

Health Benefits of Nutritional Supplements

Selected Abstracts

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Forward

The importance of nutrition for human health has long been recognized. Prior to 1960, interest in this field largely focused on the etiology and prevention of acute nutrient deficiency diseases such as scurvy, rickets, and pellagra. Some 50 essential nutrients (vitamins, minerals, antioxidants, cofactors, essential amino acids, essential fatty acids) were identified, and recommended daily intakes for those essential nutrients (e.g. Recommended Dietary Allowances or RDAs) were developed. These recommendations, in turn, proved to be valuable in eradicating acute nutrient deficiency diseases.

During the past 20-30 years, attention has shifted to the role of diet and nutrition in the pathogenesis of chronic degenerative diseases. Heart disease, some cancers, osteoporosis, type II diabetes, and macular degeneration are all known to have dietary risk factors, many of which involve chronic nutrient deficiencies. Importantly, these associations have been much more difficult to study, in large measure because of the time frames involved. Chronic degenerative diseases develop over decades (lifetimes), and it is extremely challenging to conduct research programs for such extended periods. Nevertheless, advances in epidemiological and clinical research have helped us learn a great deal about the impacts (positive and negative) of diet and essential nutrient intakes on long-term health.

During the past decade, the scientific and healthcare communities have paid increasing attention to the role of nutritional supplements (as components of diet) in preventing and treating chronic disease. Hundreds of scientific studies have been conducted and published. These studies span a broad range of health issues. They have employed a wide variety of methodologies. And they have produced both positive and negative results. In some areas (e.g. the role of calcium and vitamin D supplements in slowing the progression of osteoporosis, and the role of folic acid supplements in preventing certain birth defects), results have been consistent, and benefits have been well accepted. In other areas (e.g. the role of antioxidant supplementation in preventing heart disease), results have been less consistent, and conclusions remain controversial. In any event, research on the health benefits of nutritional supplements is progressing, and evidence continues to mount that nutritional supplements offer a convenient and cost effective means for promoting health, over both the short- and long-terms.

The following is a collection of abstracts from about 100 scientific papers describing research on the health benefits of nutritional supplements. This collection is not exhaustive. Papers were selected on the basis of scientific merit and relevance to the field. The majority describes positive results, but in some, negative results are reported. Our objective in compiling this list was to provide readers with a good cross section of the scientific literature so that they could develop a sense for the current state of research in this field and draw their own conclusions concerning the role of supplementation in healthcare. References for many more papers are given in our bibliography entitled *Health Benefits of Nutritional Supplements: Selected Readings* .

For convenience, the abstracts have been sorted by health issue; namely Cardiovascular Health, Cancer Prevention, Strong Bones, Healthy Pregnancies/Healthy Babies, Sound Metabolism, Robust Immune Function, Acute Vision, and Other.

Acute Vision

Prospective cohort study of antioxidant vitamin supplement use and the risk of age-related maculopathy.

Christen WG, Ajani UA, Glynn RJ, Manson JE, Schaumberg DA, Chew EC, Buring JE, Hennekens CH. 1999. Am J Epidemiol 149(5):476-84

In a prospective cohort study, the authors examined whether self-selection for antioxidant vitamin supplement use affects the incidence of age-related maculopathy. The study population consisted of 21,120 US male physician participants in the Physicians' Health Study I who did not have a diagnosis of age-related maculopathy at baseline (1982). During an average of 12.5 person-years of follow-up, a total of 279 incident cases of age-related maculopathy with vision loss to 20/30 or worse were confirmed by medical record review. In multivariate analysis, as compared with nonusers of supplements, persons who used vitamin E supplements had a possible but nonsignificant 13% reduced risk of age-related maculopathy (relative risk = 0.87, 95 percent confidence interval (CI) 0.53-1.43), while users of multivitamins had a possible but nonsignificant 10% reduced risk (relative risk = 0.90, 95% CI 0.68-1.19). Users of vitamin C supplements had a relative risk of 1.03 (95% CI 0.71-1.50). These observational data suggest that among persons who self-select for supplemental use of antioxidant vitamin C or E or multivitamins, large reductions in the risk of age-related maculopathy are unlikely. Randomized trial data are accumulating to enable reliable detection of the existence of more plausible small-to-moderate benefits of these agents alone and in combination on age-related maculopathy.

Long-term vitamin C supplement use and prevalence of early age-related lens opacities.

Jacques PF, Taylor A, Hankinson SE, Willett WC, Mahnken B, Lee Y, Vaid K, Lahav M. 1997. Am J Clin Nutr 66(4):911-6

We designed the present study to examine the cross-sectional relation between age-related lens opacities and vitamin C supplement use over a 10-12-y period before assessment of lens status in women without diagnosed cataract or diabetes. This design avoids biased measurement of nutrient intake that results when knowledge of lens opacities influences nutrition-related behavior or its reporting. The participants were 247 Boston-area women aged 56-71 y selected from the Nurses' Health Study cohort with oversampling of women with high or low vitamin C intakes. Lens opacities were graded with the Lens Opacification Classification System II. Use of vitamin C supplements for > or = 10 y (n = 26) was associated with a 77% lower prevalence of early lens opacities (odds ratio: 0.23; 95% CI: 0.09, 0.60) at any lens site and a 83% lower prevalence of moderate lens opacities (odds ratio: 0.17; 95% CI: 0.03, 0.85) at any lens site compared with women who did not use vitamin C supplements (n = 141) after adjustment for age and other potentially confounding variables. Women who consumed vitamin C supplements for < 10 y showed no evidence of a reduced prevalence of early opacities. These data, together with data from earlier experimental and epidemiologic studies, suggest that long-term consumption of vitamin C supplements may substantially reduce the development of age-related lens opacities.

A one year study of the macular pigment: the effect of 140 days of a lutein supplement.

Landrum JT, Bone RA, Joa H, Kilburn MD, Moore LL, Sprague KE. 1997.
Exp Eye Res 65(1):57-62

A low density of macular pigment may represent a risk factor for age-related macular degeneration (AMD) by permitting greater blue light damage. This study was carried out to determine the effects on macular pigment optical density of dietary supplementation with lutein, one of the pigment constituents. Two subjects consumed lutein esters, equivalent to 30 mg of free lutein per day, for a period of 140 days. Macular pigment optical density was determined by heterochromatic flicker photometry before, during, and after the supplementation period. Serum lutein concentration was also obtained through the analysis of blood samples by high-performance liquid chromatography. Twenty to 40 days after the subjects commenced taking the lutein supplement, their macular pigment optical density began to increase uniformly at an average rate of 1.13 +/- 0.12 milliabsorbance units/day. During this same period, the serum concentration of lutein increased roughly tenfold, approaching a steady state plateau. The optical density curve eventually levelled off 40 to 50 days after the subjects discontinued the supplement. During the same 40 to 50 days, the serum concentration returned to baseline. Thereafter, little or no decrease in optical density was observed. The mean increases in the macular pigment optical density were 39% and 21% in the eyes of the two subjects respectively. In conclusion, the modest period of supplementation has been estimated to have produced in the subjects a 30 to 40% reduction in blue light reaching the photoreceptors, Bruch's membrane, and the retinal pigment epithelium, the vulnerable tissues affected by AMD.

Antioxidant vitamins and nuclear opacities: the longitudinal study of cataract.

Leske MC, Chylack LT Jr, He Q, Wu SY, Schoenfeld E, Friend J, Wolfe J. 1998.
Ophthalmology 105(5):831-6

OBJECTIVE: The association of antioxidant nutrients and risk of nuclear opacification was evaluated in the Longitudinal Study of Cataract. **DESIGN:** Nutritional data were collected at baseline on the 764 participants, which included assessment of dietary intake, use of vitamin supplements, and plasma levels of vitamin E. Ophthalmologic and other data were collected at baseline and at yearly follow-up visits, including lens photographs, which were graded using the Lens Opacities Classification System III protocol. **MAIN OUTCOME MEASURES:** Analyses examined whether the nutritional factors at baseline were related to increases in nuclear opacification at follow-up. The MULCOX2 approach, an extension of the Cox regression model, was used. Results are presented as relative risks (RRs) and 95% confidence intervals. **INTERVENTION:** Intervention was not applicable. **RESULTS:** The risk of nuclear opacification at follow-up was decreased in regular users of multivitamin supplements (RR = 0.69; 0.48-0.99), vitamin E supplements (RR = 0.43; 0.19-0.99), and in persons with higher plasma levels of vitamin E (RR = 0.58; 0.36-0.94). **CONCLUSIONS:** In regular users of multivitamin supplements, the risk of nuclear opacification was reduced by one third; in regular users of vitamin E supplements and persons with higher plasma levels of vitamin E, the risk was reduced by approximately half. These results are similar to those obtained in our earlier case-control study. Because these data are based on observational studies only, the results are suggestive but inconclusive. The possible effect of nutritional supplements on the lens requires confirmation by ongoing clinical trials.

Vitamin supplement use and incident cataracts in a population-based study.

Mares-Perlman JA, Lyle BJ, Klein R, Fisher AI, Brady WE, VandenLangenberg GM, Trabulsi JN, Palta M. 2000. Arch Ophthalmol 118(11):1556-63

OBJECTIVE: To determine the relationship between vitamin supplement use and the 5-year incidence of nuclear, cortical, and posterior subcapsular cataract in the Beaver Dam Eye Study cohort. **DESIGN:** The 5-year incidence of cataract, determined from slitlamp (nuclear cataract) and retroillumination (cortical and posterior subcapsular cataract) photographs, was assessed in a population-based cohort of persons participating in baseline (1988-1990) and follow-up (1993-1995) examinations. Detailed data regarding the type, dosage, and duration of supplement use were obtained by in-person interviews at follow-up. **PARTICIPANTS:** Residents of Beaver Dam, Wis, aged 43 to 86 years, were identified by private census. Of the 3684 participants in both baseline and follow-up examinations, 3089 were eligible for incident cataract analysis in the present study. **RESULTS:** Compared with nonusers, the 5-year risk for any cataract was 60% lower among persons who, at follow-up, reported the use of multivitamins or any supplement containing vitamin C or E for more than 10 years. Taking multivitamins for this duration lowered the risk for nuclear and cortical cataracts but not for posterior subcapsular cataracts (odds ratios [95% confidence intervals] = 0.6 [0.4-0.9], 0.4 [0.2-0.8], and 0.9 [0.5-1.9], respectively). Use of supplements for shorter periods was not associated with reduced risk for cataract. Measured differences in lifestyle between supplement users and nonusers did not influence these associations, nor did variations in diet as measured in a random subsample. **CONCLUSIONS:** These data add to a body of evidence suggesting lower risk for cataract among users of vitamin supplements and stronger associations with long-term use. However, the specific nutrients that are responsible cannot be ascertained at this time, and unmeasured lifestyle differences between supplement users and nonusers may explain these results. Arch Ophthalmol. 2000;118:1556-1563

The use of vitamin supplements and the risk of cataract among US male physicians.

Seddon JM, Christen WG, Manson JE, LaMotte FS, Glynn RJ, Buring JE, Hennekens CH. 1994. Am J Public Health 84(5):788-92

OBJECTIVES. The purpose of this study was to examine prospectively the association between reported use of vitamin supplements and risk of cataract and cataract extraction. **METHODS.** The study population consisted of 17,744 participants in the Physicians' Health Study, a randomized trial of aspirin therapy and beta-carotene among US male physicians 40 to 84 years of age in 1982 who did not report cataract at baseline and provided complete information about vitamin supplementation and other risk factors for cataract. Self-reports of cataract and cataract extraction were confirmed by medical record review. **RESULTS.** During 60 months of follow-up, there were 370 incident cataracts and 109 cataract extractions. In comparison with physicians who did not use any supplements, those who took only multivitamins had a relative risk of cataract of 0.73 after adjustment for other risk factors. For cataract extraction, the corresponding relative risk was 0.79. Use of vitamin C and/or E supplements alone was not associated with a reduced risk of cataract, but the size of this subgroup was small. **CONCLUSIONS.** These data suggest that men who took multivitamin supplements tended to experience a decreased risk of cataract and support the need for rigorous testing of this hypothesis in large-scale randomized trials in men and women.