly higher.

## **Overall conclusions**

- 7.46 Data from the NDNS indicate that older adults exceed maximum recommendations for intakes of saturated fat, free sugars and salt and fail to meet recommendations for fruit and vegetables, fibre and oily fish, similar to the overall UK adult population. Energy intakes decline with age. Mean energy intakes were below EARs in both the 65 to 74 years and 75 years and over groups although this is likely to be at least partly due to underreporting. A high percentage of older adults in the NDNS were living with overweight or obesity, particularly in the 65 to 74 years age group, in which the prevalence was higher than in the 19 to 64 years age group, and the prevalence of underweight was low. The prevalence of overweight and obesity in older adults suggests that energy intakes are likely to be adequate. Mean protein intakes met the RNI in men and women age 65 years and over although they also showed a decline with age. Intakes of saturated fat and, for men, free sugars were higher in older adults age 75 years and over.
- 7.47 There was some evidence of low micronutrient intakes, particularly in women and in the 75 years and over age groups, and of poor status for vitamin D and folate, and to a lesser extent for iron and vitamin B12. SACN noted the usefulness of the NDNS in providing information on nutritional intake and status in older adults, though recognised that the information was based on a limited number of participants, particularly those aged 80 years and over. Data collected over 8 years for this age group was pooled to give sufficient numbers for analysis. Based on the available data there was no evidence of poorer diets in the 80 years and over age group. However, although the NDNS sample is designed to be representative of the population in each age group, it is possible that the sample may underrepresent those who have long term health conditions which make it more difficult to take part in a survey.

- 7.48 This position statement identified large gaps in the evidence for older adults for many outcomes and a number of important limitations including: small numbers of RCTs or PCS included in the meta-analyses; RCTs with short durations; cross-sectional studies considered alongside PCS; large differences in the health status of older adults; and insufficient evidence to draw conclusion in older adults in black, Asian and minority ethnic groups.
- 7.49 The majority of the evidence identified in this position statement focused on musculoskeletal health outcomes, including sarcopenia (muscle strength, muscle mass, physical performance), frailty and bone health. It was not possible to draw conclusions on the association between BMI and musculoskeletal health as evidence from systematic reviews reported on different outcomes of musculoskeletal health and most evidence was from cross-sectional studies. Evidence from meta-analyses of RCTs suggested no significant effect of protein supplements on measures of musculoskeletal health in older adults. Evidence from systematic reviews of observational studies on the association between dietary protein intake and musculoskeletal health was unclear. However, different measures of musculoskeletal health were considered in the various systematic reviews and the studies had a number of limitations (discussed above).
- 7.50 SACN published its report on Vitamin D and Health in 2016. The 4 vitamin D systematic reviews with meta-analyses identified in the current position statement, and not included in the previous SACN analysis, do not provide enough evidence to change the conclusions of the 2016 SACN report on Vitamin D and Health.
- 7.51 There was very little evidence from RCTs on dietary patterns and musculoskeletal outcomes. Evidence from observational studies suggested adherence to 'healthy' diets or a Mediterranean dietary pattern improved measures of musculoskeletal health. However, different definitions of a 'healthy' diet were used and much of the evidence was from cross-sectional studies. Overall, the evidence was too mixed to draw conclusions.
- 7.52 Evidence that was available from 1 systematic review of PCS on a Mediterranean dietary pattern and cancer broadly reflected the wider evidence base for the general adult population, that 'healthier' dietary patterns may reduce the risk of some cancers.
- 7.53 There was mixed evidence from 1 systematic review that compliance with a Mediterranean dietary pattern reduced the risk of CVD in older adults.
- 7.54 No systematic reviews were identified which looked specifically at the relationship between dietary fats and cardiovascular health outcome in older adults. This aligns with the SACN review on Saturated Fats and Health (SACN, 2019) which concluded that there was limited evidence on saturated fats and health in older adults and that this evidence did not provide a basis for changing existing recommendations for this age group (SACN, 2019).

- 7.55 For the outcomes of overall mortality and morbidity, immune function, weight change and quality of life, there were gaps in the evidence and a limited number of systematic reviews specifically studying older adults age 65 years and over.
- 7.56 As SACN published its Statement on Diet, Cognitive Impairment and Dementias in 2018, nutrition and cognition were not considered in this position statement. The 2018 position statement concluded that adherence to a Mediterranean dietary pattern was associated with a reduced risk of mild cognitive impairment and dementias, including Alzheimer's disease. There was no evidence of protective effects for any of the individual nutrients thought to account for the health benefits of a Mediterranean dietary pattern (SACN, 2018).
- 7.57 Based on the current review of the available literature, there is not enough evidence for SACN to consider conducting a full risk assessment on older adults at this time. SACN will continue to consider older adults as a population group of interest within relevant future risk assessments.

## 8 Research recommendations

- 8.1 This position statement has identified an overall need for high quality evidence from RCTs and longitudinal studies on nutrition-related outcomes for older adults living in the community.
- 8.2 Throughout the development of this position statement, a number of limitations in the available evidence were identified (see chapter 5). It is therefore recommended that future research:
- considers nutrition and health in adults aged 85 years and over
  - considers nutrition in older adults from black, Asian and minority ethnic groups
  - makes use of opportunities for sub-analysis or re-analysis of data from existing studies with a greater focus on older adults
  - better defines participants, for example, providing clear information on age range and health status
  - provides more specific details on nutritional interventions, for example the type and amount of protein used
  - standardises outcome measures, in particular for measures of musculoskeletal health
  - takes account of mediating factors related to oral health such as swallowing or poor dentition
  - uses study designs that enable more definitive conclusions to be drawn regarding potentially effective components of the diet in older adults.
- 8.3 A number of gaps in the evidence were identified during the development of this position statement. Further research is required to define the role of dietary patterns and/or specific nutrients on healthy ageing, including but not limited to the following areas:
- cardiovascular health
  - cancer
  - gastrointestinal tract health
  - eye health
  - hydration
  - skin and wound healing
  - appetite control and energy balance
  - oral health
  - immune health.

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# Annexes

# Annex 1 - International energy and nutrient recommendations for older adults

**Table 1: International energy and macronutrient recommendations for older adults**

Nutrient recommendations	Organisation and country				
	UK Dietary Reference Values (COMA 1991 <sup>a</sup> ; 1994 <sup>b</sup> ; SACN 2011 <sup>c</sup> ; 2019 <sup>d</sup> )	European Food Safety Authority (EFSA) (2017) (Europe) (65 years and older)	Nordic Council of Ministers (2012) (Nordic countries) (61 to 74 years)	US Department of Health and Human Service and US Department of Agriculture (2015) (USA) (65 years and older)	Australian Government Department of Health and the New Zealand Ministry of Health (2013) (Australia and New Zealand) (>70 years)
<b>Energy</b>	<p>EAR:</p> <p>65-74 years: Male: 2342kcal/day (9.8MJ/day) Female: 1912kcal/day (8.0MJ/day)</p> <p>75 years and over Male: 2294kcal/day (9.6MJ/day) Female: 2840kcal/day (7.7MJ/day)</p>	<p>AR:</p> <p>60 to 69 years: Male: 8.4 to 12.1 MJ/day Female: 6.8 to 9.7 MJ/day</p> <p>70 to 79 years: Male: 8.3 to 11.9 MJ/day Female: 6.8 to 9.6 MJ/day</p>	<p>Males: 8.5 to 10.9 MJ/day Females: 7.1 to 9.1 MJ/day</p>	<p>Broken down to following ages: 66-70, 71-75 and 76 &amp;Up (all recommending the same): Males: 2000kcal to 2600kcal Females 1600 to 2000 kcal</p> <p>(Daily nutritional goals are based on females: 1600kcal and Males: 2000kcal and are for adults aged over 51 years)</p>	<p>Males: 9.5 MJ to 12.1 MJ/day Females: 7.1 MJ to 9.1 MJ/day</p>

Nutrient recommendations	Organisation and country				
	UK Dietary Reference Values (COMA 1991 <sup>a</sup> ; 1994 <sup>b</sup> ; SACN 2011 <sup>c</sup> ; 2019 <sup>d</sup> )	European Food Safety Authority (EFSA) (2017) (Europe) (65 years and older)	Nordic Council of Ministers (2012) (Nordic countries) (61 to 74 years)	US Department of Health and Human Service and US Department of Agriculture (2015) (USA) (65 years and older)	Australian Government Department of Health and the New Zealand Ministry of Health (2013) (Australia and New Zealand) (>70 years)
<b>Protein</b>	RNI (all adults) 0.75g/kg body weight/day Equivalent to: 65-74 years and 75 years and over Male: 53.3g/day Female: 46.5g/day	AR (all adults): Male: 0.66 g/day Female: 0.66g/day  PRI (all adults): Male: 0.83 g/day Female: 0.83 g/day  <i>The Panel noted that the protein requirement for older adults are considered to be equal to that of adults, but the protein to energy ratio may be higher than younger age groups.</i>	≥65years: 15-20% of energy (1.1-1.3g/kg BW)	AMDR: 10-35% of energy* RDA: 51 years and up: Male: 54g Female: 46g	RDI: Male: 81g/day (1.07g/kg) Female: 57g/day (0.94 g/kg)  EAR: Male: 65 g/day (0/86g/kg BW) Female: 46g/day (0.75 g/kg BW)
<b>Total fat</b>	DRV (all adults) About 35% of energy	RI (all adults): 20-35 % of energy	25-40% of energy (recommendation from age 2 up)	AMDR: 20-35% of energy*	At or below 35% of energy*
<b>Saturated fat</b>	DRV (all adults) No more than about 10% of total dietary energy	As low as possible (all adults)	<10% energy		

Nutrient recommendations	Organisation and country				
	UK Dietary Reference Values (COMA 1991 <sup>a</sup> ; 1994 <sup>b</sup> ; SACN 2011 <sup>c</sup> ; 2019 <sup>d</sup> )	European Food Safety Authority (EFSA) (2017) (Europe) (65 years and older)	Nordic Council of Ministers (2012) (Nordic countries) (61 to 74 years)	US Department of Health and Human Service and US Department of Agriculture (2015) (USA) (65 years and older)	Australian Government Department of Health and the New Zealand Ministry of Health (2013) (Australia and New Zealand) (>70 years)
<b>Total carbohydrate</b>	DRV (all adults) Approximately 50% of total dietary energy	RI (all adults): 45-60% of energy	45-60% of energy	AMDR: 45-65% of energy* RDA: 51 years and up: Male: 130g Female: 130g	45-65% of energy*
<b>Fibre</b>	DRV (all adults) 30g/day	AI (all adults): 25 g/day	>3g/MJ Male: ≥35g/day Female: ≥25g/day	14g/1000kcal (based on AI): Male: 28g/day Female: 22.4g/day	AI: Male: 30g/day Female: 25g/day

RD1: Reference daily intake; EAR: Estimated average requirement; AI: Adequate intake; RDA: recommended dietary allowance; AMDR: acceptable macronutrient disruption range; BW: body weight; RI: Reference intake; PRI: Population reference intake; AR: Average requirement; SC: Satisfactory contribution

\*unclear if the recommendation is for total energy or food energy.

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<sup>h</sup> Nordic Nutrition Recommendations 2011. Integrating Nutrition and Physical Activity. 5<sup>th</sup> edition. <http://dx.doi.org/10.6027/Nord2014-002>

<sup>i</sup> Dietary Guidelines for Americans 2015-2020 eighth edition <https://health.gov/our-work/food-nutrition/2015-2020-dietary-guidelines/guidelines/>

<sup>j</sup> Australian Government National Health and Medical Research Council; New Zealand Ministry of Health Nutrient Reference Values for Australia and New Zealand

**Table 2: International micronutrient recommendations for older adults**

Nutrient recommendations	Organisation and country				
	UK	European Food Safety Authority (EFSA) (2017) (Europe) (65 years and older)	Nordic Council of Ministers (2012) (Nordic countries) (61 to 74 years)	US Department of Health and Human Service and US Department of Agriculture (2015) (US) (65 years and older)	Australian Government Department of Health and the New Zealand Ministry of Health (2013) (Australia and New Zealand) (>70 years)
<b>Folate (as dietary folate equivalents)</b>	<p>RNI 65 years and over Male: 200µg/day Female: 200µg/day</p> <p>LRNI 65 years and over Male: 100µg/day Female: 100µg/day</p>	<p>AR (all adults): Male: 250 µg/day Female: 250 µg/day</p> <p>PRI (all adults): Male: 330 µg/day Female: 330 µg/day</p>	<p>RI (all adults): Male: 300 µg/day Female: 300 µg/day</p>	<p>RDA (51 years and up): Male: 400 mcg Female: 400 mcg</p>	<p>RDI: Male: 400 µg/day Female: 400 µg/day</p> <p>EAR: Male: 320 µg/day Female: 320 µg/day</p>
<b>Vitamin B12 (Cobalamin)</b>	<p>RNI 65 years and over Male: 1.5µg/day Female: 1.5µg/day</p> <p>LRNI 65 years and over Male: 1.0µg/day Female: 1.0µg/day</p>	<p>AI (all adults): Male: 4.0 µg/day Female: 4.0 µg/day</p>	<p>RI: (all adults) Male: 2 µg/day Female: 2 µg/day</p>	<p>RDA (51years and up): Male: 2.4mcg/day Female: 2.4 mcg/day</p>	<p>RDI: Male: 2.4 µg/day Female: 2.4 µg/day</p> <p>EAR: Male: 2.0 µg/day Female: 2.0 µg/day</p>

Nutrient recommendations	Organisation and country				
	UK	European Food Safety Authority (EFSA) (2017) (Europe) (65 years and older)	Nordic Council of Ministers (2012) (Nordic countries) (61 to 74 years)	US Department of Health and Human Service and US Department of Agriculture (2015) (US) (65 years and older)	Australian Government Department of Health and the New Zealand Ministry of Health (2013) (Australia and New Zealand) (>70 years)
<b>Vitamin D</b>	RNI (all adults) Male: 10µg/day Female: 10µg/day	AI (all adults): Male 15 µg/day Female: 15 µg/day  ESFA note that under the conditions of assumed minimal cutaneous vitamin D synthesis. In the presence of endogenous cutaneous vitamin D synthesis, the requirement for dietary vitamin D is lower or may be even zero.	RI: 61-74 years: Male: 10 µg/day Female: 10 µg/day  ≥75 years: Male: 20 µg/day Female: 20 µg/day	RDA: 51-70 years: Male: 600 IU Female: 600 IU 71 years and up: Male: 800IU Female: 800 IU	AI: Male: 15.0 µg/day Female: 15.0 µg/day

Nutrient recommendations	Organisation and country				
	UK	European Food Safety Authority (EFSA) (2017) (Europe) (65 years and older)	Nordic Council of Ministers (2012) (Nordic countries) (61 to 74 years)	US Department of Health and Human Service and US Department of Agriculture (2015) (US) (65 years and older)	Australian Government Department of Health and the New Zealand Ministry of Health (2013) (Australia and New Zealand) (>70 years)
<b>Calcium</b>	RNI 65 years and over Male: 700mg/day Female: 700mg/day  LRNI 65 years and over Male: 400mg/day Female: 400mg/day	AR (adults ≥ 25 years): Male: 750 mg/day Female: 750 mg/day  PRI (adults ≥ 25 years): Male: 950 mg/day Female: 950 mg/day	RI (all adults): Male: 800 mg/day Female: 800 mg/day	RDA: Male: 51-70 years: 1000 mg 71 years and up: 1200 mg Female: 51 years and up: 1200 mg	RDI: Male: 1300 mg/day Female: 1300 mg/day  EAR: Male: 1100 mg/day Female: 1100 mg/day
<b>Iron</b>	RNI 65 years and over Male: 8.7mg/day Female: 8.7mg/day  LRNI 65 years and over Male: 4.7mg/day Female: 4.7mg/day	AR (all adults): Male: 6 mg/day Female (postmenopausal adults): 6 mg/day  PRI (all adults): Male: 11 mg/day Female (postmenopausal adults): 16 mg/day	RI: Male: 9 mg/day (all adults) Female: 9 mg/day (post menopause)	RDA (51 years and up): Male: 8 mg Female: 8 mg	RDI: Male: 8 mg/day Female: 8mg/day  EAR: Male: 6 mg/day Female: 5 mg/day

RDI: Reference daily intake; EAR: Estimated average requirement; AI: Adequate intake; RDA: Recommended dietary allowance;  
RI: Recommended intake; PRI: Population reference intake; AR: Average requirement; SC: Satisfactory contribution

## Annex 2 - National Diet and Nutrition Survey data for older adults: food consumption, nutrient intakes, blood and urine analytes, body mass index and self-reported general health

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**Table 1: Self-reported health and conditions limiting day-to-day activities in adults and older adults**

Interview question	Response categories	19-64 years			65-74 years			75 years and over		
		Men	Women	All	Men	Women	All	Men	Women	All
		%	%	%	%	%	%	%	%	%
<b>Self-assessed general health</b>	Very good	36	35	35	31	23	27	21	19	20
	Good	41	46	44	43	49	46	39	35	37
	Fair	19	13	16	21	22	22	31	40	36
	Bad	2	5	4	5	5	5	7	4	5
	Very bad	1	1	1	0	1	0	2	1	2
<b>Reported physical or mental health condition or illness lasting more than 12 months</b>	% reporting	32	32	32	46	64	56	68	70	69
<b>Condition/illness reported to affect:</b>	Percentages based on those who reported a condition									
<b>Vision</b>	% mentioned	2	3	3	25	9	15	13	9	11
<b>Hearing</b>	% mentioned	7	3	5	5	17	12	29	22	25
<b>Mobility</b>	% mentioned	35	38	36	54	48	51	49	64	57
<b>Learning/concentration</b>	% mentioned	7	9	8	19	12	15	10	10	10
<b>Mental health</b>	% mentioned	20	21	20	3	7	6	3	5	4
<b>Stamina/breathing difficulties</b>	% mentioned	23	22	23	20	23	22	25	31	29
<b>Social/behaviour</b>	% mentioned	1	4	3	0	4	2	0	0	0
<b>Other impairment</b>	% mentioned	6	11	8	0	9	6	24	4	13
<b>None of these</b>	% mentioned	36	36	36	33	34	34	21	19	20
<b>Condition affects ability to carry out day to day activities?</b>	Percentages based on those who reported a condition									
	Yes, a lot (%)	17	19	18	19	25	23	33	30	31
	Yes, a little (%)	28	37	33	25	25	25	30	47	39

Interview question	Response categories	19-64 years			65-74 years			75 years and over		
		Men	Women	All	Men	Women	All	Men	Women	All
<b>Day to day activities affected for how long?</b>	Percentages based on those who reported a condition									
	less than 6 months %	3	1	2	0	0	0	1	6	4
	6-12 months %	4	11	7	4	3	3	8	10	9
	More than 12 months %	93	89	91	96	97	97	91	84	86
<b>Does the condition limit or prevent shopping?</b>	Percentages based on those who reported a condition									
	Limits shopping%	17	22	20	12	19	16	28	35	32
	Prevents shopping %	3	1	2	5	6	8	11	12	12
<b>How does it limit or prevent shopping?</b>	Percentages based on those who reported a condition									
	Walking problems % mentioned	56	50	58	75	96	90	81	92	88
	Sight problems % mentioned	5	6	6	51	18	27	11	5	7
	Can't carry shopping % mentioned	61	66	63	90	83	85	71	69	70
	Tires easily % mentioned	41	38	39	75	64	67	47	39	42
	Other difficulties % mentioned	37	25	31	0	13	10	9	12	11
<b>Does the condition limit or prevent food preparation?</b>	Percentages based on those who reported a condition									
	Limits %	9	18	13	8	26	19	14	31	24
	Prevents %	2	0	1	10	0	4	7	6	6

Interview question	Response categories	19-64 years			65-74 years			75 years and over		
		Men	Women	All	Men	Women	All	Men	Women	All
<b>How does it limit or prevent food preparation?</b>	Percentages based on those who reported a condition									
Problems using hands	% mentioned	16	51	37	54	53	53	28	49	42
Problems walking	% mentioned	22	35	30	60	15	29	62	35	43
Problems standing	% mentioned	63	55	58	86	79	81	79	46	56
Problems with sight	% mentioned	7	4	5	49	5	18	20	5	9
Chronic ill health	% mentioned	25	26	25	23	0	7	0	4	3
Tires easily	% mentioned	13	33	25	80	35	49	57	30	38
Other difficulties	% mentioned	16	23	20	14	16	15	0	8	6
<b>In the last two weeks did you have to cut down your usual activities due to this condition or other illness or injury?</b>	Percentages based on those who reported a condition									
	% reported yes	9	15	12	8	21	15	15	13	14
<b>On how many days?</b>	Percentages based on those who reported cutting down on usual activities									
	1-5 days %	47	53	51	27	35	33	17	41	30
	6-10 days %	30	19	23	44	31	34	39	25	31
	More than 10 days %	24	28	26	29	34	33	44	33	39
Number of participants		450	632	1082	71	110	181	70	84	154

Data source: National Diet and Nutrition Survey (NDNS) years 7&8 dataset (2014/15-15/16)

**Table 2: Body Mass Index and percentages underweight, overweight and obese in adults and older adults**

Body Mass Index (BMI) (kg/m <sup>2</sup> )	Age groups (years)											
	Years 7&8 2014/15-15/16 <sup>1</sup>									Years 1-8 2008/09-15/16 <sup>2</sup>		
	19-64			65-74			75+			80+		
	Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All
mean	27.6	27.0	27.3	29.0	28.0	28.5	26.8	26.8	26.8	26.6	26.8	26.7
median	27.2	25.8	26.6	28.3	27.8	28.1	27.0	26.0	26.5	26.5	26.0	26.4
Std deviation	4.9	5.8	5.4	4.5	5.5	5.0	4.0	4.8	4.5	4.0	4.8	4.4
2.5 <sup>th</sup> percentile	20.2	19.0	19.3	21.8	16.9	19.3	17.4	18.0	17.5	17.4	18.0	17.8
97.5 <sup>th</sup> percentile	39.8	41.1	40.0	40.2	40.7	40.7	33.7	36.8	36.6	33.7	37.2	35.7
% underweight (BMI <18.5)	1.1	1.9	1.5	0.4	3.4	2.0	7.1	2.8	4.6	3.8	2.2	2.9
% healthy weight (BMI 18.5- <25)	29.7	41.8	35.6	12.4	28.8	21.0	24.3	39.2	32.9	29.2	41.9	36.5
% overweight (BMI 25- <30)	45.5	31.9	38.8	51.1	37.9	44.2	45.8	35.4	39.8	44.5	37.9	40.7
% obese (BMI 30-<40)	21.0	21.7	21.4	31.5	25.0	28.1	22.8	22.6	22.7	22.3	16.4	18.9
% morbidly obese (BMI ≥40)	2.7	2.8	2.7	4.4	4.8	4.6	0	0	0	0.2	1.6	1.0
% overweight or obese including morbidly obese	69.2	56.5	62.9	87.1	67.7	76.9	68.6	58.0	62.5	67.0	55.9	60.6
Number of participants	426	580	1006	64	97	161	50	64	114	95	158	253

Data sources:

<sup>1</sup> National Diet and Nutrition Survey (NDNS) years 7&8 dataset (2014/15-15/16)

<sup>2</sup> National Diet and Nutrition Survey (NDNS) years 1-8 dataset (2008/09-15/16)

**Table 3: Energy and macronutrient intakes for adults and older adults <sup>1,2</sup>**

Energy and macronutrient intakes (Dietary recommendation <sup>5</sup> )		Age groups (years)											
		Years 7&8 2014/15-15/16 <sup>1</sup>									Years 1-8 2008/09-15/16 <sup>2</sup>		
		19-64			65-74			75+			80+		
		Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All
<b>Total energy (kcal)</b>	kcal/day (mean)	2091	1632	1860	1940	1483	1693	1824	1344	1556	1770	1442	1585
	kcal/day (median)	2072	1596	1806	1977	1399	1637	1747	1379	1518	1735	1425	1548
	2.5 <sup>th</sup> percentile	1008	715	816	986	681	799	1130	679	709	837	719	755
	97.5 <sup>th</sup> percentile	3379	2765	3140	2703	2439	2625	2851	2002	2616	2839	2110	2502
	EAR (kcal/day)	2500	2000	--	2342	1912	--	2294	1840	--	2294	1840	--
	Mean intake as % EAR	84	82	--	83	78	--	80	74	--	77	79	--
<b>Total energy (MJ)</b>	MJ/day (mean)	8.79	6.87	7.82	8.16	6.24	7.12	7.67	5.66	6.55	7.42	6.08	6.66
	MJ/day (median)	8.71	6.72	7.61	8.33	5.86	6.89	7.35	5.82	6.40	7.30	6.01	6.53
	2.5 <sup>th</sup> percentile	4.25	3.03	3.39	4.16	2.87	3.37	4.76	2.87	2.98	3.83	3.03	3.21
	97.5 <sup>th</sup> percentile	14.14	11.64	13.20	11.36	10.23	11.06	11.95	8.44	10.99	12.34	8.92	10.62
	EAR (MJ/day)	10.5	8.4	--	9.8	8.0	--	9.6	7.7	--	9.6	7.7	--
	Mean intake as % EAR	84	82	--	83	78	--	80	74	--	77	79	--
<b>Protein</b>	g/day (mean)	87.4	66.6	76.9	79.5	64.0	71.1	70.9	56.3	62.7	69.7	59.0	63.6
	% total energy (mean)	17.0	16.7	16.9	16.6	17.8	17.3	15.7	17.1	16.5	16.0	16.6	16.4
	(RNI 53.3 g/d males; 46.5 g/d females; for age 50+ years)	16.1	16.5	16.4	16.3	16.9	16.4	15.2	16.8	16.3	15.5	16.4	16.0
	2.5 <sup>th</sup> percentile	10.7	9.5	10.1	10.1	11.3	11.1	10.6	11.4	10.9	11.0	11.0	11.0
	97.5 <sup>th</sup> percentile	26.5	25.0	25.9	23.5	27.1	24.9	20.8	25.1	23.2	23.3	23.5	23.5
	Mean	1.04	0.97	1.01	0.93	0.93	0.93	0.96	0.89	0.92	0.95	0.93	0.94
<b>Protein (g/kg body weight)</b>	Median	1.00	0.94	0.97	0.94	0.88	0.92	0.91	0.82	0.87	0.89	0.90	0.89
	2.5 <sup>th</sup> percentile	0.41	0.39	0.40	0.49	0.45	0.48	0.23	0.33	0.34	0.41	0.43	0.45
	97.5 <sup>th</sup> percentile	1.89	1.66	1.77	1.48	1.46	1.49	1.85	1.63	1.96	1.81	1.76	1.79
	RNI: 0.75g protein per kg body weight	81	73	77	76	70	73	82	56	67	75	68	71
	% meeting recommendation												

Energy and macronutrient intakes (Dietary recommendation <sup>5</sup> )	Age groups (years)												
	Years 7&8 2014/15-15/16 <sup>1</sup>									Years 1-8 2008/09-15/16 <sup>2</sup>			
	19-64			65-74			75+			80+			
	Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All	
<b>Carbohydrate</b> (≥ 50% of total energy)	g/day (mean)	249	199	224	236	182	207	221	166	190	217	180	196
	% total energy (mean)	45.1	46.2	45.7	46.0	45.8	45.9	45.8	46.5	46.2	46.3	46.7	46.5
	% total energy (median)	45.9	46.2	46.1	44.7	45.9	45.6	44.7	46.3	45.7	46.2	47.5	47.0
	2.5th percentile	29.0	31.8	30.1	32.6	24.0	32.1	35.2	27.0	34.4	33.0	29.9	33.0
	97.5th percentile	60.3	63.5	62.2	61.6	60.5	61.6	59.9	56.9	59.1	59.4	58.9	58.9
<b>Free sugars</b> (≤ 5% total energy)	g/day (mean)	64.3	50.0	57.1	62.0	42.1	51.2	60.5	37.7	47.8	56.1	46.6	50.7
	% total energy (mean)	11.1	11.2	11.1	11.8	10.4	11.0	12.5	10.4	11.3	12.0	11.8	11.9
	% total energy (median)	9.9	10.1	10.0	10.7	9.2	9.9	12.7	9.4	10.1	11.1	10.9	11.1
	2.5th percentile	1.8	2.3	1.9	1.3	2.3	1.7	3.6	2.2	2.3	2.3	2.3	2.3
	97.5th percentile	26.2	23.5	24.6	26.9	25.9	27.2	25.8	20.3	23.0	25.4	23.2	23.2
% meeting recommendation	13	13	13	7	20	14	12	11	11	15	12	13	
<b>AOAC fibre</b> (30g/day)	g/day (mean)	20.7	17.4	19.0	19.5	17.4	18.4	18.3	15.1	16.5	18.1	15.7	16.7
	g/day (median)	19.6	16.5	17.9	18.8	16.6	17.6	18.0	14.5	15.7	17.8	15.6	16.3
	2.5th percentile	7.5	7.1	7.4	8.8	4.2	7.3	5.7	3.0	3.5	7.6	7.1	7.4
	97.5th percentile	39.6	32.1	36.6	32.7	33.0	32.7	31.7	27.5	31.4	31.5	27.5	29.6
	% meeting recommendation	13	4	9	9	6	7	10	2	6	6	0	3
<b>Fat</b> (≤ 33% total energy)	g/day (mean)	76.6	62.4	69.5	69.3	55.3	61.8	72.1	52.9	61.4	68.7	56.8	62.0
	% total energy (mean)	32.6	33.8	33.2	31.8	33.4	32.7	35.2	35.1	35.1	34.8	35.1	35.0
	% total energy (median)	32.8	34.2	33.5	31.4	33.3	32.3	34.5	35.5	35.2	34.5	35.1	34.7
	2.5th percentile	20.0	19.1	19.8	19.2	18.9	19.6	19.6	23.9	23.1	24.8	25.7	25.7
	97.5th percentile	44.9	45.7	45.7	43.1	44.0	43.9	46.3	48.8	47.5	46.9	47.7	46.9

Energy and macronutrient intakes (Dietary recommendation <sup>5</sup> )	Age groups (years)											
	Years 7&8 2014/15-15/16 <sup>1</sup>									Years 1-8 2008/09-15/16 <sup>2</sup>		
	19-64			65-74			75+			80+		
	Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All
<b>Saturated fat</b> g/day (mean) % total energy (mean) (≤ 10% total energy) % total energy (median) 2.5th percentile 97.5th percentile	27.5	22.8	25.1	26.0	21.7	23.7	29.1	21.9	25.1	27.8	23.7	25.5
	11.6	12.2	11.9	11.9	13.0	12.5	14.0	14.6	14.3	14.0	14.5	14.3
	11.5	12.3	11.7	12.0	12.3	12.1	13.9	14.0	14.0	13.8	13.9	13.9
	5.9	5.5	5.6	6.4	6.2	6.6	5.8	8.5	8.0	8.7	8.4	8.5
	18.7	19.5	18.9	19.1	20.2	19.2	20.2	22.2	22.2	20.1	22.3	22.1
<b>Cis-monounsaturated fat</b> g/day (mean) % total energy (mean) No specific recommendation % total energy (median) 2.5th percentile 97.5th percentile	29.0	23.2	26.1	25.4	19.1	22.0	25.5	17.7	21.1	24.0	19.0	21.1
	12.3	12.5	12.4	11.6	11.6	11.6	12.5	11.7	12.1	12.1	11.8	11.9
	12.1	12.3	12.2	11.2	11.6	11.5	12.2	11.7	11.9	12.1	11.7	11.9
	7.0	6.5	7.0	6.8	5.8	6.0	7.9	7.5	7.6	7.0	7.8	7.7
	19.5	18.5	18.9	18.0	17.6	17.7	16.6	15.6	16.5	15.9	16.5	16.5
<b>Cis- n3 polyunsaturated fat</b> g/day (mean) % total energy (mean) % total energy (median) No recommendations set for cis n-3 PUFA overall 2.5th percentile 97.5th percentile	2.2	1.8	2.0	2.2	1.8	2.0	1.9	1.5	1.7	2.0	1.6	1.8
	0.9	1.0	1.0	1.0	1.1	1.1	1.0	1.0	1.0	1.0	1.0	1.0
	0.8	0.9	0.9	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.9	0.9
	0.4	0.5	0.4	0.5	0.4	0.5	0.4	0.4	0.4	0.4	0.4	0.4
	2.0	2.0	2.0	1.9	2.1	2.1	1.7	2.4	1.8	1.7	2.4	2.1
<b>Cis-n6 polyunsaturated fat</b> g/day (mean) (No further increase in average intakes and the proportion of the population consuming in excess of about 10% of energy should not increase) % total energy (mean) % total energy (median) 2.5th percentile 97.5th percentile	11.3	9.2	10.2	9.2	7.5	8.3	9.0	6.8	7.8	8.6	7.0	7.7
	4.8	5.0	4.9	4.3	4.5	4.4	4.6	4.4	4.5	4.4	4.4	4.4
	4.6	4.7	4.6	4.1	4.5	4.4	4.2	3.9	4.1	4.3	4.1	4.2
	2.6	2.7	2.7	2.3	2.5	2.3	2.6	2.2	2.3	2.3	2.3	2.3
	8.7	9.3	9.0	7.2	7.0	7.1	7.4	9.4	9.0	6.4	8.5	6.6

Energy and macronutrient intakes (Dietary recommendation <sup>5</sup> )	Age groups (years)											
	Years 7&8 2014/15-15/16 <sup>1</sup>									Years 1-8 2008/09-15/16 <sup>2</sup>		
	19-64			65-74			75+			80+		
	Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All
<b>Salt</b> g/day (mean)	6.0	4.7	5.3	5.3	4.0	4.6	5.2	3.7	4.4	5.3	4.1	4.7
Excludes discretionary salt g/day (median)	5.8	4.4	5.0	5.0	3.9	4.4	5.3	3.7	4.3	5.4	4.0	4.4
2.5 <sup>th</sup> percentile	2.1	1.4	1.9	2.1	1.6	2.1	2.7	1.4	1.7	2.2	1.6	1.8
97.th percentile	10.9	8.7	9.8	9.1	6.9	8.2	8.0	5.8	7.4	9.5	7.1	8.1
Number of participants	450	632	1082	71	110	181	70	84	154	134	201	335
	19-64 years <sup>3</sup>			65 years and over <sup>4</sup>								
	Men	Women	All	Men	Women	All						
<b>Salt</b> <sup>4</sup> (24 hour urinary sodium) g/day (mean)	9.2	7.6	8.4	8.7	6.7	7.6						
g/day (geometric mean)	8.3	6.8	7.5	--	--	--						
g/day (median)	--	--	--	8.0	6.2	7.0						
(≤ 6g/d) 2.5th percentile	3.2	2.3	2.7	3.8	2.6	2.7						
97.5th percentile	20.8	14.8	17.8	15.3	13.2	14.7						
% meeting recommendation	26	35	31	27	47	38						
Number of participants	286	310	596	133	137	270						

Data sources: <sup>1</sup> National Diet and Nutrition Survey (NDNS) years 7&8 (Roberts et al., 2018)

<sup>2</sup> National Diet and Nutrition Survey (NDNS) years 1-8 dataset 2008/09-15/16

<sup>3</sup> Assessment of salt intake from urinary sodium in adults in England 2018/19

<sup>4</sup> National Diet and Nutrition Survey (NDNS) years 1-4 (2008/09-11/12) Bates et al 2014

<sup>5</sup> Dietary recommendations are based on the following:

**Total energy** – Recommendations from SACN Dietary Reference Values for Energy (2011)

**Protein** – RNI figures were obtained from COMA Dietary Reference Values for Food Energy and Nutrients for the United Kingdom (1991). RNI for men and women aged 50+ years (based on 0.75g protein/kg/d and a body weight of 62kg for women and 71kg for men).

**Fat (including total fat saturated, cis monounsaturated, cis n-3 and cis n-6 polyunsaturated fatty acids)**. Recommendations from COMA Dietary Reference Values for Food Energy and Nutrients for the United Kingdom 1991 and COMA Nutritional aspects of cardiovascular disease (1994).

**Carbohydrate** - recommended population average from SACN Carbohydrates and Health (2015).

**Free sugars** - recommendation from SACN Carbohydrate and Health (2015). The definition of free sugars includes: all added sugars in any form including honey and syrups; all sugars naturally present in fruit and vegetable juices, spreads, purees and pastes, and similar products in which the structure has been broken down; all naturally occurring sugars in drinks (except for dairy-based drinks) and lactose and galactose added as ingredients.

**Salt** - recommendation from SACN Salt and Health (2003).

**Dietary fibre** - recommendation from SACN Carbohydrate and Health report (2015).

'--' no data available



**Table 4a: Micronutrient intakes from food sources for adults and older adults <sup>1,2</sup>**

Micronutrient intakes		Age groups (years)									Years 1-8 2008/09-15/16 <sup>2</sup>		
		19-64			65-74			75+			80+		
		Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All
<b>Vitamin A</b>	µg/day (mean)	921	825	873	877	906	893	1336	895	1090	1442	1087	1242
	µg/day (median)	624	626	625	707	724	719	866	652	737	970	856	905
	mean as % RNI	132	138	135	125	151	139	191	149	168	207	179	193
	% below LRNI	16	10	13	6	7	7	5	10	8	3	4	4
<b>Retinol (from food and supplements)</b>	µg/day (mean)	n/a	n/a	n/a	558	569	564	1000	611	783	1026	622	798
	% above 1500µg/day	n/a	n/a	n/a	7	7	7	11	7	9	12	8	10
<b>Thiamin (B1)</b>	mg/day (mean)	1.69	1.37	1.53	1.70	1.38	1.52	1.54	1.26	1.38	1.46	1.27	1.35
	mg/day (median)	1.59	1.30	1.44	1.51	1.25	1.42	1.52	1.18	1.35	1.50	1.27	1.30
	mean as % RNI	169	171	170	188	172	180	171	180	176	162	181	173
	% below LRNI	1	2	2	0	0	0	2	6	4	1	5	3
<b>Riboflavin (B2)</b>	mg/day (mean)	1.76	1.42	1.59	1.75	1.53	1.63	1.84	1.32	1.55	1.74	1.48	1.60
	mg/day (median)	1.60	1.39	1.49	1.59	1.41	1.55	1.68	1.31	1.45	1.63	1.43	1.50
	mean as % RNI	136	129	132	135	139	137	141	120	130	134	135	135
	% below LRNI	6	14	10	1	7	4	3	13	9	7	6	6
<b>Niacin (B3)</b>	mg/day (mean)	43.0	30.9	36.9	38.0	28.9	33.1	30.6	25.9	28.0	31.4	26.3	28.5
	mg/day (median)	40.3	29.8	34.3	38.3	26.9	31.0	29.1	25.4	26.8	29.9	25.5	27.8
	mean as % RNI	261	234	247	245	230	237	203	214	209	208	217	213
	% below LRNI	0	1	0	0	0	0	1	0	1	1	1	1
<b>Vitamin (B6)</b>	mg/day (mean)	2.26	1.54	1.90	1.96	1.45	1.68	1.58	1.30	1.43	1.83	1.63	1.72
	mg/day (median)	1.95	1.43	1.64	1.87	1.37	1.53	1.50	1.20	1.34	1.69	1.57	1.61
	mean as % RNI	206	171	188	196	181	188	158	186	174	183	233	211
	% below LRNI	0	0	0	0	0	0	0	0	0	0	0	0

Micronutrient intakes		Age groups (years)											
		Years 7&8 2014/15-15/16 <sup>1</sup>									Years 1-8 2008/09-15/16 <sup>2</sup>		
		19-64			65-74			75+			80+		
	Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All	
<b>Vitamin B12</b>	µg/day (mean)	5.8	4.5	5.1	6.3	4.8	5.5	6.8	4.5	5.5	7.2	5.1	6.0
	µg/day (median)	5.0	4.1	4.5	5.5	4.5	4.9	5.6	3.8	4.7	5.7	4.3	4.8
	mean as % RNI	384	299	341	421	322	368	452	300	367	481	341	402
	% below LRNI	2	3	2	2	0	1	3	0	1	1	1	1
<b>Folate</b>	µg/day (mean)	267	214	240	278	219	246	238	195	214	244	212	226
	µg/day (median)	249	200	223	264	209	231	216	177	194	223	200	213
	mean as % RNI	134	107	120	139	109	123	119	97	107	121	105	113
	% below LRNI	3	6	5	0	3	2	3	8	6	2	9	6
<b>Vitamin C</b>	mg/day (mean)	84.1	81.9	83.0	87.8	76.4	81.6	77.2	64.1	69.9	70.6	73.3	72.1
	mg/day (median)	67.1	70.1	68.6	75.2	68.2	70.9	73.0	50.8	55.1	66.3	66.6	66.5
	mean as % RNI	210	205	207	220	191	204	193	160	175	176	183	180
	% below LRNI	1	1	1	0	1	0	1	4	3	2	4	3
<b>Vitamin D (from food)</b>	µg/day (mean)	2.9	2.5	2.7	3.9	3.2	3.5	3.3	2.5	2.8	3.6	2.8	3.1
	µg/day (median)	2.5	2.1	2.3	3.8	2.5	3.1	3.1	2.1	2.6	2.9	2.5	2.5
	mean as % RNI	29	25	27	39	32	35	33	25	28	36	28	31
<b>Vitamin D (incl. supplements)</b>	µg/day (mean)	4.5	3.9	4.2	5.5	6.5	6.0	4.6	5.8	5.3	4.9	4.7	4.8
	µg/day (median)	2.6	2.5	2.6	4.2	3.9	4.1	3.8	2.8	3.2	3.7	2.9	3.3
	mean as % RNI	45	39	42	55	65	60	46	58	53	49	47	48
<b>Vitamin E</b>	mg/day (mean)	10.9	9.3	10.1	9.5	7.9	8.7	9.2	6.8	7.9	8.8	7.2	7.9
	mg/day (median)	10.1	8.6	9.3	9.3	7.2	8.2	9.0	6.1	7.6	8.2	7.0	7.4
	97.5 <sup>th</sup> percentile	23.6	18.4	21.7	16.7	14.8	16.9	15.7	16.5	16.0	16.5	15.4	16.4
	2.5 <sup>th</sup> percentile	3.6	3.1	3.5	3.5	3.1	3.5	3.9	1.3	1.9	3.3	2.3	2.6
<b>Iron</b>	mg/day (mean)	11.6	9.3	10.5	10.9	8.9	9.8	10.2	7.8	8.8	10.1	8.3	9.1
	mg/day (median)	11.0	9.0	10.0	10.4	8.8	9.7	8.9	7.3	8.3	9.6	8.0	8.6
	mean as % RNI	134	76	104	126	102	113	117	89	102	116	95	104
	% below LRNI	2	27	15	0	8	4	2	12	8	2	7	5

Micronutrient intakes		Age groups (years)												
		Years 7&8 2014/15-15/16 <sup>1</sup>									Years 1-8 2008/09-15/16 <sup>2</sup>			
		19-64			65-74			75+			80+			
		Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All	
<b>Calcium</b>	mg/day (mean)		897	746	821	887	764	820	885	693	778	858	747	795
	mg/day (median)		834	710	766	864	733	800	890	620	749	845	733	753
	mean as % RNI		128	107	117	127	109	117	126	99	111	122	107	113
	% below LRNI		7	11	9	0	11	6	4	10	8	3	10	7
<b>Magnesium</b>	mg/day (mean)		302	238	270	286	231	256	246	205	223	238	207	220
	mg/day (median)		285	229	255	270	224	241	236	189	213	231	207	216
	mean as % RNI		101	88	94	95	85	90	82	76	79	79	77	78
	% below LRNI		14	11	13	6	11	9	22	27	25	25	20	22
<b>Potassium</b>	mg/day (mean)		3145	2588	2865	3183	2687	2915	2824	2251	2504	2716	2402	2539
	mg/day (median)		3074	2560	2784	3053	2589	2840	2835	2200	2397	2607	2427	2524
	mean as % RNI		90	74	82	91	77	83	81	64	72	78	69	73
	% below LRNI		11	23	17	4	22	14	16	34	26	18	25	22
<b>Iodine</b>	µg/day (mean)		172	140	156	183	157	169	191	134	159	191	157	172
	µg/day (median)		158	131	142	167	138	145	173	129	152	166	144	156
	mean as % RNI		123	100	111	131	112	121	136	96	114	136	113	123
	% below LRNI		9	15	12	2	6	4	4	9	7	5	6	6
<b>Selenium</b>	µg/day (mean)		55	44	50	54	41	47	45	35	39	48	36	42
	µg/day (median)		52	41	46	52	37	43	43	29	37	41	33	37
	mean as % RNI		74	73	74	72	68	70	60	58	59	65	61	63
	% below LRNI		25	47	36	34	57	46	39	76	60	47	68	59
<b>Zinc</b>	mg/day (mean)		9.7	7.6	8.7	9.0	7.5	8.2	8.6	6.6	7.5	8.7	7.1	7.8
	mg/day (median)		9.3	7.5	8.3	9.1	7.4	7.7	8.0	6.3	6.8	8.1	6.5	7.2
	mean as % RNI		102	109	106	95	108	102	91	94	93	91	101	97
	% below LRNI		7	8	8	5	3	4	8	12	10	12	7	9
	Number of participants		450	632	1082	71	110	181	70	84	154	134	201	335

Data sources:

<sup>1</sup> National Diet and Nutrition Survey (NDNS) years 7&8 (Roberts et al., 2018)

<sup>2</sup> National Diet and Nutrition Survey (NDNS) years 1-8 dataset 2008/09-15/16

**Table 4b: Reference nutrient intakes (RNI) and Lower reference nutrient intakes (LRNI) by age and sex are shown in the table below**

Dietary Reference Value		19 to 64 years				65 to 74 years				75+ years			
		Men		Women		Men		Women		Men		Women	
		RNI	LRNI	RNI	LRNI	RNI	LRNI	RNI	LRNI	RNI	LRNI	RNI	LRNI
Vitamin A	µg/day	700	300	600	250	700	300	600	250	700	300	600	250
Thiamin	mg/1000kcal	0.4	0.23	0.4	0.23	0.4	0.23	0.4	0.23	0.4	0.23	0.4	0.23
	mg/day	1.0	0.6	0.8	0.5	0.9	0.5	0.8	0.4	0.9	0.5	0.7	0.4
Riboflavin	mg/day	1.3	0.8	1.1	0.8	1.3	0.8	1.1	0.8	1.3	0.8	1.1	0.8
Niacin equivalent	mg/1000kcal	4.4	6.6	4.4	6.6	6.6	4.4	6.6	4.4	6.6	4.4	6.6	4.4
	mg/day	16.5	11.7	13.2	9.4	15.5	10.3	12.6	8.4	15.1	10.1	12.1	8.1
Vitamin B6	µg/g protein	15	11	15	11	15	11	15	11	15	11	15	11
	mg/day	1.1	1.0	0.9	0.7	1.0	0.9	0.8	0.7	1.0	0.8	0.7	0.6
Vitamin B12	µg/day	1.5	1.0	1.5	1.0	1.5	1.0	1.5	1.0	1.5	1.0	1.5	1.0
Folate	µg/day	200	100	200	100	200	100	200	100	200	100	200	100
Vitamin C	mg/day	40	10	40	10	40	10	40	10	40	10	40	10
Vitamin D <sup>2</sup>	µg/day	10	-	10	-	10	n/a	10	n/a	10	n/a	10	n/a
Iron	mg/day	8.7	4.7	14.8 <sup>1</sup> 8.7 <sup>2</sup>	8.0 <sup>1</sup> 4.7 <sup>2</sup>	8.7	4.7	8.7	4.7	8.7	4.7	8.7	4.7
Calcium	mg/day	700	400	700	400	700	400	700	400	700	400	700	400
Magnesium	mg/day	300	190	270	150	300	190	270	150	300	190	270	150
Potassium	mg/day	3500	2000	3500	2000	3500	2000	3500	2000	3500	2000	3500	2000
Zinc	mg/day	9.5	5.5	7.0	4.0	9.5	5.5	7.0	4.0	9.5	5.5	7.0	4.0
Iodine	µg/day	14	70	140	70	140	70	140	70	140	70	140	70
Selenium	µg/day	75	40	60	40	75	40	60	40	75	40	60	40

<sup>1</sup> 19-50 years

<sup>2</sup> 51-64 years

**Table 5: Blood and urinary analytes for adults and older adults<sup>1</sup>**

Blood and urinary analytes		Age groups (years)								
		Years 7&8 2014/15-15/16 <sup>a</sup>			Years 1-8 2008/09-15/16 <sup>b</sup>					
		19-64 years			65-74 years			75 years and over		
		Men	Women	All	Men	Women	All	Men	Women	All
<b>25-OH vitamin D</b> <b>nmol/l</b>	mean	44.0	48.0	46.1	48.1	47.4	47.7	42.2	44.1	43.3
	median	40.9	45.6	43.3	48.8	46.8	47.2	37.9	43.1	39.9
	2.5 <sup>th</sup> percentile	13.5	13.2	13.7	12.3	15.7	12.7	10.8	11.8	10.8
	97.5 <sup>th</sup> percentile	93.7	93.7	94.3	94.8	90.5	94.8	82.8	91.4	91.2
	Threshold for deficiency 25nmol/l <sup>2</sup>	19	16	17	15	16	15	24	29	27
	Number of participants	222	298	520	170	250	420	101	171	272
<b>Serum vitamin B12</b> <b>pmol/l</b>	mean	271	276	273	260	296	280	252	269	261
	median	256	260	257	241	292	263	219	241	235
	2.5 <sup>th</sup> percentile	147	134	144	138	131	131	125	122	125
	97.5 <sup>th</sup> percentile	453	493	475	499	590	575	501	497	501
	Threshold for deficiency <sup>3</sup> 150pmol/l	3	4	3	4	5	5	8	7	8
	Number of participants	224	298	522	173	256	429	103	167	270
<b>Holotranscobalamin</b> <b>(vitamin B12)</b> <b>pmol/l</b>	mean	70	68	69	[83]	90	87	**[ ]	[88]	77
	median	67	63	65	[81]	88	88	[ ]	[83]	74
	2.5 <sup>th</sup> percentile	25	26	26	[32]	20	30	[ ]	[32]	21
	97.5 <sup>th</sup> percentile	136	156	145	[156]	157	157	[ ]	[130]	140
	Threshold for deficiency <sup>4</sup> 32pmol/l	5	8	7	[2]	5	3	[ ]	[1]	5
	Number of participants	223	297	520	35	58	93	27	30	57

Blood and urinary analytes		Age groups (years)									
		Years 7&8 2014/15-15/16 <sup>a</sup>			Years 1-8 2008/09-15/16 <sup>b</sup>						
		19-64 years			65-74 years			75 years and over			
		Men	Women	All	Men	Women	All	Men	Women	All	
<b>Plasma retinol µmol/l</b>	mean	1.95	1.72	1.84	2.01	1.87	1.93	1.94	1.89	1.91	
	median	1.94	1.66	1.76	1.98	1.76	1.86	1.86	1.91	1.89	
	2.5 <sup>th</sup> percentile	1.14	0.98	1.04	1.08	1.15	1.10	1.04	0.76	0.78	
	97.5 <sup>th</sup> percentile	2.82	2.76	2.80	3.13	3.24	3.16	3.07	3.20	3.18	
	Threshold for low vitamin A status: Below 0.35µmol/l 0.35-0.70 µmol/l <sup>5</sup>	% < 0.35µmol/l	0	0	0	0	0	0	0	0	0
	% ≥ 0.35 and ≤0.70 µmol/l	0	0	0	0.6	0.4	0.5	0	0.6	0.3	
	Number of participants	218	297	515	169	254	424	99	168	267	
<b>Plasma ferritin µg/l</b>	mean	145	54	99	182	114	145	138	110	122	
	median	132	42	71	129	84	105	97	80	94	
	2.5 <sup>th</sup> percentile	18	7	8	13	11	12	9	13	10	
	97.5 <sup>th</sup> percentile	349	167	313	491	347	478	489	389	483	
	Threshold for low plasma ferritin 15µg/l <sup>6</sup>	% below 15µg/l	2	12	7	3	4	4	5	6	5
	Number of participants	217	297	514	171	257	428	103	172	275	
<b>Haemoglobin and plasma ferritin (combined index)</b>	% below threshold for both haemoglobin <sup>7</sup> and plasma ferritin <sup>6</sup>	1	5	3	2	1	2	1	5	3	
	Number of participants	205	279	484	163	228	391	94	140	234	
<b>Haematocrit l/l</b>	mean	0.46	0.40	0.43	0.43	0.41	0.42	0.42	0.40	0.41	
	median	0.46	0.40	0.43	0.44	0.41	0.42	0.42	0.40	0.41	
	2.5 <sup>th</sup> percentile	0.40	0.35	0.36	0.37	0.34	0.35	0.29	0.32	0.32	
	97.5 <sup>th</sup> percentile	0.51	0.47	0.51	0.51	0.47	0.49	0.52	0.47	0.51	
	Threshold for low status <sup>8</sup>	< 0.36l/l	0	7	4	2	6	4	14	23	19
		0.36-0.40l/l	6	54	30	12	33	23	13	25	20
	Number of participants	216	287	503	167	244	411	102	163	264	

Blood and urinary analytes		Age groups (years)									
		Years 7&8 2014/15-15/16 <sup>a</sup>			Years 1-8 2008/09-15/16 <sup>b</sup>						
		19-64 years			65-74 years			75 years and over			
		Men	Women	All	Men	Women	All	Men	Women	All	
<b>Red cell folate</b>	Geometric mean	531	485	508	625	662	645	586	661	630	
	2.5 <sup>th</sup> percentile	261	192	206	235	287	253	235	287	253	
	97.5 <sup>th</sup> percentile	1141	1260	1197	1280	1917	1810	1280	1917	1810	
	Threshold for increased risk of anaemia 305nmol/l <sup>9</sup>	% below 305nmol/l	3	11	7	7	5	6	8	5	6
		Number of participants	220	293	513	171	227	398	92	143	235
<b>Total serum folate</b>	mean	13.9	14.6	14.2	18.0	20.7	19.5	16.8	20.3	18.8	
	2.5 <sup>th</sup> percentile	5.5	5.2	5.4	6.7	6.3	6.3	6.1	6.9	6.34	
	97.5 <sup>th</sup> percentile	33.3	48.6	43.4	53.8	68.8	64.7	42.4	89.1	89.1	
	Threshold for folate deficiency 7nmol/l <sup>10</sup>	% below 7 nmol/l	8	11	10	4	4	4	5	3	3
	Threshold for possible folate deficiency 13nmol/l	% below 13 nmol/l	46	45	46	26	20	23	27	23	25
	Number of participants	225	300	525	173	258	431	99	170	270	
<b>Erythrocyte glutathione reductase activation coefficient (EGRAC) (riboflavin status)</b>	mean	1.33	1.38	1.36	1.31	1.31	1.31	1.32	1.30	1.31	
	median	1.29	1.34	1.32	1.27	1.29	1.28	1.25	1.27	1.26	
	75 <sup>th</sup> percentile	1.41	1.45	1.43	1.38	1.38	1.38	1.38	1.36	1.36	
	90 <sup>th</sup> percentile	1.54	1.64	1.57	1.51	1.48	1.49	1.54	1.55	1.55	
	% above 1.3 <sup>11</sup>	47	61	54	41	45	43	39	36	37	
	Number of participants	221	293	514	168	239	407	97	147	244	
<b>Pyridoxal-5-phosphate (PLP) (Vitamin B6) nmol/l</b>	mean	63.7	48.3	55.9	45.9	53.1	49.8	36.4	50.5	44.9	
	median	55.0	41.6	47.4	36.9	40.0	39.4	30.3	33.8	31.8	
	2.5 <sup>th</sup> percentile	16.9	12.3	13.4	57.3	62.2	60.1	40.8	56.6	52.5	
	97.5 <sup>th</sup> percentile	204.6	131.7	156.1	122.3	174.5	150.2	104.5	199.0	170.6	
		Number of participants	219	297	516	175	238	413	97	148	245

Blood and urinary analytes	Age groups (years)									
	Years 7&8 2014/15-15/16 <sup>a</sup>			Years 1-8 2008/09-15/16 <sup>b</sup>						
	19-64 years			65-74 years			75 years and over			
	Men	Women	All	Men	Women	All	Men	Women	All	
<b>Urinary iodine concentration</b> $\mu\text{g/l}$	$\mu\text{g/L}$ (median)	105	105	105	122	111	117	146	169	152
	% below 50 $\mu\text{g}/^{12}$	12	16	14	9	13	11	9	4	6
	Number of participants	376	522	898	95	140	235	75	86	161

Data sources: <sup>a</sup> National Diet and Nutrition Survey (NDNS) years 7&8 (Roberts et al., 2018).

<sup>b</sup> National Diet and Nutrition Survey (NDNS) years 1-8 dataset 2008/09-15/16

\*\* data and bases for a variable with a cell size between 30 and 49 are presented in square brackets. In this case it should be noted that the lower or upper 2.5th percentiles represent data from at most 2 participants. For cell sizes below 30, bases have been presented in square brackets, but data have not been presented.

<sup>1</sup> Threshold of 25 nmol/L is used to define the concentration below which risk of vitamin D deficiency increases. Scientific Advisory Committee on Nutrition (2016) Vitamin D and Health. [www.gov.uk/government/publications/sacn-vitamin-d-and-health-report](http://www.gov.uk/government/publications/sacn-vitamin-d-and-health-report). The 25-OHD data presented here were obtained using the Diasorin Liaison analyser and have been standardised using the procedures of the Vitamin D Standardisation Program to isotope dilution-LCMS/MS international reference methods:

VDSP - Sempos CT, Vesper HW, Phinney KW, Thienpont LM, Coates PM. Vitamin D status as an international issue: national surveys and the problem of standardization. *Scand J Clin Lab Invest Suppl* (2012); 243: 32–40.

ODIN - Cashman KD, Dowling KG, Škrabáková Z., et al., Vitamin D deficiency in Europe – pandemic? *AJCN* (2016); 103(4): 1033-44.

<sup>2</sup> WHO. Conclusions of a WHO technical consultation on folate and vitamin B12 deficiencies. *Food and Nutrition Bulletin*. 2008; 29: S238–S244.

<sup>3</sup> Holotranscobalamin is a relatively recently established marker and thresholds indicating deficiency are under debate. 32pmol/L is suggested as a marker of biochemical holotranscobalamin deficiency, the concentration below which urinary methylmalonic acid is likely to be raised. *Annals of Clinical Biochemistry*. 2012. (49) 184-189

<sup>4</sup> Bates CJ, Thurnham DI, Bingham SA, Margetts BM, Nelson M. Biochemical Markers of Nutrient Intake. In: *Design Concepts in Nutritional Epidemiology*. 2nd Edition. OUP (Oxford, 1997), pp 170–240. The evidence for this threshold is confined mainly to (non elderly) adults

<sup>5</sup> Ferritin: 5y+ males <15mg/L, 5y+ females <15mg/L.

<sup>6</sup> Haemoglobin: 15y+ males <130g/L, 15y+ females (non-pregnant) <120g/L.

<sup>7</sup> Haematocrit: Dacie JV, Lewis SM. *Practical Haematology*. 9th Edition.

<sup>8</sup> Institute of Medicine. 1998. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/6015>

<sup>8</sup> WHO. Serum and red blood cell folate concentrations for assessing folate in populations. *Vitamins and Mineral Nutrition Information System*. 2015; 01.1-7.

<sup>9</sup> WHO. Serum and red blood cell folate concentrations for assessing folate in populations. *Vitamins and Mineral Nutrition Information System*. 2015; 01.1-7. The percentage with serum folate below 13nmol/L includes those with serum folate below 7nmol/L

<sup>10</sup> Erythrocyte glutathione reductase activation coefficient (EGRAC) was measured to assess vitamin B2 status Hill MH, Bradley A, Mustaq S, Williams EA, Powers HJ. Effects of methodological variation on assessment of riboflavin status using the erythrocyte glutathione reductase activation coefficient assay. *British Journal of Nutrition*, 2009; 102 (2): 273-8

<sup>11</sup> The median iodine concentration for the population has been presented rather than the mean iodine concentration as recommended in the World Health Organization (WHO), *Assessment of iodine deficiency disorders and monitoring their elimination* ([http://whqlibdoc.who.int/publications/2007/9789241595827\\_eng.pdf](http://whqlibdoc.who.int/publications/2007/9789241595827_eng.pdf)). As the data are based on spot urine samples, the percentage below 100  $\mu\text{g/L}$  does not necessarily indicate the percentage of the population who are iodine deficient. The distribution data should be interpreted in terms of guidelines published by WHO ([http://whqlibdoc.who.int/publications/2007/9789241595827\\_eng.pdf](http://whqlibdoc.who.int/publications/2007/9789241595827_eng.pdf)) in order to establish population status from these results



**Table 6: Consumption of selected food groups for adults and older adults**

Consumption of selected food groups		Age groups (years)											
		Years 7&8 2014/15-15/16 <sup>1</sup>									Years 1-8 2008/09-15/16 <sup>2</sup>		
		19-64			65-74			75+			80+		
		Men	Women	All	Men	Women	All	Men	Women	All	Men	Women	All
<b>5-A-Day fruit and vegetable portions</b>	mean	4.2	4.2	4.2	4.3	4.3	4.3	3.8	3.2	3.4	4.0	3.8	3.9
	median	3.8	3.6	3.7	3.4	4.2	3.6	3.3	2.3	2.8	3.6	3.5	3.5
	Portions/day	1.0	0.8	0.9	0.6	0.6	0.6	0.9	0.0	0.5	0.5	0.6	0.6
	2.5th percentile	11.0	9.5	9.9	11.4	9.4	11.1	9.3	7.7	9.1	10.4	8.4	10.1
	97.5th percentile	29	32	31	31	32	32	18	20	19	26	29	27
<b>Red and processed meat</b>	mean	77	47	62	73	54	63	66	43	53	73	54	62
	median	66	43	54	75	47	59	62	36	45	66	44	57
	g/day	0	0	0	0	0	0	0	0	0	2	0	0
	2.5th percentile	216	132	194	149	139	148	160	115	144	183	144	164
	97.5th percentile												
<b>Oily fish</b>	mean	8	8	8	17	12	15	12	8	10	13	10	11
	median	0	0	0	0	0	0	0	0	0	0	0	0
	g/day	0	0	0	0	0	0	0	0	0	0	0	0
	2.5th percentile	53	50	51	83	50	74	49	48	50	68	54	67
	97.5th percentile												
Number of participants		450	632	1082	71	110	181	70	84	154	134	201	335

Data sources:

<sup>1</sup> National Diet and Nutrition Survey (NDNS) RP years 7&8 (2014/15-15/16) (Roberts et al., 2018)

<sup>2</sup> 80 years and over: National Diet and Nutrition Survey (NDNS) years 1-8 dataset (2008/09-2015/16)

**Table 7a: Energy and macronutrient intakes for older adults by presence of own teeth**

Energy and macronutrient intake by presence of own teeth		65-74 years						75+ years						
		Men		Women		All		Men		Women		All		
		Own teeth		Own teeth		Own teeth		Own teeth		Own teeth		Own teeth		
		None	Some	None	Some	None	Some	None	Some	None	Some	None	Some	
<b>Total energy</b> MJ/day	mean	8.43	8.32	6.07	6.45	7.09	7.30	6.76	7.73	5.90	6.10	6.24	6.85	
	2.5 <sup>th</sup> percentile	4.03	4.53	3.50	3.61	3.69	3.83	3.54	3.72	3.17	3.20	3.18	3.23	
	97.5 <sup>th</sup> percentile	11.64	12.53	9.22	9.88	11.08	11.92	11.24	11.45	9.18	8.92	9.50	10.68	
EAR: Men 9.6MJ/day; Women 7.7 MJ/day														
<b>Protein</b> RNI 53.3 g/d males; 46.5 g/d females;	g/day	mean	77.4	81.6	60.4	66.9	67.7	73.6	62.1	72.2	57.8	60.2	59.5	65.7
		2.5 <sup>th</sup> percentile	38.7	33.5	31.5	38.0	34.8	35.3	39.1	33.9	33.4	31.8	34.3	32.5
		97.5 <sup>th</sup> percentile	123.1	118.7	99.2	101.4	110.0	114.8	101.9	112.3	90.3	95.2	101.9	104.0
	% total energy	mean	15.9	16.8	17.1	17.9	16.6	17.4	15.8	16.0	16.8	16.9	16.4	16.5
		2.5 <sup>th</sup> percentile	9.7	10.9	10.6	12.1	10.6	11.3	9.5	10.9	10.6	11.3	10.6	11.2
		97.5 <sup>th</sup> percentile	23.9	23.8	25.3	24.9	25.3	24.4	22.0	24.7	23.5	24.5	23.5	24.7
<b>Carbohydrate</b>	g/day	mean	239	239	183	187	207	210	203	218	176	180	187	197
		2.5 <sup>th</sup> percentile	126	124	96	84	96	93	113	107	72	82	83	92
		97.5 <sup>th</sup> percentile	342	389	289	303	338	372	346	347	289	276	314	319
	% total energy	mean	45.2	45.2	47.7	45.7	46.6	45.5	47.3	44.7	47.0	46.5	47.1	45.7
		2.5 <sup>th</sup> percentile	31.7	29.3	36.7	31.2	34.8	30.6	25.2	32.6	35.1	30.4	33.0	32.3
		97.5 <sup>th</sup> percentile	60.1	60.7	69.0	59.4	60.1	59.6	60.1	57.9	59.6	59.0	59.6	58.7
DRV: ≥ 50% energy from carbohydrate														
<b>Free sugars</b>	g/day	mean	64.6	59.1	43.4	43.0	52.5	50.3	58.0	57.1	42.0	45.8	48.2	50.9
		2.5 <sup>th</sup> percentile	7.9	7.6	0.1	6.3	3.3	6.5	8.0	11.1	4.6	12.9	4.6	12.1
		97.5 <sup>th</sup> percentile	131.5	154.5	145.7	114.3	131.5	134.1	126.9	134.9	116.6	106.5	116.5	123.2
	% total energy	mean	12.0	10.9	11.1	10.2	11.5	10.5	13.8	11.4	10.8	11.7	11.9	11.5
		2.5 <sup>th</sup> percentile	2.4	1.7	0.0	1.9	1.3	1.9	1.7	3.3	2.2	3.7	2.2	3.3
		97.5 <sup>th</sup> percentile	25.6	26.9	46.0	22.5	27.6	23.1	32.6	22.6	23.2	22.3	25.2	22.3
DRV: ≤ 5% total energy from free sugars														

Energy and macronutrient intake by presence of own teeth			65-74 years						75+ years					
			Men		Women		All		Men		Women		All	
			Own teeth		Own teeth		Own teeth		Own teeth		Own teeth		Own teeth	
			None	Some	None	Some	None	Some	None	Some	None	Some	None	Some
<b>AOAC fibre</b> DRV: 30g/day)	g/day	mean	18.4	21.0	15.4	18.0	16.7	19.4	15.0	18.7	14.3	17.3	14.6	17.9
		2.5 <sup>th</sup> percentile	8.5	10.5	4.8	8.4	6.7	9.1	7.4	7.6	7.7	6.4	7.4	7.1
		97.5 <sup>th</sup> percentile	30.8	33.8	33.9	31.7	33.9	33.2	27.3	32.7	23.2	30.0	24.8	31.5
<b>Fat</b>  DRV: ≤ 33% total energy from fat	g/day	mean	77.2	71.9	55.2	57.8	64.7	64.2	62.1	72.0	54.9	55.7	57.7	63.1
		2.5 <sup>th</sup> percentile	33.7	29.9	24.9	25.4	26.9	27.1	28.9	28.6	26.9	23.5	28.6	25.8
		97.5 <sup>th</sup> percentile	145.7	121.3	97.8	99.6	126.6	112.0	105.7	122.3	92.3	95.5	105.7	112.1
	% total energy	mean	34.2	32.4	34.1	33.6	34.1	33.1	34.6	35.0	35.1	34.3	34.9	34.6
		2.5 <sup>th</sup> percentile	20.6	20.9	18.2	21.1	20.3	20.9	22.3	22.9	26.2	20.9	24.0	22.6
		97.5 <sup>th</sup> percentile	47.2	43.7	45.8	46.6	47.2	44.1	45.7	46.5	46.5	47.7	46.5	47.0
<b>Saturated fat</b>  DRV: ≤ 10% total energy from saturated fat	g/day	mean	30.2	26.9	22.1	22.3	25.6	24.3	24.9	28.8	23.1	22.7	23.8	25.5
		2.5 <sup>th</sup> percentile	9.3	10.3	6.8	8.6	9.3	8.9	9.1	49.5	9.9	9.1	9.1	9.1
		97.5 <sup>th</sup> percentile	59.0	49.1	36.8	42.0	51.7	45.7	49.5	50.7	43.2	40.8	49.5	47.7
	% total energy	mean	13.3	12.1	13.6	12.9	13.4	12.5	13.8	13.9	14.7	13.9	14.3	13.9
		2.5 <sup>th</sup> percentile	6.7	6.9	5.6	6.8	6.3	6.8	7.7	7.6	8.4	6.5	8.4	7.1
		97.5 <sup>th</sup> percentile	20.3	17.6	19.8	20.5	20.3	19.7	20.5	19.9	22.3	22.1	21.7	20.5
Number of participants			59	275	90	377	149	652	80	174	146	210	226	384

Data source: NDNS years 1-8 combined (2008/09-2015/16);

**Table 7b: Micronutrient intakes for older adults by presence of own teeth**

Micronutrient intakes by presence of own teeth		65-74 years						75 years and over					
		Men		Women		All		Men		Women		All	
		Own teeth		Own teeth		Own teeth		Own teeth		Own teeth		Own teeth	
		None	Some	None	Some	None	Some	None	Some	None	Some	None	Some
<b>Vitamin A</b> µg/day retinol equivalents  RNI Men 700µg/day Women 600 µg/day; LRNI: Men 300µg/day; Women 250µg/day	mean	1578	1377	953	1134	1222	1244	1019	1554	997	1048	1006	1279
	2.5 <sup>th</sup> percentile	266	280	162	213	234	250	210	290	216	215	216	244
	97.5 <sup>th</sup> percentile	10988	6359	2509	5104	9040	5506	5316	8225	4548	3108	4548	6945
	% below LRNI	6	3	5	3	5	3	9	4	3	4	5	4
<b>Riboflavin</b> mg/day  RNI: Men 1.3mg/day; Women 1.1mg/day; LRNI: Men/Women: 0.8mg/day	mean	1.90	1.84	1.40	1.63	1.62	1.72	1.44	1.87	1.44	1.49	1.44	1.66
	2.5 <sup>th</sup> percentile	0.83	0.70	0.62	0.70	0.62	0.70	0.67	0.89	0.63	0.71	0.67	0.76
	97.5 <sup>th</sup> percentile	3.61	3.33	2.42	3.04	3.36	3.24	3.08	3.48	2.45	2.78	2.62	3.29
	% below LRNI	2	4	10	3	7	3	16	1	9	5	11	3
<b>Folate</b> µg/day  RNI: Men/Women 200µg/day; LRNI: Men/Women 100µg/day	mean	300	298	203	242	245	268	207	268	195	226	200	245
	2.5 <sup>th</sup> percentile	94	122	106	110	94	115	109	129	90	95	95	102
	97.5 <sup>th</sup> percentile	543	539	378	432	485	488	433	479	368	388	405	445
	% below LRNI	4	1	2	1	3	1	1	1	9	3	6	2
<b>Vitamin D</b> µg/day <b>Includes supplements</b>  RNI: Men/Women 10µg/day	mean	4.85	5.39	3.71	5.93	4.20	5.69	3.98	4.95	4.33	6.07	4.19	5.56
	2.5 <sup>th</sup> percentile	0.64	0.86	0.54	0.65	0.57	0.70	1.17	0.71	0.58	0.67	0.69	0.67
	97.5 <sup>th</sup> percentile	12.07	17.61	12.46	25.82	12.46	22.73	16.96	14.16	17.51	27.19	16.96	24.46
<b>Iron</b> mg/day  RNI: Men/Women 8.7mg/day LRNI: Men/Women 4.7mg/day	mean	10.9	11.6	8.7	9.6	9.6	10.5	8.7	10.6	8.1	9.0	8.3	9.7
	2.5 <sup>th</sup> percentile	4.6	5.6	3.2	4.7	3.4	5.2	4.3	5.2	3.7	3.9	4.3	4.2
	97.5 <sup>th</sup> percentile	23.1	19.2	13.9	16.5	21.2	18.5	14.6	18.1	14.2	16.4	14.3	16.5
	% below LRNI	3	1	6	2	5	2	3	2	6	6	5	4

Micronutrient intakes by presence of own teeth		65-74 years						75 years and over					
		Men Own teeth		Women Own teeth		All Own teeth		Men Own teeth		Women Own teeth		All Own teeth	
		None	Some	None	Some	None	Some	None	Some	None	Some	None	Some
<b>Calcium</b> mg/day RNI: Men/Women 700 mg/day LRNI: Men/Women 400 mg/day	mean	906	923	713	806	796	859	717	897	747	742	735	813
	2.5 <sup>th</sup> percentile	494	434	303	360	347	369	341	405	284	343	341	361
	97.5 <sup>th</sup> percentile	1769	1728	1223	1529	1510	1567	1832	1536	1389	1343	1517	1405
	% below LRNI	0	2	11	6	6	4	8	2	10	6	9	4
<b>Iodine</b> µg/day RNI: Men/Women 140 µg/day LRNI: Men/Women 70 µg/day	mean	218	200	148	170	178	184	160	206	153	159	156	181
	2.5 <sup>th</sup> percentile	78	71	53	54	57	58	62	83	42	59	52	65
	97.5 <sup>th</sup> percentile	431	417	290	353	361	382	378	530	293	302	348	361
	% below LRNI	2	2	9	4	6	3	6	1	8	5	7	3
<i>Number of participants</i>		59	275	90	377	149	652	80	174	146	210	226	384

Data source: NDNS years 1-8 combined (2008/09-2015/16)

**Table 8a: Energy and macronutrient intakes for older adults by use of dentures**

Energy and macronutrient intake by use of dentures		65-74 years						75+ years						
		Men		Women		All		Men		Women		All		
		Denture use		Denture use		Denture use		Denture use		Denture use		Denture use		
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	
<b>Total energy</b> MJ/day	mean	8.40	8.30	6.24	6.52	7.11	7.38	7.47	7.42	6.01	6.08	6.60	6.73	
	2.5 <sup>th</sup> percentile	4.03	4.93	3.46	3.73	3.50	3.86	3.83	3.72	3.03	3.65	3.17	3.65	
	97.5 <sup>th</sup> percentile	11.64	12.53	9.55	9.96	11.08	11.96	11.24	10.12	9.18	8.87	10.71	10.07	
EAR: Men 9.6MJ/day; Women 7.7 MJ/day														
<b>Protein</b> RNI 53.3 g/d males; 46.5g/d females	g/day	mean	79.5	81.9	64.4	67.1	70.5	74.2	69.0	69.6	59.3	59.4	63.2	64.4
		2.5 <sup>th</sup> percentile	33.5	40.2	38.5	32.2	35.7	35.1	39.1	32.0	31.8	37.0	33.7	33.9
		97.5 <sup>th</sup> percentile	118.7	122.5	99.2	101.4	114.8	112.7	102.0	113.0	102.6	95.0	102.0	106.1
	% total energy	mean	16.3	16.9	17.8	17.7	17.2	17.3	15.8	16.0	17.0	16.6	16.5	16.3
		2.5 <sup>th</sup> percentile	10.7	11.0	12.5	11.2	11.7	11.0	11.3	10.9	10.8	11.3	11.0	11.1
		97.5 <sup>th</sup> percentile	23.1	24.1	25.1	24.9	24.5	24.4	22.0	25.4	24.5	24.1	23.9	24.7
<b>Carbohydrate</b>	g/day	mean	241	236	186	187	208	211	216	211	180	176	195	193
		2.5 <sup>th</sup> percentile	101	125	86.1	90.0	93	94	113	107	79	82	80	103
		97.5 <sup>th</sup> percentile	379	389	314	303	342	374	347	312	289	274	321	311
	% total energy	mean	45.5	45.0	47.0	45.1	46.4	45.1	45.7	45.1	47.2	45.9	46.6	45.5
		2.5 <sup>th</sup> percentile	33.9	29.3	34.6	29.3	33.9	29.3	29.5	32.6	34.5	29.4	33.0	30.4
		97.5 <sup>th</sup> percentile	60.1	60.7	59.4	60.3	59.4	60.3	57.5	57.9	59.6	59.0	59.4	58.7
<b>Free sugars</b>	g/day	mean	62.5	58.4	44.1	42.2	51.5	50.1	58.8	55.5	45.2	43.1	50.7	49.1
		2.5 <sup>th</sup> percentile	6.2	8.0	5.6	5.5	5.6	6.9	12.7	11.1	5.0	14.3	8.0	12.1
		97.5 <sup>th</sup> percentile	139.1	154.5	103.3	114.7	125.2	140.1	134.9	134.6	114.3	94.6	123.2	103.7
	% total energy	mean	11.7	10.6	10.9	9.8	11.2	10.2	12.5	11.6	11.5	11.1	11.9	11.3
		2.5 <sup>th</sup> percentile	2.0	1.7	1.8	1.7	1.8	1.7	3.0	3.1	2.3	3.5	2.5	3.4
		97.5 <sup>th</sup> percentile	25.6	26.9	23.2	23.1	25.6	23.1	25.2	24.0	23.2	19.2	23.2	23.4
DRV: ≤ 5% total energy from free sugars														

Energy and macronutrient intake by use of dentures			65-74 years						75+ years					
			Men		Women		All		Men		Women		All	
			Denture use		Denture use		Denture use		Denture use		Denture use		Denture use	
			Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
<b>AOAC fibre</b> DRV: 30g/day)	g/day	mean	19.5	21.2	16.9	18.2	17.9	19.7	17.3	18.0	15.6	17.7	16.2	17.8
		2.5 <sup>th</sup> percentile	8.5	11.0	7.6	8.5	7.6	9.7	7.4	7.3	7.4	7.1	7.4	7.3
		97.5 <sup>th</sup> percentile	37.3	33.8	31.4	31.7	33.6	32.8	30.0	33.9	27.2	30.1	29.6	31.5
<b>Fat</b>	g/day	mean	74.7	71.4	55.6	58.9	63.3	65.0	70.2	67.8	54.8	56.6	61.0	62.1
		2.5 <sup>th</sup> percentile	28.3	34.6	22.9	26.6	23.8	27.3	28.9	28.5	25.8	29.8	25.8	29.3
		97.5 <sup>th</sup> percentile	145.7	116.3	97.5	99.7	122.2	112.0	126.6	112.1	92.1	116.1	105.7	112.1
DRV: ≤ 33% total energy from fat	% total energy	mean	33.3	32.3	33.5	33.9	33.4	33.1	35.3	34.4	34.4	34.9	34.7	34.6
		2.5 <sup>th</sup> percentile	20.6	20.9	18.7	20.3	19.8	20.9	22.8	22.6	22.1	23.9	22.8	23.1
		97.5 <sup>th</sup> percentile	46.3	43.6	45.6	48.2	45.8	44.1	46.9	44.6	46.6	50.1	46.5	47.1
<b>Saturated fat</b>	g/day	mean	28.3	26.9	21.8	22.6	24.4	24.7	28.6	26.6	22.9	22.7	25.2	24.6
		2.5 <sup>th</sup> percentile	8.1	12.1	7.4	9.6	7.7	10.1	9.1	11.1	9.1	9.3	9.1	10.5
		97.5 <sup>th</sup> percentile	59.0	47.7	38.9	42.5	50.0	45.7	53.8	45.9	42.2	40.8	49.3	45.3
DRV: ≤ 10% total energy from saturated fat	% total energy	mean	12.5	12.1	13.1	13.0	12.8	12.6	14.3	13.4	14.3	14.0	14.3	13.7
		2.5 <sup>th</sup> percentile	6.1	6.9	6.1	7.6	6.1	7.1	8.3	7.6	8.4	6.5	8.4	6.5
		97.5 <sup>th</sup> percentile	19.3	18.6	19.1	20.7	19.3	20.1	20.5	18.4	22.3	20.5	22.1	20.3
Number of participants			139	195	234	233	373	428	254	356	246	110	500	466

Data source: NDNS years 1-8 combined (2008/09-2015/16);

**Table 8b: Micronutrient intakes for older adults by use of dentures**

Micronutrient intakes by use of dentures		65-74 years						75 years and over					
		Men		Women		All		Men		Women		All	
		Denture use		Denture use		Denture use		Denture use		Denture use		Denture use	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
<b>Vitamin A</b> µg/day retinol equivalents RNI Men 700µg/day Women 600 µg/day LRNI: Men 300µg/day; Women 250µg/day	mean	1554	1317	1019	1176	1235	1245	1439	1350	1042	1010	1202	1175
	2.5 <sup>th</sup> percentile	262	304	230	205	236	274	290	289	240	197	238	229
	97.5 <sup>th</sup> percentile	10988	5790	3982	5104	7538	5347	7124	8224	4548	2603	5851	6945
	% below LRNI	5	3	4	3	5	3	5	5	4	4	4	5
<b>Riboflavin</b> mg/day RNI: Men 1.3mg/day; Women 1.1mg/day LRNI: Men/Women: 0.8mg/day	mean	1.91	1.81	1.53	1.64	1.69	1.72	1.71	1.78	1.51	1.42	1.59	1.60
	2.5 <sup>th</sup> percentile	0.61	0.84	0.65	0.79	0.62	0.81	0.77	0.67	0.66	0.65	0.71	0.67
	97.5 <sup>th</sup> percentile	3.74	3.29	2.68	3.09	3.27	3.24	3.48	2.80	2.50	2.73	3.14	2.78
	% below LRNI	5	2	7	3	6	2	7	4	6	5	7	5
<b>Folate</b> µg/day RNI: Men/Women 200µg/day; LRNI: Men/Women 100µg/day	mean	289	304	225	245	251	274	241	263	208	228	221	245
	2.5 <sup>th</sup> percentile	94	149	106	125	99	136	109	111	90	95	96	102
	97.5 <sup>th</sup> percentile	527	549	378	468	485	500	424	527	368	407	397	518
	% below LRNI	3	0	2	1	3	1	1	1	6	4	4	2
<b>Vitamin D</b> µg/day <b>Includes supplements</b> RNI: Men/Women 10µg/day	mean	5.14	5.41	5.27	5.82	5.21	5.62	4.27	5.18	4.93	6.40	4.7	5.8
	2.5 <sup>th</sup> percentile	0.57	0.98	0.61	0.70	0.58	0.82	1.13	0.63	0.67	0.72	0.67	0.71
	97.5 <sup>th</sup> percentile	17.6	17.5	23.2	25.8	19.2	22.7	16.8	13.9	24.5	33.6	20.2	27.2
<b>Iron</b> mg/day RNI: Men/Women 8.7mg/day LRNI: Men/Women 4.7mg/day	mean	11.2	11.7	9.1	9.7	10.0	10.7	10.0	10.2	8.5	9.1	9.1	9.6
	2.5 <sup>th</sup> percentile	4.6	6.1	4.3	4.8	4.4	5.4	4.7	5.2	3.9	4.4	4.2	4.4
	97.5 <sup>th</sup> percentile	21.2	19.2	15.2	16.6	19.1	18.1	17.6	16.3	14.3	15.7	16.4	15.7
	% below LRNI	3	0	5	2	4	1	3	2	6	5	5	4



Micronutrient intakes by use of dentures		65-74 years						75 years and over					
		Men		Women		All		Men		Women		All	
		Denture use		Denture use		Denture use		Denture use		Denture use		Denture use	
		Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
<b>Calcium</b> mg/day	mean	913	925	776	803	831	862	829	866	759	716	787	789
	2.5 <sup>th</sup> percentile	386	453	325	360	337	369	387	341	327	361	339	342
	97.5 <sup>th</sup> percentile	1631	1766	1447	1553	1542	1567	1536	1460	1396	1177	1514	1418
	% below LRNI	4	1	6	7	5	4	3	5	9	4	6	5
RNI: Men/Women 700 mg/day LRNI: Men/Women 400 mg/day													
<b>Iodine</b> µg/day	mean	206	201	159	172	178	186	183	205	159	153	169	179
	2.5 <sup>th</sup> percentile	57	71	52	67	52	71	62	82	52	59	58	59
	97.5 <sup>th</sup> percentile	428	417	381	322	410	365	391	646	295	317	344	361
	% below LRNI	3	2	7	3	5	2	4	1	6	5	5	3
RNI: Men/Women 140 µg/day LRNI: Men/Women 70 µg/day													
Number of participants		139	195	234	233	373	428	151	103	246	110	317	213

Data source: NDNS years 1-8 combined (2008/09-2015/16)

**Table 9a Energy and macronutrient intakes for older adults by reported difficulty chewing**

Energy and macronutrient intakes by difficulty chewing			65-74 years						75+ years					
			Men Difficulty chewing		Women Difficulty chewing		All Difficulty chewing <sup>a</sup>		Men Difficulty chewing		Women Difficulty chewing		All Difficulty chewing <sup>b</sup>	
			A little	No	A little	No	A little	No	A little	No	A little	No	A little	No
<b>Total energy</b> EAR: Men 9.6 MJ/day; Women 7.7 MJ/day	MJ/day	mean	8.16	8.26	6.43	6.34	7.11	7.23	7.60	7.43	6.42	5.93	7.06	6.55
		25 <sup>th</sup> percentile	2.73	4.53	3.68	3.50	3.68	3.86	4.87	3.54	3.03	3.20	3.17	3.21
		97.5 <sup>th</sup> percentile	11.21	12.47	10.19	9.55	11.21	11.64	11.24	11.64	8.92	9.18	11.24	10.62
<b>Protein</b>	g/day	mean	77.9	81.0	64.6	65.7	69.9	72.8	68.0	70.5	60.9	59.3	64.7	63.9
		2.5 <sup>th</sup> percentile	25.3	35.7	31.5	38.0	29.1	36.8	45.9	33.9	29.6	31.8	39.0	32.3
		97.5 <sup>th</sup> percentile	123.1	116.7	103.7	98.3	108.2	113.7	101.9	112.3	95.0	102.6	95.0	105.1
RNI 53.3 g/d males; 46.5 g/d females;	% total energy	mean	16.3	16.8	17.1	17.9	16.8	17.4	15.3	16.3	16.2	17.1	15.7	16.8
		2.5 <sup>th</sup> percentile	9.1	11.2	10.6	12.3	10.2	11.7	11.9	10.6	11.7	11.2	11.7	10.9
		97.5 <sup>th</sup> percentile	21.6	23.9	24.9	25.3	24.4	24.6	22.0	25.2	20.7	25.4	21.9	25.4
<b>Carbohydrate</b>	g/day	mean	238	234	190	185	209	208	213	214	197	174	205	190
		2.5 <sup>th</sup> percentile	93	124	104	84	96	92	132	107	92	75	95	79
		97.5 <sup>th</sup> percentile	379	363	314	303	379	342	346	347	306	276	319	314
DRV: ≥ 50% energy from carbohydrate	% total energy	mean	46.4	44.9	46.9	45.9	46.7	45.5	44.3	45.5	48.3	46.4	46.2	46.0
		2.5 <sup>th</sup> percentile	33.9	29.3	32.7	29.5	33.9	29.5	32.6	31.1	35.9	30.4	32.6	30.4
		97.5 <sup>th</sup> percentile	61.0	60.1	69.0	59.4	62.7	59.6	56.9	57.9	59.4	59.5	59.3	58.9
<b>Free sugars</b>	g/day	mean	61.8	57.9	50.0	41.5	54.7	49.1	62.7	53.7	53.6	41.7	58.5	46.6
		2.5 <sup>th</sup> percentile	6.2	8.0	2.6	5.5	5.1	6.4	12.7	8.9	12.9	5.9	12.9	8.9
		97.5 <sup>th</sup> percentile	142.9	140.1	145.7	112.1	142.9	129.7	140.8	130.3	114.3	94.1	120.8	116.5
DRV: ≤ 5% total energy from free sugars	% total energy	mean	11.5	10.8	12.1	9.9	11.9	10.3	12.8	11.3	13.0	10.9	12.9	11.1
		2.5 <sup>th</sup> percentile	1.5	1.7	0.8	1.8	1.5	1.7	3.3	2.3	3.4	3.5	3.3	2.3
		97.5 <sup>th</sup> percentile	26.9	25.6	46.0	22.5	27.6	23.1	25.4	22.9	23.6	22.8	25.4	22.9

Energy and macronutrient intakes by difficulty chewing			65-74 years						75+ years					
			Men Difficulty chewing		Women Difficulty chewing		All Difficulty chewing <sup>a</sup>		Men Difficulty chewing		Women Difficulty chewing		All Difficulty chewing <sup>b</sup>	
			A little	No	A little	No	A little	No	A little	No	A little	No	A little	No
<b>AOAC fibre</b>  DRV: 30g/day)	g/day	mean	20.2	20.6	16.9	17.8	18.2	19.1	17.0	18.2	17.1	16.4	17.0	17.1
		2.5 <sup>th</sup> percentile	6.1	10.1	4.8	8.4	6.1	9.0	7.6	7.3	2.9	8.0	7.6	7.4
		97.5 <sup>th</sup> percentile	39.2	33.2	32.1	31.7	33.8	32.7	27.8	31.5	55.1	29.6	29.0	30.1
<b>Fat</b>  DRV: ≤ 33% total energy from fat	g/day	mean	70.6	72.0	58.4	56.5	63.2	63.6	73.4	67.9	57.4	54.4	66.0	60.0
		2.5 <sup>th</sup> percentile	21.9	30.5	26.9	24.9	22.9	26.9	37.6	28.5	26.9	23.5	28.5	25.8
		97.5 <sup>th</sup> percentile	124.5	122.2	99.7	97.8	109.1	112.0	122.3	112.8	87.9	100.2	110.8	109.5
	% total energy	mean	32.9	32.6	34.2	33.3	33.7	33.0	36.3	34.4	33.8	34.5	35.2	34.4
		2.5 <sup>th</sup> percentile	23.6	20.6	18.8	20.2	20.3	20.4	26.3	22.3	23.1	23.7	24.7	22.6
		97.5 <sup>th</sup> percentile	44.8	44.1	48.5	44.5	48.2	44.1	48.2	44.5	44.1	47.7	46.9	46.2
<b>Saturated fat</b>  DRV: ≤ 10% total energy from saturated fat	g/day	mean	26.2	27.1	22.7	21.8	24.1	24.3	29.5	27.1	24.7	22.0	27.3	24.1
		2.5 <sup>th</sup> percentile	7.7	10.3	8.9	8.1	7.7	8.9	13.3	9.1	9.9	8.6	11.8	9.0
		97.5 <sup>th</sup> percentile	45.0	51.4	42.5	39.7	45.0	47.0	50.7	47.7	41.0	42.2	49.5	47.7
	% total energy	mean	12.2	12.2	13.2	12.9	12.8	12.6	14.5	13.6	14.6	13.8	14.5	13.7
		2.5 <sup>th</sup> percentile	6.9	6.5	5.7	6.8	6.8	6.7	8.6	7.7	8.8	6.9	8.8	7.1
		97.5 <sup>th</sup> percentile	19.1	19.1	20.7	20.1	20.7	19.3	20.5	18.8	22.2	22.3	22.2	21.1
Number of participants			49	299	81	369	125	648	59	179	72	257	131	436

Data source: NDNS years 1-8 combined (2008/09-2015/16);

<sup>a</sup> In the 65-74 year age group 25 participants reported a fair amount of difficulty chewing food and 2 participants reported a great amount of difficulty. Intakes are not reported for these groups due to small cell sizes

<sup>b</sup> In the 75 + year age group 32 participants reported a fair amount of difficulty chewing food and 11 participants reported a great amount of difficulty. Intakes are not reported for these groups due to small cell sizes

**Table 9b: Micronutrient intakes for older adults by reported difficulty chewing**

Micronutrient intakes by difficulty chewing		65-74 years						75 years and over					
		Men		Women		All		Men		Women		All	
		Difficulty chewing		Difficulty chewing		Difficulty chewing		Difficulty chewing		Difficulty chewing		Difficulty chewing	
		A little	No	A little	No	A little	No	A little	No	A little	No	A little	No
<b>Vitamin A</b> µg/day retinol equivalents	mean	1307	1435	908	1124	1066	1268	1511	1404	963	1055	1258	1199
	2.5 <sup>th</sup> percentile	77	292	193	213	162	256	297	250	244	206	244	221
	97.5 <sup>th</sup> percentile	10705	7121	2778	5104	4022	5790	6945	7124	5111	4397	6945	5316
	% below LRNI	10	3	5	3	7	3	4	5	3	4	4	5
RNI Men 700µg/day Women 600 µg/day LRNI: Men 300µg/day; Women 250µg/day													
<b>Riboflavin</b> mg/day	mean	1.85	1.83	1.54	1.60	1.66	1.71	1.76	1.75	1.57	1.44	1.67	1.57
	2.5 <sup>th</sup> percentile	0.61	0.79	0.67	0.70	0.61	0.71	0.75	0.84	0.63	0.65	0.75	0.71
	97.5 <sup>th</sup> percentile	3.36	3.41	2.94	2.76	3.36	3.21	3.08	3.47	2.42	2.73	3.08	2.84
	% below LRNI	6	3	7	4	6	4	8	2	7	5	8	4
RNI: Men 1.3mg/day; Women 1.1mg/day; LRNI: Men/Women: 0.8mg/day													
<b>Folate</b> µg/day	mean	299	298	228	238	256	266	257	252	208	219	234	233
	2.5 <sup>th</sup> percentile	70	122	106	113	92	117	119	109	67	90	112	96
	97.5 <sup>th</sup> percentile	539	543	471	423	539	482	464	450	346	399	445	434
	% below LRNI	6	1	1	1	3	1	0	1	4	6	2	4
RNI: Men/Women 200µg/day; LRNI: Men/Women 100µg/day													
<b>Vitamin D</b> µg/day <b>Includes supplements</b>	mean	5.92	5.17	4.64	5.76	5.15	5.49	4.32	4.90	6.65	5.21	5.40	5.08
	2.5 <sup>th</sup> percentile	0.92	0.82	0.67	0.61	0.92	0.61	1.31	0.67	0.41	0.68	0.69	0.67
	97.5 <sup>th</sup> percentile	26.51	17.07	14.80	25.82	14.80	22.50	13.52	16.78	38.28	24.72	24.46	22.20
RNI: Men/Women 10µg/day													

Micronutrient intakes by difficulty chewing		65-74 years						75 years and over					
		Men		Women		All		Men		Women		All	
		Difficulty chewing		Difficulty chewing		Difficulty chewing		Difficulty chewing		Difficulty chewing		Difficulty chewing	
		A little	No	A little	No	A little	No	A little	No	A little	No	A little	No
<b>Iron</b> mg/day	mean	11.5	11.5	9.1	9.6	10.0	10.5	10.1	10.2	8.7	8.7	9.4	9.3
	2.5 <sup>th</sup> percentile	3.7	5.6	3.4	4.7	3.7	5.2	5.6	4.3	2.0	4.2	5.5	4.3
	97.5 <sup>th</sup> percentile	23.1	19.5	18.2	15.3	19.1	18.1	15.5	17.6	19.5	15.3	19.5	16.3
	RNI: Men/Women 8.7mg/day LRNI: Men/Women 4.7mg/day	% below LRNI	6	1	6	2	6	1	0	3	4	6	2
<b>Calcium</b> mg/day	mean	913	902	779	789	832	841	854	845	804	720	831	772
	2.5 <sup>th</sup> percentile	238	447	327	360	327	377	405	384	284	343	373	346
	97.5 <sup>th</sup> percentile	1808	1547	1717	1447	1717	1515	1832	1460	1210	1389	1790	1396
	RNI: Men/Women 700 mg/day LRNI: Men/Women 400 mg/day	% below LRNI	5	1	9	6	7	4	1	3	6	7	3
<b>Iodine</b> µg/day	mean	187	203	155	167	168	184	198	192	166	153	183	169
	2.5 <sup>th</sup> percentile	51	74	71	52	55	59	62	72	52	52	62	59
	97.5 <sup>th</sup> percentile	427	415	326	355	353	382	530	407	285	293	391	337
	RNI: Men/Women 140 µg/day LRNI: Men/Women 70 µg/day	% below LRNI	10	1	2	5	5	3	6	1	4	7	5
Number of participants		44	279	81	369	125	648	59	179	72	257	131	436

Data source: NDNS years 1-8 combined (2008/09-2015/16);

**Table 10: Median nutrient intakes for people aged 85 years and over in NDNS and the Newcastle 85+ study**

Median intake/day	NDNS 85 years and over <sup>1</sup>			Newcastle 85 years and over <sup>2,3</sup>		
	Men	Women	All	Men	Women	All
Energy (kcal)	1628	1401	1534	1848	1471	1588
Carbohydrate (g)	199	169	177	228	177	194
Carbohydrate % food energy	46.5	47.6	46.9	46.8	46.8	46.8
Fat (g)	62.9	52.7	59.0	74.7	60.4	65.8
Fat % food energy	37.4	36.3	36.5	36.4	37.2	36.8
Protein (g)	65.6	56.4	60.5	73.0	54.5	61.3
Protein % food energy	15.5	17.4	16.6	15.9	15.5	15.7
Folate (µg)	219	196	205	245	189	208
Vitamin B12 µg	6.0	4.3	4.9	3.4	2.6	2.9
Vitamin D µg	3.5	2.4	2.6	2.3	1.8	2.0
Calcium mg	767	725	733	829	683	731
Iron mg	9.6	8.1	8.5	10.5	7.8	8.7
Number of participants	50	97	147	302	491	793

Data sources:

<sup>1</sup> NDNS years 1-8 (2008/09-2015/16)

<sup>2</sup> Mendonca N et al (2016) Macronutrient intake and food sources in the very old: analysis of the Newcastle 85+ study

<sup>3</sup> Mendonca N et al (2016) Micronutrient intakes and food sources in the very old: analysis of the Newcastle 85+ study

## Annex 3 - Search strategy

The databases Medline, Embase, Cochrane, and Food Science and Technology Abstracts were searched. The following search strategy was applied on all (with variations to account for differences in the databases):

- 1 Aged/
- 2 "AGED, 80 AND OVER"/
- 3 Frail Elderly/
- 4 exp Aging/
- 5 (old\* or senior\* or elder\* or aged or ageing or aging or geriatric\* or senescence\* or frail\*).ti.
- 6 (advanc\* adj2 (age or years or aging or ageing)).ti.
- 7 or/1-6
- 8 EATING/
- 9 exp FOOD/
- 10 Energy Intake/
- 11 Nutritional Requirements/
- 12 Food Preferences/
- 13 Feeding Behavior/
- 14 Nutritional Status/
- 15 DIET/
- 16 APPETITE/
- 17 exp MALNUTRITION/di, dh, dt, su, th [Diagnosis, Diet Therapy, Drug Therapy, Surgery, Therapy] (26708)
- 18 (malnutrition or malnourish\* or under?nutrition under?nourish\* or emaciated or starving or hunger).tw.
- 19 exp Food Deprivation/
- 20 ((food or nutrition\* or energy or kalori\* or diet\* or eating or vitamin\* or protein\* or supplement\*) adj (supplement\* or adequate\* or deficienc\* or intake or choice\* or habit\* or preference\* or quality or decision\* or pattern\*)).tw.

21 ((poor or low) adj (appetite\* or diet quality or protein intake)).tw.  
22 nutritional determinant\*.tw.  
23 or/8-22  
24 Health/  
25 well?being.tw.  
26 healthy ag?ing.tw.  
27 exp COGNITION/  
28 exp Mental Health/  
29 exp Health Status/  
30 exp METABOLISM/  
31 exp Physical Fitness/  
32 exp Motor Skills/  
33 exp "Quality of Life"/  
34 or/24-33  
35 7 and 23 and 34  
36 limit 35 to (english language and yr="1990 -Current")  
37 limit 36 to "reviews (best balance of sensitivity and specificity)"  
38 (review\* or meta\*analys\* or overview\* or umbrella or systematic).ti.  
39 36 and 38  
40 37 or 39



## Annex 4 - Characteristics of meta-analyses and systematic reviews

### Annex 4.1 – Included studies by outcome

Studies that meet inclusion criteria			
Outcome	Number of publications	First author <sup>1</sup>	Publication type
Mortality	3 (2 MA, 1 SR)	<b>Milne 2006</b> Tyrovolas 2010 <b>Winter 2014</b>	<b>MA</b> SR <b>MA</b>
Musculoskeletal health	26 (13 MA, 1 NMA <sup>2</sup> , 12 SR)	<b>Antoniak 2017</b> <b>Beudart 2018</b> Bloom 2018 <b>Coehlo-Junior 2018a</b> <b>Coehlo-Junior 2018b</b> Cruz-Jentoft 2014 Dedeyne 2017 <sup>3</sup> <b>Dewansingh 2018</b> Eglseer (2016) Feng 2017 <b>Giné-Garriga 2015</b> Lorenzo-López 2017 Mello 2014 <b>Milne 2006</b>	<b>MA</b> <b>MA</b> SR <b>MA</b> <b>MA</b> SR SR <b>MA</b> SR SR <b>MA</b> SR SR <b>MA</b> SR

<sup>1</sup> Note: publications may have more than one outcome and therefore may appear in this column more than once.

<sup>2</sup> Network meta-analysis

<sup>3</sup> In addition, includes weight loss as an outcome.

Studies that meet inclusion criteria			
		<sup>4</sup> Nowson 2018 <sup>5</sup> Pedersen 2014 Rosendahl-Riise 2017 Roman-Viñas 2018 <b>Silva 2018</b> Stanaway 2017 <b>ten Haaf 2018</b> <b>Tieland 2017</b> <b>Trevisan 2018</b> <b>Tricco 2017</b> <b>Wu 2017</b> <b>Xu 2015</b>	SR SR SR <b>MA</b> SR <b>MA</b> <b>MA</b> <b>MA</b> <b>NMA<sup>2</sup></b> <b>MA</b> <b>MA</b>
Cardiovascular health	4 SR	Nowson 2018 Ruxton 2016 Stanaway 2017 Tyrovolas 2010	SR SR SR SR
Cancers	1 SR	Tyrovolas 2010	SR
Immune health	1 SR	Ruxton 2016	SR
Weight change	3 (2 MA)	<b>Dewansingh 2018</b> <b>Milne 2006</b>	<b>MA</b> <b>MA</b>
Quality of life	2 SR	Govindaraju 2018 Ruxton 2016	SR SR

<sup>4</sup> In addition, includes non-fatal CV events as an outcome.

<sup>5</sup> In addition, includes mortality as an outcome.

## Annex 4.2 – Excluded publications on full text

Paper	Reason
Anagnostis P, Dimopoulou C, Karras S, Lambrinouadaki I & Goulis DG (2015) Sarcopenia in post-menopausal women: Is there any role for vitamin D? <i>Maturitas</i> . 82(1):56-64.	Not a systematic review or meta-analysis.
Annweiler C & Beauchet O (2015) Questioning vitamin D status of elderly fallers and nonfallers: a meta-analysis to address a 'forgotten step'. <i>Journal of Internal Medicine</i> . 277(1):16-44.	Review on vitamin D published before 2016.
Annweiler C, Schott AM, Berrut G, Fantino B & Beauchet O (2009) Vitamin D-related changes in physical performance: a systematic review. <i>The Journal of Nutrition, Health &amp; Aging</i> . 13(10):893-898.	Review on vitamin D published before 2016.
Artaza-Artabe I, Sáez-López P, Sánchez-Hernández N, Fernández-Gutierrez N & Malafarina V (2016) The relationship between nutrition and frailty: Effects of protein intake, nutritional supplementation, vitamin D and exercise on muscle metabolism in the elderly. A systematic review. <i>Maturitas</i> . 93:89-99.	Excluded because considered outcome (malnutrition) not within remit.
Ashor AW, Siervo M, Lara J, Oggioni C, Afshar S & Mathers JC (2015) Effect of vitamin C and vitamin E supplementation on endothelial function: a systematic review and meta-analysis of randomised controlled trials. <i>British Journal of Nutrition</i> . 113(8):1182-1194.	Age group did not meet inclusion criteria.
Autier P, Mullie P, Macacu A, Dragomir M, Boniol M, Coppens K, et al (2017) Effect of vitamin D supplementation on non-skeletal disorders: a systematic review of meta-analyses and randomised trials. <i>Lancet Diabetes &amp; Endocrinology</i> . 5(12):986-1004.	Age group did not meet inclusion criteria.
Bandayrel K & Wong S (2011) Systematic Literature Review of Randomized Control Trials Assessing the Effectiveness of Nutrition Interventions in Community-Dwelling Older Adults. <i>Journal of Nutrition Education and Behavior</i> . 43(4):251-262.	Excluded because paper relates to risk management.
Barnard K & Colón-Emeric C (2010) Extraskkeletal effects of vitamin D in older adults: cardiovascular disease, mortality, mood, and cognition. <i>American Journal of Geriatric Pharmacotherapy</i> . 8(1):4-33.	Review on vitamin D published before 2016.

<p>Batsis, J. A., Gill, L. E., Masutani, R. K., Adachi-Mejia, A. M., Blunt, H. B., Bagley, P. J., Lopez-Jimenez, F. and Bartels, S. J. (2017) Weight loss interventions in older adults with obesity: a systematic review of randomized controlled trials since 2005. <i>Journal of the American Geriatrics Society</i>. <a href="https://doi.org/10.1111/jgs.14514">https://doi.org/10.1111/jgs.14514</a></p>	<p>Excluded because only 1 RCT met inclusion criteria and this RCT is covered in MA by Gine-Garriga.</p>
<p>Bauer J, Biolo G, Cederholm T, Cesari M, Cruz-Jentoft AJ, Morley JE, et al (2013) Evidence-Based Recommendations for Optimal Dietary Protein Intake in Older People: A Position Paper From the PROT-AGE Study Group. <i>Journal of the American Medical Directors Association</i>. 14(8):542-559.</p>	<p>Not a systematic review or meta-analysis.</p>
<p>Blumberg JB, Frei B, Fulgoni VL, Weaver CM &amp; Zeisel SH (2017) Contribution of Dietary Supplements to Nutritional Adequacy in Various Adult Age Groups. <i>Nutrients</i>. 9(12).</p>	<p>Not a systematic review or meta-analysis.</p>
<p>Booth SL (2007) Vitamin K status in the elderly. <i>Current Opinion in Clinical Nutrition and Metabolic Care</i>. 10(1):20-23.</p>	<p>Not a systematic review or meta-analysis.</p>
<p>Buijsse B, Feskens EJ, Schlettwein-Gsell D, Ferry M, Kok FJ, Kromhout D, et al (2005) Plasma carotene and alpha-tocopherol in relation to 10-y all-cause and cause-specific mortality in European elderly: the Survey in Europe on Nutrition and the Elderly, a Concerted Action (SENECA). <i>American Journal of Clinical Nutrition</i>. 82(4):879-886.</p>	<p>Not a systematic review or meta-analysis.</p>
<p>Campbell SE, Seymour DG, Primrose WR, Almazan C, Arino S, Dunstan E, et al (2004) A systematic literature review of factors affecting outcome in older medical patients admitted to hospital. <i>Age and Ageing</i>. 33(2):110-115.</p>	<p>Excluded because nutritional information not detailed.</p>
<p>Campbell, A. D., Godfryd, A., Buys, D. R. and Locher, J. L. (2015) Does participation in home-delivered meals programs improve outcomes for older adults? Results of a systematic review. <i>Journal of Nutrition in Gerontology &amp; Geriatrics</i>. 34(2): 124-167.</p>	<p>Exclude because a narrative review with no report on outcome data.</p>
<p>Carpenter CR, Shelton E, Fowler S, Suffoletto B, Platts-Mills TF, Rothman RE, et al (2015) Risk factors and screening instruments to predict adverse outcomes for undifferentiated older emergency department patients: a systematic review and meta-analysis. <i>Academic Emergency Medicine</i>. 22(1):1-21.</p>	<p>Outcome did not fit the inclusion criteria; this is a systematic review of screening instruments.</p>

Cawood A L; Elia M ; Stratton R J (2012) Systematic review and meta-analysis of the effects of high protein oral nutritional supplements. <i>Ageing Research Reviews</i> . 11 (2):278-296.	Excluded because review relates to risk management.
Cho Y, Cudhea F, Park JH, Lee JT, Mozaffarian D, Singh G, et al (2016) Estimating change in cardiovascular disease and diabetes burdens due to dietary and metabolic factors in Korea 1998-2011: A comparative risk assessment analysis. <i>BMJ Open</i> . 6 (12) (no pagination)(e013283).	Not a systematic review or meta-analysis.
Clements SJ & S RC (2018) Diet, the intestinal microbiota, and immune health in aging. <i>Critical Reviews in Food Science and Nutrition</i> . 58(4):651-661.	Not a systematic review or meta-analysis.
Colonetti T, Grande AJ, Milton K, Foster C, Alexandre MC, Uggioni ML & Rosa MI (2017) Effects of whey protein supplement in the elderly submitted to resistance training: systematic review and meta-analysis. <i>Int J Food Sci Nutr</i> 68(3), 257-264.	Excluded because review does not exclude resistance training as effect.
Cumming RG & Nevitt MC (1997) Calcium for prevention of osteoporotic fractures in postmenopausal women. <i>Journal of Bone and Mineral Research</i> . 12(9):1321-1329.	Population does not meet inclusion criteria; many primary studies consider populations in care homes or hospitals; discussion not separated by setting.
Darling AL, Millward DJ, Torgerson DJ, Hewitt CE & Lanham-New SA (2009) Dietary protein and bone health: a systematic review and meta-analysis. <i>American Journal of Clinical Nutrition</i> . 90(6):1674-1692.	Age group did not meet inclusion criteria.
Demling RH (2009) Nutrition, anabolism, and the wound healing process: an overview. <i>Eplasty</i> . 9:e9.	Not a systematic review or meta-analysis.
Fabiani R, Naldini G & Chiavarini M. (2019) Dietary Patterns in Relation to Low Bone Mineral Density and Fracture Risk: A Systematic Review and Meta-Analysis. <i>Adv Nutr</i> doi: 10.1093/advances/nmy073. [Epub ahead of print]	Age of study participants did not meet inclusion criteria.
Favaro-Moreira NC, Krausch-Hofmann S, Matthys C, Vereecken C, Vanhauwaert E, Declercq A, et al (2016) Risk Factors for Malnutrition in Older Adults: A Systematic Review of the Literature Based on Longitudinal Data. <i>Advances in Nutrition</i> . 7(3):507-522.	Excluded because considered outcome (malnutrition) was not within remit.

Hoffmann M R; Senior P A; Mager D R (2015) Vitamin D supplementation and health-related quality of life: a systematic review of the literature. <i>Journal of the Academy of Nutrition and Dietetics</i> . 115: 2212-2672	Age group did not meet inclusion criteria.
Host A, McMahon AT, Walton K & Charlton K (2016) Factors Influencing Food Choice for Independently Living Older People-A Systematic Literature Review. <i>Journal of Nutrition in Gerontology and Geriatrics</i> . 35(2):67-94.	Excluded as 'most studies were qualitative in nature'.
Kehoe, L., Walton, J., and Flynn, A. (2019) Nutritional challenges for older adults in Europe: current status and future directions. <i>Proceedings of the Nutrition Society</i> . Published online: 30 January 2019.	Not a systematic review or meta-analysis
Kiesswetter E, Poggiogalle E, Migliaccio S, Donini LM, Sulmont-Rosse C, Feart C, et al (2018) Functional determinants of dietary intake in community-dwelling older adults: a DEDIPAC (DEterminants of Diet and Physical ACTivity) systematic literature review. <i>Public Health Nutrition</i> . 21(10):1886-1903.	Excluded as the investigated exposures could not be categorised as nutrition.
Kim JE, O'Connor LE, Sands LP, Slobodnik MB & Campbell WW (2016) Effects of dietary protein intake on body composition changes after weight loss in older adults: a systematic review and meta-analysis. <i>Nutrition Reviews</i> . 74(3):210-224.	Age group did not meet inclusion criteria.
Kim JE, O'Connor LE, Sands LP, Slobodnik MB & Campbell WW (2016) Effects of dietary protein intake on body composition changes after weight loss in older adults: a systematic review and meta-analysis. <i>Nutrition Reviews</i> . 74(3):210-224.	Age group did not meet inclusion criteria.
Kuo HK, Sorond FA, Chen JH, Hashmi A, Milberg WP & Lipsitz LA (2005) The role of homocysteine in multisystem age-related problems: a systematic review. <i>Journals of Gerontology. Series A: Biological Sciences and Medical Sciences</i> . 60(9):1190-1201.	Excluded as the investigated exposures could not be categorised as nutrition.
Lara, J., Hobbs, N., Moynihan, P. J., Meyer, T. D., Adamson, A. J., Errington, L., Rochester, L., Sniehotta, F. F., White, M. & Mathers, J. C. (2014) Effectiveness of dietary interventions among adults of retirement age: a systematic review and meta-analysis of randomized controlled trials. <i>BMC Medicine</i> .	Excluded because outcome not relevant.

<p>Latham NK, Anderson CS &amp; Reid IR (2003) Effects of vitamin D supplementation on strength, physical performance, and falls in older persons: a systematic review. <i>Journal of the American Geriatrics Society</i>. 51(9):1219-1226.</p>	<p>Review on vitamin D published before 2016.</p>
<p>Makino S, Ikegami S, Kume A, Horiuchi H, Sasaki H &amp; Orii N (2010) Reducing the risk of infection in the elderly by dietary intake of yoghurt fermented with <i>Lactobacillus delbrueckii ssp. bulgaricus</i> OLL1073R-1. <i>British Journal of Nutrition</i>. 104(7):998-1006.</p>	<p>Not a systematic review or meta-analysis.</p>
<p>Malafarina, V., Uriz-Otano, F., Gil-Guerrero, L. and Iniesta, R. (2013) The anorexia of ageing: Physiopathology, prevalence, associated comorbidity and mortality. A systematic review. <i>Maturitas</i> 74: 293-302</p>	<p>Analysis of biomarkers with no well-defined health outcomes.</p>
<p>Medical Advisory Secretariat (2008) Prevention of falls and fall-related injuries in community-dwelling seniors: an evidence-based analysis. <i>Ont Health Technol Assess Ser</i>. 8(2):1-78.</p>	<p>Review on vitamin D published before 2016.</p>
<p>Michael YL, Whitlock EP, Lin JS, Fu R, O'Connor EA &amp; Gold R (2010) Primary care-relevant interventions to prevent falling in older adults: a systematic evidence review for the U.S. Preventive Services Task Force. <i>Annals of Internal Medicine</i>. 153(12):815-825.</p>	<p>Review on vitamin D published before 2016.</p>
<p>Miles, L. M., Mills, K., Clarke, R., and Dangour, A. D. (2015) Is there an association of vitamin B12 status with neurological function in older people? A systematic review. <i>British Journal of Nutrition</i>, 114, 503–508.</p>	<p>Excluded because study populations reside both in the community and in hospitals.</p>
<p>Mocchegiani E, Costarelli L, Giacconi R, Malavolta M, Basso A, Piacenza F, et al (2014) Micronutrient-gene interactions related to inflammatory/immune response and antioxidant activity in ageing and inflammation. A systematic review. <i>Mechanisms of Ageing and Development</i>. 136-137:29-49.</p>	<p>Not a systematic review or meta-analysis.</p>
<p>Munk T, Tolstrup U, Beck AM, Holst M, Rasmussen HH, Hovhannisyan K, et al (2016) Individualised dietary counselling for nutritionally at-risk older patients following discharge from acute hospital to home: a systematic review and meta-analysis. <i>Journal of Human Nutrition and Dietetics</i>. 29(2):196-208.</p>	<p>Excluded because paper relates to risk management.</p>

Murad MH, Elamin KB, Abu Elnour NO, Elamin MB, Alkatib AA, Fatourechi MM, et al (2011) Clinical review: The effect of vitamin D on falls: a systematic review and meta-analysis. <i>Journal of Clinical Endocrinology and Metabolism</i> . 96(10):2997-3006.	Review on vitamin D published before 2016.
Nascimento-Souza, M. A., Paiva, P. G., Martino, H. S. D. and Ribeiro, A. Q. (2018) Dietary total antioxidant capacity as a tool in health outcomes in middle-aged and older adults: a systematic review. <i>Critical reviews in food science and nutrition</i> . 58:6, 905-912	Excluded because age of study participants > 65 y.
Ng TY & Kellett J (2018) Improving nutritional intake and well-being in older adults living in the community: a review of current health promotion interventions. <i>Nutrition &amp; Dietetics</i> . 75(Suppl. S1):100-100.	Not a systematic review or meta-analysis.
Paddon-Jones D & Leidy H (2014) Dietary protein and muscle in older persons. <i>Current Opinion in Clinical Nutrition and Metabolic Care</i> . 17(1):5-11.	Not a systematic review or meta-analysis.
Pettingill H, Walton K & Charlton K (2016) The impact of meal services on the nutritional intake of community-living older adults: a systematic literature review. <i>Nutrition &amp; Dietetics</i> . 73(Suppl. S1):82-83.	Not a systematic review or meta-analysis.
Poggiogalle, E., Migliaccio, S., Lenzi, A. and Donini, L. M. (2014) Treatment of body composition changes in obese and overweight older adults: insight into the phenotype of sarcopenic obesity. <i>Endocrine</i> 47 (3): 699-716.	Considers weight loss treatment which is outside of criteria; only 2 RCTs meet age/setting criteria, 1 of which is in meta-analysis by Gine-Garriga, and other RCT has very small participant numbers.
Poscia, A., Milovanovic, S., La, Milia, D, I., Duplaga, M., Grysztar, M., Landi, F., Moscato, U., Magnavita, N., Collamati, A. and Ricciardi, W. (2017) Effectiveness of nutritional interventions addressed to elderly persons: umbrella systematic review with meta-analysis. <i>European Journal of Public Health</i> . 28(2): 275-283.	Not a systematic review but an umbrella review of systematic reviews, excluded because study settings not separated in result.
Puts MTE, Toubasi S, Andrew MK, Ashe MC, Ploeg J, Atkinson E, et al (2017) Interventions to prevent or reduce the level of frailty in community-dwelling older adults: a scoping review of the literature and international policies. <i>Age and Ageing</i> . 46(3):383-392.	Excluded because nutritional information not detailed.
Rasheed S & Woods RT (2013) Malnutrition and quality of life in older people: a systematic review and meta-analysis. <i>Ageing Research Reviews</i> . 12(2):561-566.	Excluded because nutritional information not detailed.



Roman B, Carta L, Martinez-Gonzalez MA & Serra-Majem L (2008) Effectiveness of the Mediterranean diet in the elderly. <i>Clinical Interventions in Aging</i> . 3(1):97-109.	Not a systematic review or meta-analysis.
Salazar N, Valdés-Varela L, González S, Gueimonde M & de Los Reyes-Gavilán CG (2017) Nutrition and the gut microbiome in the elderly. <i>Gut Microbes</i> . 8(2):82-97.	Not a systematic review or meta-analysis.
Schroll M (2003) Aging, food patterns and disability. <i>Forum of Nutrition</i> . 56:256-258.	Not a systematic review or meta-analysis.
Schultz, T. J., Roupas, P., Wiechula, R., Krause, D., Gravier, S., Tuckett, A., Hines, S. and Kitson, A.(2016) Nutritional interventions for optimizing healthy body composition in older adults in the community: an umbrella review of systematic reviews. <i>JBIC Database Of Systematic Reviews And Implementation Reports</i>	Excluded because it is an umbrella review of systematic reviews.
Soysal P, Isik AT, Carvalho AF, Fernandes BS, Solmi M, Schofield P, et al (2017) Oxidative stress and frailty: A systematic review and synthesis of the best evidence. <i>Maturitas</i> . 99:66-72.	Excluded as the investigated exposures could not be categorised as nutrition.
Stephen AI & Avenell A (2006) A systematic review of multivitamin and multimineral supplementation for infection. <i>Journal of Human Nutrition and Dietetics</i> . 19(3):179-190.	Excluded because study group was adults in general.
ter Borg, S., Verlaan, S., Hemsworth, J., Mijnders, D. M., Schols, J. M., Luiking, Y. C., and de Groot, L. C. (2015) Micronutrient intakes and potential inadequacies of community-dwelling older adults: a systematic review. <i>British Journal of Nutrition</i> . 113 (8): 1195-1206.	Excluded because paper reviews population status of micronutrients, no intervention.
ter Borg, S., Verlaan, S., Mijnders, D. M., Schols, J. M., de Groot, L. C. and Luiking, Y. C. (2015) Macronutrient Intake and Inadequacies of Community-Dwelling Older Adults, a Systematic Review. <i>Annals of Nutrition &amp; Metabolism</i> . 66(4):242-255.	Excluded because paper reviews population status of macronutrients, no intervention.
Trabal, J. and Farran-Codina, A. (2015) Effects of dietary enrichment with conventional foods on energy and protein intake in older adults: a systematic review. <i>Nutrition Reviews</i> 73(9):624–633	Excluded because only 1 primary study out of 9 set in the community and results/discussion not separated.
Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, et al (2019) ESPEN guideline on clinical nutrition and hydration in geriatrics. <i>Clinical Nutrition</i> . 38(1):10-47.	Considered evidence is for disease treatment or management.

<p>Witard OC, Wardle SL, Macnaughton LS, Hodgson AB &amp; Tipton KD (2016) Protein considerations for optimising skeletal muscle mass in healthy young and older adults. <i>Nutrients</i>. 8 (4) (no pagination)(181).</p>	<p>Excluded as this a narrative review.</p>
<p>Wu L &amp; Sun D (2017) Consumption of Yogurt and the Incident Risk of Cardiovascular Disease: A Meta-Analysis of Nine Cohort Studies. <i>Nutrients</i>. 9(3).</p>	<p>Age group did not meet inclusion criteria.</p>

## Annex 4.3 – Data extracted from meta-analyses/systematic reviews

Table 4.3.1: Data extracted from systematic reviews and meta-analyses

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Antoniak &amp; Greig (2017)</b></p> <p><b>Study design</b> Systematic review with meta-analysis</p> <p><b>Aim of study/ research question:</b> To evaluate the effectiveness of combined resistance exercise training and vitamin D3 supplementation on musculoskeletal health in older adults.</p> <p><b>Countries:</b> not stated</p> <p><b>Funding source:</b> Stated: This research received no grant from any funding agency in the public, commercial or not-for-profit sectors. Author AEA is supported and funded by the National Osteoporosis Society via the Linda Edwards</p>	<p><b>Search period:</b> before March 2016</p> <p><b>Databases searched:</b> Science Direct, MEDLINE, PubMed, Google Scholar, Cochrane Central Register of Controlled Trials</p> <p><b>Language restrictions:</b> none stated</p> <p><b>Inclusion criteria:</b> RCTs with participants aged <math>\geq 65</math> years or mean age <math>\geq 65</math> years, intervention: resistance exercise training (RET) and vitamin D supplementation, measures of muscle strength, function, muscle power, body composition, serum vitamin D/calcium status or quality of life, compared results with a control group.</p> <p><b>Exclusion criteria:</b> if participants were supplemented with additional protein or any supplement/medication with a known anabolic effect on muscle tissue.</p>	<p><b>Number of studies:</b> 3 RCTs (Note: this SR included 7 RCTs in total, of which only 3 RCTs had relevant interventions)</p> <p><b>Study population:</b></p> <ul style="list-style-type: none"> <li>• Subject included in MA: n=266 (17 + 44 + 205)</li> <li>• All subjects in 3 primary studies: n=518 (17 + 92 + 409)</li> <li>• Age (mean): 67 to 77y</li> <li>• Sex (M:F): &gt;90% female</li> <li>• Duration: 16w, 9m, 2y</li> <li>• Community dwelling</li> <li>• for each of the 3 RCTs included in MA, baseline 25-hydroxyvitamin D levels were <math>&gt;30</math>nmol/L</li> </ul> <p><b>Intervention and control:</b></p> <p><b>1 RCT:</b> Resistance exercise training (RET) 3x per week and 1920 IU D3+800mg Ca/day <b>vs</b> RET 3x per week and 800mg Ca/day</p> <p><b>1 RCT:</b> RET 2x1.5hour per week or sedentary and 400 IU D3+800mg Ca/day <b>vs</b></p>	<p><b>Results showing significant improvement in intervention arm compared to control:</b></p> <ul style="list-style-type: none"> <li>• <b>muscle strength (lower limb)</b> MA of 3 RCTs, n=266, intervention period 16w, 9m, 2 y; SMD = 0.98, 95% CI 0.73, 1.24; <math>p &lt; 0.001</math>, <math>I^2 = 70\%</math></li> </ul> <p><b>Results showing no significant effect in intervention arm compared to control:</b></p> <ul style="list-style-type: none"> <li>• <b>timed up and go test</b> MA of 2 RCTs, n=249, intervention period 9m, 2 y; MD = -0.21 (unit ns), 95%CI -0.68, 0.26, <math>p = 0.37</math>; <math>I^2 = 0\%</math></li> <li>• <b>bone mineral density (femoral neck)</b> MA of 2 RCTs, n=249, intervention period 9m, 2 y; MD = 0.02 (unit ns), 95%CI -0.01, 0.05, <math>p = 0.15</math>; <math>I^2 = 0\%</math></li> <li>• <b>bone mineral density (spine)</b> MA of 2 RCTs, n=249, intervention period 9m, 2 y; MD = 0.02 (unit ns), 95%CI -0.03, 0.07, <math>p = 0.41</math>; <math>I^2 = 44\%</math></li> </ul>	<p><b>Authors' conclusion:</b></p> <ul style="list-style-type: none"> <li>• tentative support for the additive effect of combined RET and vitamin D3 supplementation for the improvement of muscle strength</li> <li>• no evidence of benefit of vitamin D3 supplementation alone</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>• Five out of the 6 RCTs included in the systematic review did not adjust for confounding</li> </ul> <p><b>Authors' limitation:</b></p> <ul style="list-style-type: none"> <li>• meta-analysis included 2 or 3 studies</li> <li>• meta-analyses may have been skewed due to the high weighting of one study with a large number of participants (n=205)</li> <li>• the two smaller studies did not account for confounding factors</li> <li>• none of the RCTs reported inclusion/ exclusion criterion for vitamin D</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
<p>Memorial PhD Studentship.</p> <p><b>Declaration of interest:</b> Stated as: None declared</p>	<p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>• muscle strength (lower limb)</li> <li>• timed up and go</li> <li>• femoral neck bone mineral density [BMD];</li> <li>• spine BMD</li> </ul> <p><b>Statistical analysis:</b> fixed-effect meta-analysis; effect sizes expressed as standardised mean differences (SMD) (e.g. for muscle strength) or as mean differences (MD) (e.g. for timed up and go test and bone mineral density); heterogeneity assessed via <math>X^2</math> test.</p>	<p>RET 2x1.5hours per week or sedentary and 800mg Ca/day</p> <p><b>1 RCT:</b> RET 2x/week for 12 months, 1x/week for next 12 months or sedentary and 800 IU D3/day</p> <p><b>vs</b> RET 2x/week for 12 months, 1x/week for next 12 months or sedentary and placebo/day</p> <p><b>Evaluation of study quality:</b> Assessed for risk of bias using <i>Cochrane Risk of Bias tool</i>; the 3 studies were judged to have unclear risk of bias. Quality of evidence of outcomes was assessed using Grading of Recommendation, Assessment, Development, and Evaluation (GRADE); 4 grades: high, moderate, low or very low) All studies: moderate quality</p> <p>Publication bias assessed as part of GRADE.</p>		<p>status, although at baseline serum vitamin D was not significantly different between the groups within each of the 3 RCTs.</p>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Beudart et al (2018)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> To review association between nutritional supplementation on muscle strength, muscle mass and physical performance.</p> <p><b>Funding source:</b> This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. C.B. is supported by a Fellowship from the FNRS (Fonds National de la Recherche Scientifique de Belgique—FRS-FNRS). However, most of the primary studies (87%) were industry sponsored or received specific grant from funding agencies in the public, commercial, or not-for-profit sectors.</p>	<p><b>Search period:</b> up to February 2016</p> <p><b>Databases searched:</b> MEDLINE, Embase, Cochrane</p> <p><b>Inclusion criteria:</b> age &gt; 60 y; in English; RCTs (double-blind setting); supplements (incl. protein, essential amino acids (EAA), <math>\beta</math>-hydroxy <math>\beta</math>-methylbutyrate (HMB), fatty acids, dehydroepiandrosterone (DHEA), creatine) versus placebo</p> <p><b>Exclusion criteria:</b> conference abstracts, interventions with additional elements such as exercise, interventions of energy deficit to promote weight loss, populations with specific health conditions such as diabetes.</p> <p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>• muscle mass: dual energy x-ray absorptiometry or bioimpedance spectroscopy</li> <li>• muscle strength: handgrip strength, knee flexor strength, knee extensor strength, hip abductor/adductor, hip flexor, ankle dorsiflexion, lower limb</li> <li>• physical performance: Short Physical Performance Battery</li> </ul>	<p><b>Number of studies:</b> 23 RCTs (Note: 19 RCTs in community-dwelling subjects (of which 2 RCTs in frail subjects); 4 RCTs in residential care setting),</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• age &gt; 60 y (mean age 64 to 83 y)</li> <li>• setting: 19 studies, community dwelling; 4 studies, residential care</li> <li>• intervention period from 5 d to 2 y</li> <li>• sample sizes from 14 to 280</li> <li>• 14 RCTs with both male and females (4 RCTs comprising only women, 5 RCTs comprising only men)</li> </ul> <p><b>Statistical analysis:</b> Mean differences and standard mean differences for continuous outcomes. <math>p &lt; 0.10</math> to detect heterogeneity.</p> <p><b>Evaluation of study quality:</b></p> <ul style="list-style-type: none"> <li>• Use of the Jadad score (0-5): excellent=5; good=3/4; poor<math>\leq</math>2. 7 RCTs rated excellent 12 RCTs rated good 4 RCTs rated poor</li> <li>• Use of GRADE to define quality of body of evidence: high, moderate, low, very low. All studies low or very low quality.</li> <li>• Risk of bias rated as serious or very serious in all studies (for reasons such as unclear allocation concealment or blinding procedure).</li> </ul>	<p><b>Note:</b> For meta-analyses, it was not stated which primary studies were included. For primary studies, effect sizes were not stated, and study characteristics were unclear.</p> <p><b>Muscle mass</b></p> <ul style="list-style-type: none"> <li>• protein supplementation: MA of 2 RCTs for lean body mass showed no significant effect MD 0.43, 95% CI -2.41, 3.27 (unit ns)</li> <li>• EAA supplementation: MA of 4 RCTs for lean body mass showed no significant effect MD 0.76, 95% CI -1.19, 2.70 (unit ns)</li> <li>• creatine supplementation: 1 of 4 RCTs showed a significant effect</li> <li>• DHEA: No effect with in any of 4 RCTs</li> <li>• HMB: MA of 2 RCTs showed significant effect for leg lean mass but not total lean body mass</li> </ul> <p><b>Muscle strength</b></p> <ul style="list-style-type: none"> <li>• protein supplementation: MA of 3 RCTs for handgrip strength showed no significant effect MD 0.48, 95% CI -0.61, 1.56 (unit ns)</li> <li>• EAA supplementation: MA of 3 RCTs for handgrip strength showed no significant effect MD 2.82, 95% CI -1.05, 6.68 (unit ns) (<math>I^2=94\%</math>, <math>p &lt; 0.001</math>).</li> <li>• creatine supplementation: 2 of 6 RCTs showed significant effect (very heterogeneous)</li> <li>• DHEA: 3 RCTs, no effect</li> <li>• HMB supplementation (2RCTs): <ul style="list-style-type: none"> <li>○ 1 RCT with no effect on grip strength, but significant increase in leg extension peak torque;</li> <li>○ 1 RCT no difference in muscle strength</li> </ul> </li> </ul> <p><b>Physical performance</b></p> <ul style="list-style-type: none"> <li>• protein supplementation: 2 RCTs, no effect</li> </ul>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• Evidence for positive effects of supplementation was inconsistent and limited.</li> <li>• Heterogeneity of studies was very high.</li> <li>• Inconsistent positive effects observed for creatine, essential amino acids and <math>\beta</math>-hydroxy <math>\beta</math>-methylbutyrate but results only concerned one aspect of muscle (i.e., mass, power or function).</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>• No detail on confounding or adjustments were provided in the systematic review.</li> </ul> <p><b>Authors' limitations:</b></p> <ul style="list-style-type: none"> <li>• Protein supplementation varied widely, range 20 to 45 g/d; essential amino acid supplementation range 2.5 g/d to 15 g/d.; variation in supplement protocols and in duration.</li> <li>• Any results should be interpreted with caution, some meta-analyses only included 2 studies.</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Declarations of interest:</b> Stated: Authors have no conflict of interest.</p>	<p>test, Timed Up and Go test, amongst others</p>		<ul style="list-style-type: none"> <li>• EAA supplementation: 4 RCTs, mixed results <ul style="list-style-type: none"> <li>○ 1 RCT: significant improvement in 2/6 exercise tests</li> <li>○ 1 RCT: improvement in walking test only</li> <li>○ 1 RCT: maintenance of timed chair rise in intervention rather than deterioration in control</li> <li>○ 1 RCT: no association in 2/3 tests</li> </ul> </li> <li>• creatine supplementation: 1 RCT, no effect</li> <li>• HMB supplementation: 2 RCTs, no effects</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Bloom et al (2018)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> To examine the association between diet quality and the individual components of sarcopenia (muscle mass, muscle strength, and physical performance)</p> <p><b>Funding source:</b> None stated. Acknowledged support from Medical Research Council and the NIHR Southampton Biomedical Research Centre.</p> <p><b>Declarations of interest:</b> Dr Cooper has received lecture fees and honoraria from Amgen, Danone, Eli Lilly, GSK, Medtronic, Merck, Nestle, Novartis, Pfizer, Roche, Servier, Shire, Takeda, and UCB outside of the submitted work. Other</p>	<p><b>Search period:</b> Performed in August 2016 with no date restrictions</p> <p><b>Databases searched:</b> MEDLINE, Embase, Web of Science Core Collection, CINAHL, AMED, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, DARE</p> <p><b>Inclusion criteria:</b> published in peer-reviewed journal, in English, all participants aged &gt;50 y, measurement of diet quality and one of the four outcomes, observational or RCT.</p> <p><b>Exclusion criteria:</b> diet quality and lifestyle score, diet measured as individual foods or nutrients or food groups, subjectively measured outcomes.</p> <p><b>Dietary assessment method:</b> FFQ, 24-h recall, diet records or diet history. Diet quality as measured using dietary patterns (including a priori dietary indices) or a posteriori (or data-driven) methods, or a measure of dietary variety.</p> <p><b>Outcomes:</b></p>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• 21 total (11 PCS, 10 XS) in community dwelling populations;</li> <li>• 2 further studies that were not exclusively in community dwelling populations are not considered here</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• n = 171 to 3957; 8 studies had &lt;1000 participants.</li> <li>• Countries: USA x 2, Korea, Germany x 2, Canada, Japan x 2, UK x 3, Italy x 3, Finland, Israel, Spain x 2, Australia, Hong Kong, Iran</li> </ul> <p><b>Exposure assessment:</b> Diet quality was measured using different methods. 17 of the included studies included a priori measures of diet quality (i.e., diet indices); 15 different diet indices were used. The most common a priori method used was assessment of adherence to a Mediterranean diet. 8 studies used a posteriori or data-driven methods, namely principal component analysis or factor analysis, and cluster analysis, to assess diet quality.</p> <p><b>Evaluation of study quality:</b> Risk of bias assessed using 10 criteria (study setting, design, population, reliability of measurements, losses to follow-up, etc.) resulting in 3 grades: high risk, medium risk and low risk. High risk of bias: 1 XS Medium risk of bias: 6 XS, 5 PCS</p>	<p><b>Muscle mass (4 studies):</b> <b>1 PCS 3 XS:</b></p> <ul style="list-style-type: none"> <li>• showed positive association with diet quality (3 x medium, 1 x high risk of bias); studies considered to provide weak evidence</li> <li>• 1 PCS (n = 542; mean age = 72 y; follow-up not stated; Japan, medium risk of bias) no association of dietary variety score with decline in appendicular skeletal muscle mass (ASM) (OR = 0.28, 0.07-1.07, p for trend = 0.068)</li> <li>• 1 XS (n=1435, age &gt; 65y, Korea, medium risk of bias) showed a “Westernized Korean” pattern to be associated with a 74% increased abnormality of ASM/Wt (kg) by logistics analysis, compared with the “Traditional Korean” pattern.</li> <li>• 1 XS (n=1509, mean age 68.2, Germany, medium risk of bias) showed higher adherence to a Mediterranean-style diet to be associated with a positive effect on appendicular lean mass/BMI in women, but not in men.</li> <li>• 1 XS (n=171, mean age 68.1, Australia, high risk of bias) showed no association of lean body mass with Healthy Eating Index, and a weak negative association with Healthy Diet Indicator (r=1.19, p=0.03) for women, but not for men.</li> </ul> <p><b>Muscle strength (10 studies):</b> <b>6 PCS, 4 XS:</b></p> <ul style="list-style-type: none"> <li>• studies considered to provide limited evidence for a link between healthier diet and a lower risk of declines in muscle strength</li> <li>• 6 PCS (n = 156 to 1872; mean age = 69 y to 78 y; follow-up not stated; risk of bias: 2 low, 4 medium risk). Diet quality was assessed using: <ul style="list-style-type: none"> <li>• a priori: 2x Dietary Variety Score (DVS); 2 x Mediterranean Dietary Score (MeDi score); Mediterranean Diet Adherence Screener</li> </ul> </li> </ul>	<p><b>Authors’ conclusions:</b></p> <ul style="list-style-type: none"> <li>• evidence from observational studies associates higher diet quality with benefits in physical performance. Findings for other outcomes inconclusive.</li> <li>• Some evidence suggestive of differences between men and women but findings inconsistent.</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>• The authors graded the included evidence using a quality assessment tool. Studies ranged from medium to low risk of unadjusted/residual confounding.</li> <li>• Some studies used adjusted statistical models and some did not</li> </ul> <p><b>Authors’ limitations:</b></p> <ul style="list-style-type: none"> <li>• No meta-analysis because the definitions of exposure and outcomes varied widely between studies. Studies were diverse in terms of design, setting, participants included, as well as confounding factors adjusted for in some statistical models but not others.</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
<p>authors declare no conflict of interest.</p>	<ul style="list-style-type: none"> <li>• Muscle mass: anthropometry, DXA, BIA, CT, or MRI.</li> <li>• Muscle strength: Handgrip, quadriceps, or muscle quality index.</li> <li>• Physical performance: short physical performance battery, gait/walking speed, timed get-up and-go test, balance, stair climb power test.</li> <li>• Sarcopenia: combined outcomes of muscle mass, muscle strength or physical performance.</li> </ul>	<p>Low risk of bias: 3 XS, 5 PCS</p>	<p>(MEDAS); Canadian Healthy Eating Index; (1 PCS used both MeDi score and MEDAS)</p> <ul style="list-style-type: none"> <li>• a posteriori: 5 x dietary pattern established through data driven factor analysis</li> </ul> <p><b>Individual studies:</b></p> <ul style="list-style-type: none"> <li>• 1 PCS (n=575 women, mean age = 78y, medium risk of bias, 4 years follow-up) The age-related decline in muscle strength was lower in people who frequently ate soy products or green and yellow vegetables, but no association was found with DVS.</li> <li>• 1PCS (n=690, mean age =73y, medium risk of bias, 3 years follow-up). No association was observed for grip strength and MeDi score.</li> <li>• 1PCS (n=1815, mean age=69y, low risk of bias, 3.5 years follow-up). No significant association was observed for MeDi score and MEDAS.</li> <li>• 1PCS (n=1872, mean age = 69y, low risk of bias, 3.5 years follow-up). No association was observed with westernised and “prudent” (Mediterranean-like) diet pattern.</li> <li>• 1PCS (n=781, mean age=72y, medium risk of bias, 4 years follow-up). ORs for decline in grip strength was 0.43 (95% CI = 0.19–0.99), for the highest category of DVS as compared with the lowest category.</li> <li>• 1PCS (n=156 men and women with type 2 diabetes, medium risk of bias, mean age = 75y, 3 years follow-up). Diet quality (Canadian Healthy Eating Index) alone had no effect on MS Maintenance.</li> <li>• 1XS (n=2983, mean age =66y, low risk of bias) Men and women with high prudent diet scores had higher grip strength (no statistics reported). After adjusting for fish consumption, this association was no longer significant in men. For</li> </ul>	



Study	Methods	Included studies	Results	Limitations/comments
			<p>women the association remained significant (regression coefficient of 0.17, 95% CI = 0.00 to 0.34 kg per unit change in score, p = 0.044).</p> <ul style="list-style-type: none"> <li>• 1XS (n=1392, mean age = 70y, low risk of bias). Total HEI-2005 scores were positively associated with knee extensor power (p for trend = 0.05). Those with HEI-2005 scores in Quartile 4 had a greater knee extensor power compared with those with HEI-2005 scores in the lowest quartile (p = 0.04). The associations were no longer statistically significant after further adjustment for PA.</li> <li>• 1XS (n=192, mean age = 83y, low risk of bias). No association of grip strength with MeDi score was observed.</li> <li>• 1XS (n=304, mean age = 86y, medium risk of bias). No correlation was found for hand grip strength with Mediterranean Style Dietary Pattern Score (MSDPS).</li> </ul> <p><b>Physical performance (13 studies):</b>  <b>7 PCS, 6 XS:</b></p> <ul style="list-style-type: none"> <li>• risk of bias: 6 studies low risk; 7 medium, 1 high</li> <li>• all studies found some association between healthier diet pattern &amp; physical performance.</li> <li>• consistent evidence for link between healthier diet and physical performance.</li> <li>• 7 PCS studies (n = 690 to 5350; baseline mean Age 51 to 75; follow-up 3-16 y, risk of bias: 4 low risk, 4 medium risk). Diet quality assessed using: <ul style="list-style-type: none"> <li>• a priori: 3 x MeDi score; 1 x MeDi score &amp; MEDAS; 1 x Nordic Diet Score</li> <li>• a posteriori: 1 x principal component analysis; Component analysis; 1 x factor analysis</li> </ul> </li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
			<ul style="list-style-type: none"> <li>• 1 PCS (n=705, baseline mean age 74y, medium risk of bias, 3 years follow-up). At baseline, higher adherence to Mediterranean diet was associated with better lower body performance. Participants with higher adherence experienced less decline in SPPB score, which was of 0.9 points higher (<math>p &lt; 0.0001</math>) at the 3-year-follow, 1.1 points higher (<math>p = 0.0004</math>) at the 6-year follow-up and 0.9 points higher (<math>p = 0.04</math>) at the 9-year follow-up compared to those with lower adherence. Among participants free of mobility disability at baseline, those with higher adherence had a lower risk (HR (hazard ratio) = 0.71, 95% CI = 0.51–0.98, <math>p = 0.04</math>) of developing mobility disability (defined as SPPB <math>\geq</math> 9 points).</li> <li>• 1 PCS (n=1201, baseline mean age 75y, low risk of bias, 8 years follow-up). Mediterranean diet adherence and rapid 20 m walking speed; the association remained significant after adjustment for total body-fat-percent (<math>p = 0.012</math>).</li> <li>• 1 PCS (n=5350, baseline mean age 51y, medium risk of bias, 16 years follow-up). No association was reported for “Healthy-foods” dietary pattern.</li> <li>• 1 PCS (n=1072, baseline mean age 61y, low risk of bias, 10 years follow-up). In a fully adjusted model, the overall Senior Fitness Test (SFT) score was 0.55 (95% CI = 0.22, 0.88) points higher per 1 unit increase in the Nordic Diet Score (NDS). Women in the higher per 1 unit increase in the NDS. Women in the highest fourth of the NDS had on average 5 points higher SFT score compared with those in the lowest fourth (<math>p</math> for trend 0.005). No such association was observed in men. Women with the highest score had 17% better result in the walk test, 16% better arm curl and 20% better chair stand results compared with those with the lowest score (all <math>p</math> values <math>&lt; 0.01</math>).</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
			<ul style="list-style-type: none"> <li>• 1 PCS (n=690, baseline mean age 73y, medium risk of bias, 6 years follow-up). After a 6-year follow-up, higher adherence to a Mediterranean dietary pattern at baseline was associated with a lower risk of low walking speed (OR = 0.48 (95% CI = 0.27, 0.86)).</li> <li>• 1 PCS (n=1815, baseline mean age 69y, low risk of bias, 3.5 years follow-up). Being in the highest tertile of the MEDAS score (highest Mediterranean diet adherence) was associated with reduced risk of slow walking (OR = 0.53; 95% CI = 0.35–0.79). No association was observed with MeDi score.</li> <li>• 1 PCS (n=1872, baseline mean age 69y, low risk of bias, 3.5 years follow-up). A greater adherence to the prudent pattern (Mediterranean-like) showed a non-statistically significant tendency to a lower risk of slow walking speed.</li> <li>• 1 PCS (n=772, baseline mean age 72y, medium risk of bias, 4 years follow-up). ORs for decline in usual gait speed was 0.43 CI: 0.19–0.99), respectively, for the highest category of dietary variety score as compared with the lowest category.</li> <li>• 1 XS (n=628, mean age 68y, medium risk of bias). There were no significant associations between the dietary pattern and physical performance when controlling for confounders.</li> <li>• 1 XS (n=2791, mean age 71y, medium risk of bias). MeDi score (high vs. low) was associated with faster walking speed after adjusting for confounders in a logistic regression model (OR = 0.71, p =0.034, 95% CI = 0.511–0.974].</li> <li>• 1 XS (n=2132, mean age 70y, low risk of bias). There was no significant association between adherence to a healthy dietary pattern and low walking speed.</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
			<ul style="list-style-type: none"> <li>• 1 XS (n=192, mean age 83y, low risk of bias). There was a significant inverse association between “low walking speed” and the MED score; there was an association between a high diet quality and a lower risk of low walking speed. Compared with the lowest quartile (least healthy diet), the participants in the highest quartile (most healthy diet) had a significantly decreased risk of low walking speed (OR (95% CI) = 0.29 (0.09–1.00), p for trend = 0.043).</li> <li>• 1 XS (n=304, mean age 86y, medium risk of bias). A statistically significant association (Regression coefficient = 1.0006; Std. Error = 0.4780; p-value = 0.0363) between participants with the highest adherence to the Mediterranean diet (fourth highest adherence to the Mediterranean diet (fourth quartile) and high physical performance (SPPB &gt; 7) was found.</li> <li>• 1 XS (n=171, mean age 68, high risk of bias Men showed weak positive associations between Healthy Diet Indicator (HDI) score and SPPB (short physical performance battery) (r = 0.26, p = 0.04).</li> </ul> <p><b>Sarcopenia (2 studies):</b>  <b>PCS, 1 XS:</b></p> <ul style="list-style-type: none"> <li>• 1 PCS (n=3957, mean age = 72 y, 4 years follow-up, China, low risk of bias) found in baseline high vegetable/fruit pattern associated with lower likelihood of prevalent sarcopenia in older men (From data driven factor analysis of FFQ: adjusted OR = 0.60, 95% CI = 0.36–0.99, p for trend = 0.034); no associations in women. Men in the highest quartile of Diet Quality Index-International (DQI-I) had reduced likelihood of sarcopenia (adjusted OR = 0.50, 95% CI = 0.31–0.81, p for trend = 0.004)</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
			<p>compared with men in the lowest quartile. No such associations were observed in women.</p> <ul style="list-style-type: none"> <li>• 1 XS (n=300, mean age = 67 y, Iran, medium risk of bias) found greater adherence to Mediterranean diet pattern had lower odds ratio for sarcopenia compared to those with the lowest adherence to Mediterranean diet pattern. Participants in the highest tertile of the Mediterranean diet pattern had a lower odds ratio for sarcopenia than those in the lowest tertile (OR = 0.42; 95% CI = 0.18–0.97; p for trend = 0.04). No association with Western and mixed dietary patterns.</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Coelho-Júnior et al (2018a)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> To investigate the association of relative protein intake and physical function.</p> <p><b>Funding source:</b> Stated: This research received no external funding. The authors are grateful to the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for funding this research via scholarships to HJCJ (PhD visiting: 88881.190185/2018-01). BR had financial support from the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) and CNPq (BPQ).</p> <p><b>Declarations of interest:</b></p>	<p><b>Search period:</b> published in or before August 2018</p> <p><b>Databases searched:</b> MEDLINE, Scopus, CINAHL, AMED, Ageline, EMBASE and Cochrane Central</p> <p><b>Inclusion criteria:</b> observational studies, which investigated association of relative protein intake and physical function, longitudinal studies if baseline data for participants included age &gt; 60 y, direct assessment of physical function domain, provision of at least 2 groups of protein intake, mean values and method of dispersion, English language</p> <p><b>Exclusion criteria:</b> RCTs, quasi-experimental, cross-over studies, nutritional interventions associated with other interventions (e.g. exercise), participants institutionalized or with health conditions.</p> <p><b>Dietary assessment method:</b> 24-h diet recall, 3-d diet intake, 4-d diet record, FFQ and semi-quantitative FFQ</p> <p><b>Outcomes:</b></p>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• 4 PCS</li> <li>• 2 XS</li> <li>• 1 case-control</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• n=8654</li> <li>• community dwelling</li> <li>• mean age 67.8 to 83.0 y</li> <li>• mean BMI 23.7 to 29.5 kg/m<sup>2</sup></li> <li>• 29% reported fall in 12 m before investigations</li> <li>• 3 studies (healthy individuals), 2 studies (post-menopausal women), 1 study (sarcopenic older adults), 1 study (diabetics)</li> <li>• Countries: UK, Netherlands, Finland, Canada. 2 x USA, China</li> <li>• Protein intake categorised by quartiles of intake: low (&lt;0.8 g/kg/day), middle (0.8–0.99 g/kg/day), high (≥1.0 g/kg/day), very high (≥1.2 g/kg/day)</li> <li>• No follow-up time stated for PCS</li> </ul> <p><b>Evaluation of study quality:</b> Use of Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) instrument. Scores from 17-20</p>	<p><b>Very high protein intake versus low protein intake (3 studies):</b></p> <ul style="list-style-type: none"> <li>• Lower limb muscle functioning (2 PCS; 1 XS; total n = 3225) (measuring knee extensor strength or SPPB or walking speed): Small and significant ES (no units stated) ES=0.18, 95% CI 0.01,0.35, p=0.04 X<sup>2</sup>=15.56, p=0.004, I<sup>2</sup>=74%</li> </ul> <p><b>High protein intake versus low protein intake:</b></p> <ul style="list-style-type: none"> <li>• <u>Upper-limb strength</u> (IHG) (2 PCS; 1 XS; total n = 5315) No significant differences between groups ES=-0.36, 95% CI -1.15,0.44, p=0.38 X<sup>2</sup>=4.16, p=0.12, I<sup>2</sup>=52%</li> <li>• <u>Lower-limb strength</u> (chair rise, knee extensor) (2 PCS; 1 XS; total n = 842) No significant difference ES=-0.09, 95% CI -0.26,0.08, p=0.30 X<sup>2</sup>=3.75, p=0.29, I<sup>2</sup>=20%</li> <li>• <u>Walking speed</u> (10-m WS or 6-m WS) (2 PCS; total n = 4243) Small and significant ES observed ES=0.06, 95% CI 0.02, 0.11, p=0.003 X<sup>2</sup>=27.52, p=0.00001, I<sup>2</sup>=89%</li> </ul> <p><b>Middle protein intake versus high protein intake:</b></p> <ul style="list-style-type: none"> <li>• <u>Upper-limb strength</u> (IHG) (1 PCS; 1 XS; 1 CC; total n = 653) No significant differences between groups (considerable heterogeneity) ES=1.09, 95% CI -3.78, 5.96; p=0.66 X<sup>2</sup>=25.07, p&lt;0.00001, I<sup>2</sup>=92%</li> <li>• <u>Lower-limb strength</u> Lower-limb muscle strength was evaluated by chair-rise. A meta-analysis of two studies observe a moderate non-significant difference</li> </ul>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• Very high protein intake (≥ 1.2 g/kg/d) and high protein intake (≥ 1.0 g/kg/d) showed better lower limb physical functioning and walking speed performance in comparison with low intakes intake (&lt; 0.8 g/kg/d).</li> <li>• High protein intakes do not show an association with handgrip strength or chair rise ability.</li> <li>• Provides additional evidence to support the argument of higher protein guidelines for older adults.</li> </ul> <p><b>Confounding:</b></p> <ul style="list-style-type: none"> <li>• Nine out of 10 included studies were adjusted for variables including age, sex, BMI, education, economic status, smoking status, alcohol consumption, chronic disease status, and cognitive function</li> </ul> <p><b>Authors' limitations:</b></p> <ul style="list-style-type: none"> <li>• Lack of adequate description in primary studies of the efforts to</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
<p>Stated: The authors declare no conflict of interest.</p>	<ul style="list-style-type: none"> <li>• isometric handgrip strength (IHG)</li> <li>• walking speed (WS)</li> <li>• knee extensor strength</li> <li>• short physical performance battery (SPPB)</li> <li>• chair rise</li> </ul> <p><b>Statistical analysis:</b> MA conducted using Revman V.5. Effect size (ES) measured using standard mean difference (SMD) or mean difference and reported with 95% CIs. Random-effects model used to calculate pooled ES. Heterogeneity detected using Q-statistics and I<sup>2</sup> for consistency.</p>		<p>between the groups (ES = 0.49; 95% CI= -0.01 to 0.99, p = 0.05). A non-significant heterogeneity was found across studies (I<sup>2</sup> = 0.72, df = 1, p = 0.40, I<sup>2</sup> = 0%)</p> <ul style="list-style-type: none"> <li>• Mobility: 1 PCS; 1 XS; 1 CC; total n = 653 No significant differences between groups (considerable heterogeneity) ES=0.17, 95% CI -0.12, 0.46, p=0.26 X<sup>2</sup>=56.46, p&lt;0.00001, I<sup>2</sup>=96%</li> </ul>	<p>investigate sources of bias and design of study sizes.</p> <ul style="list-style-type: none"> <li>• Categories based on quartiles of intakes and therefore low intake does not necessarily represent a low protein intake and it may be better for future studies to design groups based on proposed cut-offs for older adults.</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Coelho-Junior et al (2018b)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> To investigate the relationship between protein intake and frailty.</p> <p><b>Funding source:</b> Stated: This research received no external funding.</p> <p><b>Declarations of interest:</b> Stated: The authors declare no conflict of interest.</p>	<p><b>Search period:</b> studies published in or before July 2018</p> <p><b>Databases searched:</b> MEDLINE, Scopus, Cochrane Library</p> <p><b>Inclusion criteria:</b> observational studies investigating frailty as primary or secondary outcome, age &gt; 60 y., frailty defined by validated scale, information given for high and low protein intake, studies in English.</p> <p><b>Inclusion for meta-analysis (MA):</b> at least 2 groups divided by high or low protein intakes, prevalence of frailty in each group, total sample size of group.</p> <p><b>Primary outcome:</b></p> <ul style="list-style-type: none"> <li>• Frailty</li> </ul> <p><b>Exclusion criteria:</b> RCTs, quasi-experimental studies, cross-over studies, where nutritional interventions were associated with another intervention such as exercise, studies where participants were classified as frail according to reduced physical or cognitive function.</p> <p><b>Dietary assessment method:</b> primarily by FFQ, self-reported diet history, 24 h dietary recall.</p>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• 10 studies in total (7 XS, 3 PCS)</li> <li>• 4 XS included in MA (n=9091)</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• 10 studies</li> <li>• community dwelling</li> <li>• n=50,284 (total)</li> <li>• 7 XS: n=18,120 (France, Germany, Italy, Japan, US)</li> <li>• 3 PCS: n=32,164 (US, Spain); mean duration of follow-up 3.7 y</li> <li>• mean age not stated but all participants &gt;60 y.</li> </ul> <p><b>Evaluation of study quality:</b> With use of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) criteria: all studies scored between 19 and 22.</p> <p>Funnel plots for both meta-analyses were asymmetrical indicating that potential publication bias may influence results. Egger's linear regression test indicated possible publication bias when Kobayashi (2013) was included but not Kobayashi (2017).</p>	<p><b>High protein intake was negatively associated with frailty status when high protein intake is compared with low protein intake</b></p> <p>2 MAs based on 3 XS. For both MAs:</p> <ul style="list-style-type: none"> <li>• mean age 73.2 to 75.6 y</li> <li>• countries: France, 2 x Japan</li> <li>• each study defined low/high protein intake levels differently, e.g. based on tertile, quartile, quantiles, or as above or below 1g/kg body weight</li> </ul> <p>MA based on 3 XS including Kobayashi (2013)</p> <ul style="list-style-type: none"> <li>• OR 0.67, 95% CI 0.56, 0.82, p&lt;0.0001</li> <li>• I<sup>2</sup>=39%, p=0.18 indicating heterogeneity may not be important</li> </ul> <p>MA based on 3 XS including Kobayashi (2017)</p> <ul style="list-style-type: none"> <li>• OR 0.66, 95% CI 0.54, 0.80, p&lt;0.0001</li> <li>• I<sup>2</sup>=49%, p=0.12 indicating heterogeneity may be moderate</li> </ul> <p>2 out of the 3 PCS found an association between higher protein intake and frailty risk (data not reported).</p>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• Main findings suggest low consumption of protein is associated with frailty prevalence in older adults.</li> <li>• Study quality demonstrated that reports were of very good quality.</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>• No detail on confounding or adjustments were provided in the systematic review</li> </ul> <p><b>Authors' limitations:</b></p> <ul style="list-style-type: none"> <li>• Findings from meta-analysis based on cross-sectional studies only.</li> <li>• Main variables differently defined in papers including adaptations of some of the criteria assessing frailty, and these modifications have direct implications in the findings.</li> <li>• absence of subgroup analyses, and use of crude OR since the influence of important covariates such as type of protein (animal or vegetable) were not taken into consideration.</li> <li>• total protein intake measured whereas investigations in the context of physical</li> </ul>



Study	Methods	Included studies	Results	Limitations/comments
	<p><b>Frailty measurements:</b> Frailty phenotype proposed by Fried et al (2001) was used in 3 of the studies in the MA and Kihon checklist (KCL) used in 1 study.</p> <p><b>Statistical analysis:</b>  MA conducted using Revman V.5. An inverse variance random-effect model was used to calculate the pooled effect size. Funnel plots and Egger's regression analysis used to detect publication bias.  Heterogeneity detected using Q-statistics and I<sup>2</sup> for consistency.</p>			<p>function usually measure relative protein intake.</p> <ul style="list-style-type: none"> <li>• STROBE primarily created for use with observational studies, here used for PCS, too.</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Cruz-Jentoft et al (2014)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> Compared with control, does nutrition supplementation improve measures of muscle mass, muscle strength, and physical performance?</p> <p><b>Funding source:</b> Supported by an unrestricted educational grant provided by Abbott Nutrition (AN) to European Union Geriatric medicine Society (EUGMS).</p> <p><b>Declarations of interest:</b> AN had the right to have an observer member at the working group (WG) meetings. Members of the WG received no salary or other incomes from EUGMS or AN.</p>	<p><b>Search period:</b> January 2000 to October 2013</p> <p><b>Databases searched:</b> PubMed and Dialog database</p> <p><b>Inclusion criteria:</b> Nutrition RCTs whose outcome measures included muscle mass and at least one measure of muscle strength or physical performance, even when the population studied was not defined as sarcopenic. Well-defined populations of adults aged <math>\geq 50</math> years</p> <p><b>Exclusion criteria:</b> Studies not meeting inclusion criteria.</p> <p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>• muscle mass plus at least one measure of</li> <li>• a) muscle strength OR</li> <li>• b) physical performance</li> </ul>	<p><b>Number of studies:</b> 11 RCTs (12 RCTs were identified, 1 of which was of institutionalised older adults)</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• n = 14 to 155</li> <li>• mean age = 65 to 81 years</li> <li>• living in the community</li> </ul> <p><b>Interventions:</b></p> <ul style="list-style-type: none"> <li>• protein supplementation (usually with other nutrients providing extra calories) (4 studies, n = 62 to 98, duration = 24 weeks to 18 months)</li> <li>• amino acid (mainly leucine) supplementation (2 studies, n = 14 &amp; 155, duration = 3 months)</li> <li>• <math>\beta</math>-hydroxy <math>\beta</math>-methylbutyric acid (HMB; a bioactive metabolite of leucine) supplementation (4 studies, n = 19 to 98, duration = 8 to 24 weeks)</li> <li>• fatty acid supplementation (1 study with <math>\alpha</math>-linolenic acid, n = 51, duration = 12 weeks)</li> </ul> <p><b>Evaluation of study quality:</b> 11-point Physiotherapy Evidence Database (PEDro) scale:</p> <ul style="list-style-type: none"> <li>• 0 to 3 points: low quality</li> <li>• 4 to 6 points: moderate quality</li> <li>• 7 to 10 points: high quality</li> </ul>	<p><b>Effect sizes were not stated</b></p> <p><b>Protein supplementation:</b></p> <ul style="list-style-type: none"> <li>• 4 RCTs (1 moderate and 3 high quality studies) fail to show a consistent effect of protein supplementation on muscle mass or function</li> </ul> <p><b>Essential amino acid (EAA) supplementation:</b></p> <ul style="list-style-type: none"> <li>• 2 high quality RCTs provide very limited evidence indicating that EAA supplementation may have some effects on muscle mass and function.</li> </ul> <p><b>HMB (<math>\beta</math>-hydroxy <math>\beta</math>-methylbutyric acid) supplementation:</b></p> <ul style="list-style-type: none"> <li>• 4 high quality RCTs showed some effects on muscle mass and function, but sample sizes were low (n = 19 to 98)</li> </ul> <p><b>Fatty acid supplementation:</b></p> <ul style="list-style-type: none"> <li>• 1 high quality RCT of <math>\alpha</math>-linolenic acid supplementation in combination with resistance exercise training (RET) showed no effect of muscle mass or muscle strength when compared to RET + placebo</li> </ul>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• review failed to show a consistent effect of protein supplementation, although the number of studies found using strict selection criteria was very low.</li> <li>• EAAs and HMB seem to have some effects on muscle mass and muscle function that need to be confirmed in larger trials.</li> <li>• For omega 3-fatty acids only one negative study was found in this review.</li> <li>• Interventions that evaluated the combined effects of exercise and nutrition sometimes suggested a potential additive effect, although this needs further research.</li> <li>• solid evidence on which to base recommendations for patients with sarcopenia is not available.</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>• No detail on confounding or adjustments were provided in the systematic review.</li> </ul> <p><b>Authors' limitations:</b> Authors note the limited evidence base available.</p>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Dedeyne et al (2017)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> to determine the effect of multi-domain compared to mono-domain interventions on frailty status and score, cognition, muscle mass, strength and power, functional and social outcomes in frail or pre-frail elderly (≥65 years).</p> <p><b>Funding source:</b> internal funding by the University of Leuven, KU Leuven</p> <p><b>Declarations of interest:</b> The authors report no conflicts of interest.</p>	<p><b>Search period:</b> until September 14, 2016</p> <p><b>Databases searched:</b> PubMed, EMBASE, CINAHL, PEDro, CENTRAL, Cochrane Central register of Controlled Trial</p> <p><b>Inclusion criteria:</b> 1) randomized controlled trials, quasi-experimental studies, or prospective or retrospective cohort studies with control groups; 2) testing of a multi-domain intervention to prevent or treat frailty in people aged ≥65 years; 3) classification in terms of (pre)frailty status according to an operationalized definition; and 4) primary outcomes including one or more of the following: frailty status or score, muscle mass, strength or power, physical functioning, and cognitive or social outcomes.</p> <p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>• frailty status</li> <li>• cognition</li> <li>• muscle mass</li> <li>• muscle strength</li> <li>• and power</li> <li>• functional outcomes</li> </ul> <p><b>Exclusion criteria:</b></p>	<p><b>Number of studies:</b> 12 RCTs (24 articles)</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• n = 31 to 246</li> <li>• mean age 71 to 79 years</li> <li>• intervention duration 3 to 6 months (5 studies included a follow-up at 3 to 9 months)</li> <li>• Countries: 5 x Europe, 2 x USA, 5 x Asia</li> </ul> <p><b>Intervention:</b> Combined interventions from two or more the following domains:</p> <ul style="list-style-type: none"> <li>• exercise therapy (Ex),</li> <li>• supplementation of proteins [NuP]</li> <li>• supplementation of vitamins and minerals [NuVM],</li> <li>• milk fat globule membrane [NuMF]</li> <li>• nutritional advice [NuAd]),</li> <li>• hormone (Hor),</li> <li>• cognitive (Cog)</li> <li>• psychosocial (PS)</li> </ul> <p><b>Evaluation of study quality:</b> Studies were evaluated by two independent researchers using the Methodological index for nonrandomized studies (MINORS). The 12 MINORS criteria resulted in a total quality score ranging from 0 (low quality) to 24 (high quality).</p>	<p><b>Most results presented in this SR are for combinations of interventions. Only some RCTs presented results that allowed the effect of just the nutritional intervention to be assessed.</b></p> <p><b>Frailty</b> <b>1 RCT</b> (n=246; community dwelling; mean age 70y; duration = 6 months; Singapore; quality score: 22 of 24) showed, at 6 month post-intervention follow-up only, significant change in NuP + NuVM group compared to control for:</p> <ul style="list-style-type: none"> <li>• <b>frailty status:</b> OR =2.98 [95% CI =1.10; 8.07] (p&lt;0.01)</li> <li>• <b>frailty score</b> (0–5 points): mean change = -0.63 [95% CI = -0.92; -0.34]) (p&lt;0.05)</li> </ul> <p><b>Muscle mass</b> <b>1 RCT</b> (n=62; community dwelling; mean age 78y; duration = 24 weeks; Netherlands; quality score: 21 of 24) showed Ex + NuP + NuVM group significantly improved compared to Ex group for:</p> <ul style="list-style-type: none"> <li>• <b>appendicular muscle mass:</b> Ex + NuP + NuVM: +4.48%; Ex: -1.04%; (p&lt;0.001)</li> <li>• <b>total muscle mass:</b> Ex + NuP + NuVM: +2.75%; Ex: -0.66%; (p&lt;0.01)</li> </ul> <p><b>Muscle Strength</b> <b>1 RCT</b> (n=52; setting not reported; mean age 79y; duration = 3 months; Japan; quality score: 19 of 24) showed Ex + NuP group significantly improved compared to Ex group for:</p> <ul style="list-style-type: none"> <li>• <b>leg press rate:</b> Ex + NuP: 13.9%±36.0%; Ex: 2.7%±12.5%; (p&lt;0.05)</li> </ul>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• The limited but promising data highlight the potential of the physical exercise component as a standard intervention combined with at least a nutritional intervention.</li> <li>• Multi-domain interventions were found to be more effective than mono-domain interventions for improving frailty status and physical functioning.</li> <li>• , a multi-domain intervention tended to yield more positive outcomes for muscle mass and strength.</li> <li>• Eventually, understanding the contribution of each mono-domain intervention would pave the way to optimize and prioritize the frailty syndrome management.</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>• No detail on confounding or adjustments were provided in the systematic review.</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
	<p>Studies that did not compare groups in view of the delivered multi-domain intervention were excluded.</p> <p>A multi-domain intervention was defined as an intervention that intervenes in at least two different domains, including exercise therapy (Ex), nutritional intervention (supplementation of proteins [NuP], supplementation of vitamins and minerals [NuVM], milk fat globule membrane [NuMF], or nutritional advice [NuAd]), hormone (Hor), cognitive (Cog) or psychosocial (PS) interventions.</p>		<ul style="list-style-type: none"> <li>● <b>knee extension rate:</b> Ex + NuP: 9.5%±26.3%; Ex: -0.8%±18.2%; (p&lt;0.01)</li> </ul> <p><b>Physical activity</b></p> <p><b>1 RCT</b> (n=246; community dwelling; mean age 70y; duration = 6 months; Singapore; quality score: 22 of 24) showed significant improvement in NuP + NuVM group compared to control group at</p> <ul style="list-style-type: none"> <li>● <b>intervention end:</b> NuP + NuVM (mean change =96.2 [95% CI =57.8; 134.7], no units stated); control group (mean change =20.5 [95% CI =-17.0; 58.1], no units stated); (p&lt;0.01)</li> <li>● <b>6 months follow-up:</b> NuP + NuVM (mean change =110.1 [95% CI =71.9; 148.2], no units stated); control group (mean change =34.8 [95% CI =-2.99; 72.6], no units stated); (p&lt;0.01)</li> </ul> <p><b>Dynamic balance</b></p> <p><b>1 RCT</b> (n=96; community dwelling; mean age 83y; duration = 9 months; Sweden; quality score: 17 of 24) showed Ex + NuAd group had significantly decreased (p&lt;0.05) score step test (mean change =-1.1 [95% CI =-3.2; 1], no units stated) compared to Ex group (mean change =3.2 [95% CI =0.9; 5.5], no units stated).</p> <p><b>1 RCT</b> (n=52; setting not reported; mean age 79y; duration = 3 months; Japan; quality score: 19 of 24) showed Ex + NuP group had significantly improved (p&gt;0.05) functional reach test rate (11.0%±22.0%) compared to Ex group (1.0%±17.0%).</p>	<p><b>Authors' limitations:</b> Studies used diverse frailty definitions resulting in heterogeneous study populations</p>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Dewansingh et al (2018)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> to assess the effectiveness of dairy components on nutritional status and physical fitness</p> <p><b>Funding source:</b> This work was supported by Friesl and Campina (dairy cooperative)</p> <p><b>Declarations of interest:</b> The first author (Dewansingh) was an intern at Friesl and Campina until August 31, 2015. Author Van den Heuvel is an employee at Friesl and Campina. Other co-authors have no conflict of interest.</p>	<p><b>Search period:</b> until 2 March 2016</p> <p><b>Databases searched:</b> MEDLINE and Scopus</p> <p><b>Inclusion criteria:</b> Adults aged 55 y or older; randomized, double-blind, placebo-controlled trials; interventions based on dairy, or dairy specific components (incl. protein or amino acids); articles written in English. The control group was required to receive a placebo tablet or capsule or a “regular” food product that was compared with the intervention substance.</p> <p><b>Exclusion criteria:</b> Studies based upon only dietary advice; animal studies; renal dysfunction; regular or usual care as reference in case intervention consisted of supplement; small amounts of intervention component where there could not be an expected effect based on outcomes relevant for these review and meta-analysis</p> <p><b>Primary outcomes:</b></p> <ul style="list-style-type: none"> <li>body weight (BW)</li> <li>lean body mass (LBM)</li> </ul>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>Total for all outcomes: 36 RCTs</li> <li>10 RCTs in total included in MA for body weight (BW) (8 RCTs) and lean body mass (LBM) (8 RCTs)</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>n= 11 to 141</li> <li>mean age: 71 to 86 y</li> <li>duration 10 days to 6 months</li> <li>9 RCTs in community-dwelling adults (incl. 1 RCT of 57 men with type 2 diabetes (Leenders, 2011));</li> <li>1 RCT of 103 nursing home residents (Bjorkman, 2012)</li> <li>Countries: Finland, Iceland, Netherlands x 5, Spain, USA x 2</li> </ul> <p><b>Intervention:</b></p> <ul style="list-style-type: none"> <li>protein (7.4 to 45 g/d)</li> <li>amino acids (leucine 2.5g/d)</li> </ul> <p><b>Statistical analysis:</b> Meta-, subgroup, sensitivity analyses and funnel plots were performed when at least 3 studies per outcome measure were found. MA results are reported as estimated pooled mean differences (MD) with 95% confidence intervals.</p> <p><b>Evaluation of study quality:</b> Standardized assessment protocol from the Cochrane Collaboration with a score system for 11 criteria</p>	<p><b>Body weight:</b></p> <ul style="list-style-type: none"> <li>All MAs for body weight included 1 RCT of 103 nursing home residents</li> <li>MA of 8 RCTs (n=418) of protein/amino acid supplementation (incl. 1 RCT of 57 men with type 2 diabetes): MD = 1.13 kg; 95% CI 0.59, 1.67; p&lt;0.0001; I<sup>2</sup>=0%</li> <li>MA limited to 5 RCTs (n=330) using mixture of amino acids: MD = 2.16 kg; 95% CI, 0.93- 3.38; p=0.0006; I<sup>2</sup>=0%</li> <li>MA limited to 5 RCTs (n=264) with duration ≥6 months (incl. 1 RCT of 57 men with type 2 diabetes): MD = 2.09 kg; 95% CI, 0.88-3.29; p=0.0007; I<sup>2</sup> = 0%</li> <li>MA limited to 5 RCTs (n=330) with protein intake ≥20 g/d: MD = 1.55 kg; 95% CI, 0.75-2.35; p=0.0001; I<sup>2</sup>=0%</li> <li>MA restricted to 4 RCTs (n=179) including exercise training component to both intervention and control groups. MD = 0.78 kg; 95% CI, 0.06-1.51; p = 0.03; I<sup>2</sup>=0%</li> </ul> <p><b>Lean body mass:</b></p> <ul style="list-style-type: none"> <li>MA of 8 RCTs (n=474) of protein supplementation (included 1 RCT of 103 nursing home residents and 1 RCT of 57 men with type 2 diabetes): MD = 0.03 kg; 95% CI -0.03, 0.39; p=0.87; I<sup>2</sup>=0%</li> <li>MA of 4 RCTs (n=303) of protein supplementation combined with exercise: MD= -0.18 kg; 95% CI -0.61, 0.26; p=0.42; I<sup>2</sup>=0%</li> </ul> <p><b>Leg strength:</b></p> <ul style="list-style-type: none"> <li>MA of 6 RCTs (n=417) – non-significant effect on leg strength (SMD 0.05; 95% CI, -0.14 to 0.24; I<sup>2</sup> = 0%; p = 0.60). No significant effect on leg strength was found after limiting to 4 trials</li> </ul>	<p><b>Authors’ conclusions:</b></p> <ul style="list-style-type: none"> <li>protein supplementation increases BW. The increase in BW tends to be explained by differences in LBM but only when supplementing doses of protein higher than 20 g/d or when giving protein supplementation to (pre-)frail or compulsorily inactive older adults.</li> <li>No effect from protein supplementation on physical fitness, measured by body composition components (e.g., LBM), muscle strength, or physical performance, was ascertained.</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>Only 4 of the 36 trials scored below a 3 (good) for confounding adjustment</li> </ul> <p><b>Authors’ limitations:</b></p> <ul style="list-style-type: none"> <li>The low number of studies included, especially for the meta-, subgroup, and sensitivity analysis</li> <li>Most of the trials did not publish the mean change with its accompanying standard deviation or the correlation coefficient</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
			<p>that used 6 months of protein supplementation (n = 193; SMD 0.05; 95% CI, -0.20 to 0.30; I<sup>2</sup> = 0%; p = 0.68)</p>	<ul style="list-style-type: none"> <li>resistance-type exercise training was given to both the nutritional intervention and the control groups to increase the number of included trials and, therefore, statistical power</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Eglseer et al (2016)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> To highlight the correlations of sarcopenia with the nutritional status of adults 60 and older.</p> <p><b>Funding source:</b> None stated</p> <p><b>Declarations of interest:</b> The authors have disclosed no potential conflicts of interest, financial or otherwise.</p>	<p><b>Search period:</b> 2009-2014</p> <p><b>Databases searched:</b> MEDLINE (PubMed), CINAHL, EMBASE, PASCAL, The Cochrane Library</p> <p><b>Inclusion criteria:</b> cross-sectional design; study participants were 60 or older; relationship between nutritional status and sarcopenia represented at least a secondary objective variable.</p> <p><b>Exclusion criteria:</b> None stated</p> <p><b>Nutritional status assessment methods:</b></p> <ul style="list-style-type: none"> <li>• anthropometric measurements, e.g. BMI, waist circumference</li> <li>• malnutrition screening tools, including Mini Nutritional Assessment (MNA) both in the short form (MNA-SF) and long form (MNA-LF). One study used 'Seniors in the Community: Risk Evaluation for Eating and Nutrition' (SCREEN II)</li> </ul> <p><b>Primary outcome:</b> Sarcopenia</p>	<p><b>Number of studies:</b> 33 mainly cross-sectional studies (28 of these were in community-dwelling older adults)</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• Subject numbers: n= 48 to 4,000 (2 studies with n&lt;100)</li> <li>• Living in the community in 28 out of 33 studies</li> <li>• Study locations: United States, Korea, Brazil, European countries, incl. Italy, Turkey, Germany, and France.</li> <li>• Mean age not included although inclusion criteria states participants &gt;60 y.</li> </ul> <p><b>Evaluation of study quality:</b></p> <ul style="list-style-type: none"> <li>• Strengthening the Reporting of Observational Studies in Epidemiology (STROBE);</li> <li>• Of 42 articles that were reviewed with regard to their methodological quality, 33 were included in the systematic review</li> </ul>	<p><b>Anthropometric parameters (e.g. BMI or waist circumference) and sarcopenia assessed on the basis of e.g. muscle mass, muscle strength, physical performance:</b></p> <ul style="list-style-type: none"> <li>• 18 studies in total</li> <li>• 12 reported a negative association, between the risk of sarcopenia and anthropometric parameters e.g. higher BMI was associated with higher muscle mass, greater muscle strength or improved physical performance</li> <li>• 6 studies reported positive associations between anthropometric parameters and sarcopenia.</li> </ul> <p><b>Anthropometric parameters and sarcopenia assessed through the EWGSOP tool (European Working Group on Sarcopenia in Older People):</b></p> <ul style="list-style-type: none"> <li>• 7 studies in total: all studies showed a negative association between sarcopenia and anthropometric parameters; 'participants with sarcopenia were demonstrated to have a significantly lower BMI and poorer nutritional status than participants without sarcopenia.'</li> </ul> <p><b>Malnutrition screening tools and sarcopenia:</b></p> <ul style="list-style-type: none"> <li>• In total, 8 studies used nutrition screen tools (MNA-SF, MNA-LF or SCREEN II)</li> <li>• 6 studies showed that individuals with sarcopenia had a poorer nutritional status and increased risk of malnutrition compared to those without sarcopenia</li> </ul> <p><b>Protein intake and sarcopenia</b></p> <ul style="list-style-type: none"> <li>• 6 studies in total</li> <li>• 2 studies reported individuals with sarcopenia had significantly lower protein intakes than those without sarcopenia</li> </ul>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• Sarcopenia is a highly prevalent condition among older adults. Despite methodological differences within the studies examined in the current systematic literature review, it was shown that sarcopenia is mainly associated with malnutrition.</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>• No detail on confounding or adjustment was provided in the systematic review.</li> </ul> <p><b>Authors' limitations:</b></p> <ul style="list-style-type: none"> <li>• None stated</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
			<ul style="list-style-type: none"> <li>• 4 studies (incl. 2 large cohorts found no association)</li> </ul> <p><b>Calcium intake</b></p> <ul style="list-style-type: none"> <li>• 1 study found that participants with sarcopenia had significantly lower daily calcium intakes as compared with participants without sarcopenia</li> </ul> <p><b>Anorexia</b></p> <ul style="list-style-type: none"> <li>• 3 studies showed a significant positive association between anorexia (defined as reduced nutritional intake) and sarcopenia</li> </ul>	



Study	Methods	Included studies	Results	Limitations/comments
<p><b>Feng et al (2017)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> To identify risk or protective factors (diet-related) associated with frailty.</p> <p><b>Funding source:</b> Author Zeyun Feng is supported by a fellowship from the China Medical Board-Collaborating Program in Evidence-based Health Policy-making (grant number: CMB-CP14-190). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The views presented here are those of the authors and should not be attributed to the China Medical Board or its directors, officers, or staff.</p> <p><b>Declarations of interest:</b></p>	<p><b>Search period:</b> search carried out in September 2016 (range of included papers 2012 to 2016)</p> <p><b>Databases searched:</b> MEDLINE Ovid, Embase, Web of Science, PsychINFO Ovid, CINAHL EBSCOhost, Google Scholar</p> <p><b>Inclusion criteria:</b> original science article, assessment of frailty (primary outcome), primary objective to identify lifestyle factor associated with frailty; age <math>\geq 60</math> y., longitudinal study design, community-dwelling population, clear definition and validated tool for assessment of frailty.</p> <p><b>Dietary assessment method:</b> For Mediterranean diet, Mediterranean Diet Score (MeDi score) or Mediterranean Diet Adherence Screener (MEDAS) score; for dietary patterns, Diet Quality Index International score (DQI); for resveratrol, total dietary resveratrol (TDR) or total urinary resveratrol (TUR).</p> <p><b>Primary outcome:</b></p> <ul style="list-style-type: none"> <li>Frailty (using Fried's frailty criteria and the FRAIL (Fatigue, Resistance, Ambulation, Illness, and Loss of Weight Index) scale)</li> </ul>	<p><b>Number of studies:</b> 7 PCS (Other PCS omitted here because of non-nutrition-related exposure, such as smoking, socioeconomic status, psychological factors)</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>Sample size, range 1155 to 4000</li> <li>Duration, range 3 y to 9 y</li> <li>Age, <math>\geq 60</math> y or <math>\geq 65</math> y (mean age not stated)</li> <li>Italy (2), Spain (4), China-Hong Kong (1)</li> <li>All community-dwelling</li> </ul> <p><b>Evaluation of study quality:</b> Assessed using Quality of Reporting of Observational Longitudinal Research checklist.</p> <p><b>Statistical analysis:</b> Only included data from multivariable adjusted models, negative and positive associations, including those not reporting p values; use of logistic regression.</p>	<p><b>Mediterranean diet and frailty:</b> 2 PCS with significant negative association (<math>p &lt; 0.05</math>) between Mediterranean dietary pattern and frailty</p> <ul style="list-style-type: none"> <li>1 PCS using MeDi score (<math>n=1815</math>, age <math>\geq 60</math>y, follow-up 3.5 y, Spain)</li> <li>1 PCS using high adherence to Mediterranean dietary pattern (<math>n=690</math>, age <math>\geq 65</math>y, follow-up 6y, Italy)</li> </ul> <p>2 PCS with no significant association between Mediterranean dietary pattern and frailty</p> <ul style="list-style-type: none"> <li>1 PCS using MeDi score (<math>n=2724</math>, age <math>\geq 65</math>y, follow-up 3.9y, Hong Kong)</li> <li>1 PCS using MEDAS (<math>n=1815</math>, age <math>\geq 60</math>y, follow-up 3.5y, Spain)</li> </ul> <p><b>Other dietary patterns/nutrients and frailty:</b></p> <ul style="list-style-type: none"> <li>1 PCS with a significant negative association (<math>p &lt; 0.05</math>) between a higher Diet Quality Index International (DQI) score and frailty (<math>n=2724</math>, age <math>\geq 65</math>y, follow-up 3.9y, Hong Kong)</li> <li>1 PCS with no significant association between a "vegetables-fruits" pattern or "meat-fish" pattern and frailty (<math>n=2724</math>, age <math>\geq 65</math>y, follow-up 3.9y, Hong Kong)</li> <li>1 PCS with significant negative association (<math>p &lt; 0.01</math>) between higher consumption of fruit/vegetable and frailty (<math>n=2198</math>, age <math>\geq 60</math>y, follow-up 3.5y, Spain)</li> <li>1 PCS with significant negative association between protein consumption (including total proteins, animal proteins and higher MUFAs) and frailty. (<math>n=1822</math>, age <math>\geq 60</math>y, follow-up 3.5y, Spain)</li> <li>1 PCS with no significant association between consumption of vegetable-based protein, saturated fatty acids (SFAs), <math>\alpha</math>-linolenic acid (ALA), linoleic acid (LA), carbohydrates, simple sugars, polysaccharides, or long-chain <math>\omega</math>-3 fatty</li> </ul>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>A broad range of sociodemographic, physical, biological, lifestyle, and psychological factors show a longitudinal association with frailty. Significant lifestyle factors include a higher Diet Quality Index International (DQI) score, higher fruit/vegetable consumption and higher tertile of all measures of habitual dietary resveratrol exposure.</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>The authors note that associations were only reported from fully adjusted models.</li> </ul> <p><b>Authors' limitations:</b></p> <ul style="list-style-type: none"> <li>Significant associations found in some studies but not others, reasons may include different population characteristics, lack of power in certain studies, different or short study durations, differing frailty assessment tools (note that Fried's tool, which was most commonly used, does not take into account psychological or</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
<p>Stated: The authors have declared that no competing interests exist.</p>			<p>acids and frailty (n=1822, age ≥ 60y, follow-up 3.5y, Spain)</p> <ul style="list-style-type: none"> <li>• 1 PCS with significant negative association (p&lt;0.05) between low-fat milk and yoghurt intake and frailty (n=1871, age ≥ 60y, follow-up 3y, Spain)</li> <li>• 1PCS with no significant association of whole milk, whole-fat yogurt, low-fat yogurt, cheese or whole milk OR yoghurt and frailty (n=1871, age ≥ 60y, follow-up 3y, Spain)</li> <li>• 1 PCS reported negative association (p&lt;0.05) when comparing higher and lower tertiles of habitual dietary resveratrol exposure (TDR, TUR, and TDR+TUR) with frailty (n=322, age ≥ 65y, follow-up 9y, Italy).</li> </ul>	<p>social components, only physical aspects of frailty).</p>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Gine-Garriga et al (2015)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> Analysis of current evidence for dietary interventions (modification rather than designed for weight loss) to improve physical function</p> <p><b>Funding source:</b> Not stated</p> <p><b>Declarations of interest:</b> Stated: Maria Giné-Garriga, Eulàlia Vidal-Garcia, Natàlia Gómara-Toldrà, Blanca Roman-Viñas, and Marta Roqué-Fíguls declare that they have no conflict of interest.</p>	<p><b>Search period:</b> up to September 2014</p> <p><b>Databases searched:</b> MEDLINE</p> <p><b>Inclusion criteria:</b> 65 y, with or without non-communicable diseases, community living</p> <p><b>Exclusion criteria:</b> participants with disability, institutionalised or in hospital, dietary supplementation interventions</p> <p><b>Dietary assessment method:</b> Mediterranean diet assessed using score by Trichopoulou et al, food intake assessments</p> <p><b>Primary outcome:</b></p> <ul style="list-style-type: none"> <li>• Functional capacity</li> <li>• Strength</li> <li>• Balance</li> <li>• Mobility</li> <li>• Gait (measured by Short Physical Performance Battery (SPBB), modified Physical Performance Test, Timed Up and Go test, strength measurement tools, the chair stand test, a walking test, and other measurements of balance and mobility)</li> </ul>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• 7 studies (4 RCT, 2 PCS, 1 XS)</li> <li>• 1 PCS and 1 RCT are not included here as results combined diet and exercise in the intervention.</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• community-dwelling</li> <li>• mean age: 4 studies &gt; 65y; 3 studies &gt; 70 y.</li> <li>• RCT sample range, n=80 to 146</li> <li>• XS and PCS range, n=935 to 2225</li> <li>• Follow-up: 1 PCS 3, 6, and 9 y; 1 PCS 8 y.</li> <li>• Study locations not stated</li> </ul> <p><b>Diet interventions:</b> energy deficit of 500 to 750 Kcal plus behavioural therapy, personalised diet counselling and group session education, increase in fruit &amp; vegetable intake from &lt;2-5 daily portions. 2 studies included nutritional supplements + dietary modification.</p> <p><b>Statistical analysis:</b> Effect estimates measured by risk ratios or mean differences. If there was low heterogeneity between studies in terms of populations, interventions, and outcomes, pooled estimates of effect were obtained. MA applying inverse-variance method under a random-effects model. Statistical heterogeneity was assessed through I<sup>2</sup></p>	<p><b>MA of diet and gait speed</b></p> <ul style="list-style-type: none"> <li>• 3 RCTs, 1 PCS</li> </ul> <p>Gait speed of participants in the diet alone intervention groups was not significantly different than participants in the control group (MD=0.04 m/s; 95 % CI 0.00 to 0.09; I<sup>2</sup>=0 %; 4 studies, 2407 participants). A combination of diet plus exercise had a significant effect on gait speed (95% CI 0.06 to 0.21, I<sup>2</sup>= 0%, 2 studies, 103 participants)</p> <ul style="list-style-type: none"> <li>• <b>MA of diet and balance</b></li> <li>• 2 RCTs (study characteristics only provided for 1 RCT: mean age 80.5y; follow-up 3 and 6 months)</li> <li>• Data provided on the one leg balance stand for the comparisons of diet alone and diet plus exercise. Neither diet alone intervention (MD=1.12 (no unit stated); 95 % CI -2.79 to 5.04; I<sup>2</sup>=0 %; 2 trials, 51 participants) nor combination of diet + exercise (MD=3.47; 95 % CI -6.72 to 13.67; I<sup>2</sup>=92 %; 2 studies, 53 participants) showed a consistent effect on balance measures. The results are highly heterogeneous for the combined intervention comparison.</li> </ul> <p><b>Functional capacity</b> could not be analysed by MA but:</p> <ul style="list-style-type: none"> <li>• 1 XS (n=1456, mean age 75.2y) reported women in third tertile for dairy intake had 26% lower odds for a slow timed up and go test (P=0.04).</li> <li>• 1 RCT (n=80, mean age 71y) reported participants did not improve lower extremity physical function measures with the chair-stand test after 16 weeks eating diet rich in fruit &amp; vegetables (at least 5 portions/day compared to 2 portions/day).</li> </ul>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• No evidence for diet alone contributing to improvements in physical function. However, when exercise is combined with the dietary intervention, there is some evidence for a significant increase in walking speed but not for balance outcomes (data not included in this table).</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>• No detail on confounding or adjustments were provided in the systematic review</li> </ul> <p><b>Authors' limitations:</b></p> <ul style="list-style-type: none"> <li>• Notable challenges in applying inclusion criteria, for example, studies of participants with moderate dependence in mobility were included but participants with basic ADL (activities of daily living scale) were excluded.</li> <li>• Both diet and exercise interventions were extremely heterogeneous.</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
		<p><b>Study quality:</b>            Because of different study designs, no sensitivity analysis performed.            Risk of bias for RCTs using domain analysis from Cochrane handbook: 3 RCT, low risk; 1 RCT high risk            PCS &amp; XS assessed using Newcastle-Ottawa scale: 1 PCS, high quality; 1 PCS unclear quality; 1 XS, low quality.</p>		

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Govindaraju et al (2018)</b></p> <p><b>Study design</b> Systematic review</p> <p><b>Aim of study/ research question:</b> To review the evidence for an association between dietary patterns and self-reported quality of life (QoL) or self-rated health status.</p> <p><b>Funding source:</b> No external funding</p> <p><b>Declaration of interest:</b> None</p>	<p><b>Search period:</b> January 1975 to March 2018</p> <p><b>Databases searched:</b> Medline, Embase, Psycinfo, Cochrane, Cinhal plus, Ageline, Web of Sciences, Scopus.</p> <p><b>Inclusion criteria:</b> mean age of 60 y (if ages across all groups then include if the results were stratified for &gt;60 y), in any setting.</p> <p><b>Exclusion criteria:</b> foreign language publications, clinical views, conference papers, reviews, case studies, or not peer-reviewed.</p> <p><b>Dietary assessment method:</b> FFQ, diet history including 24 h recall, dietary screening tool (DST), computerised diet history.</p> <p><b>Primary outcome:</b> Quality of life (QoL by any validated method (for example, SF-12, SF-36. World Health Organization QoL (WHOQOL), European QoL (EUROQOL)).</p>	<p><b>Number of studies:</b> 12 (5 PCS, 7 XS) (Excluded Alcobierre et al. because mean age &lt;60y; and Lewis et al., and Rifai et al., because populations had disease diagnosis)</p> <p><b>Study populations:</b></p> <ul style="list-style-type: none"> <li>studies in any setting were included (primary paper check confirmed majority in community and one from osteoporosis initiative)</li> <li>3 studies, n=&lt;1000; 4 studies 1000&lt;n&lt;3000; 4 studies n&gt;3000</li> <li>mean age &gt; 60 y, studies done across age groups were considered if stratified results were available for ages 60 and above</li> <li>Countries: Europe (7), USA (4), Hong Kong (1), Australia (2), multicentre (1) (location not stated for each study separately)</li> </ul> <p><b>Evaluation of study quality:</b></p> <ul style="list-style-type: none"> <li>SR followed PRISMA.</li> <li>Quality assessed with Effective Public Health Practice Project (EPHPP) <i>Quality Assessment Tool for Quantitative Studies</i>: 8 studies rated as moderate quality, 1 study rated as weak and 3 studies high quality.</li> </ul>	<ul style="list-style-type: none"> <li>1 PCS, n=1911, ≥60 y (quality: strong) Higher PREDIMED (modified MeDi score) score was associated with slightly better physical component score. Compared to those in the lowest tertile, physical component score: b = 0.55 (-0.48 to 1.59) for tertile 2, 1.34 (0.21 to 2.47) for tertile 3. PREDIMED score not significantly associated with a better mental component score (MCS). [MCS: tertile 2, b = -0.25 (-1.31 to 0.80) and tertile 3, b = 0.56 (-0.58 to 1.71)] MeDi score not associated with physical component score or mental component score</li> <li>1 PCS, n=895, 67 y (quality: moderate) Adherence to dietary guidelines at baseline was associated with significantly better QoL in four domains after 5 years. Participants in the highest vs. lowest quartile of baseline total diet scores had adjusted mean scores 5.6, 4.0, 5.3, and 2.6 units higher in these SF36 domains 5 years later</li> <li>1 PCS, n=2457, 60 y (quality: strong) Older adults with better quality diets report better health-related QoL, with additional associations with emotional wellbeing observed in women. Better diet quality by dietary guidelines index (DGI) was associated with better self-reported HRQoL on the physical function (OR = 1.56, 95% confidence intervals (CI): 1.22–1.99), bodily pain (OR = 1.29, CI: 1.01, 1.63), general health (OR = 1.72, CI: 1.36, 2.19), energy (OR = 1.51, CI: 1.19, 1.92), emotional wellbeing (OR = 1.36, CI: 1.08, 1.72) and physical component score (OR = 1.46, CI: 1.15, 1.86). A higher recommended food score (RFS) was associated with better HRQoL on the physical function (OR = 1.43, CI: 1.13–1.82), general health (OR = 1.41, CI: 1.12, 1.78), energy (OR = 1.55, CI:</li> </ul>	<p><b>Authors' conclusions</b> Healthy dietary patterns (for example, Mediterranean diet) were associated with better self-rated health and QoL (in 9 out of 11 studies).</p> <p>Confounding: Fourteen out of 15 studies scored 'strong' for addressing confounders, 1 study scored 'moderate' and no studies scored 'weak'.</p> <p><b>Authors' limitations</b> Self-reported diet and self-reported QoL by questionnaire, both subject to bias. Also subject to random and systematic errors characteristic of epidemiological-scale dietary assessments.</p>

Study	Methods	Included studies	Results	Limitations/comments
			<p>1.22, 1.96) and emotional wellbeing (OR = 1.41, CI: 1.12, 1.77)</p> <p>MeDi score in the top quartile was associated with a better score on the energy scale (OR = 1.53, CI: 1.11, 2.10). An association between MeDi score and general health was also observed after adjustment for smoking and physical activity (OR = 1.52, CI: 1.11, 2.08)</p> <ul style="list-style-type: none"> <li>• 1 PCS, n=480, 73 y (quality: weak) No association observed between diet quality and risk of deterioration of health status. Risk of deterioration in health status resulting from low dietary quality: OR (95% CI): Men 1.1 (0.5, 2.3); women 1.4 (0.7, 2.7)</li> <li>• 1 PCS, n=2376 ≥60 y (quality: strong) No significant association between Mediterranean dietary pattern index (UAM-MDP) and physical component score and mental component scoreA</li> <li>• 1 XS, n=3378, 72.5 y (quality: moderate) Better dietary quality is associated with better self-rated physical and mental health. Physical component score: <math>\beta = 0.0689</math> (<math>p &lt; 0.0001</math>); mental component score: <math>\beta = 0.0693</math> (<math>p &lt; 0.0001</math>)</li> <li>• 1 XS, n=1389, 69 y (quality: moderate) Those with a favorable diet had reduced odds of having a low global Health Related quality of life (HRQoL); OR (95% CI): 0.79 (0.63–0.99)</li> <li>• 1 XS, n=351, 71 y (quality: moderate) Adherence to a Mediterranean dietary pattern was positively related to both physical component score and mental component score of SF12 (non-significant for physical component score for men). Regression coefficients for the relationship between Mediterranean diet score with women (mental component score (0.07, CI:(-</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
			<p>0.96 to 0.23, <math>p &lt; 0.001</math>) and physical component score (0.19, CI (0.04 to 0.34, <math>p = 0.020</math>)) and men (mental component score (0.01, CI: -0.12–0.29, <math>p = 0.004</math> and physical component score (0.05, CI: 0.17–0.20, <math>p = 0.060</math>))</p> <ul style="list-style-type: none"> <li>• 1 XS n=4470, 61.3 y (quality: moderate) Higher adherence to Mediterranean diet (aMED) is associated with better QOL. Those with higher aMED showed significantly higher physical component score (quintile 5: <math>50 \pm 8.5</math> compared to quintile 1: <math>47.2 \pm 9.8</math>; <math>p &lt; 0.0001</math>) and mental component score (quintile 5: <math>54.5 \pm 7.6</math> compared to quintile 1: <math>53.2 \pm 8.8</math>; <math>p &lt; 0.0001</math>)</li> <li>• 1 XS, n=641, 73 y (quality: moderate) Diet quality was positively associated with physical functioning (<math>\beta = 0.10</math>, <math>P_s &lt; 0.005</math>) and vitality (<math>\beta = 0.095</math>, <math>P_s = 0.01</math>)</li> <li>• 1 XS, n=4009, men 81.3 y, women 82 y (quality: moderate) Poor diet quality, as assessed by the dietary screening tool (DST), is associated with lower HRQoL. Health and activities limitation index (HALex) scores were significantly lower for participants with dietary intakes categorized as unhealthy (&lt;60) (0.70, 95% CI 0.69, 0.72, <math>p &lt; 0.05</math>) or borderline (60–75) (0.71, 95% CI 0.70, 0.73, <math>p &lt; 0.05</math>) compared to those scoring in the healthy range (&gt;75) (0.75, 95% CI 0.73, 0.77)</li> <li>• 1 XS n=1724, 76.0 y (quality: moderate) Men in the “pasta eaters” cluster had greater risk of reporting poor health (odds ratio [OR] 1.91; 95% CI, 1.21–3.01) than the “healthy” cluster. Women in the “biscuits and snacking” cluster (n = 162; 15%) had greater risk of poor perceived health (OR 1.69; 95% CI, 1.15–2.48) compared to “healthy” eaters</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Lorenzo-López et al (2017)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> An evaluation of nutritional status (micro- and macronutrients, dietary patterns, malnutrition) and frailty</p> <p><b>Funding source:</b> Stated: This work was supported by the Xunta de Galicia, FrailNet network IN607C, 2016/08</p> <p><b>Declarations of interest:</b> Stated: The authors declare that they have no competing interests</p>	<p><b>Search period:</b> January 2005 and February 2017</p> <p><b>Databases searched:</b> PubMed, Web of Science, Scopus</p> <p><b>Inclusion criteria:</b> community dwelling or institutionalised, age 65 y, good definition of frailty as outcome, only studies of nutritional status and frailty, English or Spanish only, undernutrition or malnutrition but not obesity.</p> <p><b>Exclusion criteria:</b> Abstracts, reviews, books, book chapters, letters, conference abstracts, short surveys, studies based on the description of a protocol, interventional studies, as well as studies based on perspective/comments from authors.</p> <p><b>Primary outcome:</b> Frailty</p> <p><b>Dietary assessment method:</b> FFQ; brief-type diet history questionnaire (BDHQ), Mediterranean diet score (MeDi score) by Trichopoulou et al, and modified version by Fung et al; malnutrition assessed by mini-nutritional assessment (MNA) and short-form MNA (SF-</p>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• 19 studies (14 XS, 5 PCS)</li> <li>• 2 XS studies with institutionalised patients and their results not included here.</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• n=22,270 (63.2% women)</li> <li>• living in the community</li> <li>• mean age 74.5 ± 7.0 y</li> <li>• 8 studies in Europe, 7 in Asia, 4 US</li> <li>• not included here are 2 XS studies in institutionalised or mixed populations (n=1237 participants)</li> </ul> <p><b>Data:</b> No meta-analysis owing to large heterogeneity.</p> <p><b>Evaluation of study quality:</b> assessed using Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)</p>	<p><b>Micronutrients and frailty (1 PCS, 4XS)</b></p> <p>In all 5 studies, frailty syndrome was independently associated with a low intake of specific micronutrients:</p> <ul style="list-style-type: none"> <li>• 1 XS (Europe (Italy); n = 802; age, mean ± SD: 74.1 ± 6.5 years; 56% women found that a low intake of certain micronutrients (vitamins D, E, and C, and folate) was significantly related to frailty independent of energy intake (OR 2.12, 95% CI: 1.29–3.50).</li> <li>• 1 XS (Asia (Japan); n = 2108; age, mean ± SD: 74.7 ± 5.0 years; 100% women, multicentre study among three generations, found that 10 of 12 micronutrients studied (vitamin A, α-carotene, β-carotene, β-carotene equivalent, cryptoxanthin, vitamin D, α-tocopherol, vitamin B6, folate, and vitamin C) were associated with a lower prevalence of frailty (no effect size stated).</li> <li>• 1 XS from Women’s Health and Aging Studies (WHAS) I and II (USA; n = 703; age, range: 70–79 years; 100% women) showed that older women with increased concentrations of methylmalonic acid (MMA: a marker of vitamin B12 tissue deficiency) had 40% to 60% greater odds of being pre-frail (p-values &lt;0.07) and 1.66 to 2.33 times greater odds of being frail (p-values &lt;0.02) compared to patients who were not frail.</li> <li>• 1 XS of same sample (USA; n = 754; age, mean (range): 74.7 (70–80 years); 100% women) reported the age-adjusted odds ratios of being frail were higher for older women with lower levels of serum total carotenoids, α-tocopherol, 25-hydroxyvitamin D, and vitamin B6 (age-adjusted OR for Q1 vs. Q2-Q3-Q4 2.50, 95% CI 1.51–4.14; 1.64, 95% CI 0.95–2.84, 1.71, 95% CI 1.00–2.94; and 1.79, 95% CI 0.99–3.24, respectively). Importantly, after adjusting for age,</li> </ul>	<p><b>Authors’ conclusions:</b></p> <ul style="list-style-type: none"> <li>• Nutrition is important in the development of frailty.</li> <li>• Five of the articles studied the association between micronutrients and frailty and reported that low intake of specific micronutrients increased the risk of being frail.</li> <li>• Among the micronutrients that were studied, most of them had sequentially decreasing levels in non-frail, pre-frail, and frail older people. One important implication of the inverse association between micronutrients and frailty is that the intake of specific nutrients may affect the health of older people and may lead to the development of frailty, five studies considered the role of macronutrient and protein intake in frail patients. Three of those studies found that higher protein intake was associated with lower frailty risk, while only 1 study found that it was actually the overall distribution of the protein throughout daily meals</li> </ul>



Study	Methods	Included studies	Results	Limitations/comments
	<p>MNA), and various laboratory techniques.</p> <p><b>Outcomes measured:</b> Frailty based on frailty phenotype (Fried et al), or modified version, or on the Study of Osteoporotic Fractures (SOF) Frailty Index or on the FRAIL scale.</p>		<p>sociodemographic status, smoking status, and body mass index, the association between micronutrients and frailty was strongest for total carotenoids, <math>\beta</math>-carotene, and lutein/zeaxanthin.</p> <ul style="list-style-type: none"> <li>1 PCS of cohort from the WHAS-I study (USA; n = 766; age, mean <math>\pm</math> SD: 78.2 <math>\pm</math> 7.6 years; 100% women), showed that women in the lowest quartile of serum carotenoids and <math>\alpha</math>-tocopherol had a significantly increased risk of becoming frail over a 3-y period (HR for Q1 vs. Q2-Q3-Q4 1.30, 95% CI 1.01–1.92; and 1.39, 95% CI 1.02–1.89, respectively). By applying a multivariate grouped-time Cox proportional hazards model, the number of nutrient deficiencies was also related to an increased risk of becoming frail.</li> </ul> <p><b>Macronutrients and frailty</b> (5 studies: 1 PCS, 4 XS) 3 XS found that a higher protein intake was associated with a lower risk of frailty</p> <ul style="list-style-type: none"> <li>1 XS (Italy, n = 802; age, mean <math>\pm</math> SD: 74.1 <math>\pm</math> 6.5 years; 56% women) found significant association between low protein intake (lowest quintile) and frailty after adjusting for energy intake (OR 1.98, 95% CI 1.18–3.31)</li> <li>1 XS (Japan; n = 2108; age, mean <math>\pm</math> SD: 74.7 <math>\pm</math> 5.0 years; 100% women) showed a significant association (adjusted OR for Q5 vs. Q1) for higher intakes of protein and lower prevalence of frailty (total protein (0.66, 95% CI 0.46–0.96) and plant protein (0.66, 95% CI 0.45–0.95). For animal protein intake the association was non-significant (0.73, 95% CI 0.50–1.06).</li> <li>1 XS Europe (Paris); n = 1345; age, mean <math>\pm</math> SD: 75.6 <math>\pm</math> 5.1 years; 60.4% women, found that a 1 g/kg protein intake was associated with a lower prevalence of frailty, after adjusting for sociodemographic and clinical factors.</li> </ul>	<p>that was significantly associated with frailty.</p> <ul style="list-style-type: none"> <li>Three studies that examined the relationship between overall diet quality and frailty revealed that the quality of the diet is inversely associated with the risk of being frail, thus providing convergent evidence that a potentially modifiable factor, such as dietary intake, may play a crucial role in frailty status. This review found 2 studies that showed that a high intake of foods with high dietary antioxidant capacity, such as vegetables, fruits, coffee, and green tea, was associated with a lower risk of developing frailty.</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>The authors mentioned that several associations were strongest after adjusting for age, socio-economic status, smoking status and BMI but did not provide any more specific information such as which or how many individual studies adjusted for confounding.</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
			<p>2 studies reported that the amount of protein intake was not associated with frailty.</p> <ul style="list-style-type: none"> <li>1 XS (Germany; n = 194; age, mean (range): 83.0 (75–96 years); 66.0% women) found that the amount of protein intake was not associated with frailty or any of its individual criteria (the authors only found a significant trend concerning low physical activity). However, the distribution of protein intake throughout the day was significantly associated with frailty. Specifically, frail older adults showed a more uneven distribution of protein intake throughout the day with a lower morning intake and a higher midday intake than pre-frail and non-frail participants.</li> <li>1 PCS (USA; n = 5925; age, mean <math>\pm</math> SD: 75.0 <math>\pm</math> 5.7 years; 100% men). A cross-sectional analysis of baseline data showed higher intakes of fibre and carbohydrates (Q5 v Q1) to be significantly associated with a decreased risk of being frail (OR 0.51; 95% CI 0.36–0.73; OR 0.65; 95% CI 0.45–0.94). A higher fat intake was significantly associated with an increased risk of being frail (1.61; 95% CI 1.12–2.31) Notably, protein intake was not associated with the risk of frailty (no effect size reported)</li> </ul> <p><b>Dietary patterns and frailty (1 PCS)</b>  1 PCS (China; n = 2724; age, mean <math>\pm</math> SD: 71.8 <math>\pm</math> 4.8 years; 50.3% women; follow-up 4 years) After adjustment for age and sex, there was no association of incident frailty and a “snacks-drinks milk products” pattern, a “vegetables-fruits” pattern, or a “meat-fish” pattern.</p> <ul style="list-style-type: none"> <li>1 PCS (China; n = 2724; age, mean <math>\pm</math> SD: 71.8 <math>\pm</math> 4.8 years; 50.3% women; follow-up 4 years) higher score of the “snacks-drinks milk products”</li> </ul>	<p><b>Authors’ limitations:</b></p> <ul style="list-style-type: none"> <li>Most primary studies were cross-sectional in design, no analysis of other mediating factors such as swallowing, poor dentition. Large heterogeneity in outcome measurements</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
			<p>significantly decreased the risk of being frail (OR 0.58, 95% CI 0.36–0.91). Better diet quality (higher Diet Quality Index-International scores) significantly decreased the risk of being frail (OR 0.59, 95% CI 0.42–0.85, respectively). No Hasselblad &amp; Hedges' d effect size was observed. There was no association of Mediterranean-Diet Score, “vegetables-fruits” pattern, or “meat-fish” pattern with incident frailty.</p> <p><b>Diet quality and frailty:</b> (2 PCS, 1 XS) overall diet quality was inversely associated with risk of being frail in 3 studies</p> <ul style="list-style-type: none"> <li>• 1 XS (Germany; n = 192; age, mean ± SD: 83.0 ± 4.0 years; 64.6% women) a healthy diet (assessed through a modified version of Mediterranean Diet Score) significantly decreased the risk of being frail (Q4 of the MeDi score, OR 0.26, 95% CI 0.07–0.98.</li> <li>• 1 PCS (China; n = 2724; age, mean ± SD: 71.8 ± 4.8 years; 50.3% women; follow-up 4 years) Participants with a higher Diet Quality Index-International score (representing a more balanced diet in terms of energy and nutrient intake) had a reduced risk of frailty (OR 0.59, 95% CI 0.42–0.85). No association was found between MeDi score and frailty.</li> <li>• 1 PCS (USA; n = 5925; age, mean ± SD: 75.0 ± 5.7 years; 100% men; follow-up 4.6 years) Diet Quality Index Revised (DQI-R) score, was inversely associated with the risk of intermediate status or frailty status relative to a robust status (OR for Q5 vs. Q1: 0.82, 95% CI 0.60–1.11; and 0.18, 95% CI 0.03–0.97, respectively)</li> </ul> <p><b>Antioxidant capacity of the diet and frailty</b> (1 PCS, 1 XS) both studies showed that a higher anti-</p>	

Study	Methods	Included studies	Results	Limitations/comments
			<p>oxidant capacity is associated with lower odds of frailty.</p> <ul style="list-style-type: none"> <li>• 1 XS (Japan; n = 2121; age, mean <math>\pm</math> SD: 74.7 <math>\pm</math> 5.0 years; 100% women) found that a higher dietary total antioxidant capacity (TAC) (as assessed by FRAP, ORAC, TEAC, and TRAP assays) was inversely associated with frailty (adjusted OR for Q5 vs. Q1: 0.35, 95% CI 0.24–0.53; 0.35, 95% CI 0.23–0.52; 0.40, 95% CI 0.27–0.60; and 0.41, 95% CI 0.28–0.62, respectively).</li> <li>• 1 PCS (Italy; n = 769; age, mean <math>\pm</math> SD: 72.7 <math>\pm</math> 5.8 years; 55.4% women; follow-up of 3, 6 &amp; 9 years) investigated the association of frailty and habitual dietary resveratrol exposure, assessed by total dietary resveratrol (TDR), total urinary resveratrol (TUR), and TDR + TUR. The concentrations of TDR, TUR, and TDR + TUR were inversely associated with frailty risk after 3-years of follow-up but not after 6- and 9-years of follow-up (OR at 3 years of follow-up for T1 vs. T3: 0.17, 95% CI 0.05–0.63; 0.32, 95% CI 0.09–1.11; and 0.11, 95% CI 0.03–0.45, respectively).</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Mello, Engstrom and Alves (2014)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> To identify the socio-demographic, psycho-behavioural, health related, nutritional and lifestyle factors associated with frailty.</p> <p><b>Funding source:</b> Not stated</p> <p><b>Declarations of interest:</b> Not stated</p>	<p><b>Search period:</b> 2001 to March 2013</p> <p><b>Databases searched:</b> MEDLINE, Scopus, LILACS, ISI Web of Knowledge</p> <p><b>Inclusion criteria:</b> Original scientific articles published in Brazilian or international periodicals; publication from 2001 to March 2013; study population 60 years or older; observational study design (cross-sectional, cohort or case-control); individual selection by probabilistic sample or article showing the sampling design; and identification of factors associated with frailty in the elderly as the principal or secondary objective.</p> <p><b>Exclusion criteria:</b> Studies not using the Fried et al 2001 definition of frailty.</p> <p><b>Primary outcome:</b> Frailty</p> <p><b>Outcomes measured:</b> Frailty defined as three or more of the five components of frailty defined by Fried et al 2001.</p> <ul style="list-style-type: none"> <li>• Self-reported unintentional weight loss of 4.5kg or 5% of</li> </ul>	<p><b>Number of studies:</b> 35 in total (8 cohorts (not stated if PCS) and 27 XS).</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• Sample size ranged from 77 to 40,657, with most including more than 600.</li> <li>• 32 studies included adults aged 65 or over, 3 included those aged 60 or over. Mean age not given.</li> <li>• Local community-dwelling, non-institutionalised</li> <li>• North American (12 studies), European (11 studies), Latin American (9 studies), Asians (3 studies)</li> </ul> <p><b>Evaluation of study quality:</b> An adapted version of the <i>Newcastle-Ottawa Scale</i>. Studies not graded on whether risk of bias was low, medium or high overall.</p> <p><b>Statistical analysis:</b> Statistical technique used by each study recorded.</p>	<p><b>This SR did not report on primary studies' study location, sample size, population age or effect estimates)</b></p> <p><b>Frailty:</b> <b>BMI</b> was considered by 14 studies in total (3 cohorts, 11 XS):</p> <ul style="list-style-type: none"> <li>• No association with frailty was reported by 5 studies (XS)</li> <li>• Some association with frailty was found in 9 studies (3 cohorts, 6 XS) of which some found association in multiple BMI categories.</li> </ul> <p>4 studies found association with BMI in general (2 cohorts, 2 XS)</p> <ul style="list-style-type: none"> <li>• a positive association was reported by 3 studies (1 cohort, 2 XS)</li> <li>• an inverse association was reported by 1 cohort</li> </ul> <p>3 studies found association with obesity measured by BMI (1 cohort, 2 XS)</p> <ul style="list-style-type: none"> <li>• All 3 studies found a positive association with frailty, of which 1 XS showed a positive association for women only</li> </ul> <p>3 studies found association with overweight measured by BMI (1 cohort, 2 XS)</p> <ul style="list-style-type: none"> <li>• A positive association with frailty was reported by 2 studies (1 cohort, 1 XS)</li> <li>• A negative association was reported by 1 XS</li> </ul> <p>1 XS found association with non-obese (black?) measured by BMI</p> <p>2 studies found positive association of frailty with underweight measured by BMI (1 cohort, 1 XS).</p> <p><b>Self-reported weight loss</b> was considered by 2 studies (1 cohort, 1 XS). The cohort study showed</p>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• The principal socio-demographic, psycho-behavioural, health-related, nutritional and life-style factors positively associated with frailty were: age, female gender, black race/colour, cardiovascular diseases, number of comorbidities/diseases, functional incapacity, poor self-rated health, depressive symptoms, BMI and smoking. Inversely associated factors were schooling, income, cognitive function and alcohol use. Underweight elderly according to BMI and those with a higher proportion of overweight according to BMI showed a higher prevalence of frailty.</li> </ul> <p><b>Confounding</b></p> <ul style="list-style-type: none"> <li>• The systematic review reported that 16 out of the 35 included studies did not adjust for confounding. No further information was provided.</li> </ul> <p><b>Authors' limitations:</b></p>

Study	Methods	Included studies	Results	Limitations/comments
	<p>body weight in the previous year</p> <ul style="list-style-type: none"> <li>• Self-reported fatigue assessed by the following: “I feel tired all the time” and “I could not get going” from the depression scale of the CES-D</li> <li>• Decreased grip strength, measured by dynamometer in the dominant hand, stratified by gender and BMI quartiles</li> <li>• Low level of physical activity measured as weekly expenditure level in kcal, with information obtained from the reduced version of the <i>Minnesota Leisure Time Activity Questionnaire</i>, stratified by gender</li> <li>• Decreased gait speed in seconds, calculated by recording the time to walk 4.6m at a comfortable pace, stratified by gender and mean height</li> </ul>		<p>no association with frailty. The XS showed a positive association.</p> <p><b>Waist circumference</b> was considered by 3 studies (3 XS). Two XS show a positive association with frailty and the other XS showed no association.</p> <p><b>Waist/hip ratio</b> was considered by 1 study (XS). The study showed a positive association with frailty.</p> <p><b>Low appetite</b> was considered by 2 studies (1 cohort, 1 XS), both of which reported a positive association with frailty.</p> <p><b>Food intake</b> (no details stated) was considered by 1 study (cohort). The study reported no association with frailty.</p>	<p>Most of the studies adopted a cross-sectional design, which does not allow establishing a cause-and-effect relationship between the independent variables and the outcome. In addition, 18 studies performed bivariate analyses and a total of 16 studies did not adjust for potential confounders.</p> <p>74% of studies performed some variation on the five components of frailty proposed by Fried et al.</p> <p>As the review only included studies using the Fried et al (2001) definition of frailty some good studies might have been excluded.</p>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Milne et al (2006)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> To investigate an association between protein and energy supplementation and mortality</p> <p><b>Funding source:</b> By the Medical Research Council, UK; Chief Scientist Office of the Scottish Executive Health Department, UK, and the Student Awards Agency for Scotland, UK.</p> <p><b>Declarations of interest:</b> Potential conflict of interest: Dr Potter was principal; investigator for a trial included in the review.</p>	<p><b>Databases searched and time periods:</b> Cochrane Central Register of Controlled Trials (issue 2, 2005), MEDLINE (1966 to June 2005), Embase (1980 to March 2004), HealthStar (1975 to March 2001), CINAHL (1982 to March 2004), BIOSIS (1985 to March 2004) and CAB abstracts (1973 to March 2004).</p> <p><b>Inclusion criteria:</b> randomised or quasi randomised trials with a minimum intervention of 1 week, minimum mean age 65 y. Intervention supplements include: commercial supplements, milk-based supplements and fortified foods.</p> <p><b>Exclusion criteria:</b> cancer sufferers, interventions which included specially designed immunomodulatory supplements or supplements of amino acids.</p> <p><b>Outcomes</b></p> <ul style="list-style-type: none"> <li>• all-cause mortality</li> <li>• co-morbidities or complications</li> <li>• percentage change in weight</li> <li>• percentage change in mid-arm muscle circumference</li> </ul>	<p><b>Number of studies:</b> 21 RCTs in total (MA includes study populations in hospital and institutions, but results are grouped post hoc for analysis by setting.)</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• mixed groups with various geriatric conditions</li> <li>• sub-analysis for participants living at home</li> <li>• age &gt; 65 y (not stated for individual studies)</li> </ul> <p><b>Duration:</b> 8 weeks or more in 81% of trials in community settings.</p> <p><b>Interventions:</b> aimed to provide between 175 kcal (732 kJ) and 1000 kcal (4.2 MJ) and between 10 g and 36 g of protein daily. Most supplements included vitamins and minerals.</p> <p><b>Evaluation of study quality:</b> Scores are available in supplementary material. All trials reported as having low scores. Few studies reported blinding or intention-to-treat analysis.</p> <p><b>Statistical analysis:</b> Peto odds ratios, combining results using fixed-effect models with 95% confidence limits. Calculations of weighted mean difference (WMD) for percentage weight change and percentage mid-arm muscle circumference change using a fixed-effects model.</p>	<p><b>Mortality:</b></p> <ul style="list-style-type: none"> <li>• MA of 8 RCTs (n=596) showed no evidence for a reduction in mortality for people living at home and receiving supplements, regardless of nutritional status (Peto OR=1.05, 95% CI 0.57, 1.95). No statistical heterogeneity.</li> <li>• MA of 4 RCTs (n=357) showed that supplementation in participants undernourished at baseline and no effect on mortality Peto OR=1.03, 95% CI 0.53, 2.02</li> <li>• MA of 4 RCTs (n=261) showed that supplementation in participants nourished at baseline and no effect on mortality Peto OR=1.14, 96% CI 0.22, 5.81</li> </ul> <p><b>Morbidity and other complications:</b></p> <ul style="list-style-type: none"> <li>• MA of 7 RCTs (n=506) showed no effect of supplementation on morbidity or complication in people at home (Peto OR=1.01, 95% CI 0.63, 1.64, I<sup>2</sup>=45.9%). Example morbidities include incomplete wound healing, infective complications, total complications excluding death.</li> </ul> <p><b>Weight change:</b></p> <ul style="list-style-type: none"> <li>• MA of 16 RCTs (n=1070) showed significant increase in weight change in supplemented group. Pooled weighted mean difference for percentage weight change = 2.23, 95% CI 1.70, 2.76; I<sup>2</sup>=14%</li> </ul> <p><b>Mid-arm muscle circumference:</b></p> <ul style="list-style-type: none"> <li>• MA of 6 RCTs (n=343) showed no statistically significant difference for supplemented vs control group. Pooled weighted mean difference for percentage change = 0.68, 95% CI -1.23, 2.60</li> </ul>	<p><b>Authors' conclusions:</b> Few studies reported evidence that suggested any change in mortality, morbidity, or function for those given supplements at home</p> <p>We observe a pattern that suggests a reduction in mortality for those who are undernourished at baseline [...] and are offered higher energy supplements.</p> <p>However, results suggest supplements can improve the nutritional status of older people as evidenced by consistent increased weight gain (which could be fat, muscle or water). Confounding: No detail on confounding or adjustments were provided in the systematic review</p> <p><b>Confounding:</b> No detail on confounding or adjustments were provided in the systematic review.</p> <p><b>Authors' limitations:</b> Many trials were small or had short follow-up times and subject to bias where outcome assessors knew</p>

Study	Methods	Included studies	Results	Limitations/comments
		<p>Heterogeneity assessed via I<sup>2</sup> test (cut-off for statistical significance 50%) and when evidence suggested heterogeneity, random-effects model used. Subgroup analysis for mortality data. Publication bias assessed by funnel plot.</p>		<p>which patients took supplements. Generally, studies considered to be of poor quality.</p> <p>Source of the funding for individual primary studies was unclear, a few studies were co-authored by an employee of the manufacturer of the oral supplement or were fully funded by the manufacturer.</p> <p>In trials of longer duration, major problems of adherence reported (24% to 45 % of participants). These may have been a result of gastrointestinal side effects by participants.</p>



Study	Methods	Included studies	Results	Limitations/comments
<p><b>Nowson et al (2018)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> To review the evidence for an association between dietary factors and cardiovascular disease (CVD) events, cognition and mental health, physical health and frailty.</p> <p><b>Funding source:</b> Financial support was provided by Meat and Livestock, Australia Ltd. (stated that no input into the review).</p> <p><b>Declarations of interest:</b> Dr Nowson reports grants from Nestle Health Services, grants and consultancy fees from Meat and Livestock Australia and Dairy Health Nutrition Consortium outside the submitted work. Also, a member of Australian Division of World Action on Salt and Health</p>	<p><b>Search period:</b> January 1994 to December 2015</p> <p><b>Databases searched:</b> MEDLINE, CINAHL, Scopus and Informit</p> <p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• mean age ≥65 y</li> <li>• living in the community or in residential aged care facilities; findings in care facilities not reported here.</li> </ul> <p><b>Exclusion criteria:</b> case-control studies, studies of serum/plasma concentration of nutrients, alcohol intake, herbal/amino acids/supplement intake, nutritional interventions, and studies of intermediary markers such as hypertension.</p> <p><b>Dietary assessment method:</b></p> <ul style="list-style-type: none"> <li>• FFQ, 24-h recall, diet records or diet history</li> <li>• Mediterranean diet assessed using Mediterranean Diet Score (MeDi score) by Trichopoulou et al.</li> </ul> <p><b>Outcomes</b></p> <ul style="list-style-type: none"> <li>• non-fatal CVD events identified through hospital records, annual examinations, telephone calls or population registries</li> </ul>	<p>19 studies (9 RCT, 6 PCS, 4 XS) (Excluding those studies with cognitive outcomes)</p> <p><b>Study participants</b></p> <ul style="list-style-type: none"> <li>• number, range 192 to 24,417</li> <li>• mean age not stated for individual studies but &gt;65 y given in inclusion criteria</li> <li>• living in the community</li> </ul> <p><b>Evaluation of study quality:</b> Quality of individual XS and PCS assessed using modified Newcastle-Ottawa Scale based on selection, comparability and outcome resulting in low, medium or high rating (1 high, 7 medium, 2 low). Quality of RCTs assessed using <i>Cochrane's collaboration tool for assessing risk of bias</i> (3 RCTs: all unclear/low rating). <i>The Grades of Recommendation, Assessment, Development and Evaluation (GRADE)</i> used to assess quality of evidence-based statements: A, excellent to D, poor.</p> <ul style="list-style-type: none"> <li>• Mediterranean dietary patterns and CVD events: evidence grade B</li> <li>• All others: evidence grade C</li> </ul>	<p><b>Mediterranean diet and non-fatal CVD events</b></p> <p><u>Significant associations</u></p> <p>1 RCT (n=7447, 4.8 y follow-up, Spain; low risk of bias)</p> <ul style="list-style-type: none"> <li>• 28% reduced risk of CVD event with Mediterranean diet supplemented with nuts (0.72, 95% CI 0.54,0.96)</li> <li>• 30% reduced risk of CVD event with Mediterranean diet supplemented with olive oil (0.70, 95% CI 0.54, 0.92)</li> </ul> <p>1 PCS (n=3328, 11.3 y follow-up, UK; medium quality)</p> <ul style="list-style-type: none"> <li>• 34% significantly reduced risk for CHD events with 5-point increase on Elderly Dietary Index (EDI, is modified MeDi score) (no CI or p-value stated)</li> <li>• No significant association found for EDI and CVD events</li> </ul> <p><u>Non-significant associations</u></p> <p>1 PCS (n=2568, 9.0 y follow-up, US, high quality) reported</p> <ul style="list-style-type: none"> <li>• no significant association of MeDi score and ischaemic stroke or myocardial infarction (T1 vs. T3: HR 1.03; 95% CI: 0.61, 1.73; HR 0.65; 95% CI: 0.38, 1.12, respectively)</li> </ul> <p>1 PCS (n=2735, 5.7 y follow-up, Hong Kong, medium quality)</p> <ul style="list-style-type: none"> <li>• no significant association of MeDi score and ischaemic stroke or haemorrhagic stroke (no CI or p-value stated)</li> </ul> <p><b>Frailty</b> <i>Mediterranean diet and frailty</i></p> <ul style="list-style-type: none"> <li>• 3 studies (2 PCS, 1 XS). All showed significant inverse associations:</li> </ul>	<p><b>Authors' conclusions:</b> Good evidence that Mediterranean diet adherence reduced risk of non-fatal cardiovascular events. Some evidence that adherence to a Mediterranean dietary pattern may decrease likelihood of frailty, and modest increase in protein may be associated with decreased risk of frailty.</p> <p>The evidence supports the appropriateness of the recommending aspects of the Mediterranean dietary pattern, particularly the use of olive oil and nuts, inclusion of daily serving of vegetables, [...] to optimise health and function in older people.</p> <p>There may be low-level quality evidence suggesting protein intakes may benefit from being higher than current RNI to assist in reducing frailty.</p> <p><b>Confounding:</b> The authors stated that 'a few' included studies did not adjust for confounders but no specific information was provided.</p>

Study	Methods	Included studies	Results	Limitations/comments
<p>(AWASH) and World Action on Salt and Health (WASH) but does not receive financial support from them.</p>	<ul style="list-style-type: none"> <li>falls and fractures were self-reported or checked via medical records</li> <li>other physical determinants and frailty (muscle mass and strength measured in a variety of ways).</li> </ul>		<ul style="list-style-type: none"> <li>1 PCS (n=690, 6.0 y follow-up; Italy, medium quality) ↑ 4 points MeDi score ↓ 70% odds for developing frailty (no CI or p-value stated)</li> <li>1 PCS (n= 1872, 3.5 y follow-up; Spain, medium quality) ↑ 3 points MeDi score ↓ 41% odds for developing frailty (no CI or p-value stated)</li> <li>1 XS (n=192; Germany, low quality) ↑ 6 points MeDi score ↓ risk of frailty reduced by 20% (no CI or p-value stated)</li> </ul> <p><i>Protein intake and frailty</i></p> <ul style="list-style-type: none"> <li>4 studies (1PCS, 3 XS). All showed significant inverse associations:</li> <li>1 PCS (n=24,417, 3.9 y follow-up; US, medium quality) 20% ↑ in protein (i.e. ≥1.44 g/kg/d) ↓ 35% risk of frailty (no CI or p-value stated)</li> <li>1 XS (n=1345; France, medium quality) Protein intake set at ≥1 g/kg body weight ↓ 59% risk of frailty (no CI or p-value stated)</li> <li>1 XS (n=802; Italy, medium quality) low protein intake (&lt;66 g/d: women, &lt;55 g/d) 2-fold more likely to be frail (no CI or p-value stated)</li> <li>1 XS (n=2108, Japan, low quality) Up to ~35% ↓ likelihood for frailty with increasing quintiles of total protein intake (no CI or p-value stated)</li> <li>1 RCT (n=54, 1 y follow-up, Chile): for the relevant intervention groups, no results were reported</li> </ul> <p><b>Protein intake combined with resistance training and muscle mass and strength (7 RCTs)</b></p> <p><u>Significant associations (3 RCTs)</u></p> <ul style="list-style-type: none"> <li>1 RCT (n=101, 1 y follow-up, Chile; X unclear/low of bias) showed increase hand grip strength for 15g protein supplement + resistance exercise (n=31) compared to only supplementation (n=28), only exercise (n=16) or neither (n=26).</li> </ul>	<p><b>Authors' limitations:</b> XS studies subject to confounding. Difficult to ascertain if those who have a good appetite and are eating a variety of foods (characteristic of Mediterranean diets) are less frail as a result of what they are eating or if their varied dietary pattern is indicative of their better health status. Quality ratings in some studies were low.</p>

Study	Methods	Included studies	Results	Limitations/comments
			<p>Protein supplementation did not affect limb strength or walking capacity.</p> <ul style="list-style-type: none"> <li>• 1 RCT (n=62, 6 months follow-up, Netherlands; low risk of bias) showed greater skeletal muscle mass for 30 g/d milk protein supplementation combined with resistance training compared to resistance training plus placebo. No difference between both groups was found for leg strength or short physical performance battery.</li> <li>• 1 RCT (n=100, 4 months follow-up, Australia; low risk of bias) showed increased lean body mass and muscle strength for increased red meat consumption (2x80 g/d) combined with resistance training compared to resistance training plus rice/pasta placebo.</li> </ul> <p><u>Non- significant associations (4 RCTs)</u></p> <ul style="list-style-type: none"> <li>• 1 RCT (n=75, 6 months follow-up, Canada; low risk of bias) showed no difference in physical performance, muscle strength and lean mass for milk protein supplementation (40g/d) combined with resistance training compared to resistance training plus placebo</li> <li>• 1 RCT (n=62, 9 months follow-up, France; unclear/high risk of bias) showed no difference in leg extension, gait velocity, stair walking or chair rise for 200 kcal nutritional supplement providing 15/d protein combined with exercise compared to exercise plus placebo, or placebo plus memory activity</li> <li>• 1 RCT (n=53, 6 months follow-up, Netherland; unclear/high risk of bias) showed no difference in muscle strengths tests for milk protein supplementation (15 g/d) combined with resistance training compared to resistance training plus placebo</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
			<ul style="list-style-type: none"> <li>• 1 RCT (n=161, 3 months follow-up, Iceland; unclear/high risk of bias) showed no difference in muscle strength for milk protein supplementation (20g/d) combined with resistance training when compared to resistance training plus placebo</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Pedersen &amp; Cederholm (2014)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> To assess the evidence behind the dietary requirement of protein and to assess the health effects of varying protein intake in healthy elderly persons in order to evaluate the evidence for an optimal protein intake</p> <p><b>Funding source &amp; declarations of interest:</b> The authors have not received any funding or benefits from industry or elsewhere to conduct this study.</p>	<p><b>Search period:</b> 2000 to 2011</p> <p><b>Databases searched:</b> PubMed and SweMed</p> <p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• mean age of &gt;65 years in settings similar to the Nordic countries</li> <li>• old adults under ‘free-living conditions’</li> <li>• original articles, MAs and SRs</li> <li>• intervention studies, prospective cohort studies, case-control studies</li> <li>• studies reporting protein intake from foods</li> <li>• English language or any Nordic language</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• observational studies with less than 1-year follow-up</li> <li>• N-balance studies shorter than 14 days</li> <li>• single meal postprandial studies</li> <li>• cross-sectional studies</li> <li>• isolated protein supplements or amino acids</li> <li>• disabled/frail elderly</li> <li>• studies without Caucasians or with Caucasians as a minority group</li> <li>• secondary prevention studies addressing adiposity or obesity</li> </ul>	<p><b>Number of studies:</b> 17 studies (3 RCT, 13 PCS, 1 XS)</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• n= 12 to 2066</li> <li>• mean age not stated, but age ranges given for the majority of studies</li> <li>• old adults under ‘free-living conditions’</li> </ul> <p><b>Evaluation of study quality:</b></p> <ul style="list-style-type: none"> <li>• according to guidelines for the 5th edition of the Nordic Nutrition Recommendations (grade A (highest): n=0; B: n=14; C: n=4)</li> </ul> <p><b>Note:</b> This systematic review also included 5 primary studies on nitrogen balance and 1 study on glomerular filtration rates. As these areas are outside the scope of this position statement these studies’ results are not presented here.</p>	<p><b>No effect sizes were reported in this SR. Study locations (country) and follow-up periods were also not reported.</b></p> <p><b>Muscle mass</b> (3 studies)</p> <p><b>1 RCT</b> (grade B; n=12; age 66 to 79 y; all women) significant positive association for total protein intake; marginal protein intake (0.45 g/kg BW) resulted in a decrease in muscle mass from 17.0kg to 14.7 kg</p> <p><b>1 PCS</b> (grade B; n=2066; age 70 to 79 y)</p> <ul style="list-style-type: none"> <li>• significant positive association for total protein intake; highest quintile of protein intake (≈19% energy) showed 40% lower loss of total lean mass (LM) and non-bone appendicular LM (aLM) compared to lowest quintile (≈11% energy) significant positive association also for animal protein intake; but not vegetable protein intake</li> </ul> <p><b>1 PCS</b> (grade C; n=862; age 75 ± 3 y; all women, 6 years follow-up)</p> <ul style="list-style-type: none"> <li>• significant positive association for total protein intake; top tertile protein intake (1.6 g/kg) had 5% higher LM/aLM compared to the lowest tertile (0.84 g/kg)</li> </ul> <p><b>Bone mineral density (BMD) and content (BMC)</b> (4 studies)</p> <p><b>1 RCT</b> (grade C; n=32; mean age of high protein group 65 ± 10 y; low protein group 72 ± 10 y)</p> <ul style="list-style-type: none"> <li>• No results reported for comparison of both intervention groups</li> <li>• for BMC change from baseline in high protein group: significant positive association reported for BMC and total protein intake</li> </ul>	<p><b>Authors’ conclusions:</b> For muscle mass the evidence is suggestive regarding the association between muscle mass and a total protein intake in the range of 13 to 20% of energy intake.</p> <p>For BMD, the evidence is suggestive for a positive association with total protein intake.</p> <p>The evidence is inconclusive for:</p> <ul style="list-style-type: none"> <li>• bone loss</li> <li>• fracture risk</li> <li>• risk of falls</li> <li>• all-cause mortality</li> </ul> <p><b>Confounding:</b> 21 out of 23 included studies adjusted for confounders. Most included the common confounders such as age, sex and BMI and some also included confounders specific to the study populations such as hospital visits.</p> <p><b>Authors’ limitations:</b> Most of the evidence is from observational studies, which are prone to be affected by</p>

Study	Methods	Included studies	Results	Limitations/comments
	<ul style="list-style-type: none"> <li>• studies on athletes</li> </ul> <p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>• muscle mass and strength</li> <li>• bone mineral content &amp; density</li> <li>• bone loss</li> <li>• fracture risk</li> <li>• all-cause mortality</li> </ul> <p><b>Dietary assessment method:</b></p> <ul style="list-style-type: none"> <li>• mainly food frequency questionnaires</li> </ul>		<p><b>1 PCS</b> (grades B; n = 1077; age 75 ± 3 y, 100% women, follow-up not reported)</p> <ul style="list-style-type: none"> <li>• significant positive association for BMD at the hip and total protein intake (p&lt;0.05 for highest compared to lowest tertile of protein intake)</li> </ul> <p><b>1 PCS</b> (grades C; n = 862; age 75 ± 3 y, 100% women, 5 years of follow-up)</p> <ul style="list-style-type: none"> <li>• significant positive association for BMC and total protein intake; highest tertile protein intake had 5% higher whole-body BMC compared to lowest tertile</li> </ul> <p><b>1 PCS</b> (grades B; n = 572; 71y; 58% Women, 4 years follow-up); study considered total, animal and vegetable protein intake</p> <ul style="list-style-type: none"> <li>• significant positive association (women only) for BMD at the hip and animal protein intake and a significant inverse association (men and women) for vegetable protein</li> </ul> <p><b>Bone loss</b> (5 studies)</p> <p><b>1 RCT</b> (grade B; n=342; age ≥ 65 y RCT intervention was combined calcium and vitamin D supplementation compared to placebo)</p> <ul style="list-style-type: none"> <li>• significant inverse association within the intervention group for total protein intake (but not for animal or vegetable protein) over 3 years with less total body (p=0.046) and femoral neck (p=0.001) BMD loss, when comparing highest to lowest tertile</li> </ul> <p><b>1 PCS</b> (grade B; n=615; age 68 to 91 y)</p> <ul style="list-style-type: none"> <li>• significant inverse association for total protein intake and 4-year bone loss at femur (p=0.02) and spine (p=0.02) when comparing highest to lowest</li> </ul>	<p>underreporting of actual protein intakes.</p>

Study	Methods	Included studies	Results	Limitations/comments
			<p>quartile of protein. Results were also significant for animal, but not vegetable protein intake.</p> <p><b>1 PCS</b> (grade B; n=742, all women; age &gt; 65y)</p> <ul style="list-style-type: none"> <li>• significant positive association for 3.6-year bone loss and animal/vegetable protein ration but not total, animal or vegetable protein intake (no statistics stated).</li> </ul> <p><b>1 PCS</b> (grade B; n=572; age 55 to 92 y)</p> <ul style="list-style-type: none"> <li>• for men and women combined no significant association for total, animal or vegetable protein intake and 4-year bone loss</li> </ul> <p><b>1 PCS</b> (grade C; n=92, all women; age 55 to 92 y)</p> <ul style="list-style-type: none"> <li>• NS association for 3-year bone loss and total protein intake.</li> </ul> <p><b>Fracture risk</b> (3 studies)</p> <ul style="list-style-type: none"> <li>• <b>1 PCS</b> (grade B; n = 946; mean age ca. 75y) showed significant inverse association for total protein when comparing upper 3 to lowest quartile (HR 0.63, 95% CI: 0.41 to 0.97)</li> <li>• <b>1 PCS</b> (grades C; n = 1035; age ≥ 65) showed significant positive association for animal protein, and ratio of animal/vegetable protein (no statistics stated) but when adjusted for bone mineral density it became insignificant</li> <li>• <b>1 case-control study</b> (grade B; 1167 cases &amp; 1334 controls; 2 age groups: 50 to 69 y &amp; 70 to 89 y) <ul style="list-style-type: none"> <li>▪ in age group 50 to 69 y significant inverse association for total/animal/vegetable (Q4 v Q1 OR 0.35, 95%CI 0.21 to 0.59; 0.43, 0.22 to 0.82; 0.52, 0.27 to 0.997 respectively)</li> <li>▪ in age group 70 to 89 y no significant association</li> </ul> </li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
			<p><b>Risk of falls</b> (1 study)</p> <p><b>1 PCS</b> (grade C; n = 807; age 75 ± 5 y, 12 months follow-up)</p> <ul style="list-style-type: none"> <li>• no significant association for total/animal/vegetable protein</li> </ul>	



Study	Methods	Included studies	Results	Limitations/comments
<p><b>Roman-Vinas and Serra-Majem (2018)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> To review the relationship between Mediterranean diet score (MeDi score) and healthy ageing measured by physical function.</p> <p><b>Funding source:</b> None stated</p> <p><b>Declarations of interest:</b> Statement of no conflict of interest</p>	<p><b>Search period:</b> September 2013 to February 2018</p> <p><b>Databases searched:</b> Medline</p> <p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• PCS or XS</li> <li>• age &gt;65 y</li> <li>• measurements of Mediterranean dietary pattern, health status, functional capacity or QoL;</li> <li>• the review does not specify any requirement regarding participants' living conditions, but the majority of included primary studies were stated as including community dwelling participants</li> </ul> <p><b>Exclusion criteria:</b> publications without abstracts, studies of food or nutrients alone, studies on the effect on gene expression, and studies on individuals &lt;65 y.</p> <p><b>Dietary assessment method:</b></p> <ul style="list-style-type: none"> <li>• 24-h recall, FFQ, validated diet history (1 study gave no details of methodology).</li> <li>• Mediterranean diet assessed using different scales (for example, MeDi score by Trichopoulou, a-MeDi by Fung)</li> </ul>	<p><b>Number of studies:</b> 2 PCS, 4 XS</p> <p><b>Primary outcome:</b> physical function</p> <p><b>Study participants</b></p> <ul style="list-style-type: none"> <li>• number, range 192 to 5789</li> <li>• mean age stated for individual studies, inclusion criteria &gt;65 y.</li> <li>• all community dwelling</li> </ul> <p><b>Evaluation of study quality:</b></p> <ul style="list-style-type: none"> <li>• Newcastle-Ottawa Scale</li> <li>• All 5 studies of fair quality</li> </ul>	<p><b>1 PCS</b>, Senior-ENRICA (n=1630, follow-up 3.5 y, mean age 68 y, Spain); agility and mobility assessed based on Rosow and Breslau scale; overall physical function assessed based on SF12.</p> <ul style="list-style-type: none"> <li>• no association for MeDi score (Trichopoulou) and physical function</li> <li>• significant association of MEDAS (highest vs lowest tertile) and: <ul style="list-style-type: none"> <li>• impairment in agility (OR = 0.70, 95% CI 0.49 to 0.98)</li> <li>• impairment in mobility (OR = 0.62, 95% CI 0.42 to 0.92)</li> <li>• impairment in overall physical functioning (OR = 0.61, 95% CI 0.45 to 0.81)</li> </ul> </li> </ul> <p><b>1 PCS</b> (includes the 2 cohorts UAM and Senior-ENRICA)</p> <p><b>(i) UAM</b> (n=2376, 2 y follow-up, mean age 70 y, Spain); dietary assessment through non-validated Mediterranean dietary pattern index; physical function assessed through physical component summary of SF36</p> <ul style="list-style-type: none"> <li>• no associations for Mediterranean dietary pattern index (highest vs lowest tertile) and physical function</li> </ul> <p><b>(ii) Senior-ENRICA</b> (n=1911, 3y follow-up, mean age 68 y, Spain); dietary assessment MeDi score and MEDAS; physical function assessed through physical component summary of SF12</p> <ul style="list-style-type: none"> <li>• no association for MeDi score (highest vs lowest tertile) and physical function</li> <li>• significant association for MEDAS (highest vs lowest tertile) and increased physical function (beta coefficient = 1.34, 95% CI 0.21 to 2.47)</li> </ul>	<p><b>Authors' conclusions:</b> Higher adherence to Mediterranean dietary pattern can help maintain a higher physical function or strength performance or quality of life.</p> <p><b>Confounding:</b> The authors mention that some of the included studies were adjusted for confounding, but no further detail was provided.</p> <p><b>Authors' limitations:</b> Study results not always comparable as outcomes measured different variables under category of physical function/healthy ageing. Mediterranean diets also evaluated differently for example wholegrains separated in some studies but included with refined CHOs in others. Some studies were from Mediterranean countries and had much higher intakes of fruit and vegetables than US studies at baseline.</p>

Study	Methods	Included studies	Results	Limitations/comments
	<p><b>Primary Outcomes:</b></p> <ul style="list-style-type: none"> <li>• Functional capacity or QoL by questionnaire (SF12/36) or survey (sometimes self-reported).</li> <li>• Physical health measured by hand-grip strength, knee extensor strength and walking tests; Short Physical Performance Battery (SPPB).</li> <li>• Katz Scale of Activities of Daily Living (ADL) score ranging from 5 (no functional limitations) to 15 (severe limitations)</li> </ul>		<p><b>1 XS</b> (n=192; mean age = 83.4 y, Germany); Highest vs lowest quartile of MeDi score showed significant inverse association for:</p> <ul style="list-style-type: none"> <li>• Frailty (OR=0.19, 95% CI 0.05 to 0.82)</li> <li>• Low grip strength (OR=0.44, 95% CI 0.18 to 1.09)</li> <li>• Low walking speed (OR=0.29, 95% CI 0.09 to 1.00)</li> </ul> <p><b>1 XS</b>, NHANES (n=2791, mean age = 71.19 y, USA); MeDi score tertiles (trend) significantly associated with:</p> <ul style="list-style-type: none"> <li>• physical function score (p for trend = 0.001)</li> <li>• muscle strength (p for trend = 0.002)</li> <li>• walking speed (p for trend &lt; 0.001)</li> </ul> <p>Other statistical comparisons:</p> <ul style="list-style-type: none"> <li>• MeDi score as continuous variable: each 1-point increase in score increased odds of faster walking by 6% (OR=0.94, CI 95% 0.88-0.99)</li> <li>• Adjusted logistic regression for MeDi score did not predict slow walking speed (T1 vs T3: OR=0.75, CI 95% 0.54, 1.05);</li> </ul> <p><b>1 XS</b>, MAHBAT ZAHAV (n=1786, mean age 74.9 y, Israel); physical function assessed based on Katz Scale of Activities of Daily Living (ADL)</p> <ul style="list-style-type: none"> <li>• MeDi score tertiles (trend) significantly associated with better physical function (ADL Scale) (p for trend &lt;0.001)</li> <li>• Mediterranean diet adherence (highest vs lowest MeDi score tertile) was associated with fewer disabilities (ADL scale) (OR =0.51, CI 95% 0.28 to 0.93)</li> <li>• Each increase in 1 point of the MeDi score ↓ risk for disability (above the median) by 11% (OR = 0.89, CI 95% 0.81 to 0.98)</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
			<p><b>1 XS</b>, TRELONG (n=304, population likely to be mostly community dwelling, mean age = 86.3 y, Italy); dietary assessment through Mediterranean-style dietary pattern score (MSDPS) by Rumawas; physical function assessed through Short Physical Performance Battery (SPPB) and hand grip strength</p> <ul style="list-style-type: none"> <li>• Mediterranean dietary pattern (highest vs lowest MSDPS quartile) associated with increased physical function in SPPB (p&lt;0.05)</li> <li>• Mediterranean dietary pattern (highest vs lowest MSDPS quartile) not associated with hand grip strength.</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Rosendahl-Riise et al (2017)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> To investigate the association of vitamin D supplementation (with and without calcium) and measurements of muscle strength and mobility</p> <p><b>Funding source:</b> Funding support was provided by the Norwegian Seafood and Research Fund (FHF).</p> <p><b>Declarations of interest:</b> The authors declare that they have no conflicts of interest.</p>	<p><b>Search period:</b> up to 13 April 2016</p> <p><b>Databases searched:</b> PubMed, Embase, Medline, Web of Science and the Cochrane Library</p> <p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• RCTs</li> <li>• Community-dwelling older adults &gt;65 years of age;</li> <li>• Vitamin D supplementation – all forms and all doses, with or without calcium supplements or dietary advice</li> <li>• measures of muscle strength and mobility</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• none stated</li> </ul> <p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>• muscle strength; hand grip strength (HGS) assessed in MA</li> <li>• mobility; timed-up-and-go test (TUG) assessed in MA</li> </ul>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• 15 RCTs included in SR</li> <li>• 10 RCTs included in MA</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• mean age ranged from 61.5y to 81y</li> <li>• 2 RCTs had mean age &lt; 65 years; results for these 2 RCTs are not reported here; however, 1 RCT (mean age 61.5 years) was included in MA of hand grip strength</li> </ul> <p><b>Duration:</b></p> <ul style="list-style-type: none"> <li>• 4 months to 20 months</li> </ul> <p><b>Interventions:</b></p> <ul style="list-style-type: none"> <li>• daily D<sub>3</sub> oral (7 RCTs): 400 to 4000 IU/day</li> <li>• bolus D<sub>3</sub> oral (2 RCTs): 8400 IU/week; 150,000 IU every 3 months</li> <li>• bolus D<sub>2</sub> injection (1 RCT): 600,000 IU x 1 injection</li> <li>• 1,25-dihydroxyvitamin D<sub>3</sub> (2 RCTs): 0.25 µg/day oral; 0.5 µg/day oral</li> <li>• 25-hydroxyvitamin D<sub>3</sub> (1 RCT): 20 µg/day or 140 µg/week oral</li> <li>• alfacalcidol (1 RCT): 0.5 mg (20 000 IU)/day oral</li> </ul> <p><b>Evaluation of study quality:</b> CONSORT statement checklist for assessing quality of randomised clinical trials</p> <p><b>Statistical analysis:</b></p> <ul style="list-style-type: none"> <li>• MAs: random effects model</li> </ul>	<p><b>Meta-analyses:</b></p> <p><b>Muscle strength (hand grip strength)</b></p> <ul style="list-style-type: none"> <li>• MA of 7 RCTs (n= 1406; follow-up 24 weeks to 12 months); MA included 1 RCT (n=305) with mean age 61.5 years (MA weight 17.9 %)</li> <li>• baseline 25-hydroxyvitamin D levels ranged from 32 to 82 nmol/L</li> <li>• Interventions: <ul style="list-style-type: none"> <li>◦ vitamin D<sub>3</sub> (5 RCTs): 3 RCTs 400 IU or 1000 IU/day vs placebo; 1 RCT 2000 IU/day vs 400 IU/day; 1 RCT 150,000 IU/3 months vs placebo</li> <li>◦ 1,25-dihydroxyvitamin D<sub>3</sub> (2 RCTs): 1 RCT 0.5 µg/day vs placebo; 1 RCT 0.25 µg/day plus 125 IU D<sub>3</sub>/day vs 125 IU D<sub>3</sub>/day</li> </ul> </li> <li>• no significant change in hand grip strength MD 0.2 kg (95% CI -0.3 to 0.7 kg]</li> <li>• In a sensitivity analysis, there was a significant effect of vitamin D supplements on hand grip strength when the 3 RCTs that included participants deficient in vitamin D were removed (MD 0.40, 95% CI 0.37 to 0.43; 4 RCTs, 930 participants).</li> </ul> <p><b>Mobility (TUG)</b></p> <ul style="list-style-type: none"> <li>• MA of 5 RCTs (n= 1260; follow-up 10 week to 20 months)</li> <li>• baseline 25-hydroxyvitamin D levels ranged from 44 to 67 nmol/L</li> <li>• Interventions (all compared to placebo): <ul style="list-style-type: none"> <li>◦ vitamin D<sub>3</sub>: 4 RCTs 800 IU/day; 1000 IU/day; 2000 IU/day; and 150,000 IU/3 months</li> <li>◦ vitamin D<sub>2</sub>: 1 RCT 1000 IU/day</li> </ul> </li> <li>• significant decrease in timed-up-and-go-test MD -0.31 s (95% CI -0.51 to -0.10 s)</li> </ul>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• no improvement in muscle strength after administration of vitamin D with or without calcium supplements</li> <li>• small but significant improvement of mobility</li> </ul> <p><b>Confounding:</b></p> <ul style="list-style-type: none"> <li>• The authors graded the included evidence using CONSORT. Several RCTs scored well for additional/subgroup/adjusted analysis, but no more specific information was provided on confounding factors in individual studies.</li> </ul> <p><b>Authors' limitations:</b></p> <ul style="list-style-type: none"> <li>• the small number of studies available for the meta-analysis, mainly as a result of heterogeneity of the measurements used</li> <li>• the variation in study populations, with a wide range of comorbidities</li> <li>• heterogeneity between studies that could not be resolved by subgroup analyses</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
		<ul style="list-style-type: none"> <li>Subgroup analysis to explore possible reasons for observed heterogeneity, subgroup analysis was conducted with predefined study characteristics: baseline vitamin D status, oral administration of the supplement, daily dose of vitamin D, placebo group, supplementation with vitamin D2 or D3, and advice on calcium supplementation</li> </ul>	<p><b>Systematic Review:</b></p> <ul style="list-style-type: none"> <li>8 RCTs (n = 21 to 689; mean age 73 to 81 years; intervention period 16 weeks to 9 months; baseline 25-hydroxyvitamin D levels 25 to 83 nmol/L) found that supplementation with vitamin D and/or calcium did not have a beneficial effect on mobility and/or muscle strength</li> <li>5 RCTs (n = 26 to 302; mean age 69 to 77 years; intervention period 10 weeks to 12 months, baseline 25-hydroxyvitamin D levels 44 to 70 nmol/L) reported that supplementation with vitamin D and/or calcium resulted in improvements in mobility and/or muscle strength. Of these 5 RCTs, 1 RCT reported improvements only in those with lowest physical permeance measures at baseline and 1 RCT reported improvements only in those with low 25-hydroxyvitamin D<sub>3</sub> at baseline.</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Ruxton et al (2016)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> To investigate the association between micronutrients (such as fatty acids and various vitamins) and healthy ageing markers.</p> <p><b>Funding source:</b> Funding for the review was provided by the Health Supplements Information Service (<a href="http://www.hsis.org">www.hsis.org</a>) which is supported by an unrestricted grant from the Proprietary Association of Great Britain.</p> <p><b>Declarations of interest:</b> The content of this paper reflects the opinion of the authors who declare the above conflict of interest.</p>	<p><b>Search period:</b> from 2005 through February 2015</p> <p><b>Databases searched:</b> PubMed (MEDLINE)</p> <p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• RCTs published in English</li> <li>• older adults &gt;50 y</li> <li>• participants free from acute conditions at baseline</li> <li>• specification of intervention dose /level</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• pharmacological interventions;</li> <li>• exploratory or pilot trial</li> <li>• intervention pre- or post-operative</li> </ul> <p><b>Outcomes</b> Markers of healthy ageing</p> <ul style="list-style-type: none"> <li>• Immune health</li> <li>• Protein synthesis</li> <li>• Muscle mass</li> <li>• Metabolic factors</li> <li>• Vitamin status</li> <li>• Mood</li> </ul>	<p><b>Number of studies:</b> 9 RCTs (SR includes 34 RCTs in total, most omitted owing to not meeting criteria for different reasons, e.g. cognitive outcomes, age of study group &lt;65 y etc.)</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• age, mostly &gt;60 y (1 RCT with 55 to 70 y; in 1 RCT, age is not adequately described but reference to post-menopausal women and healthy men)</li> <li>• setting not stated</li> <li>• study location not stated</li> </ul> <p><b>Evaluation of study quality:</b> Jadad scale for reporting RCTs (quality ranked between 1 and 5 with higher scores indicating better quality)</p>	<p><b>Immune health (5 RCTs)</b></p> <ul style="list-style-type: none"> <li>• 1 RCT, n=51 (age 65.4 y) 14 g/d of ALA or placebo combined with resistance training for 12 weeks: IL6 ↓ in the supplemented arm indicating ↓ inflammation (unclear if significant, no p-value or effect size stated) (study quality 5)</li> <li>• 1 RCT, n=62 (age 53 to 70 y) placebo (corn oil) or oil providing 1.35, 2.7, or 4.05 g/d EPA per day for 12 weeks. lower neutrophil burst at higher EPA intake compared with younger adults (unclear if significant, no p-value or effect size stated) (study quality 3)</li> <li>• 1 RCT, n=202 (age ≥64 y), placebo or 5, 10, 15 mg/d of D<sub>3</sub> for 22 weeks: ↑ in 25(OH)D<sub>3</sub> but no significant effect on cytokine production (no effect size stated) (study quality 4)</li> <li>• 1 RCT, n=147 (age 55 to 70 y) 15 mg or 30 mg Zn/d for 6 months. 15 mg supplement may help to maintain T helper/cytotoxic T lymphocyte ratio &amp; enhance adaptive immunity. High (30 mg) dose may affect B cell counts which may exacerbate age -related immunological changes (unclear if significant, no p-value or effect size stated) (study quality 3)</li> <li>• 1 RCT, n=95 (age 60 to 75 y) 2-month, double-blind RCT. Supplement containing moderate amounts of retinol, b-carotene, a-tocopherol, ascorbic acid and selenium or placebo. Reduction of 2.3% in intrinsic apoptosis of lymphocytes was found in the supp. groups of elderly people compared to control (P &lt; 0.001), UV-induced apoptosis of human lymphocytes was attenuated by micronutrient supplementation (unclear if significant, no p-value or effect size stated) (study quality 5)</li> </ul>	<p><b>Authors' conclusions:</b> Out of the total of 34 RCTs studied only a few RCTs reported statistically significant health benefits.</p> <p>Vitamin, mineral and fatty acid intakes are in need of improvement to help elderly populations achieve optimal diet quality and support healthy ageing.</p> <p><b>Confounding:</b> No detail on confounding or adjustments were provided in the systematic review.</p> <p><b>Authors' limitations:</b> Full details of methods are not always reported in each paper (such as methods of blinding or compliance rates) contributing to lower quality study scores (≤3).</p>

			<p><b>Protein synthesis (1 RCTs)</b></p> <ul style="list-style-type: none"> <li>• 1 RCT, n=16 (age ≥65 y, 8-w duration, received: 4 g/d containing 1.86 g EPA, and 1.50 g DHA or an equal amount of corn oil (placebo). Omega-3 fatty acid supplementation augmented the hyperaminoacidaemia-hyperinsulinaemia-induced ↑ in the rate of muscle protein synthesis (p &lt; 0.01) (no effect size stated) (study quality 2)</li> </ul> <p><b>Muscle mass (1 RCTs)</b></p> <ul style="list-style-type: none"> <li>• 1 RCT, n=51 (age 65.4 y, 12 w duration, double-blind); ALA in flax oil (~14 g/d) or placebo + resistance training (3 days a week). ALA supplementation led to a significantly greater increase in knee flexor muscle thickness in males (p &lt; 0.05) (no effect size stated) (study quality 5)</li> </ul> <p><b>Coronary artery calcification (1 RCTs)</b></p> <ul style="list-style-type: none"> <li>• 1 RCT, n=388 (age ns; healthy men and post-menopausal women; 3 y double-blind RCT). Allocated to receive: 500 microg/d phylloquinone, or a multivitamin alone. In a subgroup of participants those who were ≥85% adherent to supp. had less coronary artery calcification (CAC) progression in the phylloquinone group than the control (p = 0.03) (no effect size stated). Of those with pre-existing CAC, those receiving phylloquinone had 6% less progression than did those who received the multivitamin alone (p = 0.04) (study quality 4)</li> </ul> <p><b>Vitamin status (1 RCTs)</b></p> <ul style="list-style-type: none"> <li>• 1 RCT, n=387, healthy middle-aged adults (55–70 years) and older adults(70–85 years), 6-months RCT. Allocated to receive 15 or 30 mg/d Zn or placebo for 6 m. Plasma vitamin A levels ↑ significantly with zinc dose and period of treatment, particularly at 6 months (for 15 mg/d</li> </ul>	
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Study	Methods	Included studies	Results	Limitations/comments
			<p>Zn; <math>p &lt; 0.05</math> for 15 mg/d; <math>p &lt; 0.0001</math> for 30 mg/d (study quality 5)</p> <p><b>Quality of life/mood (1 RCTs)</b></p> <ul style="list-style-type: none"> <li>• 1 RCT, n=182 (no age stated 16-w duration double-blind) Intervention 1-daily multivitamin; control not stated. Qualitative analysis showed that multivitamin use <math>\uparrow</math> energy levels (<math>p = 0.022</math>) (especially for females) and enhanced mood (<math>p = 0.027</math>) (no effect sizes stated) (study quality 5))</li> </ul>	



Study	Methods	Included studies	Results	Limitations/comments
<p><b>Silva et al (2018)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> Review the association between Mediterranean dietary patterns and musculoskeletal function</p> <p><b>Funding source</b> Stated: None</p> <p><b>Declarations of interest</b> Stated: There are no conflicts of interest.</p>	<p><b>Search:</b> carried out on 8 September 2016 and 28 November 2016 (eligible studies ranged from 2011 to 2017)</p> <p><b>Databases searched:</b> MEDLINE, Embase, Web of Science, Scopus, CINAHL, LILACS, SciELO; further search for grey literature using Google Scholar and ProQuest</p> <p><b>Inclusion criteria:</b> observational studies investigating Mediterranean dietary patterns and frailty, functional disability or sarcopenia in community dwelling individuals aged <math>\geq 60</math> y; Mediterranean dietary pattern defined a priori comparing high score with low score, no language restriction, no period restriction</p> <p><b>Exclusion criteria:</b> diseased patients, or with low physical function at baseline; institutionalized patients, patients with inadequate caloric consumption, evaluation of dietary patterns derived a posteriori; reviews, letters and editorials.</p> <p><b>Mediterranean diet assessment method:</b> scales or scores</p>	<p><b>Number of studies:</b> 11 (8 PCS, 3 XS) 1 study omitted here because mean age=48 y.</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• n=16,999</li> <li>• mean age range: 68 to 84 years</li> <li>• living in the community</li> <li>• follow-up: 3.5 to 9 years</li> <li>• countries: UK, 2 x France, 2 x Spain, Germany, Italy, Israel, USA, 2 x China</li> </ul> <p><b>Statistical analysis:</b> Random effects meta-analysis using DerSimonian and Laird method; heterogeneity tested using chi-squared test with a p value of <math>p &lt; 0.10</math> (adopted because chi-square has low power in MA with few studies). The most addressed confounding variables: age, sex, BMI, energy intake, educational level, chronic diseases/comorbidities, depression, alcohol, smoking status, and physical activity.</p> <p><b>Evaluation of study quality:</b> Use of Joanna Briggs Institute tools; studies included assessed as having a low risk of bias</p>	<p><b>Mediterranean dietary patterns and frailty (5 studies)</b> MA of 4 PCS (n=5789; mean age 68 to 82 y; follow-up ns; France, Italy, Spain, China)</p> <ul style="list-style-type: none"> <li>• higher Mediterranean diet adherence compared with lowest Mediterranean diet adherence associated with reduced risk of frailty OR=0.42, 95% CI 0.28 to 0.65, <math>I^2=24.9\%</math>, <math>p=0.262</math></li> </ul> <p>1 XS (n=192, mean age 84y, Germany)</p> <ul style="list-style-type: none"> <li>• inverse association between higher Mediterranean diet adherence and frailty OR=0.19, 95% CI 0.05 to 0.82</li> </ul> <p><b>Functional disability (5 studies)</b> MA of 3 PCS (n=3493; mean age 68 to 76 y; follow-up ns; Germany, Spain, country ns for 1 study)</p> <ul style="list-style-type: none"> <li>• higher Mediterranean diet adherence inversely associated with functional disability OR=0.75, 95% CI 0.61 to 0.93, <math>I^2=0.0\%</math>, <math>p=0.78</math></li> </ul> <p>1 XS (n=1786; mean age 75 y; Israel)</p> <ul style="list-style-type: none"> <li>• higher Mediterranean diet adherence inversely associated with disabilities OR=0.51, 95% CI 0.27 to 0.93</li> </ul> <p>1 XS (n=2791; mean age 71 y; USA)</p> <ul style="list-style-type: none"> <li>• higher Mediterranean diet adherence not associated with disabilities OR 0.75, 95% CI 0.54 to 1.04</li> </ul> <p><b>Sarcopenia (2 study)</b> 1 PCS (n=2948; mean age 74 y; follow-up ns; China)</p> <ul style="list-style-type: none"> <li>• indicated no association of Mediterranean diet adherence and sarcopenia OR 0.80 (0.53 – 1.22)</li> </ul>	<p><b>Authors' conclusions:</b> Both cohort and cross-sectional data show that a higher adherence to a Mediterranean dietary pattern is associated with a decreased probability for developing frailty and functional disability. Longitudinal data failed to show an association between adherence to a Mediterranean diet and the risk of sarcopenia in a Chinese cohort study. This result may be explained due to lower consumption of olive oil, nuts and wine in the population (compared to those in a Mediterranean region).</p> <p><b>Confounding:</b> All included studies addressed confounding, including variables age, sex, BMI, energy intake, educational level, chronic diseases/ comorbidities, depression, alcohol, smoking status, and physical activity.</p> <p><b>Authors' limitations:</b> MA performed from pooled ORs from adjusted measures. No meta-regression or other</p>

Study	Methods	Included studies	Results	Limitations/comments
	<p>defined a priori, most commonly MeDi score (Trichopoulou et al.); Fung et al. adapted Greek version of MeDi score to be applied to non-Mediterranean country; also used MeDi score using dietary consumption data</p> <p><b>Outcomes measured:</b></p> <ul style="list-style-type: none"> <li>• Frailty – frailty phenotype by Fried et al. (2001); also 1 study used modified criteria by Morley et al. (2012)</li> <li>• Functional disability – Activities of Daily Living scale (ADL scale); Instrumental ADL (IADL); Short Physical Performance Battery, Physical Function questionnaire; Rosow-Breslau scale, SP-12</li> <li>• Sarcopenia – measuring sarcopenic parameters such as muscle mass (using dual-energy x ray) or appendicular lean muscle mass, muscle strength (grip strength) and physical performance; Asian Working Group for Sarcopenia’s definition</li> </ul>			<p>sensitivity analyses because studies &lt;10.</p> <p>Measures of heterogeneity did not use length of time participants were in the study.</p>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Stanaway et al (2017)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> Association between dietary nitrate supplementation and physiological performance and health-based parameters such as cardiovascular (CV) health.</p> <p><b>Funding source:</b> None stated</p> <p><b>Declarations of interest:</b> Stated: authors declare no conflict of interest</p>	<p><b>Search period:</b> to May 2017</p> <p><b>Databases searched:</b> PubMed, Ovid, Science Direct, and Web of Science</p> <p><b>Inclusion criteria:</b> primary research in peer-reviewed journals, in English, using a randomised, crossover, placebo-controlled design; aged 50+, healthy or mixed health study group, intervention of inorganic dietary nitrate such as beetroot juice.</p> <p><b>Exclusion criteria:</b> studies using multiple supplementation protocols involving other supplements in addition to nitrate had to show a clear separation in the effect of nitrates</p> <p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>• Physiological performance,</li> <li>• CV health-based parameters such as blood pressure</li> </ul>	<p><b>Number of studies:</b> 12 RCTs</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• randomised, crossover involving a placebo and nitrate treatment arm</li> <li>• age range 59.2 to 74.7 y</li> <li>• n=175 (total across all studies)</li> <li>• 5 RCTs with healthy participants</li> <li>• 6 RCTs with mixed or participants diagnosed with disease such as diabetes, peripheral arterial disease (PAD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD) or with risk factors for cardiovascular disease</li> <li>• 6 RCTs double-blinded, 1 RCT single-blinded, 4 open-label</li> <li>• setting not stated</li> </ul> <p><b>Intervention:</b></p> <ul style="list-style-type: none"> <li>• most RCTs used inorganic nitrate in the form of beetroot juice</li> <li>• 2 studies used beetroot gel and a high nitrate diet</li> <li>• Placebo used nitrate-depleted beetroot juice or low nitrate diet, 1 RCT used a nitrate-depleted gel</li> <li>• dose range 6.1 to 12.4 mmol/d</li> <li>• supplementation period varied from acute (2-4h before testing) to chronic (14 days)</li> </ul> <p><b>Evaluation of study quality:</b> risk of bias assessed using a bias hierarchy checklist described by Wright et al. including 4 key areas: selection, performance, detection and</p>	<p>Effect sizes or p-values were mostly not reported in this review.</p> <p>Dietary nitrate supplementation resulted in a significant increase in all NO indices (plasma nitrate and nitrite levels), in all studies.</p> <p><b>Physiological performance:</b> 5 RCTs</p> <ul style="list-style-type: none"> <li>• 1 RCT (n=15; age 69.6 y; COPD patients; acute supplementation 2.5h prior) showed significantly improved time to exhaustion during submaximal cycling test (p=0.031)</li> <li>• 1 RCT (n=20; age 69 y; heart failure patients; 7d supplementation) showed significantly improved time to exhaustion during submaximal cycling test (p=0.02)</li> <li>• 1 RCT (n=8; age 67 y; PAD patients; acute supplementation 3h prior) showed significantly improved walking duration before onset of pain (18%) and maximum walking time (17%)</li> <li>• 1 RCT (n=12; mean age 63.5 y; healthy adults; 3d supplementation) showed significantly reduced VO<sub>2</sub> response time from rest to walking (p&lt;0.05) following 3 days of supplementation. No significant change in 6m walking test</li> <li>• 1 RCT (n=19; mean age 64.7 y; healthy adults; 7d supplementation) showed no significant effect on O<sub>2</sub> consumption, 10-m walking test, hand-grip strength, up-and-go test, or repeat chair rise test</li> </ul> <p><b>Cardiovascular outcomes:</b> <u>Blood pressure (10 RCTs)</u> 5 RCTs resulted in a significant decrease in systolic blood pressure (SBP). Of these 5 RCTs, 4 also showed a decrease in diastolic blood pressure (DBP):</p>	<p><b>Authors' conclusions:</b> Dietary nitrate supplementation (NO<sub>3</sub><sup>-</sup>) has positive effects on physiological performance and there is some evidence indicating benefits to cardiovascular health.</p> <p>Specifically, for physiological performance supplementation may prolong time to exhaustion and increase VO<sub>2</sub> response time. Some evidence suggestive of positive outcomes for CV health (reduced blood pressure and mean arterial pressure).</p> <p><b>Confounding:</b> No detail on confounding or adjustments were provided in the systematic review.</p> <p><b>Authors' limitations:</b> Disparity in findings may be a result of variances between study designs, such as differing time periods between intervention and physiological performance test having a possible effect on absorption.</p>

Study	Methods	Included studies	Results	Limitations/comments
		<p>attrition bias. All studies considered to be good to excellent (1 reviewer).</p>	<ul style="list-style-type: none"> <li>• 1 RCT (n=15; age 69.6 y; COPD patients; acute supplementation 2.5h prior) showed significant decrease in SBP and DBP</li> <li>• 1 RCT (n=20; age 69 y; heart failure patients; 7d supplementation) showed significant decrease in SBP (DBP not reported)</li> <li>• 1 RCT (n=8; age 67 y; PAD patients; acute supplementation 3h prior) showed significant decrease in SBP and DBP</li> <li>• 1 RCT (n=12; mean age 63.5 y; healthy adults; 3d supplementation) showed significant decrease in SBP and DBP</li> <li>• 1 RCT (n=17; mean age 72 y; CKD patients; acute supplementation 4h prior) showed significant decrease in SBP and DBP</li> </ul> <p>5 RCTs reported no change in blood pressure:</p> <ul style="list-style-type: none"> <li>• 1 RCT (n=19; mean age 64.7 y; healthy adults; 7d supplementation) showed no significant change in blood pressure</li> <li>• 1 RCT (n=20; mean age 70.5 y; adults with risk factor for CVD; acute supplementation 2h prior) showed no significant change in SBP or DBP</li> <li>• c showed no significant change in blood pressure</li> <li>• 1 RCT (n=8; mean age 72.5 y; healthy adults; 3d supplementation) showed no significant change in blood pressure</li> <li>• 1 RCT (n=15; mean age 59.2 y; healthy adults; acute supplementation (lead time ns)) showed no significant change in blood pressure</li> </ul> <p><u>Mean arterial pressure (MAP) (2 RCTs)</u></p> <ul style="list-style-type: none"> <li>• 1 RCT (n=27; mean age 67.2 y; diabetes patients; 14 d supplementation) showed no change in MAP (p = 0.012)</li> </ul>	<p>Small sample sizes and few studies investigating some outcome variables.</p> <p>In addition, health status of adults differed between studies (notably some studies showing improvement in CV health targeted a diseased population such as heart failure patients).</p>

Study	Methods	Included studies	Results	Limitations/comments
			<ul style="list-style-type: none"> <li>• 1 RCT (n=17; mean age 72 y; CKD patients; acute supplementation 4h prior) showed a significant decrease in MAP (p=0.012)</li> </ul> <p><u>Endothelial function 3 RCTs</u></p> <p>2 RCTs showed significant improvements</p> <ul style="list-style-type: none"> <li>• 1 RCT (n=8; age 67 y; PAD patients; acute supplementation 3h prior) showed increased blood flow to working muscles, using near infrared spectroscopy</li> <li>• 1 RCT (n=20; mean age 70.5 y; adults with risk factor for CVD; acute supplementation 2h prior) showed improved brachial flow-mediated dilation (FMD) (77%), blood flow velocity (BFV) (31%) and reactive hyperaemia (RH) (18%).</li> </ul> <p>1 RCT showed no improvement</p> <ul style="list-style-type: none"> <li>• 1 RCT (n=27; mean age 67.2 y; diabetes patients; 14 d supplementation) showed no significant effect on FMD or Doppler perfusion</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Ten Haaf et al (2018)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> Review the effect of protein supplementation and physical performance (in non-frail older adults specifically)</p> <p><b>Funding source:</b> Stated: no funding received for this study</p> <p><b>Declarations of interest:</b> Stated: none of the authors reported a conflict of interest related to the study</p>	<p><b>Search period:</b> Up to 15 May 2018</p> <p><b>Databases searched:</b> MEDLINE, Embase, Web of Science</p> <p><b>Inclusion criteria:</b> average age of <math>\geq 50</math> y, non-frail and community dwelling participants, RCTs with minimum duration of 4 weeks, protein intervention</p> <p><b>Exclusion criteria:</b> participants with diseases such as cancer, cardiovascular disease, lung disease, etc., assisted-living or immobilized participants, interventions of restricted energy intake or nonoral intake, non-English, conference proceedings, and articles with abstracts only or study protocols only</p> <p><b>Outcomes</b></p> <ul style="list-style-type: none"> <li>Lean body mass (dual energy x-ray absorptiometry, hydrostatic weighing, whole-body air plethysmography or hydro densitometry)</li> <li>Muscle thigh cross-sectional area (computerised tomography or MRI)</li> <li>Muscle strength (isometric upper body and lower extremity test)</li> </ul>	<p><b>Number of studies:</b> 11 RCTs (Further primary studies included exercise as part of intervention but are omitted here.)</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>n=768 protein supplementation only</li> <li>n=914 protein supplementation with concomitant resistance training</li> <li>Age range 57 to 74 y</li> <li>study location (e.g. country) not stated</li> <li>community dwelling</li> <li>Intervention period 9 to 109 weeks</li> <li>Protein intervention: Ricotta, milk, 2 x milk protein, 2 x whey, 3 x essential amino acids, omnivores diet</li> </ul> <p><b>Statistical analysis:</b> Random-effects meta-analyses for lean body mass, muscle strength and physical performance (SMD=0.2 small, SMD=0.5 medium, SMD=0.8 large). Sensitivity analyses performed. Q statistics indicate statistical significant heterogeneity at <math>p &lt; 0.10</math>. Funnel plot used to examine publication bias, none found.</p> <p><b>Evaluation of study quality:</b> Use of a modified Downs and Black checklist, with a total of 27 points possible: &lt;15 poor; 15-19 moderate, 20-24 good, <math>\geq 25</math> excellent Studies scored from 15-26 (2 excellent; 6 good, 3 moderate)</p>	<p><b>1. Protein supplementation only (11 RCTs total)</b></p> <p><b>No significant effects of protein supplementation:</b></p> <ul style="list-style-type: none"> <li>Lean body mass (10 RCTs used DXA, 1 RCT did not state method of measurement) (11 RCTs; n=718; mean age 61y to 74y; duration 6 weeks to 78 weeks) SMD 0.11, 95% CI -0.06 to 0.28, <math>p=0.19</math> <math>I^2=0.0\%</math>, <math>p=0.99</math> indicating no significance of heterogeneity</li> <li>Handgrip strength (7 RCTs; n=479; mean age 70y to 74y; duration 6 weeks to 104 weeks) SMD 0.58, 95% CI -0.08 to 1.24, <math>p=0.08</math> <math>I^2=89.6\%</math>, <math>p=0.001</math> indicating significant heterogeneity</li> <li>Lower extremity muscle strength (3 RCTs; n=380; mean age 61y, 71y and 74y; duration 6, 78 and 104 weeks) SMD 0.03, 95% CI -0.20 to 0.27, <math>p=0.78</math> <math>I^2=0.0\%</math>, <math>p=0.85</math> indicating no significance of heterogeneity</li> <li>Gait speed (7 RCTs; n=487; mean age 61y to 74y; duration 6 to 78 weeks) SMD 0.41, 95% CI -0.04 to 0.85, <math>p=0.08</math> <math>I^2=76.4\%</math>, <math>p &lt; 0.001</math> indicating significant heterogeneity</li> <li>Chair-rise ability (7 RCTs; n=588; mean age 61y to 74y; duration 6 to 104 weeks) SMD 0.10, 95% CI -0.08 to 0.28, <math>p=0.26</math> <math>I^2=0.0\%</math>, <math>p=0.96</math> indicating no significance of heterogeneity</li> </ul> <p><b>2. Protein supplementation during concomitant resistance exercise (18 RCTs total)</b></p> <p><b>No significant effects of protein supplementation during concomitant resistance exercise</b></p>	<p><b>Authors' conclusions:</b> No evidence that protein supplementation in non-frail older adults has any association with improvements in lean body mass, upper and lower body muscle strength, gait speed, or chair-rise ability.</p> <p>Borderline significant findings given for handgrip strength and gait speed, however, the high heterogeneity hampered the results. Further, participants in those studies had handgrip strength below normal allowing for large improvements.</p> <p><b>Confounding:</b> The authors used a quality assessment tool which included an analysis of confounding in the individual RCTs. Scores ranged from 'poor' to 'good' for adjustment for confounding.</p> <p><b>Authors' limitations:</b> Protein intakes differed between studies in terms of type of protein, amount and timing. Also, the mean habitual intake was larger than recommendation of 0.8</p>

Study	Methods	Included studies	Results	Limitations/comments
	<ul style="list-style-type: none"> <li>Physical performance test such as timed up and go, short physical performance test</li> </ul>		<ul style="list-style-type: none"> <li>Lean body mass (11 RCTs used DXA, 2 hydrostatic weighting, 1 Bod Pod, 1 hydro densitometry) (15 RCTs; n=981; mean age 55y to 74y; duration 10-78 weeks) SMD 0.08, 95% CI -0.06 to 0.21, p =0.29 I<sup>2</sup>=0.0%, p=0.98 indicating no significance of heterogeneity</li> <li>Muscle cross-sectional area (7 RCTs; n=148; mean age 55y to 72y; duration 12-24 weeks) SMD 0.09, 95% CI -0.23 to 0.42, p =0.57 I<sup>2</sup>=0.0%, p=0.99 indicating no significance of heterogeneity</li> <li>Upper body muscle strength (10 RCTs; n=613; mean age 57y to 74y; duration 10 to 78 weeks) SMD 0.11, 95% CI -0.07 to 0.29, p =0.23 I<sup>2</sup>=0.0%, p=1.0 indicating no significance of heterogeneity</li> <li>Lower Extremity muscle strength (16 RCTs; n=981; mean age 57y to 74y; duration 12-78 weeks) SMD 0.11, 95% CI -0.06 to 0.27, p =0.23 I<sup>2</sup>=23.4%, p=0.17 indicating no significance of heterogeneity</li> <li>Gait Speed (8 RCTs; n=840; mean age 61y to 74y; duration 12 to 78 weeks) SMD 0.13, 95% CI -0.03 to 0.28, p =0.10 I<sup>2</sup>=0.0%, p=0.71 indicating no significance of heterogeneity</li> <li>Chair-rise performance (7 RCTs; n=685; mean age 61y to 74y; duration 12 to 78 weeks) SMD 0.01, 95% CI -0.16 to 0.17, p =0.95 I<sup>2</sup>=0.0%, p=0.86 indicating no significance of heterogeneity</li> </ul>	g/kg/d, which may therefore allow for a large enough protein intake to counteract age-related anabolic resistance.

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Tieland et al (2017)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> Review the association between protein or amino acid supplementation and muscle mass and strength</p> <p><b>Funding source:</b> Not stated</p> <p><b>Declarations of interest:</b> Stated: None of the authors had any personal or financial conflicts of interest (1 investigator authored 1 of the primary studies but other investigators evaluated the primary study)</p>	<p><b>Search:</b> performed in July 2016</p> <p><b>Databases searched:</b> MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL)</p> <p><b>Inclusion criteria:</b> RCTs, double-blinded, mean age <math>\geq 65</math> y, duration minimum 7 d, English, outcomes and measurements as detailed below only.</p> <p><b>Exclusion criteria:</b> cross-sectional, retrospective studies or studies as letters, commentaries, editorials, case reports, reviews or duplicate publications from the same studies. Or studies with additional interventions (such as physical exercise).</p> <p><b>Outcomes</b></p> <ul style="list-style-type: none"> <li>• Muscle mass: hydro densitometry (underwater weighing), bio impedance analysis (BIA), whole-body air plethysmography (BodPod), computed tomography (CT), magnetic resonance imaging (MRI) and dual energy X-ray absorptiometry (DXA)</li> <li>• Muscle strength: limited to 3 discrete measurements of maximal strength capacity, including handgrip strength and (double) leg 1-RM</li> </ul>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• MA on 8 RCTs</li> <li>• Individual participant data analysis on 6 RCTs (pooled analysis)</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• MA n=557; average age 67 to 88 y</li> <li>• Pooled analysis n=486; mean age 75 y</li> <li>• study location (e.g. country) not stated</li> <li>• 4 RCTs were in healthy populations; 4 RCTs contained populations with diabetes, sarcopenia, assisted daily living (ADL)-dependent, frailty</li> <li>• 1 RCT in residential care habitants. For other 7 RCTs not stated if study populations were community dwelling or not</li> </ul> <p><b>Intervention</b> (all randomly allocated)</p> <ul style="list-style-type: none"> <li>• Protein/amino acid: leucine alone, mixture of essential amino acids (EAA) or milk-based protein (1 RCT with 2 mixtures of EAA (i) 20% leucine, (ii) 40% leucine)</li> <li>• Dose: weighted mean 23.9 g/d; range 6-30 g/d</li> <li>• Duration range: 84-730 days</li> </ul> <p><b>Statistical analysis:</b> <i>Intention-to-treat (ITT) population</i></p> <ul style="list-style-type: none"> <li>• MA: random-effects model with treatment effects calculated from mean changes post- to pre-intervention and SD-change for each</li> </ul>	<p><b>Meta-analysis</b> No significant difference between protein intervention and control group on:</p> <p><b>lean body mass</b> (8 RCTs n=557; duration 12 weeks to 104 weeks; note 1 RCT contributing 15% weight, participants in residential care)</p> <ul style="list-style-type: none"> <li>• MD: 0.014 kg; 95% CI -0.152; 0.18</li> <li>• I<sup>2</sup>=0.0%, p=0.99 indicating no significance of heterogeneity</li> </ul> <p><b>handgrip strength</b> (6 RCTs; n=471; duration 12 weeks to 104 weeks; note 1 RCT contributing 18% weight; participants in residential care)</p> <ul style="list-style-type: none"> <li>• MD: -0.002 kg; 95% CI -0.182; 0.179</li> <li>• I<sup>2</sup>=0.0%, p=0.99 indicating no significance of heterogeneity</li> </ul> <p><b>leg press strength</b> (3 RCTs; n=151; duration 12 weeks to 24 weeks; note included 1 RCT of frail participants)</p> <ul style="list-style-type: none"> <li>• MD: 2.26 kg; 95% CI -0.56; 5.08</li> <li>• I<sup>2</sup>=97.4%, p=0.000 indicating significant heterogeneity</li> </ul> <p><b>leg extension strength</b> (4 RCTs n=165; duration 12 weeks to 24 weeks; note included 1 RCT of frail participants)</p> <ul style="list-style-type: none"> <li>• MD: 0.75 kg; 95% CI: -1.96, 3.47</li> <li>• I<sup>2</sup>=97.7%, p=0.00 indicating significant heterogeneity</li> </ul> <p><b>Pooled analysis</b> No significant difference between protein and placebo treatment on:</p> <ul style="list-style-type: none"> <li>• lean body mass (n=412: p=0.78),</li> <li>• leg press strength (n=121: p=0.50),</li> </ul>	<p><b>Authors' conclusions:</b> No evidence to suggest either protein or amino acid supplementation is associated with an increase in muscle mass or strength.</p> <p><b>Confounding:</b> No details on confounding or adjustments were provided in the systematic review.</p> <p><b>Authors' limitations:</b> Amount of protein supplementation varied between studies, half reported protein and or amino acids <math>\leq 7.5</math> g/d and it is not known if this amount is enough to augment muscle mass gain; 1 RCT increased intake to 25-30 g and still showed no beneficial effect.</p> <p>Source of protein also varied between studies.</p> <p>Not all primary studies reported habitual dietary intake of participants.</p> <p>Duration varied, with 7 out of 8 studies lasting <math>\leq 24</math> weeks which may not be enough time to show an effect.</p>



Study	Methods	Included studies	Results	Limitations/comments
	<p>strength tests for leg press and/or leg extension</p>	<p>group. Between studies heterogeneity calculated using <math>I^2</math>.</p> <ul style="list-style-type: none"> <li>• Pooled analysis of baseline characteristics for the independent participant data analysis (IPD) using independent sample T-test.</li> </ul> <p><b>Evaluation of study quality:</b></p> <ul style="list-style-type: none"> <li>• Use of Cochrane Collaboration giving 'low risk', 'high risk' or 'unclear risk' of bias: assessed as low risk of bias in all studies.</li> <li>• Begg's funnel plots created for each outcome variable (muscle mass, leg strength and handgrip strength) to assess publication bias, in addition to Egger's test.</li> </ul>	<ul style="list-style-type: none"> <li>• leg extension strength (n=121: p=0.16)</li> <li>• handgrip strength (n=318: p=0.37)</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Trevisan et al (2018)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> Evaluation of the association between nutritional status (BMI, malnutrition assessment) and risk of falls or risk of recurrent falls.</p> <p><b>Funding source:</b> None indicated</p> <p><b>Declarations of interest:</b> Stated: no conflicts of interest</p>	<p><b>Search period:</b> up to October 2017</p> <p><b>Databases searched:</b> PubMed (and websites such as Google Scholar)</p> <p><b>Inclusion criteria:</b> Community-based PCS, ≥ 60% of the participants aged ≥ 65 y, language restriction: 8 European languages, ≥2 categories of nutritional status or ≥ 2 quantitative categories of BMI falls</p> <p><b>Exclusion criteria:</b> hospitalised patients, or those with diseases with a high risk of falls such as Parkinson disease</p> <p><b>Exposures measured:</b> Malnutrition assessed using Mini Nutritional Assessment (MNA) tool: ≤23.5 MNA (or &lt;12 short-form MNA, SF-MNA) defining malnourished or at risk of malnutrition population; &gt;23.5 or ≥ 12 SF-MNA for well-nourished; other methods of nutritional status in primary studies also accepted.</p> <p><b>Primary outcome:</b></p> <ul style="list-style-type: none"> <li>• At least 1 fall during follow-up</li> <li>• ≥ 2 falls within a 6-month period (recurrent falls)</li> </ul>	<p><b>Number of studies:</b> 36 PCS considering BMI</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• community-dwelling</li> <li>• mean age, range: ≥ 64 y to 90 y (1 PCS with participants in the range 50 to 79 y)</li> <li>• number of participants: n=137 to n=73,168 (WHI, US) (19 PCS with n&lt;1000)</li> <li>• follow-up 1 month to 11 y (14 PCS ≤ 1 y, 24 PCS ≤ 2 y)</li> </ul> <p><b>Statistical analysis:</b></p> <ul style="list-style-type: none"> <li>• random effects dose-response MA to evaluate BMI and risk of falls/recurrent falls; the mean or median BMI value per BMI category assigned to RR</li> <li>• sensitivity analysis using leave-1 out analysis</li> <li>• heterogeneity assessed by chi-squared test with p&lt;0.10; I<sup>2</sup> evaluation with &lt;25% defining low heterogeneity, 25%-75% moderate, and &gt;75% high heterogeneity</li> </ul> <p><b>Evaluation of study quality:</b></p> <ul style="list-style-type: none"> <li>• Newcastle-Ottawa 0-9 scale; a score of ≥7 (high study quality) was reached for 83% of studies.</li> <li>• Publication bias assessed by Egger's regression and funnel plots.</li> </ul>	<p><b>Pooled analysis BMI and risk of experiencing at least 1 fall</b> (32 PCS, n=144,934, follow-up 6 months to 11 years)</p> <ul style="list-style-type: none"> <li>• Nonlinear association (p overall &lt;.001, p for nonlinearity 0.003 with a U-shape, a nadir between 24.5 and 30.0, and the lowest risk between 26.0 and 28.0).</li> <li>• Compared to BMI of 23.5 kg/m<sup>2</sup>, the pooled RR of any fall were: <ul style="list-style-type: none"> <li>• 1.09 (95% CI 1.04, 1.15) for BMI 17.0 kg/m<sup>2</sup></li> <li>• 0.98 (95% CI 0.95, 1.01) for BMI 27.5 kg/m<sup>2</sup></li> <li>• 1.07 (95% CI 0.92, 1.24) for BMI 37.5 kg/m<sup>2</sup></li> </ul> </li> <li>• Low heterogeneity for BMI &lt;25.0 kg/m<sup>2</sup> and moderate BMI ≥25.0 kg/m<sup>2</sup></li> <li>• No publication bias (p=0.92)</li> <li>• No differences by sex, age, follow-up, frequency of fall assessment, study quality. More relevant differences between unadjusted and adjusted data (p=0.06) and using location as criterion (p=0.03) (especially between studies from Europe and from the USA (p=0.02)).</li> <li>• Sensitivity analysis between studies indicate risk of an injurious fall seemed to decrease with increasing BMI and ranged from: 1.06 (95% CI 0.77, 1.46) for a BMI of 17.0 kg/m<sup>2</sup> to 0.79 (95% CI 0.46, 1.37) for a BMI of 37.5 kg/m<sup>2</sup>.</li> <li>• Pooled results were not substantially influenced by individual studies in the leave-1-out sensitivity analysis. Further sensitivity analysis showed no substantial differences.</li> </ul> <p><b>Pooled analysis BMI and risk of recurrent falls</b> (23 PCS; n=120,185; follow-up 6 months to 6 years)</p> <ul style="list-style-type: none"> <li>• No linear or nonlinear relationship (p for linearity 0.39, p overall for splines 0.28). With BMI=23.5 kg/m<sup>2</sup> as reference,</li> <li>• pooled RR of recurrent falls:</li> </ul>	<p><b>Authors' conclusions:</b> BMI may be associated with risk of falls in community dwelling older adults. BMI (both underweight and obese) may be associated with higher risk of falls in comparison to normal or overweight BMIs (24.5-30.0 kg/m<sup>2</sup>). The U-shaped curve for BMI and risk of falls appears similar to that for BMI and mortality for older populations, where lowest mortality falls between BMI 24.0 and 30.9 kg/m<sup>2</sup>.</p> <p>No association between BMI and recurrent falls although increased risk was observed for underweight people.</p> <p><b>Confounding:</b> Of the 36 studies included in the review, 22 adjusted for confounders including age, sex, and previous falls. The remaining 14 studies did not adjust for confounding.</p> <p><b>Authors' limitations:</b> Overweight participants may be selected study population who have escaped detrimental health consequences of obesity.</p>

Study	Methods	Included studies	Results	Limitations/comments
			<ul style="list-style-type: none"> <li>• 1.07 (95% CI 0.98,1.16) for BMI 17.0 kg/m<sup>2</sup></li> <li>• 0.98 (95% CI 0.94, 1.02) for BMI 27.5 kg/m<sup>2</sup></li> <li>• 0.97 (95% CI 0.81, 1.16) for BMI 37.5 kg/m<sup>2</sup></li> <li>• Low heterogeneity for BMI &lt;25.0 kg/m<sup>2</sup> and moderate BMI ≥25.0 kg/m<sup>2</sup></li> <li>• No publication bias (p=0.66)</li> <li>• No differences by sex, follow-up or other criteria, but borderline differences by age (&lt;75 vs ≥ 75 y) with lower ages having more falls.</li> <li>• Pooled results not substantially influenced by individual studies in the leave-1-out sensitivity analysis.</li> </ul>	<p>Age-related decrease in height may overestimate BMI and lead to BMI misclassification.</p> <p>A first fall may affect mobility and increase fear of falling both contributing to decreased probability of recurrent fall. Furthermore, different time periods to measure recurrent falls may have limited study of the relationship.</p>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Tricco et al (2017)</b></p> <p><b>Study design:</b> Systematic review, meta-analysis and network meta-analysis</p> <p><b>Aim of study/ research question:</b> To assess the potential effectiveness of interventions for preventing falls</p> <p>Funding source: Research Knowledge Synthesis Grant by Canadian Institutes of Health (CIHR)</p> <p><b>Declarations of interest:</b></p> <ul style="list-style-type: none"> <li>• Tier 2 Canada Research Chair in Knowledge Synthesis grant.</li> <li>• CIHR Banting Postdoctoral Fellowship Program grant</li> <li>• Tier 2 Canada Research Chair in Integrated Knowledge Translation in Rehabilitation Sciences grant</li> </ul>	<p><b>Search period:</b> until April 2017</p> <p><b>Databases searched:</b> MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Ageline databases</p> <p><b>Inclusion criteria:</b> All types of RCTs (e.g. cluster, crossover) examining fall-prevention interventions (whether single or multifactorial) for adults aged 65 years or older in all settings (e.g., community, acute care) were included. Potential comparators were usual care, other fall-prevention interventions, and placebo.</p> <p><b>Exclusion criteria:</b> none stated</p> <p><b>Primary outcomes:</b></p> <ul style="list-style-type: none"> <li>• Injurious falls</li> <li>• fall-related hospitalizations</li> </ul> <p><b>Secondary outcomes:</b></p> <ul style="list-style-type: none"> <li>• rate of falls</li> <li>• number of fallers</li> <li>• number of fall-related emergency department visits</li> <li>• number of fall-related physician visits</li> <li>• number of fractures</li> </ul>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• Total 283 RCTs; n = 159,910</li> <li>• Network meta-analysis: 54 RCTs; n = 41,596</li> </ul> <p><b>Study participants</b> (for all 283 RCTs):</p> <ul style="list-style-type: none"> <li>• mean age 78 y</li> <li>• 74% women</li> <li>• follow-up durations: <ul style="list-style-type: none"> <li>• ≤26 weeks for 150 RCTs (53%)</li> <li>• ≤1year for 223 RCTs (79%)</li> </ul> </li> <li>• no data on baseline vitamin D status was reported</li> </ul> <p><b>Intervention components:</b></p> <ul style="list-style-type: none"> <li>• Calcium (ca)</li> <li>• Clinic-level quality improvement (e.g., case management) (cl-qi)</li> <li>• Dietary modifications (di)</li> <li>• Multifactorial assessment and treatment (e.g., comprehensive geriatric assessment) (mf)</li> <li>• Osteoporosis treatment (op-tx)</li> <li>• Patient-level quality improvement (pa-qi)</li> <li>• Usual care (uc)</li> <li>• Vitamin D (vi-d)</li> <li>• 20 additional intervention components were assessed but were not of relevance to the results presented here</li> </ul> <p><b>Statistical analysis:</b> Random-effects network meta-analyses were conducted for connected networks of included RCTs</p>	<p><b>Network meta-analysis (NMA)</b></p> <ul style="list-style-type: none"> <li>• 54 RCTs, n= 41 596 participants, range of follow-up durations not stated</li> </ul> <p><b>NMA: Statistically significant results for intervention combinations that differ only in nutritional intervention components</b></p> <p><b>Injurious Falls</b></p> <ul style="list-style-type: none"> <li>• (40 treatments, 54 studies, n= 41,596)</li> <li>• ca+cl-qi+mf+vi-d vs cl-qi+mf: OR 0.14 (95% CI 0.03 to 0.64);</li> </ul> <p><b>Number of Fallers</b></p> <ul style="list-style-type: none"> <li>• (78 treatments, 158 studies, 107,300 patients)</li> <li>• ca+vi-d vs ca: OR 0.69 (95% CI 0.49 to 0.98)</li> </ul> <p><b>Fractures</b></p> <ul style="list-style-type: none"> <li>• (44 treatments, 68 studies, 86,491 patients)</li> <li>• ca+vi-d vs uc: OR 0.82 (95% CI 0.67 to 1.00)</li> <li>• ca+vi-d vs vi-d: OR 0.76 (95% CI 0.60 to 0.96)</li> <li>• ca+op-tx+vi-d vs op-tx+vi-d: OR 0.27 (95% CI 0.08 to 0.96)</li> </ul> <p><b>NMA: Statistically significant risk reductions for those combined interventions that included a nutrition component, in comparison to usual care:</b></p> <p><b>Number of injurious falls</b></p> <ul style="list-style-type: none"> <li>• ca+vi-d+cl-qi+mf vs uc</li> <li>• OR 0.12 (95%CI, 0.03 to 0.55)</li> <li>• absolute risk difference (ARD) -2.08 (95%CI, -3.56 to -0.60)</li> </ul> <p><b>Number of fallers</b></p> <ul style="list-style-type: none"> <li>• ca+vi-d+di+cl-qi+pa-qi vs uc</li> <li>• OR 0.36 (95% CI 0.14 to 0.93)</li> </ul>	<p><b>Authors' conclusions:</b> The analysis identified combinations of interventions likely to be more effective than usual care for preventing injurious falls.</p> <p>Exercise alone and various combinations of interventions were associated with lower risk of injurious falls compared with usual care. Choice of fall-prevention intervention may depend on patient and caregiver values and preferences.</p> <p><b>Confounding:</b> No detail on confounding or adjustments were provided in the systematic review. The</p> <p><b>Authors' limitations:</b> Because of the large number of comparisons in the network meta-analyses, multiplicity may have elevated the rate of false positives in the statistically significant results (type I error). Although P scores are based on the treatment effect</p>

Study	Methods	Included studies	Results	Limitations/comments
<ul style="list-style-type: none"> <li>membership with the Ontario Chiropractic Association</li> <li>Associate editor for the Canadian Medical Association Journal</li> <li>support from the Faculty of Medicine and Dentistry and the Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta</li> <li>Tier 1 Canada Research Chair in Knowledge Translation grant</li> </ul>	<ul style="list-style-type: none"> <li>costs (e.g., to the health care system)</li> <li>number of intervention-related harms (e.g., muscle soreness from exercise)</li> <li>quality of life</li> </ul>	<p>when more than 10 RCTs were available and the number of RCTs was greater than the number of intervention nodes.</p> <p>Across all outcomes, pairwise random-effects meta-analysis was conducted. Effect estimates are reported as odds ratios (ORs) for dichotomous outcomes and mean differences for continuous outcomes.</p> <p><b>Evaluation of study quality:</b> Cochrane Effective Practice and Organisation of Care (EPOC)</p>	<ul style="list-style-type: none"> <li>ARD -1.03 (95% CI -1.99 to -0.08)</li> </ul> <p><b>Number of fractures</b></p> <ul style="list-style-type: none"> <li>ca+op-tx+vi-d vs uc</li> <li>OR 0.22 (95% CI 0.09 to 0.54)</li> <li>ARD -1.51 (95% CI -2.41 to -0.62)</li> </ul> <p><b>Number of hip fractures</b></p> <ul style="list-style-type: none"> <li>ca+op-tx+vi-d vs uc</li> <li>OR 0.18 (95% CI 0.05 to 0.62)</li> <li>ARD -1.70 (95% CI -2.92 to -0.48)</li> </ul> <p><b>Pairwise meta-analysis:</b></p> <ul style="list-style-type: none"> <li>the range of follow-up durations for included studies were not stated</li> </ul> <p><b>Number of fallers:</b></p> <ul style="list-style-type: none"> <li>vi-d vs uc (7 RCTs, n = 17966): OR 0.98 (95% CI 0.83 to 1.16)</li> <li>ca+vi-d vs uc (3 RCTs, n = 4167): OR 0.95 (95% CI 0.84 to 1.07)</li> <li>ca+vi-d vs ca (5 RCTs, n = 1389): OR 0.73 (95% CI 0.58 to 0.9)</li> </ul> <p><b>Fractures:</b></p> <ul style="list-style-type: none"> <li>ca vs uc (2 RCTs, n = 4114): OR 0.94 (95% CI 0.81 to 1.1)</li> <li>ca+vi-d vs uc (3 RCTs, n = 5524): OR 0.81 (95% CI 0.66 to 0.99)</li> <li>ca vs ca+vi-d (6 RCTs, n = 6462): OR 0.98 (95% CI 0.84 to 1.15)</li> <li>vi-d vs ca+vi-d (2 RCTs, n = 3046): OR 0.85 (95% CI 0.69 to 1.04)</li> <li>vi-d vs uc (6 RCT, n=21,018): OR 1.09 (96% CI 0.92 to 1.3)</li> </ul>	<p>estimates and their associated CIs, it is recommended that the P score values be interpreted along with the network meta-analysis point estimates and their precision.</p> <p>Some of the planned subgroup analyses and sensitivity analyses were not conducted because of insufficient data. Although the point estimate was similar to the overall OR, the results were no longer statistically significant for the injurious falls network meta-analysis when only studies with a low risk of contamination bias were included. However, because most of the studies (67%) were assessed as having an unclear risk of contamination bias, the power of this sensitivity analysis was limited by the lower number of studies that could be included. This limitation suggests that improvements in reporting are required. Most network meta-analyses included numerous interventions, with sparse data for the treatment comparisons.</p>

Study	Methods	Included studies	Results	Limitations/comments
			<p><b>Hip Fractures</b></p> <ul style="list-style-type: none"> <li>• uc vs vi-d (4 RCTs, n = 18099): OR 1.29 (95% CI 0.99 to 1.67)</li> <li>• ca+vi-d vs uc (2 RCTs, n = 2886): <b>OR 0.67 (95% CI 0.54 to 0.83)</b></li> <li>• ca+vi-d vs ca (3 RCTs, n = 2918): OR 1.17 (95% CI 0.79 to 1.71)</li> </ul> <p><b>Harms: Gastrointestinal symptoms</b></p> <ul style="list-style-type: none"> <li>• ca+vi-d vs uc (2 RCTs, n = 3853): OR 1.05 (95% CI 0.52 to 2.09)</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Tyrovolas and Panagiotakos (2010)</b></p> <p><b>Study design:</b> Systematic review</p> <p><b>Aim of study/ research question:</b> A narrative review of the evidence for an association between diet, particularly Mediterranean dietary patterns, with risk of cancer or cardiovascular disease.</p> <p><b>Funding source:</b> No information</p> <p><b>Declarations of interest:</b> Stated as none</p>	<p><b>Search period:</b> 1985 through 2009</p> <p><b>Databases searched:</b> PubMed and Scopus</p> <p><b>Inclusion criteria:</b> original research published in English</p> <p><b>Exclusion criteria:</b> not stated</p> <p><b>Primary outcomes:</b></p> <ul style="list-style-type: none"> <li>• mortality</li> <li>• cardiovascular disease risk</li> <li>• cancer risk</li> </ul> <p><b>Dietary assessment method:</b></p> <ul style="list-style-type: none"> <li>• For EPIC cohort, dietary intakes collected by self or interviewer-administered questionnaires; for MEDIS cohort</li> <li>• Mediterranean diet recorded using MedDietScore (range 0-55);</li> <li>• in MEDIS study, principal component analysis (PCA) used to assess dietary patterns.</li> </ul>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• 9 (7 PCS, 2 XS)</li> <li>• SR includes further studies but were omitted from this table because age groups were outside of inclusion criteria</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• number, range n=785 to 99,744</li> <li>• age &gt; 65 y (Habits in Later Life Only study does not state specific age but refers to population as elderly)</li> <li>• community living</li> </ul> <p><b>Evaluation of study quality:</b> Evaluation method or risk of bias not stated</p>	<p><b>Mortality:</b></p> <p><b>1 PCS</b> (SENECA, Europe, n=1281, 10 y follow-up; age 70 y to 75 y)</p> <ul style="list-style-type: none"> <li>• an increasing number of unhealthy lifestyle behaviours were related to a higher mortality rate (log rank test: <math>p &lt; 0.001</math>).</li> <li>• mortality risk (men) with low-quality diet= 1.25 (95% CI 0.93 to 1.68)</li> <li>• Mortality risk (women) with low-quality diet= 1.26 (95% CI 0.88 to 1.81)</li> <li>• For subjects with three unhealthy lifestyle behaviours (low-quality diet, smoking, physical inactivity) mortality risk increased three- to fourfold (no 95%CI or p-value stated).</li> </ul> <p><b>1 PCS</b> (HALE, Europe, n=2339, 10-y follow-up; age 70 y to 90 y)</p> <ul style="list-style-type: none"> <li>• Mediterranean diet associated with 23% lower risk of death (moderate alcohol use was associated with a further 22% reduction in mortality risk) (no 95%CI or p-value stated)</li> <li>• those with a healthful diet and lifestyle factors (in relation to alcohol, smoking, exercise) had less than half the mortality rate for all-cause, CHD, CVD and cancers (compared to those with no healthful diet and lifestyle factors) (no 95%CI or p-value stated)</li> </ul> <p><b>1 XS</b> (Habits in Later Life Only, Japan, Sweden, Australia, Greece; n=785 elderly, age not stated)</p> <ul style="list-style-type: none"> <li>• legume intake associated with reduction in mortality hazard ratio (no effect size or p-value stated)</li> </ul>	<p><b>Authors' conclusions:</b> Some evidence to suggest a combination of lifestyle factors are associated with morbidity and mortality. More specifically, high adherence to Mediterranean diet is associated with reduced risk of CVD and some types of cancer. The beneficial health effect has been attributed to surrogate markers including blood pressure, lipids, inflammation etc.</p> <p><b>Confounding:</b> The authors stated that they graded the included evidence on factors including confounding. However, no further details were provided and so the extent of confounding is unclear.</p> <p><b>Authors' limitations:</b> Geographical variation in genetic risk for cancer and CVD may over- or underestimate observed results. Furthermore, gene-diet interactions observed in some studies may influence the effect size.</p>

Study	Methods	Included studies	Results	Limitations/comments
			<p><b>Cardiovascular disease risk</b></p> <p><b>1 XS</b> (MEDIS; Mediterranean islands (Cyprus and Greek islands); n=1190; mean age men 76 y, women 74 y)</p> <ul style="list-style-type: none"> <li>• High fish intake inversely associated with CV risk factors (systolic blood pressure p=0.026; fasting glucose p&lt;0.001; total serum cholesterol p=0.012; triglyceride level p=0.024) (no effect sizes stated)</li> <li>• Multinomial logistic progression showed reduction of 100g/week in fish consumption associated with 19% higher likelihood of having 1 additional CV risk factor (such as hypertension, hypercholesterolemia, diabetes or obesity)</li> <li>• Principal component analysis showed cereal intake pattern to be associated with 28.4% ↓ hypercholesterolemia (OR=0.716, p=0.001), 25% ↓ diabetes (OR=0.75, p=0.009), 33% ↓ obesity (OR=0.67, p=0.001); no association was found for high fat foods (OR=1.048, p=0.06), dairy or fruit (no effect size or p-value stated).</li> </ul> <p><b>1 XS</b> (Habits in Later Life Only, Japan, Sweden, Australia, Greece; n=785 elderly, age not stated)</p> <ul style="list-style-type: none"> <li>• greater adherence to the Mediterranean diet was associated with 21% lower odds of having one additional risk factor (i.e., hypertension, hypercholesterolemia, diabetes, obesity) in women and with 14% lower odds in men (no 95%CI or p-value stated)</li> </ul> <p><b>Cancer risk</b></p> <p><b>5 PCS</b> (EPIC, Europe, n=99,744; 10-y follow-up, age &gt;65 y)</p> <ul style="list-style-type: none"> <li>• prostate cancer (n=1104 incident cases): no association with fruit and vegetables (RR=1.00, 95% CI 0.79 to 1.26)</li> </ul>	



Study	Methods	Included studies	Results	Limitations/comments
			<ul style="list-style-type: none"> <li>• colorectal cancer: protective association from hi-fibre intake (RR=0.58, 95% CI 0.41 to 0.85 for highest vs lowest quintile); for women significant protective association with nut and seed intake (no effect size or p-value stated)</li> <li>• colorectal cancer: elevated fish intake (&gt;80 g/d vs. &lt;10 g/d) significantly reduced colorectal cancer risk (HR=0.69, 95% CI, 0.54 to 0.88, p for trend &lt;0.001)</li> <li>• colorectal cancer: no significant association for red or processed meat intake (HR=1.35, 95% CI 0.96 to 1.88; highest &gt;160 g/d vs. lowest &lt;20 g/d; p for trend=0.03)</li> <li>• lung cancer: association with fruit intake (HR=0.60, 96% CI 0.46 to 0.78, p trend = 0.0099); no association with vegetable intake (no effect size or p-value stated)</li> </ul>	

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Winter et al (2014)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> To determine the association between BMI and all-cause mortality risk in adults over 65 years</p> <p><b>Funding source:</b> It is noted that 'no financial support was received for this article'.</p> <p><b>Declarations of interest:</b> The first author (Winter) declared to be an employee of Nestle Health Science, Australia. None of the other authors declared conflict of interest.</p>	<p><b>Search period:</b> 1990 to September 2013</p> <p><b>Databases searched:</b> MEDLINE, CINAHL, Cochrane Library</p> <p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• PCS in community living adults aged over 65 years</li> <li>• PCS that reported RR or HRs and corresponding 95% CI of all-cause mortality, had a minimum follow-up of 5y and had ascertained baseline BMI and smoking status.</li> <li>• Studies that included full details of statistical models, including the confounding factors.</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Studies that reported HR only for weight in kg or weight change rather than BMI</li> <li>• Reported &lt;3 quantitative categories of BMI</li> <li>• Studies in wholly non-white populations</li> </ul> <p><b>Primary outcome:</b></p> <ul style="list-style-type: none"> <li>• all-cause mortality</li> </ul>	<p><b>Number of studies:</b></p> <ul style="list-style-type: none"> <li>• 32 PCS</li> </ul> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>• n (all studies) = 197,940 (348 to 28,466)</li> <li>• Age &gt;65 years</li> <li>• Community living</li> <li>• Follow-up 5 to 29 years</li> </ul> <p><b>Statistical analysis:</b></p> <ul style="list-style-type: none"> <li>• A2-stage random-effects meta-analysis</li> <li>• BMI was modelled by using restricted cubic splines with 3 knots chosen at the 5th, 50th, and 95th percentiles of the distribution. Pooled HRs for each 1-unit increment of BMI were reported.</li> <li>• Studies that reported results only by subgroups of age or sex were combined by using a within-study fixed-effects meta-analysis to derive common risk estimates.</li> <li>• Separate meta-analyses were performed stratified by sex, geographical region (North America compared with Europe), measured compared with self-reported anthropometric variables, never-smokers, exclusion of early deaths (deaths within the first 1 to 5 y of follow-up), exclusion of adjustment for intermediary factors in the obesity-mortality causal pathway (e.g., hypertension, diabetes, or</li> </ul>	<p><b>BMI and all-cause mortality:</b></p> <p>The association between BMI and mortality was found to be U-shaped. Compared with a reference BMI of 23.0 to 23.9 kg/m<sup>2</sup>, the mortality risk was:</p> <ul style="list-style-type: none"> <li>• lowest for BMI 27.0 to 27.9 kg/m<sup>2</sup> (HR: 0.90 95% CI 0.88 to 0.92)</li> <li>• for BMI 19.0 to 19.9 kg/m<sup>2</sup>, increased by 28% (HR 1.28, 95% CI 1.24 to 1.32) and increased by more than 28% for those with lower BMIs</li> <li>• for BMI 35.0 to 35.9 kg/m<sup>2</sup>, increased by 21% (HR 1.21, 95% CI 1.10 to 1.33) and increased by more than 21% for those with higher BMIs.</li> </ul> <p>When comparing broad BMI ranges with a reference BMI range of 21.0 to 24.9 kg/m<sup>2</sup>, the mortality risks were:</p> <ul style="list-style-type: none"> <li>• for BMI &lt;21 kg/m<sup>2</sup> (HR 1.37, 95% CI: 1.30 to 1.46)</li> <li>• for BMI 25 to 29.9 kg/m<sup>2</sup> (HR 0.90, 95% CI: 0.87 to 0.93)</li> <li>• for BMI 30.0 to 34.9 kg/m<sup>2</sup> (HR 0.96, 95% CI: 0.90, 1.02)</li> <li>• for BMI &gt;35.0 kg/m<sup>2</sup> (HR 1.18, 95% CI: 1.00 to 1.39).</li> </ul> <p><b>Subgroup analysis:</b></p> <ul style="list-style-type: none"> <li>• for never-smokers (n = 51,514) the mortality curve shifted left; the lowest mortality risk moved to BMI 26.0–26.9 kg/m<sup>2</sup> (HR: 0.94; 95% CI: 0.91, 0.97) from BMI 27.0 to 27.9 kg/m<sup>2</sup> in the main meta-analysis</li> <li>• there were no notable differences in results between men and women.</li> </ul> <p>Subgroup analyses confirmed the increased risk of mortality at BMI &lt;23.0 kg/m<sup>2</sup> and BMI &gt;33.0 kg/m<sup>2</sup> compared with a reference BMI of 23.0 to 23.9 kg/m<sup>2</sup> for studies:</p>	<p><b>Authors' conclusions:</b></p> <ul style="list-style-type: none"> <li>• For older populations, being overweight was not found to be associated with an increased risk of mortality; however, there was an increased risk for those at the lower end of the recommended BMI range for adults.</li> </ul> <p><b>Confounding:</b></p> <ul style="list-style-type: none"> <li>• Only primary studies that stated confounding factors were included; confounding factors are stated in review and include age, sex, marital status, education, smoking status, employment status and pre-existing diseases. The results of fully adjusted models were used in meta-analyses.</li> </ul> <p><b>Authors' limitations:</b></p> <ul style="list-style-type: none"> <li>• analysis assessed only mortality risk associated with BMI rather than weight change or body composition, and weight change may be more important for older adults in terms of health risks.</li> <li>• analysis was limited to all-cause mortality rather than to morbidity or</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
		<p>hyperlipidemia), and absence of preexisting disease.</p> <ul style="list-style-type: none"> <li>• Nonlinearity of the meta-analysis was assessed by testing the null hypothesis that the coefficient of the second spline was equal to zero.</li> <li>• Statistical heterogeneity was assessed by using multivariate generalization of the <math>I^2</math> statistic (2 cut-off points)</li> <li>• Publication bias was evaluated by using funnel plots and Egger's regression test</li> </ul>	<ul style="list-style-type: none"> <li>• using only measured BMIs (but not self-reported BMIs)</li> <li>• with no adjustment for intermediary factors</li> <li>• with exclusion of early deaths</li> <li>• of populations with no pre-existing disease</li> </ul>	<p>cause-specific mortality, which may have different associations with BMI.</p> <ul style="list-style-type: none"> <li>• all results were pooled together to determine mortality risk for adults aged &gt;65 y. For the younger age groups within this range, the risks of higher BMI may be greater than for those in the older age groups (&gt;75 y).</li> <li>• only predominantly white populations were included because the BMI mortality relation may differ according to race or ethnicity.</li> <li>• few primary studies provided details of levels of physical activity, and it may be that a mix of activity levels of individuals in the BMI categories influenced the results of the meta-analyses.</li> </ul>

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Wu &amp; Pang (2017)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> To evaluate the effect of vitamin D, administered either alone or in combination with calcium, on falls in older adults.</p> <p><b>Funding source:</b> Key program of Clinical Specialty Disciplines of Ningbo (2013-88), Hua-Mei foundation (2017HMKY17)</p> <p><b>Declarations of interest:</b> H. Wu and Q. Pang declare that they have no competing interests.</p>	<p><b>Search period:</b> up to 31 December 2016</p> <p><b>Databases searched:</b> PubMed and the Cochrane Library</p> <p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Older adults (mean age <math>\geq 60</math> years) dwelling both inside and outside of hospital (to note that the journal article does not state which primary studies were inside or outside hospital)</li> <li>Double-blind randomized, controlled trials (RCTs) of vitamin D in elderly populations that examined fall results, and that reported odds ratios (ORs) and 95% confidence intervals (CIs) or cross-table data.</li> </ul> <p><b>Exclusion criteria:</b> Case reports and series; reviews focussing solely on specialist populations (Parkinson's disease, e.g. stroke, Alzheimer's disease, myasthenia gravis)</p> <p><b>Primary outcome:</b></p> <ul style="list-style-type: none"> <li>risk of having at least one fall</li> </ul>	<p><b>Number of studies:</b> 26 RCTs</p> <p><b>Study participants:</b></p> <ul style="list-style-type: none"> <li>n (all studies) = 32,686 (26 to 4727)</li> <li>mean age = <math>67 \pm 2</math> to <math>92 \pm 6</math> years</li> <li>study settings not stated</li> <li>study locations not stated</li> <li>no data on baseline vitamin D status was reported</li> </ul> <p><b>Intervention:</b></p> <ul style="list-style-type: none"> <li>duration: 1 month to 60 months</li> <li>daily vitamin D dosage: <ul style="list-style-type: none"> <li>200 to 1100 IU/day</li> <li>in 11 studies: dosage 800 IU/day</li> </ul> </li> <li>long-term dosage: <ul style="list-style-type: none"> <li>in 6 studies total dosage ranged from 300,000 IU once during 36 months intervention to 100,000 IU/4 weeks</li> </ul> </li> <li>calcium dosage: <ul style="list-style-type: none"> <li>in 14 studies vitamin D was supplemented with 500 to 1200 mg calcium/day</li> </ul> </li> </ul> <p><b>Statistical analysis:</b></p> <ul style="list-style-type: none"> <li>odds ratios incl. 95% CI were calculated for each study and each meta-analysis</li> <li>random-effect model was used when there was heterogeneity in the meta-analysis (<math>I^2 &gt; 50\%</math>), otherwise a fixed-effect model was applied.</li> </ul>	<p><b>Odds ratios for falls are presented in 5 meta-analyses (these MA include primary studies of older adults both inside and outside hospital)</b></p> <p><b>Vitamin D2:</b></p> <ul style="list-style-type: none"> <li>Meta-analysis of 6 RCTs (n= 13,545; duration 5 months to 24 months)</li> <li>OR = 0.77 (95% CI 0.58 to 1.03); p = 0.08</li> <li><math>I^2 = 79\%</math>, p &lt; 0.001</li> </ul> <p><b>Vitamin D3:</b></p> <ul style="list-style-type: none"> <li>Meta-analysis of 6 RCTs (n= 8,199; duration 6 months to 60 months)</li> <li>OR = 1.08 (95% CI 0.98 to 1.20); p = 0.14</li> <li><math>I^2 = 42\%</math>, p = 0.130</li> </ul> <p><b>Vitamin D + calcium vs placebo:</b></p> <ul style="list-style-type: none"> <li>Meta-analysis of 8 RCTs (n= 11,879; duration 12 to 45 months, and 1 RCT 3 months)</li> <li>OR = 0.91 (95% CI 0.84 to 0.99); p = 0.04</li> <li><math>I^2 = 42\%</math>, p = 0.10</li> </ul> <p><b>Vitamin D + calcium vs calcium alone:</b></p> <ul style="list-style-type: none"> <li>Meta-analysis of 7 RCTs (n= 1,706; duration 1 months to 24 months)</li> <li>OR = 0.67 (95% CI 0.55 to 0.81); p &lt; 0.0001</li> <li><math>I^2 = 0\%</math>, p = 0.45</li> </ul> <p><b>Vitamin D + calcium vs placebo or calcium alone:</b></p> <ul style="list-style-type: none"> <li>Meta-analysis of 14 RCTs (n= 13,585; duration 3 months to 24 months)</li> <li>OR = 0.87 (95% CI 0.80 to 0.94); p=0.0004</li> <li><math>I^2 = 46\%</math>, p = 0.03</li> </ul>	<p><b>Authors' conclusions:</b> Combined calcium plus vitamin D supplementation is statistically significantly associated with a reduction in fall risks across various populations.</p> <p><b>Confounding:</b> No detail on confounding or adjustments were provided in the systematic review. The authors noted that publication bias has likely affected the results.</p> <p><b>Authors' limitations:</b> A publication bias has likely affected the results presented in this review. The dietary sources of vitamin represent a co-intervention that could introduce noise to the signal produced by the intervention in unblinded studies and may bias the results toward the null.</p>

Study	Methods	Included studies	Results	Limitations/comments
		<b>Evaluation of study quality:</b> No evaluation of study quality is noted in the study.		

Study	Methods	Included studies	Results	Limitations/comments
<p><b>Xu et al (2015)</b></p> <p><b>Study design:</b> Systematic review and meta-analysis</p> <p><b>Aim of study/ research question:</b> Evaluate the effectiveness of leucine on muscle protein synthesis, lean body mass and leg lean mass accretion</p> <p><b>Funding source:</b> Stated: The present study was supported by the Science and Technology Project of Zhejiang Province (grant no. 2013C33122).</p> <p><b>Declarations of interest:</b> Stated: There are no conflicts of interest.</p>	<p><b>Search period:</b> up to 31 December 2013</p> <p><b>Databases searched:</b> MEDLINE, Cochrane, Embase, Google Scholar</p> <p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• RCTs</li> <li>• age <math>\geq</math> 65 years</li> <li>• clearly defined level of leucine supplementation</li> <li>• English language</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• non-randomised controlled trials</li> <li>• letters, comments, editorials, and case reports</li> </ul> <p><b>Primary outcome:</b></p> <ul style="list-style-type: none"> <li>• Muscle protein synthesis: stable isotope infusion test to assess muscle protein fractional synthetic rate. Studies used the same measure of muscle protein fractional synthetic rate (%/h).</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>• lean body mass</li> <li>• leg lean mass accretion</li> </ul>	<p><b>Number of studies:</b> 9 RCTs (only 6 RCTs used in MA) (6 RCTs with parallel arms; 3 RCTs crossover) Note:</p> <ul style="list-style-type: none"> <li>• 4 RCTs had participants with conditions ranging from polymyalgia rheumatica, diabetes and cancer; other 5 RCTs had 'healthy' or 'healthy and lean' populations.</li> </ul> <p><b>Study participants</b></p> <ul style="list-style-type: none"> <li>• mean ages: 66.5 y to 75 y</li> <li>• study setting: <ul style="list-style-type: none"> <li>◦ 7 RCTs: community dwelling</li> <li>◦ 1 RCT: hospitalised patients</li> <li>◦ 1 RCT: cancer patients with unclear setting</li> </ul> </li> <li>• study countries not stated</li> <li>• total number ranged from 8 to 57</li> <li>• 5 RCTs, all subjects male</li> </ul> <p><b>Intervention:</b></p> <ul style="list-style-type: none"> <li>• 4 RCTs: acute supplementation given once only and outcome measured after a few hours</li> <li>• 5 RCTs: long-term (range from 10 days to 6 months)</li> <li>• acute: 2.8 g/d to 17.6 g/d</li> <li>• long-term: 2.8 g/d to 16.1 g/d</li> </ul> <p><b>Primary outcome:</b></p> <ul style="list-style-type: none"> <li>• muscle protein synthesis</li> </ul> <p><b>Secondary outcomes:</b></p> <ul style="list-style-type: none"> <li>• lean body mass</li> <li>• leg lean mass accretion</li> </ul>	<p><b>Muscle protein fractional synthetic rate:</b> MA of 4 RCTs (n=79)</p> <ul style="list-style-type: none"> <li>• Note: 2 RCTs (69.4% weight) included participants with (i) cancer [unclear setting] and (ii) bed rest [hospitalised]; 2 RCTs acute studies (supplemented once), measurements taken after 5 h and 6.5 h; 2 RCTs longer term intervention periods of 10 d and 3 m</li> <li>• fixed effects model: SMD 1.04 (95% CI 0.56 to 1.52); <math>p &lt; 0.001</math></li> <li>• random effects model: SMD 1.08 (95% CI 0.50 to 1.67); <math>p &lt; 0.001</math></li> <li>• <math>Q = 4.36</math>, <math>p = 0.225</math>, <math>I^2 = 31.16\%</math></li> <li>• The results indicated that the muscle protein fractional synthetic rate after intervention significantly increased in the leucine group compared with the control group.</li> </ul> <p><b>Lean body mass:</b> MA of 4 RCTs (n=121)</p> <ul style="list-style-type: none"> <li>• Note: 2 RCTs (69.2% weight) with participants with diabetes (community dwelling) or bed rest (hospitalised); 4 RCTs considered longer-term interventions from 10 d to 6 m</li> <li>• fixed and random effects model: SMD 0.18 (95% CI -0.18 to 0.54); <math>p = 0.318</math></li> <li>• <math>Q = 2.37</math>, <math>p = 0.499</math>, <math>I^2 = 0.0\%</math></li> <li>• The results showed that the change in lean body mass after intervention did not significantly differ between the leucine group and the control group.</li> </ul> <p><b>Leg lean mass:</b> MA of 3 RCTs (n=107)</p> <ul style="list-style-type: none"> <li>• Note: 2 RCTs (72.9% weight) with participants with diabetes (community dwelling) or bed rest</li> </ul>	<p><b>Authors' conclusions:</b> The findings suggest that either long-term or acute leucine supplementation could increase the muscle protein fractional synthetic rate. However, there is no evidence that leucine supplementation increases lean body mass or leg lean mass.</p> <p><b>Confounding:</b> No detail on confounding or adjustments were provided in the systematic review</p> <p><b>Authors' limitations:</b> The discrepancy among these studies may be due to the differences in the amount of leucine administered, the time of administration and the population studied. Of the studies included in the present meta-analysis, both the levels of leucine and the duration of dosing differed.</p>

Study	Methods	Included studies	Results	Limitations/comments
		<p><b>Statistical analysis:</b></p> <ul style="list-style-type: none"> <li>• Means and standard errors of means summarise before and after intervention measurements.</li> <li>• Heterogeneity assessed using Cochran’s Q statistic with <math>p &lt; 0.1</math> to indicate statistical significance. <math>I^2</math> statistic defined: 0–24%, no heterogeneity; 25–49%, moderate heterogeneity; 50–74%, large heterogeneity; 75–100 %, extreme heterogeneity.</li> <li>• If heterogeneity existed between studies (a Q statistic with <math>P &lt; 0.1</math> or <math>I^2 &gt; 50\%</math>), then use of random-effects model (DerSimonian–Laird method). Otherwise, fixed-effects model used (Mantel–Haenszel method).</li> </ul> <p><b>Evaluation of study quality:</b></p> <ul style="list-style-type: none"> <li>• Cochrane risk of bias tool, funnel plot could not be used owing to the small number of studies.</li> <li>• All studies evaluated as having a low risk of bias and being of high quality.</li> </ul>	<p>(hospitalised); all 3 RCTs considered longer-term interventions from 10 d to 6 m</p> <ul style="list-style-type: none"> <li>• fixed and random effects model: SMD 0.006 (95% CI -0.32 to 0.44); <math>p = 0.756</math></li> <li>• <math>Q = 0.59</math>, <math>p = 0.752</math>, <math>I^2 = 0.0\%</math></li> <li>• There was no significant difference in change in leg lean mass after intervention between the subjects treated with leucine or placebo.</li> </ul> <p><b>Sensitivity analysis</b> carried out by removing 1 study at a time from analysis concluding that no 1 study influenced the findings.</p>	

## Annex 4.4 – Mapping tables: primary studies included in meta-analysis/systematic reviews

The primary studies included within each systematic review or meta-analysis have been mapped to establish overlap. These are tabled below grouped by outcome: musculoskeletal health (Table 4.4.1) and cardiovascular events, cancer, all-cause mortality and weight change (Table 4.4.2).

**Table 4.4.1 Mapping of primary studies from SR/MA with musculoskeletal health as outcome**

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
Abe (2014)	observational	ns									X																			1
Agergaard (2015)	RCT	17	X																											1
Al Snih (2007)	PCS, USA	12725																								X				1
Aleman-Mateo (2014)	RCT	98																				X								1
Alexandre (2014)	observational	ns									X																			1
Alves (2013)	RCT, Brazil	25		X																										1
Annweiler (2010)	observational	ns									X																			1
Arnarson (2013)	RCT, Iceland	141								X																				1
Asp (2012)	observational	ns									X																			1
Atkins (2014)	PCS, UK	3328														X														1
Atlantis (2010)	PCS, Australia	1000																								X				1
Bartali (2006)	XS, Italy	802					X							X		X														3
Bastos-Barbosa (2012)	XS	ns													X															1
Bea (2017)	PCS, USA	73168																							X					1
Beasley (2010)	PCS, USA	24,417					X									X														2
Bell (2017)	RCT	99																				X								1



PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																										
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap
Berdot (2009)	PCS, France	6343																						X					1
Berggren (2008)	RCT, Sweden	199																								X		X	2
Bergland (2003)	PCS, Norway	307																						X					1
Bermon (1998)	RCT, France	16		X																									1
Berraho (2010)	PCS, France	3646																									X		1
Berrington (2010)	PCS	28466																									X		1
Berry (2015)	RCT	15																			X								1
Bhurtun (2012)	PCS, Finland	434																						X					1
Bischoff (2003)	RCT, Switzerland	122																							X		X		2
Bischoff (2006)	RCT	64																									X		1
Bischoff-Ferrari (2012)	RCT	20																	X										1
Bjorkman (2011)	RCT																											X	2
Blain (2010)	PCS, France	1300																									X		1
Blaum (2005)	XS	ns												X															1
Bollwein (2012)	XS, Germany	192			X		X							X		X		X		X									6
Bollwein (2013)	XS, Germany	194												X															1
Bongue (2011)	PCS, France	1759																						X					1
Bonnefoy (2003)	RCT, France	62														X													1
Brady (2014)	observational	ns									X																		1
Breeze (2006)	PCS, UK	4862																									X		1
Broe (2017)	RCT	48																									X		1
Burleigh (2007)	RCT, UK	203																							X		X		2
Bunout (2001)	RCT	98						X																					1
Bunout (2004)	RCT, Chile	101	X												X														2

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
Carlsson (2011)	RCT	94																					X							1
Castenada (1995)	RCT	12																				X								1
Castenada (2000)	RCT, USA	12															X													1
Ceglia (2013)	RCT	21																	X											1
Chalé (2013)	RCT, USA	75/80						X (80)		X (75)																				2
Chan (2013)	PCS, Hong Kong	2735				X									X															2
Chan (2015)	PCS, Hong Kong	2724										X		X						X										3
Chan (2016)	PCS, Hong Kong	2948/3967			X 3967															X 2948										2
Chanet (2017)	RCT	24																				X								1
Chapuy (2002)	RCT, France	583																							X		X			2
Chung (2013)	observational	ns									X																			1
Clemson (2015)	PCS, Australia	1000																						X						1
Cornish (2009)	RCT	51						X																						1
Corrada (2006)	PCS, USA	13451																								X				1
Dahl (2013)	PCS, Sweden	882																								X				1
Dawson-Hughes (2002)	RCT, USA	342															X													1
Dawson-Hughes (2004)	RCT, USA	32															X													1
De Oliveira (2016)	RCT	20																			X									1
Decullier (2010)	PCS, France	7396																						X						1
Del Favero (2012)	RCT, Brazil	18		X																										1

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
Delmonico (2009)	XS	ns									X																			1
Deutz (2011)	RCT	24																										X	1	
Deutz (2013)	RCT, USA	18/19		X (18)				X (19)																						2
Devine (2016)	PCS, Australia	1077															X													1
Dey (2001)	PCS, Sweden	2590																								X				1
Dhesi (2004)	RCT, UK	139																	X						X		X			3
Dillon (2009)	RCT	14		X				X														X	X					X		5
Dolan (2007)	PCS, USA	8029																								X				1
Doré (2015)	PCS, USA	1619																							X					1
Dretakis (2010)	observational	ns									X																			1
Dupuy (2013)	XS	ns									X																			1
Eggebeen (2016)	RCT	20																			X									1
Endeshaw (2009)	XS	ns												X																1
Estruch (2013)	RCT, Spain	7447													X															1
Faulkner (2009)	PCS, USA	8329																							X					1
Feart (2011)	PCS, France	1179																		X										1
Ferrando (2010)	RCT, USA	22		X (21)						X (22)																				2
Figueiredo (2014)	XS	ns									X																			1
Flakoll (2004)	RCT	57						X																						1
Flicker (2005)	RCT, Australia	625																							X		X			2
Flicker (2010)	PCS, Australia	9240																								X				1
Flynn (1999)	RCT, USA	39		X																										1
Fougère (2016)	XS, Italy	304			X													X												2

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
Gale (2007)	PCS, UK	348																								X				1
Garcia-Esquinas (2016)	PCS, Spain	2198										X																		1
Gardener (2011)	PCS, USA	2568													X															1
Gariballa (2013)	observational	ns									X																			1
Gassmann (2009)	PCS, Germany	622																							X					1
Geirsdottir (2013)	observational	ns									X																			1
Gilchrist (2013)	RCT	27																			X									1
Gilchrist (2014)	RCT	27																			X	X								2
Glendenning (2012)	RCT, Australia	see (n)																							X		X		3	
Gomez (2017)	PCS, Canada	1662																							X					1
Graafmans (1996)	RCT	354																									X			1
Grabowski (2001)	PCS, USA	7527																								X				1
Grady (1991)	RCT	98																	X											1
Granic (2016)	PCS, UK	791			X																									1
Grant (2005)	RCT	2643																									X			1
Gregorio (2014)	XS, USA	387				X																								1
Gualano (2014)	RCT, Brazil	30	X																											1
Gulsvik (2009)	PCS, Norway	788																								X				1
Halil (2014)	observational	ns									X																			1
Hannan (2000)	PCS, USA	615															X													1
Harwood (2004)	RCT, UK	64																							X		X			2
Hashemi (2015)	XS, Iran	300			X																				X		X			1
Himes (2011)	PCS, USA	10755																						X						1

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																										
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap
Hirsch (2006)	XS	ns													X														1
Hooker (2016)	PCS, USA	5834																							X				1
Houston (2008)	PCS, USA	2066															X												1
Hubbard (2010)	XS	ns													X														1
Hwang (2012)	observational	ns									X																		1
Ikeda (2016)	RCT								X																				2
Isanejad (2016)	PCS, Finland	381				X																							1
Ispoglou (2016)	RCT	16																				X	X						2
Jakobi (2001)	RCT, Canada	12		X																									1
Janssen (2007)	PCS, USA	4968																									X		1
Janssen (2008)	PCS, USA	4982																									X		1
Janssen (2010)	RCT	70																	X										1
Jürschik (2012)	XS	ns													X														1
Kalula (2016)	PCS, South Africa	632																							X				1
Karckainen (2010)	RCT, Finland	3139																								X		X	2
Katsanos (2006)	RCT	20																										X	1
Keller (2005)	PCS, Canada	539																									X		1
Kelly (2013)	RCT	12																			X								1
Kemmner (2017)	RCT	17																			X								1
Kenjale (2011)	RCT	8																			X								1
Kenny (2003)	RCT	65																											1
Kerstetter (2015)	RCT, USA	208		X																			X						2
Kiely (2015)	PCS, USA	736																							X				1
Kim (2012)	RCT	78/155						X															X						2

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
								155																78						
Kobayashi (2013)	XS, Japan	2108					X							X		X														3
Kobayashi (2017)	XS, Japan	2108					X																							1
Kobayashi (2014)	XS, Japan	2121												X																1
Kojima (2012)	PCS, Japan	165																							X					1
Kojima (2015)	PCS, Japan	575			X																									1
Koopman (2006)	RCT	8																										X	1	
Koopman (2008)	RCT	8																										X	1	
Kukuljan (2009)	RCT	86																				X								1
Kulminski (2008)	PCS, USA	4791																								X				1
Kvamme (2012)	PCS, Norway	16711																								X				1
Kwan (2012)	PCS, Taiwan	280																						X						1
Lagari (2013)	RCT	86																		X										1
Lana (2015)	PCS, Spain	1871										X																		1
Landi (2012)	observational	ns									X																			1
Landi (2013)	observational	ns									X																			1
Larocque (2015)	PCS, USA	4645				X																								1
Larsen (2005)	RCT, Denmark	4607																							X		X			2
Latham (2003)	RCT	224																									X			1
Law (2006)	RCT, UK	3717																							X		X			2
Leclerc (2009)	PCS, Canada	868																						X						1
Leenders (2011)	RCT, The Netherlands	57								X																		X		2
Leenders (2012)	RCT	141																					X							1
León-Muñoz (2014)	PCS, Spain	1815			X							X								X										3

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
León-Muñoz (2015)	PCS, Spain	1872			X										X															2
Lin (2016)	PCS, Taiwan	953																						X						1
Lips (2010)	RCT	593																	X											1
Luukinen (1996)	PCS, Finland	788																						X						1
Malmivaara (1993)	PCS, Finland	2437																						X						1
Markofski (2018)	RCT	24																				X								1
Martin (2011)	XS, UK	628			X																									1
Masel (2014)	XS	ns												X																1
Matteini (2008)	XS, USA	703												X																1
Mazza (2007)	PCS, Italy	1275																								X				1
McAuley (2011)	PCS, USA	981																								X				1
McTigue (2006)	PCS, USA	18651																								X				1
Meijers (2012)	PCS, The Netherlands	2971																						X						1
Meng (2009)	PCS, Australia	862															X													1
Michelon (2006)	XS, USA	754												X	X															2
Milaneschi (2011)	PCS, Italy	705			X								X																	2
Miller (2002)	PCS, Australia	1396																								X				1
Miller (2012)	RCT	8																			X									1
Misra (2011)	PCS, USA	946															X													1
Mitchell (2017)	RCT	29																				X								1
Nanri (2018)	XS, Japan	5638					X																							1
Neelemaat (2012)	RCT, The Netherlands	204																							X		X			2

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
Neville (2013)	RCT	80											X																	1
Ng (2015)	PCS, Singapore								X																					1
Nikolov (2016)	XS, Germany	1509			X																									1
Norton (2016)	RCT	60																				X								1
O'Loughlin (1993)	PCS, Canada	409																						X						1
Oh (2014)	XS, Korea	1435			X																									1
Ottenbacher (2009)	PCS	ns													X															1
Perala (2016)	PCS, Finland	1072			X																									1
Percheron (2003)	RCT, France	280		X																										1
Perez-Tasigchana (2016)	PCS, Spain	2376, 1911																X												1
Pfeifer (2000)	RCT, Germany	148																							X		X			2
Pfeifer (2009)	RCT	242																	X								X			2
Pirotta (2015)	RCT	26																	X											1
Pluijm (2006)	PCS, The Netherlands	1365																						X						1
Presley (2011)	RCT	14																			X									1
Price (2006)	PCS, UK	9984																								X				1
Prince (2008)	RCT, Australia	302																							X		X			2
Promislow (2002)	PCS, USA	572															X													1
Queiroz (2014)	observational	ns									X																			1
Rabassa (2015)	PCS, Italy	769										X		X																2
Radavelli-Bagatini (2013)	XS	1456											X																	1



PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
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Rahi (2016)	XS, Canada	1345				X	X							X		X														4
Rahi (2017)	PCS, France	560																		X										1
Rapuri (2003)	PCS, USA	92															X													1
Rawson (2000)	RCT, USA	17		X																										1
Reis (2009)	PCS, USA	3748																								X				1
Reyez-Ortiz (2004)	PCS, USA	1391																						X						1
Robinson (2008)	XS, UK	2983			X																									1
Rodríguez-Molinero (2015)	PCS, Spain	520																						X						1
Rondanelli (2014)	observational	ns									X																			1
Rydwik (2008)	RCT, Sweden	166							X				X																	2
Sai (2010)	PCS, USA	137																						X						1
Sanders (2010)	RCT, Australia	2256																							X		X			2
Sandoval-Insusti (2016)	PCS, Spain	1822					X					X																		2
Sato (2005)	RCT, Japan	96																							X		X			2
Schilp (2013)	RCT	146											X																	1
Schnittger (2012)	XS	ns												X																1
Scognamiglio (2004)	RCT, Italy	95		X																										1
Scott (2017)	PCS, Australia	1486																						X						1
Sellmeyer (2001)	PCS, USA	742															X													1
Semba (2006)	PCS, USA	766												X	X															2
Seo (2013)	observational	ns									X																			1
Shahar (2012)	PCS, USA	1201			X								X																	2
Sheehan (2013)	PCS, Ireland	606																						X						1

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
Shikany (2014)	XS, USA	5925					X																							1
Shikany (2014)	PCS, USA	5925					X							X																2
Sieber (2014)	observational	ns									X																			1
Siervo (2016)	RCT	19																			X									1
Smee (2015)	XS, Australia	171			X																									1
Smith (2007)	RCT, UK	9440																							X		X			2
Smoliner (2014)	observational	ns									X																			1
Songpatanasilp (2009)	RCT	72																		X										1
Sreekumaran Nair (2006)	RCT, USA	144		X																										1
Stalenhoef (2002)	PCS, The Netherlands	287																						X						1
Stessman (2009)	PCS, Israel	2408																								X				1
Stout (2013)	RCT, USA	43/98		X (43)				X (98)																						2
Struijk (2018)	PCS, Spain	1630																X		X										2
Sun (2016)	PCS, USA	7609																							X					1
Szanton (2009)	XS	ns													X															1
Talegawkar (2012)	PCS, Italy	690			X							X				X				X										4
Tayback (1990)	PCS, USA	2568																								X				1
Ten Haaf 2018	XS, The Netherlands	140				X																								1
Tieland, Dirks et al (2012)	RCT, The Netherlands	62						X		X																				2

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
Tieland, Rest et al (2012)	RCT, The Netherlands	65		X				X		X (61)													X							4
Tinetti (1988)	PCS, USA	336																						X						1
Trivedi (2003)	RCT, UK	2038																							X		X		2	
Uusi-Rasi (2015)	RCT	409	X																										1	
Vellas (1998)	PCS, USA	482																						X					1	
Verdijk (2009)	RCT, The Netherlands	26								X																			1	
Verhoeven (2009)	RCT, The Netherlands	29/30		X (30)						X (29)																			2	
Verlaan (2015)	Case-control, UK	136				X																							1	
Villareal (2006)	RCT, USA	56		X																									1	
Villareal (2011)	RCT, USA	53											X																1	
Visscher (2004)	PCS, Finland	1559																								X			1	
Volpato (2014)	observational	ns									X																		1	
Von Heideken Wågert (2009)	PCS, Sweden	109																						X					1	
Vukovich (2001)	RCT	31						X																					1	
Wee (2011)	PCS, USA	20975																								X			1	
Wengreen (2004)	Case-control, USA	2501															X												1	
Wiroth (2001)	RCT, France	14		X																									1	
Witham (2010)	RCT	105																									X		1	
Woo (2009)	PCS, China	4000																						X					1	
Wood (2014)	RCT	305																	X										1	
Woods (2005)	PCS	ns												X															1	

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS																											
First author, year	Study design, country (where stated in review)	Sample size	Antoniak (2017)	Beaudart (2018)	Bloom (2018)	Coelho-Junior (2018a)	Coelho-Junior (2018b)	Cruz-Jentoft (2014)	Dedeyne (2017)	Dewansingh (2018)	Egiseer (2016)	Feng (2017)	Gine-Garriga (2015)	Lorenzo-Lopez (2017)	Mello (2014)	Nowson (2018)	Pedersen (2014)	Roman-Vinas (2018)	Rosendahl-Riise (2017)	Silva (2018)	Stanaway (2017)	Ten Haaf (2018)	Tieland (2017)	Trevisan (2018)	Tricco (2017)*	Winter (2014)	Wu (2017)	Xu (2015)	Overlap	
Wu (2009)	XS	ns													X															1
Wu (2014)	observational	ns									X																			1
Xia (2009)	RCT	142																	X											1
Xu (2012)	XS, USA	2132			X																									1
Xu (2015)	PCS, China	447																							X					1
Yokoyama (2017)	PCS, Japan	781, 772			X																									1
Yu (2014)	observational	ns									X																			1
Zbeida (2014)	XS, Israel	2791; 1786			X													X		X										3
Zhu (2010)	RCT	302																	X											1
Zhu (2015)	RCT, Australia	196		X																		X	X							3
Zoltick (2011)	PCS, USA	807															X													1
Zunzunegui (2012)	PCS, SPAIN	1008																								X				1

\*Tricco (2017) included 283 primary studies in total. Only those primary studies that were also included in the other reviews are noted here.

**Table 4.4.2 Mapping of primary studies from SR/MA for cardiovascular events and risk factors, cancer, all-cause mortality outcomes and weight change**

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS							Overlap
First author (year)	Study design, country	Sample size	Dewansingh (2018)	Govindaraju (2018)	Milne (2006)	Pedersen (2014)	Ruxton (2016)	Stanaway (2017)	Tyrovolas (2010)	
Bates (2010)	PCS, UK	1100				X				1
Berry (2015)	RCT	15						X		1
Bingham (2003)	PCS, European countries	ns							X	1
Bjorkman, 2012	RCT, Finland	103	X							1
Broqvist (1994)	RCT	22			X					1
Chalé (2013)	RCT, USA	75	X							1
De Oliveira (2016)	RCT	20						X		1
Dontas (2007)	XS	ns							X	1
Edington (2004)	RCT	100			X					1
Eggebeen (2016)	RCT	20						X		1
Eneroth (2004)	RCT	53			X					1
Ferrando (2010)	RCT, USA	22	X							1
Ford (2014)	XS, USA	4009		X						1
Gilchrist (2013)	RCT	27						X		1
Gopinath (2014)	PCS, Australia	895		X						1
Gray-Donald (1995)	RCT	50			X					1
Hampson (2003)	RCT	51			X					1
Haveman-Nies (2002)	PCS, European countries	1281							X	1
Haveman-Nies (2003)	PCS, Europe	480		X						1
Jenab (2004)	PCS, European countries	ns							X	1
Kelly (2013)	RCT	12						X		1
Kemmner (2017)	RCT	17						X		1
Kenjale (2011)	RCT	8						X		1
Key (2004)	PCS, European countries	ns							X	1
Knoops (2004)	PCS, European countries	2339							X	1

PRIMARY STUDY			SYSTEMATIC REVIEW/META-ANALYSIS							Overlap
First author (year)	Study design, country	Sample size	Dewansingh (2018)	Govindaraju (2018)	Milne (2006)	Pedersen (2014)	Ruxton (2016)	Stanaway (2017)	Tyrovolas (2010)	
Leenders (2011)	RCT, The Netherlands	57	X							1
Miller (2004)	PCS, European countries	ns							X	1
Miller (2012)	RCT	8						X		1
Milte (2015)	PCS, Australia	2457		X						1
Mosher (2009)	XS, USA, UK, Canada	641		X						1
Norat (2005)	PCS, European countries	ns							X	1
Panagiotakos (2007)	PCS, Mediterranean countries	1190							X	1
Perez-Tasigchana (2016a)	PCS, Spain	2376		X						1
Perez-Tasigchana (2016b)	PCS, Spain	1911		X						1
Presley (2011)	RCT	14						X		1
Price (2005)	RCT	136			X					1
Sameiri (2008)	XS, France	1724		X						1
Sarris (2012)	RCT	182					X			1
Schlesinger (2014)	XS, Germany	1389		X						1
Shepherd (2016)	RCT	15						X		1
Siervo (2016)	RCT	19						X		1
Steiner (2003)	RCT	85			X					1
Tieland (2012)	RCT, The Netherlands	61	X							1
Tieland (Dirks (2012)	RCT, The Netherlands	62	X							1
Trabal, 2015	RCT, Spain	30	X							1
Verhoeven (2009)	RCT, The Netherlands	29	X							1
Veronese (2016)	XS, USA	4470		X						1
Woo (2010)	XS, Hong Kong	3378		X						1
Wouters-Wesseling (2003)	RCT	101			X					1
Zaragoza-marti (2018)	PCS, Spain	351		X						1

## Annex 4.5 – AMSTAR 2 assessment

Table 4.5.1 AMSTAR 2 assessment of systematic reviews and meta-analyses (rows in grey are AMSTAR 2 critical domains)

	Antoniak & Greig 2017	Beaudart 2017	Bloom 2018	Coelho-Júnior 2018a	Coelho-Júnior 2018b	Cruz-Jentoft 2014	Dedeyne 2017	Dewansingh 2018	Eglseer 2016	Feng 2017
1. PICO <sup>1</sup>	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Protocol	P/Y	N	P/Y	N	N	N	P/Y	N	N	P/Y
3. Study design <sup>2</sup>	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
4. Search strategy <sup>*3</sup>	P/Y	P/Y	P/Y	Y	Y	P/Y	Y	P/Y	Y	Y
5. Study selection duplicate	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
6. Data extraction in duplicate	Y	N	Y	Y	Y	N	Y	Y	N	Y
7. Excluded studies	N	N	N	N	N	N	Y	N	N	N
8. Included studies	P/Y	Y	P/Y	P/Y	P/Y	P/Y	P/Y	Y	N	P/Y
9. Risk of bias tool*	Y	Y	Y	P/Y	P/Y	N	Y	Y	P/Y	P/Y
10. Funding of included studies	N	Y	N	Y	Y	N	N	N	N	N
11. Statistical analysis*	N	N	N/A	N	Y	N/A	N/A	N	N/A	N/A
12. Impact of RoB assessed	N	N	N/A	Y	Y	N/A	N/A	Y	N/A	N/A
13. RoB discussed*	Y	Y	Y	Y	Y	N	Y	Y	N	Y
14. Heterogeneity discussed	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
15. Publication bias investigated*	Y	N	N/A	N	Y	N	N/A	Y	N/A	N/A
16. Conflict of interest declared	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Overall confidence rating</b>	<b>LOW</b>	<b>CRITICALLY LOW</b>	<b>MODERATE</b>	<b>LOW</b>	<b>MODERATE</b>	<b>CRITICALLY LOW</b>	<b>MODERATE</b>	<b>LOW</b>	<b>LOW</b>	<b>MODERATE</b>

	<b>Gine-Garriga 2015</b>	<b>Govindaraju 2018</b>	<b>Lorenzo-Lopez 2017</b>	<b>Mello 2014</b>	<b>Milne 2006</b>	<b>Nowson 2018</b>	<b>Pedersen 2014</b>	<b>Roman-Vinas 2018</b>	<b>Rosendahl-Rise 2017</b>
1. PICO <sup>1</sup>	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Protocol	N	P/Y	N	N	P/Y	N	P/Y	N	P/Y
3. Study design <sup>2</sup>	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
4. Search strategy <sup>*3</sup>	N	Y	P/Y	P/Y	P/Y	P/Y	P/Y	N	Y
5. Study selection duplicate	Y	Y	Y	Y	Y	Y	Y	N	Y
6. Data extraction in duplicate	Y	Y	N	Y	Y	Y	N	N	N
7. Excluded studies	N	N	Y	N	N	N	Y	N	N
8. Included studies	P/Y	P/Y	P/Y	N	Y	P/Y	Y	P/Y	P/Y
9. Risk of bias tool*	P/Y	P/Y	P/Y	Y	Y	Y	Y	N	Y
10. Funding of included studies	N	N	Y	N	Y	N	N	N	N
11. Statistical analysis*	Y	N/A	N/A	N/A	Y	N/A	N/A	N/A	Y
12. Impact of RoB assessed	N	N/A	N/A	N/A	Y	N/A	N/A	N/A	N
13. RoB discussed*	Y	N	N	Y	Y	Y	Y	N	N
14. Heterogeneity discussed	Y	Y	N	Y	Y	Y	N	N	Y
15. Publication bias investigated*	N	N/A	N/A	N/A	Y	N/A	N/A	N/A	N
16. Conflict of interest declared	Y	Y	Y	N	Y	Y	Y	Y	Y
<b>Overall confidence rating</b>	<b>LOW</b>	<b>LOW</b>	<b>LOW</b>	<b>LOW</b>	<b>HIGH</b>	<b>MODERATE</b>	<b>MODERATE</b>	<b>CRITICALLY LOW</b>	<b>CRITICALLY LOW</b>



	Ruxton 2016	Silva 2018	Stanaway 2017	Ten Haaf 2018	Tieland 2017	Trevisan 2018	Tricco 2017	Tyrovolas 2010	Winter 2014	Wu 2017	Xu 2015
1. PICO <sup>1</sup>	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Protocol	N	Y	N	N	Y	N	Y	N	N	N	N
3. Study design <sup>2</sup>	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
4. Search strategy <sup>*3</sup>	N	Y	Y	P/Y	P/Y	P/Y	Y	N	Y	Y	P/Y
5. Study selection duplicate	N	Y	N	Y	N	N	Y	N	Y	Y	Y
6. Data extraction in duplicate	N	Y	Y	Y	N	Y	Y	N	N	Y	Y
7. Excluded studies	N	N	N	N	Y	N	N	N	N	N	Y
8. Included studies	P/Y	P/Y	P/Y	P/Y	Y	P/Y	Y	Y	P/Y	P/Y	Y
9. Risk of bias tool*	P/Y	Y	P/Y	Y	Y	Y	N	N	N	N	Y
10. Funding of included studies	N	N	N	N	N	N	N	N	N	N	N
11. Statistical analysis*	N/A	Y	N/A	Y	Y	Y	Y	N/A	Y	Y	Y
12. Impact of RoB assessed	N/A	Y	N/A	Y	Y	Y	Y	N/A	N	N	Y
13. RoB discussed*	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y
14. Heterogeneity discussed	N	Y	Y	Y	N	Y	Y	N	Y	Y	Y
15. Publication bias investigated*	N/A	Y	N/A	Y	Y	Y	Y	N/A	Y	Y	N
16. Conflict of interest declared	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
<b>Overall confidence rating</b>	<b>LOW</b>	<b>MODERATE</b>	<b>MODERATE</b>	<b>MODERATE</b>	<b>MODERATE</b>	<b>MODERATE</b>	<b>MODERATE</b>	<b>CRITICALLY LOW</b>	<b>CRITICALLY LOW</b>	<b>CRITICALLY LOW</b>	<b>LOW</b>

N = no; N/A = not applicable; P/Y = partial yes; Y = yes

\* AMSTAR 2 critical domain

<sup>1</sup> PICO- population, intervention, control group, outcome

<sup>2</sup> Considered this was not applicable since RCTs are preferable to other type of study designs

<sup>3</sup> Marked as 'yes' if met the following: searched 2 databases; provided key word and/or search strategy; searched reference lists of included studies; searched trial/study registries/conducted search within 24 months of completion of the review.

## Annex 4.6 – Exposures and outcomes considered by meta-analysis/systematic reviews

	Mortality	Musculoskeletal health	Cardiovascular health	Cancers	Immune health	Weight change	Quality of life
<b>Dietary patterns</b>							
<b>Healthy diet</b>	Tyrovolas 2010	Bloom 2018 Feng 2017 Gine-Garriga 2015 Lorenzo-López 2017	Nowson 2018 Tyrovolas 2010	Tyrovolas 2010 (cancers)			Govindaraju 2018
<b>Mediterranean diet</b>	Tyrovolas 2010	Gine-Garriga 2015 Lorenzo-López 2017 Nowson 2018 Roman-Vinas 2018 Silva 2018 Feng 2017	Nowson 2018 Tyrovolas 2010	Tyrovolas 2010 (cancers)			Govindaraju 2018
<b>Food</b>							
<b>Fish</b>		Feng 2017	Tyrovolas 2010				
<b>Fruit and vegetables</b>		Feng 2017 Gine-Garriga 2015	Nowson 2018 Tyrovolas 2010				
<b>Dairy</b>		Feng 2017 Gine-Garriga 2015	Tyrovolas 2010				
<b>Energy</b>	Milne 2006	Milne 2006				Milne 2006	

	Mortality	Musculoskeletal health	Cardiovascular health	Cancers	Immune health	Weight change	Quality of life
<b>Macronutrients</b>							
<b>Protein</b>		Beudart 2018 Coelho-Júnior 2018a & 2018b Cruz-Jentoft 2014 Dedeyne 2017 Dewansigh 2018 Eglseer 2016 Lorenzo-López 2017 Milne 2016 Nowson 2018 Pedersen 2014 ten Haaf, 2018 Tieland 2017 Xu 2015				Dewansigh 2018 Milne 2006	
<b>Essential amino acid supplements (and HMB)</b>		Beudart 2018 Cruz-Jentoft 2014 Tieland 2017 Xu 2015					

	Mortality	Musculoskeletal health	Cardiovascular health	Cancers	Immune health	Weight change	Quality of life
<b>Micronutrients</b>							
Micronutrients		Lorenzo-López 2017	Ruxton 2016		Ruxton 2016		Ruxton 2016
Individual fatty acids		Cruz-Jentoft 2014			Ruxton 2016		
Vitamin D		Antoniak 2017 Rosendahl-Riise 2017 Tricco 2017 Wu & Pang 2017					
Dietary nitrate supplementation		Stanaway 2017	Stanaway 2017				
Dietary antioxidant capacity		Lorenzo-López 2017					
<b>Health Status</b>							
Weight (e.g. BMI, overweight, underweight)	Winter 2014	Eglseer 2016 Mello 2014 Trevisan 2018					
<b>Interventions</b>							
Nutritional advice (education/ counselling)		Dedeyne 2017					

## Annex 4.7 – Summary of the evidence from the individual systematic reviews and meta-analyses for each outcome

**Table 4.7.1 – Evidence on mortality provided by included systematic reviews**

Author (n=2)	Mortality
<b>BMI</b>	
Systematic review with meta-analysis	
Winter et al (2014)	↑ (32 PCS) <sup>1</sup>
<b>PROTEIN AND ENERGY</b>	
Systematic review with meta-analysis	
Milne et al (2006)	– (8 RCTs)
<b>DIETARY PATTERNS</b>	
Systematic review without meta-analysis	
Tyrovolas and Panagiotakos (2010)	<b>Mixed</b> (2 PCS) <sup>2</sup>

Direction of effect/association for reported outcomes:

↑ increased; ↓ decreased; – no effect/association

<sup>1</sup> Greater risk of mortality in those with a lower and a higher BMI (lowest risk observed between BMI of approximately 25 and 30 kg/m<sup>2</sup>).

<sup>2</sup> Measured 'diet quality' or Mediterranean diet score. Significant association between a high Mediterranean diet score and mortality, no association between diet quality and mortality.

**Table 4.7.2 – Evidence on musculoskeletal health outcomes provided by included systematic reviews**

Author (n=26)	Sarcopenia (n=1)	Muscle Strength (n=12)	Muscle Mass (n=12)	Physical Performance (n=11)	Frailty (n=10)	Bone Health (n=2)	Risk of Fracture (n=2)	Risk of Falls (n=5)	Recurrent Falls (n=1)
<b>BMI</b>									
<b>Systematic review with meta-analysis</b>									
Trevisan et al (2018)								↓ (36 PCS)	– (23 PCS)
<b>Systematic review without meta-analysis</b>									
Eglseer et al (2016)		↑ (12 CSS)	↑ (12 CSS)	↑ (12 CSS)					
Mello, et al (2014)					Unclear <sup>1</sup> (4 PCS + 10 CSS)				

Author (n=26)	Sarcopenia (n=1)	Muscle Strength (n=12)	Muscle Mass (n=12)	Physical Performance (n=11)	Frailty (n=10)	Bone Health (n=2)	Risk of Fracture (n=2)	Risk of Falls (n=5)	Recurrent Falls (n=1)
<b>PROTEIN</b>									
<b>Systematic review with meta-analysis</b>									
Beudart et al (2018)		– (2 to 6 RCTs)	– (2 to 4 RCTs)	– (2 RCTs)					
Dewansigh et al (2018)		– (6 RCTs)	– (8 RCTs)						
Ten Haaf et al (2018)		– (3 to 7 RCTs)	– (10 RCTs)	– (7 RCTs)					
Tieland et al (2017)		– (3-6 RCTs)	– (8 RCTs)						
Xu et al (2015)			<b>Unclear</b> <sup>2</sup> (3-4 RCTs)						
Milne et al (2016)			– (6 RCTs)						
Coelho-Junior et al (2018a)		<b>Unclear</b> <sup>3</sup> (few PCS/CSS/CCS)		<b>Unclear</b> <sup>4</sup> (few PCS/CSS/CCS)					

Author (n=26)	Sarcopenia (n=1)	Muscle Strength (n=12)	Muscle Mass (n=12)	Physical Performance (n=11)	Frailty (n=10)	Bone Health (n=2)	Risk of Fracture (n=2)	Risk of Falls (n=5)	Recurrent Falls (n=1)
Coelho-Junior et al (2018b)					↓ (4 CSS)				
<b>Systematic review without meta-analysis</b>									
Dedeyne et al (2017)		↑ (1 RCT)	↑ (1 RCT)	↑ (3 RCTs)	↓ <sup>5</sup> (1 RCT)				
Cruz-Jentoft et al (2014)			– <sup>6</sup> (1-4 RCTs)	– (1-4 RCTs)					
Pedersen & Cederholm (2014)			↑ (1 RCT + 1 PCS)			<b>Unclear</b> <sup>7</sup> (few RCTs/PCS)	<b>Unclear</b> <sup>8</sup> (1 PCS)	– (2 PCS)	
Nowson et al (2018)		– (1 RCTs)	– (1 RCTs)		↓ (1 PCS + 3 CSS)		– (1 RCT)	– (1 RCT)	
Lorenzo-Lopez et al (2017)					<b>Unclear</b> <sup>9</sup> (1 PCS + 4 CSS)				
Egiseer et al (2016)	<b>Unclear</b> <sup>10</sup> (2 PCS + 4 CSS)								



Author (n=26)	Sarcopenia (n=1)	Muscle Strength (n=12)	Muscle Mass (n=12)	Physical Performance (n=11)	Frailty (n=10)	Bone Health (n=2)	Risk of Fracture (n=2)	Risk of Falls (n=5)	Recurrent Falls (n=1)
<b>PROTEIN AND EXERCISE</b>									
<b>Systematic review with meta-analysis</b>									
Dewansigh et al (2018)			– (4 RCTs)						
Ten Haaf et al (2018)		– (10-16 RCTs)	– (8 RCTs)	– (7 RCTs)					
<b>Systematic review without meta-analysis</b>									
Dedeyne et al (2017)		↑ (1 RCT)	↑ (1 RCT)	Unclear <sup>11</sup> (1 RCT)					
Nowson et al (2018)		Unclear <sup>12</sup> (7 RCTs)	Unclear <sup>13</sup> (7 RCTs)						
<b>VITAMIN D</b>									
<b>Systematic review with meta-analysis</b>									
Rosendahl-Riise et al (2017)		– (7 RCTs)		↑ (5 RCTs)					
Wu & Pang (2017)								– (6 RCTs)	
Tricco et al (2017)							– <sup>14</sup> (5 to 158 RCTs)	– (6 RCTs)	

Author (n=26)	Sarcopenia (n=1)	Muscle Strength (n=12)	Muscle Mass (n=12)	Physical Performanc e (n=11)	Frailty (n=10)	Bone Health (n=2)	Risk of Fracture (n=2)	Risk of Falls (n=5)	Recurrent Falls (n=1)
<b>VITAMIN D AND CALCIUM</b>									
<b>Systematic review with meta-analysis</b>									
Rosendahl- Riise et al (2017)		– (7 RCTs)							
Wu & Pang (2017)								↓ (14 RCTs)	
Tricco et al (2017)							– (6 RCTs)	↓ (5 RCTs)	
<b>VITAMIN D AND EXERCISE</b>									
<b>Systematic review with meta-analysis</b>									
Antoniak & Greig (2017)		↑ (3 RCTs)		– (2 RCTs)		– (2 RCTs)			

Author (n=26)	Sarcopenia (n=1)	Muscle Strength (n=12)	Muscle Mass (n=12)	Physical Performanc e (n=11)	Frailty (n=10)	Bone Health (n=2)	Risk of Fracture (n=2)	Risk of Falls (n=5)	Recurrent Falls (n=1)
<b>OTHER NUTRITIONAL/ DIETARY INTERVENTIONS</b>									
<b>Systematic review without meta-analysis</b>									
Cruz-Jentoft et al (2014)		− <sup>15</sup> (11 RCTs)	− <sup>16</sup> (11 RCTs)						
Lorenzo- Lopez et al (2017)					↓ <sup>17</sup> (5 PCS + 14 CSS)				
Stanaway et al (2017)				<b>Unclear</b> <sup>18</sup> (11 RCTs)					
<b>DIETARY QUALITY AND PATTERN</b>									
<b>Systematic review with meta-analysis</b>									
Silva et al (2018)	− (1 PCS)				↓ <sup>19</sup> (4 PCS)				
Gine- Garriga et al (2015)				− (3 RCTs + 1 PCS)					

Author (n=26)	Sarcopenia (n=1)	Muscle Strength (n=12)	Muscle Mass (n=12)	Physical Performance (n=11)	Frailty (n=10)	Bone Health (n=2)	Risk of Fracture (n=2)	Risk of Falls (n=5)	Recurrent Falls (n=1)
<b>Systematic review without meta-analysis</b>									
Bloom et al (2018)	<b>Mixed + unclear</b> (1 PCS + 1 CSS) <sup>20</sup>	— <sup>21</sup> (6 PCS + 4 CSS)	↑ <sup>22</sup> (1 PCS + 2 CSS)	↑ <sup>23</sup> (7 PCS + 6 CSS)					
Lorenzo-Lopez et al (2017)					<b>Mixed</b> <sup>24</sup> (5 PCS + 14 CSS)				
Nowson et al (2018)					↓ (2 PCS + 1 CSS)				
Feng et al (2017)					<b>Mixed</b> <sup>25</sup> (1-2 PCS)				
Roman-Vinas & Serra-Majem (2018)				— <sup>26</sup> (2 PCS + 1 CSS)					

PCS: prospective cohort study, CCS: cross sectional study, RCT: randomised controlled trial

Direction of effect/association for reported outcomes: ↑ increased; ↓ decreased; — no effect/ association

Disagreement between studies: Unclear

Heterogeneity resulting in varied outcomes (e.g. looking at different dietary patterns): Mixed

Note: sarcopenia is comprised of low muscle mass and function and low physical ability. Where sarcopenia is the outcome, results are documented for each of these three columns

- <sup>1</sup> Both positive and inverse associations reported.
- <sup>2</sup> No significant difference in lean body mass (4 RCTs) or leg lean mass (3 RCTs) with leucine supplementation, there was a significant improvement in muscle protein fractional synthetic rate significantly increased with leucine supplementation.
- <sup>3</sup> Several outcomes with either no or small significant effects.
- <sup>4</sup> Several outcomes with either no or small significant effects.
- <sup>5</sup> Protein was given with vitamin and mineral supplements.
- <sup>6</sup> 'Some effects' were seen with HMB supplementation but sample size low and stats not reported.
- <sup>7</sup> Range of bone outcomes assessed; based on small number of studies for each outcome and associations seen for women and animal protein but inverse associations for men and vegetable protein, for example.
- <sup>8</sup> Range of bone outcomes assessed; based on small number of studies for each outcome and associations seen for women and animal protein but inverse associations for men and vegetable protein, for example.
- <sup>9</sup> Disagreement in study findings.
- <sup>10</sup> Two studies reported individuals with sarcopenia had significantly lower protein intakes than those without sarcopenia whilst 4 studies found no association.
- <sup>11</sup> Protein supplementation increased function reach test but decreased step score.
- <sup>12</sup> 'some' evidence of an effect from 3 RCTs, no effect found in 4 RCTs.
- <sup>13</sup> 'some' evidence of an effect from 3 RCTs, no effect found in 4 RCTs.
- <sup>14</sup> Meta-analysis of 5 RCTs and network meta-analysis of 158 RCTs.
- <sup>15</sup> No effect of  $\alpha$ -linolenic acid supplementation in combination with resistance exercise training.
- <sup>16</sup> No effect of  $\alpha$ -linolenic acid supplementation in combination with resistance exercise training.
- <sup>17</sup> Inverse associations with low serum carotenoids and alpha-tocopherol (in women), Low micronutrient intake, low antioxidant capacity and resveratrol exposure.
- <sup>18</sup> 1 study found no effect of dietary nitrate and 1 study found an effect.
- <sup>19</sup> Higher Mediterranean diet adherence associated with reduced risk of fragility and inversely associated with functional disability.
- <sup>20</sup> Higher fruit and vegetable lowered sarcopenia in men but not women in 1 PCS and Mediterranean diet lowered sarcopenia in 1 CSS.
- <sup>21</sup> No significant association between 'healthy diet' and muscle strength
- <sup>22</sup> 'Dietary quality' improved muscle mass
- <sup>23</sup> 'Healthier diet' improved multiple metrics of physical performance
- <sup>24</sup> No association with Mediterranean diet score, fruit-veg pattern or meat-fish pattern, significant decrease in fragility with higher intakes of snack-drinks milk products.
- <sup>25</sup> Significantly associated with higher Diet Quality Index, higher fruit/veg consumption and habitual dietary resveratrol and higher Med diet score, negative association with low-fat milk and yoghurt, no association with fruit-veg pattern or meat-fish pattern, no association with other single food or food group.
- <sup>26</sup> No association with Mediterranean diet score.

**Table 4.7.3 – Evidence on cardiovascular health outcomes provided by included systematic reviews**

Author (n=4)	Non-fatal cardiovascular event	Cardiovascular risk factors	Blood pressure	Coronary artery calcification
<b>MEDITERRANEAN DIETARY PATTERN</b>				
Systematic review without meta-analysis				
Nowson et al (2018)	<b>Unclear</b> (1 RCT + 3 PCS) <sup>1</sup>			
Tyrovolas and Panagiotakos (2010)		↓ (2 CSS) <sup>2</sup>		
<b>NITRATE</b>				
Systematic review without meta-analysis				
Stanaway et al (2017)			– (10 RCTs) <sup>3</sup>	
<b>PHYLLOQUINONE</b>				
Systematic review without meta-analysis				
Ruxton et al (2016)				– (1 RCT) <sup>4</sup>

Direction of effect/association for reported outcomes:

↑ increased; ↓ decreased; – no effect/association

Disagreement between studies: **Unclear**

<sup>1</sup> Non-fatal cardiovascular events included ischemic heart disease and stroke. The RCT reported reduced risk of cardiovascular events with daily consumption of nuts or olive oil. One PCS reported reduced CHD but the other two reported no association.

<sup>2</sup> Most aspects of Mediterranean diet reduced CVD risk (high med diet score as well as higher fish and cereal intake. No association with fruit and vegetable intake).

<sup>3</sup> 4 RCTs in healthy participants, 6 either mixed or in participants with CVD risk factors. Nitrate mostly given in the form of beetroot juice. Effects said to be inconsistent, no statistics provided.

<sup>4</sup> Insufficient evidence for SACN to comment on the results

**Table 4.7.4 – Evidence on cancer outcomes provided by included systematic reviews**

Author (n=1)	Colorectal cancer	Colon cancer	Lung cancer	Prostate cancer
<b>DIETARY PATTERNS</b>				
Systematic review without meta-analysis				
Tyrovolas and Panagiotakas (2010)	↓ (1PCS) <sup>1</sup>	↓ (1PCS) <sup>2</sup>	↓ (1PCS) <sup>3</sup>	– (1PCS) <sup>4</sup>

Direction of effect/association for reported outcomes:

↑ increased; ↓ decreased; – no effect/association

<sup>1</sup> From increased fibre and fish intakes

<sup>2</sup> From increased nuts and seeds intake (women only) and reduced red meat intakes

<sup>3</sup> From increased fruit intake (but not vegetables)

<sup>4</sup> From increased fruit and vegetable intake

**Table 4.7.5 – Evidence on immune health outcomes provided by included systematic reviews**

Author (n=1)	Markers of immune health
<b>FATTY ACIDS AND MICRONUTRIENTS</b>	
Systematic review without meta-analysis	
Ruxton et al (2016)	<b>Mixed</b> (9 RCTs) <sup>1</sup>

Heterogeneity in intervention/ exposure resulting in varied outcomes: Mixed

<sup>1</sup> Based on very limited data the systematic review suggests there may be some effects of fatty acids or micronutrients on some aspects of immune health, but not others.

**Table 4.7.6 – Evidence on weight change provided by included systematic reviews**

Author (n=2)	Weight change
<b>PROTEIN</b>	
Systematic review with meta-analysis	
Dewansingh et al (2018)	↑ (8 RCTs) <sup>1</sup>
Milne et al (2006)	↑ (16 RCTs) <sup>2</sup>

Direction of effect/association for reported outcomes:

↑ increased; ↓ decreased; – no effect/association

<sup>1</sup> No information was included in the systematic review about the baseline weight status of study participants, specifically whether they fell into the under- or overweight or obese categories

<sup>2</sup> Information on the baseline health and nutritional status of the study participants varied

**Table 4.7.7 – Evidence on quality of life outcomes provided by included systematic reviews**

Author (n=2)	Quality of life
<b>DIETARY PATTERNS</b>	
Systematic review without meta-analysis	
Govindaraju et al (2018)	<b>Unclear</b> (5 PCS, 7 CSS) <sup>1</sup>
<b>MICRONUTRIENTS</b>	
Systematic review without meta-analysis	
Ruxton et al (2016)	↑ (1 RCT) <sup>2</sup>

Direction of effect/association for reported outcomes:

↑ increased; ↓ decreased; – no effect/association

Disagreement between studies: **Unclear**

<sup>1</sup> Evidence inconsistent, no statistics provided.

<sup>2</sup> Increased self-reported energy levels and enhanced mood



## Annex 5 - Glossary

25-hydroxyvitamin D (25(OH)D)	A metabolite of vitamin D produced in the liver from vitamin D. Circulates in the blood and is a marker of exposure to vitamin D, reflecting vitamin D supply from cutaneous synthesis and the diet.
Alzheimer's Disease	The most common type of dementia, characterised by a slow, progressive deterioration in cognitive function. Problems with day-to-day memory are often noticed first, but other symptoms may include difficulties with word finding, problem solving, decision making or visual perception.
Anabolic resistance	Abnormal response of muscle to previously well-established anabolic stimuli, resulting in reduced muscle mass and strength.
Atherosclerosis	A potentially serious condition where arteries become clogged with fatty deposits called plaques, or atheroma. These deposits are made up of cholesterol, fatty substances, cellular waste products, calcium and fibrin. It can build up in the artery walls and, over time, narrowing them and reducing blood flow.
Atrophic gastritis	Gastritis occurs when the lining of the stomach becomes inflamed after it's been damaged. It is a common condition with a wide range of causes.
Body mass index (BMI)	<p>BMI is used to standardise body weight for different heights.</p> <p>BMI is calculated by weight in kilograms divided by height in metres squared (weight (kg)/height (m<sup>2</sup>)).</p> <p>BMI ranges:</p> <ul style="list-style-type: none"><li>• below 18.5 kg/m<sup>2</sup> – underweight range</li><li>• between 18.5 and 24.9 kg/m<sup>2</sup> – healthy weight range</li><li>• between 25 and 29.9 kg/m<sup>2</sup> – overweight range</li><li>• between 30 and 39.9 kg/m<sup>2</sup> – obese range.</li></ul> <p>(For children and young people aged 2 to 18, the BMI calculation takes into account age and sex as well as height and weight)</p>

Bone mineral content (BMC)	The mass of bone mineral in a skeletal unit (generally measured in grams (g), occasionally in g/cm cross-sectional width).
Bone mineral density (BMD)	The density of bone mineral in a skeletal unit (g/cm <sup>3</sup> ). When measured by single or dual-energy X-ray techniques it represents the mass of bone mineral measured within a scanned area (g/cm <sup>2</sup> ) and is not a true density measurement.
Cardiovascular disease	A general term for conditions affecting the heart or blood vessels. It can be categorised into 3 types: coronary heart disease, cerebrovascular disease or peripheral vascular disease.
Cerebrovascular disease	Includes ischaemic and haemorrhagic stroke, which occurs when the arterial supply to parts of the brain is blocked, or blood escapes from a ruptured blood vessel (cerebral haemorrhage).
Cognitive impairment	Mild cognitive impairment (MCI) is defined as a slight decline in cognitive abilities, including memory and thinking skills, but not to such an extent that it hinders activities of daily living. MCI is not a form of dementia, but a person with MCI is at an increased risk of developing dementia (including Alzheimer's disease).
Confounding variable (confounder)	Associated independently with both the health outcome under study and the exposure of interest. The effect of an association between an exposure and outcome is distorted by the presence of one or more (confounding) variables.
Coronary artery calcification	The accumulation of calcium deposits in the coronary arteries which supply the heart muscle.
Coronary heart disease	A complete or partial narrowing of the coronary arteries which supply the heart muscle. Includes myocardial infarction (MI) and other manifestations of coronary atherosclerosis.
Dementias	Dementia is caused by a variety of diseases and injuries that primarily or secondarily affect the brain. The most common types of dementia are: Alzheimer's disease (AD) (including early-onset AD); vascular dementia; dementia with Lewy bodies; frontotemporal dementia or mixed dementia.

Diabetes	A metabolic disorder involving impaired metabolism of glucose due to either failure of secretion of the hormone insulin, insulin-dependent or type 1 diabetes, OR impaired responses of tissues to insulin, non-insulin-dependent or type 2 diabetes.
Dietary Reference Values (DRVs)	<p>DRVs describe the distribution of nutrient and energy requirements in a population. They comprise:</p> <p><b>Estimated Average Requirement (EAR):</b> half of a group in a population will need more than this amount and half will need less;</p> <p><b>Reference Nutrient Intake (RNI):</b> the intake that will be adequate to meet the needs of 97.5% of the population;</p> <p><b>Lower Reference Nutrient Intake (LRNI):</b> the intake which will meet the needs of only 2.5% of the population.</p>
Doubly labelled water (DLW) method	An isotope-based technique that is considered the gold standard for measuring energy expenditure in free-living individuals.
Dual-energy X-ray absorptiometry (DXA)	A technique used to measure bone mineral density and skeletal muscle mass.
Estimated Average Requirement (EAR)	See Dietary Reference Values
Fixed effects model	A model that calculates a pooled effect estimate using the assumption that all observed variation between studies is caused by the play of chance. Studies are assumed to be measuring the same overall effect.
Frailty	Frailty results in people being less able to adapt to stress factors such as acute illness, injury or changes in their environment, personal or social circumstances. Such changes are more likely to result in adverse health outcomes and loss of independence. Frailty is more common in older age.
Free sugars	All added sugars in any form; all sugars naturally present in fruit and vegetable juices, purées and pastes and similar products in which the structure has been broken down; all sugars in drinks (except for dairy-based drinks); and lactose and galactose added as ingredients.

Hazard ratio (HR)	The hazard ratio is a comparison of the effect of different variables on survival or other outcomes that develop over time.
Heterogeneity	<p>The variation in study outcomes between studies.</p> <p>Heterogeneity is used generically to refer to any type of significant variability between studies contributing to a meta-analysis that renders the data inappropriate for pooling. This may include heterogeneity in diagnostic procedure, intervention strategy, outcome measures, population, study samples, or study methods.</p> <p>The term heterogeneity can also refer to differences in study findings. Statistical tests can be applied to compare study findings to determine whether differences between the findings are statistically significant. For example, significant heterogeneity between estimates of effect from intervention studies suggests that the studies are not estimating a single common effect. In the presence of significant heterogeneity, it is more appropriate to describe the variations in study findings than to attempt to combine the findings into one overall estimate of effect.</p>
International units	Vitamin D intake is expressed in International Units (IU) or in micrograms ( $\mu\text{g}$ ). For vitamin D, 1 microgram is considered equivalent to 40 international units (IU).
Lower Reference Nutrient Intake (LRNI)	See Dietary Reference Values
Malnutrition	<p>The National Institute for Health and Care Excellence (NICE) defines a person as being malnourished (NICE; CG32 2006) if they have:</p> <ul style="list-style-type: none"> <li>• a body mass index (BMI) of less than <math>18.5 \text{ kg/m}^2</math></li> <li>• unintentional weight loss greater than 10% within the past 3 to 6 months</li> <li>• a BMI of less than <math>20 \text{ kg/m}^2</math> and unintentional weight loss greater than 5% in the past 3 to 6 months.</li> </ul>
Macronutrients	Nutrients that provide energy - fat, protein and carbohydrate.

Mediterranean dietary patterns	Mediterranean dietary patterns incorporate the traditional healthy living habits of people from countries bordering the Mediterranean Sea, including France, Greece, Italy and Spain. The Mediterranean diet varies by country and region, so it has a range of definitions. Mediterranean dietary patterns are most commonly assessed through the intake of the following dietary components: higher intakes of vegetables, fruit, legumes, cereals and fish; higher ratio of mono- to saturated fatty acid intake; lower intake of dairy products and meat; and a regular but moderate alcohol intake.
Meta-analysis	<p>A quantitative pooling of estimates of effect of an exposure on a given outcome, from different studies identified from a systematic review of the literature.</p> <p>Meta-analysis is a specific method of statistical synthesis that is used in some systematic reviews, where the results from several studies are quantitatively combined and summarised. The pooled estimate of effect from a meta-analysis is more precise (that is, has narrower confidence intervals) than the findings of each of the individual contributing studies, because of the greater statistical power of the pooled sample.</p>
Myocardial infarction	Myocardial infarction is a serious medical emergency in which the supply of blood to the heart is suddenly blocked, usually by a blood clot.
Mobility	A person's ability to move independently and safely from one place to another. The most common risk factors for mobility impairment are older age, low physical activity, obesity, strength or balance impairment, and chronic diseases such as diabetes or arthritis.
Monounsaturated fats	Unsaturated fats have some of the hydrogen atoms missing and have been replaced by a double bond between the carbon atoms. If there is one double bond, the fat is known as a monounsaturated fatty acid.
Nutrient deficiency	Impaired function due to inadequate supply of a nutrient required by the body.

Odds ratio (OR)	A measure of association between an exposure and an outcome. The OR represents the odds that an outcome will occur given a particular exposure, compared with the odds of the outcome occurring in the absence of that exposure. The OR is adjusted to address potential confounding.
Phylloquinone	Also known as vitamin K <sub>1</sub> or phytomenadione.
Pooled analysis	A statistical technique for combining the results of multiple epidemiological studies.
Polypharmacy	The routine use of several medications at the same time by a patient.
Polyunsaturated fats	Unsaturated fats have some of the hydrogen atoms missing and have been replaced by a double bond between the carbon atoms. If there is more than one double bond the fat is known as a polyunsaturated fatty acid.
Prospective cohort study (PCS)	An observational study in which a defined group of people (the cohort) is followed up over time. The outcomes of people in subsets of this cohort are compared, to examine people who were exposed or not exposed (or exposed at different levels) to a particular intervention or other factor of interest. A prospective cohort study assembles participants and follows them into the future.
Quality of life	Quality of life is defined by the WHO as “individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”. It is a broad ranging concept, incorporating in a complex way a person’s physical health, psychological state, level of independence, social relationships, personal beliefs and relationship to salient features of the environment.
Random effects model	A statistical model in which both within-study sampling error (variance) and between-studies variation are included in the assessment of the uncertainty (confidence interval) of the results of a meta-analysis.

Randomised controlled trial (RCT)	An experiment in which two or more interventions, possibly including a control intervention or no intervention, are compared by being randomly allocated to participants. In most trials one intervention is assigned to each individual but sometimes assignment is to defined groups of individuals (for example, in a household) or interventions are assigned within individuals (for example, in different orders or to different parts of the body).
Relative Risk (RR)	The ratio of the rate of disease or death among people exposed to a factor, compared with the rate among the unexposed, usually used in cohort studies (World Cancer Research Fund & American Institute for Cancer Research, 2007).
Reference Nutrient Intake (RNI)	See Dietary Reference Values.
Residual confounding	Occurs when one or more confounders (see above) have not been adequately controlled for in analysis or where such variables cannot be identified.
Reverse causality	A type of bias in observational studies where the proposed cause (dietary exposure or lack of it) precedes the observed effect (health or disease outcome)
Risk factor	Social, economic or biological status, behaviours or environments which are associated with or cause increased susceptibility to a specific disease, ill health, or injury.
Safe intake	Safe Intakes are set for some nutrients if there is insufficient reliable data to establish DRVs. They are based on a precautionary approach and are 'judged to be a level or range of intake at which there is no risk of deficiency, and below a level where there is a risk of undesirable effects
Sarcopenia	Sarcopenia is a muscle disease (muscle failure) rooted in adverse muscle changes that accrue across a lifetime. It is associated with increased likelihood of adverse outcomes including falls, fractures, physical disability and mortality.

Saturated fats	A saturated fat is a fat that has as many hydrogen atoms as they can hold (i.e. they are 'saturated' with hydrogen atoms). When hydrogen atoms are missing, carbon atoms form double bonds. Generally saturated fats are solid at room temperature.
Sensitivity analysis	An analysis used to determine how sensitive the results of a study or systematic review are to changes in how it was done. Sensitivity analyses are used to assess how robust the results are to uncertain decisions or assumptions about the data and the methods that were used.
Stroke	A serious life-threatening medical condition that occurs when blood supply to part of the brain is cut off.
Systematic review	A systematic review is a method of identifying, appraising, and synthesising research evidence. The aim is to evaluate and interpret all the available research that is relevant to a particular review question. A systematic review differs from a traditional literature review in that the latter describes and appraises previous work but does not specify methods by which the reviewed studies were identified, selected, or evaluated. In a systematic review, the scope (for example, the review question and any sub-questions and/or sub-group analyses) is defined in advance, and the methods to be used at each step are specified. The steps include: a comprehensive search to find all relevant studies; the use of criteria to include or exclude studies; and the application of established standards to appraise study quality. A systematic review also makes explicit the methods of extracting and synthesising study findings.
Timed up and go	A test of mobility which measures the time a person takes to rise from an armchair, walk 3 meters, turn, walk back, and sit back down again.



## Annex 6 - Abbreviations

25(OH)D	25-hydroxy vitamin D
AMD	age-related macular degeneration
AMSTAR	A Measurement Tool to Assess Systematic Reviews
BIA	bioelectrical impedance analysis
BMD	bone mass density
BMI	body mass index
CAB	Centre for Ageing Better
CHD	coronary heart disease
CI	confidence interval
COMA	Committee on Medical Aspects of Food and Nutrition Policy
COPD	chronic obstructive pulmonary disease
CSS	cross-sectional study
CT	computerised tomography
CVD	cardiovascular disease
DHEA	dehydroepiandrosterone
DLW	doubly labelled water
DQI	diet quality index
DRV	dietary reference values
DXA	dual-energy x-ray
EAA	essential amino acids
EAR	estimated average requirement
EGRAC	erythrocyte glutathione reductase activation coefficient
EPIC	Epic Elderly Study

EVM	Expert Group on Vitamins and Minerals
EWGSOP	European Working Group on Sarcopenia in Older People
FSA	Food Standards Agency
GIT	gastrointestinal tract
HALE	Healthy Ageing: A Longitudinal Study in Europe
HMB	$\beta$ -hydroxy $\beta$ -methylbutyrate
HR	hazard ratio
HSE	Health Survey for England
I <sup>2</sup>	heterogeneity (a measure of)
IU	international units
kcal	kilocalories
LiLACS NZ	The Life and Living in Advanced Age: A Cohort Study in New Zealand
MD	mean difference
MEDAS	Mediterranean diet adherence screener
MeDi score	Mediterranean diet score
MJ	megajoules
MRI	magnetic resonance imaging
MUFA	monounsaturated fats
MSDPS	Mediterranean-style dietary pattern score
NA	not applicable
NDNS	The National Diet and Nutrition Survey
NDS	Nordic Diet Score
NHS	National Health Service
NICE	The National Institute for Health and Care Excellence
ONS	Office for National Statistics

OR	odds ratio
PAD	peripheral arterial disease
PCS	prospective cohort study
PHE	Public Health England
PLP	pyridoxal-5-phosphate
PUFA	polyunsaturated fats
RCT	randomised controlled trial
RET	resistance exercise training
RNI	reference nutrient intake
RR	relative risk
SACN	Scientific Advisory Committee on Nutrition
SD	standard deviation
SIGN	Scottish Intercollegiate Guidelines Network.
SMD	standardised mean difference
SPPB	short physical performance battery
UK	United Kingdom
WHO	World Health Organization
XS	cross-sectional study