Menopause: The Journal of The North American Menopause Society
Vol. 8, No. 2, pp. 84–95

CONSENSUS OPINION

The role of calcium in peri- and postmenopausal women: consensus opinion of The North American Menopause Society

ABSTRACT

Objective: The North American Menopause Society (NAMS) established a goal to review the published medical data and develop an evidence-based consensus opinion regarding the role of calcium in peri- and postmenopausal women.

Design: In building this consensus opinion, NAMS followed the general principles established for evidence-based guidelines. As part of that process, NAMS appointed a panel of clinicians and researchers acknowledged to be experts in the field of calcium. Their advice was used to assist the NAMS Board of Trustees in developing this consensus opinion.

Results: Adequate calcium intake (in the presence of adequate vitamin D intake) has been shown to prevent bone loss and reduce fracture risk in peri- and postmenopausal women. Although calcium is not as effective as antiresorptive agents (e.g., estrogen, selective estrogen-receptor modulators, or bisphosphonates), it is an essential component of antiresorptive agent therapy for osteoporosis. Calcium has also been associated with beneficial effects in several nonskeletal disorders, primarily hypertension, colorectal cancer, obesity, and nephrolithiasis, although the extent of those effects and mechanisms involved have not been fully explored. Estimates of adequate intakes of calcium for peri- and postmenopausal women are based on evidence relating to osteoporosis prevention. At least 1,200 mg/day of calcium is required for most women; levels greater than 2,500 mg/day are not recommended. To ensure adequate calcium absorption, a daily intake of 400–600 IU of vitamin D is recommended, either through sun exposure or through diet or supplementation. Since no accurate test to determine calcium deficiency exists, clinicians should focus instead on ensuring that a woman consumes enough calcium to meet the recommended levels.

Conclusion: Although the most definitive role for calcium in peri- and postmenopausal women is in bone health, it is clear that adequate calcium intake has implications that encompass a woman's overall health. Based on the available evidence, a strong statement can be made regarding the importance of ensuring adequate calcium intake in all women, particularly those in peri- or postmenopause.

Key Words: Calcium – Menopause – Perimenopause – Bone mass – Fractures – Osteoporosis – Hypertension – Obesity – Nephrolithiasis – Colorectal cancer.

Received November 27, 2000.

The Board of Trustees of The North American Menopause Society (NAMS) developed this consensus opinion with assistance from the following panel of experts: Robert P. Heaney, MD (Chair); Bess Dawson-Hughes, MD; J. C. Gallagher, MD; Robert Marcus, MD; and Jeri W. Nieves, PhD.

Address reprint requests to NAMS, P.O. Box 94527, Cleveland, OH 44101, USA.

Calcium, an essential nutrient for the human body, has received substantial interest in both the medical literature and lay press regarding its role in osteoporosis and several other chronic diseases, including hypertension and colon cancer. In response to the growing body of clinical trial data, The North American Menopause Society

(NAMS) has created this consensus opinion to address issues related to the role of calcium in the peri- and postmenopausal woman.

In building this consensus opinion, NAMS followed the general principles established for evidence-based guidelines detailed in several publications.[1–3] NAMS conducted a search of the literature on MEDLINE for clinical trials evaluating the role of calcium supplementation in diseases and disorders related to peri- and postmenopausal women.

In addition, recognized experts on calcium were solicited to serve on an advisory board. If the evidence was contradictory or inadequate to form a conclusion, opinion-based decisions were made. The consensus-building process of NAMS was described in a previous issue.[4]

PHYSIOLOGIC ROLE OF CALCIUM

Calcium is the most abundant mineral in the human body. Approximately 99% of the total calcium stores are contained in the skeletal structure. The remaining stores are in the cells of soft tissue (0.9%) and in the bloodstream and extracellular fluid (0.1%), where they exert effects on the cardiovascular, nervous, and muscular systems.

Calcium requirements for skeletal maintenance fluctuate throughout a woman's life. During the teen years, calcium requirements are high because of the demands of a rapidly growing skeleton. Low calcium intake during that time may impede reaching peak bone mass, which can increase the risk of osteoporosis later in life. During a woman's 20s, less calcium is required as bone turnover stabilizes (i.e., bone formation and resorption rates become balanced) and peak adult bone mass is achieved. Calcium requirements remain stable until menopause. When a woman reaches menopause, the bone resorption rate increases and bone mass declines, associated with the fall in ovarian estrogen production. Calcium needs rise at that time because of a decrease in the efficiency of utilization of dietary calcium, which is also associated with the fall in ovarian estrogen production.

The amount of calcium needed is also affected by the decrease in intestinal absorption that occurs with age. Calcium absorption increases transiently during the adolescent growth spurt and, briefly, during pregnancy. At other times, calcium absorption averages 20–30%.[5,6] This efficiency declines slowly with age. By age 65, calcium absorption efficiency is typically 50% below that of adolescent peak absorption. One factor that may limit calcium absorption is a lack of vitamin D, resulting from age-related declines in several functions, including ingestion, dermal synthesis,[7] renal enzymatic activity,[8,9] and intestinal responsiveness.[10]

Dietary factors limiting calcium absorption include consuming oxalic acid (found in spinach and some other greens), consuming large amounts of grains that contain phytates (e.g., wheat bran), and, possibly, consuming tannins (found in tea). Evidence indicates that other dietary components, such as fat, phosphorus, magnesium, and caffeine, have negligible effects on calcium absorption at generally applicable intake levels.[11] Calcium, on the other hand, has been shown to lower the rate of iron absorption in single-meal tests;[12,13] however, in general, the body up-regulates iron absorption to compensate.[14] Nevertheless, it is generally advised that iron supplements not be taken with calcium.

The importance of an adequate calcium intake for skeletal health is well established. In addition, calcium is associated with beneficial effects in several nonskeletal disorders, primarily hypertension, colorectal cancer, obesity, and nephrolithiasis, although the extent of those effects and mechanisms involved have not been fully explored. Low calcium intake also may be associated with premenstrual syndrome.[15]

Thus, although the best attested role of calcium in peri- and postmenopausal women is in bone health, it is clear that adequate calcium intake has implications that encompass a woman's overall health. Based on the available evidence, a strong statement can be made regarding the importance of ensuring adequate calcium intake in all women, particularly those in peri- or postmenopause.

OSTEOPOROSIS

The skeletal disorder osteoporosis is characterized by compromised bone strength, predisposing bone to an increased risk of fracture. Bone strength reflects bone mass, bone density, bone architecture, bone size, and bone material quality. Bone mass in peri- and postmenopausal women is determined by peak bone mass achieved during growth and the amount of bone loss thereafter. Results of standard noninvasive densitometric techniques to assess bone status are expressed as bone mineral content (BMC) or bone mineral density (BMD). BMC is expressed as grams of mineral and BMD as grams of mineral per area or volume. Bone quality reflects a broad range of different features, including bone architecture, bone remodeling activity, and accumulated fatigue damage (e.g., microfractures).

Most cases of osteoporosis occur in postmenopausal women, and the incidence increases with age. In the United States, approximately 15% of women aged 50

or older have osteoporosis, with another 35–50% having low bone mass.[16]

In the United States, it has been estimated that more than 40% of women over age 50 will suffer an osteoporotic fracture;[17] the usual fracture sites are the vertebrae, hip, pelvis, ribs, distal forearm, and other limb bones. Up to 90% of all hip and spine fractures in elderly women can be attributed to osteoporosis.[18] The event precipitating a fracture can range from a traumatic high-impact fall to normal lifting and bending. Falls seem to be the most common precipitating event for all categories of fracture (wrist, spine, and hip).

Bone fractures are associated with significant morbidity and mortality. Women with hip fractures have up to 20% mortality the first year; 50% of cases will have some long-term loss of mobility and independence, with 25% of these women requiring long-term care.[19] Clinical (as opposed to silent) spine compression fractures have a 15–20% excess mortality, in addition to their effect on quality of life.[20]

The primary clinical goal of osteoporosis therapy is to prevent fracture by slowing or preventing bone loss, maintaining bone strength, and minimizing or eliminating factors that may contribute to falls. With the emergence of parathyroid hormone as a therapeutic agent, the goal of stimulating new bone formation is available for some patients. Evidence has clearly established the importance of adequate calcium intake in programs focused on bone. However, because osteoporosis is a complex disorder, maintaining an adequate calcium intake is just one aspect of a comprehensive skeletal health program for the peri- or postmenopausal woman.

Bone density studies

Scientific evidence confirms that the decline in circulating levels of 17β-estradiol is the predominant factor influencing the accelerated bone loss associated with menopause.[21] Bone loss at the spine begins about 1.5 years before the last menstrual period and occurs at a rate of approximately 3% per year for about 5 years, amounting to a total BMD loss of approximately 15%. Bone mass at the hip declines at a rate of about 0.5% per year before and after menopause, and sustains an additional loss of approximately 5–7% across the menopause transition period.[22]

It is well established that supplemental calcium can reduce the rate of postmenopausal bone loss, especially 5 or more years after menopause.[23] However, calcium in usual doses does not prevent menopause-associated bone loss as effectively as estrogen or an antiresorptive agent.[24] Nevertheless, it is clear that calcium potentiates both the bone-sparing and antifracture efficacy of antiresorptive agents.[25–27]

Calcium Monotherapy

The use of calcium monotherapy (i.e., without an antiresorptive agent, although combined with vitamin D in some studies) has been shown to reduce or halt bone loss in healthy postmenopausal women as well as in postmenopausal women with substantial bone loss or previous fracture.[23,28–35] A review of more than 20 studies found that postmenopausal women receiving calcium supplementation had bone losses of 0.014% per year compared with 1.0% per year in untreated women.[10] In longer-term trials, the beneficial effects of calcium supplementation were sustained for up to 4 years.[35–37]

Most evidence indicates that the benefits of calcium on BMD are dependent on time since menopause, with a more pronounced effect seen in women 5 or more years postmenopause.[23,33,36,38] In a 3-year trial with older women (aged ≥65 years), 500 mg/day supplemental calcium (with vitamin D) was found to significantly reduce the loss of total body BMD compared with placebo after 1 and 3 years of therapy.[29] Despite calcium's lower efficacy in peri- and early postmenopausal women, these populations need to maintain optimal calcium intake for general health considerations and to prevent additional loss of BMD above that due to diminished estrogen levels.

Calcium appears to potentiate the effect of exercise on BMD in postmenopausal women. In a review of 17 trials evaluating the benefits of exercise (e.g., resistance training, low- to high-impact exercises) and calcium intake on bone,[39] adding calcium supplementation to the exercise groups significantly improved BMD. The benefits of exercise, however, were observed only in those with daily calcium intakes above 1,000 mg.

Calcium Plus an Antiresorptive Agent

The antiresorptive agent estrogen is prescribed either alone as estrogen replacement therapy (ERT) or combined with a progestogen as hormone replacement therapy (HRT). In studies of early (≤5 years) postmenopausal women that compared ERT/HRT without calcium versus calcium monotherapy[40] or compared ERT/HRT with or without calcium supplementation,[41] calcium alone was not as effective as ERT/HRT alone in reducing estrogen-withdrawal bone loss. However, supplemental calcium did improve the efficacy of ERT/HRT.[26]

A review of trials administering calcium in addition to the active treatment (either an oral estrogen or nasal calcitonin) supports those conclusions.[26] In postmenopausal women receiving estrogen, high calcium intakes (1,183 mg/day, through both diet and supplements) significantly increased BMD at various skeletal sites when compared with estrogen therapy combined with low calcium intakes (563 mg/day): 2.1–3.3% versus 0.4–1.3%, respectively. Similar results were observed in the trials evaluating the effects of calcium supplementation with nasal calcitonin. In these studies, lumbar spine BMD increased 2.1% with calcitonin (200 IU/day) plus calcium (1,466 mg/day) compared with a decline of 0.2% with calcitonin given without calcium.

Because of the well-established need for adequate calcium intake, the key trials with either a selective estrogen-receptor modulator (SERM) or a bisphosphonate have not used a true placebo control.[42–50] Instead, all participants received calcium. Although it is likely that calcium potentiates the positive BMD effects of these agents, as it does for ERT/HRT, this conclusion can only be surmised.

Bone fracture studies

Reduced BMD is recognized as an important risk factor for osteoporotic fractures. In observational studies,[51–54] postmenopausal women who had suffered a hip fracture had significantly reduced BMC compared with age-matched controls. Women with low calcium absorption also have an increased risk for hip fractures, especially those with low calcium intakes.[55] Calcium's established benefits on BMD in controlled trials, combined with the causal relationship between low BMD and higher fracture rates, led to investigations of calcium in reducing fractures.

Calcium Monotherapy

In the presence of adequate vitamin D, calcium has been found to reduce the incidence of spine, hip, and other fractures.[28,29,56] In a large (N = 3,270) controlled trial of healthy, elderly French women (mean age, 84 years) who had low vitamin D levels and low calcium intakes, women who received supplemental vitamin D (800 IU/day) and calcium (1,200 mg/day) for 18 months had significantly fewer nonvertebral fractures (32%) and hip fractures (43%) than placebo recipients.[56] Another well-controlled trial in older postmenopausal women (aged ≥65 years) found that 500 mg/day of calcium plus 700 IU/day of vitamin D for 3 years significantly reduced the relative risk of any first nonvertebral fracture (RR, 0.4; 95% CI, 0.2–0.8).[29] A reduction in vertebral fracture rate was also seen in a study of 93 vitamin D-replete elderly women (mean age 72.1 years) given calcium supplementation (800 mg/day).[28]

In controlled clinical trials of calcium supplementation without concomitant vitamin D,[33,37] calcium (mean dose, 1,050 mg/day) reduced fracture rates, showing risk reductions of 25–70%. In the largest of these studies (N = 197),[33] calcium (1,200 mg/day) significantly lowered the spine fracture incidence in postmenopausal women (aged >60 years) with prior spine fracture and low calcium intakes, but not in women without a history of fracture. Among those with a fracture on entry, women not receiving calcium supplements were 2.8 times more likely to suffer another fracture.

Calcium Plus an Antiresorptive Agent

In trials demonstrating the efficacy of antiresorptive agents in fracture prevention, all study participants received calcium plus adequate vitamin D.[57–62] However, because the trials were not placebo-controlled for calcium, it can only be inferred that combination therapy with an antiresorptive agent and calcium is more effective at reducing fractures than calcium monotherapy. On the other hand, it cannot be assumed that antiresorptive agents would lower fracture rates in women with low calcium intake.

The efficacy of the SERM raloxifene in lowering the risk for vertebral fractures was established in the Multiple Outcomes of Raloxifene Evaluation (MORE) trial,[57] a double-blind, placebo-controlled study of 7,705 postmenopausal women with osteoporosis. The bisphosphonates alendronate and risedronate have each been shown to reduce the risk of vertebral and hip fractures in women with low bone density,[58–61] although their effects on fractures were dependent on the prevalent fracture status of women at entry into trial. Intranasal calcitonin also has been found to reduce vertebral fractures.[62]

Conclusions

Calcium, alone or with vitamin D, is not as effective in reducing menopause-related bone loss as are ERT/HRT, SERMs, or bisphosphonates. Calcium plus vitamin D can reduce the risk of fracture, particularly in the elderly, but it is no substitute for an antiresorptive agent in early postmenopausal women. However, calcium and vitamin D are both essential components of osteoporosis therapy with all antiresorptive agents.

COLORECTAL CANCER

The third most common malignancy in US women is colorectal cancer, and the risk increases with age. The incidence is six times higher in women aged 65 years and older compared with women aged 40–64 years.[63]

Low calcium intake is one of the risk factors associated with an increased incidence of colorectal cancer. A recent review of epidemiological studies concluded that high calcium intake appeared to decrease proliferation of colorectal epithelial cells (shown to promote tumor formation in animal studies) and lower the risk for colorectal adenoma.[64] However, clinical trial data are not fully consistent.

The association between high calcium intake and decreased proliferation of colorectal epithelial cells has been observed in several trials.[65–70] Calcium (up to 1,200 mg/day from either diet or supplementation) reduced colorectal cancer turnover in high-intake groups.[65–67] The largest trial (N = 193) found that calcium supplementation (1,000 or 2,000 mg/day) normalized the distribution of proliferating cells in the colorectal mucosa without affecting the proliferation rate.[68] However, two randomized trials using 1,200 mg of calcium daily did not find reduced epithelial cell proliferation.[69,70]

In studies of calcium and colorectal adenoma development, most findings support an inverse association between high calcium intake and cancer risk, although statistical significance has been reached in only a few studies.[64] In the largest controlled study (N = 930 men and women with a recent history of colorectal adenomas), 1,200 mg/day of calcium significantly reduced the risk of recurrent colorectal adenomas (RR, 0.85; 95% CI, 0.74–0.98).[71] A similar positive effect (although not statistically significant) has been observed in other prospective trials.[72–74] A prospective cohort study of nearly 90,000 women free of colorectal cancer at study entry also found an association (again not statistically significant) between calcium intake and lowered risk of colorectal cancer.[75]

Considerable research in experimental animals has clearly established the protective role of calcium in colon carcinogenesis.[76] Although the human studies have not all been positive, their findings are consistent with these animal data.

The controlled trials of calcium supplementation and colon cancer in humans have typically used calcium carbonate as the calcium source, based on the assumption that one calcium source is much the same as another. However, calcium phosphate has been shown to bind bile acids more efficiently than calcium carbonate and has worked better in the animal models than has the carbonate salt. Furthermore, high milk diets (in which the calcium source is effectively calcium phosphate) yield a colonic residue less irritating to mucosal cells than do diets in which supplements of the carbonate salt are used.[77] More research is needed to clarify the difference, if any, between various calcium salts and their role in colorectal cancer prevention.

Conclusions

Based on the generally consistent animal and human data, a case can be made that high calcium intake provides some chemoprotective properties against colorectal cancer. The data, however, are not sufficient to support a general recommendation that women take calcium solely to prevent colorectal cancer. However, since women should consume at least a minimum amount of calcium required for skeletal health, they may receive an added colorectal cancer benefit.

HYPERTENSION

The incidence of hypertension becomes more common with aging. Postmenopausal women are at great risk, with more than 50% of US women affected beyond age 55.[78]

Considerable epidemiologic and clinical trial data exist on the relationship between calcium intake and blood pressure. Although data from observational studies are equivocal, most controlled clinical trials have found that calcium has a beneficial effect on hypertension.

Analyses of pooled data from calcium intervention trials in hypertensive women[79–82] have concluded that supplemental calcium intake significantly lowers blood pressure (systolic: −0.15 mm Hg/100 mg per day of calcium; diastolic: −0.051 mm Hg/100 mg per day of calcium).[80] Because of the heterogeneity of hypertension, calcium intake did not have an effect on all active-treatment cohorts, although some subsets did show efficacy.

In both hypertensive and normotensive women and men, trials have found that high calcium intake from supplements produced small (2–5 mm Hg), but statistically significant, decreases in blood pressure. Dietary sources for calcium have produced similar effects. In a study of the DASH (Dietary Approaches to Stop Hypertension) diet,[83] which used fruits and vegetables and low-fat dairy products as the primary source of calcium, diastolic and systolic blood pressure declines of 3.0 and 5.5 mm Hg, respectively, were observed.

For white women, the calcium requirement for bone probably provides optimal protection against hyperten-

sion as well. It may be the opposite for black women, who utilize dietary calcium more efficiently, and thereby have denser bones with the same or lower calcium intake.[84] However, their calcium intake requirement is at least as high as for white women.[83] This is because hypertension may be the principal expression of inadequate calcium intake in blacks. For blacks, it may be more appropriate to peg calcium requirements to a cardiovascular, rather than a skeletal, endpoint.

Conclusions

Trials have demonstrated that calcium intake is associated with a beneficial effect on hypertension. However, the data are not sufficient to support a general recommendation that women take calcium solely to prevent or treat hypertension. Women may experience an added hypertension benefit from consuming the minimum amount of calcium required for skeletal health.

NEPHROLITHIASIS

Another condition, nephrolithiasis, is relatively common among both women and men. Although some concern has been expressed that high intake of calcium may increase the risk of developing renal calculi, several lines of evidence suggest that increasing calcium consumption up to or beyond 1,500 mg/day, as desired for osteoporosis therapy, actually reduces the risk.

The most convincing evidence of this inverse association comes from the standard use of calcium carbonate to treat the syndrome of intestinal hyperoxalosis and also from the Nurses' Health Study. In the Nurses' Health Study (N = 91,731 women),[85] those with dietary calcium intakes above 1,000 mg/day had a lower risk of developing an initial renal calculus than did women with lower calcium intakes (RR, 0.65; 95% CI, 0.50–0.83). However, women consuming less than 500 mg/day of calcium from a supplement had an increased risk compared with women taking less than 100 mg/day (RR, 1.20; 95% CI, 1.02–1.41). The authors suggested that the higher risk with supplements may have been related to the timing of calcium intake in relation to meals or to the oxalate content of those meals. In 67% of women, the supplements either were not consumed with a meal or the meal had a low oxalate content. More likely, this was a chance occurrence, since supplements ingested at more than 500 mg/day exhibited no increased risk.

Conclusions

Calcium intakes of up to 1,500 mg/day do not appear to increase the risk of developing renal calculi and probably reduce the risk appreciably. For peri- and postmenopausal women at high risk for developing renal calculi, foods may be the best sources of calcium. If calcium supplementation is needed, each dose should be taken with a large glass of water.

OBESITY

In women, the incidence of obesity (i.e., body mass index $\geq$30.0) increases until age 60, then decreases. According to NHANES III data, approximately 52% of women 50–59 years of age are either overweight or obese, a percentage that drops to about 41% in women 60–74 years old.[86]

A potential link between an increased risk of obesity and low calcium intake has only recently become apparent. An analysis of observational data has suggested an association based on findings that children and adolescents with high milk intakes weighed less and had less body fat than those with low milk intakes.[87] This conclusion was supported by an analysis of the NHANES III database that found a highly significant stepwise, inverse correlation between dietary calcium intake and the risk of obesity.[88] In a reanalysis of three calcium intake trials,[89] investigators found a similar inverse relationship between BMI and calcium intake in two studies of perimenopausal women as well as significant weight loss in a controlled trial of calcium supplementation in older women.

One plausible mechanism to explain the clinical and epidemiological observations is that low calcium intake, which increases parathyroid hormone and 1,25-dihydroxyvitamin D levels, stimulates the adipose cell metabolism to switch from lipolysis to lipogenesis, which in turn increases fat storage.

Conclusions

Although limited data suggest a statistically strong, inverse correlation between the risk of obesity and dietary calcium intake, available studies indicate that calcium intake explains only a small portion of the variability in body weight in postmenopausal women. Nevertheless, as for the other nonskeletal disorders addressed in this consensus opinion, ensuring an adequate calcium intake for skeletal purposes may confer small weight-control benefits as well.

OPTIMAL INTAKES

The primary factor influencing the amount of calcium absorbed is the amount of calcium ingested. Thus,

TABLE 1. *Recommended daily elemental calcium intakes in peri- and postmenopausal women*

National Academy of Sciences	
Age 31–50	1,000 mg
Age 51 and older	1,200 mg
National Institutes of Health	
Premenopausal women aged 25–50	1,000 mg
Postmenopausal women younger than age 65 using ERT	1,000 mg
Postmenopausal women not using ERT	1,500 mg
All women older than age 65	1,500 mg

Adapted from NIH[21] and the Standing Committee on Dietary Reference Intakes.[11]

attention should be focused on achieving optimal intakes of calcium, as well as vitamin D.

Calcium

The body's calcium requirements for optimal skeletal health vary by age, peaking during adolescence and then declining somewhat during early and middle adulthood. Calcium requirements rise again after midlife, particularly in postmenopausal women, owing in large part to estrogen-related shifts in intestinal calcium absorption and renal conservation.

Most experts support the published recommendations for daily calcium consumption from either the National Institutes of Health (revised in 1994)[21] or the National Academy of Sciences (revised in 1997).[11] Recommendations related to peri- and postmenopausal women are presented in Table 1.

The recommended calcium intakes are based on the total calcium content of various foods. To achieve maximum calcium absorption, food selection decisions should reflect the food's calcium bioavailability and the presence in the meal of other foods that may inhibit calcium absorption. Calcium requirements should optimally be met by food sources, with a calcium supplement added, if needed.[21]

The side effect profile from recommended levels of calcium intake is insignificant. No calcium intervention trials have reported any serious side effect associated with these levels.

The use of higher calcium intakes produces no currently recognized health benefits to women, and side effects can occur. Intakes greater than 2,500 mg/day (the upper limit for healthy adults set by the National Academy of Sciences) can increase the risk for hypercalcemia, which, in extreme cases, can lead to kidney failure.

Calcium supplements should be considered contraindicated in women with a renal calculus until the specific cause has been determined and the woman reassessed. It is not necessary to measure urine calcium excretion before increasing calcium intake to recommended levels in women who have not had a renal calculus. In general, women with a renal calculus should have their urine calcium excretion measured.

Vitamin D

The nutrient vitamin D is essential for the intestinal absorption of calcium. Ensuring sufficient vitamin D intake is fundamental to all prevention and treatment programs for postmenopausal osteoporosis.

The current recommended dietary intake for vitamin D is 400 IU/day for women aged 51–70 years and 600 IU/day for women older than age 70.[11] The National Osteoporosis Foundation recommends intakes of up to 800 IU/day for women at risk of deficiency because of inadequate sunlight exposure, such as elderly, chronically ill, housebound, institutionalized women, or those who live in northern latitudes.[90] The safe upper limit of vitamin D is 2,000 IU/day.[11] Higher doses may introduce risks such as hypercalciuria and hypercalcemia, and should be avoided.

Sources of vitamin D include sunlight, vitamin D-fortified dairy products, fatty fish, cod liver oil, and supplements. Daily requirements can usually be met with a multivitamin supplement (typically containing 400 IU vitamin D) plus moderate sun exposure. Many elderly women (>65 years) who have little or no sun exposure and rely on multivitamins alone for vitamin D intake may have suboptimal vitamin D levels.[91] Currently, there is no worldwide consensus on criteria for acceptable serum 25-hydroxyvitamin D [25(OH)D] values, but if minimization of parathyroid hormone concentration is used, as some suggest, the lower end of the normal 25(OH)D concentration would be in the range of 28–32 ng/mL (70–80 nmol/L). Taking vitamin D at the same time as a calcium supplement is not necessary, although it can be a convenient way to obtain adequate levels of both nutrients.

Magnesium

Another nutrient, magnesium, is sometimes mentioned as a necessary supplement for the protection of bone health and/or for absorption of calcium. Although magnesium is a necessary nutrient for the metabolic activity of all cells, in most trials focused on BMD or osteoporotic fracture, benefits of calcium were observed without magnesium supplementation. Moreover, a study with calcium absorption as the endpoint found that 789–826 mg/day of magnesium, more than double the daily average magnesium intake (280 mg) for postmenopausal women, had no effect on calcium absorption.[92]

Two studies[93,94] that did report an increase in BMD in postmenopausal women who received magnesium-containing supplements were small and not well controlled, and they do not present persuasive evidence of a beneficial magnesium effect. However, in frail elderly women and women with gastrointestinal disease, magnesium supplements may be needed.[95,96]

Conclusions

Estimates of adequate intakes of calcium, vitamin D, and magnesium for peri- and postmenopausal women are based on evidence relating to osteoporosis prevention. At least 1,200 mg/day of calcium is required for most women; levels greater than 2,500 mg/day are not helpful. A daily intake of 400–600 IU of vitamin D is recommended, either through sun exposure or through dietary intake or a supplement. The current evidence does not support magnesium supplementation for most peri- and postmenopausal women who ingest a balanced diet.

ASSESSMENT OF CALCIUM DEFICIENCY

No single laboratory test can accurately detect calcium deficiency. Tests for serum calcium and urine calcium, as well as those for BMD, have been used; however, each has important limits in clinical utility. Serum calcium levels are maintained within normal ranges even in the face of dietary calcium deficiency. The use of urine calcium is limited by its large range of normal values. Bone density is influenced by many factors other than diet; thus, its measurement cannot be considered a specific test of calcium deficiency.

In the absence of specific laboratory tests for calcium deficiency, an assessment of dietary calcium intake offers a quick and inexpensive option. However, such an assessment relies on the woman's subjective recollections of her food intake and serving sizes, which are often inaccurate. Moreover, inadequate dietary intake is only one aspect of calcium insufficiency. Others include inefficient absorption and excessive obligatory loss, neither of which is readily measurable in clinical practice.

In general, postmenopausal women in the United States and Canada have calcium intakes that are low, with median intakes of approximately 600 mg/day.[84,97] Specific populations of postmenopausal women at extra risk for inadequate calcium intake include women who are lactose intolerant, follow a vegetarian diet, or have poor eating habits.

Conclusions

Since no accurate test to determine calcium deficiency exists, clinicians should focus instead on ensuring that a woman consumes enough calcium to meet the recommended levels through diet and, when necessary, supplementation.

CALCIUM SOURCES

There are three categories of calcium sources: foods, calcium-fortified foods, and supplements.

Foods and fortified foods

Dietary sources are the preferred means of obtaining adequate calcium intake because there are other essential nutrients found in high-calcium foods. For most US residents, dairy products (e.g., milk, cheese, yogurt, ice cream) are the major contributors of dietary calcium, providing approximately 70% of the total calcium intake of postmenopausal women aged 60 years and older.[98] Dairy products have a high calcium content, high calcium bioavailability, and relatively low cost. Reduced-fat or low-fat products contain at least as much calcium per serving as high-fat dairy products, and they offer an alternative to the higher-fat products for those concerned about weight and lipid profiles.

Nondairy food sources of calcium include leafy green vegetables, a few types of nuts (e.g., almonds), and dried beans; however, the content is less concentrated than in dairy products, and the calcium in some foods (e.g., spinach) is not well absorbed. Other foods containing high levels of calcium include canned salmon and sardines (both eaten with bones).

Many calcium-fortified foods are available, including orange and fruit juices, cereals, bread, nutrition bars, and selected soy products (see Table 2). Although some of these foods have been shown to exhibit good bioavailability for their added calcium, most have not been tested.

An estimated 25% of the US population and 70% of the world's population exhibit some degree of lactase nonpersistence (i.e., inability to metabolize lactose in dairy products),[99,100] which in some individuals may produce diarrhea, bloating, and gas when dairy products are consumed (i.e., lactose intolerance). Lactase nonpersistence is more common among people of Asian, African, and South American descent. Other gastrointestinal problems (e.g., celiac disease, irritable bowel syndrome, Crohn's disease, gastrointestinal infection), or their treatment with intestinal antibiotics,

TABLE 2. *Calcium content of foods*

Food	Serving size	Approximate calcium per serving (mg)
Milk		
Whole or skim	1 cup (8 oz)	290–315
Chocolate, whole, low fat	1 cup	280–285
Powdered nonfat milk	1 tsp	50
Ice cream, soft, hardened	1/2 cup	90–100
Cheese		
American	1 oz	175
Cheddar	1 oz	200
Cottage	1/2 cup	70
Cream	2 tbsp	20–40
Mozzarella, part skim	1 oz	210
Parmesan	1 tbsp	70
Ricotta, part skim	4 oz	335
Yogurt[a]		
Whole milk, plain	1 cup	295
Low fat, plain, fruit	1 cup	340–450
Frozen, flavored	1 cup	160–240
Fish, shellfish		
Sardines in oil (with bones)	3 oz	370
Salmon	3 oz	170–210
Vegetables, nuts		
Almonds, dry roasted	1/4 cup	100
Beans, kidney	1 cup	50
Beans, baked, canned	1 cup	130
Beans, refried, canned	1 cup	190
Bok choy, raw	1 cup	160–250
Broccoli, fresh, cooked	1 cup	120–180
Cabbage, fresh, cooked	1 cup	50
Collards, fresh, cooked	1 cup	300–350
Figs, dried	10 figs	270
Soybeans, cooked	1 cup	175
Soybean curd (tofu)[b]	4 oz	30–155
Turnip greens	1 cup	200
Fortified foods[c]		
Calcium-fortified milk	1 cup	500
Calcium-fortified soy milk product	1 cup	80–300
Cereal with added calcium (without milk)	1 cup	100–1,000
Fruit juice with added calcium	1 cup	225–300
Breakfast bars	1 bar	200–500

[a] Yogurt varies in serving size, fat, and calcium content. Check labels for calcium content and calories.
[b] The calcium content of tofu processed with calcium salts can be as much as 300 mg/4 oz. The label should provide specific information.
[c] Unfortified breads and cereals are relatively low sources of calcium but still contribute substantially to calcium intake because these foods constitute a large part of the diet.

can cause lactose intolerance, either temporary or permanent.[101]

Many women with lactase nonpersistence can tolerate milk normally if they never stop drinking it in youth or if they increase intakes gradually, thereby conditioning their intestinal flora to produce lactase.[100] Those few who remain intolerant may substitute yogurt and lactase-treated milk. True milk intolerance or allergy is rare. Calcium supplements should be considered if dietary preferences or lactase deficiency restrict consumption of dairy foods.

Supplements

Calcium supplements offer a convenient alternative to women unable to consume enough calcium from diet alone. Wide selections of supplements are available, varying in size, type of preparation (e.g., tablet, chewable tablet, dissolvable tablet, liquid), and price. They also vary in elemental calcium content and absorbability.

The two most common calcium supplements consist of calcium carbonate or calcium citrate.

Calcium carbonate contains the highest percentage of elemental calcium (40%). Calcium carbonate products are typically less expensive than most other types of calcium supplements and are the most widely used calcium supplement. Calcium citrate (tetrahydrated form) contains 21% elemental calcium. Calcium carbonate and calcium citrate are equally well absorbed if taken with meals, the normal way of assimilating any nutrient.[102]

Other calcium products on the market include the following:

- Effervescent calcium supplements, typically calcium carbonate and citric acid. These are combined with materials that facilitate dissolving in water or orange juice to aid swallowing and improve absorption.
- Calcium citrate malate, which usually costs more than calcium carbonate.
- Supplements containing calcium that is chelated to an amino acid (e.g., bisglycinocalcium); these exhibit superior absorbability, although also at a higher cost.
- Bone meal, dolomite, or oyster shell supplements. In the past, some of these have contained toxic contaminants, especially lead;[103] however, a more recent analysis of the most commonly used brands did not reveal toxic levels of contaminants.[104]

The total calcium dose in a supplement is based on the amount of elemental calcium it contains. For example, 1,250 mg of calcium carbonate (which contains 40% elemental calcium) provides 500 mg of elemental calcium. Most products list the available elemental calcium. Recommended calcium levels (either reference values or dietary recommended intakes) refer to elemental calcium.

To maximize absorption, calcium supplements should be taken in doses of 500 mg or less throughout the day, and usually with meals. Consumption of calcium supplements with meals can also minimize the potential for rare gastrointestinal side effects.

Conclusion

Foods should be the primary source of calcium intake. Dairy products are among the best sources of calcium based on their high elemental calcium content, high absorption rate, and low cost relative to total nutritional value. Supplements and fortified foods are an alternative source for women not able to consume enough dietary calcium. Although achieving adequate calcium intake is the primary goal, a level of caution may be needed to avoid consuming more than 2,500 mg/day, owing to the abundance of supplemental calcium sources.

RESEARCH NEEDS

While much is known about the role of calcium in peri- and postmenopausal women, additional research is needed to further the understanding of this important nutrient. Some suggested areas for research include the following:

- Determine the optimal calcium intake during various stages of peri- and postmenopause.
- Determine the optimal calcium requirements in different ethnic populations, and the appropriate functional indicator for each. To date, bone status has been used for all ethnic groups as the functional indicator of calcium deficiency; however, for blacks, blood pressure may be the more appropriate indicator.
- Measure the long-term effects of calcium intake on bone remodeling.
- Examine the dose-response relationships between varying calcium intakes combined with antiresorptive agents regarding efficacy on bone loss and/or fractures.
- Evaluate the long-term effects of increased calcium intake on the incidence of colorectal cancer.
- Further define the role of calcium in the prevention of obesity and hypertension.

Acknowledgments: NAMS appreciates the contributions of the following panel of experts: *Robert P. Heaney, MD* (Chair), John A. Creighton University Professor, Creighton University, Omaha, Nebraska; *Bess Dawson-Hughes, MD*, Professor of Medicine, Chief, Calcium and Bone Metabolism Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, Massachusetts; *J. C. Gallagher, MD*, Professor of Medicine, Department of Bone Metabolism, Creighton University Medical Center, Omaha, Nebraska; *Robert Marcus, MD*, Professor of Medicine, Stanford University School of Medicine, Director, Aging Study Unit, Geriatrics Research, Education and Clinical Center, Palo Alto Veterans Affairs Health Center, Palo Alto, California; *Jeri W. Nieves, PhD*, Assistant Professor of Clinical Epidemiology, The Joseph L. Mailman School of Public Health, Columbia University and Helen Hayes Hospital, New York, New York. The development of this manuscript was supported by an unrestricted educational grant from SmithKline Beecham Consumer Healthcare.

REFERENCES

1. Grilli R, Magrini N, Penna A, Mura G, Liberati A. Practice guidelines developed by specialty societies: the need for a critical appraisal. *Lancet* 2000;355:103–6.
2. Feder G. Guidelines for clinical guidelines. *BMJ* 1998;317:427–8.
3. Scottish Intercollegiate Guidelines Network. *SIGN guidelines: an introduction to SIGN methodology for the development of evidence-based clinical guidelines.* Accessed at: http://www.sign.ac.uk/. Accessed June 23, 2000.
4. Boggs PP, Utian WH. The North American Menopause society develops consensus opinions [editorial]. *Menopause* 1998;5:67–8.
5. Heaney RP, Recker RR, Stegman MR, Moy AJ. Calcium absorption in women: relationships to calcium intake, estrogen status, and age. *J Bone Miner Res* 1989;4:469–75.
6. O'Brien KO, Abrams SA, Liang LK, Ellis KJ, Gagel RF. Increased efficiency of calcium absorption during short periods of inadequate calcium intake in girls. *Am J Clin Nutr* 1996;63:579–83.
7. Holick MF, Matsuoka LY, Wortsman J. Age, vitamin D, and solar ultraviolet [letter]. *Lancet* 1989;2(8671):1104–5.
8. Slovik DM, Rosenthal DI, Doppelt SH, et al. Restoration of spinal bone in osteoporotic men by treatment with human parathyroid hormone (1-34) and 1,25-dihydroxyvitamin D. *J Bone Miner Res* 1986;1:377–81.
9. Gallagher JC, Riggs BL, Eisman J, Hamstra A, Arnaud SB, DeLuca HF. Intestinal calcium absorption and serum vitamin D metabolites in normal subjects and osteoporotic patients: effect of age and dietary calcium. *J Clin Invest* 1979;64:729–36.
10. Nordin BE. Calcium and osteoporosis. *Nutrition* 1997;13:664–86.
11. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Institute of Medicine. *Dietary reference intakes: calcium, phosphorus, magnesium, vitamin D, and fluoride.* Washington, DC: National Academy Press, 1997.
12. Dawson-Hughes B, Seligson FH, Hughes VA. Effects of calcium carbonate and hydroxyapatite on zinc and iron retention in postmenopausal women. *Am J Clin Nutr* 1986;44:83–8.
13. Deehr MS, Dallal GE, Smith KT, Taulbee JD, Dawson-Hughes B. Effects of different calcium sources on iron absorption in postmenopausal women. *Am J Clin Nutr* 1990;51:95–9.
14. Ilich-Ernst JZ, McKenna AA, Badenhop NE, et al. Iron status, menarche, and calcium supplementation in adolescent girls. *Am J Clin Nutr* 1998;68:880–7.
15. Thys-Jacobs S, Starkey P, Bernstein D, Tian J, for the Premenstrual Syndrome Study Group. Calcium carbonate and the premenstrual syndrome: effects on premenstrual and menstrual symptoms. *Am J Obstet Gynecol* 1998;179:444–52.
16. Looker AC, Orwoll ES, Johnston CC, et al. Prevalence of low femoral bone density in older U.S. adults from NHANES III. *J Bone Miner Res* 1997;12:1761–8.
17. Melton LJ III, Chrischilles EA, Cooper C, Lane AW, Riggs BL. Perspective: how many women have osteoporosis? *J Bone Miner Res* 1992;7:1005–10.
18. Melton LJ III, Thamer M, Ray NF, et al. Fractures attributable to osteoporosis: report from the National Osteoporosis Foundation. *J Bone Miner Res* 1997;12:16–23.
19. US Congress Office of Technology Assessment. *Hip fracture outcomes in people age 50 and over—background paper.* Washington, DC: US Government Printing Office, 1994. Publication OTA-BP-H-120.
20. Cooper C, Atkinson EJ, Jacobsen SJ, O'Fallon WM, Melton LJ III. Population-based study of survival after osteoporotic fractures. *Am J Epidemiol* 1993;137:1001–5.
21. National Institutes of Health. NIH Consensus Development Panel

on Optimal Calcium Intake. Optimal calcium intake. *JAMA* 1994; 272:1942–8.
22. Recker RR, Lappe J, Davies K, Heaney R. Characterization of perimenopausal bone loss: a prospective study. *J Bone Miner Res* 2000;15:1965–73.
23. Dawson-Hughes B, Dallal GE, Krall EA, et al. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. *N Engl J Med* 1990;323:878–83.
24. Heaney RP. Calcium, dairy products and osteoporosis. *J Am Coll Nutr* 2000;19:83S–99S.
25. Davis JW, Ross PD, Johnson NE, Wasnich RD. Estrogen and calcium supplement use among Japanese-American women: effects upon bone loss when used singly and in combination. *Bone* 1995; 17:369–73.
26. Nieves JW, Komar L, Cosman F, Lindsay R. Calcium potentiates the effect of estrogen and calcitonin on bone mass: review and analysis. *Am J Clin Nutr* 1998;67:18–24.
27. Honkanen RJ, Alhava E, Saarikoski S, Kroger H, Tupperainen M. Interaction of calcium and HRT in the prevention of bone loss and fractures in early postmenopausal women. *J Bone Miner Res* 1999;14(Suppl 1):S181.
28. Chevalley T, Rizzoli R, Nydeggar V, et al. Effects of calcium supplements on femoral bone mineral density and vertebral fracture rate in vitamin-D-replete elderly patients. *Osteoporos Int* 1994;4:245–52.
29. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age and older. *N Engl J Med* 1997;337:670–6.
30. Devine A, Dick IM, Heal SJ, Criddle RA, Prince RL. A 4-year follow-up study of the effects of calcium supplementation on bone density in elderly postmenopausal women. *Osteoporos Int* 1997; 7:23–8.
31. Elders PJ, Netelenbos JC, Lips P, et al. Calcium supplementation reduces vertebral bone loss in perimenopausal women: a controlled trial in 248 women between 46 and 55 years of age. *J Clin Endocrinol Metab* 1991;73:533–40.
32. Peacock M, Liu G, Carey M, et al. Effect of calcium or 25OH vitamin D3 dietary supplementation on bone loss at the hip in men and women over the age of 60. *J Clin Endocrinol Metab* 2000;85: 3011–19.
33. Recker RR, Hinders S, Davies KM, et al. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *J Bone Miner Res* 1996;11:1961–6.
34. Reid JR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Effect of calcium supplementation on bone loss in postmenopausal women. *N Engl J Med* 1993;328:460–4.
35. Riggs BL, O'Fallon WM, Muhs J, O'Connor MK, Kumar R, Melton LJ III. Long-term effects of calcium supplementation on serum parathyroid hormone level, bone turnover, and bone loss in elderly women. *J Bone Miner Res* 1998;13:168–74.
36. Elders PJ, Lips P, Netelenbos JC, et al. Long-term effect of calcium supplementation on bone loss in perimenopausal women. *J Bone Miner Res* 1994;9:963–70.
37. Reid JR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: a randomized controlled trial. *Am J Med* 1995;98:331–35.
38. Aloia JF, Vaswani A, Yeh JK, Ross PL, Flaster E, Dilmanian FA. Calcium supplementation with and without hormone replacement therapy to prevent postmenopausal bone loss. *Ann Intern Med* 1994;120:97–103.
39. Specker BL. Evidence for an interaction between calcium intake and physical activity on changes in bone mineral density. *J Bone Miner Res* 1996;11:1539–44.
40. Riis B, Thomsen K, Christiansen C. Does calcium supplementation prevent postmenopausal bone loss? A double-blind, controlled clinical study. *N Engl J Med* 1987;316:173–7.
41. Haines CJ, Chung TK, Leung PC, Hsu SY, Leung DH. Calcium supplementation and bone mineral density in postmenopausal women using estrogen replacement therapy. *Bone* 1995;16: 529–31.
42. Cummings SR, Black DM, Thompson DE, et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: results from the Fracture Intervention Trial. *JAMA* 1998;280:2077–82.
43. Delmas PD, Bjarnason NH, Mitlak BH, et al. Effects of raloxifene on bone mineral density, serum cholesterol concentrations, and uterine endometrium in postmenopausal women. *N Engl J Med* 1997;337:1641–7.
44. Evans RA, Somers NM, Dunstan CR, Royle H, Kos S. The effect of low-dose cyclical etidronate and calcium on bone mass in early postmenopausal women. *Osteoporos Int* 1993;3:71–5.
45. Fogelman I, Ribot C, Smith R, Ethgen D, Sod E, Reginster JY, for the BMD-MN Study Group. Risedronate reverses bone loss in postmenopausal women with low bone mass: results from a multinational, double-blind, placebo-controlled trial. *J Clin Endocrinol Metab* 2000;85;1895–900.
46. Grey AB, Stapleton JP, Evans MC, Tatnell MA, Ames RW, Reid IR. The effect of the antiestrogen tamoxifen on bone mineral density in normal late postmenopausal women. *Am J Med* 1995; 99:636–41.
47. Lufkin EG, Witaker MD, Nickelsen T, et al. Treatment of established postmenopausal osteoporosis with raloxifene: a randomized trial. *J Bone Miner Res* 1998;13:1747–54.
48. Meunier PJ, Vigno E, Garnero P, et al, for the Raloxifene Study Group. Treatment of postmenopausal women with osteoporosis or low bone density with raloxifene. *Osteoporos Int* 1999;10:330–6.
49. Ryan PJ, Blake GM, Davie M, et al. Intermittent oral disodium pamidronate in established osteoporosis: a 2 year double-masked placebo-controlled study of efficacy and safety. *Osteoporos Int* 2000;11:171–6.
50. Sebaldt RJ, Ioannidis G, Adachi JD, et al. 36 month intermittent cyclical etidronate treatment in patients with established corticosteroid induced osteoporosis. *J Rheumatol* 1999;26:1545–9.
51. Cummings SR, Black DM, Nevitt MC, et al, for the Study of Osteoporotic Fractures Research Group. Bone density at various sites for prediction of hip fractures. *Lancet* 1993;34:72–5.
52. Melton LJ III, Atkinson EJ, O'Fallon WM, Wahner HW, Riggs BL. Long-term fracture prediction by bone mineral assessed at different skeletal sites. *J Bone Miner Res* 1993;8:1227–33.
53. Perloff JJ, McDermott MT, Perloff KG, et al. Reduced bone-mineral content is a risk factor for hip fractures. *Orthop Rev* 1991; 20:690–8.
54. Spector TD, McCloskey EV, Doyle DV, Kanis JA. Prevalence of vertebral fracture in women and the relationship with bone density and symptoms: the Chingford Study. *J Bone Miner Res* 1993;8: 817–22.
55. Ensrud KE, Duong T, Cauley JA, et al, for the Study of Osteoporotic Fractures Research Group. Low fractional calcium absorption increases the risk for hip fracture in women with low calcium intake. *Ann Intern Med* 2000;132:345–53.
56. Chapuy MC, Arlot ME, Duboeuf F, et al. Vitamin D3 and calcium to prevent hip fractures in elderly women. *N Engl J Med* 1992;327: 1637–42.
57. Ettinger B, Black DM, Mitlak BH, et al, for the Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. *JAMA* 1999;282:637–45.
58. Black DM, Cummings SR, Karpf DB, et al. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. *Lancet* 1996;348:1535–41.
59. Harris ST, Watts NB, Genant HK, et al, for the Vertebral Efficacy With Risedronate Therapy (VERT) Study Group. Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis: a randomized controlled trial. *JAMA* 1999;282:1344–52.
60. Liberman UA, Weiss SR, Broll J, et al, for the Alendronate Phase

III Osteoporosis Treatment Study Group. Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis. *N Engl J Med* 1995;333:1437–43.
61. Reginster J, Minne HW, Sorensen OH, et al. Randomized trial of the effects of risedronate on vertebral fractures in women with established postmenopausal osteoporosis. *Osteoporos Int* 2000;11:83–91.
62. Chesnut CH, Silverman S, Andriano K, et al. A randomized trial of nasal spray salmon calcitonin in postmenopausal women with established osteoporosis: the prevent recurrence of osteoporotic fractures study. *Am J Med* 2000;109:267–76.
63. American Cancer Society. *Cancer facts & figures–1999*. Atlanta, GA: American Cancer Society, 1999.
64. Jänne PA, Mayer RJ. Chemoprevention of colorectal cancer. *N Engl J Med* 2000;342:1960–8.
65. Holt PR, Atillasoy EO, Gilman J, et al. Modulation of abnormal colonic epithelial cell proliferation and differentiation by low-fat dairy foods: a randomized controlled trial. *JAMA* 1998;280:1074–9.
66. Lipkin M, Newmark H. Effect of added dietary calcium on colonic epithelial-cell proliferation in subjects at high risk for familial colonic cancer. *N Engl J Med* 1985;313:1381–4.
67. Thomas MG, Thomson JP, Williamson RC. Oral calcium inhibits rectal epithelial proliferation in familial adenomatous polyposis. *Br J Surg* 1993;80:499–501.
68. Bostick RM, Fosdick L, Wood JR, et al. Calcium and colorectal epithelial cell proliferation in sporadic adenoma patients: a randomized, double-blinded, placebo-controlled clinical trial. *J Natl Cancer Inst* 1995;87:1307–15.
69. Baron JA, Tosteson TD, Wargovich MJ, et al. Calcium supplementation and rectal mucosal proliferation: a randomized controlled trial. *J Natl Cancer Inst* 1995;87:1275–7.
70. Cascinu S, Ligi M, Del Ferro E, et al. Effects of calcium and vitamin supplementation on colon cell proliferation in colorectal cancer. *Cancer Invest* 2000;18:411–6.
71. Baron JA, Beach M, Mandel JS, et al. Calcium supplements for the prevention of colorectal adenomas. *N Engl J Med* 1999;340:101–7.
72. Hofstad B, Almendingen K, Vatn M, et al. Growth and recurrence of colorectal polyps: a double-blind 3-year intervention with calcium and antioxidants. *Digestion* 1998;59:148–56.
73. Hyman J, Baron JA, Dain BJ, et al. Dietary supplemental calcium and the recurrence of colorectal adenomas. *Cancer Epidemiol Biomarkers Prev* 1998;7:291–5.
74. Bonithon-Kopp C, Kronborg O, Giacosa A, Rath U, Faivre J, for the European Cancer Prevention Organisation Study Group. Calcium and fibre supplementation in prevention of colorectal adenoma recurrence: a randomised intervention trial. *Lancet* 2000;356:1300–6.
75. Martinez ME, Giovannucci EL, Colditz GA, et al. Calcium, vitamin D, and the occurrence of colorectal cancer among women. *J Natl Cancer Inst* 1996;88:1375–82.
76. Lipkin M, Newmark H. Calcium and the prevention of colon cancer. *J Cell Biochem Suppl* 1995;22:65–73.
77. Lupton JR. Dairy products and colon cancer: mechanisms of the protective effect [editorial]. *Am J Clin Nutr* 1997;66:1065–6.
78. American Heart Association. *2000 heart and stroke statistical update.* Dallas, TX: American Heart Association, 1999.
79. Allender PS, Cutler JA, Follmann D, Cappuccio FP, Pryer J, Elliott P. Dietary calcium and blood pressure: a meta-analysis of randomized clinical trials. *Ann Intern Med* 1996;124:825–31.
80. Birkett NJ. Comments on a meta-analysis of the relation between dietary calcium intake and blood pressure. *Am J Epidemiol* 1998;148:223–8.
81. Bucher HC, Cook RJ, Guyatt GH, et al. Effects of dietary calcium supplementation on blood pressure. *JAMA* 1996;275:1016–22.
82. Griffith LE, Guyatt GH, Cook RJ, Bucher HC, Cook DJ. The influence of dietary and nondietary calcium supplementation on blood pressure: an updated metaanalysis of randomized controlled trials. *Am J Hypertens* 1999;12:84–92.
83. Appel LJ, Moore TJ, Obarzanek E, et al, for the DASH Collaborative Research Group. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 1997;336:1117–24.
84. Alaimo K, McDowell MA, Briefel RR. Dietary intake of vitamins, minerals, and fiber of persons ages 2 months and over in the United States: third National Health and Nutrition Examination survey, phase 1, 1988–91. *Adv Data* 1994;258:1–28.
85. Curhan GC, Willett WC, Speizer FE, Spiegelman D, Stampfer MJ. Comparison of dietary calcium with supplemental calcium and other nutrients as factors affecting the risk for kidney stones in women. *Ann Intern Med* 1997;126:497–504.
86. Kuczmarski RJ, Flegal KM, Campbell SM, Johnson CL. Increasing prevalence of overweight among US adults. The National Health and Nutrition Examination Surveys, 1960 to 1991. *JAMA* 1994;272:205–11.
87. Heaney RP. Calcium intake and the prevention of chronic disease. In: Wilson T, Temple N, eds. *Frontiers in nutrition*. Totowa, NJ: Humana Press, 2000.
88. Zemel MB, Shi H, Greer B, Dirienzo D, Zemel PC. Regulation of adiposity by dietary calcium. *FASEB J* 2000;14:1132–8.
89. Davies KM, Heaney RP, Recker RR, et al. Calcium intake and body weight. *J Clin Endocrinol Metab* 2000;85:4635–8.
90. National Osteoporosis Foundation. *Physician's guide to prevention and treatment of osteoporosis.* Washington, DC: National Osteoporosis Foundation, 1998.
91. Chapuy MC, Preziosi P, Maamer M, et al. Prevalence of vitamin D insufficiency in an adult normal population. *Osteoporos Int* 1997;7:439–43.
92. Spencer H, Fuller H, Norris C, Williams D. Effect of magnesium on the intestinal absorption of calcium in man. *J Am Coll Nutr* 1994;13:485–92.
93. Abraham GE. The importance of magnesium in the management of primary postmenopausal osteoporosis. *J Nutr Med* 1991;2:165–78.
94. Stendig-Lindberg G, Tepper R, Leichter I. Trabecular bone density in a two-year controlled trial of peroral magnesium in osteoporosis. *Magnes Res* 1993;6:155–63.
95. Durlach J, Bac P, Durlach V, Rayssiguier Y, Bara M, Guiet-Bara A. Magnesium status and ageing: an update. *Magnes Res* 1998;11:25–42.
96. Rude RK, Olerich M. Magnesium deficiency: possible role in osteoporosis associated with gluten-sensitive enteropathy. *Osteoporos Int* 1996;6:453–61.
97. MacLean D. Nova Scotia Heart Health Program, Health and Welfare Canada, Nova Scotia Department of Health. *The report of the Nova Scotia nutrition survey.* Halifax, NS, 1993.
98. Fleming KH, Heimbach JT. Consumption of calcium in the US: food sources and intake levels. *J Nutr* 1994;124:1426S–30S.
99. Heaney RP. Bone mass, nutrition, and other lifestyle factors. *Nutr Rev* 1996;54:S3–S10.
100. Suarez FL, Savaiano DA, Levitt MD. Review article: the treatment of lactose intolerance. *Aliment Pharmacol Ther* 1995;9:589–97.
101. Suarez FL, Savaiano DA, Levitt MD. A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med* 1995;333:1–4.
102. Heaney RP, Dowell MS, Barger-Lux MJ. Absorption of calcium as the carbonate and citrate salts, with some observations on method. *Osteoporosis Int* 1999;9:19–23.
103. Bourgoin BP, Evans DR, Cornett JR, et al. Lead content in 70 brands of dietary calcium supplements. *Am J Public Health* 1993;83:1155–60.
104. Ross EA, Szabo NJ, Tebbett IR. Lead content of calcium supplements. *JAMA* 2000;284:1425–9.