

The Whitehall-Robins Supplement

A Selection of Recent Findings in the Field of Nutrition

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Vitamin E and C are safe across a broad range of intakes [Review Article].

Intake of these two antioxidants are rarely low enough to cause deficiency in Western population, however, low intake of these antioxidants might increase the risk of several chronic diseases. Because of their antioxidants properties, several studies suggested that supplements of vitamin E, vitamin C or both may lower the risk of specific chronic diseases such as Alzheimer's disease, macular degeneration, some types of cancer, cataracts and heart disease. Recent clinical trials failed to demonstrate benefit and a recent meta-analysis for vitamin E supplementation suggested a potential for harm. Such conflicting results created confusion among consumers and health professionals. To review the safety of vitamin E and C either individually or in combination, scientific experts authored this authoritative safety evaluation, which is published as a review article to provide guidance when it comes to the safety profile of vitamins E and C. It is worth mentioning that recently, the Recommended Dietary Allowances (RDAs) for vitamin E have been increased by approximately 50% for men and by almost 100% for women compared to the previous RDAs. Similarly, the new RDAs for vitamin C have been increased by 25% for women and 50% for men. A safe tolerable upper intake (UL) was set at 1,000 mg for vitamin E and 2,000 mg for vitamin C in adults. These safety levels were revisited in this review article following some of the recent negative findings from clinical trials with vitamins E and C supplementation. After extensive review of the available evidence the experts conclude in this review article, "The UL is not intended to apply to the most sensitive persons in sensitive subpopulations, such as those with phenylketonuria or Wilson's disease but, instead, to apply to the healthy general population, including its normal range of variation. The recommendations are entirely based on the available scientific evidence; the main caveat is that healthy persons should not routinely take the vitamins in amounts higher than the UL. Beyond that, the recommendations support the consensus of published studies that vitamin E doses up to 1,000 mg/d and vitamin C doses up to 2,000 mg/d are safe for use by the general population. Many clinical trials show the safety of combinations of vitamins E and C at the amount identified for their independent UL values."

[Hathcock JN, et al. *Am J Clin Nutr* 2005;81:736-745]

The association of calcium and vitamin D with risk of colorectal adenomas.

There is growing evidence from animal and human studies that calcium and more recently vitamin D are important nutrients associated with colorectal cancer. The evidence suggests that calcium and vitamin D may reduce the risk of colorectal cancer by several mechanisms such as binding of long-chain fatty acids and bile acids in the small intestine, hence protecting the colonic epithelial cells from potential mutagens as well as effects on cell proliferation. The majority of colorectal cancers are thought to originate from adenomatous polyps. This association was evaluated in the Polyp Prevention Trial (PPT), a multicenter, randomized clinical trial that investigated the effects of high-fiber, high-fruit and vegetable, low-fat diet on the recurrence of adenomatous polyps in the colon. Extensive and detailed dietary and supplemental data were collected annually for all participants and were available for analysis to investigate this association. In this study, there were no overall significant associations between adenoma recurrence and dietary calcium and vitamin D intakes. However, supplemental calcium and vitamin D use during follow-up were inversely associated with adenoma recurrence. Compared to non users of calcium and vitamin D supplements, there was approximately a 20% reduction in the risk of adenoma recurrence. Slightly stronger associations were observed for the prevention of multiple recurrences. The authors conclude, "This trial cohort provides some evidence that calcium and vitamin D intake may be inversely associated with adenoma recurrence."

[Hartman TJ, et al. *J Nutr* 2005;135:252-259]

Obesity, weight gain and the risk of kidney stones.

Kidney stones are a common and major cause of morbidity with a life-time prevalence of 10% in men and 5% in women. About 80% of kidney stones contain calcium and calcium oxalate stones are the most common form of kidney stones. Identifying modifiable risk factors is important for the prevention and treatment of this condition. Obesity is associated with insulin resistance, which in turn might lead to the formation of calcium containing kidney stones. This study utilized data from three large cohorts comprising of nearly 250,000 participants in total. One of the cohorts involved men who were between the age of 40-75 years at baseline, the second was among women between the age of 34-59 years at baseline, and the third cohort was among women between the age of 27-44 years at baseline.

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The objective of this study was to determine if weight, weight gain, body mass index (BMI), and waist circumference are associated with the incidence of symptomatic kidney stone. The results of this study confirmed that obesity and weight gain are associated with an increased risk of symptomatic kidney stones. This association could not be explained by differences in the intake of dietary factors that affect risk. There was an indication that the magnitude of the increased risk may be higher in women.

[Taylor EN, et al. *JAMA* 2005; 293:455-462]

Effect of moderate alcohol consumption on cognitive function in women.

Excess alcohol intake impairs the brain, however, the effect of moderate consumption is unclear. Moderate alcohol intake is associated with a decreased risk of cardiovascular disease. Cognitive impairment and cardiovascular disease share common risk factors, therefore, a cognitive benefit from moderate alcohol intake is plausible. This hypothesis was evaluated in a subset of women participating in a large ongoing cohort study who were 70 to 81 years old. In this study, women consuming less than 15.0 g of alcohol (about one drink/day) had significantly better mean cognitive scores than nondrinkers. Women who drank less than 15.0 g of alcohol per day had a risk of cognitive impairment that was approximately 20% lower than among nondrinkers. There was no significant difference in cognitive performance between nondrinkers and those drinking 15.0 g - 30.0 g (1-2 drinks) of alcohol per day. Also, there were no significant differences in risks according to the alcoholic beverage (e.g., beer or wine) and no interaction with the apolipoprotein E genotype. Several mechanisms have been proposed to explain this benefit on cognition. It is suggested that moderate alcohol intake may help preserve brain vasculature, may prevent subclinical strokes, and thus result in better cognitive function. The authors conclude, "Although the adverse effects of excessive alcohol intake are well known and caution should be exercised in recommending even moderate alcohol intake, our results combined with those of other studies suggest that women who consume up to one drink per day have less cognitive impairment and better cognitive function than nondrinkers."

[Stampfer MJ, et al. *N Engl J Med* 2005; 352:245-253]

Suggested Readings

Folate and colorectal neoplasia: relation between plasma and dietary markers of folate and adenoma recurrence.

[Martinez ME, et al. *Am J Clin Nutr* 2004; 79:691-697]

Homocysteine levels and the risk of osteoporotic fractures.

[Van Meurs JBJ, et al. *N Engl J Med* 2004;350:2033-2041]

A prospective study of plasma selenium levels and prostate cancer risk.

[Li H, et al. *J Natl Cancer Inst* 2004;96:696-703]

Low maternal dietary intake of iron, magnesium, and niacin are associated with spina bifida in the offspring.

[Groenen PMW, et al. *J Nutr* 2004;134:1516-1522]

Serum selenium is associated with plasma homocysteine concentrations in elderly humans.

[Gonzalez S, et al. *J Nutr* 2004;134:1736-1740]

Relation between intake of vitamins C and E and the risk of diabetic retinopathy in the Atherosclerosis Risk in Communities Study.

[Millen AE, et al. *Am J Clin Nutr* 2004; 79:865-873]

Selenium and colorectal adenoma: Results of a pooled analysis.

[Jacobs EW, et al. *J Natl Cancer Inst* 2004;96:1669-1675]

Multivitamin use and the risk of preterm birth.

[Vahratian A, et al. *Am J Epidemiol* 2004;160:886-892]

Maternal calcium intake and offspring blood pressure.

[Gillman MW, et al. *Circulation* 2004;110:1990-1995]

Association between serum concentration of 25-hydroxyvitamin D3 and periodontal disease in the US population.

[Dietrich T, et al. *Am J Clin Nutr* 2004;80:108-113]