Mineral water as food for bone: an overview

Barbara Pampaloni [1], Maria Luisa Brandi [2]
[1] Bone Clinic, Casa di Cura Villa Donatello, Florence, Italy
[2] F.I.R.M.O. Italian Foundation for the Research on Bone Disease, Florence, Italy

ABSTRACT

Water is a primary asset and contributes significantly to human health. Although water requirements vary from person to person, an intake of 1.5-2 L per day is known to guarantee proper hydration, and is essential to maintaining the body's water balance.

Water for human use includes "water" (treated or not) intended to be drinkable, used for the preparation of food and drinks, and for other domestic uses, and "natural mineral water", meaning waters that "originate from an aquifer or from a groundwater basin, which flow from one or more natural or reamed (perforated) springs and which have specific hygienic characteristics and, possibly, health properties".

According to European legislation (Directive 2009/54/EC), mineral waters can be classified on the basis of analysis of their main chemical-physical characteristics. Natural mineral waters can also be classified into many categories on the basis of their mineral composition and principal component. Natural mineral waters are known to have many beneficial (and non-beneficial) effects on human health and several studies have explored their properties and their role in different physiological and pathological conditions.

Despite concerns about possible negative effects due to the plasticizers and/or endocrine disruptors that may be present in bottled mineral waters, their consumption is widespread.

Calcium-rich mineral waters (calcium content >150 mg/L) supply excellent amounts of highly bioavailable calcium and are a very useful way of taking in calcium regularly and in a well distributed way throughout the day, without experiencing side effects; they therefore contribute to the achievement of the recommended intakes.

Mineral waters can also be used as supplements to reduce the risk of deficiency of other micronutrients important for bone health such as boron, strontium and fluoride. Finally, gut microbiota is emerging as a key player in bone turnover regulation due to its ability to modulate the immune system, controlling inflammation and also influencing calcium absorption and vitamin D levels. Intestinal dysbiosis may promote bone mass loss in older people and after menopause. For this reason, the maintenance of a healthy and efficient intestinal microbiota is considered fundamental in the management of skeletal pathologies, both to prevent them and to support possible drug therapies.

KEYWORDS

Natural mineral waters, calcium, magnesium, boron, strontium, fluoride, bone health.

Introduction

Water is an essential element for life. The fact that it covers about 70% of the Earth's surface and makes up about 60-70% of the human body is enough to give an idea of the importance of the relationships between water, health and the ecosystem. Most of the world's waters are unavailable, being preserved in ice form in the polar caps and in Greenland. Of the free waters, only about 1% consists of fresh water that collects in basins, lakes and rivers, or flows underground, and of this 1% only a small part can be used for human needs. And now, with pollution-related climate change clearly under way, the amount of water that can be used by people is destined to decline still further. A key aspect of climate change is its impact on the Earth's water cycle, through which water is continuously distributed from our oceans to the atmosphere, soil, rivers and lakes, and then returned to our seas and oceans. Climate change is

Article history
Received 29 Jul 2022 – Accepted 29 Aug 2022

Contact
Maria Luisa Brandi; marialuisa.brandi@unifi.it; marialuisa@marialuisabrandi.it
F.I.R.M.O. Italian Foundation for the Research on Bone Diseases,
Via Reginaldo Giuliani 195/A, 50141 Florence, Italy

increasing water vapor levels in the atmosphere and making water availability less predictable. Climate change has also increased the average water temperature of rivers and lakes, shortening the length of the ice cover seasons. These changes, together with the increase in river flows in winter and their reduction in summer, are having important impacts on water quality and freshwater ecosystems. Some of the changes triggered by climate change exacerbate other pressures on aquatic habitats, including pollution. For example, a river flow reduced as an effect of decreased rainfall will result in a higher concentration of pollutants, as there is less water to dilute them [1].

Although water is such an important element for life and plays a fundamental protective role for human health, its contribution to maintaining health, as well as its use as real food which provides human body with essential nutrients, is very often ignored, especially in richer countries.

The human body is made up of about 60% water, well distributed between the extra and intracellular compartments, which contain respectively about 35% and 65% of all the water contained in the body. Water is used by our body for several functions: the distribution of nutrients and molecules through the bloodstream, the elimination of waste products and toxins, and the lubrication of membranes and cells; it is also used to support organs, tissues and joints. Since the human body contains no mechanism allowing us to accumulate and store water, we need to ensure a daily supply of it, sufficient to keep the level of water in the body constant and efficient. Although a certain amount of water is introduced through solid foods in our diet - fruit and vegetables, in particular, can contain up to 85% water - an intake of approximately 1.5/2 L per day is still essential to ensure adequate hydration and to maintain the body's water balance. This amount may vary as needs differ according to age, level of physical activity, personal circumstances and weather conditions [2].

Given the fundamental importance of water, countries across the world define recommended intake levels for their populations. Table I shows the recommended daily amounts for different age groups and physiological conditions in Italy [3].

Water for human use includes "water" (treated or not) intended to be drinkable, used for the preparation of food and beverages, and for other domestic uses, and "natural mineral water". According to Italian law, drinking water must be "clear, odorless, tasteless, colorless and harmless, that is, free of pathogenic microorganisms and chemical substances harmful to humans" and safe on the basis of verification of its microbiological, physical and chemical parameters [4].

Natural mineral water can be clearly distinguished from ordinary drinking water by the purity and preservation of the springs from which it is obtained, by the presence of constant levels of minerals (trace elements or other constituents), and by any effects they may cause.

According to European legislation (Directive 2009/54/EC) [5], and its subsequent implementation in Italian law [6], natural mineral waters are those that "originate from an aquifer or from a groundwater basin, which flow from one or more natural or reamed (perforated) springs and which have specific hygienic characteristics and, possibly, health properties". Moreover, composition, temperature and other essential characteristics of natural mineral waters must remain constant at source even in the presence of natural variations, including changes in flow.

In the United States, the Food and Drug Administration (FDA), the regulatory agency for food and beverages, is the body responsible for regulating bottled water as food. The FDA identifies mineral waters as "water containing not less than 250 parts per million (PPM) of total dissolved solids (TDS) taken from a spring with one or more wells, or from a geologically and physically protected underground spring" [7].

Table I Recommended daily intake of water for the Italian population.

	AGE RANGES	ADEQUATE INTAKE (mL/day)
Infants		
	6-12 months	800
Children-Teenagers		
	1-3 years	1200
	4-6 years	1600
	7-10 years	1800
Males	11-14 years	2100
	15-17 years	2500
Females	11-14 years	1900
	15-17 years	2000
Adults		
Males	18 -29 years	2500
	30 -59 years	2500
	60-74 years	2500
	≥75 years	2500
Females	18-29 years	2000
	30-59 years	2000
	60-74 years	2000
	≥75 years	2000
Pregnancy		
		+350
Breastfeeding		
		+700

Most of the mineral waters consumed in the world are stored in plastic bottles. Several studies have focused on the safety of bottled mineral waters and one of the main concerns over their use concerns the possible migration of chemicals from plastic containers to the water. Plastic bottles can release free monomers, which, after migrating into the water and being absorbed by the human body, can potentially interfere with endocrine systems. This phenomenon, which can occur with stored food in general, can be amplified in food products that are consumed in large quantities, as ascertained in the case of water. Bisphenol A is one of the best characterized endocrine disruptors commonly used in the plastic food packaging production industry. Such disruptors may migrate into food, especially if the packaging is stored under conditions that favor this. Favorable conditions include long storage times, high temperatures, and exposure to sunlight and UV rays [8].

Despite concerns about possible negative effects due to the possible presence of plasticizers and/or endocrine disruptors that may be present in bottled mineral waters, they continue to be widely consumed. In recent years, bottled mineral water consumption has significantly increased worldwide. According to a U.S. and International Developments and Statistics report, the United States, Western European countries, and several Asian nations have seen an increase in their bottled water markets [2].

As recently reported in the Libro Bianco "Il valore dell'acqua 2021", Italy consumes 200 liters per capita per year, and is the world's leading consumer of bottled mineral water (compared to a European average of 118 liters). It is also the EU's second largest pumper of water for potable use, drawing 153 m^3 per capita per year (twice the European average) [9].

According to the Italian National Institute of Statistics (ISTAT), 46.5% of Italians do not drink tap water. Parents, in particular, often prefer to give their children bottled mineral water. Considering the good quality of water supplied by local waterworks, this practice is, for most of Italy, at least partially unjustified. As mentioned, Italy consumes more bottled mineral water (an average of 155 L/person/year) than any other European nation [10].

As we have outlined, water in all its forms is fundamental for human survival. In particular, drinking water can be considered in two ways: "a drink" if we refer to a liquid that hydrates human body, or "food" if we consider its mineral, nutritious content.

"Natural mineral water" means microbiologically pure water, the term denoting absence of the main indicators of contamination, such as parasites and pathogenic microorganisms [2]. A natural mineral water can be defined as such in the presence of the following:

- a detailed description of the hydrogeological basin from which it originates, including the nature of the soil and the way in which the water was collected
- a detailed physico-chemical analysis, performed to define its final characteristics (source flow rate, source temperature, anions, cations, trace elements, presence of toxic elements)
- microbiological analysis, performed to ensure that the main indicators of contamination are not present.

This information shall be clearly indicated on the label, which will also include possible beneficial physiological effects on human health, if supported by appropriate clinical and scientific studies [5, 11].

The water can also be classified on the basis of its "fixed residue 180 ºC", that is, the amount of residual mineral salts (in mg) after evaporation of 1 liter of water at 180 ºC.

Finally, it is also possible to classify natural mineral waters, into many categories, on the basis of the presence of certain specific minerals. According to Directive 2009/54/EC, mineral waters can currently be classified as:

- bicarbonate water, if the bicarbonate content is >600 mg/L
- sulphate water, if the sulphate content is >200 mg/L
- chlorinated water, if the chloride content is >200 mg/L
- calcium water, if the calcium content is >150 mg/L
- magnesian water, if the magnesium content is >50 mg/L
- fluorinated water, if the fluoride content is >1 mg/L (more than 1.5 mg/L fluoride is not suitable for children under 7 years of age)
- acid water, if the CO2 content is >250 mg/L
- sodium water, if the sodium content is >200 mg/L. The note "Suitable for a low-sodium diet" may be added to labels if the sodium content is <20 mg/L.

Calcic and magnesian waters

Mineral waters with a calcium (Ca) content >150 mg/L are defined as "calcic waters". They supply excellent amounts of highly bioavailable Ca, and are therefore a very useful way of taking Ca regularly and in a well distributed way throughout the day, without experiencing side effects; they therefore contribute substantially to the achievement of the recommended intakes.

Several studies on osteoporosis prevention and therapies based on Ca supplements have shown that mineral water can be usefully transformed from "food" into "nutrient". If properly consumed, in fact, calcic water can be considered an excellent Ca supplement.

As effectively summarized in the table published in 2019 by Vannucci *et al.* [12], the past thirty years have seen many publications on the effectiveness of mineral water for maintaining adequate Ca intake. In a cross-sectional study involving 21 healthy men aged 18-50 years, recruited from the German general population, Greupner *et al.* evaluated the bioavailability of Ca from three mineral waters with different mineral concentrations, from milk, and from a calcium carbonate supplement (CaCo3). Serum and urine analysis results indicated that the bioavailability of Ca from mineral water with different levels of mineralization, milk and food supplements was comparable [13].

Calcium-rich mineral water is a calorie-free and fat-free source of Ca that contributes to the optimal supply. In this context, individuals' usual patterns of mineral water consumption should be considered, because greater intake during the day can increase the bioavailability of Ca.

The amount of Ca in drinking water is variable, ranging from negligible levels to values higher than those contained in several dairy products. This variability depends on the origin of the water, the treatment it underwent, and the distribution system used. In many areas of China, to ensure the quality and safety of classically produced tap water, the government has widely implemented direct drinking water (DDW) systems in several public spaces, including school campuses. DDW is obtained from municipal tap water using a series of advanced water treatment technologies and can be consumed safely without further treatment. The result of such systems, however, is a purified very low mineral water that, widely consumed by the population, can drastically reduce the mineral intake thus posing several health risks.

Huang *et al.* conducted a retrospective cohort study in 660 children aged 10-13 years divided into two groups who, for four years, were given, at school, drinking water with normal or very low mineral content, respectively. They evaluated the relationships between water consumption and bone remodeling in these children, and concluded that consumption of very low mineral water, even though it is not the only source of daily drinking water, might be associated with osteoblast inhibition, bone resorption activation, bone mineral reduction, and height development retardation. The authors considered these effects to be attributable to the fact that, by consuming this water, children did not achieve the recommended Ca intake [14].

Although drinking water may be extremely important in achieving recommended levels of Ca, its consumption is regularly omitted in food intake surveys, and not all chemical composition tables show the Ca content of water.

In Europe the mineral content of water varies greatly, and that applies to both tap water and bottled waters. Stoot *et al.* analyzed 126 brands of carbonated or sparkling water, in 10 countries, and confirmed this great variability in the mineral composition of water across Europe. The lowest average concentration of Ca (about 43 mg/L) was found in Italy, and the highest (91 mg/L) in Switzerland [15].

Concentrations of Ca and magnesium (Mg) in drinking water in Europe vary considerably due to the composition of the bedrock, i.e., the source of the water supply. Although there is no regulation imposing minimum Ca and Mg or water hardness levels, many studies agree that the presence of Ca and Mg is beneficial for health.

Even though the current position of the World Health Organization [16,17] is that the strength of evidence is insufficient to propose guidelines for Ca, Mg or water hardness levels, Kozisek, in a paper published in 2020, looked at whether EU member states have rules on levels of these minerals and of hardness of drinking water. The author observed that there are several studies suggesting that Ca- and Mg-rich mineral waters have a protective and beneficial effect on many chronic diseases including neurological disturbances, amyotrophic lateral sclerosis, preeclampsia in pregnant women, high blood pressure, and metabolic syndrome. And many publications have also shown that a lack of Ca or Mg in drinking water seems to cause lower bone mass density (BMD), a higher incidence of fractures, and disturbed bone development in children [18].

In recent review, Rosborg and Kozisek (2020) evaluated six epidemiological studies carried out in Taiwan and Slovakia on water hardness and water Mg content. The studies showed that the presence of Mg and hardness of water were associated with a lower risk of certain neoplasms, in particular esophageal, colon, rectal, prostate and breast cancers [19].

Even though the health benefits of this type of water appear clear, consumption of water with very high levels of Ca and Mg may be reduced by lower acceptability of the water due to its taste. Moreover, the high level of total dissolved solids may raise fears of increased risk of kidney stones. That said, there is evidence that Ca can reduce the risk of certain types of kidney stones by reducing urinary oxalate excretion [20].

Although the importance of the presence of these minerals in water intended for human consumption is evident, there is still no clear European directive setting minimum limits for the presence of Ca and Mg in public drinking water.

The decision on limit values was left to the member states, taking into account local conditions: the minimum concentrations of calcium and magnesium or of total solids dissolved in softened or demineralized water could be established taking into account the characteristics of the water entering these processes [21].

It would therefore be desirable for these health observations to be translated into a single directive establishing the characteristics of drinking water intended for human use, also because, as Kozisek concludes: "Concentrations of Ca and Mg in sources of drinking water in Europe vary considerably due to composition of the bedrock, from which water source originates. We can find a wide range of water hardness from very soft to extremely hard, and even though these drinking waters may comply with all microbiological and toxicological requirements, their consumption may influence the health of populations supplied" [18].

On the other hand, the problem of the effect of mineralized water on human health has long been addressed globally. The study conducted by Cormick and colleagues, published in 2020, aimed to evaluate the Ca content of waters from Argentine waterworks and of bottled natural mineral waters, to assess how it may help the population to meet recommended intakes. Data on the mineral content of waters from the United States show an average of 34 mg/L for tap water coming from surface sources, 52 mg/L for tap water coming from ground sources, and 100 mg/L for mineral waters. Data from Spain show an average Ca concentration of about 38.9 mg/L for public drinking waters and 39.6 mg/L for mineral waters. Cormick *et al.* showed that, in Argentina, most tap or commercially available bottled waters had Ca levels well below 50 mg/L. The samples the authors analyzed had an average Ca level of 13.1-15.8 mg/L with those from water supply systems and those from private wells found to have similar values. Considering that the recommended Ca intake is about 1000 mg/day, these results show that the Ca concentration in the evaluated Argentinian waters could cover 1.3 to 1.9% of the required amount per liter of water consumed. The authors conclude that Ca contained in waters distributed in Argentina, both tap and commercially bottled, do not significantly contribute to achieving the recommended amounts. So, given the benefits that arise from proper Ca intake, and in the light of the low Ca intake reported in different regions of the world, increasing the amount of Ca in tap water and commercially bottled water could be a valid means of bringing about a "universally and fair improvement of calcium intake". Strategies to increase the Ca content of water should therefore be developed [22].

Published in 2002, a study conducted in France by Galan *et al.* showed that mineral water, depending on the amount of Ca it provides, can contribute up to a quarter of an individual's total daily Ca intake. Subjects who regularly drink mineral-rich water have a significantly higher Ca intake than those who drink low mineral or tap water. The authors also noted that only mineral water can bring about significant differences in dietary Mg intake. Depending on the concentration of Mg, mineral water can contribute from 6% to 17% of total daily Mg intake. People who drink water rich or moderately rich in Mg have a significantly higher intake than those who drink water low in minerals or tap water. These authors, too, conclude that a mineralized water can significantly contribute to improving intake of Ca and Mg, and is also a valid option for those who cannot or do not want to consume dairy products [23].

A recent review published by Rondanelli *et al.* in 2021 shows that Mg has been considered of fundamental importance for bone health since 2009, the year in which a European Food Safety Agency (EFSA) panel concluded that "a cause-and-effect relationship has been established between the dietary intake of magnesium (Mg) and maintenance of normal bone". In the light of the numerous studies analyzed, the authors remarked that "from the various studies carried out since 2009 on the serum concentration of Mg and its relationship with bone, it has been shown that lower values are linked to the presence of osteoporosis, and that about 30-40% of the subjects analyzed (mainly menopausal women) have hypomagnesemia. Considering the intervention studies published to date on supplementation with Mg, most have used this mineral in the form of citrate, carbonate or oxide, with a dosage varying between 250 and 1800 mg. In all studies a benefit in terms of both bone mineral density and fracture risk was found" [24].

It is therefore clear that adequate intake of Mg through diet has a protective effect on the onset of osteoporotic fractures, especially in the female population. Women meeting the recommended Mg intake had a 27% decreased risk of future fractures [25].

A study conducted 20 years ago in the SU.VI.MAX cohort in France showed that subjects who drank Mg-rich water had significantly higher intakes of Mg than those who drank oligomineral water or tap water [23].

It is worth noting that bioavailability of Mg from water is generally greater than from food, and while it is relatively easy to fortify water, it is practically impossible to add Mg to foods. Moreover, using water rich in Mg for cooking, in particular for boiling foods, can help to reduce mineral losses from food [26].

A magnesian water can be considered an excellent alternative source in order to achieve optimal intake of Mg, even as a possible alternative to oral supplements (as in the case of calcic waters).

An extensive Norwegian study of elderly people living in urban and rural communities provided interesting information about the effects of Mg in drinking water distributed through municipal aqueducts and the risk of hip fracture. Norway has a high incidence of hip fractures that varies according to degree of urbanization. The hypothesis behind the study was that this variation could reflect a difference in environmental factors and in particular could be due to variations in the concentration of Ca and Mg supplied to the population through municipal drinking water. So, Dahal *et al*. set up a study with the precise purpose of investigating the association between the presence of Ca and Mg in municipal drinking water and the risk of hip fracture, taking into account degree of urbanization, variation between geographical regions, type of water source (surface or groundwater), and acidity (pH) of the water. Fracture events recorded by NOREPOS (Norwegian Epidemiologic Osteoporosis Studies) between 1999 and 2008 were analyzed. The composition of the water from about 500 aqueducts that supply 64% of the Norwegian population was analyzed and its mineral characteristics were related to hip fractures recorded in subjects (men and women between the ages of 50 and 85) who used the analyzed water as drinking water. The study was conducted between years 1994 and 2000 with the participants being observed for a period of between 3 and 14 years. During that time 5,433 fracture events in men and 13,493 in women were identified. The study concluded that both men and women aged 50-85 who drink municipal water with a relatively high concentration of Mg had a significantly reduced risk of hip fracture. On the basis of these results, the authors argued that one possibility, currently not exploited, to improve the mineral status of the Norwegian elderly could be to add Mg to municipal drinking water [27].

In 2015 a further study was published whose purpose was to assess in particular the possible association between Ca in municipal drinking water and the risk of hip fracture in the same sample of Norwegian men and women, and whether this risk could be modified by the simultaneous presence of different levels of trace minerals. The study considered a large population covering about two thirds of the Norwegian population and analyzed 19000 hip fracture events. It is interesting to note that a lower risk of hip fracture was shown in men who consumed, daily, water with a higher Ca content, and that this inverse association between the amount of Ca in drinking water and hip fracture was even more marked when the copper level in the water was high The results showed that the presence of copper changed the relationship between the quantity of calcium and the risk of hip fracture and that it was possible to evince an inverse association between calcium in drinking water and hip fracture risk in men that was stronger when the copper concentration in the water was high [28].

Strongly mineralized waters are a great resource for ensuring an optimal supply of mineral salts through diet, which in turn contributes in a substantial way to the maintenance of good skeletal health. The mineral composition of drinking water depends on the geological characteristics of the source zone and the local distribution systems. It is important to be aware of the mineral characteristics of water, as substances that can be important for skeletal health may be present in low concentrations.

Trace minerals: strontium, boron, fluoride

Strontium

Strontium (Sr) is also a mineral that contributes to the maintenance of the health of our skeleton; in fact, up to 99% of the Sr present in our body is stored in the bone. Strontium promotes bone growth and helps to prevent and treat osteoporosis. Strontium ranelate is an organic salt widely used in the treatment of osteoporosis. Strontium is taken in through food and drink and, in particular, mineral waters. It is a mineral well known to compete with calcium for absorption, which is why a correct Ca/Sr ratio is considered important for osteoporosis prevention. Although Sr can be considered an important element for public health, the WHO has not established limits for the presence of Sr in drinking water [17].

A recent study published by Peng *et al*., in 2021, evaluated Sr levels in samples of public water collected in 314 Chinese cities. The study assessed the health risks, in different age groups and in different regions, in relation to the presence of Sr in drinking water and therefore its intake. In the study, performed between December 2019 and January 2020, the authors estimated that daily intake of Sr through public drinking water amounted to 24-42% of total daily intake of Sr correlation analysis showed a significantly positive correlation between Sr concentration and lumbar bone mineral density in the elderly population, and concluded that the Sr present in the drinking water could have a positive effect on the prevention of osteoporosis [29].

Thus, although this is an element that needs to be carefully assessed, because of its competition with calcium for absorption and the essential need to keep its levels under control, its administration in adequate doses through drinking water could probably be an important factor in the prevention of bone health issues.

Boron

Boron is a widespread trace element in nature, which humans take in mainly through diet (food and drinking water). To date, observations collected from the scientific literature suggest positive effects of boron on human health and metabolism, but human data are still scarce.

A diet rich in boron is characterized by high consumption of fruits, leafy vegetables, nuts, legumes, fermented drinks of vegetable origin (wine, cider and beer), and coffee.

The concentration of boron in foods varies according to the quantity of boron in soil, thus dietary intake of boron varies widely, depending on the quality of drinking water and amount and types of plant foods consumed, plants being the only organisms able to metabolize inorganic boron compounds and convert them into forms that are effectively assimilated by animal and human cells [30].

There are no specific recommendations regarding intake of boron. According to the WHO, 0.2-0.6 mg/day in drinking water and 1.2 mg/day through diet can be considered adequate intakes. However, "boron intake" of 1-13 mg/day has been suggested to be an "acceptable safety interval" for adults. A varied diet rich in plant foods is thought to provide up to 1.5-3.0 mg/day of boron; reported dietary boron intake in the European Union ranges from 0.8 to 1.9 mg/day [31].

The EFSA, on the other hand, after performing several observations on every possible toxic effect of boron and after assessing it toxicodynamics, suggested that 10 mg/day (in the form of boric acid and borates) constitutes the maximum safe dose for the adult population [32].

In a recent study, published in 2022, Weber *et al.* identified a correlation between boron plasma concentration, diet, and cardio-metabolic risk in the general population. The study evaluated plasma boron concentrations in around 1000 subjects, aged 19-77 years, recruited from the general HEALTY population, with the aim of identifying dietary, anthropometric and cardio-metabolic correlates of these concentrations. The researchers concluded that higher boron intake corresponded to better metabolic profiles, characterized by lower body mass index and lower concentration of C-reactive protein, resulting in a lower cardio-metabolic risk profile [30].

Boron has long been considered a critical element for bone health. Studies published to date on boron efficacy on bone metabolism have established that supplementation of 3 mg/day is useful to support bone health (in order to prevent and maintain adequate BMD). This dose is much lower than the upper level indicated by EFSA (daily dose of 10 mg).

A study by Boyacioglu *et al.* in 53 postmenopausal women aged 50-60 investigated the relationship between daily intake of boron, blood levels of osteocalcin, and polymorphisms of the gene encoding it. This Turkish study involved 25 women from "boron rich" regions and 28 women from "low boron" regions. The data analysis showed significantly higher serum levels of osteocalcin in postmenopausal subjects naturally exposed to higher boron concentrations than in subjects from low boron areas, but no statistically significant correlation was found between boron exposure levels and the presence of some polymorphisms of the osteocalcin gene. Although the authors could not make any conclusive observations about the effects of boron intake on BMD, they observed that the level of osteocalcin was higher in the group exposed to boron. Therefore, it is possible to hypothesize that regular intake of water containing more than 1 mg/L of boron can positively affect bone metabolism in postmenopausal women [33].

In the light of the newest observations on the effects of boron, Rondanelli *et al.* concluded that: "Given the recent discoveries on the various beneficial effects of boron on human health, it may be necessary to evaluate whether to classify it among the essential microelements for humans." [32].

Fluoride

Fluoride is another element commonly found in water intended for human consumption. Fluoride is the 13th most abundant anion in the lithosphere. It is present in all the water resources of our planet in variable quantities and proportions. The levels of fluoride in lakes, rivers and canals depend on the topography of the river basins of these bodies of water. The levels of fluoride in groundwater depend on the quality of the minerals present in the rocks through which the water passes [34].

Total daily exposure to fluoride, which is related to the concentration of the mineral in drinking water, the amount drunk, and the levels present in food, may vary significantly depending on geographical area.

As reported by the WHO, fluoride dissolved in drinking water is frequently absorbed in proportions exceeding 90%. Average absorption of dietary fluoride is in the range 30-60%, varies from region to region, and is influenced by dietary composition. In humans, fluoride is considered a chemical element of great importance for health. There are several epidemiological studies on the possible long-term effects of exposure to fluorides by ingestion through water. The fluoride content of human bones varies from 300 to 7000 pg/g of dry tissue depending on total fluoride exposure [31]. To date many studies clearly establish that fluoride mainly produces effects on skeletal tissues in bones and teeth, although low concentrations of fluoride provide protection against dental caries, especially in children.

In relation to the amount of fluoride contained in water, the following phenomena can be observed: dental fluorosis, bone problems, osteoporosis, skeletal fluorosis, neurological disorders, thyroid disorders and growth retardation, as well as muscle damage following deadly toxic doses. The term fluorosis covers a wide spectrum of clinical manifestations related to fluoride toxicity. In the body, ionic fluoride rarely exists in blood;

most ingested fluoride is trapped by bone tissue. In bone, fluoride accumulates in the lattice of bone crystal, where it stimulates new bone formation locally. The newly formed bone outgrowths (exostoses) lead to several clinical syndromes. Effects on bone increase with drinking water fluoride concentrations in exceeding 2 mg/L. Skeletal fluorosis (with changes in bone structure) can occur when water contains 3-6 mg/L. Skeletal deformities generally develop at concentrations of above 10 mg/L. The WHO has set an upper limit of 1.5 mg/L for fluoride in drinking water, although several countries have set their own standards according to their circumstances [31].

Italian waters are usually sufficiently rich in fluoride, so much so that it is not advisable to add it to drinking water or use it as a pharmacological supplement. Nationally, Italy has an average water fluoride concentration of about 1 mg/L. This may explain the lack of measures and regulations concerning the artificial addition of fluoride to drinking water [35].

Emilie Helte and colleagues, in a study published in 2021, assessed the associations of urinary fluoride, and fluoride taken in through drinking water and diet, with BMD and fracture incidence in a prospective cohort of postmenopausal women living in an area where natural fluoride concentrations in municipal drinking water ranged from 0 to 1 mg/L. Between 2003 and 2009, about 8,300 women under the age of 85, living in the Uppsala area, were enrolled. Urine and blood samples were collected and a food frequency questionnaire was administered to estimate dietary and drinking water fluoride intake. Finally, bone mass assessments were carried out by performing bone density scans. As reported by the authors, the results of the study show that "the risk of hip fracture was increased among Swedish women who had the highest levels of urine fluoride excretion and the highest estimated fluoride intake from beverages and food relative to women with the lowest levels of each exposure" and that "long-term consumption of tap water with a fluoride concentration of 1 mg/L, which is below the 1.5 mg/L maximum concentration recommended by the WHO, may adversely affect bone health in postmenopausal women." [36].

In the light of this study, it can therefore be concluded that a low but constant fluoride intake, even at doses below the prescribed limit, may be harmful for bone health.

An even more recent study proposes an analysis of the mechanism by which fluoride could have harmful effects on the organism, calling into question the intestinal microbiota.

Shi-quan Zhu *et al*. evaluated the effects of exposure to different amounts of fluoride in drinking water in group of 72 female mice fed a standard diet and water containing 25, 50 or 100 mg/L fluoride. After 70 days, colic tissue and colon content were collected, to carry out histological assessments and microbiota analysis, with the aim of describing differences in microbiota structure at phylum level. The results showed a clear change in the composition of the microbiota in relation to the level of exposure to fluoride. In particular, a decrease in the amount of short-chain fatty acids (SCFAs), known to be associated with good microbiota health, was observed. Histopathological lesions of the colic tissue were also observed, with shortening and atrophy of the glands, necrosis of enterocytes, and a decrease in the number of caliciform cells. The authors concluded that high dietary fluoride concentrations have a profound effect on the intestinal mucosa, disrupting the intestinal microbiota profile, reducing the amount of SCFAs, which can lead to the onset of intestinal inflammation, and promoting an increase in the expression of IL-17A and IL-22, thereby modifying the homeostasis of the colon [37].

Gut microbiota is increasingly recognized to play a leading role in bone turnover regulation, due to its the ability to modulate the immune system, controlling inflammation and also influencing calcium absorption and vitamin D levels. Intestinal dysbiosis may promote bone mass loss in older people and after menopause.

The composition of gut microbiota can be modified in different ways: through the use of antibiotics or drugs, the adoption of new eating habits, or the use of prebiotics and probiotics. All these changes can strongly affect bone health in a favorable or unfavorable way. Most experimental data produced in mice have shown that gut microbiota modulation by the use of probiotics is able to increase bone mass and reduce bone loss associated with estrogen decrease. In this sense, intestinal microbiota manipulation could become a future adjuvant treatment in the prevention of osteoporosis, osteopenia and other diseases characterized by bone loss such as periodontitis. For this reason, the maintenance of a healthy and efficient intestinal microbiota is considered one of the fundamental aspects in the management of skeletal pathologies, both to prevent them and to support possible drug therapies [38].

Conclusions

In conclusion, in addition to bottled water, known for its mineral content, drinking water distributed through national water networks could have a positive impact on bone health. Achieving optimal intake of the many minerals considered essential for skeletal health can be difficult, and mineral waters can significantly contribute to achieving the recommended dietary levels. It is important to remember, in particular, that calcium-rich waters can supply from a third to half of the recommended daily dose of calcium. Especially in certain populations, such as older people, those who are lactose intolerant, or who suffer from an eating disorder, mineralized water can be an excellent mineral supplement. Finally, in addition to providing essential minerals, water can create the right conditions to promote maximum absorption of the minerals themselves, helping to keep the intestinal microbiota efficient.

References

1. European Environment Agency. Climate change and water - Warmer oceans, floods and droughts. Published 30 Aug 2018 - Last modified 11 May 2021. Available at: https://www.eea.europa.eu/signals/signals-2018-content-list/articles/climate-change-and-water-2014. Accessed July 4, 2022.
2. Quattrini S, Pampaloni B, Brandi ML. Natural mineral waters: chemical characteristics and health effects. Clin Cases Miner Bone Metab. 2016;13(3):173-80.
3. Società Italiana di Nutrizione Umana (SINU). IV Revisione dei Livelli di Assunzione di Riferimento di Nutrienti ed energia per la

popolazione italiana (LARN) 2014. Available at: https://sinu.it/tabelle-larn-2014/. Accessed July 4, 2022.
4. Ministero della Sanità - DECRETO 26 marzo 1991 - Norme tecniche di prima attuazione del decreto del Presidente della Repubblica 24 maggio 1988, n. 236, relativo all'attuazione della direttiva CEE n. 80/778 concernente la qualita' delle acque destinate al consumo umano, ai sensi dell'art. 15 della legge 16 aprile 1987, n. 183. (GU Serie Generale n.84 del 10-04-1991). Accessed July 4, 2022.
5. Official Journal of the European Union. Directive 2009/54/Ec of the European Parliament and of the Council of 18 June 2009 on the exploitation and marketing of natural mineral waters. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX-:32009L0054&from=FR. Accessed July 4, 2022.
6. DECRETO LEGISLATIVO 8 ottobre 2011, n. 176 – Normativa. Available at: https://www.water-time.it/Media/Editor/files/Normative/Decreto%20Legislativo%20n_176%2008-10-2011.pdf. Accessed July 4, 2022.
7. National Archives. Code of Federal Regulations (CFR) – A point in time of electronic Code of Federal Regulations (eCFR). Available at: https://www.ecfr.gov/current/title-21/chapter-I/subchapter-B/part-165?toc=1. Accessed July 4, 2022.
8. Russo G, Laneri S, Di Lorenzo R, et al. Monitoring of pollutants content in bottled and tap drinking water in Italy. Molecules. 2022;27(13):3990.
9. European House Ambrosetti - Valore Acqua per l'Italia - Libro Bianco 2021. Available at: https://www.ambrosetti.eu/news/valore-acqua-per-litalia-libro-bianco-2021/. Accessed July 4, 2022.
10. Petrini C. Centro Nazionale di Epidemiologia Sorveglianza e Promozione della Salute, Istituto Superiore di Sanità. La fluorazione delle acque in Italia. Available at: https://www.epicentro.iss.it/cavo_orale/nota. Accessed July 4, 2022.
11. Elia V, Napoli E, Rizzo R. The new frontiers of Hydrology. Italian Beverage Technology. 2011; 20(66):5.
12. Vannucci L, Fossi C, Quattrini S, et al. Calcium intake in bone health: a focus on calcium-rich mineral waters. Nutrients 2018;10(12):1930.
13. Greupner T Schneider I, Hahn A. Calcium bioavailability from mineral waters with different mineralization in comparison to milk and a supplement. J Am Coll Nutr. 2017;36(5):386-90.
14. Huang Y, Ma X, Tan Y, et al. Consumption of very low mineral water is associated with lower bone mineral content in children. J Nutr. 2019;149(11):1994-2000.
15. Stoots SJM, Geraghty R, Kamphuis GM, et al. Variations in the mineral content of bottled 'carbonated or sparkling' water across Europe: a comparison of 126 brands across 10 countries. Cent European J Urol. 2021;74(1):71-5.
16. WHO, Geneva 2011. Hardness in Drinking-water. Background document for development of WHO Guidelines for Drinking-water Quality. Available at: https://apps.who.int/iris/bitstream/handle/10665/70168/WHO_HSE_WSH_10.01_10_Rev1_eng.pdf. Accessed July 4, 2022.
17. WHO (2017a). Guidelines for drinking-water quality. Fourth edition incorporating the first addendum. Geneva: World Health Organization. Available at: https://www.who.int/publications/i/item/9789241549950. Accessed July 4, 2022.
18. Kozisek F. Regulations for calcium, magnesium or hardness in drinking water in the European Union member states. Regul Toxicol Pharmacol. 2020;112:104589.
19. Rosborg, I, Kozisek F. (Eds.). Drinking Water Minerals and Mineral Balance - Importance, Health Significance, Safety Precautions, 2nd edition. Springer Nature Switzerland AG 2019.
20. Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. N Engl J Med. 1993;328(12):833-8.
21. Council of the European Union, 2019. Safe drinking water and sanitation: Council approves EU guidelines. Available at: https://www.consilium.europa.eu/en/press/press-releases/2019/06/17/safe-drinking-water-and-sanitation-council-approves-eu-guidelines/. Accessed July 4, 2022.
22. Cormick G, Lombarte M, Minckas N, et al. Contribution of calcium in drinking water from a South American country to dietary calcium intake. BMC Res Notes. 2020;13(1):465.
23. Galan P, Arnaud MJ, Czernichow S, et al. Contribution of mineral waters to dietary calcium and magnesium intake in a French adult population. J Am Diet Assoc. 2002;102(11):1658-62.
24. Rondanelli M, Faliva MA, Tartara A, et al. An update on magnesium and bone health. Biometals. 2021;34(4):715-36.
25. Veronese N, Stubbs B, Solmi M, et al. Dietary magnesium intake and fracture risk: data from a large prospective study. Br J Nutr. 2017;117(11):1570-6.
26. Barbagallo M, Veronese N, Dominguez LJ. Magnesium in aging, health and diseases. Nutrients. 2021;13(2):463.
27. Dahl C, Søgaard AJ, Tell GS, et al. Nationwide data on municipal drinking water and hip fracture: could calcium and magnesium be protective? A NOREPOS study. Bone. 2013;57(1):84-91.
28. Dahl C, Søgaard AJ, Tell GS, et al. Population data on calcium in drinking water and hip fracture: an association may depend on other minerals in water. A NOREPOS study. Bone. 2015;81:292-9.
29. Peng H, Yao F, Xiong S, Wu Z, Niu G, Lu T. Strontium in public drinking water and associated public health risks in Chinese cities. Environ Sci Pollut Res Int. 2021;28(18):23048-59.
30. Weber KS, Ratjen I, Enderle J, Seidel U, Rimbach G, Lieb W. Plasma boron concentrations in the general population: a cross-sectional analysis of cardio-metabolic and dietary correlates. Eur J Nutr. 2022;61(3):1363-75.
31. WHO, Geneva 1996. Trace elements in human nutrition and health. 1.Trace elements - metabolism 2.Trace elements - standards 3.Nutrition 4.Nutritional requirements ISBN 92 4 156173 4 (NLM Classification: QU 130). Available at: file:///C:/Users/Hp/Downloads/9241561734_eng.pdf. Accessed July 4, 2022.
32. Rondanelli M, Faliva MA, Peroni G, et al. Pivotal role of boron supplementation on bone health: a narrative review. J Trace Elem Med Biol. 2020;62:126577.
33. Boyacioglu O, Orenay-Boyacioglu S, Yildirim H, Korkmaz M. Boron intake, osteocalcin polymorphism and serum level in postmenopausal osteoporosis. J Trace Elem Med Biol. 2018;48:52-6.
34. Solanki YS, Agarwal M, Gupta AB, Gupta S, Shukla P. Fluoride occurrences, health problems, detection, and remediation methods for drinking water: a comprehensive review. Sci Total Environ. 2022;807(Pt 1):150601.
35. Ministero della Salute. Acque potabili - Parametri – Fluoruro 2016. Available at: https://www.salute.gov.it/portale/temi/documenti/acquepotabili/parametri/FLUORURO.pdf. Accessed July 4, 2022.
36. Helte E, Donat Vargas C, Kippler M, Wolk A, Michaëlsson K, Åkesson A. Fluoride in drinking water, diet, and urine in relation to bone mineral density and fracture incidence in postmenopausal women. Environ Health Perspect. 2021;129(4):47005.
37. Zhu SQ, Liu J, Han B, et al. Fluoride exposure cause colon microbiota dysbiosis by destroyed microenvironment and disturbed antimicrobial peptides expression in colon. Environ Pollut. 2022;292(Pt B):118381.
38. D'Amelio P, Sassi F. Gut microbiota, immune system, and bone. Calcif Tissue Int. 2018;102(4):415-25.

Conflicts of Interest: *The authors declare no conflict of interest.*