Health Benefits of Nutritional Supplements

Selected Abstracts

Compiled by

Tim Wood, Ph.D.
Charles Hussey, M.S.

USANA Health Sciences
3838 West Parkway Blvd.
Salt Lake City, UT 84120

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Forward

The importance of nutrition for human health has long been recognized. Prior to 1960, interest in this field largely focused on the etiology and prevention of acute nutrient deficiency diseases such as scurvy, rickets, and pellagra. Some 50 essential nutrients (vitamins, minerals, antioxidants, cofactors, essential amino acids, essential fatty acids) were identified, and recommended daily intakes for those essential nutrients (e.g. Recommended Dietary Allowances or RDAs) were developed. These recommendations, in turn, proved to be valuable in eradicating acute nutrient deficiency diseases.

During the past 20-30 years, attention has shifted to the role of diet and nutrition in the pathogenesis of chronic degenerative diseases. Heart disease, some cancers, osteoporosis, type II diabetes, and macular degeneration are all known to have dietary risk factors, many of which involve chronic nutrient deficiencies. Importantly, these associations have been much more difficult to study, in large measure because of the time frames involved. Chronic degenerative diseases develop over decades (lifetimes), and it is extremely challenging to conduct research programs for such extended periods. Nevertheless, advances in epidemiological and clinical research have helped us learn a great deal about the impacts (positive and negative) of diet and essential nutrient intakes on long-term health.

During the past decade, the scientific and healthcare communities have paid increasing attention to the role of nutritional supplements (as components of diet) in preventing and treating chronic disease. Hundreds of scientific studies have been conducted and published. These studies span a broad range of health issues. They have employed a wide variety of methodologies. And they have produced both positive and negative results. In some areas (e.g. the role of calcium and vitamin D supplements in slowing the progression of osteoporosis, and the role of folic acid supplements in preventing certain birth defects), results have been consistent, and benefits have been well accepted. In other areas (e.g. the role of antioxidant supplementation in preventing heart disease), results have been less consistent, and conclusions remain controversial. In any event, research on the health benefits of nutritional supplements is progressing, and evidence continues to mount that nutritional supplements offer a convenient and cost effective means for promoting health, over both the short- and long-terms.

The following is a collection of abstracts from about 100 scientific papers describing research on the health benefits of nutritional supplements. This collection is not exhaustive. Papers were selected on the basis of scientific merit and relevance to the field. The majority describes positive results, but in some, negative results are reported. Our objective in compiling this list was to provide readers with a good cross section of the scientific literature so that they could develop a sense for the current state of research in this field and draw their own conclusions concerning the role of supplementation in healthcare. References for many more papers are given in our bibliography entitled Health Benefits of Nutritional Supplements: Selected Readings .

For convenience, the abstracts have been sorted by health issue; namely Cardiovascular Health, Cancer Prevention, Strong Bones, Healthy Pregnancies/Healthy Babies, Sound Metabolism, Robust Immune Function, Acute Vision, and Other.

Strong Bones

Vitamin D3 and calcium to prevent hip fractures in the elderly women.

Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD, Meunier PJ. 1992.
N Engl J Med 327(23):1637-42

BACKGROUND. Hypovitaminosis D and a low calcium intake contribute to increased parathyroid function in elderly persons. Calcium and vitamin D supplements reduce this secondary hyperparathyroidism, but whether such supplements reduce he risk of hip fractures among elderly people is not known. METHODS. We studied the effects of supplementation with vitamin D3 (cholecalciferol) and calcium on the frequency of hip fractures and other nonvertebral fractures, identified radiologically, in 3270 healthy ambulatory women (mean [+/- SD] age, 84 +/- 6 years). Each day for 18 months, 1634 women received tricalcium phosphate (containing 1.2 g of elemental calcium) and 20 micrograms (800 IU) of vitamin D3, and 1636 women received a double placebo. We measured serial serum parathyroid hormone and 25-hydroxyvitamin D (25(OH)D) concentrations in 142 women and determined the femoral bone mineral density at base line and after 18 months in 56 women. RESULTS. Among the women who completed the 18-month study, the number of hip fractures was 43 percent lower (P = 0.043) and the total number of nonvertebral fractures was 32 percent lower (P = 0.015) among the women treated with vitamin D3 and calcium than among those who received placebo. The results of analyses according to active treatment and according to intention to treat were similar. In the vitamin D3-calcium group, the mean serum parathyroid hormone concentration had decreased by 44 percent from the base-line value at 18 months (P < 0.001) and the serum 25(OH)D concentration had increased by 162 percent over the base-line value (P < 0.001). The bone density of the proximal femur increased 2.7 percent in the vitamin D3-calcium group and decreased 4.6 percent in the placebo group (P < 0.001). CONCLUSIONS. Supplementation with vitamin D3 and calcium reduces the risk of hip fractures and other nonvertebral fractures among elderly women.

Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D.

Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL. 1995.
Am J Clin Nutr 61(5):1140-5

We conducted a study to determine whether increasing vitamin D intake above the recommended dietary allowance (RDA) of 5.0 micrograms (200 IU)/d reduces bone loss in healthy postmenopausal women residing at latitude 42 degrees N. In this double-blind, randomized 2-y trial, we enrolled 247 healthy ambulatory postmenopausal women who consumed an average of 2.5 micrograms (100 IU) vitamin D/d in their usual diets. The women were given either 2.5 micrograms (100 IU) or 17.5 micrograms (700 IU) vitamin D/d. All women received 500 mg supplemental calcium per day as citrate malate. Duplicate hip and spine and single whole-body scans were performed by dual-energy x-ray absorptiometry at 6-mo intervals selected to flank the periods when 25-hydroxycholecalciferol (calcidiol) concentrations are highest (summer/fall) and lowest (winter/spring). Plasma calcidiol and serum osteocalcin were measured in these seasons in year 1. Both treatment groups lost bone mineral density from the femoral neck, but the 17.5-micrograms group lost less than (-1.06 +/- 0.34%; mean +/- SE) the 2.5-micrograms group (-2.54 +/- 0.37%, P = 0.003). Seventy percent of the benefit each year occurred in winter/spring and 30% in summer/fall. Changes in spinal and whole-body bone densities did not differ by treatment group and were minimal after 2 y. Serum osteocalcin and plasma calcidiol (2.5-micrograms group only) fluctuated with season. In conclusion, in healthy, calcium-supplemented, postmenopausal women residing at latitude 42 degrees N, an intake of 5.0 micrograms (200 IU) vitamin D/d is sufficient to limit bone loss from the spine and whole body but it is not adequate to minimize bone loss from the femoral neck.

A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women.

Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannenbaum S. 1990.
N Engl J Med 323(13):878-83

Background. The effectiveness of calcium in retarding bone loss in older postmenopausal women is unclear. Earlier work suggested that the women who were most likely to benefit from calcium supplementation were those with low calcium intakes. METHODS. We undertook a double-blind, placebo-controlled, randomized trial to determine the effect of calcium on bone loss from the spine, femoral neck, and radius in 301 healthy postmenopausal women, half of whom had a calcium intake lower than 400 mg per day and half an intake of 400 to 650 mg per day. The women received placebo or either calcium carbonate or calcium citrate malate (500 mg of calcium per day) for two years. Results. In women who had undergone menopause five or fewer years earlier, bone loss from the spine was rapid and was not affected by supplementation with calcium. Among the women who had been postmenopausal for six years or more and who were given placebo, bone loss was less rapid in the group with the higher dietary calcium intake. In those with the lower calcium intake, calcium citrate malate prevented bone loss during the two years of the study; its effect was significantly different from that of placebo (P less than 0.05) at the femoral neck (mean change in bone density [+/- SE], 0.87 +/- 1.01 percent vs. -2.11 +/- 0.93 percent), radius (1.05 +/- 0.75 percent vs. -2.33 +/- 0.72 percent), and spine (-0.38 +/- 0.82 percent vs. -2.85 +/- 0.77 percent). Calcium carbonate maintained bone density at the femoral neck (mean change in bone density, 0.08 +/- 0.98 percent) and radius (0.24 +/- 0.70 percent) but not the spine (-2.54 +/- 0.85 percent). Among the women who had been postmenopausal for six years or more and who had the higher calcium intake, those in all three treatment groups maintained bone density at the hip and radius and lost bone from the spine. CONCLUSIONS. Healthy older postmenopausal women with a daily calcium intake of less than 400 mg can significantly reduce bone loss by increasing their calcium intake to 800 mg per day. At the dose we tested, supplementation with calcium citrate malate was more effective than supplementation with calcium carbonate.

Calcium supplementation and increases in bone mineral density in children.

Johnston CC Jr, Miller JZ, Slemenda CW, Reister TK, Hui S, Christian JC, Peacock M. 1992.
N Engl J Med 327(2):82-7

BACKGROUND. Increased dietary intake of calcium during childhood, usually as calcium in milk, is associated with increased bone mass in adulthood; the increase in mass is important in modifying the later risk of fracture. Whether the increase is due to the calcium content of milk, however, is not certain. METHODS. We conducted a three-year, double-blind, placebo-controlled trial of the effect of calcium supplementation (1000 mg of calcium citrate malate per day) on bone mineral density in 70 pairs of identical twins (mean [+/- SD] age, 10 +/- 2 years; range, 6 to 14). In each pair, one twin served as a control for the other; 45 pairs completed the study. Bone mineral density was measured by photon absorptiometry at two sites in the radius (at base line, six months, and one, two, and three years) and at three sites in the hip and in the spine (at base line and three years). RESULTS. The mean daily calcium intake of the twins given placebo was 908 mg, and that of the twins given calcium supplements was 1612 mg (894 mg from the diet and 718 mg from the supplement). Among the 22 twin pairs who were prepubertal throughout the study, the twins given supplements had significantly greater increases in bone mineral density at both radial sites (mean difference in the increase in bone mineral density: midshaft radius, 5.1 percent [95 percent confidence interval, 1.5 to 8.7 percent]; distal radius, 3.8 percent [95 percent confidence interval, 1.4 to 6.2 percent]) and in the lumbar spine (increase, 2.8 percent [95 percent confidence interval, 1.1 to 4.5 percent]) after three years; the differences in the increases at two of three femoral sites approached significance (Ward's triangle in the femoral neck, 2.9 percent; greater trochanter, 3.5 percent). Among the 23 pairs who went through puberty or were postpubertal, the twins given supplements received no benefit. CONCLUSIONS. In prepubertal children whose average dietary intake of calcium approximated the recommended dietary allowance, calcium supplementation increased the rate of increase in bone mineral density. If the gain persists, peak bone density should be increased and the risk of fracture reduced.

Calcium supplementation and bone mineral density in adolescent girls.

Lloyd T, Andon MB, Rollings N, Martel JK, Landis JR, Demers LM, Eggli DF, Kieselhorst K, Kulin HE. 1993.
JAMA 270(7):841-4.

OBJECTIVE--To evaluate the effect of calcium supplementation on bone acquisition in adolescent white girls. DESIGN--A randomized, double-blind, placebo-controlled trial of the effect of 18 months of calcium supplementation on bone density and bone mass. SUBJECTS--Ninety-four girls with a mean age of 11.9 + 0.5 years at study entry. SETTING--University hospital in a small town. INTERVENTIONS--Calcium supplementation, 500 mg/d calcium as calcium citrate malate; controls received placebo pills. MAIN OUTCOME MEASURES--Bone mineral density and bone mineral content of the lumbar spine and total body were measured by dual-energy x-ray absorptiometry and calcium excretion from 24-hour urine specimens. RESULTS--Calcium intake from dietary sources averaged 960 mg/d for the entire study group. The supplemented group received, on average, an additional 354 mg/d of calcium. The supplemented group compared with the placebo group had greater increases of lumbar spine bone density (18.7% vs 15.8%; P = .03), lumbar spine bone mineral content (39.4% vs 34.7%; P = .06), total body bone mineral density (9.6% vs 8.3%; P = .05), and 24-hour urinary calcium excretion (90.4 vs 72.9 mg/d; P = .02), respectively. CONCLUSIONS Increasing daily calcium intake from 80% of the recommended daily allowance to 110% via supplementation with calcium citrate malate resulted in significant increases in total body and spinal bone density in adolescent girls. The increase of 24 g of bone gain per year among the supplemented group translates to an additional 1.3% skeletal mass per year during adolescent growth, which may provide protection against future osteoporotic fracture.

A co-twin study of the effect of calcium supplementation on bone density during adolescence.

Nowson CA, Green RM, Hopper JL, Sherwin AJ, Young D, Kaymakci B, Guest CS, Smid M, Larkins RG, Wark JD. 1997.
Osteoporos Int. 7(3):219-25.

The effect of calcium supplementation on bone mineral density (BMD) was evaluated in female twin pairs aged 10-17 years with a mean age of 14 years. Forty-two twin pairs (22 monozygotic, 20 dizygotic; (including one monozygotic pair from a set of triplets) completed at least 6 months of the intervention: 37 pairs to 12 months and 28 pairs to 18 months. BMD was measured by dual-energy X-ray absorptiometry (DXA). In a double-blind manner, one twin in each pair was randomly assigned to receive daily a 1000 mg effervescent calcium tablet (Sandocal 1000), and the other a placebo tablet similar in taste and appearance to the calcium supplement but containing no calcium. Compliance (at least 80% tablets consumed), as measured by tablet count, was 85% in the placebo group and 83% in the calcium group over the 18 months of the study, on average increasing dietary calcium to over 1600 mg/day. There was no within-pair difference in the change in height or weight. When the effect of calcium supplementation on BMD was compared with placebo at approximately 6, 12 and 18 months, it was found that there was a 0.015 +/- 0.007 g/ cm2 greater increase in BMD (1.62 +/- 0.84%) at the spine in those on calcium after 18 months. At the end of the first 6 months there was a significant within-pair difference of 1.53 +/- 0.56% at the spine and 1.27 +/- 0.50% at the hip. However, there were no significant differences in the changes in BMD after the initial effect over the first 6 months. Therefore, we found an increase in BMD at the spine with calcium supplementation in females with a mean age of 14 years. The greatest effect was seen in the first 6 months; thereafter the difference was maintained, but there was no accelerated increase in BMD associated with calcium supplementation. The continuance of the intervention until the attainment of peak bone mass and follow-up after cessation of calcium supplementation will be important in clarifying the optimal timing for increased dietary calcium and the sustained, long-term effects of this intervention.

Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: a randomized controlled trial.

Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. 1995.
Am J Med 98(4):331-5

PURPOSE: To determine the long-term effects of calcium supplements or placebo on bone density in healthy women at least 3 years postmenopause. PATIENTS AND METHODS: Eighty-six women from our previously reported 2-year study agreed to continue on their double-blind treatment allocation (1 g elemental calcium or placebo) for a further 2 years, with 78 women (40 on placebo) reaching the 4-year end point. Median (interquartile range) dietary calcium intakes for the whole group were 700 mg (range 540 to 910) per day at baseline, 670 mg (range 480 to 890) per day at 2 years, and 640 mg (range 460 to 880) per day at 4 years. The bone mineral density (BMD) of the total body, lumbar spine, and proximal femur was measured every 6 months by dual-energy, x-ray absorptiometry. RESULTS: There was a sustained reduction in the rate of loss of total body BMD in the calcium group throughout the 4-year study period (P = 0.002), and bone loss was significantly less in the calcium-treated subjects in years 2 through 4 also (difference between groups 0.25% +/- 0.11% per year, P = 0.02). In the lumbar spine, bone loss was reduced in the calcium group in year 1 (P = 0.004), but not subsequently. There was, however, a significant treatment effect at this site over the whole 4-year period (P = 0.03). In the proximal femur, the benefit from calcium treatment also tended to be greater in the first year and was significant over the 4-year study period in the femoral neck (P = 0.03) and the trochanter (P = 0.01). Nine symptomatic fractures occurred in 7 subjects in the placebo group and 2 fractures in 2 subjects receiving calcium (P = 0.037). CONCLUSIONS: Calcium supplementation produces a sustained reduction in the rate of loss of total body BMD in healthy postmenopausal women.

Effect of calcium supplementation on bone loss in postmenopausal women.

Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. 1993.
N Engl J Med 328(7):460-4

BACKGROUND. The use of calcium supplements slows bone loss in the forearm and has a beneficial effect on the axial bone density of women in late menopause whose calcium intake is less than 400 mg per day. However, the effect of a calcium supplement of 1000 mg per day on the axial bone density of postmenopausal women with higher calcium intakes is not known. METHODS. We studied 122 normal women at least three years after they had reached menopause who had a mean dietary calcium intake of 750 mg per day. The women were randomly assigned to treatment with either calcium (1000 mg per day) or placebo for two years. The bone mineral density of the total body, lumbar spine, and proximal femur was measured every six months by dual-energy x-ray absorptiometry. Serum and urine indexes of calcium metabolism were measured at base line and after 3, 12, and 24 months. RESULTS. The mean (+/- SE) rate of loss of total-body bone mineral density was reduced by 43 percent in the calcium group (-0.0055 +/-0.0010 g per square centimeter per year) as compared with the placebo group (-0.0097 +/- 0.0010 g per square centimeter per year, P = 0.005). The rate of loss of bone mineral density was reduced by 35 percent in the legs (P = 0.02), and loss was eliminated in the trunk (P = 0.04). Calcium use was of significant benefit in the lumbar spine (P = 0.04), and in Ward's triangle the rate of loss was reduced by 67 percent (P = 0.04). Calcium supplementation had a similar effect whether dietary calcium intake was above or below the mean value for the group. Serum parathyroid hormone concentrations tended to be lower in the calcium group, as were urinary hydroxyproline excretion and serum alkaline phosphatase concentrations. CONCLUSIONS. Calcium supplementation significantly slowed axial and appendicular bone loss in normal post-menopausal women.