

The Whitehall-Robins Supplement

A Selection of Recent Findings in the Field of Nutrition

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Risk assessment for vitamin D.

There is recent and compelling evidence that increased vitamin D intake may provide many health benefits beyond the well established benefit on bone health. These health benefits include reducing the risk of certain cancers, diabetes, metabolic syndromes as well as increasing physical strength in the elderly, hence reducing the risk of falls. The current daily recommendation for adult ≥ 19 y ranges between 200-600 IU vitamin D/day. This level is based on older evidence and it is less than the amounts of vitamin D which are associated with the above mentioned health benefits. When formulating recommendations for nutrient intake, safety is an important consideration. The current Tolerable Upper Intake Level (UL) for vitamin D is 2,000 IU. This level is viewed as too restrictive and is not based on current evidence. There is a general concern that higher vitamin D intakes can be potentially toxic. This review article which was authored by several well known vitamin D experts, applied risk assessment methodology to derive a revised safe UL for vitamin D₃ on the basis of all clinical trials. Vitamin D₃ and not vitamin D₂ was considered in this analysis, because it is the primary form of dietary vitamin D and is more potent than vitamin D₂. The authors provided strong evidence in support of a significantly higher UL for vitamin D. They conclude, "Collectively, the absence of toxicity in trials conducted in healthy adults that used vitamin D dose ≥ 250 $\mu\text{g}/\text{d}$ (10,000 IU vitamin D₃) supports the confident selection of this value as the UL."

[Hathcock JN, et al. *Am J Clin Nutr* 2007; 85:6-18]

Prolonged effect of calcium supplementation on risk of colorectal adenomas in a randomized trial.

Calcium supplementation with 1,200 mg as calcium carbonate has been shown to reduce the risk of recurrent colorectal adenomas in clinical trials. However, it is not known whether continued calcium supplementation is required to suppress carcinogenesis and whether there is a rebound increase in risk of large bowel cancer after cessation of supplementation use. This study tracked adenoma recurrence for an average of 7 years after completion of the randomized trial of calcium supplementation and recurrent colorectal adenoma. In this post-treatment follow-up study, the benefit of calcium supplementation on colorectal adenoma recurrence continued for 5 years after the cessation of calcium supplementation. Interestingly, the risk reduction in the calcium-treated subjects was more pronounced during the 5 years after active treatment than it was during active treatment. The exact mechanisms for such residual benefit are not clear, however, there are plausible explanations for this benefit. The hypothesized effects are either through the calcium ability to bind and precipitate bile acid and free fatty acid and/ or through a direct effect of calcium on the colon. It is worth mentioning that in this study, the randomized treatment was not associated with risk of adenomas during the next 5 years. This suggests that this benefit does not last indefinitely. The authors conclude, "The protective effect of calcium supplementation on risk of colorectal adenoma recurrence extends up to 5 years after cessation of active treatment, even in the absence of continued supplementation."

[Grau MV, *J Natl Cancer Inst* 2007; 99:129-136]

Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomized, double blind, controlled trial.

Ageing is associated with a decline in cognitive function, particularly cognitive domains related to memory and information speed. Changes in cognitive performance are linked with a higher risk of dementia. Identifying risk factors associated with age related cognitive decline is important and several factors were recently identified. Low folate and elevated homocysteine concentrations are examples of such risk factors, because of their association with poor cognitive performance. This randomized, double blind, placebo controlled study enrolled 818 men and women between the ages of 50-70 years. Participants were randomized to either 800 μg daily folic acid or placebo for 3 years to investigate whether folic acid supplementation improved cognitive performance compared to placebo. Cognitive performance was ascertained with tests that probe cognitive domains that decline with ageing. Serum folate concentrations increased by 576% and plasma total homocysteine concentrations decreased by 26% in participants taking folic acid compared to those taking placebo. In this study, folic acid supplementation had a beneficial effect on global function, specifically memory and information processing. The authors conclude, "Folic acid supplementation for 3 years significantly improved domains of cognitive function that tend to decline with age".

[Druga J, et al. *Lancet* 2007; 369:208-216]

Prenatal multivitamin supplementation and rates of congenital anomalies: A meta-analysis.

Birth defects are common medical conditions affecting 1 in 33 children born in North America. It is estimated that each year, approximately 150,000 babies are born in North America with birth defects. One of the major scientific findings in the past two decades was the importance of maternal folic acid supplementation in preventing the recurrence of neural tube defects. Since then, several lines of evidence emerged which suggest that folic acid containing multivitamins may reduce the risk of other congenital birth defects. This study, conducted a systematic review of published literature to examine the current evidence for the association between maternal folic acid containing multivitamins use and the rates of congenital anomalies other than

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neutral tube defects compared to the rates in nonusers. Based on the inclusion and exclusion criteria, 41 studies were included in this meta-analysis. Out of the 41 studies, there were 27 case control studies, 4 randomized controlled studies and 10 cohort studies. This meta-analysis provided evidence that maternal use of folic acid containing multivitamins before conception and throughout the first trimester is associated with lower risk of several congenital anomalies, including neural tube defects, cardiovascular, oral cleft, urinary tract, hydrocephalus, and limb defects. The authors conclude, "Maternal consumption of folic acid containing prenatal multivitamins is associated with decreased risk of several congenital anomalies, not only neural tube defects. These data have major public health implications, because until now fortification of only folic acid has been encouraged. This approach should be considered".

[Goh YI, et al. *J Obstet Gynaecol Can* 2006; 28:680-689]

Suggested Readings

Folate and vitamin B-12 status in relation to anemia, macrocytosis, and cognitive impairment in older Americans in the age of folic acid fortification.

[Morris MS, et al. *Am J Clin Nutr* 2007; 85:193-200]

Nutrient intakes and food consumption patterns among Ontario students in grades six, seven, and eight.

[Hanning RM, et al. *Can J Pub Health* 2007; 98:12-16]

n-3 fatty acids are positively associated with peak bone mineral density and bone accrual in healthy men: the NO2 Study.

[Högström M, et al. *Am J Clin Nutr* 2007; 85:803-807]

Vitamin D supplementation improves cytokine profiles in patients with congestive heart failure: a double-blind, randomized, placebo-controlled trial.

[Schleithoff SS, et al. *Am J Clin Nutr* 2006; 83:754-759]

Homocysteine-lowering trials for prevention of cardiovascular events: a review of the design and power of the large randomized trials.

[B-Vitamin Trialists' collaboration. *Am Heart J* 2006; 151; 282-287]

Dietary folate, vitamin B12, and vitamin B6 and the risk of Parkinson disease.

[De Lau, LML, et al. *Neurology* 2006; 67:315-318]

Randomized controlled trial of calcium in healthy older women.

[Reid IR, et al. *Am J Med* 2006; 119:777-785]

Higher baseline serum concentrations of vitamin E are associated with lower to total and cause-specific mortality in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study.

[Wright ME, et al. *Am J Clin Nutr* 2006; 84:1200-1207]

Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage.

[Ames BN. *Proc Natl Acad Sci* 2006; 103:17589-17594]

Cancer incidence and mortality and vitamin D in Black male health professionals.

[Giovannucci E, et al. *Cancer Epidemiol Biomarkers Prev* 2006; 15:2467-2472]