The Nutritional Needs of Middle-Aged and Older Adults: The European Union Perspective

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Abstract

This narrative review describes the distinct nutritional needs of middle-aged and older adults in the European Union. Literature reviews were conducted to identify sources evaluating nutritional status and interventions relevant to these populations. Emphasis was placed on dietary guidelines, systematic reviews, and meta-analyses examining relevant macronutrients and micronutrients and important diseases or conditions related to aging (e.g. cardiovascular disease, infections, osteoporosis, cognition, immunity). Middle-aged and older adults in the European Union frequently do not obtain recommended amounts of key macronutrients and micronutrients necessary for maintaining health. In addition to the nutritional benefits of a healthful diet and contact with professionals to identify nutritional barriers, problem-solving techniques and micronutrient and macronutrient goals can improve the outcomes of dietary interventions in these individuals. Nutrition education programs, particularly those with specific recommendations, are effective for improving the nutritional status of these populations. For those who do not obtain adequate amounts of macronutrients and micronutrients from their diets, adhering to dietary guidelines and, when warranted, supplementation should be considered to improve nutritional status. The findings from randomized, controlled trials suggest that dietary interventions and supplementation can correct nutritional deficiencies and inadequacies that are important to the health of middle-aged and older adults. However, it is important to evaluate nutrient intake from the diet, supplementation, and fortified food to avoid exceeding tolerable upper intake levels of certain nutrients and limit potential adverse outcomes. Medical histories, medication use, dietary patterns, and other risk factors should be considered when recommending dietary improvements and supplements in these populations.

Key words: **Aging, malnutrition, micronutrients, nutritional deficiencies.**

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Introduction

Life expectancies in European Union (EU) countries continue to rise, expanding the aging population. It has been estimated that by 2050 greater than 25% of the EU population will be ≥65 years of age, which has the potential to challenge the healthcare system (1). According to the European Health Report, important non-communicable diseases (NCDs) associated with aging include cardiovascular disease (CVD), certain cancers, and type 2 diabetes (1). Because these NCDs are the leading causes of early mortality in the EU, primary and secondary prevention efforts are needed to reduce NCD-related morbidity and mortality (1). To allow older individuals to live more independently and remain integrated in society, the World Health Organization's agenda for preventing NCDs includes increasing physical activity, reducing tobacco and alcohol use, and reducing the risk of malnutrition, a condition in which many nutrient requirements are not met (2). The European Food Safety Authority (EFSA) reference intakes for selected micronutrients in adults >50 years of age are listed in Table 1 (3).

According to a systematic review of longitudinal data, risk factors for malnutrition include frailty, excessive polypharmacy, declining physical functioning and cognition, depression, dysphagia, and institutionalization (4). Multiple physical, socioeconomic, and cultural factors affect the nutritional status of older individuals, including changes in the ability to absorb nutrients, reduced appetite, and decreased ability to chew (4, 5). Furthermore, there are multiple drug-nutrient interactions that should be considered for this population (Table 2) (6). Insufficient energy intake associated with aging is complex and may involve chronic illnesses and reduced ability and desire to prepare and eat meals (7). Micronutrient intake below recommended amounts increases NCD risks (8).

Micronutrient	Men	Women
Vitamins		
Folate*	250 μg	250 μg
Vitamin A†	750 μg	650 μg
Vitamin B_{12} (cobalamin)	4.0 μg	4.0 μg
Vitamin B_6	1.5 mg	1.3 mg
Vitamin C	90 mg	80 mg
Vitamin D	15 μg	15 μg
Vitamin E (α-tocopherol)	13 mg	11 mg
Vitamin K	70 μg	70 μg
Minerals		
Calcium	750 mg	750 mg
Magnesium	350 mg	300 mg
Potassium	3500 mg	3500 mg

*1 μg of DFE equals 1 μg of food folate=0.6 μg of folic acid from fortified food=0.5 μg of a folic acid supplement; †1 μg RE equals 1 μg of retinol, 6 μg of β-carotene, and 12 μg of other provitamin A carotenoids; DFE, dietary folate equivalent; RE, retinol equivalent.

Table 1. European Food Safety Authority (EFSA) daily reference intakes for selected micronutrients in adults >50 years of age (3)

For example, micronutrient deficiencies can cause mitochondrial decay, a mechanism contributing to aging and development of diseases including cancer and neural decay (8). A relationship has been observed between the intake of certain micronutrients (i.e. vitamins D, B_6, B_{12}, and E and folate) and frailty in older adults (9). Values for ranges of nutrient intakes in the EU are described in Table 3 (10).

This narrative review describes the nutritional needs of middle-aged (50–64 years) and older (≥65 years) adults in the EU and interventions healthcare professionals should consider. Literature searches were conducted to identify sources that evaluated the nutritional status and interventions relevant to this population, with an emphasis placed on systematic reviews, meta-analyses, and dietary guidelines. Notably, some meta-analyses also included other ages (<50 years), but those that are included primarily assessed older individuals.

Protein

Aging leads to a loss of muscle mass and strength and poor physical performance (i.e. sarcopenia) that has been associated with macro- and micronutrient deficiencies, suggesting that a high-quality diet that includes optimal protein and nutrient intake combined with physical exercise can reduce this risk (11). Sarcopenia can increase the risk for falls, fractures, disability, loss of independence, and increased mortality (11). The prevalence of sarcopenia is approximately 1–29% in community-dwelling older adults and 10–33% in those living in long-term care and acute hospital settings (12).

Adequate protein intake is important to healthy aging, and higher intakes may be necessary to compensate for the difficulty of maintaining muscle mass; however, recommendations vary by country (13). The EFSA recommendation for protein intake for adults is 0.83 g/kg/d (3), yet, the PROT-AGE Study Group recommends protein intakes in older adults of 1.0–1.2 g/kg/d (13). The authors state that those with chronic diseases, severe illnesses, injury, or malnutrition may require higher intakes (i.e. 1.2–1.5 and 2.0 g/kg/d, respectively) (13). Higher protein intake can negatively impact kidney function in those with severe kidney disease not receiving dialysis; therefore, caution should be taken in this population (13). The Nordic Nutrition Recommendations set a tentative recommendation of 1.2–1.5 g/kg/d while stressing that adequate data do not exist to estimate an optimal protein intake (14).

Protein quality, timing of administration, whether to supplement with single amino acids, and the addition of physical exercise should be considered (13). Protein supplementation immediately following resistance training exercise is beneficial for muscle mass and strength (13). A recent meta-analysis of randomized, controlled trials (RCTs) conducted with whey-, leucine-, and casein-based protein supplements combined with resistance training reported that elderly individuals adhering to this regimen improved lean body and appendicular mass, body fat and mass, muscle strength, and mobility (15). However, the International Sarcopenia Initiative stated that protein supplements alone or combined with resistance training have shown inconsistent effects on muscle mass and function in individuals ≥50 years of age (12).

Dietary fiber

Dietary fiber is critical to maintaining proper laxation and a healthy microbiome and is involved in many physiological activities including protecting against CVD (5). EFSA recommends that older adults consume 25 g/d of total fiber (3), but few meet this goal (5). The European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

Drug	Micronutrient	Consequence(s)
Acid suppressants		
Antacids	Copper, fluoride, iron, manganese, phosphorus	Decreased absorption of micronutrient
Proton-pump inhibitors	Vitamin B_{12}	Decreased absorption of vitamin B_{12} from food but not supplements
	Calcium	Decreased absorption of calcium from supplements
	Iron	Decreased absorption of iron
Histamine-2 receptor antagonists	Vitamin B_{12}	Decreased absorption of vitamin B_{12} from food but not supplements
	Calcium	Decreased absorption of calcium from supplements
	Iron	Decreased absorption of iron
Antibiotics	Biotin	Decreased biotin synthesis by intestinal bacteria
	Vitamin B_{12}	Decreased absorption of vitamin B_{12} from food, but not supplements
	Vitamin K	Decreased synthesis of vitamin K by intestinal bacteria; decreased recycling of vitamin K with cephalosporin
	Calcium	Using calcium supplements with quinolones or tetracyclines may decrease absorption of antibiotic
	Iron	Using iron supplements with quinolones or tetracyclines may decrease efficacy of antibiotic
	Magnesium	Using magnesium supplements may decrease absorption of nitrofurantoin, quinolones, or tetracyclines
	Manganese	Using tetracyclines may decrease manganese absorption
	Zinc	Using zinc supplements may decrease efficacy of quinolones and tetracyclines
Metformin	Vitamin B_{12}	Decreased absorption of vitamin B_{12}; corrected by taking B_{12} supplements with milk or calcium supplements
Anticonvulsants	Biotin	Long-term use can increase biotin requirement
	Folic acid	May interfere with dietary folate absorption
	Riboflavin	Long-term use may increase hepatic metabolism and riboflavin requirement
	Thiamin	Long-term use may increase thiamin requirement
	Vitamin B_6	High vitamin B_6 doses may decrease efficacy of phenobarbital and phenytoin
	Vitamin D	Decreased calcidiol plasma levels
	Vitamin E	Decreased vitamin E plasma levels
	Vitamin K	Increased risk for neonatal vitamin K deficiencies and hemorrhagic disease in newborns when taken during pregnancy
	Selenium	Decreased selenium plasma levels with valproic acid
	Zinc	Zinc deficiencies, especially with valproic acid
Anticoagulants		
Warfarin	Vitamin C	High vitamin C doses may decrease anticoagulant efficacy
	Vitamin E	High vitamin E doses may potentiate anticoagulant efficacy
	Vitamin K	High vitamin K intake (diet or supplement) may decrease anticoagulant efficacy; may increase risk for neonatal vitamin K deficiencies and hemorrhagic disease in newborns when taken in pregnancy
	Iodine	Potassium iodide at pharmacologic doses may decrease efficacy of warfarin
	Magnesium	Antacids containing magnesium may decrease efficacy of warfarin

Table 2. Common drug-micronutrient interactions and consequences of the interaction(s) (6)

Drug	Micronutrient	Consequence(s)
Aspirin	Vitamin C	High aspirin doses may increase excretion of vitamin C
	Vitamin K	Decreased vitamin K recycling
	Vitamin E	High vitamin E doses may potentiate antiplatelet effects
Methotrexate	Folate	Folate deficiencies requiring folic acid supplementation
Sulfasalazine	Folate	Increased folate requirement
	Vitamin K	Decreased vitamin K recycling
Cycloserine	Vitamin B_6	Vitamin B_6 deficiencies by forming inactive complex
Isoniazid	Niacin	Niacin supplementation is recommended with long-term isoniazid treatment
	Vitamin B_6	Vitamin B_6 deficiencies by forming inactive complex
	Vitamin E	Decreased vitamin E absorption
	Vitamin K	Increased risk for vitamin K deficiencies and hemorrhagic disease in newborns when taken in pregnancy
Rifampin	Vitamin K	Increased risk for vitamin K deficiencies and hemorrhagic disease in newborns when taken in pregnancy
Bisphosphonates	Calcium, iron, magnesium	Decreased bisphosphonate absorption
	Zinc	Decreased bisphosphonate and zinc absorption
Diuretics	Thiamin	Loop diuretics may increase thiamin excretion
	Calcium	Thiazides increase renal calcium absorption
	Magnesium	High-dose long-term diuretic may cause magnesium depletion
	Phosphorus	Hyperkalemia if potassium-sparing diuretics and phosphates are taken together
	Zinc	Increased zinc excretion
Colchicine	Vitamin B_{12}	Decreased vitamin B_{12} absorption from food but not supplements
Allopurinol	Iron	Increased storage of iron in the liver; users should avoid iron supplements
Cholestyramine and colestipol	Most vitamins and minerals	Decreased absorption of many vitamins and minerals

Table 2. Common drug-micronutrient interactions and consequences of the interaction(s) (6) (continued)

recommendations for managing dyslipidemia include consuming 45% to 55% of energy from carbohydrates, including fruit, vegetables, whole grains, legumes, and nuts, and 25-40 grams of total dietary fiber, such as β-glucan from oat and barley (16).

A meta-analysis of 67 RCTs reported that consuming high-fiber diets significantly reduced total and low-density lipoprotein (LDL) cholesterol, but not high-density lipoprotein cholesterol (17). Other meta-analyses of RCTs reported that using different fiber supplements significantly reduced diastolic blood pressure, an effect that was more pronounced in adults >40 years of age compared with younger adults (18), and significantly reduced glycated hemoglobin in middle-aged and older adults with type 2 diabetes (19).

Omega-3 fatty acids

Omega-3 fatty acids have anti-inflammatory properties, and higher intakes have been linked to reductions in CVD risk and cognitive impairment (5). Omega-3 fatty acids cannot be efficiently converted from dietary alpha-linolenic acid in the body; therefore, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) often do not reach adequate levels. Dietary sources of omega-3 fatty acids include oily fish, flaxseed, and walnuts (5). EFSA recommends that adults consume 0.5% of their energy in the form of alpha-linolenic acid and 250 mg/d EPA plus DHA (3). ESC and EAS recommendations include 2–3 g/d of long-chain omega-3 fatty acid supplements to reduce triglycerides and regular consumption of fish and nuts for preventing CVD (20).

Meta-analyses of RCTs conducted in adults

with or without cardiovascular comorbidities (e.g. coronary heart disease, heart failure) receiving DHA and EPA through the diet or supplementation reported a greater risk reduction among individuals with elevated triglyceride and LDL cholesterol levels (21) and significantly improved brain natriuretic peptide and serum norepinephrine levels (22). The Multicenter Osteoarthritis Study, a prospective cohort study of individuals (mean age: 60 years) with, or at high risk for, knee osteoarthritis (OA) reported that individuals with high plasma omega-3 fatty acid levels, especially DHA, had less patellofemoral cartilage loss (23). Well-controlled RCTs are necessary to support using omega-3 fatty acid supplements for OA.

Due to the association between inadequacies in omega-3 fatty acid status and cognitive decline, a number of studies have been conducted to evaluate the effects of omega-3 fatty acids on cognitive functioning. Meta-analyses of observational studies and RCTs conducted in middle-aged and older adults reported significant improvements in cognitive functioning (i.e. attention, executive functioning, memory), but no improvements in other cognitive parameters were observed (24, 25). A more recent meta-analysis of omega-3 fatty acid trials in adults (>40 years of age) did not observe improvements in cognitive functioning (26).

Folate and vitamins B_6 and B_{12}

Folate is a B-vitamin involved in the metabolism of nucleic acid precursors, DNA methylation, homocysteine metabolism, and cognition (5). Vitamin B_6 is essential for many enzymatic reactions involved in protein metabolism, while vitamin B_{12} is involved in folate metabolism and neurological functioning. Deficiencies in vitamin B_{12} can cause peripheral neuropathy and cognitive dysfunction (3, 5). EFSA recommends that adults consume 250 μg/d folate, 4.0 μg/d vitamin B_{12}, and 1.5 mg/d and 1.3 mg/d vitamin B_6, in men and women, respectively (3). Deficiencies and inadequacies in folate and vitamins B_6 and B_{12} can increase homocysteine concentrations, weaken immunity, and increase risk of CVD, stroke, cognitive dysfunction, depression, osteoporosis, and fracture risk (5, 27). In the EU up to 20% of older adults (>64 years) do not obtain adequate amounts of vitamin B_{12}, and a substantial proportion (17–46%) do not achieve adequate intake of folate (28). Older adults may have difficulty extracting vitamin B_{12} from natural food sources due to an age-related decline in gastric acid secretion (5), which reduces the ability of vitamin B_{12} to bind to intrinsic factor (29).

Meta-analyses of folic acid supplement RCTs in middle-aged and older adults reported significant risk reductions in stroke and CVD-related events (30) and significant reductions in plasma homocysteine concentration, with further reductions when vitamin B_{12} was co-administered (31).

Folic acid and vitamin B_{12} supplementation may also improve bone health, primarily due to the effects on homocysteine levels (32). However, an RCT conducted in older individuals (≥65 years) with elevated homocysteine levels supplemented with folic acid and vitamin B_{12} reported no reduction in fracture risk, aside from a sub-group of individuals >80 years of age (32).

A meta-analysis of case-control studies reported significant associations between higher folate intake and decreased risk of head and neck squamous cell carcinoma (33). Despite these potential benefits, excessive intake of synthetic folic acid can increase the risk of certain cancers (34). Therefore, it is important to determine an individual's intake of dietary folate and folic acid from supplements and fortification to avoid reaching levels that can cause adverse health outcomes.

In meta-analyses of RCTs of folic acid in subjects ≥45 years of age without dementia (35) and vitamin B_6 and B_{12} in subjects ≥40 years of age who were healthy or at risk for CVD (26), no improvements in cognitive functioning were found. Another trial that administered folic acid and vitamin B_{12} to older adults (60–74 years) reported significant improvements in overall cognitive functioning and immediate and delayed recall (36).

Vitamin A

Vitamin A is a fat-soluble vitamin found either as preformed vitamin A (retinol) in animal products such as liver and dairy, or as provitamin A carotenoids such as β-carotene in fruit and vegetables (3, 37). Vitamin A is involved in regulating cellular growth and differentiation and is required for healthy immune function and vision (3, 37). EFSA recommends that adult men and women consume 750 μg/d and 650 μg/d vitamin A (as Retinol Equivalents, Table 1), respectively, from a mixture of preformed vitamin A and provitamin A carotenoids (3).

Micronutrient	Age, years*†	Men (min, max)	Women (min, max)
Vitamins			
Folate‡	19–64	203–494 μg	131–392 μg
	>64	139–343 μg	121–335 μg
Vitamin A	>64	0.5–2.5 mg	0.4–2.3 mg
		500–2500 μg	400–2300 μg
Vitamin B_{12} (cobalamin)	19–64	1.9–9.3 μg	1.0–8.8 μg
	>64	3.1–8.2 μg	2.5–7.5 μg
Vitamin B_6	19–64	1.6–3.5 mg	1.3–2.1 mg
	>64	1.2–3.0 mg	1.2–2.9 mg
Vitamin C (ascorbic acid)	19–64	64–153 mg	62–153 mg
	>64	59–142 mg	60–160 mg
Vitamin D	19–64	1.6–10.9 μg	1.2–10.1 μg
	>64	0.7–15.0 μg	0.7–12.9 μg
Vitamin E (α-tocopherol)§	19–64	3.3–17.4 mg	4.2–16.1 mg
	>64	6.3–13.7 mg	6.7–13.7 mg
Vitamin K	Values not reported		
Minerals			
Calcium	19–64	687–1171 mg	508–1047 mg
	>64	627–1071 mg	533–959 mg
Magnesium	19–64	256–465 mg	192–372 mg
	>64	221–403 mg	179–348 mg
Potassium	19–64	2700–4400 mg	2300–3600 mg
	>64	2200–3800 mg	2200–3700 mg

*Intakes reported for individuals 19–64 years of age for all countries except the following: Greece: 22±2 years of age; Hungary: ≥18 years of age; United Kingdom: 25–64 years of age; †Intakes reported for individuals >64 years of age for all countries except Hungary (>59 years of age); ‡Folate equivalent; 1 μg food folate=0.5 μg folic acid (PGA)=0.6 μg folic acid taken with meals; §RRR-α-tocopherol equivalent=mg α-tocopherol + mg β-tocopherol x 0.5 + mg y-tocopherol x 0.25 + mg α-tocotrienol x 0.33.
DFE, dietary folate equivalent; PGA, pteroyl glutamic acid.

Table 3. Nutrient intake in the European Union based on national data (10)

A critical issue with vitamin A is its toxicity (hypervitaminosis A) caused by excessive retinol intake; middle-aged and older adults may be particularly susceptible to vitamin A toxicity (38). Additionally, several prospective cohort studies have reported that higher intakes of retinol are associated with an increased risk of hip fractures in primarily middle-aged and older adults (39), and two RCTs found that high-dose supplementation with β-carotene (alone or combined with retinol) further increased the risk of lung cancer in at-risk populations (e.g. smokers, asbestos-exposed workers) (38). However, a meta-analysis of four RCTs found no effect on lung cancer risk with retinol or β-carotene supplementation in healthy adults (40).

Vitamin D

Vitamin D plays critical roles in calcium metabolism and bone health but is also involved in other health outcomes, such as neurological conditions, autoimmune diseases, NCDs (e.g. type 2 diabetes, cancers), and infections (5, 41). EFSA recommends vitamin D intake of 15 μg/d for adults (3), while the International Osteoporosis Foundation recommends average daily intake of 20–25 μg/d for older adults (41). Older adults may be at particular risk for insufficiency and deficiency due to lower sunlight exposure, reduced ability of the skin to synthesize vitamin D from 7-dehydrocholesterol upon sunlight exposure, and limited consumption of food sources of vitamin D (e.g. fortified milk, oily fish) (5). Across the EU, the percentage of the older population (>64 years) not obtaining

adequate amounts of vitamin D is approximately 90% in most areas except Norway, Finland, and Spain (28). A systematic review of 195 studies reported that mean 25(OH)D values for those >65 years of age in the EU were 51.7 nmol/L (42). European League Against Rheumatism (EULAR) and European Federation of National Associations of Orthopaedics and Traumatology (EFORT) recommendations for preventing future fractures in those ≥50 years of age with previous fractures taking anti-osteoporosis drugs include supplementation with 800 IU/d (equivalent to 20 μg/d) vitamin D with adequate calcium intake (1000–1200 mg/d) (43). This recommendation is based on a meta-analysis of RCTs demonstrating a significant reduction in the risk of falling with 700–1000 IU/d (17.5–25 μg/d) vitamin D or 25(OH)D levels of 60–95 nmol/L (44) and a pooled analysis demonstrating a reduced risk of hip fractures with ≥800 IU/d (≥20 μg/d) vitamin D or baseline 25(OH)D levels >60 nmol/L in elderly individuals (≥65 years) (45). A separate meta-analysis of RCTs reported that vitamin D at 482–770 IU/d (12–19 μg/d) reduced the risk for non-vertebral and hip fractures by 20% (44), while a National Osteoporosis Foundation meta-analysis of RCTs reported that vitamin D supplements of 400–800 IU/d (10–20 μg/d) and calcium of 500–1200 mg/d reduced the risk of total and hip fractures by 15% and 30%, respectively (46). Evidence for the effectiveness of vitamin D supplements in reducing the risk of falling is inconsistent, and bolus doses have been shown to increase the risk for falling (47).

It has been suggested that vitamin D can have positive effects on other health outcomes, including autoimmune diseases and CVD, type 2 diabetes, and cancer (48). Deficiencies in 25(OH)D levels may also be associated with increased risk of colorectal and breast cancer, cardiovascular events, and mortality (48). Aggregated evidence from RCTs suggests that vitamin D supplementation could effectively prevent respiratory tract infections (49, 50), which caused 2.8 million deaths worldwide in 2010 (49) and affect the elderly at increased rates (50).

Calcium

Calcium is an essential mineral that is involved in promoting bone health but is also associated with other health outcomes such as controlling blood pressure (5). While EFSA recommends 750 mg/d total calcium intake in adults >50 years of age (3), EULAR/EFORT recommends 1000–1200 mg/d for preventing fractures in those using anti-osteoporosis drugs, with supplementation as necessary (43). EULAR/EFORT also cautions that calcium supplements may produce adverse gastrointestinal and possibly cardiovascular effects (43). Across the EU, the percentage of the older population (>64 years of age) not obtaining adequate amounts of calcium ranges from 48–100% (28).

A meta-analysis of 29 RCTs that evaluated calcium supplementation with or without vitamin D on bone health outcomes in middle-aged and older individuals (≥50 years of age) observed significant reductions in fracture risk and bone loss (51). Concern has been raised about the potential for calcium supplements to increase the risk for CVD, but a long-term study specifically designed to evaluate this potential found no evidence of increased risk in older women (mean age: 75 years) in relation to placebo (52). Another meta-analysis reported that total calcium intake (diet and supplementation) below the tolerable upper intake level (UL) is not associated with an increased risk for CVD (53). However, caution should be taken when recommending calcium supplementation to those already obtaining adequate dietary intake (53).

Vitamin K

Vitamin K describes a group of related fat-soluble vitamins critically involved in coagulation and bone health by activating specific proteins in the bloodstream and bone (3, 5, 54). Vitamin K_1 (phylloquinone) is the primary dietary form of vitamin K, which is found in green leafy vegetables and vegetable oils, while vitamin K_2 (menaquinone) is primarily found in animal-based or fermented foods (3, 54). EFSA recommends that adults consume 70 μg/d vitamin K (3). The mechanism of action for a class of anticoagulant therapies (e.g. warfarin) used for preventing atrial fibrillation and other cardiovascular events involves vitamin K antagonism; therefore, balancing the dose of these treatments and dietary vitamin K intake should be considered (55). However, studies have provided conflicting results; some show a negative relationship between coagulation stability and vitamin K intake and others suggest that some amount of vitamin K intake is necessary to produce an adequate response (55). A Cochrane database review reported that only one study showed this additive anticoagulant effect, indicating that the current evidence is insufficient to recommend

vitamin K for those with unstable response to warfarin (56). Supplemental vitamin K has a strong anticoagulant effect, and consuming high levels of vitamin K-rich foods may interact with anticoagulant treatment (57). Vitamin K_1 supplementation combined with calcium and vitamin D_3 has also been shown to modestly improve bone mineral content in older non-osteoporotic women; however, these effects were not observed with vitamin K_1 alone, suggesting that there may be a synergistic effect of these nutrients (58). Vitamin K_2 has also been shown to produce benefits in arterial stiffness and bone mineral density (59, 60).

Vitamin E

Vitamin E (α-tocopherol) is a fat-soluble vitamin with antioxidant properties that are critical for protecting polyunsaturated fatty acids in membrane phospholipids and plasma lipoproteins from oxidative damage (3); it is also involved in immune function (5). α-Tocopherol deficiency causes the development of neurological symptoms (e.g. ataxia) (3). EFSA recommends that adult males and females consume 13 mg/d and 11 mg/d vitamin E, respectively (3), yet those >64 years of age have been shown to consume only between 6.3 and 13.7 mg/d (10). Very few individuals meet intake recommendations for vitamin E through diet alone (5). A meta-analysis of dietary intake studies reported that vitamin E is associated with a dose-dependent reduction in lung cancer risk (61), but another meta-analysis reported no effect on total or cancer-related mortality, aside from a significant reduction in the incidence of prostate cancer when vitamin E was consumed with other nutrients (62). Another meta-analysis of RCTs reported a decreased risk of ischemic stroke but an increased risk for hemorrhagic stroke. Notably, the doses of vitamin E administered substantially exceeded recommended intake levels (63).

Vitamin C

Vitamin C is a water-soluble vitamin with strong reducing and antioxidant properties; it acts as a cofactor in several enzymatic reactions for the synthesis of carnitine, catecholamines, and pro-collagen and for metabolizing cholesterol to bile acids (3). The primary dietary sources of vitamin C include fruit and vegetables and their juices (3). EFSA recommends that adult males and females consume 90 mg/d and 80 mg/d vitamin C, respectively (3). In the EU, the proportion of individuals >64 years of age falling below the average requirement of vitamin C is 4-33% (28).

Population-based studies have shown that plasma vitamin C levels are significantly and inversely related to stroke risk (64). Furthermore, lower vitamin C levels have been linked with a greater risk for Alzheimer's disease (65, 66). Meta-analyses of RCTs have found that vitamin C supplementation significantly reduces both systolic and diastolic blood pressure (67), improves endothelial function and vasodilation in individuals with cardiometabolic risk factors (68), and decreases risk for lung cancer (69) and age-related cataracts (70).

Magnesium

Magnesium is an essential mineral for many enzymatic reactions involved in the synthesis of carbohydrates, lipids, nucleic acids, and proteins, and serves in various neurological and cardiovascular functions, including regulating blood pressure (3, 5). Magnesium is primarily found in muscle tissues and is an important component of bone (3, 5). Magnesium occurs naturally in a number of food items, including nuts, whole grains, seafood, fruit, and vegetables (3). EFSA recommends that adult men and women consume 350 mg/d and 300 mg/d of magnesium, respectively (3). There are few clear indications of magnesium inadequacies due to its various metabolic effects, and serum magnesium concentration as an indicator of status is questionable since there are no reliable biomarkers for magnesium body status (3).

Meta-analyses of prospective cohort and observational studies conducted primarily in middle-aged individuals have reported an association between higher circulating magnesium concentrations and decreased CVD risk (71), a significant inverse relationship between dietary magnesium intake and risk of metabolic syndrome (72), and a relationship between higher magnesium intake and reductions in colorectal cancer (73). Meta-analyses of RCTs that evaluated magnesium supplementation on diabetes-related outcomes reported improvements in insulin resistance (74) and fasting glucose levels (75) and significant reductions in systolic and diastolic blood pressure (76), including in individuals with insulin resistance, pre-diabetes, and other NCDs (77).

Potassium

Potassium is the primary intracellular cation responsible for maintaining fluid and electrolyte balance in the body and, hence, proper nerve conduction, muscle contraction, blood volume, and blood pressure (3, 5). Potassium occurs naturally in all foods but is particularly represented in root vegetables, fruit, whole grains, coffee, and dairy (3). EFSA recommends that adults consume 3500 mg/d of potassium, but these values can vary by country (3). Insufficient potassium intake causes hypertension and increases the risk of CVD, kidney stones, and osteoporosis (5).

A meta-analysis of prospective cohort studies reported that higher dietary potassium intake reduced the risk of stroke, which the authors attributed to reduced blood pressure (78). Although a 2006 Cochrane database review did not find substantial support for potassium supplementation for hypertension (79), a more recent meta-analysis of RCTs reported that potassium supplementation reduced systolic and diastolic blood pressure in a dose-dependent manner in hypertensive individuals (80).

Ensuring adequate nutrition in middle-aged and older adults

There is a robust body of evidence suggesting that a whole-diet approach not only lowers mortality from NCDs, but also positively impacts physical and cognitive functioning, mental health, and quality of life in older adults (81). However, too few high-quality studies have evaluated these outcomes to make clear recommendations. In addition to the nutritional benefits of a healthful diet, there are psychological benefits to eating that should not be overlooked (82). Increasing contact with professionals, identifying barriers, developing problem-solving techniques, and setting appropriate goals can improve the outcomes of dietary interventions in middle-aged and older individuals (83). Nutrition education programs have been shown to be effective for improving the nutritional status of older adults, particularly when they include specific interventions or multiple sessions (84).

Higher adherence to a Mediterranean Diet has been found to be significantly and inversely related to overall mortality in adults >65 years of age (85) and to reduced all-cause, CVD- and cancer-related mortality (86). Furthermore, a multivitamin/multimineral supplement (MVMS) that provides most micronutrients in recommended amounts can provide nutritional support for those who are unable to reach adequate micronutrient intake levels from their habitual diet, particularly for older individuals who often experience malnutrition with advancing age (87).

Healthcare providers commonly recommend MVMS to older adults, and while MVMS are generally safe (88), their benefits for improving health-related outcomes have been difficult to conclusively demonstrate (89). The Physicians' Health Study II (PHS II) observed no reduction in the risk for developing CVD (90), but there was a significant 8% reduction in the risk of all types of cancer in this middle-aged and older male population (≥50 years of age) taking a daily MVMS for a mean duration of 11 years (91). The reduction in cancer risk was 12% when excluding prostate cancer from the analysis, and even greater (27%) in men with a baseline history of cancer (91). Despite its long duration and large sample size involving more than 14,000 male physicians, PHS II was insufficiently powered to detect statistically significant effects of MVMS on any individual type of cancer (91).

PHS II also found a significant 9% reduction in total age-related cataracts and an 11% reduction in cataract surgery (92). According to a Cochrane database review, use of an MVMS with antioxidant vitamins and minerals may delay the progression of age-related macular degeneration (AMD) (93). Lutein and zeaxanthin, which are sometimes added to MVMS formulations, also seem to be beneficial for the management of AMD (94). A meta-analysis of eight RCTs utilizing lutein and zeaxanthin supplementation showed improvements in visual acuity and contrast sensitivity in subjects with AMD (95).

Conflicting evidence on cognition has been observed in older adults who use MVMS. One clinical trial in middle-aged and older men reported improvements in episodic memory, including contextual recognition (96), while another trial in healthy middle-aged and older adults reported no benefit in cognitive task performance (97). Both of these studies reported that MVMS use improved some health-related biomarkers (i.e. C-reactive protein, liver function, and vitamin B_6 and B_{12} blood levels, cholesterol, and homocysteine levels) (96, 97). A meta-analysis of 10 RCTs in primarily middle-aged and older adults reported that MVMS modestly improved some aspects of memory (98). An MVMS formulated with folic acid and vitamins

B_6 and B_{12} was shown to improve plasma homocysteine concentrations in an RCT in individuals ≥50 years of age (99), and another study in older individuals being treated with metformin demonstrated that use of an MVMS can reduce the risk for metformin-mediated deficiencies in vitamin B_{12} levels (100).

It is important that an MVMS include nutrients only in amounts that approximate reference intake values, and middle-aged and older adults who decide to use an MVMS should be aware that using additional single-nutrient supplements could result in a total intake exceeding the UL of these nutrients, increasing the risk of adverse health outcomes (87). Furthermore, there may be some individual exceptions to consider for these populations. For example, the typical dose of calcium commonly used in an MVMS may not be sufficient to promote bone health; therefore, dietary intake should be considered (89).

Conclusion

Data from RCTs suggest that dietary interventions and, when warranted, supplementation with MVMS can be used to reduce the risk of experiencing nutritional deficiencies and inadequacies that are detrimental to the health of middle-aged and older adults. For individuals who do not consume adequate protein, fiber, omega-3 fatty acids, and micronutrients from their habitual diet, supplementation may be required. The individual's medical history, medication use, dietary patterns, and other risk factors should be considered when recommending dietary supplements.

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Conflicts of Interest

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