

The Whitehall-Robins Supplement

A Selection of Recent Findings in the Field of Nutrition

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Editor's note: There is growing evidence that vitamin D has benefits beyond bone health. The four abstracts in this issue are entirely devoted to the role of vitamin D in non-skeletal conditions.

Vitamin D intake and incidence of multiple sclerosis.

Multiple sclerosis (MS) incidence increases with distance from the equator in both hemispheres. One explanation for this phenomena is that sunlight exposure and the expected increase in vitamin D synthesis may provide a protective effect against MS. Vitamin D has strong immunoregulatory effects and several studies reported that individuals with MS tend to have insufficient vitamin D levels. This study is the first prospective study that investigated the association between vitamin D and the risk of developing MS in nearly 190,000 female nurses participating in two large ongoing cohort studies. Diet was assessed at baseline and updated every four years thereafter. Comparing women in the highest quintile (= 600 IU) of total vitamin D (dietary+ supplementary sources) intake at baseline with those in the lowest quintile (= 100 IU), there was a 33% reduction in risk of MS. No association was found between dietary vitamin D and MS incidence. In this study, women who used supplemental vitamin D, mainly from multivitamins, had a 40% lower risk of MS than women who did not use vitamin D. Duration of use of multivitamins was also inversely associated with risk of MS as there was nearly a 60% reduction in the risk of MS with the use of multivitamins for = 10 years. The authors conclude "These results support a protective effect of vitamin D intake on risk of developing MS".

[Munger KL, et al. *Neurology* 2004;62:60-65]

Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain.

Chronic pain is a common condition, which is associated with some degree of long-term or short-term disability with substantial direct and indirect costs. Of the many types of chronic pain, nonspecific musculoskeletal pain (e.g. non-inflammatory arthritis, nonarticular rheumatism and non-radiating lower back pain) is frequently encountered in health clinics. Chronic nonspecific musculoskeletal pain is one consequence of hypovitaminosis D. This study was cross sectional in design and its objective was to determine the prevalence of hypovitaminosis D in primary care outpatients with persistent, nonspecific musculoskeletal pain syndromes refractory to standard therapies. The study enrolled 150 patients presented consecutively between February 2000 and June 2002 with persistent, nonspecific musculoskeletal pain. The study was conducted in Minneapolis (45° north) and it included immigrant and nonimmigrant individuals of both genders, aged 10 to 65 years, from 6 broad ethnic groups who were screened for vitamin D status by measuring their serum 25-hydroxyvitamin D levels. In this study, 93% of all patients had deficient levels of vitamin D. Of the African American, East African, Hispanic, and American Indian patients, 100% had deficient levels of vitamin D (= 20 ng/mL). Nonimmigrants had vitamin D levels as deficient as immigrants and levels of vitamin D in men were as deficient as women. The findings of this study suggest that all patients with persistent, nonspecific musculoskeletal pain are at high risk of hypovitaminosis D. The authors conclude "Because osteomalacia is a known cause of persistent, nonspecific musculoskeletal pain, screening all outpatients with such pain for hypovitaminosis D should be standard practice in clinical care".

[Plotnikoff GA, et al. *May Clin Proc* 2003;78:1463-1470]

Vitamin D intake is inversely associated with rheumatoid arthritis. Results from the Iowa Women's Health Study.

Rheumatoid arthritis (RA) is an autoimmune disorder of unknown etiology, however, genetic and nongenetic factors might be involved in its etiology. Vitamin D may have immunomodulatory effects. This study evaluated the association of dietary and supplemental vitamin D intake with the incident of RA in a large prospective cohort study of nearly 30,000 women between 55-69 years of age without the history of RA at baseline. After 11 years of follow-up, 152 cases of RA were identified in this cohort and the diagnosis of RA was validated by reviewing the cases' medical records. In this study, there was an inverse association between higher intake of vitamin D and RA risk. This association remained after adjusting for potentially confounding variables. Inverse associations were apparent for both dietary and supplemental vitamin D, however, supplementary vitamin D showed a stronger inverse association with risk of RA than did dietary vitamin D. The authors conclude "Greater intake of vitamin D may be associated with a lower risk of RA in older women, although this finding is hypothesis generating."

[Merlino LA, et al. *Arthritis & Rheumatism* 2003;50:72-77]

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Vitamin D, calcium supplementation, and colorectal adenomas: results of a randomized trial.

There is evidence that calcium and vitamin D have anticancer effects in the large bowel. Although both nutrients are metabolically related in bone and the intestine, their potential interactions in the carcinogenesis of the large intestine are not well understood. The independent and joint effects of calcium supplementation and vitamin D status was evaluated in this 4-year randomized, double blind, placebo-controlled trial of calcium carbonate (1,200 mg elemental calcium) as a chemopreventive agent for large-bowel adenoma recurrence. In this study, vitamin D status strongly modified the effect of calcium supplementation on adenoma recurrence. Calcium supplements lowered adenoma risk only among subjects with 25-(OH) vitamin D levels above the overall median (29.1 ng/ mL). Equally 25-(OH) vitamin D was associated with a reduced risk only among subjects randomly assigned to receive the calcium carbonate supplement. This suggests, that vitamin D and calcium supplementation appear largely to act jointly and not separately on colorectal carcinogenesis. The authors conclude "Further investigation is needed to understand the mechanistic basis of vitamin D/calcium interaction and to clarify the amount of intake of each nutrient required for optimum protective effects. Nevertheless, these data clearly suggest the potential for important chemopreventive effects from calcium and vitamin D."

[Grau MV, et al. *J Natl Cancer Inst* 2003;95:1765-1771]

Suggested Readings

Vitamin C and risk of coronary heart disease in women.

[Osganian SK, et al. *J Am Coll Cardiol* 2003;42: 246-252]

The use of B vitamin supplements and peripheral arterial disease risk in men are inversely related.

[Merchant AT, et al. *J Nutr* 2003;133: 2863-2867]

Multivitamin use and colorectal cancer incidence in a US cohort: does timing matter?

[Jacobs EJ, et al. *Am J Epidemiol* 2003;158:621-628]

Gestational calcium supplementation and blood pressure in the offspring.

[Hatton DC, et al. *Am J Hypertens* 2003;16:801-805]

Long-latency deficiency disease: insight from calcium and vitamin D.

[Heaney RP. *Am J Clin Nutr* 2003;78:912-919]

Malnutrition in institutionalized seniors: the iatrogenic component.

[Wendland BE, et al. *J Am Geriatr Soc* 2003;51:85-90]

Lycopene, β -carotene, and colorectal adenomas.

[Erhardt JG, et al. *Am J Clin Nutr* 2003;78: 1219-1224]

Longitudinal calcium intake is negatively related to children's body fat indexes.

[Skinner JD, et al. *J Am Diet Assoc* 2003;103:1626-1631]