

**Modification of the Effect of Vitamin E Supplementation on the Mortality of Male Smokers by Age and Dietary Vitamin C.** Harri Hemilä and Jaakko Kaprio. *Am J Epidemiol* 2009;169(8):946-953.

The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study (1985–1993) recruited 29,133 Finnish male cigarette smokers, finding that vitamin E supplementation had no overall effect on mortality. The authors of this paper found that the effect of vitamin E on respiratory infections in ATBC Study participants was modified by age, smoking, and dietary vitamin C intake; therefore, they examined whether the effect of vitamin E supplementation on mortality is modified by the same variables. During a median follow-up time of 6.1 years, 3,571 deaths occurred. Age and dietary vitamin C intake had a second-order interaction with vitamin E supplementation of 50 mg/day. Among participants with a dietary vitamin C intake above the median of 90 mg/day, vitamin E increased mortality among those aged 50–62 years by 19% (95% confidence interval: 5, 35), whereas vitamin E decreased mortality among those aged 66–69 years by 41% (95% CI: –56, –21). Vitamin E had no effect on participants who had a dietary vitamin C intake below the median. Smoking quantity did not modify the effect of vitamin E. This study provides strong evidence that the effect of vitamin E supplementation on mortality varies between different population groups. Further study is needed to confirm this heterogeneity. **Key words:** aging; antioxidants; oxidative stress; population characteristics; randomized controlled trial; smoking; survival rate.

**Dietary  $\beta$ -Tocopherol and Linoleic Acid, Serum Insulin, and Waist Circumference Predict Circulating Sex Hormone-Binding Globulin in Premenopausal Women.** Fatima Nayeem et al. *J Nutr* 2009;139(6):1135-1142.

Reduced levels of circulating sex hormone-binding globulin (SHBG) are implicated in the etiology of sex steroid-related pathologies and the metabolic syndrome. Dietary correlates of serum SHBG remain unclear and were studied in a convenient cross-sectional sample of healthy 30- to 40-y-old women ( $n = 255$ ). By univariate analyses, serum SHBG correlated negatively with several indices of the metabolic syndrome, such as BMI, waist circumference, hip circumference ( $r = -0.36$  to  $-0.44$ ;  $P < 0.0001$ ), fasting serum insulin ( $r = -0.41$ ;  $P < 0.0001$ ), serum triglycerides ( $r = -0.27$ ;  $P < 0.0001$ ), serum glucose ( $r = -0.23$ ;  $P < 0.001$ ), and plasma testosterone ( $r = -0.19$ ;  $P = 0.002$ ). Serum SHBG correlated positively with serum HDL-cholesterol ( $r = 0.33$ ;  $P < 0.0001$ ), plasma progesterone ( $r = 0.17$ ;  $P = 0.007$ ), and dietary intake of  $\beta$ -tocopherol ( $r = 0.17$ ;  $P = 0.006$ ), and negatively with that of fructose ( $r = -0.13$ ;  $P = 0.04$ ). Principal component analysis (PCA) extracted 12 nutrient factors with eigenvalues  $> 1.0$  from 54 nutrients and vitamins in food records. Multivariate regression analyses showed that the PCA-extracted nutrient factor most heavily loaded with  $\beta$ -tocopherol and linoleic acid ( $P = 0.03$ ) was an independent positive predictor of serum SHBG. When individual nutrients were the predictor variables,  $\beta$ -tocopherol ( $P = 0.002$ ), but not other tocopherols or fatty acids (including linoleic acid), was an independent positive predictor of serum SHBG. Circulating insulin ( $P = 0.02$ ) and waist circumference ( $P = 0.002$ ), but not serum lipids, were negative independent predictors of SHBG in all regression models. Additional studies are needed in women of other age groups and men to determine whether consumption of foods rich in  $\beta$ -tocopherol and/or linoleic acid may increase serum SHBG concentrations and may thereby decrease the risk for metabolic syndrome and reproductive organ cancer.

**Vitamin E, Vitamin C, Beta Carotene, and Cognitive Function Among Women With or at Risk of Cardiovascular Disease. The Women's Antioxidant and Cardiovascular Study.** Jae Hee Kang et al. *Circulation* 2009;119(21):2772-2780.

**Background**— Cardiovascular factors are associated with cognitive decline. Antioxidants may be beneficial. **Methods and Results**— The Women's Antioxidant Cardiovascular Study was a trial of vitamin E (402 mg every other day), beta carotene (50 mg every other day), and vitamin C (500 mg daily) for the secondary prevention of cardiovascular disease. From 1995 to 1996, women  $\geq 40$  years of age with cardiovascular disease or  $\geq 3$  coronary risk factors were randomized. From 1998 to 1999, a cognitive function substudy was initiated among 2824 participants  $\geq 65$  years of age. With 5 cognitive tests, cognition was assessed by telephone 4 times over 5.4 years. The primary outcome was a global composite score averaging all scores; repeated-measures analyses were used to examine cognitive change over time. Vitamin E supplementation and beta carotene supplementation were not associated with slower rates of cognitive change (mean difference in change for vitamin E versus placebo,  $-0.01$ ;

95% confidence interval, -0.05 to 0.04;  $P=0.78$ ; for beta carotene, 0.03; 95% confidence interval, -0.02 to 0.07;  $P=0.28$ ). Although vitamin C supplementation was associated with better performance at the last assessment (mean difference, 0.13; 95% confidence interval, 0.06 to 0.20;  $P=0.0005$ ), it was not associated with cognitive change over time (mean difference in change, 0.02; 95% confidence interval, -0.03 to 0.07;  $P=0.39$ ). Vitamin C was more protective against cognitive change among those with new cardiovascular events during the trial ( $P$  for interaction=0.009). **Conclusions**— Antioxidant supplementation did not slow cognitive change among women with preexisting cardiovascular disease or cardiovascular disease risk factors. A possible late effect of vitamin C or beta carotene among those with low dietary intake on cognition warrants further study.