# The Effect of Exercise and Nutrition on Bone Health

Abdel Galil M. Abdel Gader

Department of Physiology, College of Medicine, Al Faisal University, Riyadh, Saudi Arabia

#### Abstract

Bone and skeletal muscle are the main components of the musculoskeletal system that functions as one unit to give the body shape, support, and movement. The maintenance of adequate bone health depends on a multitude of factors on the top of genetics, including nutritional factors, especially calcium, Vitamin D, and proteins, in addition to regular physical activity, particularly weight-bearing exercises and parathyroid hormone. These factors are most effective in building peak bone mass and strength during childhood and adolescence and these effects are maintained into adult life and beyond. This review will discuss how exercise and the main nutritional components perform their function in maintaining bone health, bone mineral density, and strength.

Keywords: Bone density, bone mass, calcium, exercise, Vitamin D, weight bearing

## **INTRODUCTION**

The musculoskeletal system, which refers to skeletal muscles and bones, is the largest component of the human body and functions, as one unit, to give the body shape, support, and movement. Besides, the contractions of muscle put mechanical strain on bone and in this way influence greatly bone density, size, and its strength.<sup>[1,2]</sup> The close connection of the functions of both muscles and bones becomes clear when muscles are not used or paralyzed; this results in disuse atrophy of both muscles and bones and the recovery of function results in the rebuilding of both.<sup>[3,4]</sup> However, the maintenance of optimal bone health depends on the interplay between numerous physiological, genetic, and lifestyle factors that include adequate nutrition and optimum hormone levels; besides, exercise and a deficiency in one factor cannot be compensated for by the improvement in others.

Bone is a complex tissue composed of inorganic, organic, and cellular components. The major inorganic component is hydroxyapatite, a complex calcium salt including phosphate, carbonate, magnesium, and other ions. Hydroxyapatite is interwoven with organic components such as collagens and many minor protein contributors. The major cellular components of bone are osteocytes, osteoclasts, and osteoblasts; osteoclasts being responsible for the bone breakdown and bone remodeling and osteoblasts for bone formation and the deposition of bone mineral. Bones are not inert tissues, but are metabolically

#### Access this article online

Website:

Quick Response Code:

www.journalmsr.com

**DOI:** 10.4103/jmsr.jmsr\_41\_18

active, dynamic living tissues that undergoe the biological processes of wear and repair throughout life. These processes are regulated by numerous hormones, particularly parathyroid hormone (PTH) and sex hormones (especially estrogen), in addition to Vitamin D. The current review looks at only the effects of exercise and nutrition on bone health.

## **EFFECT OF EXERCISE ON BONE HEALTH**

Regular physical exercise is essential for maintenance of optimal bone health in many ways. Other than growth and strength of both muscles and bones, the stress produced by exercise on bones benefits bones by increasing calcium deposition; accordingly, bones become denser and stronger. In contrast, physical inactivity results in a decrease of bone mass.<sup>[5,6]</sup> It is also noteworthy that bone modeling is sensitive to mechanical loading, highlighting the influential role of physical activity and this phenomenon persists throughout life.<sup>[7,8]</sup>

Rapid bone growth and building of bone density and strength prevail during childhood and adolescence and exercise during

Address for correspondence: Prof. Abdel Galil M. Abdel Gader, College of Medicine, Al Faisal University, PO Box: 50927, Riyadh 11533, Saudi Arabia. E-mail: amagader@gmail.com

Received : 29-07-2018 Accepted : 28-08-2018 **Revised :** 26-08-2018 **Published Online :** 04-10-2018

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

**How to cite this article:** Abdel Gader AM. The effect of exercise and nutrition on bone health. J Musculoskelet Surg Res 2018;2:142-7.

this period enhances these processes further and maximizes bone mass and this gain in bone mass extends into later years. In fact, the growth, development, and expansion of bones is the outcome of a continuous process of bone deposition and resorption and this bone modeling commences much earlier, during fetal life and continues until epiphyseal fusion, around the end of the second decade of life. However, bone density, mineral content, and structural strength, which depend largely on the thickness of the bone and its dimensions, do not cease after epiphyseal fusion.<sup>[9]</sup>

In a detailed 16-year report based on the results of an evidence-based review of the literature since the year 2000 covering the factors that influence the achievement of the full genetic potential for skeletal mass, Weaver et al.[10] reported a general consensus that lifestyle is one of the main factors that promote maximal bone health throughout life. Among these lifestyle factors, physical activity and calcium intake were identified as the major factors that determine peak bone mass (PBM) from late childhood and adolescence (the critical period for bone accretion) and help to prevent the development of osteoporosis in later life. Although physical activity and calcium have their own independent mechanisms of action on bone, exercise and calcium may not operate independently. For example, low dietary calcium intake or diminished bioavailability results in a reduced adaptive bone response to exercise; conversely, adequate dietary supply of calcium maximizes the benefit of physical activity during rapid bone growth during childhood and adolescence; this being the period to achieve optimal bone health and minimize the risk of osteoporosis in later years. Calcium role in bone health is dealt with below.

The precise biological mechanism whereby exercise influences bone mass has been worked to a great extent. It was shown, for more than two decades, that any increase in mechanical load placed on bone represents strains on the whole bone.[11,12] These strains result in the activation of special osteocytes, embedded within the bone, that function as mechanosensitive cells and have the unique property of mechanotransduction and can detect and respond to mechanical strain. These osteocytes, in turn, and via a sequence of molecular signals activate osteoblasts and osteoclasts and in such a way, the osteocytes control both bone formation and resorption (via the differentiation of both the osteoblasts and osteoclasts). The resulting osteogenic response represents the bone adaptation to the strain put by the physical activity and its causative muscular contraction on the bone. It is notable that the response to the strain will obviously be in the predominant loading direction of the contracting muscle and at the site of strain and deformation.<sup>[13]</sup> A detailed account of this topic can be found elsewhere.<sup>[7]</sup>

The bone adaptation responses to exercise described above serve the important physiological goal of improving bone mineral density (BMD), bone architecture, and strength and also prevent bone injuries. This effect is particularly significant in high-impact sports, such as tennis. Interestingly, those who are physically active in early childhood get further benefit of this physical activity in the form of higher bone mineral content, notably in the femoral neck and hip, when they reach adult life, than those nonexercising sedentary counterparts.<sup>[14,15]</sup> Most of these bone benefits are kept throughout life.<sup>[16]</sup> Former soccer players usually have high BMD and larger bone size and were reported to suffer a lower risk of fracture up to 30 years after they retire.<sup>[16]</sup> The practical benefit of this feature is that it is now well established that exercise is crucial for preventing/ delaying age-related bone loss and the risk of osteoporosis.<sup>[17]</sup>

There is also a general agreement that the gain in bone strength, in response to exercise particularly weight-bearing exercises, such as jumping and ball games, is maximum during childhood and early puberty.<sup>[18]</sup>

When comparing the effect of weight-bearing exercise (vertical jumping) between pre-and post-menopausal women, there was a significant increase in femoral BMD in the premenopausal women and no improvement in the postmenopausal women.<sup>[19]</sup> The mechanism responsible for this difference was related to both the reduction of the circulating estrogen levels and the loss of estrogen receptors on bone cells. This results in diminished proliferation of osteoblasts in the postmenopausal women, estrogen being an essential factor for skeletal growth as well as bone homeostasis.<sup>[20]</sup> On the other hand, males aged 60-85 years were requested to engage in unilateral 12-month leg hopping exercise, with the other leg kept at rest as a control. At the end of the exercise period, a marked increase in BMD was observed in the femur more on the exercising leg than on the resting leg.<sup>[21]</sup> This was attributed more to prevention and/or delaying the expected aging bone changes, which no doubt is the benefit of exercise to bone health. Besides delaying the aging process and maintaining bone health, physical activity has added benefit in improving general body fitness and health.

As to the question how often exercise should be practiced in order to maintain bone health, and strength, there is a general agreement that the exercise bout should continue for 30 min and repeated 3–4 times per week, bearing in mind to give muscles at least 1 day rest between exercise bouts. It is also believed that too much exercise, as seen in some types of competitive sports, can be harmful and may result in reduced BMD and stress fractures.<sup>[3]</sup>

As to which type of exercise is best for bone, all types of exercises are good for bone since any muscle contraction is in real fact against bone or at least some degree of stress is borne by bone. However, weight resistance and weight-bearing exercises are best for improving bone health, enhancing bone mass and slowing bone loss throughout life. Examples of such weight-bearing exercises include walking, running, jogging, and tennis which are the best for bone as they combine the stress on the bone of both muscle contraction and gravity.<sup>[9,22,23]</sup> Other related types of exercise include climbing stairs, gymnastics, and dancing. As expected, the higher the stress and its impact on the bone, the greater the benefit. Furthermore,

the effect of walking can be enhanced by holding weights in the hands while walking. Resistance exercise includes weight lifting, elastic tubing, and other wide range of machines in physical therapy departments and body fitness clubs. The focus of the exercise should be on major muscle groups in the legs, arms, and trunk. Although swimming and cycling are not weight-bearing exercises, they still contract muscles and would have some benefit to bone health. Whatever type of exercise a person likes and enjoys, he or she must do it regularly. Regular physical activity has the added advantage of improving the cardiorespiratory fitness and accordingly improving muscle strength, body balance, and reaction time and, as a result, preventing falls and fractures.<sup>[24]</sup>

## NUTRITION AND BONE HEALTH

As mentioned above, nutrition besides physical exercise and other factors are critical for the maintenance of normal bone health. Although bone mass and strength are basic biological features and accordingly are genetically determined, numerous other physiological and lifestyle modifiable factors interact together for the maintenance of normal bone health and strength, throughout life. However, adequate nutrition is an important "modifiable" (or environmental) factor that influences both bone mass accumulation during childhood and adolescence and bone loss that occurs in later life.<sup>[25]</sup>

The fact that adequate dietary calcium and protein are essential for determining bone mineral mass is well recognized to be the most critical nutritional factors to achieve optimal PBM during childhood and adolescence. However, bone mineralization besides adequate calcium requires phosphate, and the availability and utilization of all these nutritional factors is dependent on Vitamin D.<sup>[26]</sup>

The need for these nutritional ingredients is particularly critical during these early years of life to prevent bone loss and fractures in the elderly. As expected, during these early years, the rate of bone formation exceeds resorption and skeletal mass increases. Once an adult PBM is achieved, equal rates of formation and resorption maintain bone mass until the age of about 30 years when the rate of resorption begins to exceed formation and bone mass slowly decreases. Besides bone mass, bone microstructure and bone geometry also influence the risk of fractures in these late years of life.<sup>[27]</sup> Like exercise, the importance of various aspects of nutrition in bone health has been reviewed extensively in the literature.<sup>[25-34]</sup> However, this short review appraises on the scientific basis for the importance of nutrition for the maintenance of bone health.

Bones are composed mainly of a collagen protein framework that gives them flexibility and calcium phosphate mineral (hydroxyapatite) that gives them strength and rigidity. This unique combination of rigidity and flexibility allows bones to withstand extensive ranges of severity of strain. About 80%–90% of the bone mineral content is calcium and phosphorous; other ingested dietary components include protein that enters the structure of the bone framework and microelements; zinc, copper, iron, magnesium, and fluoride in addition the following Vitamins A, C, D, and K are needed for normal bone metabolism. The complex interaction between these nutritional factors, hormones, and lifestyle is still waiting for further clarification so that major bone problems such as osteoporosis and fractures can be prevented and/or managed.<sup>[35]</sup>

The body stores around 1000 g of calcium, 99% of which is in bones, reaffirming the quote "*we walk around on our calcium reserves*."<sup>[36]</sup> About 1000 mg of calcium are ingested per day, of which one-fifth is absorbed in the small intestine, a process that requires the availability of Vitamin D. Both Vitamin D and PTH elevate Ca<sup>++</sup> in blood by stimulating reabsorption of filtered calcium by the kidney tubules and by stimulating osteoclasts to mobilize calcium from bone. The other hormone involved in body calcium homeostasis is calcitonin (or thyrocalcitonin) that blocks the action of osteoclasts and actions of Vitamin D on the intestine, thereby reducing the blood levels of both calcium and phosphate. The other hormones of interest are estrogens and androgens, both stimulate bone formation during childhood and puberty. This would explain why postmenopausal women (with low estrogen) have an increased incidence of osteoporosis and bone fractures.

Calcium balance and BMD are no doubt essential for the long-term maintenance of bone health; balance refers to net outcome calcium intake and absorption and calcium losses through the kidneys, gastrointestinal tract, and the skin. This makes the dietary intake of calcium as the key factor in maintaining calcium balance and bone health throughout life, but, as mentioned earlier, in particular during the early years of life.

The vital role of calcium in the maintenance of bone health is reflected by the observation that two-thirds of osteoporotic fractures are attributable to inadequate intake of calcium.<sup>[36]</sup> That was enough to instigate the Food and Drug Administration to support the claim that the consumption of calcium-containing dietary supplement, as well as calcium-enriched foods, helps in the prevention of osteoporosis.<sup>[37]</sup>

In menopausal women, the natural decline in their estrogen levels plays a key role in increasing calcium loss through the kidneys (by reducing calcium reabsorption) and by increasing the loss of calcium in feces (by reducing absorption of calcium in the small intestine). As a result, calcium is drawn from bones in order to maintain calcium balance. The net result is a reduction in bone mass and increased risk for osteoporotic fractures. Increased dietary calcium intake becomes the most effective step to maintain satisfactory bone mass and health and prevent fractures during the menopause. The effective alternative it offered is a combination of dietary protein, Vitamin D, and calcium supplementation along with a specifically designed exercise program aiming to improve or even stop the impending muscle weakness and osteoporosis that characterize the menopause.<sup>[38]</sup>

As to the dietary sources of calcium, dairy products are its primary sources followed by calcium-enriched foods and beverages such as orange juice and other juice drinks and supplements, fruits and vegetables, and grain products. The absorption of calcium in the small intestine is influenced mainly by Vitamin D status that enhances calcium absorption. Calcium supplements were reported to be good calcium sources for those with low blood calcium levels who cannot take diets rich in calcium.<sup>[31-40]</sup> However, some reservations have been raised recently about the benefits of these supplements in the prevention of osteoporotic fractures<sup>[39]</sup> in addition to increasing the risk of renal calculus formation.<sup>[41]</sup>

The growth of bone and the maintenance of its health depend, among other basic requirements, on the dietary intake of protein.<sup>[23]</sup> In their recent systematic review and meta-analysis, Wallace *et al*.<sup>[42]</sup> reached the conclusion that high protein intake is of great benefit to mineral density and it resulted in significant reduction in hip fractures among healthy adults aged 18 years and above compared to that of low protein intake. An earlier long-term review of Medline EMBASE electronic databases of randomized clinical trials in healthy adults, which excluded calcium excretion and calcium balance, found a positive association between dietary protein intake and lumbar spine BMD. This finding gives further support to the critical benefit of protein intake to the maintenance of bone health and bone mineral content.<sup>[43]</sup>

As to phosphate and like calcium, most (about 80%) of the body phosphate is found in bones, bound with calcium to form hydroxyapatite that is responsible for BMD and its rigidity.<sup>[44]</sup> Phosphate is regulated by a complex set of processes occurring in the intestine, skeleton, and kidneys. The currently known main regulators of phosphate homeostasis include Vitamin D, PTH, and numerous peptides (phosphatonins); best identified among them is fibroblast growth factor-23.<sup>[45]</sup>

Phosphate, other than bone growth and health, is involved in many vital intracellular and extracellular functions including synthesis of proteins, energy metabolism, cell signaling, and apoptosis. Without the availability of adequate quantities of phosphate, mature chondrocytes cannot undergo apoptosis and accordingly the invasion by new blood vessels and generation of new bone is blocked. This results in rickets and delayed growth before the fusion of the epiphysis or osteomalacia in later years as a result of a deficiency in hydroxyapatite formation.<sup>[46]</sup>

Bone mineral homeostasis and acceptable bone health require adequate quantities of calcium and phosphate, and the availability of both nutrients to the body and subsequent use by bones are dependent on the active form of Vitamin D (1 $\alpha$ ,25-dihydroxy Vitamin D3; 1 $\alpha$ ,25- dihydroxycholecalciferol [1,25[OH]<sub>2</sub>D]). Thus, the absorption of nutrients by the small intestine requires both Vitamin D and PTH. Vitamin D and PTH work together to maintain or raise blood calcium levels by many mechanisms: other than promoting the intestinal absorption of calcium, stimulate the kidney tubules to reabsorb filtered calcium and also stimulate osteoclasts to release calcium from bone into the bloodstream. When the serum Ca<sup>++</sup> is too high, calcitonin blocks PTH-stimulated formation of Vitamin D in the kidney and counters Vitamin D and PTH actions on the kidney tubules.

The best dietary sources of Vitamin D are dairy products, especially milk and Vitamin D-fortified foods and nutritional supplements. Vitamin D is also produced in the skin from 7-dehydrocholesterol under the influence of ultraviolet (sun) irradiation, which in most persons, this skin source can meet their Vitamin D requirements. In this early form, 7-dehydrocholesterol is considered a prohormone that is first hydroxylated in the liver to form an intermediary metabolite, 25-hydroxyvitamin D. This metabolite is further converted in the kidney into a number of other forms, the best studied of which is the physiological form of Vitamin D (1,25[OH]<sub>2</sub>D), which sometimes is considered a hormone.<sup>[45]</sup> Vitamin D is a fat-soluble vitamin and is best absorbed when consumed with fat-containing foods.

The vital role of the combination of Vitamin D and calcium in enhancing bone density was demonstrated in numerous controlled studies in the elderly women who had experienced a reduction in osteoporotic fractures,<sup>[47-51]</sup> reduced body sway, improved body balance, and prevented falls and subsequent osteoporotic fractures.<sup>[52-54]</sup>

Finally, other nutritional requirement needed for the bone metabolic processes and for the maintenance of bone health, bone mass, and strength include the following micronutrients: vitamins and minerals: Vitamins A, C, K, and the B group of vitamins; the following minerals fluoride, copper, iron, zinc, manganese, and boron, in addition to macronutrients such as carbohydrates, fats, and soy foods,<sup>[26,30,31]</sup> which will not be discussed in this short review.

## CONCLUSION

The maintenance of adequate bone health depends on a multitude of factors on the top of the genetics, the so-called "modifiable factors," with the most significant being nutritional materials, especially calcium, Vitamin D, proteins, regular physical activity, especially weight-bearing exercise and PTH. These factors are most effective in building bone mineral content, PBM, and strength during childhood and adolescence and these effects are maintained into adult life and beyond. Although all the factors discussed or mentioned in this review are needed for the achievement of PBM especially during early years of life, the most critical nutritional factor that seems to dominate in the treatment, as well as prevention of osteoporosis, is calcium. Therefore, preventive efforts of osteoporosis take special care of administering adequate nutritional supplies of calcium and Vitamin D, the latter to ascertain the absorption and utilization of calcium. Exercise as explained above also promotes osteoblastic bone-building activity.

## Financial support and sponsorship

Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

#### **Authors' contributions**

The author of this review is responsible for the conception of this review, acquisition of references and the interpretation of their contents, drafting and revising all the article drafts, including the final draft and its approval for publication.

#### REFERENCES

- 1. Brotto M, Bonewald L. Bone and muscle: Interactions beyond mechanical. Bone 2015;80:109-14.
- 2. Sievänen H, Heinonen A, Kannus P. Adaptation of bone to altered loading environment: A biomechanical approach using X-ray absorptiometric data from the patella of a young woman. Bone 1996;19:55-9.
- Russo CR. The effects of exercise on bone. Basic concepts and implications for the prevention of fractures. Clin Cases Miner Bone Metab 2009;6:223-8.
- Bayar A, Sarikaya S, Keser S, Ozdolap S, Tuncay I, Ege A, *et al.* Regional bone density changes in anterior cruciate ligament deficient knees: A DEXA study. Knee 2008;15:373-7.
- Heaney RP, Abrams S, Dawson-Hughes B, Looker A, Marcus R, Matkovic V, et al. Peak bone mass. Osteoporosis Int 2000;1:985-1009.
- Suominen H. Muscle training for bone strength. Aging Clin Exp Res 2006;18:85-93.
- Santos L, Elliott-Sale KJ, Sale C. Exercise and bone health across the lifespan. Biogerontology 2017;18:931-46.
- Baxter-Jones AD, Faulkner RA, Forwood MR, Mirwald RL, Bailey DA. Bone mineral accrual from 8 to 30 years of age: An estimation of peak bone mass. J Bone Miner Res 2011;26:1729-39.
- Karlsson M. Has exercise an antifracture efficacy in women? Scand J Med Sci Sports 2004;14:2-15.
- Weaver CM, Gordon CM, Janz KF, Kalkwarf HJ, Lappe JM, Lewis R, et al. The national osteoporosis foundation's position statement on peak bone mass development and lifestyle factors: A systematic review and implementation recommendations. Osteoporos Int 2016;27:1281-386.
- Turner CH, Forwood MR, Rho JY, Yoshikawa T. Mechanical loading thresholds for lamellar and woven bone formation. J Bone Miner Res 1994;9:87-97.
- Forwood MR, Turner CH. Skeletal adaptations to mechanical usage: Results from tibial loading studies in rats. Bone 1995;17:1978-2058.
- Goodman CA, Hornberger TA, Robling AG. Bone and skeletal muscle: Key players in mechanotransduction and potential overlapping mechanisms. Bone 2015;80:24-36.
- Baxter-Jones AD, Kontulainen SA, Faulkner RA, Bailey DA. A longitudinal study of the relationship of physical activity to bone mineral accrual from adolescence to young adulthood. Bone 2008;43:1101-7.
- Meyer U, Ernst D, Zahner L, Schindler C, Puder JJ, Kraenzlin M, *et al.* 3-year follow-up results of bone mineral content and density after a school-based physical activity randomized intervention trial. Bone 2013;55:16-22.
- Tveit M, Rosengren BE, Nilsson JÅ, Karlsson MK. Exercise in youth: High bone mass, large bone size, and low fracture risk in old age. Scand J Med Sci Sports 2015;25:453-61.
- Borer KT. Physical activity in the prevention and amelioration of osteoporosis in women: Interaction of mechanical, hormonal and dietary factors. Sports Med 2005;35:779-830.
- Hind K, Burrows M. Weight-bearing exercise and bone mineral accrual in children and adolescents: A review of controlled trials. Bone 2007;40:14-27.
- Bassey EJ, Rothwell MC, Littlewood JJ, Pye DW. Pre- and postmenopausal women have different bone mineral density responses to the same high-impact exercise. J Bone Miner Res 1998;13:1805-13.
- Weitzmann MN, Pacifici R. Estrogen deficiency and bone loss: An inflammatory tale. J Clin Invest 2006;116:1186-94.
- Allison SJ, Poole KE, Treece GM, Gee AH, Tonkin C, Rennie WJ, *et al.* The influence of high-impact exercise on cortical and trabecular bone mineral content and 3D distribution across the proximal femur in older men: A Randomized controlled unilateral intervention. J Bone Miner Res 2015;30:1709-16.

- 22. Weaver CM. Calcium requirements of physically active people. Am J Clin Nutr 2000;72:579S-84S.
- Barlet JP, Coxam V, Davicco MJ. Physical exercise and the skeleton. Arch Physiol Biochem 1995;103:681-98.
- Gregg EW, Pereira MA, Caspersen CJ. Physical activity, falls, and fractures among older adults: A review of the epidemiologic evidence. J Am Geriatr Soc 2000;48:883-93.
- 25. Rizzoli R, Biver E, Bonjour JP, Coxam V, Goltzman D, Kanis JA, et al. Benefits and safety of dietary protein for bone health-an expert consensus paper endorsed by the European society for clinical and economical aspects of osteoporosis, osteoarthritis, and musculoskeletal diseases and by the international osteoporosis foundation. Osteoporos Int 2018; doi: 10.1007/s00198-018-4534-5.
- Caroli A, Poli A, Ricotta D, Banfi G, Cocchi D. Invited review: Dairy intake and bone health: A viewpoint from the state of the art. J Dairy Sci 2011;94:5249-62.
- Rizzoli R. Dairy products, yogurts, and bone health. Am J Clin Nutr 2014;99:1256S-62S.
- Bacciottini L, Brandi ML. Foods and new foods: The role of nutrition in skeletal health. J Clin Gastroenterol 2004;38:S115-7.
- 29. Miggiano GA, Gagliardi L. Diet, nutrition and bone health. Clin Ter 2005;156:47-56.
- Palacios C. The role of nutrients in bone health, from A to Z. Crit Rev Food Sci Nutr 2006;46:621-8.
- Sahni S, Mangano KM, McLean RR, Hannan MT, Kiel DP. Dietary approaches for bone health: Lessons from the Framingham osteoporosis study. Curr Osteoporos Rep 2015;13:245-55.
- Farsinejad-Marj M, Saneei P, Esmaillzadeh A. Dietary magnesium intake, bone mineral density and risk of fracture: A systematic review and meta-analysis. Osteoporos Int 2016;27:1389-99.
- Wallace TC, Frankenfeld CL. Dietary protein intake above the current RDA and bone health: A Systematic review and meta-analysis. J Am Coll Nutr 2017;36:481-96.
- 34. Shams-White MM, Chung M, Fu Z, Insogna KL, Karlsen MC, LeBoff MS, *et al.* Animal versus plant protein and adult bone health: A systematic review and meta-analysis from the national osteoporosis foundation. PLoS One 2018;13:e0192459.
- Ilich JZ, Kerstetter JE. Nutrition in bone health revisited: A story beyond calcium. J Am Coll Nutr 2000;19:715-37.
- Heaney RP. Bone biology in health and disease. In: Shils ME, Olson JA, Shike M, Catherine Ross A, editors. 9<sup>th</sup>ed. Philadelphia: Williams and Wilkins; 1999.
- 37. Agostini D, Zeppa Donati S, Lucertini F, Annibalini G, Gervasi M, Ferri Marini C, *et al.* Muscle and bone health in postmenopausal women: Role of protein and Vitamin D supplementation combined with exercise training. Nutrients 2018;10:1038.
- Guidance for Industry: Health Claims on Calcium and Osteoporosis; and Calcium, Vitamin D, and Osteoporosis; 2009. Available from: https://www.fda.gov/Food/GuidanceRegulation/ GuidanceDocumentsRegulatoryInformation/LabelingNutrition/ ucm152626.htm. [Last accessed on 2018 Sep 20].
- Kilim HP, Rosen H. Optimizing calcium and Vitamin D intake through diet and supplements. Cleve Clin J Med 2018;85:543-50.
- 40. US Preventive Services Task Force, Grossman DC, Curry SJ, Owens DK, Barry MJ, Caughey AB, *et al.* Vitamin D, calcium, or combined supplementation for the primary prevention of fractures in community-dwelling adults: US preventive services task force recommendation statement. JAMA 2018;319:1592-9.
- 41. Kahwati LC, Weber RP, Pan H, Gourlay M, LeBlanc E, Coker-Schwimmer M, *et al.* Vitamin D, calcium, or combined supplementation for the primary prevention of fractures in community-dwelling adults: Evidence report and systematic review for the US preventive services task force. JAMA 2018;319:1600-12.
- Wallace TC and Frankenfeld CL. Dietary Protein Intake above the Current RDA and Bone Health: A Systematic Review and Meta-Analysis J Amer Coll Nutr 2017;36:481-96.
- Darling AL, Millward DJ, Torgerson DJ, Hewitt CE, Lanham-New SA. Dietary protein and bone health: A systematic review and meta-analysis. Am J Clin Nutr 2009;90:1674-92.
- 44. Nordin BE. Calcium and osteoporosis. Nutrition 1997;13:664-86.

- Boonrungsiman S, Gentleman E, Carzaniga R, Evans ND, McComb DW, Porter AE, *et al.* The role of intracellular calcium phosphate in osteoblast-mediated bone apatite formation. Proc Natl Acad Sci U S A 2012;109:14170-5.
- Sutton AL, MacDonald PN. Vitamin D: More than a "bone-a-fide" hormone. Mol Endocrinol 2003;17:777-91.
- O'Brien KO. Combined calcium and Vitamin D supplementation reduces bone loss and fracture incidence in older men and women. Nutr Rev 1998;56:148-50.
- Baeksgaard L, Andersen KP, Hyldstrup L. Calcium and Vitamin D supplementation increases spinal BMD in healthy, postmenopausal women. Osteoporos Int 1998;8:255-60.
- Health Quality Ontario. Prevention of falls and fall-related injuries in community-dwelling seniors: An evidence-based analysis. Ont Health Technol Assess Ser 2008;8:1-78.
- 50. Lips P, Bouillon R, van Schoor NM, Vanderschueren D, Verschueren S,

Kuchuk N, *et al.* Reducing fracture risk with calcium and Vitamin D. Clin Endocrinol (Oxf) 2010;73:277-85.

- Borderud SP, Li Y, Burkhalter JE, Sheffer CE, Ostroff JS. Electronic cigarette use among patients with cancer: Characteristics of electronic cigarette users and their smoking cessation outcomes. Cancer 2014;120:3527-35.
- 52. Pfeifer M, Begerow B, Minne HW, Abrams C, Nachtigall D, Hansen C, et al. Effects of a short-term Vitamin D and calcium supplementation on body sway and secondary hyperparathyroidism in elderly women. J Bone Miner Res 2000;15:1113-8.
- Bischoff HA, Stähelin HB, Dick W, Akos R, Knecht M, Salis C, et al. Effects of Vitamin D and calcium supplementation on falls: A randomized controlled trial. J Bone Miner Res 2003;18:343-51.
- Chua GT, Wong RY. Association between Vitamin D dosing regimen and fall prevention in long-term care seniors. Can Geriatr J 2011;14:93-9.