

# The Whitehall-Robins Supplement

## A Selection of Recent Findings in the Field of Nutrition

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### **Prospective study of predictors of vitamin D status and cancer incidence and mortality in men.**

In 1937, it was hypothesized that sunlight exposure lowers cancer risk, and in 1941 an association between latitude and cancer mortality was reported. More recently, it was hypothesized that vitamin D status accounts for increased risk of colon, breast, ovarian and prostate cancers at higher latitudes. Latitude as a surrogate of solar UV-B radiation is inversely correlated with vitamin D status, however, latitude is only one of many determinants of vitamin D status. This study is the first to consider multiple determinants of vitamin D exposure, which included, dietary and supplementary vitamin D, skin pigmentation, adiposity, geographic residence, and leisure-time-physical activity in relation to cancer risk in a large ongoing cohort study of US men. The authors, quantified the relation of these 6 determinants to plasma 25-hydroxy-vitamin D [25(OH) D] levels and computed a predicted [25(OH) D] level for each of the nearly 50,000 men in this cohort based on these characteristics. From 1986 through January 31, 2000, 4,286 incident cancers and 2,025 cancer deaths were documented in this cohort. In this study, an increment of 25 nmol/L in predicted [25(OH) D] levels was associated with a 17% reduction in total cancer incidence, 29% reduction in total cancer mortality, and a 45% reduction in mortality of the digestive system cancers. The authors conclude "Low levels of vitamin D may be associated with increased cancer incidence and mortality in men, particularly for digestive system cancers. The vitamin D supplementation necessary to achieve a [25(OH) D] increment of 25 nmol/L may be at least 1,500 IU/day". It is worth mentioning that the current Recommended Dietary Allowance (RDA) for vitamin D is 200 IU and 400 IU for adults <50 y and >50 y respectively.

[Giovannucci E, et al. *J Natl Cancer Inst* 2006; 98:451-459]

### **Serum carotenoids, vitamins A and E, and 8 year lung function in a general population.**

Impaired and/or a rapid decline in lung function are strong predictors of respiratory morbidity and mortality and of all cause and cardiovascular mortality. Oxidative stress can impair lung function as well as accelerating the decline in lung function. This can lead to several ailments of the respiratory system, particularly with exposure to cigarette smoke. Antioxidants can protect the lungs against damage caused by free radicals. This study investigated whether subjects with low serum levels of antioxidants ( $\beta$ -carotene,  $\alpha$ -carotene, vitamins A and E) are at a higher risk of accelerated decline in forced expiratory volume in 1 second (FEV-1), because their lungs will be less protected against oxidative stress. The subjects in this study aged 20-44 years at the beginning of the study and they were followed up for 8 years. During the 8 year follow-up period the mean annual decrease in FEV-1 was 29.8 ml/ year after adjusting for several confounding variables. The study reported that  $\beta$ -carotene and vitamin E may protect against accelerated decline in lung function, especially in heavy smokers. The decline in FEV-1 was twice as great in heavy smokers with low levels of  $\beta$ -carotene or vitamin E. The authors conclude, "These results strongly suggest that  $\beta$ -carotene protects against the decline in FEV-1 over an 8 year period in the general population, and that  $\beta$ -carotene and vitamin E are protective in heavy smokers".

[Guenegou A, et al. *Thorax* 2006;61: 320-326]

### **Periconceptional multivitamin use reduces the risk of preeclampsia.**

Preeclampsia is a disorder of pregnancy with public health significance in developing and developed countries. Preeclampsia affects roughly 7% of first pregnancies. Nutrition has long been suspected to play a role in the etiology of preeclampsia. Recently, we came to the realization that, while preeclampsia is clinically evident late in pregnancy, the causal factors and pathophysiological changes are present months earlier. This study assessed the independent effect of regular periconceptional multivitamin use on the risk of preeclampsia. One thousand eight hundred and thirty four pregnant women enrolled in a study investigating pregnancy exposure and preeclampsia prevention were asked whether they regularly used multivitamins or prenatal vitamins in the past 6 months. Accordingly women were classified either as users or nonusers. Adjusting for several confounding variables, regular use of multivitamins was associated with a 45% reduction in preeclampsia risk compared to nonusers. The prepregnancy overweight modified this effect. Lean multivitamin users had a 71% reduction in preeclampsia risk compared to lean nonusers. In contrast, there was no relation between multivitamin use and preeclampsia among overweight women. The authors conclude "If confirmed by others, these results suggest that regular use of a multivitamin supplement in the periconceptional period may help to prevent preeclampsia, particularly among lean women".

[Bodnar LM, et al. *Am J Epidemiol* 2006; 164: 470-477]

### **Centrum use and progression of age-related cataract in the Age-Related Eye Disease Study. A propensity score approach. AREDS report No.21.**

The Age-Related Eye Disease Study (AREDS) is a clinical trial, which was designed to investigate the effect of a high-dose antioxidant formulation, which contained 500 mg of vitamin C, 400 IU of vitamin E, and 15 mg of beta-carotene on the risk of cataract development and progression. After 7 years of such an intervention, there was no statistically significant effect on the risk of development or progression of cataract.

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At the time of enrollment into the AREDS, more than half of the participants were taking some form of supplements. To standardize the usage of non-study supplements, participants who wanted to continue the use of supplements were provided with the Centrum® multivitamin. Two thirds of the participants elected to supplement with Centrum®. Because Centrum® use was not randomized, the propensity score method was used to adjust for possible selection bias and confounding. The propensity score for a person is the probability of being treated (in this case choosing to take Centrum®) conditional on the person's characteristics. This method reduces bias by balancing the different characteristics (covariates) between treatment groups.

After a median follow-up of 6.3 years, Centrum® use, adjusted for propensity score and other potentially confounding variables was associated with a 16% significant reduction in the risk of any lens opacity progression in general and this beneficial effect was particularly strong for nuclear opacity. The authors conclude "Observational data from the AREDS and other studies suggest that use of multivitamin may delay the progression of lens opacities. A National Eye Institute-sponsored clinical trial scheduled for completion in 2007 will provide additional data on Centrum use and cataract development."

[Age-Related Eye Disease Study Research Group. *Ophthalmology* 2006;113:1264-1270]

### **Suggested Readings**

**Calcium and dairy food intakes are inversely associated with colorectal cancer risk in the cohort of Swedish men.**

[Larsson Sc, et al. *Am J Clin Nutr* 2006; 83:667-673]

**Perinatal Choline influences brain structure and function.**

[Zeisel SH, et al. *Nutr Rev* 2006; 64: 197-203]

**Whole-grain and fiber intakes and periodontitis risk in men.**

[Merchant AT, et al. *Am J Clin Nutr* 2006; 83:1395-1400]

**Sensitivity of markers of DNA stability and DNA repair activity to folate supplementation in healthy volunteers.**

[Basten GP, et al. *Br J Cancer* 2006; 94:1942-1947]

**Effect of vitamin C on common cold: randomized controlled trial.**

[Sasazuki S, et al. *Eur J Clin Nutr* 2006; 60:9-17]

**The case against ergocalciferol (vitamin D2) as a vitamin supplement.**

[Houghton LA, et al. *Am J Clin* 2006; 84:694-697]

**Prospective study of fruits and vegetables and risk of oral premalignant lesions in men.**

[Maserejian NN, et al. *Am J Epidemiol* 2006; 164:556-566]

**The retinol carotenoids zeaxanthin and lutein scavenge superoxide and hydroxyl radicals: A chemiluminescence and ESR study.**

[Trevithick-Sutton CC, et al. *Mol Vision* 2006; 12:1127-1135]

**Intakes of fruits, vegetables, vitamins A, C, and E, and carotenoids and risk of renal cell cancer.**

[Lee JE, et al. *Cancer Epidemiol Biomarkers Prev* 2006; 15:2445- 2452]

**Consumption of coffee is associated with reduced risk of death attributed to inflammatory and cardiovascular diseases in the Iowa Women's Health Study.**

[Anderson LF, et al. *Am J Clin Nutr* 2006; 83:1039-1046]