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Nutrition and Lifestyle in Osteoporotic and Sarcopenic Elders - Clinical Considerations by Italian College of Rheumatologists (CreI)

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Abstract:

Osteoporosis is considered the most frequent rheumatic pathology in the elderly population. It is often accompanied by sarcopenia, defined as the progressive loss of skeletal muscle mass and strength. Together, these conditions increase the risk of falls, fractures, disability, lower quality of life, and frequent hospitalization. This means increased healthcare costs for all European countries, due to the increase in the average age and elderly population. Multiple pharmacological therapies are available for osteoporosis, but the prevention seems to be an important tool to reduce the risk of fracture and hospitalization of patients. A healthy lifestyle, consisting of the right amount of nutrients and micronutrients and physical exercise can help prevent the development of osteoporosis and sarcopenia in the elderly. This review brings together the information present in the literature on the benefits that nutrients and micronutrients, naturally present in foods, have on the prevention of these pathologies. it is suggested that a correct intake of proteins, calcium, phosphorus, magnesium, vitamin.D, vitamin C and antioxidants, vitamin K and omega 3, associated with constant physical exercise, can help to contain osteoporosis. It also indicates the right physical exercise for older osteoporotic adults. This document drawn up by the CReI-Food study group of the Italian College of Rheumatologists aims to provide, based on the most recent scientific evidence, indications on correct nutrition and lifestyle for the prevention and treatment of osteoporosis in older people.

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INTRODUCTION

Population ageing is a longstanding process transforming the demographic, social and economic facets of societies worldwide, especially in the EU [1, 2] where the old-age dependency ratio reached 31.8 in 2019 against 24.9 in the United States (USA) [3]. It is estimated that the segment of people aged 65 and older will grow from 19.7% to 29.5% of the total EU population between 2018 and 2060, with an even greater increase of people over 80 years, who will double (from 6% to 12%) in the same period (Home - Eurostat, n.d.). The rheumatic disease most represented in the elders population are OP and osteoarthritis (OA), often associated with sarcopenia. OP constitutes a major health problem. During the aging process, a gradual loss of bone mass results in osteopenia and OP. The diagnostic difference between osteopenia and OP is based on the level of bone mineral density (BMD). The World Health Organization (WHO) recommends measuring BMD at the spine, hip, or forearm using dual-energy X-ray absorptiometry devices [5]. According to the WHO criteria, osteopenia is defined as a BMD between 1.0 and 2.5 SD below that of a "young normal" adult (T score between −1.0 and −2.5), and OP as a T score of −2.5 or lower. Worldwide, 200 million people suffer from OP and 8.9 million fractures occur every year [6]. By 2050, hip fractures may exceed 21 million cases [7]. The prevalence of OP is 18.3% globally, and it is greater in women than in men (23.1 and 11.7, respectively) [8]. The direct cost of treating these osteoporotic fractures in five European countries (France, Germany, the United Kingdom, Italy, and Spain) is EUR 29 billion, while for the 27 EU Member States it is EUR 38.7 billion, a cost that is expected to increase by 25% until 2025 [9]. Effective fracture prevention by reducing the loss of bone mass is the primary goal of those caring for old people. Other than pharmacologic agents, it is lifestyle adjustment, nutritional support, fall prevention strategies, exercise, and physical status that can treat OP or prevent further osteoporotic fracture. Each of these factors, alone or in combination, can be helpful. Sarcopenia, an involuntary loss of muscle mass often associated with osteoporosis, results in loss of muscle function and strength, reduced independent mobility, and increased risk of falls, fractures, disability, and hospital and long-term care admissions. There are several mechanisms that may be involved in the onset and progression of sarcopenia. These mechanisms involve, among others, protein synthesis, proteolysis, neuromuscular integrity, and muscle fat content [10, 11]. The prevalence of sarcopenia varies between different populations, with reported rates of 5–50% in people over 65 years of age. These variations depend on factors such as the specific techniques used to measure muscle mass and muscle function, the population under study and diagnostic criteria [12]. The European Working Group on Sarcopenia in Older People (EWGSOP) recommends that both reduced muscle mass and decreased muscle function (strength or performance) be evaluated for the diagnosis of sarcopenia [13]. The bone loss of OP, possibly associated with the loss of muscle mass in sarcopenia, reduce autonomy and quality of life in old patients, causing morbidity and mortality. For all these conditions non-pharmacological treatment based on proper nutrition and physical exercise is indicated for healthy aging [14]. In the elders, the nutritional status is influenced by changes that occur in the body composition, in its metabolism and in the functionality of its organs and systems. Over the years, the body composition presents a series of modifications: such as the reduction of skeletal muscle mass, plasma volume and body water associated with an increase in adipose tissue and the progressive reduction of the lean mass of metabolically active cell mass [15]. Energy and nutrient requirements change with age (Table **1**). Energy demand decreases while nutrient requirements remain high. It is not always easy to ensure a correct nutritional intake in the elders due to possible difficulties in chewing, swallowing, mobility, and the presence of cognitive impairment, depression, isolation, poverty, coexistence of acute and chronic diseases, side effects of drugs [12]. In this narrative review, we will describe the role of nutrition in the prevention of OP. In particular, the nutritional role of macronutrients such as proteins and micronutrients such as vitamin (Vit) D, K and C, calcium (Ca), other minerals, and polyunsaturated fatty acids (PUFAs) will be investigated. The exercise, included in the recommendations for the prevention of OP is an effective health intervention; in terms of mortality reduction, it determines benefits like pharmacological interventions. Ageing and a sedentary lifestyle are associated with declines in muscle function and cardiorespiratory fitness, resulting in an impaired capacity to perform daily activities and maintain independent functioning. However, in the presence of adequate exercise these changes in muscular and aerobic capacity are substantially attenuated. Structured exercise play important roles as preventive strategies for many chronic diseases, improves mobility, mental health, and quality of life; it is always

Table 1: Average energy requirement (AR) for adults (60 – 79 years) obtained with the interactive tool "DRV Finder" – Dietary Reference Values for European population, released by EFSA – European Food Safety Authority (2018)

ARs for energy were not calculated for adults ≥ 80 years due to lack of anthropometric data from EU countries for this age group. Ars for energy is an average and indicative value for the reference population, in clinical practice it must be adapted to the individual.

The terms for calculating the AR for energy are described in the EFSA scientific opinion on the DRV for energy [17].

AR according to the Physical Activity Level (PAL)[a]			
Sedentary	**From sedentary to moderately activity**	**Active lifestyle**	**Very active lifestyle**
PAL = 1.4	**PAL = 1.6**	**PAL = 1.8**	**PAL = 2.0**
MEN 60 – 69 Years; Kcal/day			
2017	2305	2593	2882
MEN 70 – 79 Years; Kcal/day			
1984	2267	2550	2834
WOMEN 60 – 69 Years; Kcal/day			
1628	1861	2093	2326
WOMEN 70 – 79 Years; Kcal/day			
1614	1844	2075	2305

[a]Classification of lifestyles in relation to the intensity of habitual physical activity from "Human energy requirements" - Report of a Joint FAO/WHO/UNU Expert Consultation (2001)
Sedentary or moderately active lifestyle: these people spend most of their time sitting or standing. in occupations that do not require too much physical exertion as small household chores. They do not walk long distances. use motor vehicles for transportation and do not exercise sports.
Active or very active lifestyle: these people practice jobs that require more energy than less active and sedentary lifestyles. Or they are people with sedentary jobs who regularly practice vigorous sports during the week.

advisable in the old patients [16]. The purpose of this study is to provide nutrition and lifestyle advice to all caregivers of elders with OP, considering both community-living and nursing-home.

METHODS

This narrative review was conducted by the CReI-Food study group of the Italian College of Rheumatologists (consisting of rheumatology experts, nutrition operators, and trainer operators) based on considerations included in the abstract: "what are the correct nutrition and lifestyle strategies for the prevention and treatment of osteoporosis in elders? And how nutrients and micro-nutrients can improve the symptoms?" Identification of relevant studies was conducted on PubMed [Public MEDLINE run by the National Center of Biotechnology Information (NCBI) of the National Library of Medicine of Bethesda (Bethesda, MD, USA)] using the keywords "osteoporosis" "sarcopenia" and "elder population" or "aging" combined with terms related to our fields of interest, such as diet, nutrition, physical activity, omega-3, VitD, K, C, calcium, other minerals, protein. Furthermore, we searched through the references of the chosen articles for additional studies. Our research was focused on nutrients and micro-nutrients that are part of the normal diet or taken as supplements but not on nutraceuticals as phyto-derivatives taken in pharmacological doses.

DISCUSSION

In recent years, the worldwide scientific production concerning nutrition in the elderly has increased exponentially. The most frequent rheumatic pathology in these patients is OP. It has been estimated that 50-85% of the change in bone mineral density in middle age is genetically determined however the impact of hereditary factors on both bone loss and fractures decreases with age, while the impact of style becomes more important of life [18]. Even if it remains difficult to determine what the influence of diet alone is in the context of lifestyle, due to the variables: environmental exposures, genotype of the individual and composition of the intestinal microbiota, nutrition remains a cornerstone in non-pharmacological therapy of the OP [19]. This review reports some of the nutrients and micronutrients available in foods that are among the most important and studied elements in the management of OP in elderly patients to provide an

Table 2: Key Points on the Properties of Nutrients and Micronutrients Described in this Review

Nutrients	Abbreviations	Properties
Proteins	/	Adequate protein intake increases bone mineral density and protects against fragility fracture risk only in adults with adequate Ca intake.
Calcium, Vitamin D	Ca, VitD	Adequate Ca intake and correct sun exposure or VitD intake in the treatment of OP. Ca is essential for proper bone mineralization and for carrying out important reactions within the body. VitD is a regulator of Ca metabolism and participates in bone mineralization.
Magnesium	Mg	Mg deficit has been hypothesized as a potential risk factor for osteoporotic disease and bone loss.
Phosphorous	P	It also reduced risk of osteoporosis by 45% in adults whose Ca and P intakes were within normal ranges.
Vitamin C	VitC	VitC supplementation could reduce risk of fragility fractures and increase BMD.
Antioxidant molecules	/	It is advisable to vary the choice of fruit and vegetables to ensure an adequate supply of nutrients with powerful antioxidant activities to delay aging and to enhance anti-inflammatory action.
Vitamin K2	VitK2	Low plasma concentrations of VitK2 are associated with a high risk of bone fractures. VitK2 supplementation also increases osteoblastogenesis and the production of collagen with potential beneficial effect on reduction of bone loss.
Omega-3 fatty acids	Ω-3 FAs; ω-3 FAs; n-3 FAs	The increase in fish consumption (>250g per week) and EPA and DHA supplementation, positively correlated with better BMD and mainly exert anti-inflammatory functions by promoting osteoblasts activities and inhibiting osteoclast resorption.
Eicosapentaenoic acid	EPA	
Docosahexaenoic acid	DHA	

update and facilitate the transmission of nutritional advice to the patients (Table **2**).

The Role of Nutrients and Micronutrients in Osteoporotic Elders

1. Protein Intake

Proteins are complex molecules that are important for several bodily functions and provide a source of essential amino acids; a key nutrient for skeletal health, they constitute an important component of the organic bone matrix, influence Ca metabolism and regulate serum levels of insulin-like growth factor 1 (IGF-1), an orthotropic hormone important for bone formation. The IGF-1 hormone enhances Ca and P absorption in the intestine; it is involved in the synthesis of calcitriol and increases the rate of reabsorption of phosphate from the kidney. Proteins represent approximately 30% of bone mass and 50% of bone volume. The effect of proteins on bone health may or may not be beneficial depending on the amount ingested and their plant or animal nature. A low protein intake is detrimental both to the construction of peak bone mass in childhood and adolescence, as it affects skeletal growth, and to the preservation of bone mass with age. Protein deficiency also leads to a reduction in muscle mass and strength in the older adults and is therefore a risk factor for falls. While a gradual decrease in caloric intake in the elders should be considered as an adjustment for reduced energy expenditure, adequate dietary protein is required for maintenance of bone health. An adequate protein intake is necessary not only to maintain the function of the musculoskeletal system but is also able to decrease the complications that occur after an osteoporotic fracture. Correction of poor protein nutrition in patients with a recent hip fracture has been shown to improve subsequent clinical outcome by significantly reducing the rate of complications, such as pressure sores, severe anemia, and intercurrent pulmonary or renal infections [20]. The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) recommends a dietary protein intake of 1.0–1.2 g/kg of body weight/day, with at least 20–25 g of high-quality protein at each main meal [21, 22]. The main sources of animal-based protein are found in meat, fish, poultry, eggs, and dairy products (Table **4**). Animal-based proteins are often called "complete" due to their amount of essential amino acids [23]. Vegetable proteins can be obtained from legumes, nuts, seeds, tofu, soy, tempeh, seitan. They may have poorer nutritional quality due to their variable aminoacidic profile, lower proportion of lysine, cysteine, or methionine [24]. Previously it was assumed that excessively high protein intake might induce a negative Ca balance. This hypothesis relates a higher animal

protein intake with more sulfur amino acids, which could increase acid production and bone resorption, and thus, could induce hypercalciuria and bone loss, leading to OP and an increased risk of fragility fractures [25]. More recent meta-analyses have reported that a higher protein intake is associated with a higher BMD, reduced risk of hip fracture and slower rate of bone loss. It is especially important in older people with OP and must always be accompanied by adequate dietary Ca intakes [26]. Various studies are underway to evaluate whether it is better to take animal or vegetable proteins. On the one hand they are reported lower BMD in the femoral neck and lumbar spine of vegetarians and vegans compared to omnivores, and on the other hand, no significant differences between animal and plant protein consumption were observed in relation to BMD and hip fractures [27, 28]. What is clear is that adequate protein intake increases BMD and protects against fragility fracture risk in adults with adequate Ca intake. In the relationship between vegetarian/vegan diet and bone health, the overall quality of the diet should be considered. Nutritional deficiencies can be avoided when a vegetarian or vegan diet is properly planned with high biological value proteins, variety of fruits and vegetables, legumes, whole grains, nuts, and various soy products and possibly supplemented with nutraceuticals [29].

2. Calcium and Vitamin D

Ca and VitD are part of the bone mineral matrix as calcium phosphate (hydroxyapatite crystals) and are required for bone strength. In an adult subject there are usually 1-2 kg of Ca; more than 99% is found in the skeleton, where it confers mechanical stability and constitutes a reserve necessary to maintain the normal concentration of Ca in the extracellular fluid. Given the crucial role it plays in a wide variety of cellular functions including cell division and adhesion, plasma membrane integrity, protein secretion, muscle contraction, neuronal excitability, the regulation of enzyme activity in interstitial fluids, coagulation, and other plasma proteolytic activities, the Ca concentration in the extracellular fluid must be maintained within a narrow range. Under normal conditions, its concentration is maintained by regulating the rate of passage of Ca through the intestinal and renal epithelia. This regulation is mainly achieved through the modulation of blood levels of parathyroid hormone (PTH) and 1,25-dihydroxycholecalciferol (1,25(OH)2D). Ionized Ca^{2+} in blood inhibits PTH secretion by activating calcium-sensing receptors and indirectly modulates PTH secretion through its effects on 1,25(OH)2D production. This active metabolite of VitD, in fact, inhibits the production of PTH through a negative feedback mechanism. The daily Ca absorption should correspond to the amount of Ca excreted in the urine each day. The dietary Ca requirement is determined by the need for bone development and bone maintenance, which change throughout life. The daily Population Reference Intake (PRI), recommended by the Dietary Reference Values for the EU ("DRV Finder" tool released by EFSA, 2018), is 950 mg/day [30] (Table **3**). Water is an important source of Ca. According to EFSA, a daily intake of 2 L for females and 2.5 L for males [31] should be guaranteed, because good hydration is essential to maintain body water equilibrium, even though it can vary among people, depending on age, physical activity, personal circumstances, and weather conditions [32] (Table **3**). Results of studies carried out on postmenopausal healthy women with a low dietary Ca intake (below 700 mg/day), showed that the consumption of a sulphate-rich mineral water with a high Ca content (596 mg/L) reduced circulating PTH and bone turnover markers [33]. The best way to achieve adequate Ca intake is through adhering to a healthy diet. The most important sources of Ca in the diet are dairy products (milk, yogurt, and cheese), fish (especially sardines with bones), legumes and a few vegetables and fruits (particularly nuts and seeds) (Table **4**). Sometimes dietary sources are insufficient or poorly tolerated, and, in those situations, pharmacological Ca supplementation could be useful [34]. However, the role played by Ca in reducing the risk of fractures is controversial. A meta-analysis published in 2017, which observed an over-50 living population, not in hospitals, nursing homes or assisted residences, showed that there is no significant association between taking Ca or VitD supplements or the Ca/VitD combination with the risk of hip fracture compared to placebo or no treatment. Furthermore, no significant associations were found between supplementation with Ca or VitD, or combined supplements of Ca/VitD, and the incidence of non-vertebral fractures, vertebral fractures or total fractures. In conclusion, the study showed that non-institutionalized old people who take Ca or VitD or Ca/VitD have the same probability of suffering fractures as those who do not follow any treatment [35]. If in the non-institutionalized elderly population, a campaign on proper nutrition with adequate Ca intake and correct sun exposure for a good activation of VitD can be promoted, a Ca supplement should be prescribed in patients suffering from OP, in patients taking OP therapies, patients taking glucocorticoids and

institutionalized patients. In four RCTs (n = 44,505), the evidence showed that the effect of Ca supplements in preventing fractures is weak and inconsistent [21, 36, 37]. The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases and the International Osteoporosis Foundation also concluded that current evidence reveals that supplementation with Ca alone cannot reduce the risk of fracture [38]. The EFSA Panel, in determining the daily intake of vitamin D, had to consider that the serum concentration of 25(OH)D reflects the amount of vitamin D obtained from skin synthesis and through food. From the data obtained it was determined that the adequate daily intake for the adult population is 15 µg (Table **3**). With this quantity it is possible to reach the target of 50 nmol/l of serum VitD. In the presence of an optimal skin synthesis, it is not necessary to supplement VitD [39].

3. Others Minerals: Phosphorus, Magnesium

Phosphorus (P) is the second most abundant mineral in the body after Ca. About 85% is stored in the teeth and bones (700-900 g) in the form of phosphoproteins and hydroxyapatite crystal, while the remainder is found in the tissues and vital organs: heart, brain, muscles, and liver. P is an important intracellular component both in the form of free anions and as a component of proteins, enzymes, transcription factors, energy molecules (adenosine triphosphate, creatine phosphate) and nucleic acids. It's well available in food and is absorbed in the small intestine, even in the absence of VitD although its absorption is increased through active transport mechanisms stimulated by 1,25(OH)2D. The lack of P causes rickets and growth retardation in children and osteomalacia in adults. P deficiency is a very rare condition, due to its natural occurrence in large amounts of food and to the body's high ability to absorb it. The adequate daily intake for P, based on EFSA scientific opinion is 550 mg/day for both genders, according to age group [40] (Table **3**).

A cross-sectional analysis of the data from males and females who participated in the 2005-2010 National Health and Nutrition Examination Survey (NHANES), shows that high P intake is associated with a 4.2% improvement in Bone Mineral Content (BMC) and a 2.1% improvement in BMD. It also reduced risk of osteoporosis by 45% in adults whose Ca and P intakes were within normal ranges [41] while several animal studies have recorded that high dietary P levels, especially on a low Ca diet, decreased BMD through excessive parathyroid hormone (PTH) and osteopontin (OPN, bone matrix protein) excretion [42, 43]. P can be found in foods; the highest percentages of P are found in cereal seeds (11 mg/g in wheat germ) and in legumes from 3 to 6 mg/g. Other sources are fish, eggs, meat, grains (1 to 2 mg/g), milk (about 0.9 mg/g) and vegetables (0.4 - 0.7 mg/g) (Table **4**). Magnesium ion (Mg^{2+}) is the divalent intracellular cation most present in the human cell; after potassium (K), it is the second most represented cation in the organism, with a concentration of 10 – 30 mM in the human body, of which 60% is found in the bones. Mg is also involved in the exchange of Ca and P ions across cell membranes and is essential for neuronal activity and muscle contractions. One third of skeletal Mg is in cortical bone on the surface of the hydroxyapatite crystals, improve the solubility of P and Ca hydroxyapatite and, thereby, influence crystal size and formation. Furthermore, Mg induces osteoblast proliferation, is important for bone development, stimulates bone formation and is essential for bone mineralization; its deficiency is associated with reduced bone formation [44]. Mg is also necessary for the activation of VitD because most of the enzymes involved required it [45]. Mg deficiency can have a detrimental effect on bone health directly (by enhancing osteoclast and reducing osteoblast activity, decreasing bone stiffness) and indirectly (it's functional to VitD activities). Dietary Mg deficit has been hypothesized as a potential risk factor for osteoporotic disease and bone loss. A decreased whole body and hip BMD in postmenopausal women with lower daily Mg intake was reported, however, no relationship between low Mg supplementation and increased risk of fractures was determined [46]. Epidemiologic studies have shown that elevated dietary intakes of Mg were positively and significantly related to BMD. On the opposite, inadequate dietary Mg intakes were linked to an increased rate of bone loss in postmenopausal osteoporotic women. In older subjects, a low intake of Mg causes excessive Ca release from the bone, which further worsens bone fragility and increases the risks of fractures and fall [47, 48]. Mg is found in most whole foods, such as green leafy vegetables, legumes, and nuts (Table **4**). The adequate daily intake for Mg in adults is 350 mg/day for males and 300 mg/day for females, according to EFSA scientific opinion, which also establishes the daily tolerable intake of 250 mg/day of Mg from supplements [49] (Table **3**).

4. Vitamin C and Antioxidant Molecules

VitC, also known as ascorbic acid, is a naturally occurring micronutrient; the human organism is unable

to synthesize VitC, therefore its intake must be through a healthy and balanced diet. Sources are fruits and vegetables: oranges, citrus fruits, red and green peppers, kiwis, strawberries, tomatoes, black currants, broccoli, and cabbage (Table **4**). VitC is essential for the proper functioning of multiple biological processes including biosynthesis of collagen, L-carnitine, hydroxyproline, hydroxylysine, several hormones (e.g., noradrenaline/adrenaline, peptide hormones), gene transcription, regulation of translation and elimination of tyrosine [50]. VitC is a powerful antioxidant which can be used in all pathologies characterized by increased oxidative stress. VitC can improve bone health because of its antioxidant properties. It can suppress osteoclast activity and it's a cofactor for osteoblast differentiation. VitC deficiency leads to a well described set of symptoms known as scurvy. The syndrome includes several bone symptoms: osteolysis, osteonecrosis, bone loss and pathological fractures [51]. Studies have shown a negative relationship between VitC supplementation and the risk of fragility fractures, especially femur and hip, suggesting the potential use of VitC in the treatment of OP [52]. Postmenopausal women have been shown significantly increased BMD of vertebrae, spine, and hip after VitC supplementation [53]. This positive relationship, however, has not been confirmed in other studies suggesting the need for further study and the impossibility of recommending the VitC supplementation except in selected cases. A higher dietary VitC intake was correlated with a lower risk of hip fracture and OP, as well as higher BMD, at both the femoral neck and lumbar spine sites [54]. A diet rich in fruit and vegetables must be ensured for a correct intake of VitC, remembering that the requirement can increase in smoking patients, in patients with IBD and chronic diseases characterized by an increase in oxidative stress [55]. The PRI, in according to EFSA, is 110 mg/day for males and 95 mg/day for females [56] (Table **3**). Oxidative stress is a mechanism of cellular damage determined by free radicals, chemical compounds, particles with high instability and high reactivity. Free radicals are rendered harmless by cellular detoxification processes (antioxidant enzymes). Cellular damage from excess free radicals is involved in all the mechanisms of aging and in some pathologies including OP even if, to date, it has not yet been possible to have a complete vision of the real effects of this process on the development of disease. A recent meta-analysis confirmed the role of oxidative stress in the onset of the disease. The three main enzymes that contribute to the maintenance of reactive oxygen species (ROS) levels, such as superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx), were also analyzed during the study. Both catalase and GPx activities were increased in postmenopausal OP patients, while serum SOD levels did not show significant changes [57]. Antioxidant molecules counteract oxidative stress, preventing or delaying cellular damage. The most studied molecules are minerals (selenium, manganese, zinc, and copper), as essential cofactors for the functioning of antioxidant enzymes, vitamins such as C, B2, E, carotenoids as they react with free radicals, glutathione, and polyphenols (plant extracts). The foods naturally richest in antioxidants are vegetables, so eating fruits and vegetables is the best way to ensure the antioxidant intake [58, 59]. According to what is recommended by the Mediterranean diet, it's advisable to propose the consumption of three portions of fruit and two portions of vegetables a day [60]. In addition to VitC, the main antioxidants are tocopherols, carotenes, and carotenoids, glutasinolates, phenols (anthocyanins and quercetin). Blue-violet fruits and vegetables (aubergines, radish, figs, raspberries, blueberries, blackberries, currants, black grapes, plums) are characterized by the presence of anthocyanins, carotenoids, VitC. Green fruits and vegetables (asparagus, agretti, basil, chard, broccoli, cabbage, artichokes, cucumbers, chicory, lettuce, rocket, parsley, spinach, zucchini, white grapes, kiwi) is characterized by the presence of chlorophyll, carotenoids, folic acid, VitC. Fruit and white vegetables (garlic, cauliflower, onion, fennel, mushrooms, apples, pears, leeks, celery) contain polyphenols, flavonoids, VitC. Red fruits and vegetables (tomatoes, turnips, radishes, peppers, beets, watermelons, blood oranges, cherries, strawberries) contain lycopene and anthocyanins. Yellow fruits and vegetables (oranges, lemons, tangerines, grapefruit, melons, lotuses, apricots, peaches, medlars, carrots, pumpkin, peppers, corn) contain flavonoids, carotenoids, VitC. Resveratrol is also an important antioxidant, contained in black mulberries, blueberries, red fruits, cocoa, and wine. According to the Mediterranean diet, the consumption of a glass of red wine a day can be tolerated [61]. It is advisable to vary the choice of fruit and vegetables to ensure an adequate supply of these pigments which have powerful antioxidant activities, delay aging, and have an anti-inflammatory action [62, 63].

5. Vitamin K

The generic term VitK is used for several compounds derived from 2-methyl-1,4-naphthoquinone, including

the phylloquinones or VitK1 and the menaquinones or VitK2. Phylloquinones are present in products of plant origin, especially green leafy vegetables (cabbage, broccoli, sprouts, Brussels broccoli) and peas (Table **4**). Menaquinones are synthesized by intestinal bacteria and are contained in foods of animal origin, especially in liver, meat, and dairy products. As with other fat-soluble vitamins, absorption requires normal pancreatic and biliary functions. It is only stored in small amounts as it has a high turnover, which is why continued dietary intake and colonic absorption are essential. In humans, VitK catalyzes an enzymatic carboxylation reaction of proteins involved in the coagulation factor cascade. Deficiency causes a hemorrhagic syndrome, due to inadequate synthesis of blood clotting factors. While known for its importance in the coagulation cascade, VitK has other functions as well. It participates in the carboxylation of many bone-bound proteins, regulates the genetic transcription of osteoblastic markers and regulates bone resorption by modulating the production of the osteocalcin produced by osteoblasts during their differentiation. After synthesis, osteocalcin undergoes carboxylation of glutamic acid residues by gamma-glutamyl carboxylase. This process is facilitated by VitK. The carboxylated form of osteocalcin accumulates in the bone matrix due to its strong affinity for hydroxyapatite. Several experimental studies have addressed the question of the role of VitK in bone metabolism. Low plasma concentration is associated with a high risk of bone fractures in both northern European and Asian populations of both sexes [63, 64]. In some studies, VitK2 treatment was found to be effective and safe in the treatment of osteoporosis [65]. It is involved in the modulation of RANK/RANK-L signaling (Receptor activator of nuclear factor κB and -Ligand) and in the modulation of osteoclastogenesis [66]; it also increases osteoblastogenesis and therefore the production of collagen. Some studies have confirmed the potential beneficial effect of VitK2 supplementation to reduce bone and BMD loss, however its effect on fracture risk needs to be demonstrated [67]. The efficacy of VitK on fractures and bone quality needs to be ascertained in future large trials drawn to overcome problems still unsolved after previous studies and with sufficient statistical power to detect true and clinically meaningful effects. More evidence is needed about the effects of VitK supplementation at physiological and pharmacological doses and what the required dose of VitK is to ensure bone and vascular health [68]. In adults, the adequate intake of VitK, in according to EFSA is 70 µg/day (VitK as phylloquinone) [69] (Table **3**).

Table 3: Daily Population Recommended Intake (PRI), Adequate Intake (AI), Average Requirement (AR) and Tolerable Upper Level (UL) of Ca, P, Mg, VitD, VitC, VitK and water obtained with the interactive tool "DRV Finder" – Dietary Reference Values for European population, released by EFSA – European Food Safety Authority (2018)

Research: adults, both genders, ≥60 years

	Gender	AI	AR	PRI	UL
Ca	Both genders	NA	750 mg/day	950 mg/day	2500 mg/day
Mg	Male	350 mg/day	NA	NA	250 mg/day[a]
	Female	300 mg/day	NA	NA	250 mg/day[a]
P	Both genders	550 mg/day	NA	NA	NA
VitC	Male	NA	90 mg/day	110 mg/day	NA
	Female	NA	80 mg/day	95 mg/day	NA
VitD	Both genders	15 µg/day[b]	NA	NA	100 µg/day[c]
VitK	Both genders	70 µg/day[d]	NA	NA	NA
Water	Male	2.5 Lt/day[e]	NA	NA	NA
	Female	2 Lt/day[e]	NA	NA	NA

[a]The UL refers to rapidly dissociating magnesium salts and compounds contained in supplements, it does not include Mg naturally present in foods and beverages.
[b]The AI is relate to ergocalciferol (VitD2) and cholecalciferol (VitD3). This setting assumes minimal cutaneous VitD synthesis.
[c]The UL represent the sum, of VitD2 and VitD3. In the presence of an optimal cutaneous VitD synthesis, supplementation is not necessary.
[d]The AI is based on phylloquinone (VitK1) only, due to the current evidence on menaquinones (VitK2) is insufficient.
[e]The AI relate to water from beverages and food.
AI: Adequate Intake, this value is used when the AR cannot be calculated, it's based on observations or experiments; AR: Average requirement, daily nutrient intake suitable for half of the reference population; PRI: Population Reference Intake, the daily intake of nutrients for almost of people in the reference population; UL: Upper Level, tolerable upper intake level is the maximum chronic daily intake of a nutrient.
NA: Not Available.

6. Omega 3 PUFA

Omega-3 fatty acids (Ω-3 FAs), also called n-3 FAs or ω-3 FAs, are a heterogeneous group of molecules that include monounsaturated fatty acids (MUFAs) and PUFAs. The n-3 FAs have either the only (MUFAs) or the first (PUFAs) double bond between the third and fourth carbon atom counting from the last methyl group [70]. N-3 PUFAs include alfa-linolenic acid (ALA; 18:3 n-3), stearidonic acid (SDA; 18:4 n-3), eicosapentaenoic acid (EPA; 20:5 n-3), docosapentaenoic acid (DPA; 22:5 n-3) and docosahexaenoic acid (DHA; 22:6 n-3). ALA is the precursor for the synthesis of the longer chains in the human body, where SDA is the first long-chain (LC PUFAs) elongation product, which leads to the synthesis of EPA, DPA and DHA [71]. The elongation system requires the same enzymes used in the omega-6 (ω-6 or n-6) PUFAs metabolic pathway ranging from linoleic acid (LA; 18:2 n-6) to arachidonic acid (ARA; 20:4 n-6), which are Δ-6 and Δ-5 desaturase and their respective elongases (ELOVL) [72]. Both n-6 and n-3 PUFAs are constituents of phospholipids cell membranes and are also implicated in the synthesis of eicosanoids such as prostaglandins (PGs), prostacyclin (PGI), thromboxane (TX), leukotrienes, hydroperoxytetraenoic acid, hydroxyeicosatetraenoic acid and lipoxins, which are involved in several physiological process, including inflammation, platelet aggregation, vasodilation, vasoconstriction, immune response, and cell growth and proliferation [71]. From ARA we can obtain 2-series PGs (A2, E2, I2) and TX (A2) by cyclooxygenase-2 (COX-2) action and 4-series leukotrienes (B4, C4 and E4) by lipoxygenases (5-LOX) action. (3) PGE2 and TXA2 are produced in platelets and promote inflammation, aggregation, and vasoconstrictors. Instead, EPA can be converted to 3-series PGs (B3, D3, E3, I3) and TX (A3) by COX-2 and 5-series leukotrienes by 5-LOX. These eicosanoids act like vasodilators and anti-platelet aggregation agents. Prostaglandin I2 (PGI2) derived from AA is also an inhibitor of platelet aggregation (FAO, 2010). DHA can also be metabolized to autacoids such as D-series resolvins (Resolvin D1 to Resolvin D6), protectins (Neuroprotectin D1), and maresins (MaR1 and MaR2), that can enhance the resolution of inflammation [72]. Humans is unable to synthesize PUFAs, we can only convert them from dietary ALA and LA and, considering the opposite effects of n-3 and n-6 PUFAs in regulating homeostasis, it is clear how important the role of nutrition is. Furthermore, the production rates of LC n-3 PUFAs from ALA is low, hence it's vital to include foods that are a source of EPA and DHA in the daily diet [71].

Studies on female mice shown the effect of high-dose regular fish oil against bone loss in animal model of aging. These findings correlated with a decreased activity of pro-inflammatory cytokines TNF-α and IL-6 [74]. Previous *in vitro* studies had shown that these cytokines promote bone resorption by increasing osteoclast differentiation [75]. From these results, Rahman *et al*., analyzed the dose-dependent effect of a highly purified concentrate fish oil (CFO) on female mice during aging and suggested that 4% CFO maintained higher bone mineral density. Moreover, CFO supplementation showed reduced levels of the Tartrate-Resistant Acid Phosphatase (TRAP), a bone resorption marker, and the osteoclast-stimulating-factor, RANKL, without affecting the decoy-receptor of RANKL, osteprotegerin (OPG) [76]. Some studies evaluated the effects of Ω-3 on the bone metabolism in post-menopausal women and in elders with a previous diagnosis of osteoporosis. The increase in fish consumption (>250g per week) [77] and EPA and DHA supplementation, positively correlated with better BMD and mainly exert anti-inflammatory and protective functions by promoting osteoblasts activities and inhibiting osteoclast resorption [77-81]. Kelly *et al*., in their review, described a role of the low-grade chronic inflammation (LGCI) (present in overweight and obesity people) in the development of osteoporosis. The authors purpose that a high intake of n-6 PUFAs with a low intake of n-3 PUFAs, typical of Western diet, promotes LGCI, thus contributing to osteoporosis via deregulation of mesenchymal stem cell (MSC) lineage commitment [82]. The n-3 EPA and DHA drive osteoblastic potential of MSC via increasing osteoblastic transcription factors and inhibit osteoclastogenesis suppressing the Nuclear Factor - kB (NF-kB) signalling, while n-6 ARA and derived PGE2 use the same pathways to down-regulate osteoblastogenesis and stimulate osteoclast differentiation [83]. Osteoclasts, the bone-resorbing cells, originate from myeloid progenitor or osteal macrophages. Because of this origin, they are programmed to respond to inflammatory signals, indeed, pro-inflammatory cytokines [Tumor Necrosis Factor α (TNF-α), interleukin (IL) 6, IL-1β, and IL-11] released by activated immune cells, induce osteoclast resorption activity [82, 84]. Therefore, inflammatory states in which chronic inflammation and a high dietary ratio of n-6:n-3 are present, will lead to down-regulation of osteoblastogenesis and increase the osteoclastogenesis and bone resorption. According to LARN the recommended intake of n-3 FA for adults and older should represent 0.5 - 2% of total daily

Table 4: Macro and Micronutrients Contained in 100 gr of Foods

Main source: Food Composition Tables, updated in 2019, edited by crea.gov.it Council for Agricultural Research and Economics. Second source: USDA National Nutrient Database for Standard Reference, Release 28 – 2015

Foods Source of Proteins	**gr/100 gr**	**Foods Source of Magnesium**	**mg/100 gr**	**Foods Source of Vitamin C**	**mg/100 gr**	**Foods Source of Vitamin D3**	**µg/100 gr**		
Soybean, dried	37	Wheat bran	550	Grape Grape, juice, canned	340	Halibut	27		
Bresaola, dried beef	33	Pumpkin seeds	550	Guava, fresh	243	Carp	25		
Raw ham	28	Cocoa	499	Hot peppers, fresh	229	Trout	19		
Chicken, whole, with skin, roasted	28	Dark chocolate	292	Currant, fresh	200	Swordfish	17		
Turkey, leg, with skin, baked in oven	27	Almonds, sweet, dried	264	Peppers, red and yellow	166	Mackerel	16		
Beans, dried, raw	24	Cashew nuts	260	Parsley	162	Salmon	12		
Lentils, dried, raw	23	Wheat germ	255	Raw peppers	151	Sardines	5		
Almonds, dried	22	Quinoa, raw	189	Peppers, greens	127	Egg, chicken egg, whole	2		
Lean veal, Calf, fillet, raw	21	Peanuts, toasted	175	Rocket Rocket, leaves, fresh	110	**Foods Source of Omega 3**	%		
Beef, tenderloin (fillet), lean only	21	Hazelnuts	160	Kiwi	93		ALA	EPA	DHA
Glithead, fillets, raw	21	Pistachios	158	Turnip leaves	81	Soybean, oil	6.8	-	-
Pilchard, fresh	20	Nuts	131	Cabbage	77	Flaxseed, oil, cold pressed	53.4	-	-
Chicken, whole, with skin, raw	19	Chickpeas, dried, raw	130	Papaya, fresh	60	Olive, extra virgin oil	0.77	-	-
Turkey, whole, with skin, raw	18	Corn	120	Oranges, fresh	55	Walnuts, dried	11.9	-	-
Salmon, fresh	18	Spelt, grain	112	**Foods Source of Vitamin K**	**µg/100 gr**	Wheat germ	7.4	-	-
Cod, raw	17	Milk chocolate	107	Spices, basil, dried	1714	Beans, dried, raw	33.3	-	-
Sole, fresh	17	Venere rice, raw	101	Parsley, fresh	1640	Sole	5.7	17.9	26
Sea Bass, fresh	17	**Foods Source of Phosphorus**	**mg/100 gr**	Collard, fresh or frozen	623	Cod	-	12	32.1
Mackerel, fresh	17	Pumpkin seeds	1233	Spinach, raw	540	Pilchard	5	12.5	17
Herring, fresh	17	Wheat bran	1200	Turnip	519	Mackerel	1.64	8	13.8
Ham	16	Sea bass	1150	Beets	484	Salmon	0.85	8.4	11.3
Cuttlefish, fresh	14	Wheat germ	1100	Kale	390	Anchovy	0.39	10.6	20.4
Squid, fresh	13	Skimmed milk	1100	Lettuce leaf (green), raw	102	ALA: alfa-linolenic acid; EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid			
Egg, Chicken Egg, whole	13	Gilt-head bream Glithead, fish breeding, fillets, raw	1050	Broccoli and Brussels sprouts	101				
Mussel	12	Bran	1013	Cabbage	76				
Egg, Chicken Egg, white	11	Emmenthal, cheese	700	**Foods Source of Vitamin D**	**IU/100 gr**				
Octopus, fresh	11	Grana cheese	692	Fish oil, cod liver	10000				
Clam, fresh	10	Gruyere, cheese	685	Mushrooms, brown, italian	1276				
Oyster, fresh	10	Unsweetened cocoa powder	685	Mushrooms, portabella	1135				
Foods Source of Calcium	**mg/100 gr**	Parmesan, cheese	691	Mushroom, white	1046				
Gruyere, cheese	1123	Cheese, soft	650	Halibut	1097				
Parmesan, cheese	1159	Soy, dried	591	Salmon	859				
Cheddar, cheese	810	Egg, chicken egg, yolk	586	Trout	760				
Cheese, semi soft	604	Pistachios	500	Swordfish	666				
Ricotta, cow milk, cheese	295	Cashew Nuts	490	Mackerel	643				
Milk, cow, whole	119	Pine Nuts	466						
Greek Yogurt, whole milk	150	Legumes, dried	400 – 460						
Yogurt, whole milk	125	Anchovy	196						

calories (at least 250mg of EPA and DHA) [85]. The EFSA Panel on Dietetic Products, Nutrition and Allergies provided a scientific opinion on the safety of the n-3 PUFAs supplementation and, although the data were insufficient to determine the UL for any population group, they concluded that a long-term supplemental intake of EPA and DHA combined up to about 5g/day do not raise safety concerns for adults. According to EFSA, dietary recommendations for EPA and DHA for European adults are between 250 and 500 mg/day [86]. The n-3 intake is usually inadequate because of their limited sources but a lower ratio of n-6:n-3 fatty acids is more desirable in reducing the risk of many of the chronic disease found in the western societies [87]. Some reviews summarize the dietary sources of n-3 and n-6 PUFAs. (1, 3) Most seeds and vegetable oils including canola, soybean, corn, and sunflower oils are major sources of n-6 FAs primarly LA. Instead, seeds of chia (Salvia hispanica), perilla (*Perilla frutescens*), flax (*Linum usitatissimum*), paprika (*Capsicum annuum*) and *Trichosanthes kirilowii* are abundant in n-3 ALA. Both n-3 ALA and n-6 LA can be found in walnuts and green leafy vegetables, and in low n-6:n-3 ratio in raspberry (Rubus spp.) and other berries (Vaccinium spp.) seeds oil. As mentioned above, both EPA and DHA are synthesized from ALA but in humans this process is insufficient. The conversion rate varies between 0.2 and 21% from ALA to EPA and between 0 and 9% from ALA to DHA, depending by multiple factors such sex and competitive inhibition of Δ -6 desaturase. Red meat is the main dietary source of LA, ARA and DPA which accumulates in mammalian muscle and adipose tissues [85]. Seafood contains n-3 PUFAs (EPA and DHA) that can be directly utilized from human body (Table **4**). A good source of EPA are herring, wild sardine and pollock roe. Instead, DHA is found mainly in caviar, flyingfish, herring, pollock, oyster, atlantic salmon and salmon roe. Fish oil from salmon, sardine, herring, cod liver and menhaden contains higher quantities of EPA and DHA [72, 85]. Finally, as opposed to terrestrial plants, seaweed contains n-3 and n-6 long chain PUFAs because they can synthetize them. In general, red algae have ARA and high EPA and brown algae contain much LA and ALA than EPA. Green algae contain high LA, ALA, and DHA [88].

SARCOPENIA IN OSTEOPOROSIS

Sarcopenia is defined as a syndrome characterized by the progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life, and death. The EWGSOP recommends using the presence of both low muscle mass and low muscle function (strength or performance) to diagnose sarcopenia. Therefore, the diagnosis requires documentation of criterion 1 plus documentation of criterion 2 or criterion 3 [89].

Low muscle strength (criterion 1) identified a probable sarcopenia; in addiction, low muscle quantity and/or quality (criterion 2) can confirm the diagnosis of sarcopenia; low physical performance (criterion 3), in presence of criterion 1 and 2, identified a severe sarcopenia.

An accurate assessment of muscle strength can be made using a calibrated hand-held dynamometer. The grip strength test is simple and inexpensive. As an alternative to the grip test, the chair stand test can be used to measure the strength of the leg muscles. This test measures how long it takes for the patient to stand up of his chair five times, without using his hands. Measurement of muscle quantity and quality considers the appearance and composition of the muscle and can be evaluated using the Magnetic Resonance Imaging (MRI) and computer tomography or by Dual-energy X-ray absorptiometry (DXA) or by Bioelectrical impedance analysis (BIA). Gait speed measurement is used to determine physical performance, also in association with the chair stand test [89].

Morphologically, during sarcopenia, the muscle tissue presents serious alterations in cell turnover, linked to an increase of oxidative stress, on which alterations of mitochondrial function and cellular vacuolization depend. Furthermore, a reduction in the number of cells is observed in the sarcopenic muscle satellites resulting in a significant loss of power muscle regeneration. The process of muscle aging begins with the progressive denervation of the individual motor units followed by the substantial reduction in the rapid contraction of the muscle fibers. Most of the motor units lost will be replaced by adipose tissue. The loss of muscle mass, typical of the elders, is the main cause of sarcopenia. In geriatrics it is a progressive process with increasing age. Muscle mass decreases by about 3-8% per decade after the age of 30 and this rate of decline is even higher after the age of 60 (so much so that at age 75 muscle mass is estimated to have halved compared to a healthy young woman). Sarcopenia, as a physiological process, cannot be avoided, however it is important to slow its progression through physical

activity and proper nutrition. Sarcopenia increases the risk of falls and fractures [90] and is one of the first causes to trigger progressive frailty in the elders with increasing limitations of autonomy and poor mobility, a drastic reduction in the quality of life up to the achievement of a severe disability [91]. Sarcopenia complicates not only the most common rheumatic diseases such as osteoarthritis and osteoporosis, but also cardiovascular and respiratory diseases or dementia [92, 93]. Muscular trophism represents the fundamental stimulus for the mechanical remodeling of skeletal structures for which sarcopenia is an important cause of bone quality deterioration. Osteoporosis and sarcopenia are in fact connected in many respects, and can be interpreted as a single unit, defined as a bone-muscle unit [94]. The bone-muscle unit communicates through biochemical and mechanical crosstalk. The simultaneous presence of osteoporosis and sarcopenia, the main age-related pathologies, is defined as osteosarcopenia (OS) [95]. Most studies have found that exercise improves muscle mass, strength, and function, thus may have a protective and beneficial role against sarcopenia, as well as a balanced diet can prevent and slow it [96-98]. Osteoporosis and sarcopenia are two sides of the same coin and share most of the pathogenetic mechanisms. Because of this, they can benefit from the same eating patterns. Dietary patterns, such as the Mediterranean diet, rich in PUFAs, vitamins and antioxidants that reduce oxidative stress, can have a beneficial role on muscle trophism [99]. An adequate protein intake and a good availability of VitD are also important.

PHYSICAL EXERCISE IN THE PREVENTION AND TREATMENT OF SARCOPENIA AND OSTEOPOROSIS

In this section we summarize the guidelines set out in the International Exercise Recommendations in Older Adults (ICFSR), regarding the use of physical exercise in the prevention and treatment of sarcopenia and OP. There are conditions, such as sarcopenia for which exercise may play a primary role both in prevention and in treatment. Declines in muscle function and cardiorespiratory fitness with ageing result in impaired ability to perform daily activities and maintain independence. Exercise improves muscle strength, muscle quality, muscle mass, bone density, mobility and has beneficial effects on cognitive function. The prescription of structured exercise should be based on specific outcomes (primary prevention, improvement in fitness, disease treatment) and the dosage recommendations should consider the external (exercise variable) and internal (acute response to exercise) loads. These are influenced by several factors, such as genetics, psychological, functional, and environmental factors. According to the WHO's "Global Recommendations on Physical Activity for Health" the older adults (age 65 and over) should practice 150 minutes of moderate or 75 minutes of vigorous intensity aerobic activity per week. It is also recommended the muscle strengthening activity for two or more days per week. The US Department of Health and Human Services (HHS) suggests that multicomponent exercises training, which includes balance training and muscle strengthening, at least 2 days per week, and aerobic activities of at least moderate intensity, for a duration of 30 to 45 minutes per session, performed three or more times per week appear to be most effective to increase functional ability in older people with frailty. Exercise adaptations are specific to the selected modality chosen. Resistance training, which use a resistance to muscular contraction to build strength, muscle mass and power output, is the core treatment for sarcopenia. It should be the first choice if significant deficits in muscle strength or balance are identified. Indeed, standing up requires strength and power, staying upright involves balance and walking any distance requires endurance. Attempting to ambulate those who cannot lift their body weight out of a chair or maintaining standing balance is likely to fail and increase risk of falls. Therefore, sequencing should be considered, and introduction of strength/power training, then balance exercise, and then finally aerobic exercise may be a logic progression. Moreover, resistance training may prevent muscle loss during a low-calorie diet in overweight and obese individuals. This protective effect is not achieved with aerobic training alone. The exercises should involve major muscle groups and include both multi-joint exercises, such as squat, leg press, chest press and single muscle groups, such as biceps, triceps, knee extensors. For each exercise, 2-3 sets of 8-12 repetitions are recommended, starting at 30-40% of 1RM (one Repetition Maximum) and progressing to loads of 70-80% 1RM, with 1-3 minutes rest between sets. As reported in ICFSR, different meta-analyses have shown that resistance training progressing to intensities ranging from 70 and 80% of 1RM promote greater strength gains than progressing to light (i.e., <50% of 1 RM) and moderate (i.e., < 70% of 1 RM) [100, 101]. Resistance training can be used to preserve or improve muscle power in the shortest amount of time. This

specific type of muscle training is called power training and should be prescribed, where possible, to older individuals with sarcopenia, frailty, and other co-morbidities, considering that muscle power deficits are associated with disability both in older men and even more so in the women. A special care should be taken with the execution of the exercises to avoid musculoskeletal injuries, which may represent a significant barrier for older adults intending to perform power training. Mechanical loading of the skeleton generally leads to favourable site-specific change in bone density, morphology, and strength, whereas unloading (bed rest, immobilisation, spinal cord injury or space travel) produces rapid and sometimes dramatic resorption of bone. The incidence of hip fractures is 30 – 50% lower in older adults with a history of high physical activity levels than age-matched, less active individuals. A systematic review and meta-analysis published in 2017 highlighted that combined exercise protocols that integrate different exercise training modes, such as resistance training along with impact exercise, with high mechanical strain generated against the ground during exercise, tended to be effective in improving or preserving lumbar spine, femoral neck, total hip, and total body BMD in postmenopausal women, although high impact activities, such as jumping using weighted vest, are not recommended for people with vertebral osteoporosis [102]. For high impact activities including walking, jogging, skipping, hopping, stair climbing and stepping with weighted vests, 5 – 10% of body weight in vest during exercise is recommended. To prevent falls, exercise prescriptions should include balance training, 2 – 3 repetitions of 5 – 10 different static and dynamic balance postures, up to 7 days per week. Multicomponent exercise programmes, which include various combinations of strength, power, gait, balance, and functional training, have been shown to reduce falls in older adults and can be prescribed to prevent the onset of the frailty syndrome, a state of decreased physiological reserve that makes individuals vulnerable to stress, potentially resulting in disability and increased mortality. Aerobic training can counteract the decline in the cardiorespiratory capacity due to age by inducing central and peripheral adaptations that boost maximal oxygen uptake (VO2max) and the ability of skeletal muscle to generate energy by oxidative metabolism, therefore it should be a part of exercise routine for both fit and frail older adults. Aerobic exercises for older adults may include walking with changes in pace and direction, treadmill walking, step-ups, stair climbing, stationary cycling, dancing, or aquatic exercise. However, conditions such as severe balance impairments, neuromuscular disease or lower extremity arthritis may request alternative modalities, such as cycling or aqua aerobic. It is possible to start with 5-10 minutes of training in the first weeks and progress up to 15-30 minutes, with a frequency from 3 to 7 days per week Having regard to the considerable scientific evidence on the health benefits of exercise for older adults, the use of exercise not only as a preventive medicine but also as a therapeutic agent should be encouraged, and exercise programs should be included as an integral part of the older patients care plan. To ensure adherence to the training program and allow the sedentary patient to gradually adapt to the new exercise routine, starting with a single exercise mode can be recommended. In all cases, exercise prescription should be individualized considering risk factors, medical history, musculoskeletal limitations, functional ability, tolerance, and personal preferences [16].

CONCLUSIONS

In the elders, the caloric requirement decreases while the need for micro and macronutrients remains constant. Essential micronutrients for bone mineralization are calcium, phosphorus, magnesium. An important role is entrusted to vitamins, in particular VitC and VitK and to the antioxidant molecules that can counteract the oxidative stress that causes tissue aging. The adequate intake or possible supplementation of omega-3 PUFAs (EPA and DHA) promotes osteoblastic activity and reduces osteoclastic. Among the macronutrients, an important role is played by proteins, both animal and vegetable, which improve bone and muscle trophism. An adequate protein intake is fundamental. Insufficient dietary protein intake can lead to muscle waste, resulting in unintentional loss of body weight due to accelerated degradation of muscle protein and reduced protein synthesis. It is important to help, even with nutrition associated with exercise, the maintenance of muscle mass and contain the sarcopenia that is often associated with OP. Muscular trophism represents the fundamental stimulus for the mechanical remodeling of skeletal structures for which sarcopenia is an important cause of the deterioration of bone quality resulting in an increase in the incidence of fragility fractures in older patient. The loss of muscle stimulation, as mentioned, inhibits bone remodeling. Among proteins, those rich in leucine seem to play an important role because they have anabolic properties [103]. An adequate intake of

VitD is confirmed to be able to reduce the risk of fracture, especially in patients living in residential facilities. VitD plays a decisive role in musculoskeletal metabolism. VitD deficiency correlates with muscle fiber atrophy, increased risk of chronic musculoskeletal pain, sarcopenia, and falls. Although further studies are needed, it can be affirmed that dietary interventions that include good adherence to the Mediterranean pattern, an adequate protein intake and a good availability of VitD improve muscle mass [104, 105].

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS APPROVAL

Not applicable.

CONSENT TO PARTECIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIAL

The datasets supporting the conclusions of this article are available at: https://multimedia.efsa.europa.eu/drvs/index.htm "DRV Finder" – Dietary Reference Values for European population, released by EFSA – European Food Safety Authority (2018) (Tables **1** and **3**); https://www.alimentinutrizione.it/sezioni/tabelle-nutrizionali Food Composition Tables, updated in 2019, edited by crea.gov.it Council for Agricultural Research and Economics and USDA National Nutrient Database for Standard Reference, Release 28 – 2015, https://data.nal.usda.gov/dataset/usda-national-nutrient-database-standard-reference-legacy-release (Table **4**).

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AUTHORS CONTRIBUTIONS

(a) Conception and design: R. Laurenti, M. Fioretti; (b) literature review and data collection: R. Laurenti, M. Fioretti, F.Tanzini; (c) manuscript writing: all authors; (d) the drafting of the article or its critical revision for important intellectual content: all authors; (e) final approval of manuscript: all authors.

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