



Reviewing the Evidence Base for Supplemental Antioxidant Nutrients and Cancer Prevention: What We've Learned

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A large body of research has investigated the potential role of supplemental antioxidant nutrients (beta-carotene and other carotenoids, vitamin E, vitamin C, selenium) in the prevention of cancer. This presentation will review the scientific evidence on supplemental antioxidant nutrients and cancer prevention, with an emphasis on large randomized controlled trials of these nutrients for the primary and secondary prevention of various cancers in humans. As will be discussed, results from completed trials in general indicate no clear benefit to the use of supplemental antioxidant nutrients for cancer prevention, with some studies finding evidence of harm with certain nutrient supplements in certain populations. At the same time, some studies have suggested promising leads for further evaluation, stimulating a second generation of trials involving supplemental antioxidant nutrients. One such trial is SELECT, which is an ambitious trial that evaluates supplemental vitamin E and selenium (alone and in combination) for the prevention of prostate and other cancers in 32,400 men.

Research Needs and Conclusions: The evidence base on antioxidant nutrients and cancer prevention continues to evolve. Randomized trials of supplemental antioxidant nutrients for the primary prevention of cancer are extremely lengthy and expensive, and it will be several years before results of the most recently initiated trials become available. During the interim, there is a critical need to develop and validate reliable biomarkers of oxidative stress for human and animal studies, and intermediate endpoints that can be used as surrogate endpoints for cancer prevention trials. It is currently unknown if higher measures of oxidative stress predict greater cancer incidence/preneoplasia in human populations. Also, studies aimed at exploring interactions of antioxidant nutrients and their contributions to global measures of oxidative burden are needed. Given the current evidence base, the routine use of antioxidant nutrient supplements for either the primary or secondary prevention of cancer cannot be recommended.

References:

Blot WJ, Li J-Y, Taylor PR, et al. Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. *J Natl Cancer Inst* 1993;85:1483-1492.

Clark LC, Combs GF, Turnbull BW, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. *JAMA* 1996;276:1957-1963.

Hennekens CH, Buring JE, Manson JE, et al. Lack of effect of long-term supplementation with beta carotene on the incidence of malignant neoplasms and cardiovascular disease. *N Engl J Med* 1996;334:1145-1149.

Institute of Medicine, National Academy of Sciences, Food and Nutrition Board, Panel on Dietary Antioxidants and Related Compounds. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington: National Academy Press, 2000.

Klein EA, Thompson IM, Lippman SM, et al. SELECT: the next prostate cancer prevention trial. Selenium and Vitamin E Cancer Prevention Trial. *J Urol* 2001;166(4):1311-1315.

Omenn GS, Goodman GE, Thornquist MD, et al. Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. *N Engl J Med* 1996;334:1150-1155.

The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *N Engl J Med* 1994;330:1029-1035.