Today's Dietitian
The Magazine for Nutrition Professionals
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New Research on Osteoporosis: Reducing the Risks
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Suggested CDR Learning Codes: 3020, 4040, 4050, 4180, 4190, 5130; Level 2
Suggested CDR Performance Indicators: 8.1.4, 8.1.5, 8.2.1, 8.3.6

Osteoporosis has been defined as "a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility."[1] The most prevalent metabolic bone disease in the United States, osteoporosis often is not diagnosed until a fracture manifests.[2]

According to the National Osteoporosis Foundation, roughly 9 million Americans have osteoporosis and 48 million have low bone density, leaving almost 60% of adults ages 50 and older at risk of breaking a bone. Studies also suggest that approximately one in two women and up to one in four men aged 50 and older will break a bone as a result of having osteoporosis.[3]

Risk Factors
Hereditary factors are thought to be responsible for roughly 70% of the differences in bone mass among individuals,[4] while aging and hormonal status are the two most important factors contributing to the development of osteoporosis.[1]

Research also has found that maternal health during pregnancy, the infant's birth weight, and the child's weight at the age of 1 can affect adult bone mass and that larger babies and rapid growth in the first year predict increased bone mass later in life. A study published by Dennison et al in 2005 noted an independent association of both birth weight and weight at age 1 with bone mineral content in the seventh decade in both sexes. This suggests that both prenatal and postnatal factors are important determinants of skeletal health.[5]

Uncontrollable risk factors for the development of osteoporosis include the following[1,6,7]:

- being aged 50 or older;
- being female, as women lose 30% to 40% of their cortical bone and 50% of their trabecular bone over their lifetime, while men lose 15% to 20% of their cortical bone and 25% to 30% of their trabecular bone;
- having an androgen or estrogen deficiency (Women who started menopause before turning 54, are menopausal, have amenorrhea, or had late menarche have an increased risk.);
- having a family history of osteoporosis;
- having a low body weight and/or a petite build;
- having suffered broken bones or height loss as an adult;
- having a dowager hump; and

- being white or Asian.

In addition, certain diseases and the use of certain medications greatly increase a person's risk of developing osteoporosis. Among the conditions and disorders that can increase osteoporosis risk are genetic and congenital, endocrine, inflammatory, hematologic, and neoplastic; the most common include cystic fibrosis, premature menopause, eating disorders, Cushing syndrome, diabetes mellitus, pregnancy, celiac disease, malnutrition, inflammatory bowel disease, and metastatic disease.[1]

Controllable risk factors associated with osteoporosis include dietary factors (eg, excessive salt, caffeine, and alcohol consumption; low calcium and vitamin D intake), smoking, excessive weight loss, and a sedentary lifestyle. Controlling these factors through diet and lifestyle changes can help prevent osteoporosis.

Consequences

One in two women and one in five men older than the age of 50 will suffer an osteoporotic fracture.[8] According to the National Osteoporosis Foundation, fractures that result from osteoporosis can cause chronic pain, disability, and death. These fractures also may lead to depression and loss of self-esteem, and the high morbidity and resultant reliance on others can lead to difficult interpersonal relationships and social roles for patients and their families. Only 40% of patients will rebound to their prefracture level of function following a hip fracture, and 20% of patients who have experienced a hip fracture will require long-term nursing home care.[2]

Fractures that result from osteoporosis can cause loss of height, diminished range of motion, immobility, and balance difficulties.[1] Multiple thoracic fractures may lead to the development of restrictive lung disease, while lumbar fractures could alter the abdominal anatomy, thus causing constipation, abdominal pain, distention, reduced appetite, and early satiety.

Hip fractures are associated with an 8.4% to 36% increase in mortality within one year; men have a higher increase in mortality than do women following a hip fracture. Mortality is also increased following vertebral fracture.[2]

Early diagnosis and treatment of osteoporosis are of the utmost importance in preventing these life-changing consequences.

Diagnosis

Osteoporosis is diagnosed via bone mineral density measurement or the occurrence of a hip or vertebral fracture without major trauma as an adult. Secondary causes of osteoporosis are excluded via blood and urine tests.[2]

Dual-energy X-ray absorptiometry (DXA) is used to assess bone mineral density. Bone mineral density testing is recommended for the following groups of individuals[2]:

- women aged 65 and older and men aged 70 and older, regardless of clinical risk factors;

- younger postmenopausal women, women in the menopausal transition, and men aged 50 to 69 with clinical risk factors for fracture;
- adults who suffer a fracture after age 50; and
- adults with a chronic medical condition (eg, rheumatoid arthritis) or taking a medication (eg, glucocorticoids in a daily dose of 5 mg or more of prednisone or equivalent for three months or more) associated with low bone mass or bone loss.

DXA results are expressed in the form of a t score, which is compared with control subjects who have peak bone mineral density. The difference between the patient's bone mineral density and the average bone mineral density of the reference population is divided by the standard deviation of the reference population and is used to calculate the t score and z score. The z score compares the bone mineral density of a reference population matched for age, sex, and ethnicity.[2]

Another test, Vertebral imaging to diagnose vertebral fractures, is recommended for the following individuals[2]:

- women aged 70 and older and all men aged 80 and older;
- women aged 65 to 69 and men ages 75 to 59 with a bone mineral density t score of -1.5 or below; and
- postmenopausal women aged 50 to 64 and men aged 50 to 69 with specific risk factors, including low trauma fracture (occurred without a traumatic event such as a car accident), historical height loss of 1.5 inches or more, prospective height loss of 0.8 inches or more (Prospective height loss is determined via sequential measurements of an individual's height to determine whether it has decreased over time.), or recent or ongoing long-term glucocorticoid treatment.

FRAX is a tool developed by the World Health Organization (WHO) to determine the 10-year probability of hip fracture and major osteoporotic fracture (clinical vertebral, hip, forearm, or proximal humerus).[2] This assessment tool predicts fracture in men and women through the use of clinical risk factors with and without the use of femoral neck bone density. The clinical risk factors taken into account include BMI, history of fracture, parental history of hip fracture, glucocorticosteroid use, the presence of rheumatoid arthritis and other secondary causes of osteoporosis, current smoking status, and alcohol intake of three or more units daily.

Treatment of Osteoporosis

The National Osteoporosis Foundation recommends osteoporosis treatment for the following people[2]:

- those with hip or vertebral fractures, whether clinical or asymptomatic;
- those with t scores of -2.5 or less at the femoral neck, total hip, or lumbar spine;
- postmenopausal women and men aged 50 and older with low bone mass (t score between -1 and -2.5) at the femoral neck, total hip, or lumbar spine and a 10-year hip fracture probability of 3% or more or a 10-year major osteoporosis-related fracture probability of 20% or more based on the US-adapted WHO FRAX model.

Current FDA-approved treatment options for osteoporosis include bisphosphonates (alendronate, alendronate plus D, ibandronate, risedronate, and zoledronic acid), calcitonin, estrogen agonist/antagonist (raloxifene), estrogens and/or hormone therapy, parathyroid hormone (PTH(1-34), teriparatide), and RANKL inhibitor (denosumab). [2]

There are hazards associated with all medications, and those used to treat osteoporosis are no exception. The National Women's Health Network has developed a comprehensive osteoporosis fact sheet regarding the safety concerns of various osteoporosis treatments.

Regardless of which pharmacologic option is used, after three to five years of treatment, a comprehensive risk assessment should be performed. No medication therapy should continue indefinitely.[2]

Biochemical markers of bone turnover, such as resorption markers (eg, serum C-telopeptide, urinary N-telopeptide) and formation markers (eg, serum bone-specific alkaline phosphatase, osteocalcin, aminoterminal propeptide of type 1 procollagen), may be measured in certain patients and predict the danger of bone fracture independently of bone density, predict the magnitude of fracture risk reduction when repeated after three to six months of treatment, predict the rate of bone loss, predict the extent of bone mineral density improvement after therapy, help determine a patient's compliance and persistence with therapy, and help determine the duration of a "drug holiday" and if and when the medication should be reinitiated.[2]

Adults who are found to be vitamin D deficient may be treated with 50,000 IU of vitamin D once a week or a daily dose of 6,000 IU for eight to 12 weeks. Maintenance therapy of 1,500 to 2,000 IU/day is then recommended. Obese individuals or those with malabsorption or on medications that affect vitamin D metabolism may require higher doses.[2]

Surgical procedures, including vertebroplasty and kyphoplasty, may be necessary to manage osteoporotic vertebral compression fractures.[1]

Prevention: Controlling Risk Factors

Below is a discussion of the dietary and lifestyle factors mentioned previously that can affect a person's risk of developing osteoporosis.

Salt

The INTERSALT Study, an observational study involving 10,079 men and women aged 20 to 59 from 52 world populations, found no significant correlation between sodium intake and the development of osteoporosis. People from Finland and the United Kingdom were found to have a relatively high rate of osteoporosis but had lower salt intake than did those from countries with lower rates of osteoporosis, such as Hungary, Spain, and Malta. Similarly, Japanese individuals experienced fewer hip fractures than did people in white European populations, although the Japanese have one of the highest salt intakes among populations of developed countries.[10]

According to a review published in the ***Journal of the American College of Nutrition***, "Good estimates of true osteoporosis prevalence are not available for many of the populations studied by INTERSALT, and, more important, these populations differ widely in genetic susceptibility to osteoporosis, vitamin D status, and calcium intake, among other critical variables."[11]

Devine et al examined the dietary profiles of 196 individuals and found that after a two- year period, the change in bone mineral density at the total hip and an ankle site were inversely related to urine sodium content. The researchers hypothesized that by halving participants' dietary sodium intake from 2,000 to 1,000 mg/day, hip bone loss would be negated and that doubling their calcium intake, putting it in the currently recommended range, would have the same effect.[12]

Teucher et al set out to more fully characterize salt's effect on calcium metabolism and the potential impact on bone health in postmenopausal women by investigating adaptive mechanisms in response to changes in salt and calcium intake. Eleven women completed the randomized crossover trial, which consisted of four successive five-week periods of controlled dietary intervention, each separated by at least a four-week break. Participants were provided with moderately low (518 mg) and high (1,284 mg) calcium diets and moderately low (3.9 g) and high (11.2 g) sodium diets. Salt was responsible for a significant positive to negative change in bone calcium balance when consumed as part of a high-calcium diet. The kinetic data suggest that salt significantly affects calcium urinary excretion and bone calcium balance only in individuals following a high-calcium diet.[13]

The authors concluded that "low calcium intake was associated with negative bone calcium balance with both high- and low-salt diets, but with a moderately high calcium intake, the bone balance was positive when the salt intake was low but not when it was moderately high."[13]

In a more recent study published in ***Nutrients***, researchers assessed 24-hour urinary sodium and its relationship with urinary calcium and areal bone mineral density in 102 healthy nonobese women. The women were grouped to have a lower calcium intake and higher calcium intake by median split (higher calcium intake defined as 506 mg/1,000 kcal or higher).[14]

Dietary sodium intake correlated with 24-hour urinary loss, and urinary sodium levels correlated positively with urinary calcium levels for all participants and among those with lower, but not higher, calcium intakes. Urinary sodium was inversely associated with areal bone mineral density for all participants and among women with lower, but not higher, calcium intakes.[14]

The researchers concluded that "24-hour urinary sodium (a proxy for intake) is associated with higher urinary calcium loss in young women and may affect areal bone mineral density, particularly in those with lower calcium intakes."[14] So the more sodium individuals ingest, and thus excrete, the more calcium they also excrete, which is particularly true for women consuming a diet both low in calcium and high in sodium.[2]

Meeting current recommendations for potassium will decrease or arrest sodium chloride–induced calciuria, and common salt intakes will not negatively affect bone or calcium status if calcium intakes at least meet current recommendations.[11]

Also, decreasing salt intake appears to positively influence bone health. This especially may be true among individuals who also have a low intake of calcium. Getting enough dietary potassium may mitigate the negative effects of sodium on the skeleton.

Caffeine

Because caffeine appears to decrease calcium absorption and contribute to bone loss, consuming no more than three cups of coffee daily is recommended.[15] The Framingham Osteoporosis Study found that colas, but not other sodas, were associated with bone loss.[16] This may be secondary to the combination of phosphorous and caffeine found in colas. The researchers concluded that "unless additional evidence rules out an effect, women who are concerned about osteoporosis may want to avoid the regular use of cola beverages."[16]

Despite its caffeine content, tea actually may improve bone health. When Chen et al prospectively investigated the correlation between habitual tea drinking with bone mineral density and fracture risk, they found that multivariate analyses suggested a positive trend of increased total body bone mineral density occurring with regular tea drinking. However, results from the Cox proportional hazard model did not find a significant association between tea drinking and the risk of fractures at either the hip or the wrist/forearm area.[17] The authors concluded that "the results from this study indicate that the effect of habitual tea drinking on bone density is small and does not significantly alter the risk of fractures among the US postmenopausal population."[17]

The authors did note that one recent study suggested that the catechins derived from green tea stimulate osteoblastlike cells in culture, and that this is at least partly achieved via estrogen receptors. They further noted that additional investigation into whether black and green teas have different effects on bone health is needed. Furthermore, they wrote, "Because of the potential adverse effect of caffeine on bone density, we believe that not counting decaffeinated tea consumption in our study may lead to an underestimation of the strength of any positive association between bone density and tea consumption."[17]

Shen et al determined that tea and its bioactive components improve bone density, support osteoblastic activity, and suppress osteoclastic activities, all of which may decrease the risk of fracture.[18]

In some research, the catechins present in green tea appear to be especially helpful in regard to bone density. However, research into the correlation between tea consumption and bone density should be carried out using decaffeinated tea, as caffeine may negate some of the positive effects on the skeleton.

Alcohol

A very small study published in ***Menopause*** in 2012 found that abstaining from alcohol resulted in elevated markers of bone turnover and that resuming alcohol consumption reduced

these bone turnover markers. The study authors concluded that alcohol intake exaggerated the negative skeletal changes associated with menopause.[19]

It is important to keep in mind that the reduction in bone turnover markers among women who resumed drinking alcohol did not definitively decrease their fracture risk.[19]

However, female patients and clients should not be advised to consume alcohol. According to one study, women between the ages of 67 and 90 who regularly consumed more than 3 oz of alcohol each day experienced greater bone loss compared with women consuming a minimal amount of alcohol.[20]

A study published in the ***American Journal of Medicine*** in May 2008 found that, compared with individuals who abstained from alcohol, those who consumed between 0.5 and one drink per day had a lower risk of hip fracture, while people who consumed more than two drinks per day had an increased risk. A linear relationship between femoral neck density and alcohol consumption also was found. The authors, however, concluded that, "a precise range of beneficial alcohol consumption cannot be determined."[21]

Individuals who do not consume alcohol should not begin to do so just to improve their bone health, and those who do consume alcohol should limit their intake to one to two drinks per day. More research is needed to ascertain a precise amount of beneficial alcohol consumption.

Weight Loss

A prospective cohort study published in the ***Journal of the American Geriatric Society*** in 2003 looked at 6,785 elderly white women with a change in body weight and assessment of intention to lose weight, and found that the adjusted average rate of decline in total hip bone density steadily increased as the women lost weight. Women who lost 5% or more from their baseline weight experienced a -0.92% change in hip bone density annually. Additionally, higher rates of hip bone loss were seen in the women who lost weight regardless of BMI or intention to lose weight.[22]

During the average 6.6 years of follow-up after their fourth bone density test as part of the study, 400 women suffered their first hip fracture. Women who experienced weight loss had 1.8 times the risk of subsequent hip fracture compared with women who had stable or increasing weight.[22]

Among elderly women, it appears that weight loss (whether intentional or not) may decrease bone density and increase the risk of fracture.

Exercise and Osteoporosis Risk

Growing bone possesses a greater capacity to adapt to mechanical loading than does mature bone, making it crucial for girls to engage in weight-bearing activities.

A recent meta-analysis evaluating the impact of weight-bearing exercise on the bone health of female children and adolescents included 17 studies and found that weight-bearing exercise had a small but significant influence on bone mineral content and areal bone mineral density of

the lumbar spine and the size and bone mineral content of the femoral neck. The frequency of exercise was the most important factor in determining the positive effect on the skeleton; programs of weight-bearing activity three days per week resulted in significantly better effects on the bone compared with programs involving exercise on fewer than three days per week.[23]

A study published in the ***Journal of Osteoporosis*** in 2013 examined body composition and bone mineral density to compare women divided by activity level: sedentary, maintenance exercise, and federated sport team. The women did not differ in terms of age, height, weight, or BMI.[24]

Bone mineral content and nonfat soft tissue mass were higher and fat mass was lower in the sport team group compared with the other groups. The same held true for bone mineral density of the total skeleton, lumbar spine, femoral neck, and total hip. The authors concluded that a level of physical activity higher than that usually recommended benefits bone health in adult premenopausal women.[24]

Pilates and yoga help with flexibility, strength, and balance, but certain positions may be dangerous for people with osteoporosis and those at risk of breaking a bone. For people with osteoporosis, tai chi can help decrease the risk of falls; postural exercises can decrease the risk of breaking a bone (especially in the spine); and functional exercises can help with activities of daily living and decrease the risk of falling and breaking a bone. People with osteoporosis are advised to work with a physical therapist to develop a safe and effective regimen.[25]

Children and adolescents who perform weight-bearing exercise at least three times per week have increased bone mineral content and density. Premenopausal adult women may need more physical activity than usually is recommended to benefit their bones.

Tai chi may benefit those with osteoporosis, but caution should be taken when considering Pilates or yoga regimens. In these cases, individuals with osteoporosis should seek the help of a physical therapist to develop a program based on postural and functional exercises.

Smoking

According to a 2012 National Institutes of Health article, most studies suggest that smoking increases the risk of bone fracture. Furthermore, the longer someone smokes and the more cigarettes smoked, the greater the risk of fractures. Also, smokers who do suffer fractures seem to take longer to heal and have a greater chance of suffering complications as a result of the fracture than do nonsmokers. Fortunately, cessation of smoking seems to decrease the risk of low bone mass and fracture, although it may take several years for smokers to decrease their risk once they have quit.[26]

Calcium and Vitamin D

The nutrients calcium and vitamin D are best known for preventing osteoporosis. In 2010, the Institute of Medicine issued new Dietary Reference Intakes for these two nutrients, specifying an Estimated Average Requirement (EAR) of 400 IU/day of vitamin D with a Recommended

Dietary Allowance (RDA) of 600 IU/day for adults aged 19 to 70 and 800 IU/day for adults older than 70. The Upper Level Intake (ULI) for vitamin D is 4,000 IU/day.[27]

When it comes to calcium, adults between the aged of 19 and 50 have an EAR of 800 mg/day, an RDA of 1,000 mg/day, and a ULI of 2,500 mg/day. Men between the aged of 51 and 70 have an EAR of 800 mg/day and an RDA of 1,000 mg/day, while women require slightly more, with an EAR of 1,000 mg/day and an RDA of 1,200 mg/day. Both sexes in this age group have a ULI of 2,000 mg. Individuals of either sex who are older than 70 have an EAR of 1,000 mg/day, an RDA of 1,200 mg, and a ULI of 2,000 mg.[27]

According to data from the National Health and Nutrition Examination Survey 2003-2006, calcium intake by American males aged 1 and older ranges from 871 to 1,266 mg/day, while calcium intake by females ranges from 748 to 968 mg/day. Groups in which more than 50% of individuals consume an inadequate amount of calcium include boys and girls between the ages of 9 and 13, girls aged 14 to 18, women aged 51 to 70, and men and women older than 70.[28]

According to the same data, average vitamin D intake from food ranges from 204 to 288 IU/day for males and 144 to 276 IU/day for females. Levels were much higher when dietary supplements were taken into account, especially among older women. For women between the ages of 51 and 70, mean vitamin D intake from food was 156 IU/day, but is 404 IU/day with supplements. For women over the age of 70, they generally consumed 180 IU/day from food and 400 IU/day with supplements.[28]

In March 2007, a group of researchers studying nutrition and vitamin D published an editorial hypothesizing that 1,700 IU of vitamin D daily would be necessary to raise serum 25-hydroxyvitamin D (25(OH)D) levels from 50 to 80 nmol/L, stating that the desirable concentration of 25(OH)D is 75 nmol/L or higher.[29]

It's well-known that milk and milk products are rich sources of calcium, but there are many other calcium-rich foods. For example, while 8 oz of plain low-fat yogurt contains 415 mg of calcium and 1 cup of skim milk contains 306 mg, 1 cup of frozen then boiled collard greens contains 357 mg.[30]

Other sources include black-eyed peas (211 mg in 1 cup, boiled), canned salmon (181 mg in 3 oz), calcium-set tofu with calcium sulfate used as a coagulant (163 mg in 3 oz), trail mix (159 mg in 1 cup consisting of nuts, seeds, and chocolate chips), canned baked beans (154 mg in 1 cup), green peas (94 mg in 1 cup), oranges (72 mg in 1 cup), and almonds (70 mg in 1 oz).[30]

Vitamin D can be found in foods such as canned pink salmon, sardines, and mackerel; some instant oatmeals; fortified cow's milk; fortified soymilk; fortified orange juice; fortified ready-to-eat breakfast cereals; and egg yolk.[31]

For individuals who can't consume enough calcium and vitamin D from food, supplements are an option. However, because of the health risks now thought to result from taking too much

calcium in supplement forms, patients and clients should be advised to look to food first and then fill in any gaps with supplements.

Calcium and Vitamin D: Do They Prevent Fractures?

The US Preventive Services Task Force (USPSTF) has released the following statement regarding calcium and vitamin D supplementation for the primary prevention of fractures in premenopausal women or in men[32]:

> The task force concludes that the current evidence is insufficient to assess the balance of the benefits and harms of combined vitamin D and calcium supplementation for the primary prevention of fractures in premenopausal women or in men. The task force concludes that the current evidence is insufficient to assess the balance of the benefits and harms of daily supplementation with greater than 400 IU of vitamin D_3 and greater than 1,000 mg of calcium for the primary prevention of fractures in noninstitutionalized postmenopausal women. The task force recommends against daily supplementation with 400 IU or less of vitamin D_3 and 1,000 mg or less of calcium for the primary prevention of fractures in noninstitutionalized postmenopausal women.

When 16 randomized controlled trials were analyzed, random-effects model meta-analysis showed that combined vitamin D and calcium supplementation reduced fracture risk in older adults, but the effects differed according to study setting; for example, they were more pronounced among institutionalized elderly compared with community-dwelling older adults.

The Women's Health Initiative Trial, a randomized controlled trial, showed adverse outcomes associated with supplementation, including an increased risk of renal and urinary tract stones. The researchers addressed the concerns by stating the following[33]:

> Critics of this study have pointed to the low dosage (400 IU/day) of vitamin D supplementation, lack of blood 25-(OH) D measurement, poor adherence, low baseline risk of the study population, and off-study use of additional vitamin D and calcium supplements during the trial as factors that could explain the null findings. Others have suspected that the adverse outcomes of renal and urinary stones were associated with excess calcium intake from both diet and calcium supplements. These concerns raise many important issues regarding the design and conduct of future trials of dietary supplements, which need to consider the myriad differences between nutrients and drugs, especially when the background exposure to a nutrient (such as vitamin D) cannot be reliably ascertained.

In response to the USPSTF's statement, the National Osteoporosis Foundation said the recommendations do not apply to women with osteoporosis or broken bones after age 50 or those with significant risk factors for fracture. The foundation stressed that it recommends that all women aged 50 and older get 1,200 mg of calcium and 800 to 1,000 IU of vitamin D each day via combined food and supplements (if necessary). Furthermore, it reminded the public that osteoporosis medications are ineffective without calcium and vitamin D.[34]

Robert P. Heaney, MD, an endocrinologist specializing in nutrition with a focus on bone biology, osteoporosis, and human calcium and vitamin D physiology, pointed out on his Creighton University blog that the USPSTF actually said there wasn't enough evidence to make a determination about vitamin D supplementation specifically to prevent fractures in the

fragile elderly. However, he wrote that there is plenty of evidence in favor of supplementation and that it is curious that the task force recommends vitamin D supplements for the prevention of falls but not for the prevention of fractures. He further contended that no member of the task force is an expert in vitamin D biology and that poorly designed studies were used in the evaluation.[35]

Do Calcium Supplements Cause Heart Attacks?

When researchers reanalyzed data from the Women's Health Initiative, they found that women who received calcium supplements with or without vitamin D had a higher risk of cardiovascular events, especially myocardial infarction, compared with women who were given placebos. The study authors called for a reassessment of the role of calcium supplements in osteoporosis management.[36]

Wang et al pointed out that in vitro and in vivo laboratory studies have shown that calcium may affect the risk of developing cardiovascular disease (CVD) through multiple mechanisms, including blood cholesterol, insulin secretion and sensitivity, vasodilation, inflammatory profile, thrombosis, obesity, and vascular calcification. The authors also noted that results of prospective epidemiologic studies seeking a correlation between dietary calcium intake and CVD incidence or mortality in middle-aged and older adults have been inconclusive, although the pooled data do not support a significant effect. The pooled data also do not support any benefit of calcium supplementation in reducing the risk of coronary artery disease or stroke.[37]

A meta-analysis published by Bolland et al in 2010 also suggested that calcium supplementation may increase heart attack risk. The meta-analysis included double-blind, placebo-controlled trials involving at least 500 mg of calcium per day in individuals ages 40 and older. All of the studies had at least 100 participants and lasted for at least one year.[38]

Eleven studies with nearly 12,000 participants were included in the trial-level data analysis; there were 166 heart attacks in the calcium group compared with 130 in the placebo group. A separate analysis on patient-level data including more than 8,000 participants found 143 heart attacks in the calcium group and 111 in the placebo group.[38]

In total, the findings suggested that individuals who take more than the median dietary intake of calcium between the combination of food and supplements and who do not take vitamin D supplements have a 30% increased risk of suffering a heart attack. Trials concerning calcium and vitamin D given together with a placebo comparator were eligible only if vitamin D was given to both intervention and control groups because vitamin D supplementation has been associated with decreased mortality. The authors hypothesized that treating 1,000 people with calcium for five years would result in an additional 14 heart attacks and prevent 26 fractures.[38]

Wang et al discussed that meta-analysis in their review and noted that none of the included trials was specifically designed to assess the effect of calcium supplementation on CVD risk, and the numbers of CVD events in many of the trials were too small to draw clinically meaningful conclusions. Additionally, CVD events were not prespecified end points, and only two of the 15 trials had CVD events adjudicated by blinded investigators.[37]

None of the trials included in the meta-analysis reported a significant difference in CVD events between the calcium and placebo groups, and only the pooled relative risk showed a statistical significant effect. The meta-analysis depended on unpublished data. Lastly, the combined trial data appeared to suggest that calcium supplements increase the risk of myocardial infarction but not the risk of stroke or all-cause mortality.[37]

There is no proof that dietary calcium increases risk, so again it may be prudent to recommend that patients and clients attempt to get the majority of their calcium from food rather than supplements.

Do Calcium Supplements Cause Prostate Cancer?

When researchers prospectively looked at the association of dairy products and calcium intake in relation to prostate cancer risk among 29,509 men enrolled in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial,[39] they found that a greater intake of calcium and dairy products (particularly low-fat versions) were modestly associated with an increased prostate cancer risk. However, no association between calcium supplements and prostate cancer was found. This agrees with some other research and should be interpreted cautiously.[39]

In this prospective study, calcium and dairy product intake was evident for only nonaggressive forms of prostate cancer. However, two previous studies found that the association between calcium intake and prostate cancer was most marked for aggressive or fatal disease. When simultaneously evaluated in multivariate models, the risks were related to dietary calcium but not independently to dairy products; a higher calcium intake seemed to increase the risk of prostate cancer, regardless of whether the calcium came from milk products or from other foods. No relationship between calcium intake and circulating 1,25(OH)(2)D was found.[39]

The first National Health and Nutrition Examination Epidemiologic Follow-Up Study reported that low-fat milk intake was associated with an increased risk of prostate cancer development, but that the consumption of whole milk products was not associated with an increased risk. The authors concluded that removing the fat from milk also may remove other important substances, such as conjugated linolenic acid, which is believed to potentially have cancer-protective properties.[40]

Additionally, the researchers pointed out that low-fat milk has a lower vitamin D content compared with whole milk and hypothesized that calcium's suppression of circulating vitamin D may be to blame. The authors considered that the insulinlike growth factors in milk are not likely to explain the difference between low-fat and whole milk's effect on risk, as they would contain the same amount.[40]

When researchers looked at a cohort of men from the Physician's Health Study, they found that during 11 years of follow-up, men consuming more than 600 mg/day of calcium had a 32% higher risk of prostate cancer compared with men consuming 150 mg/day or fewer from dairy products. Skim milk was the dairy food most strongly related to risk, while dairy fat and protein were not significantly related to risk.[41]

The authors stated that because serum calcium concentration is tightly regulated, it is not likely to be associated with prostate cancer. Instead, they said a third factor probably mediates the effect and hypothesized that dietary calcium's suppression of the production of circulating vitamin D likely is a link.[41]

New Promise for Prevention

In the past 10 years, the understanding of food's effects on the skeleton has greatly advanced. Rather than focusing on specific vitamins and minerals, researchers instead are looking at specific foods that seem to hold promise for preventing and treating osteoporosis.

Soymilk and Dairy

Matthews et al examined the benefits of soymilk and dairy products on bone health among 337 postmenopausal white women. The women completed a lifestyle and dietary questionnaire at enrollment, and their heel bones were measured via broadband ultrasound attenuation two years later. The authors reminded readers first that soymilk contains a nonsteroidal phytoestrogen, which in some studies has been shown to have a protective effect against age-related bone loss and, in other studies, was found to protect against other chronic diseases. Second, they noted that soy phytoestrogen has been marketed as an alternative to hormone replacement therapy to prevent osteoporosis after menopause.[42]

Soymilk usually is fortified with calcium and vitamin D. The researchers discovered that women who consumed roughly 1.3 cups of soymilk daily reduced their chances of having a low t score by 57% compared with those who didn't drink soymilk. This remained true even after adjustments for other important covariates, such as dairy consumption.[42]

The study also found that women who consumed at least one serving of dairy food each day experienced a 62% reduction in the odds of having a low t score compared with those who consumed dairy foods fewer than two times per week. Of all the dairy products, only cheese showed a significantly protective effect on low t scores when evaluated separately. This is possibly due to the higher calcium and protein content of cheese per serving compared with milk.[42]

The authors concluded that postmenopausal women could benefit from drinking soymilk and/or having a regular intake of dairy products.[42]

Vitamin K

A cohort of more than 72,000 participants in the Nurses' Health Study was followed for 10 years. Women with a higher vitamin K intake had a significantly lower risk of hip fracture compared with women who had the lowest vitamin K intake. This did not change when calcium and vitamin D intake were taken into account.[43]

A cohort of 335 men and 553 women (average age of 75.2) who had participated in the Framingham Heart Study between 1988 and 1989 had their vitamin K intakes assessed via food-frequency questionnaires. Those in the highest quartile of vitamin K intake (average of 254 mcg/day) had a significantly lower risk of hip fracture compared with those in the lowest quartile (56 mcg/day). However, no correlation between vitamin K intake and bone mineral

density was found among participants of either sex. The authors noted, however, that vitamin K content might simply be indicative of consuming an overall healthful diet.[44]

Good sources of vitamin K include olive, soybean, and canola oils; mayonnaise; cooked broccoli; and raw kale, spinach, green leaf lettuce, Swiss chard, watercress, and parsley.[45]

Omega-3 Fatty Acids

Omega-3 fatty acids have been a topic of recent research regarding their effects on the skeleton. When control and ovariectomized (those whose ovaries were surgically removed) mice were fed a diet that was supplemented either with 5% corn oil or 5% fish oil, the ovariectomized mice who received the corn oil had significantly increased bone mineral density loss (20% in the distal left femur and 22.6% in lumbar vertebrae), while those that received fish oil lost only 10% in the distal left femur and had no change in the lumbar vertebrae. The authors suggested that the omega-3 fatty acids may inhibit osteoclast generation and activation.[46]

Högström et al determined that healthy young men had better bone mineral density if the fatty acid composition of the serum phospholipid fraction was rich in omega-3 fatty acids. The researchers determined that both the spinal bone mineral density at age 22 and changes in the spinal bone mineral density between the ages of 16 and 22 were significantly and positively associated with a higher serum concentration of both omega-3 fatty acids and DHA. Meanwhile, bone mineral density was negatively affected between the ages of 16 and 22 by a higher ratio of omega-6 fatty acids to omega-3 fatty acids in the phospholipid fraction.[47]

Through a series of cell-based studies, NASA scientists discovered that adding omega-3 fatty acid to cells inhibited the activation of nuclear factor kappa B, which is known to spur bone breakdown and be involved in both immunity and inflammation. Activation of nuclear factor kappa B can result in the loss of muscle and bone. Astronauts returning from short-duration shuttle missions have been found to have raised levels of nuclear factor kappa B, which don't return to normal for two weeks following mission completion.[48]

A ground-based bed-rest study was conducted on 16 subjects who were evaluated after 60 days. (Bed rest simulates some of the effects of weightlessness, including the loss of muscle and bone.) Higher intakes of omega-3 fatty acids were associated with less bone loss throughout the study duration. Furthermore, the researchers discovered that astronauts who ate more fish lost less bone mineral density than did others after space flights that lasted from four to six months.[48]

It appears that omega-3 fatty acid intake and a diet lower in omega-6 fatty acids benefit the bones.

Blueberries

A 2010 study in the ***Journal of Bone and Mineral Research*** found that rats fed rations containing 10% freeze-dried blueberry powder had significantly more bone mass than did controls whose rations contained no blueberries. When researchers exposed cultures of osteoblasts to serum from the animals, the serum from the rats in the blueberry group saw an

increase in the development of osteoblasts into mature bone cells. The serum of the blueberry-fed rats was high in phenolic acids, which are believed to stimulate bone building.[49]

Another study found that the prevention of bone cell senescence brought on by the surgical removal of the ovaries in adult rats occurred following the consumption of a diet containing blueberries immediately prior to puberty. The molecular mechanisms underlying this effect involve the prevention of collagen degradation.[50]

Therefore, animal studies have demonstrated that blueberries may be beneficial for bone health.

Dried Plums

When researchers instructed a group of 55 postmenopausal women to consume 100 g of dried plums (about 10 prunes) each day for one year and another group of 45 women to consume 100 g of dried apples each day, those who ate the dried plums had significantly higher bone mineral density in the ulna and spine than did those in the dried apple group. All of the women received daily supplements containing 500 mg of calcium and 400 IU of vitamin D, and none was on hormone replacement therapy. The effect of the dried plums was attributed to the suppression of bone resorption.[51]

Rendina et al fed adult osteopenic ovariectomized mice either a control diet or a diet supplemented with 25% dried plums, apples, apricots, grapes, or mangos for a period of eight weeks. Dried plums were the only fruit to have an anabolic effect on trabecular bone in the vertebra and to prevent bone loss in the tibia. Whole bone and spine bone mineral density improved in the mice receiving dried plum-, apricot-, and grape-supplemented diets. The dried plums, however, were the only fruit to downregulate osteoclast differentiation and upregulate osteoblast activity.[52]

Dried plums should be recommended to women who are concerned about skeletal health, as they appear to suppress bone resorption, decrease ostoclast activity, and increase osteoblast activity.

Tart Cherries

Researchers found that adding Montmorency tart cherries to mice's diet reduced the bone loss that occurs with age. Mice were assigned to a baseline group or to groups receiving 0%, 1%, 5%, or 10% cherries for 90 days. The mice who received the 5% and 10% cherry diet had higher whole-body and tibia bone density than did the control and baseline groups.[53]

Tart cherries are yet another fruit that may help improve bone health.

Fruits and Vegetables, Potassium, Magnesium, and Alkalinity

In 1999, when researchers looked at dietary intake measures associated with both baseline and four-year longitudinal change in bone mineral density among surviving members of the original cohort of the Framingham Heart Study, they found that alkalizing potassium, magnesium, and fruits and vegetables were associated with greater bone mineral density.[54]

Bone mineral density was tested at the femoral neck, trochanter, Ward's area, and radius. Specifically, higher potassium intake was significantly associated with greater bone mineral density at all four sites for men and three sites for women; magnesium was associated with greater bone mineral density at one hip site for both men and women and in the forearm for men; and fruit and vegetable intake was associated with greater bone mineral density at three sites for men and two for women. Greater potassium and magnesium intakes also were correlated with less bone mineral density loss at two hip sites, while a greater fruit and vegetable intake was associated with less decline at one hip site in men.[54]

When four-year bone mineral density change was examined, significant results were seen only for men, for whom baseline potassium and magnesium intakes (both separately and combined) were predictive of bone loss at all three hip sites in the subsequent four years.[54] Thus, alkalizing minerals (potassium and magnesium), fruits, and vegetables appear to have a protective effect on bone density, according to some research.

Researchers found that among a cohort of 266 elderly women, baseline potassium intake as measured via 24-hour potassium excretion had a positive association with bone mineral density one and five years later. In fact, women in the highest quartile of potassium excretion had a 5% higher total hip bone mineral density at one year, and a 6% higher total hip bone mineral density and 4% higher total bone mineral density at five years compared with women in the lowest quartile. The researchers concluded that, in particular, four or more servings of vegetables per day may play a role in preventing osteoporosis because of the potassium content.[55]

In a study published in ***Biological Trace Element Research***, 20 postmenopausal women were divided into two groups; one was given 1,830 mg/day of magnesium citrate for 30 days, while the other was not given any supplementation. After 30 days, the women who received the magnesium supplements had significantly decreased intact parathyroid hormone levels, significantly increased osteocalcin levels, and decreased deoxypyridinoline levels. These findings suggest that magnesium supplements may suppress bone turnover.[56] Magnesium, as previously mentioned, is alkalizing.

Potassium and magnesium appear to benefit the bones, as do fruits and vegetables but it is not known whether this is because of the produce's mineral content or whether there is another factor at play.

Bad for the Bones

In addition to looking at foods that promote bone health, researchers also are exploring whether certain foods or dietary approaches may harm bone.

Milk Acidity

As discussed in a paper published in the ***Journal of the American College of Nutrition*** in 2011, researchers set out to discover whether the hypothetical association between the generation of dietary acid as a result of dairy product consumption and the harm to human health, as often described by the lay press, is grounded in fact. The researchers noted "this theoretical association is based on the idea that the protein and phosphate in milk and dairy

products make them acid-producing foods, which cause our bodies to become acidified, promoting diseases of modern civilization." The authors contended that milk and dairy products neither produce acid when metabolized nor lead to the development of metabolic acidosis, that systemic pH is not influenced by diet, that net acid excretion is not an important influence of calcium metabolism, and that dietary phosphate does not have a negative impact on calcium metabolism.[57]

In another paper published in the same issue of the ***Journal of the American College of Nutrition***, the author contended that bone's calcium-phosphate content is similar to that measured in human milk. Both calcium and inorganic phosphate play a crucial structural role in bone formation and positively influence the activity of bone-forming and bone-resorbing cells.[58]

Inorganic phosphate plays a role in osteocyte maturation. The interaction of calcium and inorganic phosphate at both the renal and intestinal levels has important implications in the acquisition and maintenance of bone health as well as in osteoporosis management. Observational and interventional studies have suggested that calcium-inorganic phosphate salt or dairy products can exert positive effects on bone acquisition and maintenance.[58]

It appears that fears of dietary acid generation resulting from the consumption of dairy products are unfounded. In fact, dairy products appear to positively affect on the skeleton. However, soymilk is an acceptable substitution for individuals who cannot consume dairy or prefer not to.

High-Protein Diet

In Framingham, Massachusetts, 3,700 residents were divided by how much calcium they consumed via food. Among those who consumed fewer than 800 mg/day, those who ate the most protein had nearly three times the risk of hip fracture than did those who ate the least. However, among residents who consumed more than 800 mg/day, those who ate the most animal protein had an 85% lower risk of hip fracture compared with those who ate the least animal protein. As long as there is adequate calcium in a person's diet, it appears that protein is good for the bones.[59]

In the tertile analysis, among those with the highest tertile of total protein intake (median of 103 g/day), there was a decreased risk of hip fracture relative to subjects in the lowest tertile of total protein intake (median of 79 g/day) among individuals in the high-calcium group (more than 800 mg/day).[59]

The study authors noted that the high protein content of Western diets often is cited as a risk factor for osteoporosis or bone fractures. High protein intakes have been shown to affect calcium homeostasis, resulting in increased calcium excretion, but findings regarding the effect of protein on calcium balance and bone health have been mixed.[59]

Individuals who consume a diet that is high in both calcium and dietary protein appear to have a decreased risk of hip fracture. The effect of a diet that is high in dietary protein but low in calcium is not well described.

Practical Applications
RDs should advise their patients and clients to attempt to get enough calcium from foods before turning to supplements. Clients can track their calcium intake using a calculator such as that on the International Osteoporosis Foundation website and based on the Food and Agriculture Organization/WHO calcium intake recommendations.

A diet rich in fruits, vegetables, and dairy foods, with the possible addition of omega-3-fatty-acid–rich foods, olive oil, soy products, tart cherries, dried plums, and blueberries may be helpful for those wishing to prevent osteoporosis. Dietitians should recommend moderation with respect to alcohol, sodium, and caffeine intake and cessation of smoking, if applicable. A high-protein diet in individuals who consume adequate calcium does not appear to weaken bones and likely is beneficial, even among those people who are trying to lose weight.

An exercise program consisting of weight-bearing activities, muscle-bearing exercises, and physical activity geared toward improving flexibility, balance, and function should be stressed. Individuals with osteoporosis should be referred to a physical therapist for help in developing an appropriate exercise regimen.

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Patient Handout: Take Control of Your Bone Health:
http://www.todaysdietitian.com/pdf/courses/KoontzOsteoporosisHandout.pdf

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Examination

1. Which of the following is an uncontrollable risk factor for the development of osteoporosis?
A. Consuming a diet high in potassium
B. Consuming a diet high in sodium
C. Being aged 50 or older
D. Consuming a diet high in soy-based foods

2. Multiple thoracic fractures could lead to the development of which of the following?
A. Constipation
B. Restrictive lung disease
C. Abdominal pain
D. Early satiety

3. Bone mineral density testing is recommended for which of the following groups?
A. Women older than 50 and men older than 60
B. Individuals who broke more than three bones before age 18
C. Postmenopausal women aged 50 to 64 and men aged 50 to 69, depending on their risk factor profile
D. Those with a family history of osteoporosis

4. Which population group contains more than 50% of individuals who consume an inadequate amount of calcium?
A. Boys and girls between the ages of 9 and 13
B. Boys ages 14 to 18
C. Women ages 35 to 45
D. Men between the ages of 45 and 60

5. Which of the following has been hypothesized to cause an increase in cardiovascular disease among women taking calcium supplements?
A. Toxins from the supplements
B. A decrease in urine excretion secondary to calcium's effect on the renal tubules
C. A decrease in individuals' ability to reach their target heart rates while exercising
D. Changes to insulin secretion and sensitivity

6. Which of the following is accurate according to The National Osteoporosis Foundation?
A. Both men and women need 800 to 900 IU of vitamin D each day.
B. Every child and adult in America would benefit from a vitamin D supplement.
C. Vitamin D supplements are not necessary for anyone who has not suffered a broken hip.
D. Osteoporosis medications will not be effective without adequate vitamin D intake.

7. Which of the following minerals has been associated with improved bone health?
A. Iron
B. Copper
C. Magnesium
D. Boron

8. Which of the following dried fruits seems to suppress bone resorption?
A. Plums
B. Cherries
C. Apricots
D. Pineapple

9. Which of the following is true regarding exercise by women and bone mineral density?
A. Both bone mineral content and nonfat soft tissue mass are lowest in those with a federated sport team activity level.
B. Bone mineral density is lower among women with a federated sport team activity level compared with women with a sedentary activity level.
C. A level of physical activity higher than that usually recommended benefits bone health in adult premenopausal women.
D. A maintenance exercise activity level is as good as a federated sport team activity level for bone mineral density.

10. Which of the following is an FDA-approved treatment option for osteoporosis?
A. Steroids
B. Sodium fluoride
C. Parathyroid hormone 1-34
D. Calcitriol