

# The Whitehall-Robins Supplement

## A Selection of Recent Findings in the Field of Nutrition

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### **Effect of Vitamin D on falls. A meta-analysis.**

Falls among elderly individuals occur frequently and it is encountered in 30% per year of those 65 years or older and between 40%-50% of those 80 years or older. Falls in the elderly is one of the leading causes of mortality in this age group. The moderate protective effect of vitamin D on fractures has been explained primarily to its effect on bone density. However, there is growing evidence that vitamin D may also directly improve muscle strength, hence reducing the risk of fractures. This meta-analysis assessed the overall efficacy of vitamin D in preventing falls among the elderly. Only double-blind randomized, controlled trials (RCTs) of vitamin D in elderly population that examined falls (resulting from low trauma) were considered in the final analysis. This meta-analysis considered 5 RCTs that included 1237 elderly individuals treated with vitamin D for 2 months up to 3 years. The pooled results suggested that vitamin D can reduce the risk of falling by 22% and this risk reduction was statistically significant. To ascertain the appropriate vitamin D level, which is associated with a reduction in the risk of falls, the investigators conducted a sub-analysis. Despite the limited data, there was a suggestion that 400 IU of vitamin D may not be clinically effective in preventing falls, however, a significant reduction in falls was observed when 700 to 800 IU/d of vitamin D were used in the trials. There was also an indication that the observed benefit of vitamin D on falls was achieved when the total dietary calcium intake was above the median intake of 512 mg/d. This suggests that a combination of vitamin D and calcium may be important. The beneficial effect of vitamin D on the risk of falling is that the active form of vitamin D (1,25-hydroxyvitamin D), binds to a highly specific nuclear receptors in muscle tissue which leads to improved muscle function and a reduction in the risk of falling. [Bischoff-Ferrari HK, et al. *JAMA* 2004; 291: 1999-2006]

### **A randomized trial of multivitamin supplements and HIV disease progression and mortality.**

It is estimated that approximately 40 million people worldwide were infected with HIV by the end of 2003, many of whom had symptoms of the acquired immunodeficiency syndrome (AIDS). However, fewer than 8% of the 6 million patients with advanced disease who were eligible for antiretroviral treatment were receiving it. The World Health Organization (WHO) is actively working on increasing access to the treatment of AIDS patients. The WHO recommends that patients with advanced disease should receive antiretroviral treatment, while those in earlier stages should be monitored and given supportive care. As a low-cost intervention, micronutrient supplements have been proposed because of their potential benefit on immunity that might slow the progression of HIV disease. If this effect is demonstrated, supplementation could delay the onset of advanced disease and the need of antiretroviral therapy. This will eventually reduce drug-related adverse event and costs. The investigators enrolled 1,078 pregnant women infected with HIV in a double blind, placebo-controlled trial to examine the effect of daily supplements of vitamin A (preformed vitamin A and beta-carotene), multivitamins (vitamin B complex, C, and E), or both on progression of HIV disease. After a median follow-up of nearly 6 years, it was observed that multivitamin supplementation with vitamin B complex, vitamin C, and vitamin E significantly delayed the progression of disease among HIV infected women as well as a reduction in AIDS related mortality. Multivitamin use resulted in higher CD4+ and CD8+ cell counts and lower viral loads. Supplementation with vitamin A alone had a small beneficial effect and for most part not significantly different from the effect of the placebo. Adding vitamin A to the multivitamin regimen reduced the benefit for some of the examined end points. The authors conclude, "Multivitamin supplements delay the progression of HIV disease and provide an effective, low-cost means of delaying initiation of antiretroviral therapy in HIV-infected women."

[Fawzi W, et al. *N Engl J Med* 2004;351:23-32]

### **Effect of calcium supplementation on the risk of large bowel polyps.**

Recent clinical trials have demonstrated that calcium supplementation modestly reduces the risk of colorectal adenomas. Little is known about the effect of calcium supplementation on the risk of different types of colorectal lesions and whether there is an interaction between calcium supplementation and dietary calcium, fat, and fiber intakes on the risk of these polyps. To investigate the above-mentioned associations, this study analyzed data from a large randomized, double blind, multicenter trial of the effect of 1,200 mg/d of calcium carbonate or placebo on the recurrence of large bowel adenomas. After four years of follow-up, all types of polyps occurred less frequently in the calcium treatment group than in the placebo group. The protective effect was particularly strong for advanced histologic lesions, which are strongly associated with invasive colorectal cancer. Furthermore, the beneficial effect of supplemental calcium was strongest in subjects whose baseline dietary calcium intake was in the highest category. This suggests that a total calcium intake (from diet and supplement) of more than 1,200 mg/day may be necessary for an optimum chemoprotective effect. Also, there were indications that high intake of dietary fat may counter some of the benefits of supplemental calcium, however, high intake of total dietary fiber did not interfere with the beneficial effects of calcium. The suggested mechanism for such a benefit is that calcium combines with bile acids and other fats in the lumen, therefore preventing their irritating and cancer promoting effects. The authors conclude "Our results suggest that calcium supplementation may have a more pronounced antineoplastic effect on advanced colorectal lesions than on other types of polyps."

[Wallace K, et al. *J Natl Cancer Inst* 2004;96:921-925]

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### **Zinc intakes and plasma concentrations in men with osteoporosis: the Rancho Bernardo Study.**

Osteoporosis is generally considered to be a condition of postmenopausal women, however, it is less appreciated that it is also an important public health issue among elderly men. It is estimated that one in eight men over the age of 50 years of age will have an osteoporotic fracture and about 30% of hip fractures occur in men. Although protein and calcium are important nutrients for bone health, other minerals and vitamins are probably important for maintaining healthy bones, and one of these nutrients is zinc. Animal studies have shown that zinc deficiency is associated with abnormalities in bone growth, bone formation, and mineralization. In women, low zinc intake has been associated with low bone mass, and women with osteoporosis have reduced serum or plasma zinc concentrations and increased zinc excretion. There is little research about the association between zinc status and osteoporosis in men. This study is believed to be the first study that examined the independent association between dietary zinc and plasma zinc and their association with bone mineral density (BMD) and 4-year bone loss in men between the ages of 45 – 92 years. In this study, the mean dietary zinc intake was 11.2 mg, and the mean plasma zinc concentration was 12.7  $\mu\text{mol/L}$ . Plasma zinc was correlated with total zinc intake from diet and supplements. Zinc intake and plasma zinc concentrations were significantly lower in men with osteoporosis at the hip and the spine than in men without osteoporosis at these sites. BMD values for almost all skeletal sites were significantly lower in men in the lowest category of plasma zinc concentrations than men with higher plasma zinc concentrations. Plasma zinc did not predict bone loss during the 4-year interval. The authors conclude “Dietary zinc intake and plasma zinc each have a positive association with BMD in men.”

[Hyun TH, et al. *Am J Clin Nutr* 2004;80:715-721]

### **Suggested Readings**

Alcohol consumption and cardiovascular disease mortality in hypertensive men.

[Malinski MK, et al. *Arch Intern Med* 2004;164:623-628]

Calcium, vitamin D, milk consumption, and hip fractures; a prospective study among postmenopausal women.

[Feskanich D, et al. *Am J Clin Nutr* 2003; 77:504-511]

Plasma homocysteine and risk for congestive heart failure in adults without prior myocardial infarction.

[Ramachandran SV, et al. *JAMA* 2003; 289:1251-1257]

Calcium, vitamin D, dairy products, and risk of colorectal cancer in the Cancer Prevention Study II Nutrition Cohort (United States).

[McCullough ML, et al. *Cancer Causes Control* 2003; 14:1-12]

Overweight, obesity, and mortality from cancer in prospectively studied cohort of U.S. adults.

[Calle EE, et al. *N Engl J Med* 2003; 348: 1625-1638]

Dietary intakes and plasma concentrations of carotenoids and tocopherols in relation to glucose metabolism in subjects at high risk of type 2 diabetes: The Botnia Dietary Study.

[Ylonen K, et al. *Am J Clin Nutr* 2003; 77:1434-1441]

Low vitamin B-12 concentrations in patients without anemia: the effect of folic acid fortification of grain.

[Mills JL, et al. *Am J Clin Nutr* 2003; 77:1474-1477]

Prospective study of serum vitamin E levels and esophageal and gastric cancers.

[Taylor PR, et al. *J Natl Cancer Inst* 2003; 95:1414-1416]

Joint association of alcohol and folate intake with risk of major chronic disease.

[Jiang R, et al. *Am J Epidemiol* 2003; 158:760-771]

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

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