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Role of fatty acids and micronutrients in healthy ageing: a systematic review of randomised controlled trials set in the context of European dietary surveys of older adults

C. H. S. Ruxton,[1] E. Derbyshire[2] & M. Toribio-Mateas[3]

[1]Nutrition Communications, Cupar, UK
[2]Nutritional Insight Ltd, Epsom, Surrey, UK
[3]University of West London, London, UK

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Correspondence
C. H. S. Ruxton, Nutrition Communications, 26 East Road, Cupar, UK.
Tel.: +44 7973 337757
E-mail: carrie@nutrition-communications.com

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Abstract

Background: Ageing is a multifaceted and inevitable process involving a decline in health and well-being that could be ameliorated by dietary modification. We review and discuss the evidence for nutritional interventions that may support healthy ageing.
Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to identify randomised controlled trials investigating the role(s) of fatty acids and micronutrients in relation to markers of healthy ageing.
Results: European dietary surveys suggest that diets in elderly people are generally high in saturated fat, whereas intakes of vitamin D, magnesium, potassium, zinc and copper are below recommended levels. Thirty-four studies meeting the criteria were found, with 12 of these investigating the role of fatty acids and 22 considering intakes of micronutrients in relation to healthy ageing. Overall, these studies suggested that certain nutrients were consistent with healthy ageing; for example, omega-3 fatty acids were helpful for cognitive health, whereas combinations of calcium, vitamin D and K were linked with better bone health.
Conclusions: Vitamin, mineral and fatty acid intakes are in need of improvement to help elderly populations achieve optimal diet quality and support healthy ageing. This could involve the judicious use of supplements alongside dietary advice. Additional research is needed to determine optimal nutrient doses, combinations and forms in relation to desired health outcomes.

Introduction

Human life expectancy in Western countries is now twice that reported in the early Victorian era [(1)]. Average life expectancy in Europe is approximately 78 years, being slightly lower for males at 74 years and higher in females at 81 years [(2)]. Furthermore, the number of people aged ≥85 years is projected to rise to 19 million by 2020 and to 40 million by 2050 [(3)]. A consequence of this demographic change is a 'top heavy' population where the prevalence of disease and impairment rise exponentially with advancing age, which increases morbidity and reduces quality of life [(4)].

Although people are living longer, the additional years of life do not translate into extra time spent in good health. An estimated 52 million European citizens aged 55–74 years have chronic illnesses [(5)], whereas 23% of the total global disease burden is found in those aged ≥60 years [(6)]. The main causes of ill health in older people are cardiovascular diseases (30.3% of the total burden in those aged >60 years), malignant neoplasms (15.1%), chronic respiratory diseases (9·5%), musculoskeletal

diseases (7·5%), and neurological and mental disorders (6·6%) [6]. Thus, the ageing population could be the greatest healthcare challenge of the 21st Century [4] with a need for prevention strategies to reduce the impending disease burden [6].

These developments have sparked a growing interest in 'healthy ageing'. The World Health Organisation defines health not just as '*the absence of infirmity or disease*', but '*a state of complete physical, mental and social well- being*' [7]. Similarly, other publications define health as '*a state of adequate physical and mental independence in activities of daily life*' [8]. Thus, healthy ageing reflects the importance of 'sustaining health', which should ideally take a lifelong perspective [9]. Good nutrition, adequate levels of physical activity and quality healthcare all have important roles to play in achieving this [9].

Consequences of an ageing population

Ageing is defined as a multicausal process involving all of the bodies' tissues and organs, ultimately leading to impaired regulation, regeneration and structural changes [10]. Physiologically, one pivotal change is 'cellular senescence'; a process during which the bodies' cells cease to function and divide. This change is considered to contribute to age-related reductions in tissue function and regeneration [11]. Telomere length, a marker of the buffers that stabilise and cap chromosomes, can be used to predict the onset of cellular senescence because these become smaller as cells age [12]. In elderly people, accumulating levels of reactive oxygen species can disrupt biological homeostasis, contributing to internal cell and tissue damage [13]. Reducing numbers of nerve fibres along with myelin sheath damage can further impair brain and nervous system function [14].

Genetics may be responsible for approximately 25% of the variation in age at death according to linkage studies that have found a longevity locus on chromosome 3 [15]. In most cases, genes only 'load the gun' for potential adverse health outcomes, whereas certain environmental exposures are required to act as 'triggers' initiating the physiological or pathological pathways behind human health and disease [16]. Consequently, lifestyle factors such as physical activity, smoking, alcohol consumption, stress and dietary habits have important roles to play in healthier ageing [4,17].

Socially, ageing can influence general wellbeing and life satisfaction. Findings from the English Longitudinal Study of Ageing (n = 6034 older adults) revealed that feelings of loneliness and isolation were widespread. This was associated with reduced cognitive function, especially amongst those with low levels of education [18]. Older people with chronic illnesses such as coronary heart disease and arthritis also report having increased levels of depressed mood and impaired hedonic (emotional) and eudemonic (sense of purpose) meaning in life [19].

Senses, such as taste, diminish with age, which can limit food choice and appetite [20]. Sensory impairment can lead to poor nutritional status and an increased risk of malnutrition [21]. The European Nutrition for Health Alliance has estimated that malnutrition costs around £7.4 billion in the UK alone, as a result of individuals visiting their general practitioner more often or needing additional hospital care [22]. One study found malnutrition in 30% of elderly living in warden-assisted accommodation and 10% of those living at home [23]. A study of 448 geriatric outpatients found that malnutrition prevalence was 17%, whereas malnutrition 'risk' was higher at 58% [24]. Other work suggests that malnourished patients are more likely to be in hospital for longer periods compared with healthy controls (6.9 versus 4.6 days) and to have a higher likelihood of readmission [25]. Tools, such as the Malnutrition Universal Screening Tool (MUST), have helped to identify those at risk of malnutrition [26].

Other age-related health issues, such as tooth loss, dementia, dysphagia and gastrointestinal disorders [27], can also increase the risk of malnutrition. One study of 644 elderly Europeans (aged ≥65 years) found that those choosing foods that were 'easy to chew' were at high risk nutritionally [28]. Equally, denture use and poor oral health contribute to malnutrition risk [29]. Interestingly, evidence from meta-analysis has shown that interventions designed to improve the nutritional status of malnourished patients can lead to significant improvements in physical and mental quality of life [30]. Without interventions, malnutrition ultimately leads to frailty, disability, reduced mobility and poor life quality [31].

Given that most Western countries have ageing societies and there are valid concerns about how this will impact on nutritional status, quality of life and health, there is a need to determine which nutritional strategies may best support healthy ageing. This is the focus of the present review.

Materials and methods

European survey data

Data were extracted from European Dietary Surveys aiming to identify habitual intakes of fatty acids and micronutrients. A general Internet search followed by a PubMed (MEDLINE) search was carried out using the key terms 'European' combined with 'Dietary Surveys' and 'Fatty acid/Nutrient/Micronutrient Intakes'.

For the survey to be included, a full report translated into English was required. Equally, data expressing fatty

acid intakes as a percentage of energy intake or micronutrient intakes as a percentage of reference nutrient intakes (RNIs) or similar were required.

Identification of trials

Study selection

For the second part of the review, randomised controlled trials (RCTs) were identified using systematic approaches and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [32].

RCT published in English from 2005 onwards were included if they met the criteria: (i) included older adults at baseline (≥50 years); (ii) included subjects at baseline who were free from acute medical conditions; (iii) did not use multi-interventions in the form of pharmacological treatments; (iv) if the intervention used supplements, dose/level(s) of intakes should be specified; (v) the study was not an exploratory or pilot trial; (vi) interventions were not pre- or post-operative; and (vii) information needed to rank the quality of papers could be obtained from the full paper or abstract.

Search strategy

Searches were conducted using PubMed (MEDLINE) database. The search focused on identifying human RCTs of older adults aged ≥50 years. According to gerontologists, ageing begins from the fourth decade of life [10]. Equally, there is growing interest in the importance of sustaining health of the 'youngerold', defined as those aged 55–60 years [9]. Taken together, these definitions formed the basis of the chosen age cut-off.

Keyword search terms are included in Table 1 with the final search run conducted on 14 February 2015. Markers of healthy ageing were based on the main areas of age-related change, as determined by the National Institutes of Health [33]. Although studies recruiting only healthy subjects at baseline were used, those involving subjects with 'mild' cognitive impairment were permitted.

Table 1 Search criteria for the inclusion of randomised controlled trials (RCTs): human RCTs published between 2005 and 2015, conducted on older adults, aged ≥50 years

(1) Fatty acids	+	(1) Healthy ageing/telomere length
Omega-3 fatty acids		(2) Cognitive health
Eicosatetraenoic acid		(3) Bone health
Docosahexaenoic acid		(4) Eye health
Eicosapentaenoic acid		(5) Digestive health
(2) Micronutrients		(6) Metabolic health
Multivitamins/minerals		(7) Urogenital health/ prostate cancer
Micronutrient supplements		(8) Dental/periodontal health
		(9) Functional abilities/sarcopenia

Data collection and extraction

Titles and abstracts of RCT papers were identified through database searches based on the specified search terms. Using the database filters, only English language, human studies were identifed. Studies were then screened against the inclusion criteria using title screening, following by a review of the abstract and then the full paper. As shown in Fig. 1, the screening process involved a number of stages, where papers were excluded in phases.

As shown in Table 2, data extracted from each of the papers included: (i) the duration of the RCT; (ii) sample size; (iii) age of participants; (iv) the fatty acid/micronutrient intervention under investigation; (v) dose/level of intake; and (vi) effects on marker(s) of healthy ageing and levels of statistical significance (where reported).

Quality assessment

The quality of the final 34 studies was critically evaluated using the Jadad scale [34] for reporting RCTs (Table 3). Quality scores were ranked between 1 and 5, with higher scores being indicative of higher quality.

Ethical approval

Ethical approval was not deemed relevant for this review.

Results

European survey data

As shown in Table 4, European diets have a tendency to be high in saturated fat and low in certain micronutrients. In particular, total fat intakes in Scottish females [35] and low income groups [36] exceed the acceptable macronutrient distribution range (AMDR) advising that total fat intakes are between 20% and 35% of total energy intake [37]. Saturated fat intakes appear to consistently exceed recommended maximum levels set at 10% of energy intake across all European surveys [38].

With respect to polyunsaturated fatty acids (PUFAs), omega-3 intakes generally fall within the AMDR, set at 0.5–2% of energy intake, whereas omega-6 fatty acid intakes exceed the AMDR which is 2.5–9% of energy intake [37]. However, for chronic disease prevention, total PUFA intakes should lie ideally between 6% and 11% of energy intake [37]. Other studies have considered intakes of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The German Nutrition Society (2012) report highlighted EPA and DHA intakes that fell below European Food Safety Authority Adequate Intake set at 0.25 g EPA + DHA daily [39,40]. Intakes were also lower than American Heart Association guidelines, which distinguish between people without disease (0.5 g day^{-1} of EPA + DHA) and those with coronary artery diseases

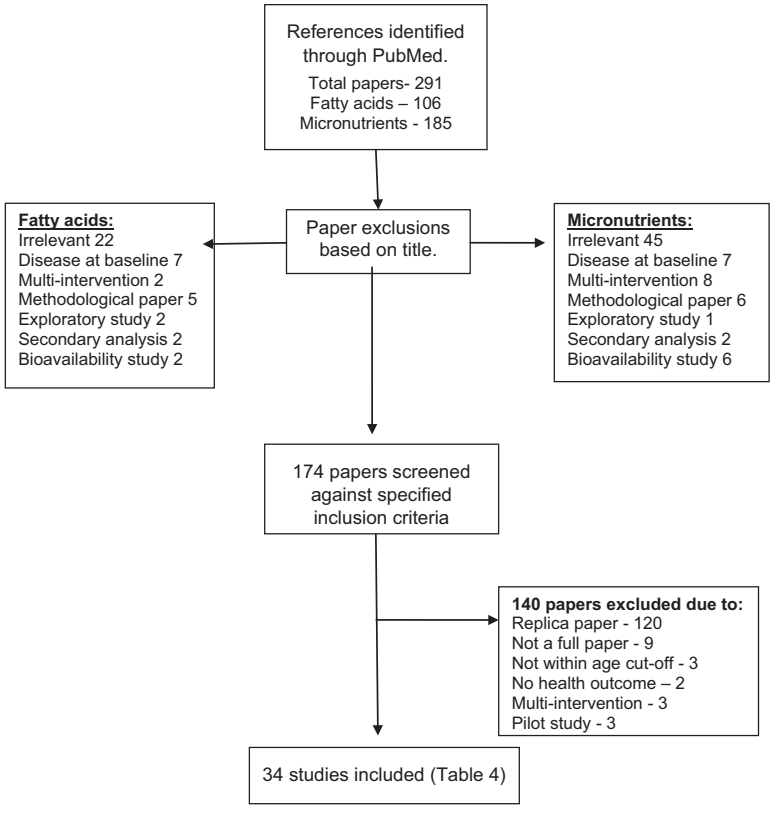

Figure 1 Flow diagram for the database search results.

(1 g day^{-1}), and hypertriglyceridaemic patients who may benefit from a higher dosage of 3–4 g day^{-1} of EPA + DHA [41]. Findings from the cross-sectional FINDIET survey concluded that the profile of fatty acids in the Finnish diet continue to miss targets [42], a situation also seen in the UK [43].

With regard to vitamin and mineral intakes, several micronutrients were under-consumed relative to national dietary guidelines. As seen in Table 5, average intakes of iron in Scottish females aged 50–64 years were 105% of the Reference Nutrient Intake [35], defined as the amount of a nutrient likely to meet the needs of most healthy individuals in a population [38]. According to data from years 1 to 3 of the UK National Diet and Nutrition Survey (NDNS), vitamin D intakes were just 38% and 29% of the RNI for males and females aged 65 years and older, respectively. There were also shortfalls in intakes of magnesium, potassium, zinc and copper intakes [44]. Using data from the latest NDNS (years 1–4) for adults aged 50–64 years, 2% were below the LRNI for iron and calcium and 1% were below the LRNI for folate [45].

Other work assessing vitamin D status in central Europe has shown that 25(OH)D status declined with age, being only 21 ng mL^{-1} for those aged 80–89 years, falling below optimal values of 30–50 ng mL^{-1} [46]. Iron deficiency anaemia is also prevalent in older age, especially amongst those aged >80 years [47]. Although more European research is needed, this has been demonstrated in US populations. For example, Price *et al.* [48] found that approximately 11% of men and 10% of women aged ≥65 years were anaemic, with these values doubling at the age of 85 years, and with prevalence rates reaching 50–60% in residential/nursing homes.

Poor diets may disproportionately affect low-income populations. The UK Low Income NDNS revealed that vitamin D intakes were 34% and 26% of the RNI for men and women respectively aged ≥65 years [36]. Intakes of magnesium, potassium, iron, zinc and copper were also under consumed when expressed as a percentage of RNI, whereas intakes of calcium, iodine and folate (for females) only just met the RNI [36]. As shown in Table 4, some of the lowest omega-3 fatty acid intakes were seen in low income populations.

Other European surveys report similar findings. For example, SENECA (Survey in Europe on Nutrition and the Elderly; a Concerted Action) pooled data from older adults aged 74–79 years from eight European countries, finding that 23.9% of men and 46.8% of women had inadequate intakes of one nutrient or more. There also appeared to be a general deficit of omega-3 fatty acids, with 60.1% of people being at risk of clinical deficiency for α-linolenic acid while 46.9% risked deficiency for

Table 2 Fatty acids, micronutrients and healthy ageing outcomes [randomised controlled trials (RCTs) only]

Reference	Sample size, age (years)	Marker of healthy ageing	Methodology	Findings
Fatty acids				
Kiecolt-Glaser *et al.* (2013)	106 healthy sedentary overweight adults, 40–85 years	Telomere length	4-month DB RCT. Received n-3 PUFAS as: (i) 2.5 g day^{-1}, (ii) 1.25 g day^{-1}, or (iii) placebo capsules	Supplementation sig. ↓ oxidative stress as measured by F2-isoprostanes ($P = 0.02$)
Konagi *et al.* (2013)	45 healthy elderly males aged 61–72 years	Brain function	12-week DB parallel RCT. Received: 0.25 g of krill oil per capsule or a placebo	n-3 PUFAs activated cognitive function during the working memory and calculation tasks
Pinazo-Durán *et al.* (2013)	66 subjects (median age 52 years)	Eye health (dry eye)	Prospective, open-label, randomised study. Those with and without dry eye took: 2 capsules per day of a fatty acid + micronutrient supp. or no supp	Levels of IL-1β, IL-6, and IL-10 in tears were sig. ↓ in the dry eye disorder group taking the supplement
Nilsson A *et al.* (2012)	40 healthy subjects. (51–72 years)	Cognitive performance Cardiometabolic risk markers	5-week cross-over placebo-controlled study. Took: 3 g n-3 fish oil daily and had a 5-week washout	n-3 PUFA resulted in better performance in the working memory test compared to placebo ($P < 0.05$) and also lowered plasma TAG ($P < 0.05$) and systolic BP ($P < 0.0001$) compared to the placebo
Sinn *et al.* (2012)	50 adults aged >65 years with MCI	Cognitive health	6-month DB RCT. Received: 1·67 g EPA + 0·16 g DHA per day, 1·55 g DHA + 0·40 g EPA day or the n-6 PUFA linoleic acid	Compared with the LA group, geriatric depression scores improved in the EPA ($P = 0·04$) and DHA ($P = 0·01$) groups and verbal fluency in the DHA gp ($P = 0·04$)
Stough *et al.* (2012)	74 healthy participants, aged 45–80 years	Cognitive function Visual acuity	90-day TB PC randomised repeated-measures trial Intervention: 1000 mg of tuna oil (252 mg DHA, 60 mg EPA, 10 mg vitamin E) or 1000 mg soybean oil (placebo)	DHA supplementation did not sig. affect cognitive function. For participants with corrected vision, those receiving DHA had sig. better right eye visual acuity post-treatment compared to the placebo ($P = 0.011$)
Smith *et al.* (2011)	16 older adults (≥65 years)	Protein synthesis	8-week RCT. Received: 4 g day^{-1} 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 ($P < 0.01$)
Dangour *et al.* (2010)	867 cognitively healthy adults, aged 70–79 years	Cognitive function	24-month DB controlled trial. Received: 200 mg EPA plus 500 mg DHA or olive oil	No sig. changes in cognitive function scores over 24 months were observed
Yurko-Mauro *et al.* (2010)	485 healthy subjects, aged ≥55 years	Cognitive decline	24-week DB RCT. Received 900 mg day^{-1} of DHA or matching placebo	DHA supplementation was associated with sig. few PAL errors ($P = 0.03$) and improved immediate and delayed Verbal Recognition Memory scores ($P < 0.02$)
Cornish and Chilibeck (2009)	Fifty-one older adults (65.4 ± 0.8 years)	Inflammatory markers Muscle mass	12-week DB RCT. Received: ALA in flax oil (~14 g day^{-1}) or placebo + resistance training (3 days a week)	ALA supplementation led to a significantly greater increase in knee flexor muscle thickness in males ($P < 0.05$)
van de Rest *et al.* (2008)	302 cognitively healthy (Mini-Mental State Examination score >21) individuals aged ≥65 years	Cognitive function	26-week DB PC trial. Received: 1800 mg day^{-1} EPA-DHA, 400 mg day^{-1} EPA-DHA, or placebo capsules	No sig. changes in any of the cognitive domains for either low-dose or high-dose fish oil supplementation were observed

Table 2 *(Continued)*

Reference	Sample size, age (years)	Marker of healthy ageing	Methodology	Findings
Rees *et al.* (2006)	93 younger (18–42 years) and 62 older males (53–70 years)	Immune function	12-week controlled DB study. Received placebo (corn oil) or oil providing 1.35, 2.7, or 4.05 g EPA per day	Older subjects incorporated EPA into plasma and mononuclear cell phospholipids more readily than younger subjects. They were also more sensitive to the immunologic effects of EPA
Micronutrients				
Dawson-Hughes *et al.* (2014)	279 men and women ≥65 years	Bone health	2-year PC trial. Received vitamin D (700 IU day^{-1}) and calcium (500 mg day^{-1}) or a placebo	In men, sclerostin levels ↑over 2 year by 13.1% in the vitamin D plus calcium-supplemented group and ↓ by 10.9%) in the placebo group ($P = 0.005$)
AREDS2 Research Group (2013)	4203 participants (50–85 years)	Age-related cataract	Multicentre RCT (4.7 years). Randomly assigned to: (i) Lutein/zeaxanthin 10 mg/ 2 mg, (ii) omega-3 LC PUFA 1 g, (iii) placebo or (iv) a combination of these	Daily supplementation with lutein/zeaxanthin had no statistically sig. overall effect on rates of cataract surgery or vision loss
Aloia *et al.* (2013)	159 post-menopausal healthy white women	Bone health	6-month DB PC parallel, longitudinal factorial study. Randomised to: (i) double placebo, (ii) calcium (1200 mg daily) plus placebo, (iii) vitamin D_3 (100 μg) plus placebo, and (iv) vitamin D_3 and calcium	Supp. of the diet with 1200 mg calcium per day reduced bone turnover markers, whereas supp. with up to 100 μg vitamin D_3 per day does not
Cauley *et al.* (2013)	36 282 post-menopausal women, 50–79 years	Bone health	RCT (mean 4.9 years). Randomised to: 1000 mg of calcium carbonate plus vitamin D (400 IU D_3) or matching placebo tablets	Women with vitamin D intakes >600 IU per day, had an ↑ risk of invasive breast cancer, hazard ratio = 1.28 (95% CI; 1.03, 1.60)
Grodstein *et al.* (2013)	5947 male physicians aged ≥65 years	Cognitive function	DB PC RCT (over 8.5 years) of a multivitamin	Cognitive performance did not differ between the multivitamin and placebo groups. Doses of vitamins may be too low or the population may be too well-nourished to benefit from a multivitamin
Knapen *et al.* (2013)	244 healthy post-menopausal women	Bone loss	36-months. Received menaquinone-7 (180 μg per day) or a placebo	MK-7 intake sig. improved vitamin K status and ↓the age-related decline in BMC and BMD at the lumbar spine and femoral neck
McAlindon *et al.* (2013)	$n = 146$ with symptomatic knee OA (mean age, 62.4 years)	Joint health	2-year DB PC clinical trial. Received: Placebo or oral cholecalciferol, 2000 IU per day, with dose escalation	Knee pain decreased in both groups with no sig. differences at any time
Prentice *et al.* (2013)	36 282 post-menopausal women	Bone health	DB, PC clinical trial (average 7 years). Randomised to: 1000 mg elemental calcium carbonate plus 400 IU of vitamin D_3 daily or placebo	Though based on subset analysis, long-term use of calcium and vitamin D appeared to ↓ the risk of hip fracture among post-menopausal women
Bischoff-Ferrari *et al.* (2012)	22 healthy post-menopausal women, mean age of 61.5 years	Lower extremity function Blood pressure Innate immunity	4-month DB RCT. Received 20 μg of HyD or 20 μg (800 IU) of vitamin D_3 per day	Women on HyD compared to vitamin D_3 had a 2.8-fold ↑ odds of maintained or improved lower extremity and a 5.7-mmHg ↓in systolic BP ($P = 0.0002$)

Table 2 *(Continued)*

Reference	Sample size, age (years)	Marker of healthy ageing	Methodology	Findings
Gaziano *et al.* (2012)	641 male physicians aged >50 years	Cancer risk	Randomised, DB, placebo-controlled trial over 11.2 years. Enrolled in a multivitamin study	Daily multivitamin supplementation modestly but sig. ↓ the risk of total cancer ($P = 0.04$)
Rossom *et al.* (2012)	2034 women aged >65 years	Cognitive impairment	RCT (over 7.8 years). Randomised to receive 1000 mg of calcium carbonate combined with 400 IU of vitamin D_3 or a placebo	There were no sig. differences in incident dementia or MCI or in global or domain-specific cognitive function between groups
Sarris *et al.* (2012)	182 participants	Energy levels/well-being Mood	16-week DB PC randomised parallel trial of once-daily multivitamin administration	Qualitative analysis showed that multivitamin use ↑ energy levels ($P = 0.022$) (especially for females) and enhanced mood ($P = 0.027$)
Walker *et al.* (2012)	900 adults aged 60–74 years	Cognitive decline	2-year RCT, received: daily oral 400 μg FA + 100 μg vitamin B_{12} supplementation (compared to placebo)	FA + vitamin B_{12} sig. improved total cognitive function score ($P = 0.032$) and immediate and delayed recall scores at 24 month versus placebo
Wallace *et al.* (2012)	42 women aged 49–71 years	Heart health (homocysteine, tHcy	12-week DB PC RCT. Received: 1 g choline per day (as choline bitartrate), or placebo supplement	Choline supplementation induced a ↓in plasma tHcy concentration at week 6 of −0·9 μmol, a change which, when compared to that observed in the placebo group 0·6 μmol, approached statistical sig. ($P = 0·058$)
Barnes *et al.* (2011)	211 younger and 202 older ≥64 years adults	Immune health	22-week RCT, received: Placebo, 5, 10, or 15 mg (1 mg = 40 IU) D_3 daily	15 μg per day D_3 supplementation sig. ↑ $25(OH)D_3$ concentrations in the older cohort but had no sig. effect on cytokine concentrations
Ma *et al.* (2011)	95 elderly people (60–75 years)	UV-induced apoptosis	2-month DB RCT. Supplement containing moderate amounts of retinol, β-carotene, α-tocopherol, ascorbic acid and selenium or placebo	A ↓ of 2.3% in intrinsic apoptosis of lymphocytes was found in the supp. groups of elderly people compared to their control gp ($P < 0.001$), UV-induced apoptosis of human lymphocytes was attenuated by micronutrient supplementation
Christen *et al.* (2010)	11 545 apparently healthy male physicians >50 years	Age-related cataract	Randomised, double-masked, PC trial (over 8 years). Received: 400 IU of vitamin E or placebo on alternate days and 500 mg of vitamin C or placebo daily.	Long-term alternate-day use of 400 IU of vitamin E and daily use of 500 mg of vitamin C had no notable beneficial or harmful effect on the risk of cataract
Shea *et al.* (2009)	388 healthy men and post-menopausal women	Coronary artery calcification	3 year DB RCT. Allocated to receive: 500 μg phylloquinone per day, or a multivitamin alone	In a subgroup of participants those who were ≥85% adherent to supp. had less CAC progression in the phylloquinone group than the control gp ($P = 0.03$). Of those with pre-existing CAC those receiving phylloquinone had 6% less progression than did those who received the multivitamin alone ($P = 0.04$)
Shea *et al.* (2008)	379 healthy men and women (60–81 years)	Bone health	3 year DB RCT. Allocated to receive: 500 μg phylloquinone per day, or a multivitamin alone	Poor vitamin K status was associated with high concentrations of cytokines involved in bone turnover

Table 2 *(Continued)*

Reference	Sample size, age (years)	Marker of healthy ageing	Methodology	Findings
Intorre *et al.* (2008)	387 healthy middle-aged (55–70 years) and older (70–85 years) adults	Vitamin status	6-month RCT. Allocated to receive 15 or 30 mg Zn per day or placebo for 6 months	Plasma vitamin A levels ↑ sig. with zinc dose and period of treatment, particularly at 6 months (for 15 mg Zn per day, $P < 0.05$ for 15 mg day^{-1} and $P < 0.0001$ for 30 mg day^{-1})
Hodkinson (2007)	147 individuals, aged 55–70 years	Immune health	6-month DB RCT. Received: 15 mg or 30 mg Zn per day for 6 months	Total Zn intake (diet plus supp.) of up to 40 mg Zn per day did not have sig. long-term effects on immune status
Kang *et al.* (2006)	6377 women ≥65 years	Cognitive function	DB PC RCT (5.6 years). 600 IU [α-tocopherol acetate], on alternate days	Long-term use of vitamin E supp. did not provide cognitive benefits among generally healthy older women

ALA, α-linolenic acid; DB, double-blind; BMC, bone mineral content; BMD, bone mineral density; BP, blood pressure; CAC, Coronary artery calcification; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FA, folic acid; gp, group; MCI, mild cognitive impairment; Paired Associate Learning (PAL) test; PC, placebo-controlled; RCT, randomised controlled trial; SES, socio-economic status; sig, significant/significantly; supp, supplement; TAG, triacylglycerides; TB, triple blind; TB, triple-blind; UV, ultraviolet.

long-chain omega-3 PUFA [49]. Similarly, in Southern France, the POLANUT cross-sectional study of older adults (>70 years, $n = 832$) [50] found that median intakes of vitamins B_6, D, calcium and magnesium were below Nutrient Reference Values, formerly known as the Recommended Daily Allowance (RDA) [51]. Another survey estimated the prevalence of dietary inadequacy amongst older adults in Europe using estimated average requirements based on Nordic and Institute of Medicine recommendations. The findings showed that the mean prevalence of inadequacy was up to 10% of the population for zinc, iron and vitamin B_{12}, between 11% and 20% for copper and vitamin C, and above 21% for vitamin D, folic acid, calcium, selenium and iodine [52].

A study mapping the prevalence of micronutrient deficiencies across eight different European countries found that over 90% of people had inadequate vitamin D intakes. Although mean vitamin and mineral intakes from foods did not pose a general concern, it was noted that inadequacies were more likely to be found in older adults [53]. Finally, data extracted from the 2004 European Nutrition and Health Report, summarising the nutritional situation of older people from 11 European Union countries concluded that total fat intakes were high, the fatty acid profile imbalanced, and that average vitamin D and folic acid intakes were below guidelines [54].

Nutrition interventions

As shown in Fig. 1, 291 RCTs were originally identified: 106 in relation to fatty acids and 185 for micronutrients. After reviewing the titles and abstracts, 117 were eliminated, leaving 174 for closer inspection. Considering the abstracts and available full papers resulted in exclusion of a further 140 papers, leaving 34 RCTs for inclusion.

Cognitive health

It has been estimated that, annually, over one-third (38.2%) of the European Union population suffer from a mental disorder [55]. Eleven RCTs investigated the role(s) of fatty acids ($n = 7$) or micronutrients ($n = 4$) in relation to markers of cognitive health. These varied in terms of their design and cognitive outcome measures.

Of the seven studies on fatty acids, most measured cognitive health, performance or decline. The majority of researchers used healthy subjects at baseline ($n = 6$), whereas one recruited participants with mild cognitive impairment (MCI) at baseline [56]. Of the six studies using healthy subjects, mixed findings were reported. In one of the largest trials, a 2-year RCT of 867 older adults (70–79 years), 200 mg EPA + 500 mg DHA taken daily did not improve memory or executive function [57].

Table 3 Quality assessment used to assess randomised controlled trials (RCTs) identified in the systematic review

Publication	Randomisation	Method of randomisation described and appropriate	Blinding mentioned	Method of blinding described and appropriate	Withdrawal and dropout of subjects provided	Total score
Fatty acids						
Kiecolt-Glaser *et al.* (2013)	1	1	1	1	0	4
Konagi *et al.* (2013)	1	1	1	1	1	5
Pinazo-Durán *et al.* (2013)	1	0	0	0	0	1
Nilsson A *et al.* (2012)	1	0	0	0	1	2
Sinn *et al.* (2012)	1	0	0	0	0	1
Stough *et al.* (2012)	1	1	1	1	1	5
Smith *et al.* (2011)	1	0	0	0	1	2
Dangour *et al.* (2010)	1	1	1	1	1	5
Yurko-Mauro *et al.* (2010)	1	1	1	1	0	4
Cornish and Chilibeck (2009)	1	1	1	1	1	5
van de Rest *et al.* (2008)	1	1	1	1	1	1
Rees *et al.* (2006)	1	0	1	0	1	3
Micronutrients						
Dawson-Hughes *et al.* (2014)	1	0	0	0	0	1
AREDS2 Research Group (2013)	1	1	1	0	1	4
Aloia *et al.* (2013)	1	0	1	1	0	3
Cauley *et al.* (2013)	1	0	0	0	1	2
Grodstein *et al.* (2013)	1	1	1	1	1	5
Knapen *et al.* (2013)	1	1	0	0	1	3
McAlindon *et al.* (2013)	1	1	1	0	0	3
Prentice *et al.* (2013)	1	1	1	1	0	4
Bischoff Ferrari *et al.* (2012)	1	0	1	1	0	3
Gaziano *et al.* (2012)	1	1	1	1	1	5
Rossom *et al.* (2012)	1	1	0	0	0	2
Sarris *et al.* (2012)	1	1	1	1	1	5
Walker *et al.* (2012)	1	1	1	1	1	5
Wallace *et al.* (2012)	1	1	1	1	0	4
Barnes *et al.* (2011)	1	1	1	0	1	4
Ma *et al.* (2011)	1	1	1	1	1	5
Christen *et al.* (2010)	1	0	1	0	1	3
Shea *et al.* (2009)	1	0	1	1	1	4
Shea *et al.* (2008)	1	0	1	1	1	4
Intorre *et al.* (2008)	1	1	1	1	1	5
Hodkinson *et al.* (2007)	1	0	1	0	1	3
Kang *et al.* (2006)	1	0	1	0	1	3

Total quality assessment score for which scores range between 1 and 5: with 1 being the lowest quality and 5 being the highest quality.

Another trial on 74 healthy adults (45–77 years) found that 90 days of DHA supplementation (252 mg day^{-1}) significantly raised plasma DHA levels but did not affect cognitive function [58]. Finally, research carried out on 302 cognitively older adults found that neither high (1800 mg), nor lower (400 mg) doses of EPA-DHA daily significantly altered cognitive outcomes [59].

Three studies using fish oils, or high-dose DHA, found positive benefits. Konagai *et al.* [60] reported that a sample of 45 males (61–72 years) randomised to take sardine oil ($P = 0.043$) or krill oil ($P = 0.004$) over 12 weeks had significantly greater changes in oxyhaemoglobin levels (a marker of brain function) during working memory tasks. Equally, a similarly sized study ($n = 40$) showed that 3 g of fish oil n-3 PUFA taken daily over 5 weeks led to significant improvements in working memory ($P < 0.05$) [61]. In terms of DHA supplementation, a clinical trial comprised of adults aged ≥55 years ($n = 485$) randomised to take 900 mg DHA or placebo daily over 24 weeks found that DHA supplementation significantly improved immediate and delayed Verbal Recognition Memory scores ($P < 0.02$) [62]. In relation to studies carried out on subjects with MCI, in a 6-month RCT, 50 older adults were allocated into three groups with daily dosages of combined DHA and EPA or a PUFA control. The first group received DHA-rich (1.55 g DHA plus 0.40 g EPA)

Table 4 Fat and fatty acid intakes of ageing Europeans

			Total fat		Saturated		Cis-n-3 fatty acids		Cis-n-6 fatty acids	
Reference and country	Age	Sex	g	%E	g	%E	g	%E	g	%E
NDNS RPS (2014), Scotland	50–64 years	M	76.0	33.4	27.8	12.2	NR	NR	NR	NR
		F	59.7	35.5	23.8	14.0	NR	NR	NR	NR
NDNS (2014) years 1–4, UK	50–64 years	M	74.0	32.4	27.6	12.0	NR	NR	NR	NR
		F	59.9	33.4	22.6	12.5	NR	NR	NR	NR
NDNS (2012) years 1–3, UK	19–64 years	M	78.8	32.9	28.8	12.0	2.2	0.9	11.4	4.8
	>65 years	M	75.4	34.9	29.3	13.6	2.3	1.1	10.1	4.7
	19–64 years	F	60.1	33.0	22.0	12.0	1.8	1.0	8.9	4.9
	>65 years	F	58.3	34.6	23.2	13.7	1.8	1.1	7.8	4.7
German Nutrition Society (2012), Germany	51–65 years	M	86.0	NR	38.0	NR	0.09 EPA 0.14 DHA	NR	NR	NR
	65–80 years	M	60.0	NR	27.0	NR	0.07 EPA 0.12 DHA	NR	NR	NR
	51–65 years	F	81.0	NR	36.0	NR	0.07 EPA 0.12 DHA	NR	NR	NR
	65–80 years	F	62.0	NR	28.0	NR	0.07 EPA 0.12 DHA	NR	NR	NR
Pot *et al.* (2012) NDNS year 1, UK	19–64 years	M/F	71.4	32.9	26.1	12.0	2.2	1.0	10.6	4.9
Nelson *et al.* (2007) LINDNS, UK*	50–64 years	M	74.9	35.0	28.6	13.3	1.9	0.9	10.3	4.8
	65 year+	M	70.2	36.0	28.3	14.1	1.4	0.8	9.5	4.9
	50–64 years	F	58.5	35.0	23.1	13.6	1.4	0.9	8.0	5.0
	>65 years	F	56.1	35.2	23.2	14.5	1.3	0.8	7.0	4.5
FINDIET (2007), Finland	20–64 years	M	76.6	30.4	32.5	12.9	3.1	1.2	11.4	8.1
		F	53.4	28.7	22.6	12.0	2.2	1.2	4.5	4.4

DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; F, female; g, grammess; M, male, NDNS, National Diet and Nutrition Survey; NR, not reported; RPS, Rolling Programme Scotland; %E, percentage energy intake.
*Energy intakes are expressed as a percentage of food energy in the LINDNS.

supplement. The second received an EPA-rich (1.67 g EPA plus 0.16 g) supplement, and the third group received 2.2 g of n-6 PUFA linolenic acid. Adults in the DHA-rich supplementation group significantly improved geriatric depression scores and self-reported physical health [56].

Of the four studies on micronutrients, one looked at potential cognitive effects of multivitamin use [63], another folic acid and B_{12} supplements [64], one used calcium carbonate with vitamin D_3 [65] and another vitamin E [66].

Grodstein *et al.* [63], as part of the US Physicians' Healthy Study II, found that daily multivitamin use did not affect cognitive function at any of the four measured time periods. It was concluded that doses of multivitamins may have been too low, or that the sample was sufficiently nourished. Amongst a sample of 900 adults (60–74 years) with elevated psychological distress at baseline, supplementation with 400 μg of folic acid and 100 μg of B_{12} over 24 months significantly improved immediate and delayed memory recall [64]. A Cochrane Review of the use of B_{12} for cognitive decline found that folic acid in combination with B_{12} was effective in reducing serum homocysteine levels [67].

Elevated plasma homocysteine (hcy) levels, also known as hyperhomocysteinaemia, have been associated with cognitive impairment and neurodegenerative disorders [68].

Rossom *et al.* [65] randomised over 4000 older women to take 1000 mg calcium carbonate + 400 IU vitamin D_3, or placebo over 7.8 years. However, no changes in dementia incidence or cognitive impairment were seen [65]. As part of the Women's Health Study, vitamin E (600 IU α-tocopherol acetate) taken on alternative days over 5.6 years was not found to significantly affect cognitive function [66].

Bone health

The average cost of osteoporotic fractures is expected to rise by 25% in 2025, mainly driven by the ageing population [69]. A total of six RCTs considered the role of micronutrients in relation to bone health, three of which looked at calcium and vitamin D. One 6-month trial in 159

Table 5 Micronutrient intakes of ageing Europeans (% reference nutrient intake)

Reference and country	Age	Sex	Vitamin A (μg)	Vitamin B_6 (mg)	Vitamin B_{12} (μg)	Folate (μg)	Vitamin C (mg)	Vitamin D* (μg)	Ca (mg)	Mg (mg)	K (mg day^{-1})	Fe (mg)	Zn (mg)	Cu (mg day^{-1})	I (μg)
NDNS RPS (2014) Scotland	50–64 years	M	NR	NR	NR	148	216	NR	119	NR	NR	137	NR	NR	NR
		F	NR	NR	NR	109	215	NR	103	NR	NR	105	NR	NR	NR
NDNS (2014, years 1–4), UK	50–64 years	M	NR	NR	NR	148	219	NR	130	NR	NR	135	NR	NR	NR
		F	NR	NR	NR	123	235	NR	110	NR	NR	110	NR	NR	NR
NDNS (2012, years 1–3), UK	19–64 years	M	137	190	391	149	219	–	129	**96**	**88**	137	104	105	133
	>65 years	M	227	171	510	148	210	**38**	135	**90**	**88**	125	**97**	118	152
	19–64 years	F	161	160	311	115	210	–	104	**84**	**72**	**79**	109	**88**	100
	>65 years	F	194	160	378	120	200	**29**	113	**82**	**74**	109	109	**90**	121
Vinas *et al.* (2011), Europe†	>64 years	M	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	16	30
		F	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	17.8	23
Nelson *et al.* (2007), LINDNS UK	50–64 years	M	192	168	509	144	191	–	127	**85**	**85**	133	100	104	141
	>65 years	M	163	151	409	129	157	**34**	119	**76**	**75**	117	**87**	**92**	132
	50–64 years	F	164	145	330	112	186	–	107	**74**	**69**	**99**	**99**	**80**	113
	>65 yearss	F	183	143	332	110	168	**26**	104	**70**	**65**	103	**98**	**74**	113
Carrière *et al.* (2007) POLANUT, France*	>70 years	M/F	NR	**67**	NR	NR	**99.8**	**15.7**	**79.2**	**67.4**	NR	102	NR	NR	NR
SENECA (1999)‡, Europe	74–79 years, 8 European countries	M	NR	5	NR	NR	NR	NR	NR	NR	NR	7.2	NR	NR	NR
		F	NR	8.9	NR	NR	NR	NR	NR	NR	NR	23	NR	NR	NR

F, female; LI, low income; M, male; NDNS, National Diet and Nutrition Survey; NR, not reported.
(–) indicates no reference intake. Intakes from food sources only.
*% Recommended Daily Allowance.
†% population below the estimated average requirement.
‡% with inadequate intakes according to the Dutch minimum requirement.
Note: Values in bold indicate that values were less than 100% of the reference nutrient intake.

healthy post-menopausal women found that daily calcium supplementation (1200 mg) on top of usual dietary intakes reduced markers of bone turnover (i.e. serum cross-linked C-telopeptide and procollagen type I N-terminal propeptide), although supplementation with up to 100 μg (4000 IU) vitamin D_3 did not [70]. The Women's Health Initiative clinical trial, consisting of 36 282 post-menopausal women, did not find any associations between calcium and vitamin D supplementation and hip fracture after an average of 11 years of follow-up [71]. Using data from the same trial, however, Prentice *et al.* [72] reported that 1000 mg of calcium plus 10 μg (400 IU) vitamin D_3 was associated with a reduced risk of hip fracture among post-menopausal women.

Another study showed that 3 years of daily supplementation with 180 μg of vitamin K_2 (menaquinone-7) reduced the age-related decline in bone mineral density of post-menopausal women, especially at the lumbar spine and femoral neck. Positive effects on bone strength were also observed [73]. Earlier work, however, by Shea *et al.* [74] found that 500 μg of vitamin K1 (phylloquinone) had no effect on markers of bone health when taken by healthy older men and women. These differences may be explained, in part, by vitamin K_2 having a higher potency and a longer half-life [73].

Serum sclerostin is a glycoprotein produced by bone-forming cells (osteocytes) that is often used as a clinical marker of bone turnover. A 2-year trial of 279 older adults (>65 years) found that 17.5 μg (700 IU) of vitamin D_3 + 500 mg calcium led to increased sclerostin levels in men but not in women. These findings suggest that men and women respond differently to vitamin D and calcium [75], indicating that different nutritional approaches may be required with advancing age.

An additional two studies looked at joint health and lower extremity function. A clinical trial of 146 adults (mean age 62.4 years) with knee osteoarthritis showed that 50 μg (2000 IU) of cholecalciferol (vitamin D_3) did not improve in knee pain, function or cartilage volume over a 2-year period [76]. Other research on 22 post-menopausal women found that daily supplementation with 20 μg (800 IU) of HyD (a crystalline form of vitamin D_3) over 4 months resulted in a 2.8-fold increased odds of maintaining or improving lower extremity function compared to standard vitamin D_3 [77].

Eye health

With advancing age, especially beyond 75 years, an increasing prevalence of cataract, age-related macular degeneration, glaucoma, diabetic retinopathy and visual impairment can impact significantly on quality of life [78]. Four studies examined the potential roles of fatty acids and micronutrients in relation to eye health.

In one study, patients with nonsevere dry eye disorders randomised to take a combined formulation of antioxidants and essential fatty acids had significantly lower expression of certain interleukins after 3 months, indicating that immune and inflammatory responses could be modulated [79]. Another study administered DHA over 90 days (as 1000 mg of tuna oil) to 74 adults aged 45–77 years, finding that DHA resulted in significantly better visual acuity compared to the placebo group in those with corrected vision [58]. Findings from the Age-Related Eye Disease Study (AREDS2), a multicentre clinical trial (n = 4203), found that daily lutein/zeaxanthin supplementation over a median period of 4.7 years did not significantly affect rates of cataract surgery or vision loss [80]. Equally, a randomised, double-blind trial comprised of 11 545 healthy males taking 400 IU of vitamin E on alternate days and 500 mg of vitamin C, or placebo daily, had no notable effect on cataract risk after 8 years of follow-up [81].

Immune health

To date, five studies have looked at the impact of nutrition on components of immune function. In one study, 51 adults were randomly allocated to receive 14 g day^{-1} of α-linolenic acid (ALA) or placebo for 12 weeks when carrying out resistance training on 3 days of the week. The results showed that, amongst older males, interleukin-6 levels were reduced in the ALA group indicating reduced inflammation [82]. Another 12-week study found that older males were more sensitive to the immunological effects of EPA, experiencing a lower neutrophil respiratory burst at higher EPA intakes (up to 4.05 g) [83]. Regading micronutrients, Bischoff-Ferrari *et al.* (2012) reported that 20 μg of HyD or vitamin D_3 led to reductions in five out of seven markers of innate immunity when taken over 4 months [77]. This was significantly more pronounced for HyD for four markers in particular: eotaxin, interleukin-2, MCP-1 and MIP-1β. Other work found that vitamin D3 supplementation, in doses up to 15 μg, did not affect cytokine production when taken by older males over 22 weeks [84]. Finally, the findings from the ZENITH study, a RCT in adults aged 50–70 years, found that moderate zinc supplementation (i.e. 15 mg day^{-1}) may help to maintain the T Helper/cytotoxic T-lymphocyte ratio and, consequently, enhance adaptive immunity. However, higher doses (i.e. approximately 30 mg day^{-1}) may affect B-lymphocyte counts, exacerbating age-related immunological changes [85].

Metabolic health

A 5-week cross-over placebo-controlled study showed that daily fish oil PUFA (3 g daily) was associated with significantly lower plasma triacylglyceride levels and

systolic blood pressure [61]. The findings from a 4-month RCT showed that women taking 20 μg HyD had significantly (−5.7 mmHg) lower blood pressure ($P = 0.0002$) [77]. In relation to choline supplementation, a 12-week trial recruiting 42 post-menopausal women found that 1 g of choline daily led to reduction in plasma homocysteine levels that approached statistical significance ($P = 0.058$) [86]. Finally, a 3-year follow-up study comprising 388 healthy adults showed that those with a history of coronary artery disease receiving 500 μg of phylloquinine daily had 6% less progression compared to those taking a standard multivitamin ($P = 0.04$) [74].

Other markers

Six studies have looked at other markers of health. As noted earlier, shorter chromosome telomeres are associated with faster biological ageing and risk of age-related disease. A double-blind 4-month trial of 106 sedentary, overweight middle-aged and older adults found that telomere length increased with decreasing n-6 : n-3 ratio, suggesting that this could affect cell ageing [87]. Another study found that supplementation with 1.86 g of EPA + 1.5 g of DHA over 8 weeks increased the rate of muscle protein synthesis, suggesting that this could be useful for sarcopenia prevention [88].

The findings from the Physicians' Health Study, a large-scale RCT carried out on US physicians aged ≥50 years, found that, after a median follow-up of 11.2 years, daily multivitamin use modestly but significantly reduced the risk of total cancer [89]. Feelings of subjective health were reported in one study with multivitamin use being associated with significantly increased energy levels and better mood, as well as a trend towards better sleep [90]. A 2-month double-blind RCT that included 95 older participants (60–75 years) found that antioxidant supplementation with moderate amounts of retinol, β-carotene, α-tocopherol, ascorbic acid and selenium significantly reduced levels of ultraviolet-induced apoptosis (cell death) by 3.1% [91]. Finally, a trial of middle and older-aged men found that long-term zinc supplementation (i.e. for 6-months) was associated with increased plasma vitamin A levels (for 30 mg of zinc daily; $P < 0.0001$) [92].

As presented in Table 3, studies varied in terms of their quality and potential risk of bias, with methods of randomisation and blinding techniques not always being adequately described. From a more general perspective, additional long-duration RCTs are needed, adequately powered by sample size. Study populations also need to be clearly defined at baseline. Some lack of associations, for example, could be a result of study populations having a good nutritional status at baseline. Also, there is a need for studies to measure and define supplement compliance more clearly. For example, infrequent use could lead to a lack of findings. In other instances, the dose of supplement given may not have been sufficiently high to generate an effect, especially in short-term studies, which could then exacerbate poor compliance. Because of the high costs of clinical trials, Morris & Tangey (2011) recommend that vitamin supplementation trials should first be conducted on individuals with insufficient nutritional status and then, if effective, progress to testing on those with adequate nutrient levels [93].

Discussion

European diets tend to be high in saturated fat and lack certain micronutrients, namely vitamin D, magnesium, potassium, zinc and copper in some groups of older people. Although omega-3 intakes (as a percentage of energy intake) generally fell within the AMDR set at 0.5–2 per set, in Germany, EPA and DHA intakes were substantially lower than Adequate Intake recommendations [40]. This highlights a pressing need for more dietary surveys to quantify fatty acid intakes, which tend to be overlooked at present. The use of dietary software that analyses the fatty acid profile of foods will also be needed to achieve this. Furthermore, although the European Micronutrient Recommendations Aligned Network of Excellence is working towards harmonising micronutrient recommendations across Europe [94], similar approaches are also needed for omega-3 fatty acids.

Although only a few RCTs reported statistically significant health benefits, there were promising findings for several nutrients. For example, increasing omega-3 intakes appeared to have a role in improving memory [60–62], reducing the risk of dry eye [79], depression scores [56] and levels of leucocyte telomere oxidative stress [87] at the same time as supporting muscle protein synthesis [88]. Folic acid and B_{12} supplementation were found to impact positively on cognitive function [64]. Combinations of calcium and vitamin D supplementation appeared to be most effective for fracture prevention [72], as well as HyD in relation to improving lower extremity function [77]. The role of vitamin K, especially menaquinone-7, in supporting bone health is emerging and requires further investigation [73]. Finally, other work suggests that multivitamin use is associated with reduced total cancer risk [89], improved energy levels and enhanced mood [90]. As shown in Table 3, 18 studies included in the review were of high quality (quality assessment scores 4 or 5). The remaining studies were not necessarily of poor quality, although full details of methods were not reported in all papers. For example, methods of blinding, reasons for

subject withdrawal or rates of supplement compliance were not always reported. Future studies should look to following CONSORT (Consolidated Standards or Reporting Trials) guidelines to support the recording of these details. This will help to minimise the risk of bias at the same time as benefitting the quality of future studies. On a final note, future trials should attempt to recruit populations with suboptimal nutrient status or intakes at baseline in order to provide the best opportunity for effective results. These are unlikely to be seen in populations who already have an optimal nutrition status [93].

With regard to translation into practice, dietitians can play a key role in guiding people to make better dietary choices throughout adulthood, with healthy ageing in mind. Partial substitution of saturated fats with omega-3 fats appears to be a valid dietary intervention for the prevention of cardiovascular disease [95]. Equally, advice is needed to narrow gaps where micronutrient shortfalls are apparent, especially amongst high-risk groups such as low income individuals or those at risk of malnutrition. Bioavailability should be considered, particularly in relation to vitamin B_{12} and the different vitamin D and calcium forms [96]. For example, the absorption of protein-bound vitamin B_{12} diminishes with age, typically as a result of higher rates of atrophic gastritis in this age group [97]. A recent study on premenopausal women also showed that a single serving of calcium carbonate powder appeared to be significantly more bioavailable than calcium citrate tablets at 4 h after ingestion [98].

Another factor is the general decline in daily volume of food consumed with advancing age due to slower gastric emptying, altered taste and lower energy requirements [95], which may make it more challenging to ensure nutrient adequacy. In addition, better management of dental health in older people could help to support status, as could the provision of vitamin and mineral supplements [95]. Vitamin D supplementation programmes may also be of benefit across vulnerable populations, such as elderly living in care homes.

In conclusion, European populations are ageing but not enjoying extra years of good health which suggests a potential transforming role for nutrition. There is emerging evidence that omega-3 fatty acids, B vitamins, vitamin D and calcium are the most promising nutrients for healthy ageing. Clearly, given the variation in the quality of RCTs, much more research is required, particularly in populations with poor nutritional status, and using differing doses and nutrient forms. As it may be challenging for elderly people to obtain all their nutrient needs from food sources, there is a positive role for supplements, e.g. multivitamins, minerals and fish oils, alongside advice on healthy eating. Indeed official advice to take vitamin D supplements is already given in several countries.

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CR led the project and wrote and edited the paper. ED conducted the background research and contributed to the writing of the paper. MTM reviewed and contributed to the writing of the ageing aspects of the paper. All authors critically reviewed the manuscript and approved the final version submitted for publication.

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