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The Beta-Carotene and Retinol Efficacy Trial: incidence of lung cancer and cardiovascular disease mortality during 6-year follow-up after stopping beta-carotene and retinol supplements.

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BACKGROUND: The Beta-Carotene and Retinol Efficacy Trial (CARET) tested the effect of daily beta-carotene (30 mg) and retinyl palmitate (25,000 IU) on the incidence of lung cancer, other cancers, and death in 18,314 participants who were at high risk for lung cancer because of a history of smoking or asbestos exposure. CARET was stopped ahead of schedule in January 1996 because participants who were randomly assigned to receive the active intervention were found to have a 28% increase in incidence of lung cancer, a 17% increase in incidence of death and a higher rate of cardiovascular disease mortality compared with participants in the placebo group. **METHODS:** After the intervention ended, CARET participants returned the study vitamins to their study center and provided a final blood sample. They continue to be followed annually by telephone and mail self-report. Self-reported cancer endpoints were confirmed by review of pathology reports, and death endpoints were confirmed by review of death certificates. All statistical tests were two-sided. **RESULTS:** With follow-up through December 31, 2001, the post-intervention relative risks of lung cancer and all-cause mortality for the active intervention group compared with the placebo group were 1.12 (95% confidence interval [CI] = 0.97 to 1.31) and 1.08 (95% CI = 0.99 to 1.17), respectively. Smoothed relative risk curves for lung cancer incidence and all-cause mortality indicated that relative risks remained above 1.0 throughout the post-intervention follow-up. By contrast, the relative risk of cardiovascular disease mortality decreased rapidly to 1.0 after the intervention was stopped. During the post-intervention phase, females had larger relative risks of lung cancer mortality (1.33 versus 1.14; $P = .36$), cardiovascular disease mortality (1.44 versus 0.93; $P = .03$), and all-cause mortality (1.37 versus 0.98; $P = .001$) than males. **CONCLUSIONS:** The previously reported adverse effects of beta-carotene and retinyl palmitate on lung cancer incidence and all-cause mortality in cigarette smokers and

individuals with occupational exposure to asbestos persisted after drug administration was stopped although they are no longer statistically significant. Planned subgroup analyses suggest that the excess risks of lung cancer were restricted primarily to females, and cardiovascular disease mortality primarily to females and to former smokers.

Carcinogenesis. 2004 Nov 25; [Epub ahead of print] Related Articles, Links

Detection of p53 and K-ras mutations in sputum of individuals exposed to smoky coal emissions in Xuan Wei county, China.

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Lung cancer mortality rates in the Xuan Wei County population are among the highest in China and are associated with exposure to indoor emissions from the burning of smoky coal. Previous studies of lung tumors from both nonsmoking women and smoking men in this region showed high frequencies of mutations, consisting mostly of G to T transversions, in the p53 tumor suppressor gene and K-ras oncogene, suggesting these mutations were caused primarily by polycyclic aromatic hydrocarbons. In this study, sputum samples from 92 individuals with no evidence of lung cancer from Xuan Wei County were screened for p53 and K-ras mutations. Sputum cells were collected on glass slides by sputum cyto-centrifugation, stained, and cyto-pathologically analyzed. Cytologically non-malignant epithelial cells were taken from each sputum sample, using a laser capture microdissection microscope, and molecularly analyzed. Cells taken from the sputum of 15 (16.3%) individuals were mutation-positive, including thirteen (14.1%) individuals each with a p53 mutation, one (1.1%) individual with a K-ras mutation, and one (1.1%) individual with a p53 and a K-ras mutation. p53 mutations were found in both the sputum of individuals with evidence of chronic bronchitis (3 of 46, or 6.5%) and those without evidence of this disease (11 of 46, or 23.9%). Therefore, mutations in the p53 gene and, to a lesser extent, the K-ras gene were frequent in non-malignant epithelial cells taken from the sputum of individuals without evidence of lung cancer who were exposed to smoky coal emissions in Xuan Wei County and were at a high risk for developing the disease.

Eur J Cancer Prev. 2004 Dec;13(6):471-80. Related Articles, Links

Dietary habits and lung cancer risk among non-smoking women.

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A case-control study was conducted to investigate the relationship between diet and the risk of lung cancer among women non-smokers and to compare with

women smokers in the same population. Data collected by personal interviews from 435 microscopically confirmed cases and 1710 controls were analysed using unconditional logistic regression. In addition to results for all study subjects, associations between diet and lung cancer risk were compared between two highly contrasting groups: smokers (odds ratio (OR) 7.03) and non-smokers (OR 1.00). A protective effect of frequent (daily or several times per week) black tea drinking appeared among non-smoking women (OR 0.65, 95% confidence interval (CI) 0.43-0.99). Among smoking women, protective effects were observed for frequent intake of milk/dairy products (OR 0.56, 95% CI 0.32-0.96), coffee (OR 0.47, 95% CI 0.25-0.88), and wine consumption (daily or weekly OR 0.60, 95% CI 0.37-0.98; monthly OR 0.60, 95%

CI 0.39-0.94). Inverse associations with the risk appeared for physical exercise for smokers only, and for the body mass index both among non-smoking and smoking women. Some items of diet may contribute to variation in risk among women in the Czech Republic; their importance seems to vary in relation to their status in smoking, the dominant factor in the aetiology of lung cancer.

Anticancer Res. 2004 Sep-Oct;24(5B):3177-84. Related Articles, Links

Aspirin use and mortality from cancer in a prospective cohort study.

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There is evidence that use of aspirin offers several potential health benefits including cancer prevention and cardiovascular disease prevention. The purpose of this study was to assess the association between aspirin use and death from cancer and cardiovascular diseases with a special emphasis on cancer mortality. MATERIALS AND METHODS: The baseline data for this prospective cohort study were collected in 1971--1975 for the first National Health and Nutrition Examination Study (NHANES I) and 1976--1980 as part of the second NHANES (NHANES II) with mortality follow-up using the National Death Index (NDI) through December 31, 1992. The main analyses were the relative risks of total mortality and cause-specific mortality for persons who used aspirin compared to persons who did not use aspirin adjusted for confounding using Cox proportional hazards. RESULTS: The proportion of aspirin users was lower among cancer cases than non-cases (58% versus 66%) and use of aspirin decreased with age. Consequently, age was a negative confounder attenuating the protective association between aspirin use and cancer and cardiovascular mortality. After adjusting for age, BMI, sex, race, poverty index, education and smoking, we observed a significant association of reduced all cause mortality among all aspirin users (relative risk [RR] = 0.88; 95% confidence interval [CI] 0.85 - 0.99) and lung cancer mortality among male aspirin users (RR = 0.69; CI 0.49-0.96). However, for women we observed adverse associations between aspirin use and bladder (RR=12.31; CI 2.98-50.80) and brain cancer mortality (RR=3.13; CI 1.09-9.00), although case numbers were small. CONCLUSION: Aspirin use appears to offer protection from all causes of mortality and lung cancer among men. In women aspirin use is associated with increased risk of bladder and brain cancer. Because of the small number of female bladder (n=15) and brain (n=20) cancer cases in this cohort the findings require confirmation.

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Lung cancer rates in men and women with comparable histories of smoking.

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BACKGROUND: Recent case-control studies suggest that, given equal smoking exposure, women may have a higher relative risk of developing lung cancer than men. Despite prospective data that conflict with this hypothesis, mechanistic studies to find a biologic basis for a sex difference continue. **METHODS:** We addressed the hypothesis directly by analyzing prospective data from former and current smokers in two large cohorts--the Nurses' Health Study of women and the Health Professionals Follow-up Study of men. We calculated incidence rates and hazard ratios of lung cancer in women compared with men, adjusting for age, number of cigarettes smoked per day, age at start of smoking, and time since quitting, using Cox proportional hazards models. We also reviewed published results from prospective analyses. **RESULTS:** From 1986 through 2000, 955 and 311 primary lung cancers were identified among 60 296 women and 25 397 men, respectively, who ranged in age from 40 to 79 years. Incidence rates per 100 000 person-years for women and men were 253 and 232, respectively, among current smokers and 81 and 73, respectively, among former smokers. The hazard ratio in women ever smokers compared with men was 1.11 (95% confidence interval = 0.95 to 1.31). Six published prospective cohort studies allowed assessment of comparative susceptibility to lung cancer by sex. None supported an excess risk of lung cancer for women. **CONCLUSIONS:** Women do not appear to have a greater susceptibility to lung cancer than men, given equal smoking exposure. Research should be focused on enhancing preventive interventions for all.